EMERGING ISSUES IN EMS AND 911

Efficacy of Prehospital Application of Tourniquets and Hemostatic Dressings To Control Traumatic External Hemorrhage

U.S. Department of Transportation
National Highway Traffic Safety Administration

EMS NHTSA
National Highway Traffic Safety Administration

NHTSA
www.nhtsa.gov

Disclaimer

This publication is distributed by the U.S. Department of Transportation, National Highway Traffic Safety Administration, in the interest of information exchange. The opinions, findings and conclusions expressed in this publication are those of the author(s) and not necessarily those of the Department of Transportation or the National Highway Traffic Safety Administration. The United States Government assumes no liability for its contents or use thereof. If trade or manufacturer's name or products are mentioned, it is because they are considered essential to the object of the publication and should not be construed as an endorsement. The United States Government does not endorse products or manufacturers.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Suggested citation: Snyder D, Tsou A, Schoelles K. Efficacy of Prehospital Application of Tourniquets and Hemostatic Dressings to Control Traumatic External Hemorrhage. DOT HS 811 999b. Washington, DC: National Highway Traffic Safety Administration. May 2014. Available at: www.ems.gov.

The majority of all road trauma deaths occur either at the scene of injury or in the prehospital setting. The World Health Organization has identified uncontrolled bleeding to be the leading cause of preventable traumatic death. Emergency Medical Services systems play a key role in helping to reduce motor vehicle-related fatalities by providing medical care at the crash scene and by quickly transporting injured patients to the most appropriate level of trauma care. This systematic review was used by the American College of Surgeons to develop an evidence-based guideline on external hemorrhage control in the prehospital setting and will help the National Highway Traffic Safety Administration (NHTSA) in its mission to save lives due to injuries from road traffic crashes. This document and the associated evidence-based guideline will help NHTSA meet its strategic goals to improve survivability from motor vehicle crashes and improve emergency care for persons injured in vehicle crashes.

Technical Expert Panel

In designing the study questions and methodology at the outset of this report, ECRI Institute consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

The list of Technical Experts who participated in developing this report follows:

Eileen Bulger, M.D.
Professor of Surgery, University of Washington
Chief of Trauma,
Harborview Medical Center
Seattle, Washington

Frank Butler, MD, CAPT, MC, USN (ret)
Chairman, Department of Defense Committee on Tactical Combat Causalty Care
Director, Prehospital Trauma Care Division, Department of Defense Joint Trauma System
Naval Hospital Pensacola
Pensacola, Florida

Drew Dawson, Director
Office of Emergency Medical Services
National Highway Traffic Safety Administration
U.S. Department of Transportation
Washington, DC

Mary Fallat, M.D.
Professor and Chief, Pediatric Surgery
University of Louisville School of Medicine
Louisville, KY

Detective Scott M. Harding, BS, NREMT-P
Prehospital Trauma Life Support, Region 1 Coordinator
National Association of Emergency Medical Technicians
Columbus, OH

Jay Johannigman, M.D.
Associate Professor of Surgery
Chief, Division of Trauma/Critical Care
University of Cincinnati Medical Center
Cincinnati, OH

Christopher Kahn, M.D. M.P.H.
Fellowship Director, EMS/Disaster Medicine Fellowship
University of California San Diego Medical Center
San Diego, CA

Gregg Margolis, Ph.D., NREMT-P
Director, Division of Health Systems and Health Care Policy
Office of the Assistant Secretary for Preparedness Response
U.S. Department of Health and Human Services
Washington, DC

Jeffrey P. Salomone, M.D.
NREMT-P Medical Director
District Medical Group
Maricopa Medical Center
Phoenix, Arizona

Peter P. Taillac, MD
Associate Professor, Surgery
Division of Emergency Medicine
University of Utah School of Medicine
Utah State EMS Medical Director,
Bureau of EMS and Preparedness
Salt Lake City, UT

Lynn J. White, M.S., CCRP
Director of Resuscitation and Accountable Care
American Medical Response
Research Consultant,
The Center for Medical Transport Research
Columbus, Ohio

Peer Reviewers

Prior to publication of the final evidence report, ECRI Institute sought input from Peer Reviewers selected by the National Highway Traffic Safety Administration. However, the conclusions and synthesis of the scientific literature presented in this report does not necessarily represent the views of individual reviewers.

Peer reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential non-financial conflicts may be retained. The list of peer reviewers follows.

Frank Butler, MD, CAPT, MC, USN (ret)
Chairman, DoD Committee on Tactical Combat Causalty Care
Director, Prehospital Trauma Care Division,
Joint Trauma System

Mary Fallat, M.D.
Professor and Chief, Pediatric Surgery
University of Louisville School of Medicine
Committee on Trauma, American College of Surgeons
Louisville, KY

Cathy Gotschall, Sc.D.
Office of Emergency Medical Services
National Highway Traffic Safety Administration
U.S. Department of Transportation,
Washington, DC

J. Stephen Higgins, Ph.D.
Office of Behavioral Safety Research
National Highway Traffic Safety Administration
U.S. Department of Transportation,
Washington, DC

Eddy Lang M.D., C.M., CCFP (EM), CSPQ
Interim Faculty Department Head
Department of Emergency Medicine
University of Calgary
Calgary, Alberta, Canada

Peter Taillac, MD
Utah Bureau of EMS and Preparedness
University of Utah School of Medicine
National Association of State EMS Officials
Salt Lake City, UT

Acknowledgments

The authors gratefully acknowledge Cathy Gotschall, Sc.D., of the Office of Emergency Medical Services in the National Highway Traffic Safety Administration, who provided oversight of the project (Prepared under Subcontract No. S2013.104SC to Millennium Services 2000+ Incorporated, DTNH22-11-C-00223). We also acknowledge the contributions of Eileen Erinoff, M.S.L.I.S., Director of the Information Center and Kristy McShea, M.S.L.S., Medical Librarian, both of ECRI Institute, for designing and conducting the literature searches.

Contents

Abbreviations and Acronyms viii
1. Introduction 1
Background 1
Condition 1
Treatment Strategies 2
Tourniquets 2
Hemostatic Agents and Dressings 3
Wound Closure Device 4
Scope and Key Questions 11
Scope of the Review 11
Key Questions 11
Use of Tourniquets 12
Use of Hemostatic Dressings 12
Analytic Framework 12
2. Methods 14
Literature Search Strategy 14
Search Strategy 14
Inclusion Criteria 15
Population 15
Intervention 15
Study Design 15
Outcomes 15
Publication Type 15
Study Selection and Data Extraction 16
Risk-of-Bias Assessment of Individual Studies 16
Data Synthesis 17
Strength of the Evidence Base 17
Applicability 17
Peer Review 18
3. Results 19
Results of Literature Searches 19
Key Question 1: Tourniquets Compared With External Pressure 20
Description of Included Studies 20
Key Points 25
Detailed Synthesis 25
Strength of Evidence 31
Applicability 34
Key Question 2: Junctional Tourniquets Compared With External Pressure 34
Description of Included Studies 35

Key Question 3: Tourniquets Compared With Other Tourniquets 35
Description of Included Studies 35
Key Question 4: Junctional Tourniquets Compared With Other Junctional Tourniquets 35
Description of Included Studies 35
Key Question 5: Tourniquets and Duration of Use 35
Strength of Evidence 36
Key Question 6: Hemostatic Dressings Compared With External Pressure 38
Description of Included Studies 38
Key Points 41
Strength of Evidence 42
Applicability 44
Key Question 7: Hemostatic Dressings Compared With Other Hemostatic Dressings 44
Description of Included Studies 44
Ongoing Clinical Trials 44
Indirect Evidence: Animal Model Studies 45
Key Points 46
Selection of Animal Studies 47
Description of studies using 30-45 seconds of free bleeding time 47
Strength of Evidence 48
Description of studies using shorter or longer free-bleeding times 50
Studies using 5 seconds or less free bleeding time 50
Studies using 1 or 2 minutes of free bleeding time 50
Studies using 3 or more minutes of free bleeding 50
Indirect Evidence: Volunteer and Simulation Studies 51
Key Points 51
Results of Volunteer and Simulation Studies 51
4. Discussion 53
Key Findings and Strength of Evidence 53
Findings in Relationship to What is Already Known 54
Applicability 54
Limitations of the Evidence Base 55
Research Gaps 55
Conclusions 56
References 57
Appendix A. Methods of Identifying the Literature A-1
Appendix B. Excluded Articles B-1
Appendix C. Evidence Tables for Indirect Evidence: Animal, Volunteer and Simulation Studies C-1

Tables

Table 1. Types of tourniquets 4
Table 2. Types of hemostatic dressings 6
Table 3. Mechanism of action of hemostatic dressings 9
Table 4. List of included studies of prehospital tourniquet use 21
Table 5. Outcomes reported in studies of prehospital tourniquets 22
Table 6. Data collection process in studies of prehospital tourniquet use 23
Table 7. Studies of prehospital tourniquets reporting data on mortality 26
Table 8. Studies of prehospital tourniquets reporting data on amputations 29
Table 9. Studies of prehospital tourniquets reporting adverse events 30
Table 10. Key Question 1: Strength of evidence grades for survival rate and amputation rate with prehospital tourniquet use 33
Table 11. Key Question 5: Strength of evidence grades for adverse events with prehospital tourniquet use 37
Table 12. List of included studies of prehospital hemostatic dressing use 38
Table 13. Outcomes reported in studies of prehospital hemostatic dressings 38
Table 14. Data collection process in studies of prehospital hemostatic dressing use 39
Table 15. Study of prehospital hemostatic dressing use reporting survival 41
Table 16. Studies of prehospital hemostatic dressing use reporting adverse events 41
Table 17. Key Question 6: Strength of evidence grades for survival and amputations with prehospital hemostatic dressing use 43
Table 18. U.S. Army Institute of Surgical Research Recommendations for Surgical Procedures, Wound Treatment, and Resuscitation for Severe Extremity Hemorrhage Swine Model 46
Table 19. Strength of evidence – Animal studies using recommended free bleeding time (30-45 seconds) in comparison to standard gauze 49

Figures

Figure 1. Analytic framework 13
Figure 2. Disposition of documents identified by searches 19
Figure 3. Survival rates (short-term) in casualties treated with a prehospital tourniquet, all studies included 28
Figure 4. Survival rates (short-term) in casualties treated with a prehospital tourniquet, only military tourniquet studies included 28
Figure 5. Amputation rates in surviving casualties treated with a prehospital tourniquet, military studies only 30

Abbreviations and Acronyms

ACS:	advanced clotting sponge (QuikClot)
CAT:	Combat Application Tourniquet
CRoC:	Combat Ready Clamp
EMS:	emergency medical services
EMT:	Emergency and Military Tourniquet
EPC:	Evidence-based Practice Center
ISS:	Injury Severity Score
JTTR:	Joint Theater Trauma Registry
QCG:	QuikClot Combat Gauze
RCT:	randomized controlled trial
SOFTT:	Special Operations Forces Tactical Tourniquet
TCCC:	Tactical Combat Casualty Care

1. Introduction

Background

Condition

In the United States, data collected by the Centers for Disease Control and Prevention indicate that traumatic injuries in 2008 accounted for 181,226 deaths.[1] According to the National Highway Traffic Safety Administration, motor vehicle crashes in 2010 were responsible for 32,885 deaths and 2,239,000 injures.[2] In contrast in the same year interpersonal violence and falls were responsible for 20,000 and 31,600 deaths, respectively.[3] Death from road injuries was the fifth leading cause of death, exceeded only by death from ischemic heart disease, lung cancer, stroke, and chronic obstructive pulmonary disease. Some of these injury-related deaths are due to traumatic external hemorrhage and exsanguination. An analysis by Kauvar et al.[4] of the National Trauma Data Bank for the years 2002–2005 found a 2.8% death rate among patients with an "isolated lower extremity trauma with an arterial component." Among the same set of patients, 6.5% suffered amputations. The authors suggested that deaths from traumatic external hemorrhage and exsanguination may be preventable with better prehospital control of hemorrhage. A smaller study of patients who died from isolated extremity injuries at two hospitals in the Houston area was reported by Dorlac et al. The study suggested if prehospital hemorrhage control been employed, some of these patients might have been saved.[5] These patients were treated primarily by gauze dressings before reaching a hospital.

One source of evidence on prehospital control of hemorrhage is the military. Over the past 10 years the U.S. military's Tactical Casualty Combat Care (TCCC) program has worked to steadily improve prehospital trauma care.[6-9] (The reader should note that "casualty" refers to an injured person and not necessarily to a fatality.) The goal of TCCC is avoid preventable deaths through a set of trauma-management guidelines designed for the battlefield before the solider reaches a medical treatment facility. The Committee on TCCC regularly evaluates the prehospital trauma literature, gets input from combat medical personnel, and looks at research performed at military research facilities to update the guidelines when needed. Before 2001, battlefield trauma care did not involve the regular use of tourniquets or hemostatic dressings for hemorrhage control.[8,9] External hemorrhage was usually managed with prolonged direct pressure. Through the TCCC's efforts, by January 2005, all combatants entering a U.S. Central Command area were directed to have a Combat Application Tourniquet (CAT) and a HemCon dressing. Evidence leading to these recommendations was gathered via military reports during early parts of the wars in Afghanistan and Iraq.[10-13]

Use of tourniquets in civilian emergency medical services (EMS) is not widespread.[14,15] Instead, most EMS providers rely on direct pressure, pressure dressings, pressure points and elevation to treat severe extremity hemorrhage, using tourniquets only as a last resort. The Guidelines for Field Triage of Injured Patients does not include a recommendation for tourniquet use because "evidence is limited regarding the use of tourniquets in civilian populations; use of tourniquets among EMS systems varies; inclusion of tourniquet use as a criterion could lead to overuse of tourniquets instead of basic hemorrhage control methods, and thus potentially result in overtriage."[1] Efforts are being made to implement aspects of TCCC into civilian trauma care, especially the use of tourniquets.[9,16-18] The recent mass-casualty event at the Boston Marathon

brought tourniquets into the public spotlight as they were used by volunteer medical staff to stop severe hemorrhage.[19] Interestingly, Boston EMS had incorporated tourniquet use and training into its protocols for several years and also adapted several of the TCCC concepts as well.[19]

Treatment Strategies

For the purposes of this report, external hemorrhage is defined as blood loss originating from a ruptured blood vessel and appearing on a body surface. External hemorrhage includes extremity hemorrhage (blood loss from a ruptured blood vessel in the arms or legs) and junctional hemorrhage (blood loss from a ruptured blood vessel in the groin proximal to the inguinal ligament, the buttocks, the gluteal and pelvis areas, the perineum, the axilla and shoulder girdle, and the base of the neck).[20]

The following section provides background on the conditions and treatments being examined in this evidence report. Details on the proper techniques for tourniquet use can be found in other resources such as the TCCC Curriculum and Guidelines.[21,22]

Tourniquets

Tourniquets have a long history of use potentially dating as far back as the 1500s.[23-25] Historical records indicate tourniquets were first used to stop blood flow prior to performing the medical amputations often necessitated by battlefield injury. Tourniquets were widely used to treat extremity bleeding in World War I, but medical officers were often dissatisfied with their use in the field; the long delays before soldiers would reach a field hospital for treatment often resulted in prolonged stoppage of blood flow and subsequent loss of the limb. Tourniquets continued to be used in subsequent major conflicts including WW II, the Korean War and the Vietnam War with apparently mixed results. However, several factors may have contributed to negative outcomes associated with tourniquet use. Tourniquets were sometimes placed when not indicated, or improperly placed; also, there continued to be significant delays in transporting wounded soldiers off the battlefield. Fears of tissue damage and limb loss appear to have discouraged civilian use. Instead, the technique of applying direct pressure followed by a pressure dressing, and pressure-point bleeding control was favored. Traumatic amputation was considered an exception to the no-tourniquet approach.

As noted, experience from the wars in Afghanistan and Iraq prompted the U.S. military to aggressively use tourniquets.[24] Most fatalities occur before the injured soldier reaches a physician, with many of the deaths due to extremity hemorrhage. Medics are now trained to apply a tourniquet first rather than direct pressure, leaving the medic free to attend to other duties. Tourniquet pressure is then maintained during transport to a medical facility.[8] According to Kragh:[26]

> The current indication for emergency tourniquet use is any compressible limb wound that the applier assesses as having potentially lethal hemorrhage. In this environment tourniquet use may be the initial and primary method to control severe hemorrhage. This is in contrast to a historical stepwise approach that used application of direct pressure and pressure points to control hemorrhage before tourniquet application.

Unlike earlier wars, injured soldiers are quickly removed from the battlefield and receive prompt medical attention, reducing the likelihood that prolonged tourniquet use will lead to tissue damage or limb loss.

Tourniquets work properly when compression of limb tissue stops arterial blood flow and no distal pulse is present.[26] Well-designed tourniquets should be easy to use, durable, and mechanically effective to ensure stoppage of arterial blood flow without excessive pressure.[27] The U.S. military, through the TCCC program, recommends three tourniquets: the CAT, the Special Operations Forces Tactical Tourniquet (SOFTT), and the Emergency and Military Tourniquet (EMT).[7] Testing by the military found that these three tourniquets were 100% effective in stopping arterial blood flow in the limbs of volunteers who applied their own tourniquets.[28] The CAT and SOFTT use a strap and a windlass for tightening and the EMT is a pneumatic tourniquet with an air bladder and an inflation bulb to produce compression. These three tourniquets are intended for use on thighs or upper arms.

A separate category of tourniquets, called junctional tourniquets, is comprised of devices designed to stop bleeding in the areas between the trunk and the limbs where a regular tourniquet cannot be applied.[20,29] The Combat Ready Clamp (CRoC) was specifically designed for difficult inguinal bleeding during combat and works by compressing the femoral artery in the inguinal or groin area. The device is collapsible and lightweight and has a rounded plastic disk to apply direct pressure over the femoral artery. A safety strap is attached to the device to hold it around the torso.

Table 1 presents information on manufacturers, design, and regulatory information for commercially available tourniquets.

Tourniquet use is associated with characteristic complications. For instance, insufficient compression will stop only venous flow (essentially creating a venous tourniquet) trapping blood in the limb with potentially life threatening consequences.[14,26] The trapped blood causes limb edema and loss of blood to the general circulation, which can hasten the onset of shock. Bleeding may actually increase with development of venous hypertension. Venous tourniquets have been associated with increased mortality.[10] Other complications include ischemia, compression, and reperfusion injury.[26,30] Muscle cells, in particular, may be more susceptible to ischemia and reperfusion effects after prolonged tourniquet use. Nerve compression may result in neuropathy and weakness; however, evidence suggests this nerve damage is typically minor and reversible.[26] The potential association between tourniquets and limb loss is examined under Key Question 1.

Hemostatic Agents and Dressings

Topical hemostatic agents may be useful for injuries (such as junctional wounds) in which tourniquet use is not feasible.[16,31,32] These agents have physical properties that allow the agent to adhere to damaged tissue and seal ruptured blood vessels or enhance natural blood clotting mechanisms to accelerate clot formation and produce a strengthened clot.

Clot-formation enhancement can be achieved through two mechanisms: concentration of clotting elements in the wound through rapid absorption of water from blood, or chemical reactions that stimulate the intrinsic coagulation pathway. The ideal agent should stop bleeding in 2 minutes or less, cause no toxicity to surrounding tissue, cause no pain or thermal injury, be ready to use with little training, be easily applied under extreme conditions, fit complex wounds, be easily removed from the wound, have a long shelf life, and be cost-effective.[31,32]

Table 2 presents information on manufacturers and regulatory information for commercially available hemostatic dressings.

Table 3 describes the mechanism of action of each hemostatic dressing.

The U.S. military has tested several hemostatic dressings, primarily using a swine model of femoral artery injury.[33] These tests suggested that QuikClot Combat Gauze and WoundStat were more consistent in stopping hemorrhage than HemCon or QuikClot. The TCCC program recommended "Combat Gauze as the first-line treatment for life-threatening hemorrhage that is not amenable to tourniquet placement."[7] WoundStat was recommended as a backup agent. QuikClot Combat Gauze was preferred over WoundStat because combat medical personnel strongly preferred a gauze-type hemostatic agent over powdered or granule hemostatic agents and because of potential thromboembolic complications associated with using WoundStat. WoundStat was subsequently dropped by the U.S. military because of potential damage to blood vessels reported in animal studies.[34]

Wound Closure Device

Innovative Trauma Care (iTraumaCare Inc., Edmonton AB, Canada) developed and marketed a temporary wound closure device called the iTClamp Hemorrhage Control System (Innovative Trauma Care). This device is applied to wound edges and then pressed closed. The skin edges are held by suture needles and a pressure bar holds the edges together to seal the wound and allow formation of a stable clot.[35] The clamp is self-locking to prevent unintentional opening. The device received clearance for marketing from the U.S. Food and Drug Administration under the 510(k) process in May 2013 (K123551). The predicate device was the Combat Ready Clamp. Indications for use are: "The iTClamp is a trauma clamp device for the temporary control of severe bleeding in the extremities, axilla and inguinal areas."

Table 1. Types of tourniquets

Product	Company* (Web site)	U.S. Food and Drug Administration (FDA) Regulations
Combat Application Tourniquet (CAT)	Composite Resources, Inc. (Combat Application Tourniquet | Composite Resources)	Class 1 – 510(k) exempt Product code: GAX (Tourniquet, nonpneumatic) Establishment Registration & Device Listing for Composite Resources Inc.
Combat Ready Clamp (CRoC)	Combat Medical Systems (CRoC Combat Ready Clamp)	Product code: DXC (clamp, vascular) 510(k) summaries: K130482 (issued 2013 Apr 29), K102025 (issued 2010, Aug 11) Indications for use: The Combat Ready Clamp is indicated for use in the battlefield to control difficult bleeds in the inguinal area.
Emergency and Military Tourniquet (EMT)	Delfi Medical Innovations (Delfi medical innovations, inc.)	Class 1 – 510(k) exempt Product code: KCY (Tourniquet, pneumatic) Establishment Registration & Device Listing for Delfi Medical Innovations

Product	Company* (Web site)	U.S. Food and Drug Administration (FDA) Regulations
SAM Medical Systems Junctional tourniquet	SAM Medical Systems (SAM Junctional Tourniquet « SAM)	Product Code: DXC (clamp vascular) 510(k) summary: K123694 (issued 2013 Mar 7) Indications for use: The SAM Junctional Tourniquet is indicated for battlefield and trauma situations: • To control difficult bleeds in the inguinal area • To immobilize a pelvic fracture
Special Operation Forces Tactical Tourniquet (SOFTT)	Tactical Medical Solutions, Inc. (Product Details -Tac Med Solutions Store)	Class 1 – 510(k) exempt Product code: GAX (Tourniquet, nonpneumatic) Establishment Registration & Device Listing for Tactical Medical Solutions, Inc.
SWAT-T	TEMS Solutions, LLC (WELCOME - SWAT-Tourniquet) Product is also distributed on Combat Medical Systems Web site: (SWAT-T Tactical Tourniquet)	Class 1 – 510(k) exempt Product code: GAX (Tourniquet, nonpneumatic) Establishment Registration & Device Listing for TEMS Solutions
TK-4 (Tourni-kwik)	H&H Medical Corp. (H&H Medical Corporation)	Class 1 – 510(k) exempt Product code: GAX (Tourniquet, nonpneumatic) Establishment Registration & Device Listing for H&H Medical Corporation

*Company names were obtained through FDA documents or from the product Web site.

Table 2. Types of hemostatic dressings

Product	Company* (Web site)	U.S. Food and Drug Administration Regulations
BloodStop	Lifescience Plus, Inc. (BloodSTOP for surface wounds | LifeScience PLUS)	Product code: FRO (Dressing, wound, drug) 510(k) summaries: K072681.pdf (issued 2007 Nov 2) K071578.pdf (issued 2007 Sep 27) Indications for use: Non-absorbable hemostatic gauze for emergency and therapeutic use in the control of bleeding from the skin and other surface wounds where temporary control of bleeding is required.
Celox	Medtrade products Ltd. (USA Home « Celox)	Product code: FRO (Dressing, wound, drug) 510(k) summaries: K113560.pdf (issued 2012 Aug 1) K110386.pdf (issued 2011 May 10) K102965.pdf (issued 2010 Dec 8) K093593.pdf (issued 2010 Jan 20) K093519.pdf (issued 2010 Jan 14) K090780.pdf (issued 2009 Nov 20) K091795.pdf (issued 2009 Nov 20) K080097.pdf (issued 2008 Jul 9) K072328.pdf (issued 2007 Dec 21) K061079.pdf (issued 2006 Jun 2) Latest indications for use: Under the supervision of a health care professional CELOX Gauze PRO / CELOX PRO Hemostatic Gauze / OMNI-STAT Gauze / OMNI-STAT Hemostatic Gauze for minor external bleeding from wounds and procedures (Rx) is indicated for use as a temporary topical dressing for bleeding control associated with minor wounds, including control of minor external bleeding and exudate from sutures and/or surgical procedures. Under the supervision of a health care professional CELOX Gauze PRO / CELOX PRO Hemostatic Gauze'/ OMNI-STAT Gauze / OMNI-STAT Hemostatic Gauze for moderate to severe external bleeding wounds (Rx) is indicated for temporary external treatment for controlling moderate to severe bleeding.

Table 2. Types of hemostatic dressings (continued)

Product	Company* (Web site)	U.S. Food and Drug Administration Regulations
HemCon, Chitoflex, Guardacare	HemCon Medical Technologies, Inc. (acquired by TriStar Wellness Solutions in May 2013) (HemCon > Home)	Product code: FRO (Dressing, wound, drug) 510(k) summaries ***HemCon dressings*** K072486.pdf (issued 2008 Aug 6) K080818.pdf (issued 2008 May 15) K043050.pdf (issued 2005 Jun 13) K030946.pdf (issued 2003 Jun 19) K023298.pdf (issued 2002 Nov 4) Latest indications for use: HemCon Bandage is a hemostatic dressing for the external temporary control of severely bleeding wounds intended for emergency use. Additionally, the HemCon Bandage also controls bleeding after hemodialysis. ***ChitoGauze/ChitoFlex*** K111163.pdf (issued 2011 May 17) [ChitoGauze] K102546.pdf (issued 2010 Nov 17) [ChitoGauze] K092357.pdf (issued 2009 Aug 25) [ChitoGauze] K090026.pdf (issued 2009 Mar 31) [ChitoGauze] K071519.pdf (issued 2007 Aug 6) [ChitoFlex] Latest indications for use: The ChitoGauze"" FUISIONW Wound Packing Kit is a hemostatic dressing for the external, temporary control of severely bleeding wounds. ***GuardaCare*** K103641.pdf (issued 2011 Jun 16) Latest indications for use: HemCon GuardaCareT'XR is a hemostatic dressing intended for the temporary control of severely bleeding wounds such as surgical wounds and traumatic injuries.
Quick Relief (QR), PRO QR, StatSeal, WoundSeal, TraumaSeal, BioSeal	BioLife, LLC (BioLife)	Product code: FRO (Dressing, wound, drug) Establishment Registration and Device Listings BioSeal Advanced; BioSeal CVC; Pro QR Powder; StatSeal; WoundSeal; WoundSeal MD; WoundSeal Rapid Response) and TraumaSeal 510(k) summaries K080210.pdf (issued 2009 Feb 10) [PRO QR (Quick Relief)] K070520.pdf (issued 2007 Nov 6) Latest indications for use: PRO QR Powder for moderate to severe external bleeding wounds is intended for emergency use of temporary external treatment for controlling moderate to severe bleeding.

Table 2. Types of hemostatic dressings (continued)

Product	Company* (Web site)	U.S. Food and Drug Administration Regulations
QuikClot Combat Gauze; QuikClot ACS	Z-Medica Corporation (ZMedica - QuikClot - Stop Bleeding Fast | Hemostatic agent)	Product code: FRO (Dressing, wound, drug) 510(k) summaries ***QuikClot hemostatic bandages*** K123387.pdf (issued 2013 Apr 12) K120782.pdf (issued 2013 Mar 20) K090620.pdf (issued 2009 Apr 8) K072474.pdf (issued 2007 Oct 16) Latest indications for use: QuikClot Combat Gauze Hemostatic Dressing is intended for use as a topical dressing for local management of bleeding wounds such as cuts, lacerations, and abrasions. It may also be used for temporary treatment of severely bleeding wounds, such as surgical wounds (operative, postoperative, dermatological, etc.) and traumatic injuries. ***QuikClot granule bandages*** K070010.pdf (issued 2007 Jan 25) [QuikClot Sport] K061767.pdf (issued 2006 Jul 19) [QuikClot ACS] K051955.pdf (issued 2005 Aug 10) [QuikClot ACS] K050769.pdf (issued 2005 Apr 14) K013390.pdf (issued 2002 May 23) Different manufacturer – On Site Gas Systems, Inc. Latest Indications for use for QuikClot ACS: This device is intended for temporary external use to control traumatic bleeding.
Rapid deployment hemostat (RDH) Modified Rapid Deployment Hemostat (MRDH)	Marine Polymer Technologies (mrdh | Why mrdh)	Product Code: KMF (Bandage, liquid) (When used only as a skin protectant, the device is exempt from the premarket notification procedures) 510(k) summaries K082703.pdf (issued 2008 Oct 14) K002550.pdf (issued 2000 Dec 20) Latest indications for use: MRDH Bandage is a trauma dressing intended for the temporary control of severely bleeding wounds such as surgical wounds (operative, postoperative, donor sites, dermatological, etc.) and traumatic injuries.

Table 2. Types of hemostatic dressings (continued)

Product	Company* (Web site)	U.S. Food and Drug Administration Regulations
TraumaDex, Bleed-X, Hemaderm	Medafor, Inc. (Medafor Inc Products and Technology, Medafor Inc. Developer of Hemostatic Technology) Note: *According to news items on Medafor's Web site (Medafor News 2002-02-12) TraumaDex is distributed by Emergency Medical Products (EMP) to emergency medical services and military personnel.*	Product code: FRO (Dressing, wound, drug) 510(k) summaries ***Hemaderm*** K033666.pdf (issued 2003 Dec 17) K021678.pdf (issued 2002 Jul 12) Latest indications for use: HemaDerm is intended for use under the care of a health care professional as a topical dressing for the temporary treatment of severely bleeding wounds, such as surgical wounds (postoperative, donor sites, dermatological,) minor cuts, and lacerations and for the temporary treatment of mild bleeding from topical ear, nose, and throat surgical wounds and nosebleeds. 510(k) Class 1 Product code: KMF (Bandage, liquid) ***TraumaDEX, Bleed-X*** K013225.pdf (issued 2001 Dec 26) Latest indications for use: TraumaDex is intended as a topical dressing for the local management of bleeding wounds such as cuts, lacerations, and abrasions. Under the care of a health care professional, TraumaDex may be used for the temporary treatment of severely bleeding wounds, such as surgical wounds (postoperative, donor sites, dermatological), cuts, lacerations, and traumatic injuries.
UltraClot (InstaClot) BallistiClot	Emergency Medical Devices, LLC (Emergency Medical Devices)	Product code: FRO (Dressing, wound, drug) 510(k) summary K082601.pdf (decision date 2008 Oct 9) - Note: according to manufacturer Web site, UltraClot OTC, UltraClot Onestep, UltraClot Gauze, and BallistiClot are covered by this 510(k). Clearance is pending for UltraClot Plug. Latest indications for use: UltraClot is intended as a hemostatic dressing for emergency external use and temporary wound treatment to achieve hemostasis of moderate to severe bleeding.

*Company names were obtained through FDA documents or from the product Web site

Table 3. Mechanism of action of hemostatic dressings

Product	Company*	Mechanism of Action as Described on the Company Web site
BloodStop	Lifescience Plus, Inc. BloodSTOP for surface wounds | LifeScience PLUS	"BloodSTOP is a natural, biocompatible, non-irritating, animal-free hemostatic agent which resembles traditional gauze. Using a proprietary formulation, cotton cellulose is etherized and oxidized to make a highly absorbent, water-soluble, hemostatic matrix." "When applied to a wound, BloodSTOP quickly absorbs blood and other body fluids, transforms into a gel to seal the wound with a protective transparent layer, actively aids in blood coagulation, and creates an environment for wound healing."

Table 3. Mechanism of action of hemostatic dressings (continued)

Product	Company*	Mechanism of Action as Described on the Company Web site
Celox	Medtrade Products, Ltd. (USA Home « Celox)	"Celox Gauze is a high density gauze, impregnated with the proven Celox granules [chitosan], individually sterile packed in a ruggedized pouch with tear notches for fast opening." • Chitosan absorbs fluid, swells, and forms a gel; • Celox electrostatically attracts red blood cells and forms a gel-like plug. • Does not rely on the body's own clotting mechanism. • No heat generated.
HemCon, Chitoflex, Chito Gauze, Guardacare	HemCon Medical Technologies, Inc. (acquired by TriStar Wellness Solutions in May 2013) (HemCon > Home)	"HemCon Bandage PRO works by becoming extremely adherent when in contact with blood. This adhesive-like action seals the wound and controls bleeding. HemCon products are fabricated from chitosan, a naturally occurring, bio-compatible polysaccharide. Because chitosan has a positive charge, it attracts red blood cells, which have a negative charge. The red blood cells create a seal over the wound as they are drawn into the bandage, forming a very tight, coherent seal."
Quick Relief (QR), PRO QR, StatSeal, WoundSeal, TraumaSeal, BioSeal	BioLife, LLC (BioLife)	"WoundSeal/BioSeal powder is composed of a hydrophilic, or water-loving, polymer and potassium ferrate. When the powder is poured onto a bleeding wound, the hydrophilic polymer instantly dehydrates the blood by absorbing only the plasma or liquid portion of the blood stacking the blood solids beneath the powder. Simultaneously the potassium ferrate dissolves, releasing iron that agglomerates (binds together) the blood solids to create an occlusive seal. As manual pressure is applied to the powder, the seal is pushed into contact with the wound. The natural glue-like nature of drying blood adheres the seal to the wound and surrounding skin. The occlusive seal that has formed in seconds stops further bleeding or oozing. Blood solids continue to stack beneath the seal, strengthening it. The natural clotting process proceeds below the seal."
QuikClot Combat Gauze; QuikClot ACS	Z-Medica Corporation (ZMedica - QuikClot - Stop Bleeding Fast | Hemostatic agent)	"QuikClot 2x2 is a soft, white, sterile, 2" x 2", nonwoven gauze impregnated with kaolin, an inert mineral that does not contain animal or human proteins or botanicals." "The intrinsic blood clotting pathway is initiated by negatively charged surfaces such as kaolin." • Kaolin promotes the activation of Factor XII (FXII) in the presence of kallikrein and high molecular weight kininogen. Activated FXII initiates the intrinsic clotting pathway via the activation of Factor XI (FXI). Activated FXI continues the coagulation pathway that ends with the formation of a fibrin clot. Kaolin promotes the activation of platelet-associated FXI and it is a distinct and separate molecule from plasma FXI. Activated platelet-associated FXI initiates the intrinsic clotting pathway in normal and FXII deficient patients. QuikClot ACS contains 3 mm diameter zeolite beads packaged in a very porous surgical mesh. Zeolite has a large surface area for fibrin formation, has the ability to activate platelets and contains a cation (Ca++) that is a cofactor in many steps of the coagulation cascade. QuikClot zeolite products adsorb water from blood, concentrating clotting factors at the site.

Table 3. Mechanism of action of hemostatic dressings (continued)

Product	Company*	Mechanism of Action as Described on the Company Web site
Rapid deployment hemostat (RDH) Modified Rapid Deployment Hemostat (MRDH)	Marine Polymer Technologies (mrdh | Why mrdh)	MRDH contains pGlcNAc fibers. "When blood contacts pGlcNAc, plasma proteins are rapidly bound and absorbed. Fibers in the matrix interact with platelets, stimulating their activation leading to the onset of the coagulation cascade. A catalytic surface for thrombin generation and accelerated fibrin clot formation results from the interaction of platelets with pGlcNAc. The fibers bind and cause agglutination of RBCs [red blood cells], resulting in the exposure of phosphatidylserine, leading to their activation and direct participation in clotting. The combination of platelet and RBC receptor-based contact with the pGlcNAc fibers results in thrombin generation and fibrin mesh formation. A hemostatic plug forms, which is augmented by additional vasoconstrictive effects due to the release of both thromboxane by activated platelets and endothelin-1 by endothelial cells."
TraumaDex, Bleed-X, Hemaderm	Medafor, Inc. Distributed by Emergency Medical Products (EMP)	HemaDerm is composed of microporous polysaccharide hemospheres, is applied as a powder, and "is designed to act as a sieve to dehydrate the blood and thus serve to accelerate the natural blood clotting process." The product then forms a gel.
UltraClot (InstaClot) BallistiClot	Emergency Medical Devices, LLC (Emergency Medical Devices, UltraClot)	The Web site indicates that a proprietary hemostatic agent is dissolved into the wound from the UltraClot pouch. The FDA documents described the agent as "comprising a clay-based powder contained in a dissolving pouch with a non-stick gauze pad backing that is placed on a moderate to severe wound and held in place until hemostasis is achieved."

*Company names were obtained through FDA documents or from the product Web site

Scope and Key Questions

Scope of the Review

The purpose of this evidence report is to present a systematic review and assessment of the biomedical and clinical literature describing prehospital treatment of external hemorrhage caused by traumatic injury. The primary focus of the report is the efficacy of prehospital application of tourniquets and hemostatic dressings to control traumatic external hemorrhage. The need for a systematic review and evidence analysis on this topic was conceived by the National Highway Traffic Safety Administration (NHTSA) during discussions with trauma stakeholders and other Federal agencies. NHTSA has partnered with ECRI Institute's Evidence-based Practice Center (EPC) to undertake this report. The ECRI Institute EPC is one of 11 EPCs designated by the Agency for Healthcare Research and Quality (AHRQ). An original set of key questions were proposed by NHTSA and then refined after discussions with ECRI Institute and experts in the military and EMS communities.

Key Questions

The key questions assessed in this evidence report were developed using the PICOTS approach (populations, interventions, comparators, outcomes, timing, and settings):

- The population of interest is individuals with extremity hemorrhages.
- The interventions of interest are commercially available tourniquets and hemostatic dressings.
- Comparators are external wound pressure and nontourniquet or nonhemostatic interventions.
- Outcomes of interest are limb salvage, hypovolemic shock, survival, and adverse effects.

- Timing is both immediate and long-term.
- The setting is prehospital before any procedures are performed in the hospital emergency department or operating theater.

Use of Tourniquets

- Key Question 1. In trauma patients with extremity hemorrhage (excludes junctional hemorrhage) who are treated in the prehospital setting by EMS personnel, what is the effect of tourniquet use (single or double) with or without external wound pressure on limb salvage, hypovolemic shock, survival, and adverse effects compared with external pressure alone or with other nontourniquet interventions?
- Key Question 2. In trauma patients with junctional hemorrhage who are treated in the prehospital setting by EMS personnel, what is the effect of specialized junctional tourniquet use with or without external wound pressure on limb salvage, hypovolemic shock, survival, and adverse effects compared with external pressure alone or with other nonjunctional tourniquet interventions?
- Key Question 3. In trauma patients with extremity hemorrhage (excludes junctional hemorrhage) who are treated in the prehospital setting by EMS personnel, do different brands or models of tourniquets differ from each other in their effect on limb salvage, hypovolemic shock, survival, and adverse effects?
- Key Question 4. In trauma patients with junctional hemorrhage who are treated in the prehospital setting by EMS personnel, do different brands or models of specialized junctional tourniquets differ from each other in their effect on limb salvage, hypovolemic shock, survival, and adverse effects?
- Key Question 5. In trauma patients with external hemorrhage (excludes junctional hemorrhage) who are treated in the prehospital setting by EMS personnel using a tourniquet—
    a. Does the incidence of adverse events vary by the duration of tourniquet use prior to removal?
    b. Does the incidence of adverse events vary depending on whether tourniquets are removed in the field versus in a facility?

Use of Hemostatic Dressings

- Key Question 6. In trauma patients with external hemorrhage (hemorrhage from any body surface) who are treated in the prehospital setting by EMS personnel, what is the effect of hemostatic dressings with or without external wound pressure on limb salvage (if an extremity involved), hypovolemic shock, survival, and adverse effects compared with using nonhemostatic gauze with or without external wound pressure?
- Key Question 7. In trauma patients with external hemorrhage (hemorrhage from any body surface) who are treated in the prehospital setting by EMS personnel, do different brands or types of hemostatic dressings differ from each other in their effect on limb salvage (if an extremity is involved), hypovolemic shock, survival, and adverse effects?

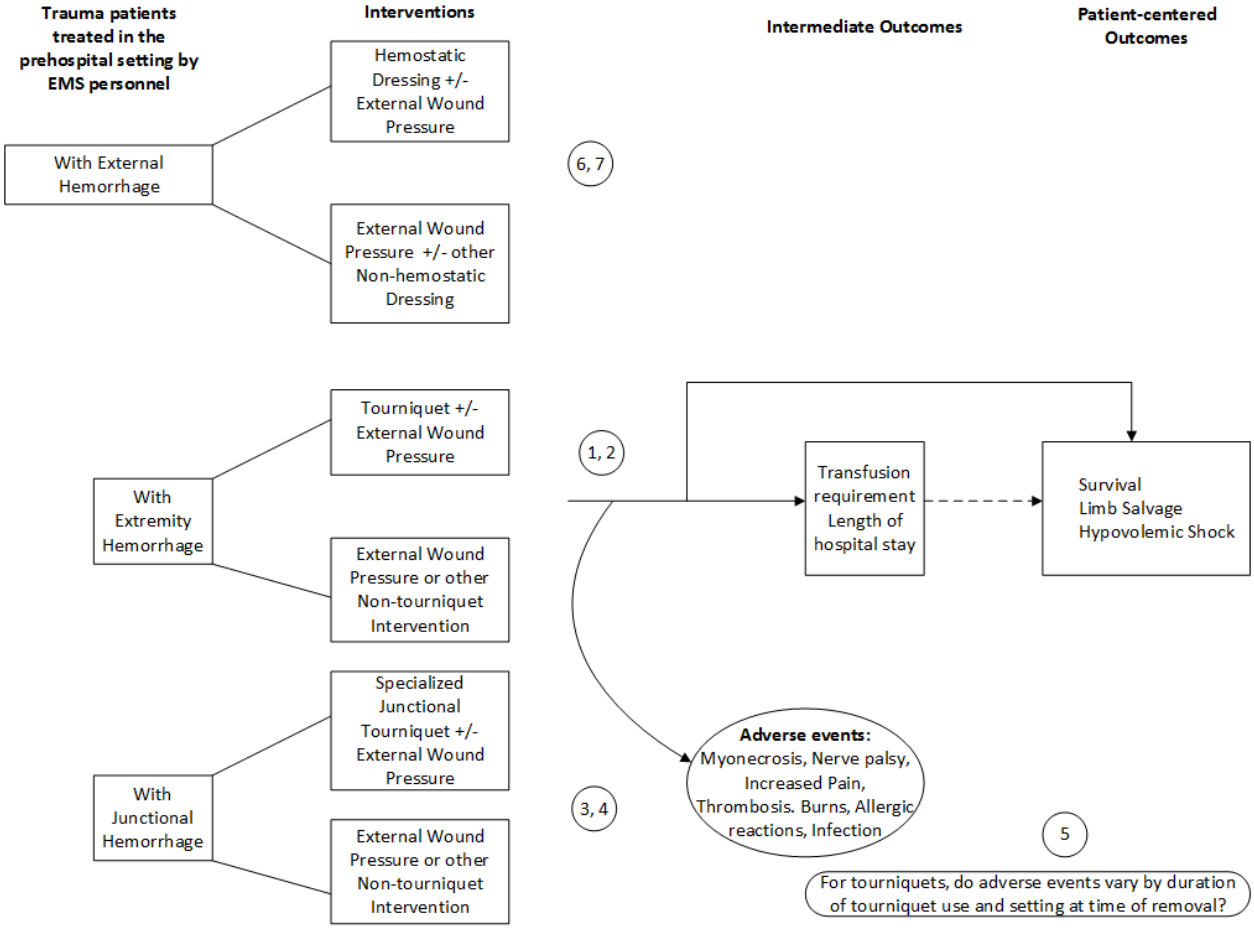
Analytic Framework

The analytic framework below (Figure 1) graphically depicts events that individuals with trauma-induced external hemorrhage experience as they are treated with a tourniquet or hemostatic dressing; it begins with identification of hemorrhage (the far left of the figure), moves

to application of various interventions, and ends with patient-oriented outcomes. Key Questions 1 through 7 are represented in the framework by a circled number.

Patient-oriented outcomes are events that directly affect patient health. This report focuses on treatment of patients with trauma-induced external hemorrhage which has the potential to result in patient death or limb amputation. Therefore, the outcomes most directly relevant to patient well-being are survival, limb salvage, and prevention of hypovolemic shock. Potential adverse events associated with tourniquet use (such as myonecrosis, nerve palsy, increased pain, infection, and thrombosis) and hemostatic dressings (such as burns, allergic reactions, infections, and tissue damage) also directly affect patients. Outcomes such as transfusion requirement and hospital length of stay have a less direct impact on patients and were considered intermediate outcomes.

Figure 1. Analytic framework



Circles indicate key questions

2. Methods

ECRI Institute partners with private and public organizations to perform scientific reviews of a variety of topics. The process of systematic review as practiced by ECRI Institute follows specific prescribed steps:

1. The investigators start with formulated "key" questions. These questions test hypotheses and are structured using the PICOTS framework. The focus is on outcomes that are relevant and important to patients (patient-oriented outcomes). The framework is depicted visually in an "analytic framework," used to show the relationship between the key questions and the outcomes used to address these questions. (See Figure 1)
2. Inclusion and exclusion criteria for studies to be used in the review are determined based on the specific key questions. Criteria may vary for each question in the review.
3. Next, an objective and comprehensive search of the medical literature and gray literature, (i.e., reports, monographs, and studies produced by government agencies, educational facilities, and corporations that do not appear in the peer-reviewed literature) is conducted. The reference lists of included studies are examined for any studies not identified by electronic searches.
4. Studies are compared with the inclusion criteria developed before examining the evidence, and those included in the review are then critically appraised, noting features of the design and conduct of the studies that create potential for bias. Risk of bias, in this context, is the extent to which the design and conduct of a single study "protect against all bias in the estimate of treatment effect."[36] Studies with a low potential for bias are typically described as being of "high quality," whereas those with high potential for bias are described as being of "low" or "poor" quality, and those of moderate quality as having intermediate potential for bias. The degree to which a study protects against bias is referred to as "internal validity." Following this appraisal, data are extracted from the included studies and analyzed or summarized as appropriate.
5. The body of evidence for each population-intervention-comparator-outcome set is assessed in terms of study designs, overall study limitations, consistency, directness, precision, publication bias, magnitude of effect and other factors to assign an evidence grade.

Literature Search Strategy

Search Strategy

To identify relevant information on the benefits and harms of prehospital application of tourniquets and hemostatic dressings, we employed the following search strategies:

- Systematic search of 13 external and internal electronic databases, including CINAHL, EMBASE, and Medline from 2001 to the present for fully published, primary, clinical studies. A detailed search strategy and a full explanation of our electronic database search are presented in Appendix A.
- Systematic search of the following databases unlimited by date for secondary publications (e.g., systematic reviews, Health Technology Assessments): The Cochrane Database of Systematic Reviews (Cochrane Reviews), Database of Abstracts of Reviews of Effects (DARE), and Health Technology Assessment and Database (HTA).

- Search for additional published and unpublished studies, which included the following steps:
    - Manual search of bibliographies listed in fully published studies
    - Search and written inquiry to regulatory agencies, including the U.S. Food and Drug Administration (FDA)
    - Search of www.ClinicalTrials.gov and www.controlled-trials.com for ongoing clinical trials
- Publications were also suggested for inclusion by individuals who commented on the draft report.

Inclusion Criteria

We used the following criteria to determine which studies identified by our searches would be included in our analysis. These criteria were developed prior to any review of the clinical literature. Inclusion and exclusion criteria were developed to specify the types of studies appropriate for addressing the Key Questions.

Population

1. *Study must have enrolled human subjects in whom a trauma-induced extremity hemorrhage is treated in a prehospital setting by EMS personnel.*
   Studies of animals were outside the scope of this assessment. However we examined this literature base in a separate part of the report.
2. *Study must report results separately for extremity and junctional hemorrhage.*

Intervention

3. *Study must evaluate the efficacy of a tourniquet or a hemostatic dressing currently marketed in the United States.*

Study Design

4. *Studies may be of any design.*
5. *Studies must have enrolled at least 5 patients per treatment group.*

Outcomes

6. *Study must have reported on at least one of the outcomes listed in the Key Questions.*
7. *The reliability and validity of all instruments measuring relevant outcomes, such as activities of daily living and function or pain, must have been addressed in the published literature.*
   However, for studies not using a validated instrument, we did not necessarily exclude the entire study—only data from instruments in which the psychometric properties were not reported in the published literature.
8. *For all outcomes, we considered only time points for which at least 50% of the enrolled participants contributed data.*

Publication Type

9. *Study must have been published in English.*

Although we recognized that in some situations, excluding non-English studies could lead to bias, we believed that the few instances in which this may occur do not justify the time and cost typically necessary for translation of studies to identify those of acceptable quality for inclusion in our review.

10. *Study was reported as a full-length, peer-reviewed article.*
    Published abstracts and letters alone do not include sufficient details about experimental methods to permit verification and evaluation of study design.[37,38]
11. *When several sequential reports from the same study center were available, we included outcome data from only the largest, most recent, or most complete report.*
    However, we used relevant data from earlier and smaller reports if the report presented pertinent data not included in the larger, more recent report. This criterion prevents double-counting of patients.

Study Selection and Data Extraction

Once the searches identified potential references, these were processed using DistillerSR (Evidence Partners, Ottawa, Canada), an online application designed specifically for the screening and data extraction phases of a systematic review. Specific forms were created for title screening, abstract screening, full text screening, and data extraction. During title screening, only titles with no obvious connection to the focus of this review were eliminated. The lead analyst screened all abstracts for their relevance to the report and segregated references into excluded, clinical studies, animal studies, and background references. Although we did not perform dual screening of abstracts, we have included a bibliography of excluded abstracts in Appendix B. After the abstract screening phase full text articles were retrieved. The full texts of clinical studies were screened by the lead analyst to ensure they contained sufficient patient numbers and reported patient-oriented outcomes. Although full text articles were not screened in duplicate, we have included a bibliography of excluded studies with reasons for exclusion in Appendix B. Data extraction forms were used to record data on clinical study design, data collection processes, patients/casualties, and outcomes. Data were extracted by a research analyst and then reviewed by the lead analyst.

Risk-of-Bias Assessment of Individual Studies

After determining which of the publications identified in our searches met our inclusion criteria, we assessed the potential for bias in these studies. Judging study quality by assessing the potential for bias is the first part of grading the strength of an evidence base according to the system detailed in the publication by Viswanathan et al.[36] In this system, the risk-of-bias assessment tool is a set of questions that explicitly evaluates the risk of bias. The questions are geared specifically for the field of research being assessed in the review.

Viswanathan et al. consider "risk of bias to refer to the extent to which a single study's design and conduct protect against all bias in the estimate of effect." Bias is systematic error—as opposed to random error—introduced into a study that leads to an underestimation or an overestimation of the true effect of an intervention.[39] In well-constructed studies, biases are minimized by appropriate study design and conduct, and changes in outcomes and differences in outcomes between groups are definitively attributed to the treatment of interest. For these

reasons, high-quality studies are those in which study design and conduct eliminate or greatly reduce the potential for bias.

Clearly, the nature of emergency medical procedures (particularly in combat situations) does not allow for well-controlled clinical studies. Typically, data collection is retrospective and captures only the procedure of interest without a defined comparison group. Consequently, the risk of bias is likely to be high. However, this does not mean the evidence collected in these studies should be summarily rejected, only that the estimate of effect size is likely to be biased and that perhaps, the true effect size will remain unknown. Nevertheless, when effects are sufficiently large, they may be judged clinically significant despite a high risk of bias.

Some aspects of study design and conduct may enhance data collection in single-arm studies. To reflect this we collected information on the following:

- Was data collection prospective?
- Was a researcher on site to assist with data collection?
- Were medics or patients interviewed about outcomes?
- Were medics or soldiers given specific instructions on how and when to use the tourniquets or hemostatic dressings?

Data Synthesis

For studies of tourniquets, we analyzed the outcomes of survival and amputation. We performed a random effects meta-analysis of available data for the military population, and considered the data on children (defined as younger than 18 years of age) and civilians separately. Statistical heterogeneity was examined using I^2, but the small number of studies in the comparisons limited our confidence in statistical measures of heterogeneity. Given the short time between injury and assessments of survival and amputation, and given that no studies had concurrent control groups (i.e., not treated with a tourniquet), survival and amputation were treated as dichotomous outcomes and analyzed as event rates with 95% confidence intervals.

For animal model studies we calculated absolute risk differences and relative risk (RR) with 95% confidence intervals for the primarily dichotomous outcomes for individual studies. We calculated odds ratio (OR) with 95% confidence intervals for individual studies in cases in which meta-analyses was possible and calculated a summary OR using a random effects model.

Strength of the Evidence Base

The overall strength of evidence for each key question and outcome was assessed using the GRADE principles.[40-42] The strength of evidence grade is a composite of the study design, study limitations (risk of bias), consistency, directness, precision, and publication bias domains. These strength of evidence grades are described as High, Moderate, Low or Very Low and reflect decreasing confidence in the estimates of the effects of interventions on outcomes.

Applicability

Applicability, sometimes referred to as generalizability, is considered separately from judgments about strength of evidence.[43] Applicability is judged from the standpoint of clinical decisionmakers regarding how relevant the evidence is to their specific practice. The evidence must be evaluated to determine whether the patient populations, settings, diseases or conditions,

interventions, comparators, and outcomes are relevant to their decisions. To assess applicability to a particular patient population, one must consider whether studies include the patients of interest or whether the eligibility criteria exclude patients with comorbidities or those in poor health. In other words, the evidence is assessed for its ability to reflect "real world" situations. For this report, we consider whether the populations (including their types of injuries), interventions, and settings described in the published studies are applicable to the civilian population, EMS providers and and a nonmilitary setting.

Peer Review

Nominations for peer reviewers were solicited from several sources, including the TEP and interested Federal agencies. Experts in emergency medical services, emergency medicine, surgery, military combat casualty care, and systematic review methods were invited to provide external peer review of the draft report. Members of the TEP also provided comments. We have addressed reviewer comments, revising the text as appropriate. A list of peer reviewers who submitted comments on the draft report is provided above.

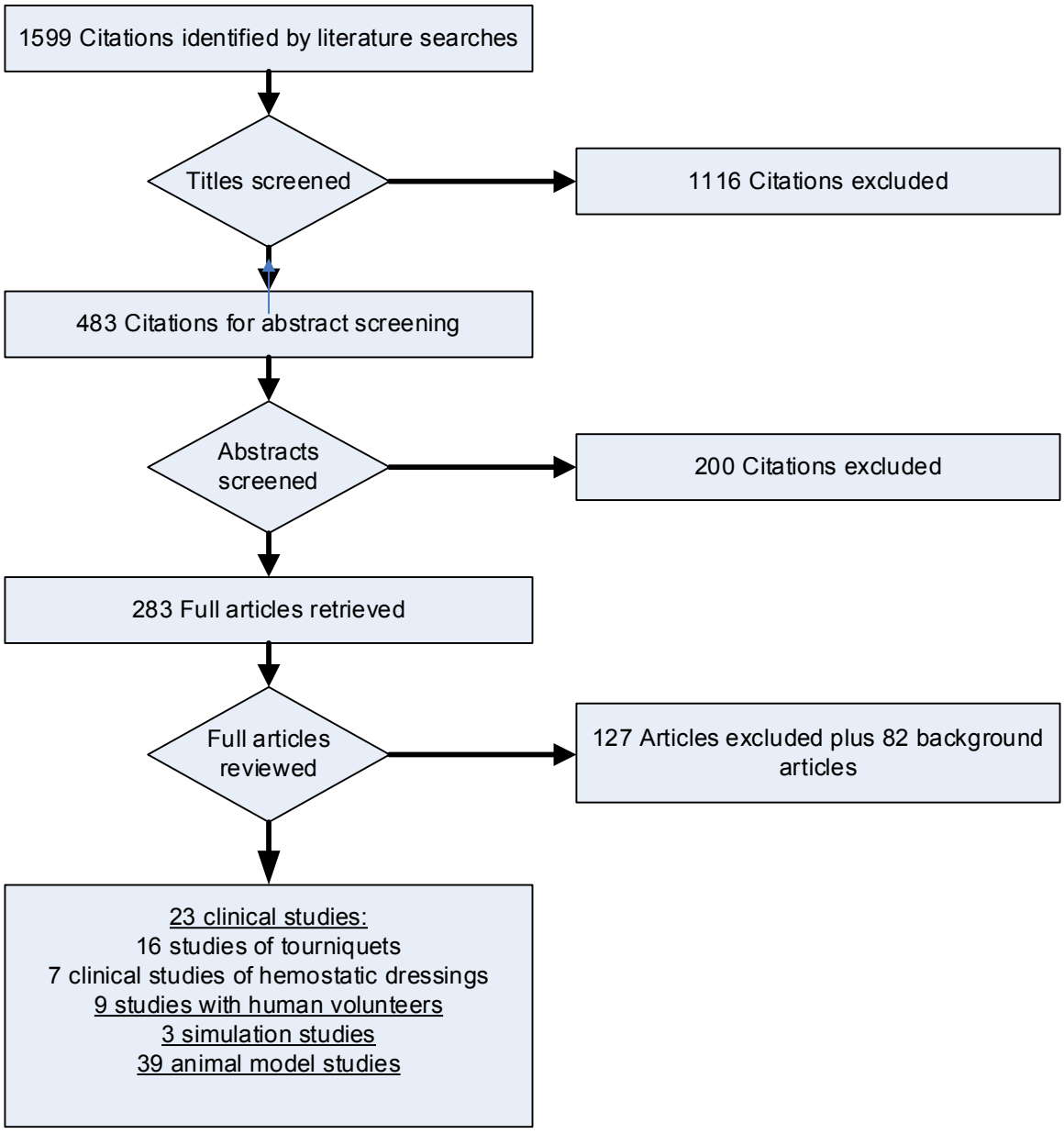
3. Results

The results chapter presents our findings, beginning with the results of our literature searches and a description of the included studies. The chapter is organized to present the findings separately for each key question. We also present information on ongoing clinical trials and an assessment of the results of animal model studies.

Results of Literature Searches

Figure 2 is an attrition diagram that provides a visualization of the disposition of references as they were evaluated for possible inclusion in the report. Our searches identified 1,599 potential citations for this report. After examining titles, abstracts, and full text we included 27 clinical studies examining tourniquets and/or hemostatic dressings that met our inclusion criteria.

Figure 2. Disposition of documents identified by searches



Identified articles excluded at the abstract level are listed in Table B-1 in Appendix B. At the abstract level, articles were excluded if they were obviously not related to the focus of the evidence report, were not published in English, or were not full length articles (abstracts only). Articles reviewed as full text and then excluded are listed in Table B-2 in Appendix B. This table provides a specific reason for exclusion of each article.

Key Question 1: Tourniquets Compared With External Pressure

Key Question 1: In trauma patients with extremity hemorrhage (excludes junctional hemorrhage) who are treated in the prehospital setting by EMS personnel, what is the effect of tourniquet use (single or double) with or without external wound pressure on limb salvage, hypovolemic shock, survival, and adverse effects compared with external pressure alone or with other nontourniquet interventions?

Description of Included Studies

We identified 20 publications of prehospital tourniquet use for trauma-induced extremity hemorrhage. However, four publications did not provide information on outcomes needed for inclusion in this report: Lairet et al.,[44] Gerhardt et al.,[45] Kragh et al.,[46] Kragh et al.[47] In two instances, the same study population was assessed in two separate publications. Kragh et al.[48] and Kragh et al.[49] used the same set of 499 patients and Kragh et al.[11] and Kragh et al.[10] used the same set of 232 patients. The 16 included publications are listed in Table 4 along with the setting where the data on tourniquet use were collected. Fourteen of the 16 studies were conducted in military settings: the U.S. military in Iraq and Afghanistan (8 studies), the U.K. military (3 studies), the Israeli military (2 studies), and Canadian military (1 study). Only one study, Kalish[50] reported data from a civilian setting. The study by Kragh et al. 2012[51] described 88 pediatric cases included in the Joint Theater Trauma Registry.

The outcomes reported in these studies are listed in Table 5. Thirteen of the 16 included studies reported data on deaths, 11 reported data on adverse events, 8 reported data on amputations, and none reported data on shock.

Seven of the studies used prospective data collection (see Table 6). Three of the studies had a researcher on site to assist with data collection. Most studies provided some general information on how the tourniquets were to be used within the study context, but only a few provided specific details on instructions given to participants. However, studies from the U.S. military were likely using TCCC practices when data were collected after 2005 and it is likely that tourniquets were used aggressively as a first option for traumatic extremity hemorrhage.

A few studies attempted to draw comparisons between casualties treated with a tourniquet and similar casualties not treated with a tourniquet (see Table 5). For instance, Kotwal et al.[12] reported the number of casualties treated with compression dressings versus tourniquets, but only reported outcomes for those treated with tourniquets. Beekley et al.[52] reported outcome data for tourniquet- and nontourniquet-treated casualties, but failed to report what prehospital treatments the nontourniquet group received. Clasper et al.[53] matched surviving tourniquet-treated casualties with surviving nontourniquet-treated casualties to examine the rate of adverse events. As Clasper et al. pointed out, "in a standard retrospective study it is likely that there would be considerable bias if simple comparison was made between the two groups as it is likely that those casualties with more severe injuries would have required a tourniquet, but those with a more severe injury are also likely to have worse outcomes and experience more complications."

Table 4. List of included studies of prehospital tourniquet use

Reference	Setting	Registry or Hospital	Period of Data Collection
Eastridge et al. 2012[13]	U.S. military Iraq/Afghanistan	Records from Armed Forces Medical Examiner System (AFMES) and Defense Medical Mortality Registry, which analyzes all active-duty deaths.	Oct 2001 to June 2011
King et al. 2012[54]	U.S. military Afghanistan	Patients presenting to a forward surgical team (FST) at Forward Operating Base Shank (Level II) in Afghanistan	Aug 2011 to Nov 2011
Kragh et al. 2012[51]	U.S. military Iraq/Afghanistan pediatric casualties	Joint Theater Trauma Registry	May 2003 to Dec 2009
Kotwal et al. 2011[12]	U.S. military Iraq/Afghanistan	Prehospital Trauma Registry (PHTR) Casualties from the 75th Ranger Regiment	Oct 2001 to March 2010
Kragh et al. 2011[49]	U.S. military Iraq	U.S. combat support hospital in Baghdad, Iraq	March 2006 to March 2007
Kragh et al. 2011[48]	U.S. military Iraq	U.S. combat support hospital in Baghdad, Iraq	March 2006 to March 2007
Brown et al. 2010[55]	U.K. military Iraq/Afghanistan	Joint Theater Trauma Registry	Aug 2003 to May 2008
Brodie et al. 2009[56]	U.K. military Iraq/Afghanistan	Joint Theatre Trauma Registry	Feb 2003 to Sept 2007
Clasper et al. 2009[53]	U.K. military Iraq/Afghanistan	Joint Theatre Trauma Register	Dec 2003 to May 20008
Kragh et al. 2009[11]	U.S. military Iraq	U.S. combat support hospital in Baghdad, Iraq	March to Oct 2006
Tien et al. 2009[57]	Canadian military Afghanistan	Role 3 multinational medical unit (MMU) at Kandahar Airfield Base and Canadian Trauma Registry	Feb 2006 to May 2006
Beekley et al. 2008[52]	U.S. military Iraq	The 31st combat support hospital in Iraq	Jan 2004 to Dec 2004
Dayan et al. 2008[58]	Israeli military	Israeli civilian emergency department	2006
Kalish et al. 2008[50]	U.S. civilian	Boston Medical center and Boston EMS Trauma Database	Jan 1999 to April 2006
Kragh et al. 2008[10]	U.S. military Iraq	U.S. combat support hospital in Baghdad, Iraq	March 2006 to Oct 2006
Lakstein et al. 2003[59]	Israeli military	Israeli defense force personnel in a military prehospital setting	Jan 1997 to Jan 2001

Table 5. Outcomes reported in studies of prehospital tourniquets

Reference	Number of Casualties Treated	Patient Characteristics	Amputations	Deaths	Shock	Adverse Events
Eastridge et al. 2012[13]	976	Not reported		X		
King et al. 2012[54]	54 treated with Combat Application Tourniquet/Special Operations Forces Tactical Tourniquet (CAT/SOFTT)	Not reported		X		X
Kragh et al. 2012[51]	88 pediatric casualties treated with CAT	72 were male and 16 were female patients. Mean age was 11 years (median, 11 years; range, 4–17 years). Injuries: explosion 64%, gunshot 30%, other 6%.		X		
Kotwal et al. 2011[12]	66 treated with tourniquets 394 treated with compression dressings	All casualties were male, with age at time of injury ranging from 18.9 to 52.9 years. Injuries: explosion 67%, gunshot 24%, blunt trauma 6%.	X	X		
Kragh et al. 2011[49]	499	96% male, average age 29 years, 16 were children and 5 elderly. Injury: explosion 75%		X		X
Kragh et al. 2011[48] Same study as Kragh et al. 2011[49] but reporting morbidities	499	96% male, average age 29 years, 16 were children and 5 elderly. Injury: explosion 75%				X
Brown et al. 2010[55]	23	Median age 26 years, range 18–42 years, not specific to tourniquet patients. Injuries for entire patient pool: explosion 62%, gunshot 38%.				X
Brodie et al. 2009[56]	70 treated with CAT	Gender and age data not reported. Injuries: explosion 86%, gunshot 14%.	X	X		X
Clasper et al. 2009[53]	22 casualties treated with tourniquets matched to 22 casualties not treated with tourniquets; all casualties had a fracture	Tourniquet group: mean age of 26.6 years, range 19–37 years. Injuries: explosion 32% Nontourniquet group: mean age of 25.7 years, range 19–37 years. Injuries: explosion 64%	X			X

Table 5. Outcomes reported in studies of prehospital tourniquets (continued)

Reference	Number of Casualties Treated	Patient Characteristics	Amputations	Deaths	Shock	Adverse Events
Kragh et al. 2009[11] Reassessment of data from Kragh et al. 2008[10]	232 total casualties were included, with 194 of these having prehospital tourniquets placed.	95% male, mean age of 29 years, range 4–70 years, 9 children and 1 elderly. Injuries: explosion 63%, gunshot 23%.	X	X		X
Tien et al. 2009[57]	6	Entire study examined 134 patients, 96% male, mean age of 26 years. Injuries: explosion 34%, gunshot 32%, blunt 22%.		X		
Beekley et al. 2008[52]	67 casualties treated with tourniquets compared with 98 patients not treated with tourniquets	Tourniquet group: 97% male, mean age of 29 years. Injuries: explosion 64%, gunshot 30%. Nontourniquet group: 96% male, mean age of 25. Injuries: explosion 70%, gunshot 27%.	X	X		X
Dayan et al. 2008[58]	5 cases with prolonged tourniquet use	All males, 20–22 years old. Injuries: explosion=1, gunshot=4.	X	X		X
Kalish et al. 2008[50]	11 civilian extremity hemorrhages	All males, mean age of 27 years, gunshot wounds 55%, stab wounds 27%, lacerations 18%.		X		X
Kragh et al. 2008[10]	232 total casualties were included, with 194 of these having prehospital tourniquets placed.	95% male, mean age of 29 years, range 4–70 years, 9 children and 1 elderly. Injuries: explosion 63%, gunshot 23%.	X	X		X
Lakstein et al. 2003[59]	91 casualties treated with silicone and improvised tourniquets	Gender and mean age not reported. Injuries: explosion 73%, gunshot 27%.	X	X		X

Table 6. Data collection process in studies of prehospital tourniquet use

Reference	Method of Data Collection	Researcher on Site	Medics or Patients Interviewed	Instructions for Tourniquet Use
Eastridge et al. 2012[13]	Retrospective	No	No	Tactical Combat Casualty Care (TCCC) training was available halfway through the period of data collection.
King et al. 2012[54]	Prospective	No	Yes	Medics were given feedback on their performance, but the paper does not specify whether instructions were provided before the study. TCCC likely.
Kragh et al. 2012[51]	Retrospective	No	No	None stated. TCCC likely.
Kotwal et al. 2011[12]	Prospective	Yes	Yes	The entire fighting force was trained in TCCC.

Table 6. Data collection process in studies of prehospital tourniquet use (continued)

Reference	Method of Data Collection	Researcher on Site	Medics or Patients Interviewed	Instructions for Tourniquet Use
Kragh et al. 2011[49]	Prospective	Yes	Yes	All deployed U.S. service personnel get tourniquet training with instructions to apply them as soon as possible to stop potentially lethal external limb bleeding; the soldiers were taught how to use the tourniquets using a simplified form of TCCC in Prehospital Trauma Life Support.
Kragh et al. 2011[48]	Prospective	Yes	Yes	TCCC practices.
Brown et al. 2010[55]	Retrospective	No	No	Medical care by the British military includes initial care for stabilization by a medic and evacuation as necessary.
Brodie et al. 2009[56]	Retrospective	No	No	C>ABC [catastrophic hemorrhage control before airway, breathing, and circulation] to reflect the importance of rapidly controlling external hemorrhage. This concept is firmly embedded in training at all levels of provider in the early management of severe trauma.
Clasper et al. 2009[53]	Retrospective	No	No	None stated
Kragh et al. 2009[11]	Prospective	No	No	TCCC practices
Tien et al. 2009[57]	Prospective	No	No	TCCC practices
Beekley et al. 2008[52]	Retrospective	No	No	At the time of the initiation of the data collection for this study (July 2004), standardized tourniquets were just starting to be deployed into Afghanistan and Iraq, but a liberalized policy of tourniquet use—using a tourniquet as a first-line treatment for extremity hemorrhage in casualties under fire—although standard in the special operations arena, had not been widely disseminated through conventional forces.
Dayan et al. 2008[58]	Retrospective	No	No	Israeli Defense Force (IDF) protocols for tourniquet use on the battlefield: amputation of a limb, multiple-site injury, uncontrolled bleeding from a major limb vessel, multiple-casualty event, and night scenario.
Kalish et al. 2008[50]	Retrospective	No	No	None stated
Kragh et al. 2008[10]	Prospective	No	No	TCCC practices
Lakstein et al. 2003[59]	Retrospective	No	No	"Physicians and medics assigned to combat missions carry tourniquets and use them routinely, minutes after injury. In addition, IDF combat soldiers are regularly equipped with tourniquets and trained to identify extremity hemorrhage and use the tourniquets to stop the bleeding." IDF indications for tourniquet use: Failure to stop bleeding by direct pressure bandaging, injury does not allow direct control of bleeding with a bandage, or objective factors, amputation, bleeding from multiple locations.

Key Points

- No studies identified for this report provide a direct comparison of tourniquets and compression for treating trauma patients with extremity hemorrhage. In the military setting, tourniquets are considered an appropriate first response to traumatic extremity hemorrhage.
- Based on 13 studies reporting mortality data for casualties treated with tourniquets, prehospital tourniquets are an effective treatment method for the prevention of death due to exsanguination. The reported survival rates for casualties treated with prehospital tourniquets ranged from 87% to 100%.
- Based on a meta-analysis of 9 studies in military settings reporting adequate data, the survival rate for casualties treated with prehospital tourniquets was 91.9% with 95% confidence intervals of 88.1% to 94.6%.
- Based on 8 studies reporting amputation data for casualties treated with tourniquets, prehospital tourniquets appear to be effective preventing amputation. The reported amputation rates for casualties treated with prehospital tourniquets ranged from 13% to 28%.
- Based on a meta-analysis of 6 studies in military settings, the amputation rate for surviving casualties treated with prehospital tourniquets was 19.2% with 95% confidence intervals of 15.8% to 23.2%.
- Insufficient evidence was available to examine the influence of prehospital tourniquet use on hypovolemic shock.
- Based on 11 studies reporting adverse-event data for casualties treated with tourniquets, prehospital tourniquets are associated with temporary nerve palsy, fasciotomies, and wound infection.

Detailed Synthesis

Key Question 1 could not be assessed directly because no studies provided a direct comparison of prehospital tourniquet use with prehospital use of compression to treat extremity hemorrhage. The available study data were primarily drawn from military experience during the wars in Iraq and Afghanistan. At the start of those wars, prehospital use of tourniquets was not a common practice. Modern tourniquets such as the CAT were not provided to most troops until late 2005 and were not universally implemented until 2007. Thus, an analysis comparing deaths associated with extremity hemorrhage before and after widespread tourniquet use could provide indirect evidence of the effectiveness of prehospital tourniquets. This comparison was undertaken by Eastridge et al. in 2012.[13] They examined all battlefield fatalities from October 2001 to June 2011 and found 976 potentially survivable deaths, of which roughly 91% were associated with hemorrhage. Extremity hemorrhage accounted for 13.5% of the hemorrhage fatalities. According to their analysis the death rate from extremity hemorrhage was 23.3 deaths per year prior to widespread systematic tourniquet use, but decreased to 17.5 deaths per year from 2006 to 2007, and further decreased to 3.5 deaths per year after full implementation of tourniquet use and training was completed. The transition from treating extremity hemorrhage with compression to the prehospital use of tourniquets as the main treatment option was associated with an 85% reduction in extremity hemorrhage–related deaths.

Results from studies reporting mortality data are presented in Table 7. The studies are consistent in reporting 87% survival or better for casualties treated with prehospital tourniquets (see Figure 3). The study by Eastridge et al. did not provide data that could be used in the meta-analysis, and the study by Dayan et al. was a special case of five casualties with prolonged tourniquet use, so neither study was included in the pooled analysis. Meta-analysis of the nine studies reporting survival for adult military casualties treated with tourniquets demonstrated a summary effect size estimate for survival of 91.9% with 95% confidence intervals of 88.1 % to 94.6% (see Figure 4). Findings in the study of children were similar (92%, with CI 84% to 96%),[51] as were those in the study of civilian casualties (91%, CI 56% to 99%).

Table 7. Studies of prehospital tourniquets reporting data on mortality

Reference	Number of Casualties Treated	Mortality	Note About Mortality Data
Eastridge et al. 2012[13]	Number of casualties treated with a tourniquet was not reported.	976 potentially survivable (PS) deaths	The primary injury/physiologic focus of PS acute mortality was associated with hemorrhage (90.9%) and airway compromise (8.0%). For the site of lethal hemorrhage "the most substantial anatomic region of hemorrhage was truncal (67.3%), followed by junctional (19.2%) and peripheral-extremity (13.5%) hemorrhage." …"Before the introduction of tourniquets, the death rate from peripheral-extremity hemorrhage was 23.3 deaths per year, which was reduced to 17.5 deaths per year during the training and dissemination period from 2006 to 2007. After full implementation, this number was reduced to 3.5 deaths per year, an 85% decrease in mortality."
King et al. 2012[54]	54 treated with Combat Application Tourniquet/Special Operations Forces Tactical Tourniquet (CAT/SOFTT) tourniquets used	No deaths at the Forward Surgical Team (Level II)	None
Kragh et al. 2012[51]	88 pediatric casualties treated with CAT tourniquets	7	Survival rate was 93%. However 6 of the deaths did not have extremity wounds or external injury that would warrant a tourniquet.
Kotwal et al. 2011[12]	66 treated with tourniquets 394 treated with compression dressings	2 treated with tourniquets	Survival rate was 94% for casualties treated with a tourniquet. The report notes that of the fatalities including extremity hemorrhage exsanguination "none were potentially survivable through additional prehospital medical intervention." No information is reported on outcomes for casualties treated with compression dressings.
Kragh et al. 2011[49]	425 treated with tourniquets	55	Survival rate was 87% for all casualties treated with tourniquets (n=499), prehospital and emergency hospital. 10 casualties with extremity hemorrhage could not be treated with a tourniquet and died.
Brodie et al. 2009[56]	70 treated with CAT	9	Survival rate was 87%. According to the report, deaths were not related to tourniquet use but were associated with more severe injuries.

Table 7. Studies of prehospital tourniquets reporting data on mortality (continued)

Reference	Number of Casualties Treated	Mortality	Note About Mortality Data
Kragh et al. 2009[11]	232 total casualties were included, with 194 of these having prehospital tourniquets placed.	22	Survival rate was 89%.
Tien et al. 2009[57]	6	0	No deaths
Beekley et al. 2008[52]	165 were identified who had traumatic extremity amputation, major extremity vascular injury, or who had a prehospital tourniquet placed. 67 casualties treated with tourniquets compared with 98 patients not treated with tourniquets	3 tourniquets 4 non-tourniquets	3 of the 67 casualties with tourniquets died (survival rate of 96%) compared to 4 of 98 casualties without tourniquets (survival rate of 96%). The study was "biased toward those patients that survived evacuation off the battlefield to the CSH [combat support hospital]. We were unable to obtain data on casualties that died before reaching surgical care during the study time period."
Dayan et al. 2008[58]	5 cases with prolonged tourniquet use	No deaths	Special report of 5 cases with nerve damage after prolonged tourniquet use.
Kalish et al. 2008[50]	11 civilian extremity hemorrhages	1	Survival rate of 91%.
Kragh et al. 2008[10]	232 casualties with tourniquet use prehospital and in the emergency department.	18	18 deaths among 256 prehospital tourniquets used (93% survival rate). Number of prehospital casualties was not reported.
Lakstein et al. 2003[59]	91 casualties treated with silicone and improvised tourniquets	0	No deaths

Figure 3. Survival rates (short-term) in casualties treated with a prehospital tourniquet, all studies included

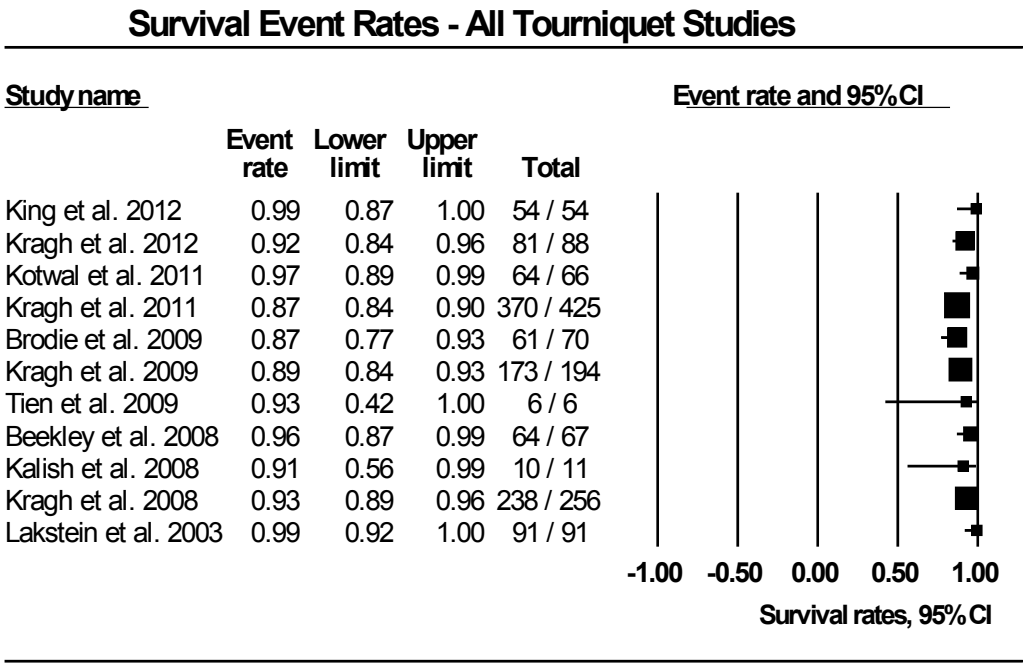
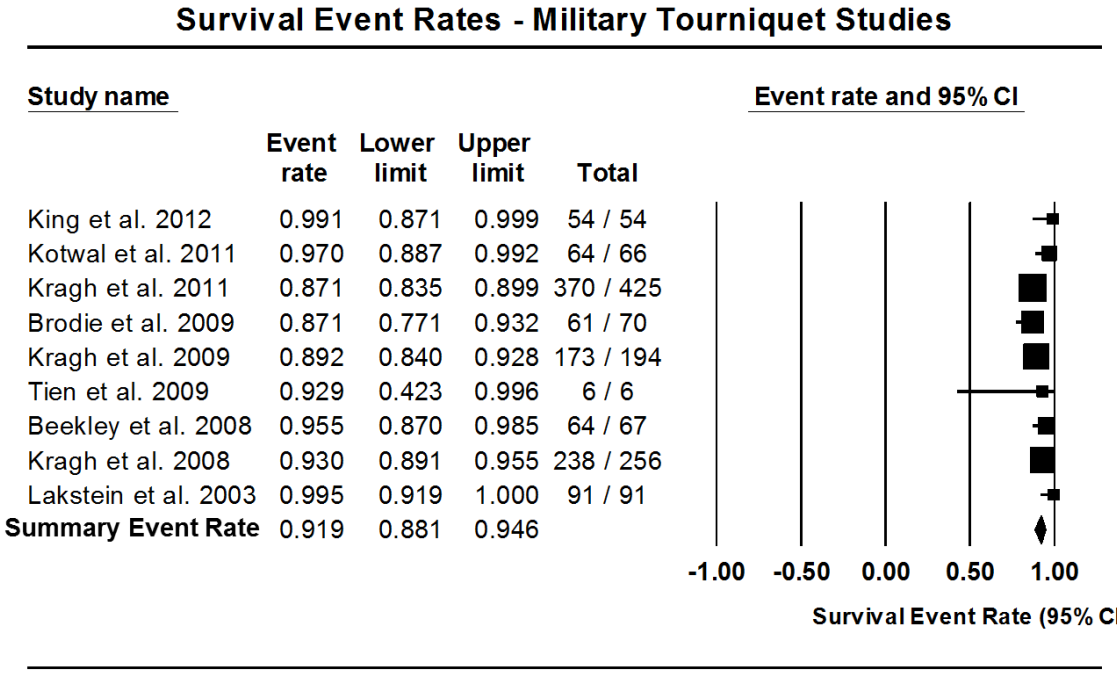


Figure 4. Survival rates (short-term) in casualties treated with a prehospital tourniquet, only military tourniquet studies included

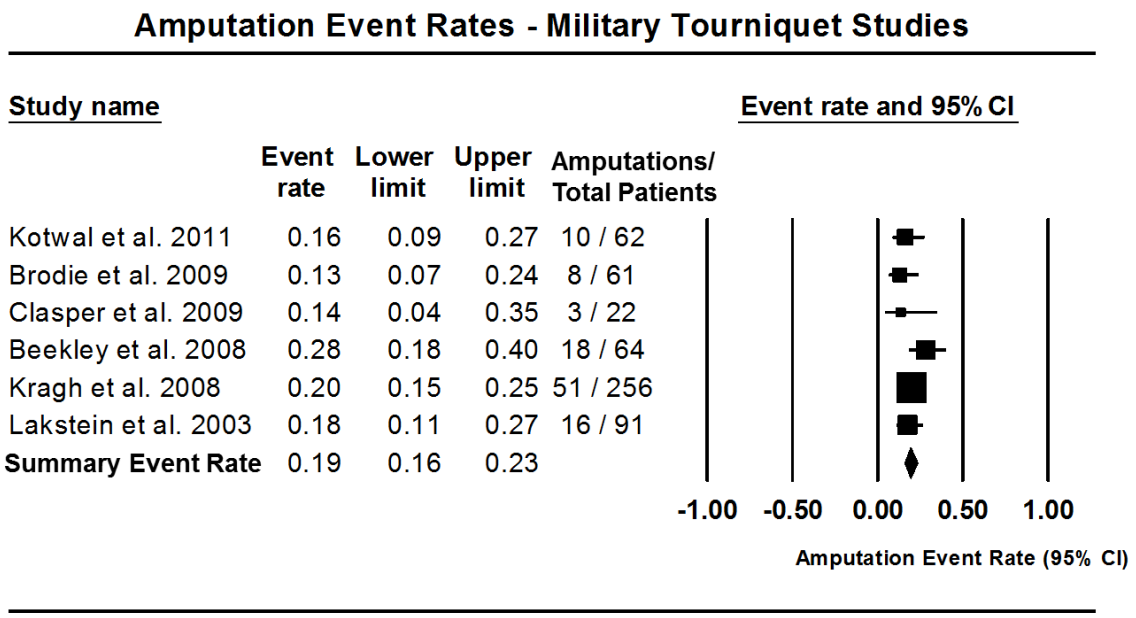


The studies providing amputation rates among casualties treated with a prehospital tourniquet reported rates of 13% to 28%. Results from studies reporting amputation data are presented in Table 8. We calculated a summary event rate estimate of 19%, with 95% confidence interval from 16% to 23% (see Figure 5). (The study by Kragh et al.[11] was not included in the analysis because the data were reported by limbs, not individual casualties.) A before-and-after analysis similar to the one performed by Eastridge et al. has not been done for amputations. Some authors have suggested that amputation rates may be higher after implementation of tourniquet use because more casualties survive the initial traumatic injury, but require limb amputations due to the severity of the injury.

Table 8. Studies of prehospital tourniquets reporting data on amputations

Reference	Number of Casualties Treated	Amputations
Kotwal et al. 2011[12]	66 casualties treated with tourniquets 394 treated with compression	10 amputations among 62 survivors. Amputation rate was 16%. No information is reported on outcomes for casualties treated with compression dressings.
Brodie et al. 2009[56]	70 treated with CAT	8 amputations among 61 survivors. Amputation rate was 13%.
Clasper et al. 2009[53]	22 casualties treated with tourniquets matched to 22 casualties not treated with tourniquets; all casualties had a fracture	3 tourniquet casualties and 3 non-tourniquet casualties. Amputation rate was 13.6%.
Kragh et al. 2009[11]	232 total casualties were included with 194 of these having prehospital tourniquets placed.	97 limbs of 307 treated with tourniquets were amputated among the 232 total casualties. Amputation rate was 32% of limbs.
Beekley et al. 2008[52]	67 treated with prehospital tourniquets 98 not treated with prehospital tourniquets	28% of tourniquet patients vs. 25% of no-tourniquet patients required debridement amputation
Dayan et al. 2008[58]	5 cases with prolonged tourniquet use	1 amputation. Amputation rate of 20%.
Kragh et al. 2008[10]	232 casualties with tourniquet use prehospital and in the emergency department. Data were reported for number of tourniquets used not per casualty.	51 amputations among 256 prehospital tourniquet uses (20% amputation rate).
Lakstein et al. 2003[59]	91 casualties treated with silicone and improvised tourniquets	16 amputations among 91 survivors. Amputation rate of 18%.

Figure 5. Amputation rates in surviving casualties treated with a prehospital tourniquet, military studies only



No studies reported data that could be used to analyze any potential connection between prehospital tourniquet use and hypovolemic shock.

Studies reporting adverse events associated with prehospital tourniquet use are listed in Table 9.

Table 9. Studies of prehospital tourniquets reporting adverse events

Reference	Number of Casualties Treated	Adverse Events
Kragh et al. 2011[49]	499	7 instances of temporary nerve palsy. 15 patients had a tourniquet applied without a medical or tactical indication. None of the limbs in the 15 patients suffered morbidity.
Kragh et al. 2011[48]	Same study as Kragh et al. 2011[49] but reporting morbidities	All patients experiencing nerve palsy at tourniquet site had prehospital use (n=8 patients). Most (82%) of the nerve palsies were in the arm. "All nerve palsies at the level of the tourniquet resolved within 3 minutes to 3 days except in one Iraqi transferred with incompletely resolved nerve palsy on the third day. Tourniquet duration was not associated with nerve palsy in that those casualties with greater than 4 hours use had none."
Brown et al. 2010[55]	23	12 infections. "The use of tourniquets to control bleeding in the field was associated with infections on univariate analysis, but this association is likely related to the severity of injury as use of tourniquet was not relevant in multivariate analysis."
Brodie et al. 2009[56]	70 treated with CAT	Two cases of compartment syndrome, one ulnar nerve palsy.

Table 9. Studies of prehospital tourniquets reporting adverse events (continued)

Reference	Number of Casualties Treated	Adverse Events
Clasper et al. 2009[53]	22 casualties treated with tourniquets matched to 22 casualties not treated with tourniquets; all casualties had a fracture	"The most common complication was superficial infection, occurring in 50% and there was no difference in the incidence between the 2 groups" [prehospital tourniquet use vs. no tourniquet use] Other types of adverse events: superficial wound infection (11 vs. 11; no difference); deep infection 7 (prehospital tourniquet) vs. 1 (no prehospital tourniquet), p <0.05; flap failure: 1 (prehospital tourniquet) vs. 0 (no tourniquet).
Kragh et al. 2009[11]	232 total casualties were included, with 194 of these having prehospital tourniquets placed.	At the time of tourniquet application in prehospital patients, shock was already present in 6 casualties, 5 of which went on to die. Of the 188 casualties (prehospital) for whom shock was not present at tourniquet application, 17 went on to die. 10 nerve palsies occurred (only combined data reported).
Beekley et al. 2008[52]	67 casualties treated with tourniquets compared with 98 patients not treated with tourniquets	"We encountered no significant adverse sequelae related to prehospital tourniquet use. The absence of neurological complications in our dataset may be related to the relatively short prehospital tourniquet times documented (mean, 70 minutes)."
Dayan et al. 2008[58]	5 cases with prolonged tourniquet use	1 nerve palsy (in patients with >20 hours tourniquet duration)
Kalish et al. 2008[50]	11 civilian extremity hemorrhages	2 patients underwent fasciotomies, which both closed prior to hospital discharge.
Kragh et al. 2008[10]	232 casualties with tourniquet use prehospital and in the emergency department. Data were reported for number of tourniquets used, not per casualty.	"Tourniquet duration may have increased risk of only two morbidities, amputation and fasciotomy." Of prehospital tourniquet uses, 139 morbidities were reported, including 49 fasciotomies, 51 amputations, 18 deaths, 9 palsies, 6 clots, 3 myonecroses, 2 acute renal failure, 1 rigor.
Lakstein et al. 2003[59]	91 casualties treated with silicone and improvised tourniquets	Neurologic complications were recorded in 7 limbs of 5 patients. "Ischemic time for these cases ranged between 109 and 187 min."

Strength of Evidence

The risk of bias associated with these studies was rated high because they are all single-arm studies with no comparison group (observational case series studies). The true effect of prehospital tourniquet use is likely combined with the effects of training and other medical interventions intended to improve prehospital care. Consequently, it is difficult to estimate the comparative effectiveness of prehospital tourniquets and compression dressings. However, it seems unlikely that the entire reduction in mortality seen after implementation of routine initial application of tourniquets should be attributed to confounding factors. Furthermore, our experts with military experience noted that initial use of tourniquets also provides practical advantages over manual compression in battlefield settings, freeing up medics to tend to other injuries or individuals.

The overall strength of evidence for Key Question 1 was assessed using the GRADE system.[40,41,60,61] These evidence grades appear in Table 10. In the GRADE system observational studies begin with an initial grade of low which may then be modified based on other factors.

Based on particular study characteristics, this rating can then be adjusted either down (depending on study limitations, consistency, directness, precision, and publications bias) or up (based on magnitude of effect, dose response, confounders). All studies in the evidence base lacked comparison groups; consequently, we downgraded by one point for study limitations.[61] Directness refers to the applicability of the study population to the population of interest. The evidence base for this question consisted primarily of injured military personnel treated with tourniquets which may not predict the effectiveness in civilian populations and settings. We considered downgrading one point for indirectness, but decided against it given the similar results seen in the one study of civilians and the one study in children.[60] The evidence base for survival was upgraded by two points for a large magnitude of effect.[62] Eastridge et al. 2012 estimated a 7-fold improvement in survival based on their estimate of 23.5 deaths per year from peripheral extremity hemorrhage prior to routine use of tourniquets in the field (2001 to 2005) and 3.5 deaths per year after full implementation (after 2007).[13] Although it is likely that confounding factors account for some of this improvement, we decided that the likelihood that tourniquets account for a large portion of the improvement warranted a two-point upgrade. After making these adjustments, the evidence base for survival was rated Moderate and for amputations was rated Very Low.

Table 10. Key Question 1: Strength of evidence grades for survival rate and amputation rate with prehospital tourniquet use

Outcome	# Studies (Total N)	Type of Studies	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome
					Study Limitations	Consistency	Directness	Precision	Publication Bias	Large Magnitude of Effect	Dose-Response	Confounders	
Survival rate	9 studies of military personnel (1,229)	Observational	91.9% (95% confidence interval [CI]: 88.1% to 94.6%)	Low	-1 Absence of comparison group	0	0	0	0	+2 (7-fold improvement over historical military data)	0	0	Moderate
Amputation rate	6 (556)	Observational	19.2% (95% CI: 15.8% to 23.2%)	Low	-1 Absence of comparison group	0	0	0	0	0	0	0	Very Low

Applicability

The studies that address Key Question 1 provide data primarily on the battlefield use of tourniquets for extremity hemorrhage. The outcomes reported in the military studies, primarily death and amputation, are likewise important in a civilian setting. The tourniquets used by the military have also been used in civilian settings, so applicability is not compromised by the types of devices used. However significant differences may exist with regard to the training of military versus EMS providers, the health of military versus civilian patients, and the nature of injuries sustained. Furthermore, because access to individual attention and hospital-based care is likely more rapid in civilian settings, the incremental benefits of pre-hospital tourniquet use over compression may be less than the benefits seen in a military context. In mass casualty events, as in combat situations, compression may be impractical, and the injured individual may need to self-apply a tourniquet. Under those circumstances, the available evidence may be more directly applicable.

Only a single study, Kalish et al.,[50] reported on the use of tourniquets in a civilian setting. The authors describe only 11 patients, all males with a mean age of 29 years and primarily with gunshot wounds. The evidence from the military's experience with gunshot wounds may be particularlyapplicable to civilian experience. However, military studies often do not separate results for gunshot wounds and explosive devices, potentially limiting extrapolation to civilian use.

In an analysis of the National Trauma Databank from 2002 to 2005, Kauvar et al. categorized lower limb injuries as due to penetrating (66%) or blunt trauma (34%). The patients ranged from 2 to 86 years of age with a mean age of 30.6 years (median of 27 years) with males accounting for 85% of the patients. Among 651 individuals with lower extremity arterial injury (common femoral, superficial femoral, popliteal and tibial) they calculated a mortality rate of 2.8% and amputation rate of 6.5%.[4] While these lower rates may reflect differences in the severity of injuries seen in civilian versus military settings, they may also reflect the fact that the data come from specialized trauma centers in the U.S.

A smaller study of patients dying from isolated extremity injuries at two hospitals in the Houston area was reported by Dorlac et al.[5] The 14 patients this study died from penetrating extremity injury primarily involving a major artery. The patients were 93% male, with an average age of 31 years, and in half the cases, had been injured by gunshot wounds. Eastridge et al.[13] reported that 22% of the fatalities from the wars in Iraq and Afghanistan were due to gunshot wounds and half of all fatalities (when excluding instantaneous deaths) occurred before the patient reached a medical treatment facility. Only 12.7% of casualties died after reaching a medical treatment facility. Soldiers treated with tourniquets were predominately males with an average age between 25 and 29 years.[11,12,49,52,53] Therefore, the evidence from military studies can be extrapolated to at least a subset of civilian patients (young males). Additional data on the benefits and harms of tourniquets in younger and older patients, especially those with peripheral vascular disease would be a valuable addition to the current evidence base.

Key Question 2: Junctional Tourniquets Compared With External Pressure

Key Question 2: In trauma patients with junctional hemorrhage who are treated in the prehospital setting by EMS personnel, what is the effect of specialized junctional tourniquet use with or without external wound pressure on limb salvage, hypovolemic shock, survival, and

adverse effects compared with external pressure alone or with other nonjunctional tourniquet interventions?

Description of Included Studies

We identified no clinical studies that addressed this question. The only studies of junctional tourniquets involved human volunteers and did not report outcomes considered in this report. The studies are described in the section on indirect evidence.

Key Question 3: Tourniquets Compared With Other Tourniquets

Key Question 3: In trauma patients with extremity hemorrhage (excludes junctional hemorrhage) who are treated in the prehospital setting by EMS personnel, do different brands or models of tourniquets differ from each other in their effect on limb salvage, hypovolemic shock, survival, and adverse effects?

Description of Included Studies

We identified no studies that addressed this question. We did identify studies comparing different types of tourniquets in healthy volunteers. Those studies are discussed later in the section on indirect evidence.

Key Question 4: Junctional Tourniquets Compared With Other Junctional Tourniquets

Key Question 4: In trauma patients with junctional hemorrhage who are treated in the prehospital setting by EMS personnel, do different brands or models of specialized junctional tourniquets differ from each other in their effect on limb salvage, hypovolemic shock, survival, and adverse effects?

Description of Included Studies

We identified no clinical studies that addressed this question. We did identify studies using anatomic pelvic simulation models to examine the Pelvic C-Clamp (two studies) and the Combat Ready Clamp (one study). These studies are described in the section on indirect evidence.

Key Question 5: Tourniquets and Duration of Use

Key Question 5: In trauma patients with external hemorrhage (excludes junctional hemorrhage) who are treated in the prehospital setting by EMS personnel using a tourniquet—

a. Does the incidence of adverse events vary by the duration of tourniquet use prior to removal?
b. Does the incidence of adverse events vary depending on whether tourniquets are removed in the field versus in a facility?

We identified four studies that correlated duration of tourniquet use with adverse events: Beekley et al.,[52] Dayan et al.,[58] Kragh et al.,[10] and Lakstein et al.[59] These studies are mentioned under adverse events for Key Question 1. Adverse events were not reported according to timing or setting of tourniquet removal.

Strength of Evidence

The overall strength of evidence for Key Question 5 was assessed using the GRADE system.[40-42] The results of the process appear in Table 11.

Table 11. Key Question 5: Strength of evidence grades for adverse events with prehospital tourniquet use

Outcome	# Studies (Total N)	Type of Studies	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome
					Study Limitations	Consistency	Directness	Precision	Publication Bias	Large Magnitude of Effect	Dose-Response	Confounders	
Nerve palsy, fasciotomies, and wound infection	11 (1,328)	Observational	The large majority of adverse events were temporary	Low	-1 (lack of comparison groups, making it difficult to determine causality)	0	0	0	0	0	0	0	Very low

Key Question 6: Hemostatic Dressings Compared With External Pressure

Key Question 6: In trauma patients with external hemorrhage (hemorrhage from any body surface) who are treated in the prehospital setting by EMS personnel, what is the effect of hemostatic dressings with or without external wound pressure on limb salvage (if an extremity involved), hypovolemic shock, survival, and adverse effects compared with using non-hemostatic gauze with or without external wound pressure?

Description of Included Studies

Our searches identified seven studies that examined the prehospital use of hemostatic dressings to control external hemorrhage (see Table 12). Five of the studies were conducted in a military setting. One study was in a civilian setting and one study gathered both military and civilian data. Only one study reported deaths as an outcome, and four studies reported the incidence of adverse events (see Table 13). Products examined in these studies included HemCon (3 studies), Celox (1 study), QuikClot granules (2 studies), and QuikClot Combat Gauze (1 study). One study did not collect information on which hemostatic dressings were used. Information on the data collection procedures is presented in Table 14.

Table 12. List of included studies of prehospital hemostatic dressing use

Reference	Setting	Registry or Hospital	Period of Data Collection
Brown et al. 2009[63]	U.S. civilian	Tualatin Valley Fire & Rescue, Aloha, OR	June 2006 to Aug 2006
Cox et al. 2009[64]	U.S. military Iraq	U.S. military medical facilities in Afghanistan	April 2006 to Oct 2006
Lairet et al. 2012[44]	U.S. military Afghanistan	Level III combat support hospital	Nov 2009 to Nov 2011
Pozza and Millner, 2010[65]	U.S. military Afghanistan	U.S. Role 2 (Enhanced Care) facility	April 2008 to October 2008
Ran et al. 2010[66]	Israel military	Israel Defense Force's Medical Corps	2009
Rhee et al. 2008[67]	U.S. civilian and U.S. military Iraq	Summary of QuikClot uses submitted to the authors by military and civilian users	Not specified, but study was completed in 2006
Wedmore et al. 2006[68]	U.S. military Iraq/Afghanistan	None	2003 to 2004

Table 13. Outcomes reported in studies of prehospital hemostatic dressings

Reference	Number of Casualties Treated	Patient Characteristics	Amputations	Survival	Shock	Adverse Events
Brown et al. 2009[63]	HemCon n=34	53% extremity wounds, 68% male, mean age of 51.5 years, range of 16–91 years.				X
Cox et al. 2009[64]	HemCon n=5, QuikClot granules n=3	7 of 8 extremity wounds, other data not reported				X

Table 13. Outcomes reported in studies of prehospital hemostatic dressings (continued)

Reference	Number of Casualties Treated	Patient Characteristics	Amputations	Survival	Shock	Adverse Events
Lairet et al. 2012[44]	Unspecified hemostatic dressings n=23, Compression n=371	For all 1,003 patients in the study, the mechanism of injury was explosion 60%, penetrating 24%, blunt 15%. 97% male, mean age of 25 years		X		
Pozza and Millner 2010[65]	Celox = 21	All gunshot wounds. All male between ages of 18 and 45 years.				X
Ran et al. 2010[66]	QuikClot Combat Gauze n=14	Injuries: blast=7, gunshot=6, stab=1. Other data not reported.				X
Rhee et al. 2008[67]	QuikClot granules n=103 (69 treated by U.S. military personnel, 20 treated by civilian trauma surgeons, 14 treated by civilian first responders)	Injuries for all patients: explosion 21%, gunshot 66%, blunt 8%, stab wound 5%.				X
Wedmore et al. 2006[68]	HemCon n=64	55% extremity wounds; bleeding was predominantly from a venous source in 33 cases, arterial source in 7 cases, and unknown in 24 cases.				X

Table 14. Data collection process in studies of prehospital hemostatic dressing use

Reference	Method of Data Collection / Comments About Data Collection	Researcher on Site	Medics or Patients Interviewed	Instructions for Dressing Use
Brown et al. 2009[63]	Prospective	Yes	Yes	"The initial approach to most external hemorrhage (lacerations, abrasions, puncture wounds) was application of manual pressure with a gauze bandage and elevation of the bleeding area if possible. This is the approach that is traditionally taught to EMS providers and it was not altered for the purpose of the study. If the gauze bandage soaked through with blood, it was to be removed and the HemCon Bandage applied as directed."
Cox et al. 2009[64]	Retrospective "Data collection in the prehospital military environment is notoriously difficult, and in this series the ongoing combat operations posed severe limitations to data collection and follow-up."	No	No	Tactical Combat Casualty Care (TCCC)

Table 14. Data collection process in studies of prehospital hemostatic dressing use (continued)

Reference	Method of Data Collection / Comments About Data Collection	Researcher on Site	Medics or Patients Interviewed	Instructions for Dressing Use
Lairet et al. 2012[44]	Prospective "The primary limitation is that the study was a convenience sample. This was not a consecutive enrollment study because of the challenges of performing this study in a combat zone. Also, given the lack of comprehensive prehospital medical record data for the Theater of Operations, we cannot confirm the true denominator of our population—those dying before arrival at our study facilities, or who were transported."	No	No	TCCC
Pozza and Millner 2010[65]	Prospective	Yes	Yes	Celox was used when hemostasis was not achieved with compression using standard pressure bandage. Celox granules were applied with a syringe. 15 soldiers were also treated with tourniquets. The tourniquets could be removed after bleeding was controlled with Celox.
Ran et al. 2010[66]	Prospective	No	No	QuikClot Combat Gauze was used after direct pressure to a central wound or a tourniquet applied to an extremity wound had failed to stop bleeding.
Rhee et al. 2008[67]	Prospective Data were collected through a survey or through direct contact with users.	No	Yes	"The current instruction for use in the combat battlefield is for external source of hemorrhage that is life threatening and uncontrolled by all other means. After ineffectiveness of these measures, Quik-Clot was to be used."
Wedmore et al. 2006[68]	Retrospective Two U.S. Army emergency physicians collected and reviewed cases. Data were collected and based on verbal and written accounts of HemCon dressing use.	No	A survey was sent to forward deployed medical personnel who initially received HemCon dressings. The survey asked if the HemCon dressing was effective in hemorrhage control.	Providers were instructed to utilize the dressings in cases in which other standard techniques had failed or if they thought there was a high likelihood of failure with standard techniques. 35 of 64 (55%) were applied to wounds located on patient extremities, 25 of 64 (39%) were applied to wounds located on the chest, groin, buttocks, and abdomen. No cavity wounds.

Key Points

- No studies identified for this report provided a direct comparison of hemostatic dressings with or without external wound pressure to non-hemostatic gauze with or without external wound pressure for the prehospital treatment of trauma patients with extremity hemorrhage.
- Only one study, Lairet et al.,[44] reported on survival in patients treated with hemostatic dressings (Table 15). While the study reported that hemostatic dressings were life-saving, it did not specify what dressings were used.
- The primary outcome reported in five studies was the ability of the hemostatic dressings to stop bleeding.
- Most studies reported no complications or adverse events (Table 16). However, QuikClot granules were associated with pain and discomfort from the exothermic reaction.

The study by Brown et al.[63] reported that HemCon controlled external hemorrhage in 27 of 34 cases (79%); in 25 cases the bleeding stopped within 3 minutes of application.

The study by Cox et al.[64] was confounded because seven of the eight patients treated with hemostatic dressings in the field were also treated with a tourniquet.

The study by Pozza and Millner[65] reported that Celox stopped bleeding in 18 gunshot wounds when first applied and in 3 additional cases with further application.

The study by Ran et al.[66] reported that QuikClot Combat Gauze successfully stopped bleeding in 11 out of 14 cases of extremity and truncal hemorrhage.

The study by Rhee et al.[67] reported that QuikClot granules were 100% effective in stopping bleeding.

In the study by Wedmore et al.,[68] medics were surveyed on their use of HemCon dressing. In 42 of the 64 cases, the dressings were used when traditional gauze dressings or pressure dressings failed to stop bleeding. In 62 of the 64 cases, HemCon successfully stopped the bleeding.

Table 15. Study of prehospital hemostatic dressing use reporting survival

Reference	Number of Casualties Treated	Deaths
Lairet et al. 2012[44]	Hemostatic dressing n=23 Non-hemostatic dressing n=371	A treating physician reported that the hemostatic dressing was lifesaving in 13 of 23 casualties (survival rate of 57%). Similar data were not reported for casualties treated with non-hemostatic dressings.

Table 16. Studies of prehospital hemostatic dressing use reporting adverse events

Reference	Number of Casualties Treated	Adverse Events
Brown et al. 2009[63]	HemCon n=34	No complications or adverse events were reported.
Cox et al. 2009[64]	HemCon n=5, QuikClot granules n=3	Among all patients treated prehospital and in-hospital, 2 of the 4 patients treated with QuikClot had burns from exothermic reactions. No adverse reactions were noted for HemCon.
Pozza and Millner 2010[65]	Celox = 21	No pain or changes to the surrounding tissue were reported.

Table 16. Studies of prehospital hemostatic dressing use reporting adverse events (continued)

Reference	Number of Casualties Treated	Adverse Events
Ran et al. 2010[66]	QuikClot Combat Gauze n=14	No complications or adverse events were reported.
Rhee et al. 2008[67]	QuikClot granules n=52	Field medics and corpsmen reported that about 25% of their uses resulted in concomitant mild to severe pain and discomfort due to the exothermic reaction from QuikClot granules. None of the medics or corpsmen thought that QuikClot caused additional injury.
Wedmore et al. 2006[68]	HemCon n=64	No adverse effects or complications were noted in the answer to the survey.

Strength of Evidence

The risk of bias associated with these studies is high because they are all single-arm studies with no comparison group. Sufficient data were not available to provide an estimate of survival rates or amputation rates in patients treated with hemostatic dressings. The overall strength of evidence for Key Question 6 was assessed using the GRADE system.[40-42] The results are reported in Table 17. Because all studies lacked comparison groups, we downgraded by one point for study limitations[61] and assessed the strength of the evidence as Very Low.

Table 17. Key Question 6: Strength of evidence grades for survival and amputations with prehospital hemostatic dressing use

Outcome	# Studies (Total N)	Type of Studies	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome
					Study Limitations	Consistency	Directness	Precision	Publication Bias	Large Magnitude of Effect	Dose-response	Confounders	
Survival rates	1 (23)	Observational	13 survivors (57%)	Low	-1 (incomplete reporting on comparison group)	0	0	0	0	0	0	0	Very Low
Amputation rates	0	0	—	—	—								—
Adverse events	6 (179)	Observational	QuikClot granules were associated with burns and pain. No other adverse events were reported.	Low	-1 (lack of comparison group)	0	0	0	0	0	0	0	Very Low

Applicability

The studies that address Key Question 6, like those for Key Question 1, provide data primarily on the battlefield use of hemostatic dressings. The applicability of these military studies to civilian needs may be tempered by the difference in settings. The primary outcome reported was bleeding control, which is likewise important in the civilian setting. Also, the particular hemostatic dressings used by the military are also available for civilian use; in these ways, the applicability of results from these military studies to the civilian context appears high.

The military's experience with hemostatic dressings may be most generalizable to the civilian context when the injuries are caused by gunshot wounds. However, many studies did not report separate outcomes for different mechanisms of injury. Notably, one study performed in civilians by Brown et al.[63] examined 34 patients, primarily male, with a wide range of ages (16–91 years). This study was unique in reporting individual patient data, allowing for better extrapolation to variable civilian settings and mechanisms of injuries.

Key Question 7: Hemostatic Dressings Compared With Other Hemostatic Dressings

Key Question 7: In trauma patients with external hemorrhage (hemorrhage from any body surface) who are treated in the prehospital setting by EMS personnel, do different brands or types of hemostatic dressings differ from each other in their effect on limb salvage (if an extremity involved), hypovolemic shock, survival, and adverse effects?

Description of Included Studies

Our searches identified no studies that directly compared hemostatic dressings for prehospital control of external hemorrhage. We did identify animal studies in which different dressing types were compared; these are described in the section on indirect evidence.

Ongoing Clinical Trials

Our search of ClinicalTrials.gov identified no ongoing or planned clinical trials involving prehospital use of tourniquets or hemostatic dressings.

Indirect Evidence: Animal Model Studies

The U.S. Military has made extensive use of animal models, especially the swine hemorrhage model, to test the effectiveness of hemostatic dressings to control severe extremity bleeding.[33] The first studies were performed by Alam and coworkers to identify an agent for immediate use by the U.S. Military and published in 2003 and 2004.[69,70] The model had to be clinically relevant to the types of traumatic lethal extremity hemorrhage that occurred in combat in Iraq and Afghanistan and provide a sufficiently rigorous test of hemostasis and survival. Alam et al. used a complex groin injury in swine involving complete division of the femoral artery and vein and free bleeding for 3 or 5 minutes before the test dressings were applied. Both studies compared QuikClot granules and TraumaDex with standard gauze; one study also examined HemCon and Fast Act. Both experiments concluded that QuikClot granules demonstrated the best hemorrhage control and mortality reduction in this model.

Since these original studies were published, several different approaches have been used in the swine hemorrhage model to test hemostatic dressings. Differences in whether or not the spleen was removed, how the injury was induced, the amount of free bleeding time, how the dressings were applied, whether or not fluid replacement was used, and the length of time and amount of manual pressure to be applied have been reported in various studies.[33] Because these differences make cross-study comparisons difficult, the U.S. Army Institute of Surgical Research (ISR) proposed a standard swine hemorrhage model in 2011.[33] This model uses Yorkshire cross-bred, castrated male pigs weighing 34 kg to 44 kg, a 6 mm punch hole in the femoral artery to produce severe bleeding, 45 seconds of free bleeding, a single use of QuikClot Combat Gauze as a comparison dressing, and 3 minutes of manual compression. The animals are observed for 150 minutes from time of injury. Surgeons are blinded to the test dressing and dressing application should be according to manufacturer's instructions. Using this model, the hemostasis rate (defined as cessation of bleeding during an observation period after release of manual compression) and survival rate are 33% when using QuikClot Combat Gauze. Table 18 provides a summary of the recommended steps for the surgical procedures, wound treatment, and resuscitation steps in the severe hemorrhage swine model proposed by ISR.

Table 18. U.S. Army Institute of Surgical Research Recommendations for Surgical Procedures, Wound Treatment, and Resuscitation for Severe Extremity Hemorrhage Swine Model[33]

Surgical Procedures
1. Animal is induced with an injection of tiletamine-zolazepam or ketamine and anesthetized with isoflurane in oxygen via a face mask.
2. Cannulate the right carotid artery for blood withdrawal and to measure blood pressure.
3. Catheterize the right jugular vein for fluid administration.
4. Grossly examine internal organs through a midline laparotomy, perform a cystostomy, and place a Foley catheter for urine collection then close the abdomen.
5. Make a 10 cm incision in the groin area parallel and close to the femoral artery. Expose the artery and dissect 5 cm free from the surrounding tissue. Avoid damage to the femoral nerve and vein.
6. If measuring wound temperature when testing dressings with potential exothermic properties suture a microelectrode to the adjacent muscle at least 1 inch away from the artery.
7. Bathe the artery with a few milliliters of 2% lidocaine to prevent vasospasm and to dilate the artery to its normal diameter.
8. Discontinue fluid maintenance and allow a 5–10 minute stabilization period to establish a mean arterial blood pressure (MAP) of 60 mm Hg or higher.
9. Collect preinjury/baseline blood samples.
10. Clamp the artery proximally and distally. Make a 6 mm-diameter arteriotomy on the anterior surface of the vessel using a 6 mm vascular punch.
11. Release the clamps and allow free bleeding for 45 seconds. Collect shed blood by suction; weigh and record as pretreatment blood loss.
Wound Treatment
1. During bleeding, open the test dressing package and apply when the free bleeding period has ended. The application should be complete in 1 minute.
2. Cover the dressing material with a folded laparotomy sponge or equivalent gauze and manually press for 3 minutes with sufficient pressure to occlude the artery and stop bleeding.
3. Pull the skin flaps over the sponge or gauze without clamping or applying additional pressure.
4. After the 3 minutes of manual compression slowly remove the pressure and observe bleeding for 3 minutes without disturbing the dressing. If no bleeding occurs during this period then initial hemostasis has been achieved.
5. If bleeding occurs after compression release or at any time during the observation period collect the shed blood by suction and weigh. Record the time when bleeding stops.
Resuscitation
1. Start fluid resuscitation after the 3 minute manual compression is completed. Infuse 500 mL of Hextend via the jugular vein at 33 mL/minute for about 15 minutes to raise and maintain MAP (mean arterial pressure) at 60 to 65 mmHg. Maintain MAP with infusion of lactated Ringers solution to a maximum of 10 L.
2. Observe the animal for 150 minutes or until death (MAP under 15 mm Hg and end tidal Pco_2 under 10 mm Hg for at least 2 minutes)
3. If available, use computed tomography to scan surviving animals for images of arterial blood flow.
4. Flex and stretch the treated leg 5 times to simulate walking to test the stability of the hemostasis.
5. Remove the hemostatic dressing and observe the clot.
6. Euthanize the animal with an intravenous injection of euthanasia solution.
7. Collect tissue samples for histology. Tissue examination should be blinded to treatment.

Key Points

- The severe extremity hemorrhage swine model has been used to test the hemostatic and survival properties of numerous hemostatic dressings but the studies are inconsistent in the duration of free bleeding time and manual compression, timing of fluid resuscitation and maintenance of blood pressure, length of observation period for assessing hemostasis and survival, and use of standard gauze dressing.

- QuikClot Combat Gauze, Celox, and HemCon were the most studied hemostatic dressings in the animal model studies.
- Analysis of 30- to 45-second free-bleeding studies of QuikClot Combat Gauze, Celox, and HemCon hemostatic dressing indicated that none of these dressings were significantly superior to standard gauze for survival rate.
- Given the wide variation in definitions and inconsistency of the hemostasis rates seen across studies, the animal model evidence base does not provide a reliable assessment of how these dressing might perform in clinical situations involving peripheral hemorrhage.

Selection of Animal Studies

Animal studies were identified in the original searches for this evidence report as described in Appendix A. We included only studies comparing FDA-cleared or approved hemostatic dressings with standard gauze or another cleared or approved hemostatic dressing in a swine or goat model of extremity bleeding. We excluded liver or other internal organ injury models.

Our searches identified 61 publications of potentially relevant animal model studies. Twenty-two were excluded for various reasons (see Table B-3 in Appendix B). The 38 included animal model studies were organized into four tables (in Appendix C) according to the duration of free bleeding time: 5 seconds or less (4 studies), 30 to 45 seconds (19 studies), 1 to 2 minutes (11 studies), and 3 or more minutes (5 studies). A single study examined the use of a locally applied clamp.[35] The animal model used was a pig unless noted in the table under the methods columns.

Most studies evaluated more than one type of hemostatic dressing, randomly allocated dressings to each animal, and blinded the person applying the dressings to the type of dressing. Two products that are no longer recommended for use by the military, QuikClot granules and WoundStat, were used as comparators in several studies of products that are still in current use.

Description of studies using 30-45 seconds of free bleeding time

QuikClot Combat Gauze, Celox, and HemCon were the most studied hemostatic dressings in the animal model studies. Hemostasis rates were reported in the majority of studies, but the protocols for determining hemostasis varied widely (e.g., whether compression was applied and if so, for how long; timing of fluid resuscitation; duration of observation for hemostasis).

Data on hemostasis and survival after 30 or 45 seconds of free bleeding (as recommended by the ISR) were selected from studies of these dressings for further analysis.

QuikClot Combat Gauze was examined in three studies;[71-73] in one of these it was compared to standard gauze.[73] Hemostasis rates were 30% in two studies[71,73] and 57% in one study.[72] (One form of Combat Gause, QuikClot Combat Gauze XL, had a hemostasis rate of 80%.[71] Survival rates ranged from 60% to 100%.

HemCon was examined in 9 studies that reported data on hemostasis,[71-79] and in an additional study that reported survival only.[80] Both the hemostasis rates and survival rates varied across studies despite using the same animal model. Six of the studies reported a hemostasis rate less than 50%[73,75-79] and three of the studies reported a hemostasis rate greater than 50%.[71,72,74] The same was true for the survival rates. Five studies reported survival rates less than 50%[73-75,78,79] and five studies[71,72,76,77,80] reported rates greater than 50%. HemCon was compared to other hemostatic dressings and to standard gauze in six studies.[73,75-77,79,80] Comparators included QuikClot Combat Gauze in three studies.[71-73]

Five studies examined Celox.[71,73-75,80] Three studies included a comparison to standard gauze,[73,75,80] three included HemCon as a comparator[71,74,80] and two included QuikClot Combat

Gauze as a comparator.[71,73] Hemostasis rates and survival rates were inconsistent across studies for all comparisons.

Neither QuikClot Combat Gauze, Celox, nor HemCon was significantly superior to standard gauze for survival. Tables of these studies are provided in Appendix C.

Strength of Evidence

For the purposes of determining the strength of evidence only the 11 studies of QuikClot Combat Gauze, HemCon, and Colex comparing these dressings to standard gauze and reported survival data were assessed. In the GRADE system randomized controlled studies start with an initial high quality of evidence grade which may then be modified based on factors than can lead to rating the quality of evidence down (study limitations, consistency, directness, precision, and publications bias) or up (magnitude of effect, dose response, confounders). We downgraded by 2 points for indirectness of the study populations (pigs vs. humans). In addition, we downgraded the animal studies by one point for publication bias, given that negative animal studies are even more unlikely to be submitted for publication or to be published if they are submitted.[81] We also downgraded the evidence comparing Celox gauze to standard nonhemostatic gauze for significant inconsistency. The evidence could also be downgraded for imprecision, given the small size of the studies and the width of the confidence intervals. The overall strength of evidence for each comparison for the outcome of survival was assessed as Very Low using the GRADE system.[40,41,60,61]

Table 19. Strength of evidence – Animal studies using recommended free bleeding time (30-45 seconds) in comparison to standard gauze

Outcome	# Studies (Total N)	Type of Studies	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome
					Study limitations	Consistency	Directness	Precision	Publication Bias	Large Magnitude of Effect	Dose-response	Confounders	
Survival: QuikClot Combat Gauze vs. standard gauze	1 study (n=16)	Randomized controlled study	Odds ratio: 8.0 (95% CI of 0.80 to 79.7, p=0.08)	High	0	0	-2	0	-1	0	0	0	Very Low
Survival: HemCon vs. standard gauze	7 studies (n=115)	Randomized controlled study	Odds ratio: 0.86 (95% CI of 0.16 to 4.67, p=0.86)	High	0	0	-2	0	-1	0	0	0	Very Low
Survival: Celox vs. standard gauze	3 studies (n=40)	Randomized controlled study	Odds ratio: 6.98 (95% CI of 0.16 to 310.96, p=0.32)	High	0	-1	-2	0	-1	0	0	0	Very Low

Description of studies using shorter or longer free-bleeding times

Studies using 5 seconds or less free bleeding time

The studies using this short duration of free bleeding time are described in a table and additional text in Appendix C. Of note, Satterly et al.[82] reported that hemostasis rates were 20% higher when applied by military personnel compared with nonmedical personnel; this increase was statistically significant. Military personnel also rated QuikClot Combat Gauze easier to use than HemCon.

The other study using trained military personnel examined various versions of HemCon and reported the best results with the double-sided bandage; hemostasis with this dressing was 76% at 4 minutes and was significantly better than standard gauze.[83] Military personnel preferred the double-sided HemCon bandage over the one-sided dressing and the powder form.

Wright et al.[84] specifically looked at tissue damage and wound healing when using QuikClot granules. Extensive tissue burns, necrosis, and impaired wound healing were noted in animals treated with QuikClot granules.

Studies using 1 or 2 minutes of free bleeding time

QuikClot Combat Gauze was examined in three studies with good results for hemostasis and survival.[85-87] Two of these studies, examining differing outcomes, reported that Combat Gauze was significantly better than standard gauze:

- Gegel et al.[85] reported that QuikClot Combat Gauze was significantly better than standard gauze at controlling blood loss and preventing further bleeding when the limb was vigorously moved.
- Causey et al.[86] reported that hemostasis using QuikClot Combat Gauze was significantly better than standard gauze when used in conditions of severe acidosis and coagulopathy.

Studies comparing hemostatic dressings did not find significant differences. All of the studies are described in additional text and a table in Appendix C.

Studies using 3 or more minutes of free bleeding

QuikClot granules and QuikClot ACS ("bagged QuikClot) were compared to various hemostatic agents and standard gauze in all five studies using 3 or more minutes of free bleeding.[69,70,88-90] In these studies of severe bleeding, QuikClot was effective at promoting hemostasis and survival. However, these QuikClot products significantly raised wound temperature. All of the studies are described in additional text and a table in Appendix C.

Indirect Evidence: Volunteer and Simulation Studies

The U.S. Military has also made extensive use of volunteer and simulation studies to test the effectiveness, reliability, and ease of use of tourniquets and abdominal clamps. These studies typically examine the ability of the tourniquet to halt blood flow to the extremities of volunteers (usually measured by Doppler ultrasound) and how much training is necessary to easily place and operate the devices. The abdominal clamps are used on specially designed pelvic models to provide training and test ease of use. Our searches identified nine studies using human volunteers to test the following devices: the Combat Application Tourniquet (CAT) (4 studies), the Emergency and Military Tourniquet (EMT) (3 studies), the Stretch, Wrap, and Tuck Tourniquet (2 studies), the Self Applied Tourniquet System (2 studies), the One-Handed Tourniquet (2 studies), the Abdominal Aortic Tourniquet (1 study), the Mechanical Advantage Tourniquet (one study), the Special Operations Forces Tactical Tourniquet (1 study), the Last Resort Tourniquet (1study), the London Bridge Tourniquet (1 study), and the K2 Tactical Tourniquet (1 study). Of the nine volunteer studies, three compared different non-commercial and commercial tourniquets (bladder tourniquet, windlass tourniquet, cargo-strap tourniquet, rubber tube, and improvised tourniquet). Three studies used anatomic pelvic simulation models to examine the Pelvic C-Clamp (2 studies) and the Combat Ready Clamp (1 study).

Key Points

- The Combat Application Tourniquet was reported to be better than 90% successful in occluding blood flow when self-applied to the leg in three studies. However, a fourth study reported only a 17% success rate when self-applied at mid-thigh and only a 8.3% success rate when the tourniquet was applied by a member of the research team.
- The Emergency and Military Tourniquet was reported to successfully occlude leg blood flow in three studies.
- Rubber and latex tubing were also reported to successfully occlude leg blood flow in three studies. Rubber and latex tubing had higher pain scores than other tourniquets.
- Tourniquets exposed to harsh environments for extended periods were less effective than new tourniquets in occluding blood flow and were more likely to break when used.
- Abdominal clamps were all examined in simulation models.
    - Occlusion of simulation bleeding was 100% reported in one study.
    - Special training is necessary for proper use of abdominal clamps.

Results of Volunteer and Simulation Studies

Evidence tables for the volunteer and simulation studies are provided in Appendix C. The CAT was tested in four studies. Wall et al. 2013[91] compared the CAT to the Stretch, Wrap, and Tuck Tourniquet (SWAT-T). Both were easy to use and produced occlusion at both the thigh (94% success) and forearm (100% success), but the CAT produced significantly more discomfort. Childers et al. 2011[92] reported that new CATs (not exposed to harsh environments) produced leg occlusion in 91% of applications compared to 63% of tourniquets previously exposed to the Afghanistan environment. Taylor et al. 2011[93] compared the CAT to the EMT when applied at mid-thigh. The CAT was successful at occluding the popliteal artery in only 16.6% of self-applications, and in only 8.3% when applied by a member of the research team. The EMT, which is not designed for self-application, and which was applied by a trained

researcher, produced occlusion in 75%. Walters et al. 2005[28] reported 100% occlusion when the CAT was applied to the leg and to the arm.

The EMT, a pneumatic device, was examined in three studies. As mentioned above, Taylor et al. 2011[93] reported 75% occlusion success when applied at mid-thigh by a trained researcher. King et al. 2006[94] reported 80% success when applied to the leg and Walters et al. 2005[28] reported 100% success for the leg and arm.

The SWAT-T was examined in two studies. As mentioned above, Wall et al. 2013[91] reported 94% and 100% occlusion success in the leg and thigh, respectively. Wall et al. 2012[95] examined just the SWAT-T and reported that the device successfully produced occlusion in 64% of applications when minimal training was provided.

The Self Applied Tourniquet System was examined in two studies. King et al. 2006[94] reported less than 50% success with leg occlusion and Walters et al. 2005[28] reported less than 80% success for leg occlusion. These results were not considered effective enough to recommend the device.

The One-Handed Tourniquet was examined in two studies. King et al. 2006[94] reported that this device did not work in any attempt at leg occlusion and Walters et al. 2005[28] reported less than 80% success for thigh occlusion. These results were not considered effective enough to recommend the device.

Basic tubing was examined in three studies. Guo et al. 2011[96] reported that leg occlusion success with rubber tubing was 60% and Swan et al. 2009[97] reported a 90% success. King et al. 2006[94] reported that latex surgical tubing was 90% successful for leg occlusion. While all three studies reported success with tubing they also all reported that tubing was the most painful.

Abdominal clamps (Pelvic C-Clamp and Combat Ready Clamp) were tested using pelvic models and simulated bleeding with the primary purpose of determining the proper training methods for use of these devices. Only the study using the Combat Ready Clamp tested occlusion using a specially designed manikin that simulated bleeding. Each study concluded that with proper training these devices could be successfully set up and used.

4. Discussion

Key Findings and Strength of Evidence

Our searches identified 16 studies that examined prehospital tourniquet use for trauma-induced extremity hemorrhage that reported outcomes selected for this report.

- No studies identified for this report provide a direct comparison of tourniquets to compression for treating trauma patients with extremity hemorrhage. In the military setting, tourniquets are considered an appropriate first response to traumatic extremity hemorrhage.
- Based on 13 studies reporting survival data for casualties treated with tourniquets, prehospital tourniquets are an effective treatment method for the prevention of death due to exsanguination. The reported survival rates for casualties treated with prehospital tourniquets ranged from 87% to 100%. Based on a meta-analysis of nine studies in military settings reporting adequate data, the survival rate for casualties treated with prehospital tourniquets is 91.9% with 95% confidence intervals of 88.1% to 94.6%. The strength of evidence was graded Moderate for improvement in survival.
- Based on eight studies reporting amputation data for casualties treated with tourniquets, prehospital tourniquets appear to be effective for preventing amputation. The reported amputation rates for casualties treated with prehospital tourniquets ranged from 13% to 28%. Based on a meta-analysis of 6 studies in military settings, the amputation rate for surviving casualties treated with prehospital tourniquets is 19.2% with 95% confidence intervals of 15.8% to 23.2%. The strength of evidence for improvement in amputation rates was graded Very Low.
- Insufficient evidence was available to examine the influence of prehospital tourniquet use on hypovolemic shock.
- Based on 11 studies reporting adverse-event data for casualties treated with tourniquets, prehospital tourniquets are associated with temporary nerve palsy, fasciotomies, and wound infection.

Our searches identified seven studies that examined the prehospital use of hemostatic dressings to control external hemorrhage. Only one study reported on survival associated with hemostatic dressing use.

- No studies identified for this report provide a direct comparison of hemostatic dressings and compression for the prehospital treatment of trauma patients with extremity hemorrhage.
- A single study reported that survival was improved but did not report adequate data for assessing the strength of evidence for this outcome.
- Indirect evidence from animal studies using 30 to 45 second free-bleeding time indicated that QuikClot Combat Gauze, Celox, and HemCon hemostatic dressings were not superior to standard gauze for survival rate. Hemostasis rates seen in these studies varied significantly. Consequently, the animal model evidence base does not provide a reliable assessment of how these dressing would perform in clinical situations involving external hemorrhage.

Findings in Relationship to What is Already Known

A systematic review and guideline from the Eastern Association for the Surgery of Trauma on management of penetrating lower extremity arterial trauma was published in 2012.[98] The guideline made the following recommendation:

> In cases of hemorrhage from penetrating lower extremity trauma in which manual compression is unsuccessful, tourniquets may be used as a temporary adjunct for hemorrhage control until definitive repair.

The authors stated that the recommendation is generally supported by data from studies based on retrospective data collection. The studies on tourniquet use examined in the guideline are the same studies identified for our report. The guideline states that "The initial approach to an arterial injury should be manual compression or a compression dressing, and the primary indication for tourniquet use should be the failure of direct pressure to control hemorrhage from an extremity vascular injury. Tourniquet time should be limited and tourniquets should be removed when definitive care is available. When correctly used, the complication rate from tourniquet use is exceedingly low." Hemostatic dressings were not considered in the guideline.

Another guideline on managing bleeding after major trauma was published by the Task Force for Advanced Bleeding Care in Trauma in 2010.[99] The guideline recommends "adjunct tourniquet use to stop life-threatening bleeding from open extremity injuries in the pre-surgical setting." The recommendation was "Grade 1C" in the GRADE system: strong recommendation, low-quality or very low-quality evidence, but with benefits clearly outweighing risk and burdens. The recommendation was based on the same studies examined in our report. The guideline states that "When uncontrolled arterial bleeding occurs from mangled extremity injuries, including penetrating or blast injuries or traumatic amputations, a tourniquet represents a simple and efficient method to acutely control hemorrhage."

Our searches identified two systematic reviews of prehospital hemostatic dressing use. They also identified the same studies identified in our report. Smith et al.[32] noted that "Anecdotal reports strongly support the use of hemostatic dressings when bleeding cannot be controlled using pressure dressings alone; however, current research focuses on studies conducted using animal models. There is a paucity of published clinical literature that provides an evidence base for the use of one type of hemostatic dressing over another in humans." Granville-Chapman et al.[100] also note that the clinical data for hemostatic dressings are scant and come from retrospective observational studies and that the available comparison data come from animal models. These authors supported the use of QuikClot granules and QuikClot ACS, in addition to HemCon as the current standard in 2010, basing their opinion on animal studies along with the sparse clinical data. The authors thought that other newer hemostatic dressings, such as QuikClot Combat Gauze and Celox, would eventually replace these two dressings.

Applicability

The data collected in the studies identified for this evidence report are partially applicable to the population of interest for this report. The available evidence for civilian use is small compared to that for military use. A recent study examined barriers to implementation of battlefield trauma care into the care of civilians with traumatic injuries.[101] The authors surveyed directors of the 31 local EMS agencies in California regarding the use of tourniquets, hemostatic dressings and TCCC principles in their regions. Of the 14 directors who responded, eight (57%) reported use of tourniquets, and only one reported use of hemostatic dressings. Reasons cited for not using tourniquets were (1) the difference in injuries encountered in civilian and military

settings, (2) perceived lack of effectiveness, and (3) concern about adverse effects. Reasons for not using hemostatic agents were (1) perceived lack of proven effectiveness, (2) concerns about adverse effects, and (3) expense.[101]

The military experience with gunshot wounds and other trauma not related to explosives may be the most relevant to the civilian setting, but studies did not typically provide data on effectiveness for injury mechanism subgroups. While civilians injured by gunshot wounds are often similar in age and sex to the military populations, it would be helpful to have more information about the performance of tourniquets in children and the elderly, particularly those with vascular comorbidities.

The types of tourniquets and dressings currently used by the military are available for use in civilian prehospital settings. However, the training in combat casualty care is heavily emphasized in the military, so proper application of these interventions in the civilian setting would require equally rigorous training.

Limitations of the Evidence Base

Emergency trauma situations are not readily amenable to rigorous randomized comparison trials. Butler and Carmona have noted "there is no ability to rely on carefully performed randomized, controlled trials to provide definitive answers to the medical decisions required in battlefield trauma care."[9] Elster et al. made the same point when discussing the implications of combat casualty care for mass casualty events.[18] They noted that "few military clinical practice guidelines are the result of standard, randomized clinical trials." Instead a "pragmatic approach adopted for military combat casualty care has allowed for rapid adoption of life saving strategies through practical methods. In this context, the evidence base supporting the military's clinical practice guidelines is driven by the results of basic science, translational large animal research, and retrospective cohort analyses."

Reviewing the evidence collected for this evidence report, we have been mindful of this problem and have attempted to adopt a "best available evidence" approach to addressing the report's key questions. However, most of the key questions proposed for this report could not be addressed with the available evidence. We identified no direct comparisons of compression to either tourniquets or hemostatic dressings. The main purpose of many studies was not to collect data on outcomes related to tourniquet or hemostatic dressing use, but instead to document the use of these interventions in a variety of settings. Other than a single report from the war zones in Iraq and Afghanistan that provided data on tourniquet use in pediatric casualties, we have no data on pediatric or elderly populations.

We have provided data from animal studies on hemostatic dressings and from human volunteer studies on tourniquets as indirect evidence regarding some of the questions addressed in this report. However, we caution against extrapolating from this data for anything aside from hypothesis generation.

Research Gaps

Data on outcomes related to civilian use of tourniquets and hemostatic dressings are extremely limited. This deficiency has already been noted in several reviews.[32,100] We identified two studies that collected information on hemostatic dressing use, but few relevant outcomes were reported in these studies. If tourniquets and hemostatic dressings are implemented widely in the civilian sector, it would be valuable to enhance the data collection for the National Trauma Databank to capture specific information about their use and outcomes. Information on the

demographics and health of patients treated, the mechanisms of injury, the types of interventions employed, the difficulty or ease of use, the control of hemorrhage, complications, limb salvage and patient survival would be extremely helpful for assessing the effectiveness and safety of these approaches. Information on the extent of training of those applying the tourniquets or dressings would also be important for interpreting the findings.

Conclusions

The military's experience treating trauma-related external hemorrhage before and after widespread use of tourniquets during the wars in Iraq and Afghanistan strongly suggests that tourniquet use saves lives. The adverse side effects associated with tourniquets appear to be manageable and do not appear to outweigh the benefits of tourniquet use. Proper training in tourniquet use, as highlighted in the TCCC program, is a key provision for making this intervention successful.

Information on the effectiveness of hemostatic dressings is centered on their ability to stop bleeding but little other outcome data related to human use have been reported in the available literature.

Published information on civilian use of tourniquets and hemostatic dressings is sparse. Prospective data collection on utilization and outcomes with these products in the civilian setting would be helpful for confirming the applicability to the general population and civilian settings.

References

1. Sasser SM, Hunt RC, Faul M, Sugerman D, Pearson WS, Dulski T, Wald MM, Jurkovich GJ, Newgard CD, Lerner EB, Cooper A, Wang SC, Henry MC, Salomone JP, Galli RL, Centers for Disease Control and Prevention (CDC). Guidelines for field triage of injured patients: recommendations of the National Expert Panel on Field Triage, 2011. MMWR Recomm Rep. 2012 Jan 13;61(RR-1):1-20. PMID: 22237112
2. NHTSA National Center for Statistics and Analysis. Traffic safety facts: 2010 data [DOT HS 811 630]. Washington (DC): U.S. Department of Transportation, National Highway Traffic Safety Administration (NHTSA); 2012 Jun. 12 p. Available at: http://www-nrd.nhtsa.dot.gov/Pubs/811630.pdf.
3. Murray CJ, Abraham J, Ali MK, Alvarado M, Atkinson C, Baddour LM, et al. The state of US health, 1990-2010: burden of diseases, injuries, and risk factors. JAMA. 2013 Jul 10;Epub ahead of print. PMID: 23842577
4. Kauvar DS, Sarfati MR, Kraiss LW. National trauma databank analysis of mortality and limb loss in isolated lower extremity vascular trauma. J Vasc Surg. 2011 Jun;53(6):1598-603. PMID: 21514772
5. Dorlac WC, DeBakey ME, Holcomb JB, Fagan SP, Kwong KL, Dorlac GR, Schreiber MA, Persse DE, Moore FA, Mattox KL. Mortality from isolated civilian penetrating extremity injury. J Trauma. 2005 Jul;59(1):217-22. PMID: 16096567
6. Butler FK Jr, Holcomb JB, Giebner SD, McSwain NE, Bagian J. Tactical combat casualty care 2007: evolving concepts and battlefield experience. Mil Med. 2007 Nov;172(11 Suppl):1-19. PMID: 18154234
7. Butler FK. Tactical Combat Casualty Care: update 2009. J Trauma. 2010 Jul;69 Suppl 1:S10-3. PMID: 20622602
8. Butler FK Jr, Blackbourne LH. Battlefield trauma care then and now: a decade of Tactical Combat Casualty Care. J Trauma Acute Care Surg. 2012 Dec;73(6 Suppl 5):S395-402. PMID: 23192061
9. Butler FK, Carmona R. Tactical combat casualty care: from the battlefields of Afghanistan and Iraq to the streets of America. Tactical Edge. 2012 Winter;86-91.
10. Kragh JF Jr, Walters TJ, Baer DG, Fox CJ, Wade CE, Salinas J, Holcomb JB. Practical use of emergency tourniquets to stop bleeding in major limb trauma. J Trauma. 2008 Feb;64(2 Suppl):S38-49; discussion S49-50. PMID: 18376170
11. Kragh JF Jr, Walters TJ, Baer DG, Fox CJ, Wade CE, Salinas J, Holcomb JB. Survival with emergency tourniquet use to stop bleeding in major limb trauma. Ann Surg. 2009 Jan;249(1):1-7. PMID: 19106667
12. Kotwal RS, Montgomery HR, Kotwal BM, Champion HR, Butler FK Jr, Mabry RL, Cain JS, Blackbourne LH, Mechler KK, Holcomb JB. Eliminating preventable death on the battlefield. Arch Surg. 2011 Dec;146(12):1350-8. PMID: 21844425
13. Eastridge BJ, Mabry RL, Seguin P, Cantrell J, Tops T, Uribe P, Mallett O, Zubko T, Oetjen-Gerdes L, Rasmussen TE, Butler FK, Kotwal RS, Holcomb JB, Wade C, Champion H, Lawnick M, Moores L, Blackbourne LH. Death on the battlefield (2001-2011): implications for the future of combat casualty care. J Trauma Acute Care Surg. 2012 Dec;73(6 Suppl 5):S431-7. PMID: 23192066
14. Lee C, Porter KM, Hodgetts TJ. Tourniquet use in the civilian prehospital setting. Emerg Med J. 2007 Aug;24(8):584-7. PMID: 17652690
15. Doyle GS, Taillac PP. Tourniquets: a review of current use with proposals for expanded prehospital use. Prehosp Emerg Care. 2008 Apr-Jun;12(2):241-56. PMID: 18379924
16. Sharpe DB, Barneby EM, Russell RJ. New approaches to the management of traumatic external haemorrhage. Trauma. 2011 Jan;13(1):47-55.
17. Lockey DJ, Weaver AE, Davies GE. Practical translation of hemorrhage control techniques to the civilian trauma scene. Transfusion. 2013 Jan;53 Suppl 1:17S-22S. PMID: 23301967
18. Elster EA, Butler FK, Rasmussen TE. Implications of combat casualty care for mass casualty events. JAMA. 2013 Aug 7;310(5):475-6.
19. Biddinger PD, Baggish A, Harrington L, D'Hemecourt P, Hooley J, Jones J, Kue R, Troyanos C, Dyer KS. Be prepared - the Boston marathon and mass-casualty events. N Engl J Med. 2013;368(21):1958-60.

20. Kragh JF Jr, Murphy C, Dubick MA, Baer DG, Johnson J, Blackbourne LH. New tourniquet device concepts for battlefield hemorrhage control. Army Med Dept J. 2011 Apr-Jun;38-48. PMID: 21607905
21. Tactical combat casualty care guidelines. Washington , DC: Military Health System; 2012 Sep 17. 14 p. Available at: http://www.health.mil/Libraries/120917_TCCC_Course_Materials/TCCC-Guidelines-120917.pdf.
22. Military Health System (MHS). Tactical combat casualty care curriculum. [Web site]. Washington (DC): Military Health System (MHS), U.S. Department of Defense; [accessed 2013 Oct 1]. [various]. Available: http://www.health.mil/Education_And_Training/TCCC.aspx.
23. Mabry RL. Tourniquet use on the battlefield. Mil Med. 2006 May;171(5):352-6. PMID: 16761880
24. Welling DR, Burris DG, Hutton JE, Minken SL, Rich NM. A balanced approach to tourniquet use: lessons learned and relearned. J Am Coll Surg. 2006 Jul;203(1):106-15.
25. Richey SL. Tourniquets for the control of traumatic hemorrhage: a review of the literature. J Spec Oper Med. 2009;9(1):56-64. PMID: 19813349
26. Kragh JF Jr. Use of tourniquets and their effects on limb function in the modern combat environment. Foot Ankle Clin. 2010 Mar;15(1):23-40. PMID: 20189115
27. Smith ER, Shapiro GL. Totally tourniquets. JEMS. 2013 Nov;:48, 50, 52.
28. Walters TJ, Wenke JC, Kauvar DS, McManus JG, Holcomb JB, Baer DG. Effectiveness of self-applied tourniquets in human volunteers. Prehosp Emerg Care. 2005 Oct-Dec;9(4):416-22. PMID: 16263675
29. Mann-Salinas EA, Kragh JF Jr, Dubick MA, Baer DG, Blackbourne LH. Assessment of users to control simulated junctional hemorrhage with the combat ready clamp (CRoC). Int J Burns Trauma. 2013;3(1):49-54. PMID: 23386985
30. Fitzgibbons PG, Digiovanni C, Hares S, Akelman E. Safe tourniquet use: a review of the evidence. J Am Acad Orthop Surg. 2012 May;20(5):310-9. PMID: 22553103
31. Kheirabadi B. Evaluation of topical hemostatic agents for combat wound treatment. US Army Med Dept J. 2011 Apr-Jun;25-37. PMID: 21607904
32. Smith AH, Laird C, Porter K, Bloch M. Haemostatic dressings in prehospital care. Emerg Med J. 2012 Nov 17;Epub ahead of print. PMID: 23161808
33. Kheirabadi BS, Arnaud F, McCarron R, Murdock AD, Hodge DL, Ritter B, Dubick MA, Blackbourne LH. Development of a standard swine hemorrhage model for efficacy assessment of topical hemostatic agents. J Trauma. 2011 Jul;71(1 Suppl):S139-46. PMID: 21795871
34. Gerlach T, Grayson JK, Pichakron KO, Sena MJ, DeMartini SD, Clark BZ, Estep JS, Zierold D. Preliminary study of the effects of smectite granules (WoundStat) on vascular repair and wound healing in a swine survival model. J Trauma. 2010 Nov;69(5):1203-9. PMID: 20068476
35. Filips D, Logsetty S, Tan J, Atkinson I, Mottet K. The iTClamp Controls Junctional Bleeding in a Lethal Swine Exsanguination Model. Prehosp Emerg Care. 2013 Oct-Dec;17(4):526-32. PMID: 23968337
36. Viswanathan M, Ansari MT, Berkman ND, Chang S, Hartling L, McPheeters LM, Santaguida PL, Shamliyan T, Singh K, Tertsvadze A, Treadwell JR. Assessing the risk of bias of individual studies in systematic reviews of health care interventions. Agency for Healthcare Research and Quality methods guide for comparative effectiveness reviews [AHRQ Publication No. 12-EGC047-EF]. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2012 Mar. 33 p. Available at: http://www.effectivehealthcare.ahrq.gov.
37. Narine L, Yee DS, Einarson TR, Ilersich AL. Quality of abstracts of original research articles in CMAJ in 1989. CMAJ. 1991 Feb 15;144(4):449-53. PMID: 1993292
38. Pitkin RM, Branagan MA, Burmeister LF. Accuracy of data in abstracts of published research articles. JAMA. 1999 Mar 24-31;281(12):1110-1. PMID: 10188662
39. Owens DK, Lohr KN, Atkins D, Treadwell JR, Reston JT, Bass EB, Chang S, Helfand M. Grading the strength of a body of evidence when comparing medical interventions-Agency for Healthcare Research and Quality and the Effective Health Care Program. J Clin Epidemiol. 2010 May;63(5):513-23. PMID: 19595577

40. Guyatt G, Oxman AD, Akl E, Kunz R, Vist G, Brozek J, Norris S, Falck-Ytter Y, Glasziou P, Debeer H, Jaeschke R, Rind D, Meerpohl J, Dahm P, Schunemann HJ. GRADE guidelines 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011 Apr;64(4):383-94. PMID: 21195583

41. Balshem H, Helfand M, Schunemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S, Guyatt GH. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol. 2011 Apr;64(4):401-6. PMID: 21208779

42. Guyatt GH, Oxman AD, Santesso N, Helfand M, Vist G, Kunz R, Brozek J, Norris S, Meerpohl J, Djulbegovic B, Alonso-Coello P, Post PN, Busse JW, Glasziou P, Christensen R, Schunemann HJ. GRADE guidelines: 12. Preparing summary of findings tables-binary outcomes. J Clin Epidemiol. 2013 Feb;66(2):158-72. PMID: 22609141

43. Atkins D, Chang S, Gartlehner G, Buckley DI, Whitlock EP, Berliner E, Matchar D. Assessing applicability when comparing medical interventions: Agency for Healthcare Research and Quality and the Effective Health Care Program. J Clin Epidemiol. 2011 Nov;64(11):1198-207. Epub 2011 Apr 3. PMID: 21463926

44. Lairet JR, Bebarta VS, Burns CJ, Lairet KF, Rasmussen TE, Renz EM, King BT, Fernandez W, Gerhardt R, Butler F, DuBose J, Cestero R, Salinas J, Torres P, Minnick J, Blackbourne LH. Prehospital interventions performed in a combat zone: a prospective multicenter study of 1,003 combat wounded. J Trauma Acute Care Surg. 2012 Aug;73(2 Suppl 1):S38-42. PMID: 22847092

45. Gerhardt RT, Berry JA, Blackbourne LH. Analysis of life-saving interventions performed by out-of-hospital combat medical personnel. J Trauma. 2011 Jul;71(1 Suppl):S109-13. PMID: 21795868

46. Kragh JF Jr, Wade CE, Baer DG, Jones JA, Walters TJ, Hsu JR, Wenke JC, Blackbourne LH, Holcomb JB. Fasciotomy rates in Operations Enduring Freedom and Iraqi Freedom: association with injury severity and tourniquet use. J Orthop Trauma. 2011 Mar;25(3):134-9. PMID: 21321506

47. Kragh JF Jr, O'Neill ML, Walters TJ, Dubick MA, Baer DG, Wade CE, Holcomb JB, Blackbourne LH. The military emergency tourniquet program's lessons learned with devices and designs. Mil Med. 2011 Oct;176(10):1144-52. PMID: 22128650

48. Kragh JF Jr, O'Neill ML, Walters TJ, Jones JA, Baer DG, Gershman LK, Wade CE, Holcomb JB. Minor morbidity with emergency tourniquet use to stop bleeding in severe limb trauma: research, history, and reconciling advocates and abolitionists. Mil Med. 2011 Jul;176(7):817-23. PMID: 22128725

49. Kragh JF Jr, Littrel ML, Jones JA, Walters TJ, Baer DG, Wade CE, Holcomb JB. Battle casualty survival with emergency tourniquet use to stop limb bleeding. J Emerg Med. 2011 Dec;41(6):590-7. PMID: 19717268

50. Kalish J, Burke P, Feldman J, Agarwal S, Glantz A, Moyer P, Serino R, Hirsch E. The return of tourniquets. Original research evaluates the effectiveness of prehospital tourniquets for civilian penetrating extremity injuries. JEMS. 2008 Aug;33(8):44-6. PMID: 18692730

51. Kragh JF Jr, Cooper A, Aden JK, Dubick MA, Baer DG, Wade CE, Blackbourne LH. Survey of trauma registry data on tourniquet use in pediatric war casualties. Pediatr Emerg Care. 2012 Dec;28(12):1361-5. PMID: 23187998

52. Beekley AC, Sebesta JA, Blackbourne LH, Herbert GS, Kauvar DS, Baer DG, Walters TJ, Mullenix PS, Holcomb JB, 31st Combat Support Hospital Research Group. Prehospital tourniquet use in Operation Iraqi Freedom: effect on hemorrhage control and outcomes. J Trauma. 2008 Feb;64(2 Suppl):S28-37; discussion S37. PMID: 18376169

53. Clasper JC, Brown KV, Hill P. Limb complications following pre-hospital tourniquet use. J R Army Med Corps. 2009 Sep;155(3):200-2. PMID: 20397360

54. King DR, van der Wilden G, Kragh JF Jr, Blackbourne LH. Forward assessment of 79 prehospital battlefield tourniquets used in the current war. J Spec Oper Med. 2012 Winter;12(4):33-8. PMID: 23536455

55. Brown KV, Murray CK, Clasper JC. Infectious complications of combat-related mangled extremity injuries in the British military. J Trauma. 2010;69(Suppl 1):S109-S114. PMID: 20622604

56. Brodie S, Hodgetts TJ, Ollerton J, McLeod J, Lambert P, Mahoney P. Tourniquet use in combat trauma: U.K. military experience. J Spec Oper Med. 2009 Winter;9(1):74-7. PMID: 19813352

57. Tien HC, Jung V, Rizoli SB, Acharya SV, MacDonald JC. An evaluation of tactical combat casualty care interventions in a combat environment. J Spec Oper Med. 2009 Winter;9(1):65-8. PMID: 19813350

58. Dayan L, Zinmann C, Stahl S, Norman D. Complications associated with prolonged tourniquet application on the battlefield. Mil Med. 2008 Jan;173(1):63-6. PMID: 18251333

59. Lakstein D, Blumenfeld A, Sokolov T, Lin G, Bssorai R, Lynn M, Ben-Abraham R. Tourniquets for hemorrhage control on the battlefield: a 4-year accumulated experience. J Trauma. 2003 May;54(5 Suppl):S221-5. PMID: 12768129

60. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, Alonso-Coello P, Falck-Ytter Y, Jaeschke R, Vist G, Akl EA, Post PN, Norris S, Meerpohl J, Shukla VK, Nasser M, Schunemann HJ, GRADE Working Group. GRADE guidelines: 8. Rating the quality of evidence--indirectness. J Clin Epidemiol. 2011 Dec;64(12):1303-10. PMID: 21802903

61. Guyatt GH, Oxman AD, Vist G, Kunz R, Brozek J, Alonso-Coello P, Montori V, Akl EA, Djulbegovic B, Falck-Ytter Y, Norris SL, Williams JW Jr, Atkins D, Meerpohl J, Schunemann HJ. GRADE guidelines: 4. Rating the quality of evidence--study limitations (risk of bias). J Clin Epidemiol. 2011 Apr;64(4):407-15. PMID: 21247734

62. Guyatt GH, Oxman AD, Sultan S, Glasziou P, Akl EA, Alonso-Coello P, Atkins D, Kunz R, Brozek J, Montori V, Jaeschke R, Rind D, Dahm P, Meerpohl J, Vist G, Berliner E, Norris S, Falck-Ytter Y, Murad MH, Schunemann HJ, GRADE Working Group. GRADE guidelines: 9. Rating up the quality of evidence. J Clin Epidemiol. 2011 Dec;64(12):1311-6. PMID: 21802902

63. Brown MA, Daya MR, Worley JA. Experience with chitosan dressings in a civilian EMS system. J Emerg Med. 2009 Jul;37(1):1-7. PMID: 18024069

64. Cox ED, Schreiber MA, McManus J, Wade CE, Holcomb JB. New hemostatic agents in the combat setting. Transfusion. 2009 Dec;49 (Suppl 5):248S-55S. PMID: 19954487

65. Pozza M, Millner RW. Celox (chitosan) for haemostasis in massive traumatic bleeding: experience in Afghanistan. Eur J Emerg Med. 2010 May 10;Epub ahead of print. PMID: 20461007

66. Ran Y, Hadad E, Daher S, Ganor O, Kohn J, Yegorov Y, Bartal C, Ash N, Hirschhorn G. QuikClot Combat Gauze use for hemorrhage control in military trauma: January 2009 Israel Defense Force experience in the Gaza Strip--a preliminary report of 14 cases. Prehosp Disaster Med. 2010 Nov-Dec;25(6):584-8. PMID: 21181695

67. Rhee P, Brown C, Martin M, Salim A, Plurad D, Green D, Chambers L, Demetriades D, Velmahos G, Alam H. QuikClot use in trauma for hemorrhage control: case series of 103 documented uses. J Trauma. 2008 Apr;64(4):1093-9. PMID: 18404080

68. Wedmore I, McManus JG, Pusateri AE, Holcomb JB. A special report on the chitosan-based hemostatic dressing: experience in current combat operations. J Trauma. 2006 Mar;60(3):655-8. PMID: 16531872

69. Alam HB, Chen Z, Jaskille A, Querol RI, Koustova E, Inocencio R, Conran R, Seufert A, Ariaban N, Toruno K, Rhee P. Application of a zeolite hemostatic agent achieves 100% survival in a lethal model of complex groin injury in Swine. J Trauma. 2004 May;56(5):974-83. PMID: 15179235

70. Alam HB, Uy GB, Miller D, Koustova E, Hancock T, Inocencio R, Anderson D, Llorente O, Rhee P. Comparative analysis of hemostatic agents in a swine model of lethal groin injury. J Trauma. 2003 Jun;54(6):1077-82. PMID: 12813325

71. Rall JM, Cox JM, Songer AG, Cestero RF, Ross JD. Comparison of novel hemostatic dressings with QuikClot combat gauze in a standardized swine model of uncontrolled hemorrhage. J Trauma Acute Care Surg. 2013 Aug;75(2 Suppl 2):S150-6.

72. Schwartz RB, Reynolds BZ, Shiver SA, Lerner EB, Greenfield EM, Solis RA, Kimpel NA, Coule PL, McManus JG. Comparison of two packable hemostatic Gauze dressings in a porcine hemorrhage model. Prehosp Emerg Care. 2011 Oct-Dec;15(4):477-82. PMID: 21870945

73. Kheirabadi BS, Scherer MR, Estep JS, Dubick MA, Holcomb JB. Determination of efficacy of new hemostatic dressings in a model of extremity arterial hemorrhage in swine. J Trauma. 2009 Sep;67(3):450-9; discussion 459-60. PMID: 19741385

74. Kheirabadi BS, Edens JW, Terrazas IB, Estep JS, Klemcke HG, Dubick MA, Holcomb JB. Comparison of new hemostatic granules/powders with currently deployed hemostatic products in a lethal model of extremity arterial hemorrhage in swine. J Trauma. 2009 Feb;66(2):316-26; discussion 327-8. PMID: 19204503

75. Arnaud F, Teranishi K, Tomori T, Carr W, McCarron R. Comparison of 10 hemostatic dressings in a groin puncture model in swine. J Vasc Surg. 639;50(3):632-9. PMID: 19700097

76. Sambasivan CN, Cho SD, Zink KA, Differding JA, Schreiber MA. A highly porous silica and chitosan-based hemostatic dressing is superior in controlling hemorrhage in a severe groin injury model in swine. Am J Surg. 2009 May;197(5):576-80; discussion 580. PMID: 19393351

77. Englehart MS, Cho SD, Tieu BH, Morris MS, Underwood SJ, Karahan A, Muller PJ, Differding JA, Farrell DH, Schreiber MA. A novel highly porous silica and chitosan-based hemostatic dressing is superior to HemCon and gauze sponges. J Trauma. 2008 Oct;65(4):884-90; discussion 890-2. PMID: 18849807

78. Ward KR, Tiba MH, Holbert WH, Blocher CR, Draucker GT, Proffitt EK, Bowlin GL, Ivatury RR, Diegelmann RF. Comparison of a new hemostatic agent to current combat hemostatic agents in a Swine model of lethal extremity arterial hemorrhage. J Trauma. 2007 Aug;63(2):276-83; discussion 283-4. PMID: 17693824

79. Acheson EM, Kheirabadi BS, Deguzman R, Dick EJ Jr, Holcomb JB. Comparison of hemorrhage control agents applied to lethal extremity arterial hemorrhages in swine. J Trauma. 2005 Oct;59(4):865-74; discussion 874-5. PMID: 16374275

80. Clay JG, Grayson JK, Zierold D. Comparative testing of new hemostatic agents in a swine model of extremity arterial and venous hemorrhage. Mil Med. 2010 Apr;175(4):280-4. PMID: 20446504

81. van der Worp HB, Howells DW, Sena ES, Porritt MJ, Rewell S, O'Collins V, Macleod MR. Can animal models of disease reliably inform human studies?. PLoS Med. 2010;7(3):e1000245. PMID: 20361020

82. Satterly S, Nelson D, Zwintscher N, Oguntoye M, Causey W, Theis B, Huang R, Haque M, Martin M, Bickett G, Rush RM Jr. Hemostasis in a noncompressible hemorrhage model: an end-user evaluation of hemostatic agents in a proximal arterial injury. J Surg Educ. 2013 Mar;70(2):206-11. PMID: 23427965

83. Sohn VY, Eckert MJ, Martin MJ, Arthurs ZM, Perry JR, Beekley A, Rubel EJ, Adams RP, Bickett GL, Rush RM Jr. Efficacy of three topical hemostatic agents applied by medics in a lethal groin injury model. J Surg Res. 2009 Jun 15;154(2):258-61. PMID: 19329126

84. Wright JK, Kalns J, Wolf EA, Traweek F, Schwarz S, Loeffler CK, Snyder W, Yantis LD Jr, Eggers J. Thermal injury resulting from application of a granular mineral hemostatic agent. J Trauma. 2004 Aug;57(2):224-30. PMID: 15345965

85. Gegel B, Burgert J, Gasko J, Campbell C, Martens M, Keck J, Reynolds H, Loughren M, Johnson D. The effects of QuikClot Combat Gauze and movement on hemorrhage control in a porcine model. Mil Med. 2012 Dec;177(12):1543-7. PMID: 23397703

86. Causey MW, McVay DP, Miller S, Beekley A, Martin M. The efficacy of Combat Gauze in extreme physiologic conditions. J Surg Res. 2012 Oct;177(2):301-5. PMID: 22785361

87. Arnaud F, Teranishi K, Okada T, Parreno-Sacdalan D, Hupalo D, McNamee G, Carr W, Burris D, McCarron R. Comparison of Combat Gauze and TraumaStat in two severe groin injury models. J Surg Res. 2011 Jul;169(1):92-8. PMID: 20070980

88. Kozen BG, Kircher SJ, Henao J, Godinez FS, Johnson AS. An alternative hemostatic dressing: comparison of CELOX, HemCon, and QuikClot. Acad Emerg Med. 2008 Jan;15(1):74-81. PMID: 18211317

89. Arnaud F, Tomori T, Saito R, McKeague A, Prusaczyk WK, McCarron RM. Comparative efficacy of granular and bagged formulations of the hemostatic agent QuikClot. J Trauma. 2007 Oct;63(4):775-82. PMID: 18090005

90. Ahuja N, Ostomel TA, Rhee P, Stucky GD, Conran R, Chen Z, Al-Mubarak GA, Velmahos G, Demoya M, Alam HB. Testing of modified zeolite hemostatic dressings in a large animal model of lethal groin injury. J Trauma. 2006 Dec;61(6):1312-20. PMID: 17159671

91. Wall PL, Duevel DC, Hassan MB, Welander JD, Sahr SM, Buising CM. Tourniquets and occlusion: the pressure of design. Mil Med. 2013 May;178(5):578-87. PMID: 23756019

92. Childers R, Tolentino JC, Leasiolagi J, Wiley N, Liebhardt D, Barbabella S, Kragh JF Jr. Tourniquets exposed to the Afghanistan combat environment have decreased efficacy and increased breakage compared to unexposed tourniquets. Mil Med. 2011 Dec;176(12):1400-3.

93. Taylor DM, Vater GM, Parker PJ. An evaluation of two tourniquet systems for the control of prehospital lower limb hemorrhage. J Trauma. 2011 Sep;71(3):591-5. PMID: 21768905

94. King RB, Filips D, Blitz S, Logsetty S. Evaluation of possible tourniquet systems for use in the Canadian Forces. J Trauma. 2006 May;60(5):1061-71. PMID: 16688072

95. Wall PL, Welander JD, Singh A, Sidwell RA, Buising CM. Stretch and wrap style tourniquet effectiveness with minimal training. Mil Med. 2012 Nov;177(11):1366-73. PMID: 23198515

96. Guo JY, Liu Y, Ma YL, Pi HY, Wang JR. Evaluation of emergency tourniquets for prehospital use in China. Chin J Traumatol. 2011 Jun 1;14(3):151-5. PMID: 21635801

97. Swan KG Jr, Wright DS, Barbagiovanni SS, Swan BC, Swan KG. Tourniquets revisited. J Trauma. 2009 Mar;66(3):672-5. PMID: 19276736

98. Fox N, Rajani RR, Bokhari F, Chiu WC, Kerwin A, Seamon MJ, Skarupa D, Frykberg E, Eastern Association for the Surgery of Trauma. Evaluation and management of penetrating lower extremity arterial trauma: an Eastern Association for the Surgery of Trauma practice management guideline. J Trauma Acute Care Surg. 2012 Nov;73(5 Suppl 4):S315-20. PMID: 23114487

99. Rossaint R, Bouillon B, Cerny V, Coats TJ, Duranteau J, Fernandez-Mondejar E, Hunt BJ, Komadina R, Nardi G, Neugebauer E, Ozier Y, Riddez L, Schultz A, Stahel PF, Vincent JL, Spahn DR, Task Force for Advanced Bleeding Care in Trauma. Management of bleeding following major trauma: an updated European guideline. Crit Care. 2010;14(2):R52. PMID: 20370902

100. Granville-Chapman J, Jacobs N, Midwinter MJ. Pre-hospital haemostatic dressings: a systematic review. Injury. 2011 May;42(5):447-59. PMID: 21035118

101. Galante JM, Smith CA, Sena MJ, Scherer LA, Tharratt RS. Identification of barriers to adaptation of battlefield technologies into civilian trauma in california. Mil Med. 2013;178(11):1227-30. PMID: 24183771

102. Zentai C, Grottke O, Spahn DR, Rossaint R. Nonsurgical techniques to control massive bleeding. Anesthesiol Clin. 2013 Mar;31(1):41-53.

103. Moriwaki Y, Toyoda H, Harunari N, Iwashita M, Kosuge T, Arata S, Suzuki N. Gauze packing as damage control for uncontrollable haemorrhage in severe thoracic trauma. Ann R Coll Surg Engl. 2013 Jan;95(1):20-5. PMID: 23317720

104. Fitzpatrick GM, Cliff R, Tandon N. Thrombosomes: a platelet-derived hemostatic agent for control of noncompressible hemorrhage. Transfusion. 2013 Jan;:53 Suppl 1:100S-106S. PMID: 23301961

105. Riha GA, Schreiber MA. Update and new developments in the management of the exsanguinating patient. J Intensive Care Med. 2013 Jan-Feb;28(1):46-57. PMID: 21747123

106. Adkins CL. Wound care dressings and choices for care of wounds in the home. Home Healthc Nurse. 2013 May;31(5):259-67. PMID: 23652977

107. Abrassart S, Stern R, Peter R. Unstable pelvic ring injury with hemodynamic instability: what seems the best procedure choice and sequence in the initial management. Orthop Traumatol Surg Res. 2013 Apr;99(2):175-82. PMID: 23462306

108. Inaba K, Branco BC, Rhee P, Putty B, Okoye O, Barmparas G, Talving P, Demetriades D. Long-term preclinical evaluation of the intracorporeal use of advanced local hemostatics in a damage-control swine model of grade IV liver injury. J Trauma Acute Care Surg. 2013 Feb;74(2):538-45. PMID: 23354248

109. Phaneuf MD, Bide MJ, Hannel SL, Platek MJ, Monahan TS, Contreras MA, Phaneuf TM, LoGerfo FW. Development of an infection-resistant, bioactive wound dressing surface. J Biomed Mater Res A. 2005 Sep 15;74(4):666-76. PMID: 16028237

110. Nitecki SS, Karram T, Ofer A, Engel A, Hoffman A. Management of combat vascular injuries using modern imaging: are we getting better? Emerg Med Int. 2013;2013:689473. Epub 2013 Jan 10.

111. Muthukumar T, Senthil R, Sastry TP. Synthesis and characterization of biosheet impregnated with Macrotyloma uniflorum extract for burn/wound dressings. Colloids Surf B Biointerfaces. 2013 Feb 01;102:694-9.

112. Sellei RM, Schandelmaier P, Kobbe P, Knobe M, Pape HC. Can a modified anterior external fixator provide posterior compression of AP compression type III pelvic injuries? Clin Orthop Relat Res. 2013 Sep;471(9):2862-8. PMID: 23604604

113. Carr D, Kieser J, Mabbott A, Mott C, Champion S, Girvan E. Damage to apparel layers and underlying tissue due to hand-gun bullets. Int J Legal Med. 2013 Apr 19. [Epub ahead of print]. PMID: 23604393

114. Metsemakers WJ, Vanderschot P, Jennes E, Nijs S, Heye S, Maleux G. Transcatheter embolotherapy after external surgical stabilization is a valuable treatment algorithm for patients with persistent haemorrhage from unstable pelvic fractures: outcomes of a single centre experience. Injury. 2013 Jul;44(7):964-8. Epub 2013 Feb 8. PMID: 23398901

115. Boonkong W, Petsom A, Thongchul N. Rapidly stopping hemorrhage by enhancing blood clotting at an opened wound using chitosan/polylactic acid/polycaprolactone wound dressing device. J Mater Sci Mater Med. 2013 Jun;24(6):1581-93. Epub 2013 Apr 24. PMID: 23612939

116. Wu J, Lemarie CA, Barralet J, Blostein MD. Amphiphilic peptide-loaded nanofibrous calcium phosphate microspheres promote hemostasis in vivo. Acta Biomater. 2013 Jun 21. [Epub ahead of print]. PMID: 23796406

117. Pavic R, Margetic P. Emergency treatment for clinically unstable patients with pelvic fracture and haemorrhage. Coll Antropol. 2012 Dec;36(4):1445-52. PMID: 23390848

118. Gansslen A, Hildebrand F, Pohlemann T. Management of hemodynamic unstable patients "in extremis" with pelvic ring fractures. Acta Chir Orthop Traumatol Cech. 2012;79(3):193-202. PMID: 22840950

119. Hauschild O, Aghayev E, von Heyden J, Strohm PC, Culemann U, Pohlemann T, Suedkamp NP, Schmal H. Angioembolization for pelvic hemorrhage control: results from the German pelvic injury register. J Trauma Acute Care Surg. 2012 Sep;73(3):679-84. PMID: 22710767

120. Pohlemann T, Culemann U, Holstein JH. Initial experience using a pelvic emergency simulator to train reduction in blood loss. Clin Orthop Relat Res. 2012 Aug;470(8):2098-103. PMID: 22311726

121. Daruwalla ZJ, Rowan F, Finnegan M, Fennell J, Neligan M. Exsanguinators and tourniquets: do we need to change our practice?. Surgeon. 2012 Jun;10(3):137-42. PMID: 22008294

122. Percival TJ, Rasmussen TE. Reperfusion strategies in the management of extremity vascular injury with ischaemia. Br J Surg. 2012 Jan;99 Suppl 1:66-74. PMID: 22441858

123. Gruen RL, Brohi K, Schreiber M, Balogh ZJ, Pitt V, Narayan M, Maier RV. Haemorrhage control in severely injured patients. Lancet. 2012 Sep;380(9847):1099-1108.

124. Palmier B. [Conditions for the survival of combat casualties in overseas operations: procedure and experience from the Afghan out-of-hospital theater]. Bull Acad Natl Med. 2012 Apr-May;196(4-5):893-907. PMID: 23550451

125. Travers S, Dubourg O, Ribeiro Parenti L, Lefort H, Albarello S, Domanski L. [Prehospital use of haemostatic dressing QuikClot ACS+ for hemorrhage control of a perineal trauma]. Ann Fr Anesth Reanim. 2012 Dec;31(12):969-71. PMID: 23164651

126. Yang JH, Lim H, Yoon JR, Jeong HI. Tourniquet associated chemical burn. Indian J Orthop. 2012 May;46(3):356-9. PMID: 22719126

127. Du L, Tong L, Jin Y, Jia J, Liu Y, Su C, Yu S, Li X. A multifunctional in situ-forming hydrogel for wound healing. Wound Repair Regen. 2012 Nov-Dec;20(6):904-10. PMID: 23110551

128. Hu G, Xiao L, Tong P, Bi D, Wang H, Ma H, Zhu G, Liu H. Antibacterial hemostatic dressings with nanoporous bioglass containing silver. Int J Nanomedicine. 2012;7:2613-20. PMID: 22745538

129. Morrison JJ, Percival TJ, Markov NP, Villamaria C, Scott DJ, Saches KA, Spencer JR, Rasmussen TE. Aortic balloon occlusion is effective in controlling pelvic hemorrhage. J Surg Res. 2012 Oct;177(2):341-7. PMID: 22591921

130. Korkmaz T, Sarikas NG, Kilicgun A, Serin E, Boran C. The mechanism of activity of ankaferd blood stopper in the control of arterial bleeding and in the process of wound healing. HealthMED. 2012;6(11):3736-3743.

131. Xie H, Lucchesi L, Teach JS, Virmani R. Long-term outcomes of a chitosan hemostatic dressing in laparoscopic partial nephrectomy. J Biomed Mater Res B Appl Biomater. 2012 Feb;100 B(2):432-6.

132. Shoffstall AJ, Atkins KT, Groynom RE, Varley ME, Everhart LM, Lashof-Sullivan MM, Martyn-Dow B, Butler RS, Ustin JS, Lavik EB. Intravenous hemostatic nanoparticles increase survival following blunt trauma injury. Biomacromolecules. 2012 Nov 12;13(11):3850-7. PMID: 22998772

133. Hansen A, McMillan L, Morrison A, Petrik J, Bradley M. Polymers for the rapid and effective activation and aggregation of platelets. Biomaterials. 2011 Oct;32(29):7034-41.

134. Wigginton JG, Roppolo L, Pepe PE. Advances in resuscitative trauma care. Minerva Anestesiol. 2011 Oct;77(10):993-1002. PMID: 21952600

135. Rtshiladze MA, Andersen SP, Nguyen DQ, Grabs A, Ho K. The 2009 Sydney shark attacks: case series and literature review. ANZ J Surg. 2011 May;81(5):345-51. PMID: 21518184

136. Kubiak BD, Albert SP, Gatto LA, Vieau CJ, Roy SK, Snyder KP, Maier KG, Nieman GF. A clinically applicable porcine model of septic and ischemia/reperfusion-induced shock and multiple organ injury. J Surg Res. 2011 Mar;166(1):e59-69. PMID: 21193206

137. Clamp JA, Moran CG. Haemorrhage control in pelvic trauma. Trauma. 2011 Oct;13(4):300-316.

138. Lustenberger T, Meier C, Benninger E, Lenzlinger PM, Keel MJ. C-clamp and pelvic packing for control of hemorrhage in patients with pelvic ring disruption. J Emerg Trauma Shock. 2011 Oct;4(4):477-82. PMID: 22090741

139. Razavi S, Ardakani HZ, Rajai S, Hollisaz M, Sadeghipoor H, Farshad A, Shojaeezadeh D, Khodai G. Trends in Prevalent Injuries among Iranian Pilgrims in Hajj. Iran J Public Health. 2011;40(2):110-5. PMID: 23113080

140. Dregelid EB, Pedersen G. Treatment of major vein injury with the hemostatic fleece TachoSil by interposing a peritoneal patch to avoid vein thrombosis: a feasibility study in pigs. J Emerg Trauma Shock. 2011 Jan;4(1):77-81. PMID: 21633573

141. Valentine R, Boase S, Jervis-Bardy J, Dones Cabral JD, Robinson S, Wormald PJ. The efficacy of hemostatic techniques in the sheep model of carotid artery injury. Int Forum Allergy Rhinol. 2011 Mar-Apr;1(2):118-22. PMID: 22287330

142. Inaba K, Rhee P, Teixeira PG, Barmparas G, Putty B, Branco BC, Cohn S, Demetriades D. Intracorporeal use of advanced local hemostatics in a damage control swine model of grade IV liver injury. J Trauma. 2011 Nov;71(5):1312-8. PMID: 22002611

143. White JM, Cannon JW, Stannard A, Burkhardt GE, Spencer JR, Williams K, Oh JS, Rasmussen TE. Direct vascular control results in less physiologic derangement than proximal aortic clamping in a porcine model of noncompressible extrathoracic torso hemorrhage. J Trauma. 2011 Nov;71(5):1278-86; discussion 1286-7. PMID: 22071929

144. Grottke O, Braunschweig T, Daheim N, Coburn M, Grieb G, Rossaint R, Tolba R. Effect of TachoSil in a coagulopathic pig model with blunt liver injuries. J Surg Res. 2011 Nov;171(1):234-9. PMID: 20452609

145. De Castro GP, MacPhee MJ, Driscoll IR, Beall D, Hsu J, Zhu S, Hess JR, Scalea TM, Bochicchio GV. New hemostatic dressing (FAST Dressing) reduces blood loss and improves survival in a grade V liver injury model in noncoagulopathic swine. J Trauma. 2011 Jun;70(6):1408-12. PMID: 21817977

146. White JM, Cannon JW, Stannard A, Spencer JR, Hancock H, Williams K, Oh JS, Rasmussen TE. A porcine model for evaluating the management of noncompressible torso hemorrhage. J Trauma. 2011 Jul;71(1 Suppl):S131-8. PMID: 21795889

147. Schnuriger B, Inaba K, Barmparas G, Rhee P, Putty B, Branco BC, Talving P, Demetriades D. A new survivable damage control model including hypothermia, hemodilution, and liver injury. J Surg Res. 2011 Jul;169(1):99-105. PMID: 20036395

148. Spector D, Perry Z, Konobeck T, Mooradian D, Shikora S. Comparison of hemostatic properties between collagen and synthetic buttress materials used in staple line reinforcement in a swine splenic hemorrhage model. Surg Endosc. 2011 Apr;25(4):1148-52. PMID: 20835722

149. Pick DL, Kolla SB, Mucksavage P, Louie MK, Sountoulides P, Kaufmann O, Olamendi S, Kaplan A, Huynh V, Ortiz-Vanderdys C, Truong HP, Said SA, Andrade L, Tongson-Ignacio J, McDougall EM, Clayman RV. Sprayed fibrin sealant as the sole hemostatic agent for porcine laparoscopic partial nephrectomy. J Urol. 2011 Jan;185(1):291-7. PMID: 21075389

150. Anilkumar TV, Muhamed J, Jose A, Jyothi A, Mohanan PV, Krishnan LK. Advantages of hyaluronic acid as a component of fibrin sheet for care of acute wound. Biologicals. 2011 Mar;39(2):81-8.

151. Hutchinson RW, Broughton D, Barbolt TA, Poandl T, Muench T, Rockar R, Johnson M, Hart J. Hemostatic effectiveness of Fibrin pad after partial nephrectomy in swine. J Surg Res. 2011 May 15;167(2):e291-8. PMID: 20451926

152. Lu C-R, Chen L, Chen W-B, Dou C-Q, Liu R, Huang Z-Q. Absorbable bandage wrapping in treatment of severe blast liver injury: a miniature swine model. Chin Med J (Engl). 2011 Nov 11;124(22):3757-3761.

153. Jagodzinski NA, Weerasinghe C, Porter K. Crush injuries and crush syndrome - A review. Part 1: The systemic injury. Trauma. 2010 Apr;12(2):69-88.

154. Williams-Johnson J, Williams E, Watson H. Management and treatment of pelvic and hip injuries. Emerg Med Clin North Am. 2010 Nov;28(4):841-59.

155. Feliciano DV. Management of peripheral arterial injury. Curr Opin Crit Care. 2010 Dec;16(6):602-8. PMID: 20852417

156. Kheirabadi BS, Mace JE, Terrazas IB, Fedyk CG, Estep JS, Dubick MA, Blackbourne LH. Safety evaluation of new hemostatic agents, smectite granules, and kaolin-coated gauze in a vascular injury wound model in swine. J Trauma. 2010 Feb;68(2):269-78. PMID: 20154537

157. Estrera AL, Gochnour DC, Azizzadeh A, Miller CC 3rd, Coogan S, Charlton-Ouw K, Holcomb JB, Safi HJ. Progress in the treatment of blunt thoracic aortic injury: 12-year single-institution experience. Ann Thorac Surg. 2010 Jul;90(1):64-71. PMID: 20609750

158. Pollak AN, Powell ET, Fang R, Cooper EO, Ficke JR, Flaherty SF. Use of negative pressure wound therapy during aeromedical evacuation of patients with combat-related blast injuries. J Surg Orthop Adv. 2010;19(1):44-8. PMID: 20371006

159. Silver dressings - Do they work?. Drug Ther Bull. 2010 Apr;48(4):38-42.

160. Sinha CVK, Anand LCS. Extremity and orthopaedic injuries. Med J Armed Forces India. 2010 Oct;66(4):342-6.

161. Dubose J, Inaba K, Barmparas G, Teixeira PG, Schnuriger B, Talving P, Salim A, Demetriades D. Bilateral internal iliac artery ligation as a damage control approach in massive retroperitoneal bleeding afterpelvic fracture. J Trauma. 2010 Dec;69(6):1507-1514.

162. Khashayar P, Amoli HA, Tavakoli H, Panahi F. Efficacy of pre-hospital care in trauma patients in Iran. Emerg Med J. 2010 Jun;27(6):430-2.

163. Mylankal KJ, Wyatt MG. Control of major haemorrhage. Surgery (Oxford). November 2010;28(11):556-562.

164. Peng HT, Shek PN. Novel wound sealants: biomaterials and applications. Expert Rev Med Devices. 2010 Sep;7(5):639-659.

165. Ahmad Z. Playing with fire and getting burnt-a retrospective analysis of injuries presenting to the emergency department during 'firework season'. Eur J Plastic Surg. 2010 Aug;33(4):199-201.

166. Rich PB, Douillet C, Buchholz V, Overby DW, Jones SW, Cairns BA. Use of the novel hemostatic textile Stasilon(R) to arrest refractory retroperitoneal hemorrhage: a case report. J Med Case Rep. 2010;4:20. PMID: 20205876

167. Takacs I, Wegmann J, Horvath S, Ferencz A, Ferencz S, Javor S, Odermatt E, Roth E, Weber G. Efficacy of different hemostatic devices for severe liver bleeding: a randomized controlled animal study. Surg Innov. 2010 Dec;17(4):346-52. PMID: 20870671

168. Rothwell SW, Settle T, Wallace S, Dorsey J, Simpson D, Bowman JR, Janmey P, Sawyer E. The long term immunological response of swine after two exposures to a salmon thrombin and fibrinogen hemostatic bandage. Biologicals. 2010 Nov;38(6):619-28. PMID: 20705479

169. Millner R, Lockhart AS, Marr R. Chitosan arrests bleeding in major hepatic injuries with clotting dysfunction: an in vivo experimental study in a model of hepatic injury in the presence of moderate systemic heparinisation. Ann R Coll Surg Engl. 2010 Oct;92(7):559-61. PMID: 20522310

170. Bochicchio GV, Kilbourne MJ, Keledjian K, Hess J, Scalea T. Evaluation of a new hemostatic agent in a porcine grade V liver injury model. Am Surg. 2010 Mar;76(3):317-20. PMID: 20349664

171. Grottke O, Braunschweig T, Philippen B, Gatzweiler KH, Gronloh N, Staat M, Rossaint R, Tolba R. A new model for blunt liver injuries in the swine. Eur Surg Res. 2010;44(2):65-73. PMID: 19996600

172. Gu R, Sun W, Zhou H, Wu Z, Meng Z, Zhu X, Tang Q, Dong J, Dou G. The performance of a fly-larva shell-derived chitosan sponge as an absorbable surgical hemostatic agent. Biomaterials. 2010 Feb;31(6):1270-7. PMID: 19880175

173. Hammes C, Moersdorf G, Refeidi A, Post S, Kaehler G. Endoscopic application of hemostatic thrombin-gelatin matrix (FloSeal) in anticoagulated pigs. Minim Invasive Ther Allied Technol. 2010;19(1):48-51. PMID: 20095898

174. Stratos I, Graff J, Rotter R, Mittlmeier T, Vollmar B. Open blunt crush injury of different severity determines nature and extent of local tissue regeneration and repair. J Orthop Res. 2010 Jul;28(7):950-7.

175. Aysan E, Bektas H, Ersoz F, Sari S, Kaygusuz A, Huq GE. Ability of the ankaferd blood stopper to prevent parenchymal bleeding in an experimental hepatic trauma model. Int J Clin Exp Med. 2010;3(3):186-191.

176. Spiro DM, Zonfrillo MR, Meckler GD. Wounds. Pediatr Rev. 2010 Aug 01;31(8):326-334.

177. Adu-Frimpong J. Genitourinary trauma in boys. Clin Pediatr Emerg Med. 2009 Mar;10(1):45-9.

178. Claudet I, Pasian N, Debuisson C, Salanne S, Rekhroukh H. Tourniquet syndrome: interest of a systematic analysis of families' social conditions to detect neglect situations. Child Abuse Negl. 2009 Sep;33(9):569-72. PMID: 19811829

179. Van Natta TL, Smith BR, Bricker SD, Putnam BA. Hilar control in penetrating chest trauma: a simplified approach to an underutilized maneuver. J Trauma. 2009 Jun;66(6):1564-9. PMID: 19509615

180. Richard MJ, Tornetta P 3rd. Emergent management of APC-2 pelvic ring injuries with an anteriorly placed C-clamp. J Orthop Trauma. 2009 May-Jun;23(5):322-6. PMID: 19390358

181. Chalkias AF. Prehospital emergency thoracotomy: when to do it?. J Emerg Prim Health Care. 2009;7(4).

182. Berend K, Levi M. Management of adult Jehovah's Witness patients with acute bleeding. Am J Med. 2009 Dec;122(12):1071-6.

183. Barnard AR, Allison K. The classification and principles of management of wounds in trauma. Trauma. 2009;11(3):163-176.

184. Bochicchio G, Kilbourne M, Kuehn R, Keledjian K, Hess J, Scalea T. Use of a modified chitosan dressing in a hypothermic coagulopathic grade V liver injury model. Am J Surg. 2009 Nov;198(5):617-22. PMID: 19887188

185. Wang Y, Lu W. [The study and clinical application of absorbable hemostatic agent]. Sheng Wu I Hsueh Kung Cheng Hsueh Tsa Chih. 2009 Aug;26(4):922-6. PMID: 19813641

186. Clay JG, Zierold D, Grayson K, Battistella FD. Dextran polymer hemostatic dressing improves survival in liver injury model. J Surg Res. 2009 Jul;155(1):89-93. PMID: 19041100

187. Adams GL, Manson RJ, Hasselblad V, Shaw LK, Lawson JH. Acute in-vivo evaluation of bleeding with Gelfoam plus saline and Gelfoam plus human thrombin using a liver square lesion model in swine. J Thromb Thrombolysis. 2009 Jul;28(1):1-5. PMID: 18629446

188. Xie H, Teach JS, Burke AP, Lucchesi LD, Wu PC, Sarao RC. Laparoscopic repair of inferior vena caval injury using a chitosan-based hemostatic dressing. Am J Surg. 2009 Apr;197(4):510-4. PMID: 18585679

189. Bjorses K, Holst J. Topical haemostatics in renal trauma--an evaluation of four different substances in an experimental setting. J Trauma. 2009 Mar;66(3):602-11. PMID: 19276727

190. Bilgili H, Kosar A, Kurt M, Onal IK, Goker H, Captug O, Shorbagi A, Turgut M, Kekilli M, Kurt OK, Kirazli S, Aksu S, Haznedaroglu IC. Hemostatic efficacy of ankaferd blood stopper in a swine bleeding model. Med Princ Pract. 2009 April;18(3):165-9.

191. Bertram JP, Williams CA, Robinson R, Segal SS, Flynn NT, Lavik EB. Intravenous hemostat: nanotechnology to halt bleeding. Sci Transl Med. 2009 Dec 16;1(11):11ra22. PMID: 20371456

192. Fischer TH, Vournakis JN, Manning JE, McCurdy SL, Rich PB, Nichols TC, Scull CM, McCord MG, Decorta JA, Johnson PC, Smith CJ. The design and testing of a dual fiber textile matrix for accelerating surface hemostasis. J Biomed Mater Res B Appl Biomater. 2009 Oct;91(1):381-9. PMID: 19489008

193. Liu Y, Kopelman D, Wu LQ, Hijji K, Attar I, Preiss-Bloom O, Payne GF. Biomimetic sealant based on gelatin and microbial transglutaminase: an initial in vivo investigation. J Biomed Mater Res B Appl Biomater. 2009 Oct;91(1):5-16. PMID: 19360881

194. Kheirabadi BS, Sieber J, Bukhari T, Rudnicka K, Murcin LA, Tuthill D. High-pressure fibrin sealant foam: an effective hemostatic agent for treating severe parenchymal hemorrhage. J Surg Res. 2008 Jan;144(1):145-50. PMID: 17583744

195. Chirinos FS. Local doctor creates clothing with tourniquets for troops. Tex Med. 2008 Feb;104(2):47-9. PMID: 18610892

196. Shokrollahi K, Sharma H, Gakhar H. A technique for temporary control of hemorrhage. J Emerg Med. 2008 Apr;34(3):319-20. PMID: 18164163

197. Hong JP, Kim YW, Lee SK, Kim SH, Min KH. The effect of continuous release of recombinant human epidermal growth factor (rh-EGF) in chitosan film on full thickness excisional porcine wounds. Ann Plast Surg. Oct 2008;61(4):457-462. PMID: 18812721

198. Cuschieri J, Freeman B, O'Keefe G, Harbrecht BG, Bankey P, Johnson JL, Minei JP, Sperry J, West M, Nathens A, Moore EE, Maier RV. Inflammation and the host response to injury a large-scale collaborative project: Patient-oriented research core standard operating procedure for clinical care x. guidelines for venous thromboembolism prophylaxis in the trauma patient. J Trauma. 2008 October;65(4):944-950.

199. Degiannis E, Zinn RJ. Pitfalls in penetrating thoracic trauma (lessons we learned the hard way...). Ulus Travma Acil Cerrahi Derg. 2008;14(4):261-7.

200. Bastos R, Baisden CE, Harker L, Calhoon JH. Penetrating thoracic trauma. Semin Thorac Cardiovasc Surg. 2008;20(1):19-25.

201. Kaneko N, Kobayashi Y, Okada Y. Anatomic variations of the renal vessels pertinent to transperitoneal vascular control in the management of trauma. Surgery. 2008 May;143(5):616-622.

202. Ong SY, Wu J, Moochhala SM, Tan MH, Lu J. Development of a chitosan-based wound dressing with improved hemostatic and antimicrobial properties. Biomaterials. 2008 Nov;29(32):4323-32. PMID: 18708251

203. Sanghi P, Virmani R, Do D, Erikson J, Elliott J, Cilingiroglu M, Matthews H, Kazi M, Ricker R, Bailey SR. A comparative evaluation of arterial blood flow and the healing response after femoral artery closure using angio-seal STS Plus and StarClose in a porcine model. J Interv Cardiol. 2008 Aug;21(4):329-36. PMID: 18573159

204. Xie H, Khajanchee YS, Shaffer BS. Chitosan hemostatic dressing for renal parenchymal wound sealing in a porcine model: implications for laparoscopic partial nephrectomy technique. J Soc Laparoendosc Surg. 2008 Jan-Mar;12(1):18-24. PMID: 18402734

205. Leixnering M, Reichetseder J, Schultz A, Figl M, Wassermann E, Thurnher M, Redl H. Gelatin thrombin granules for hemostasis in a severe traumatic liver and spleen rupture model in swine. J Trauma. 2008 Feb;64(2):456-61. PMID: 18301215

206. Delgado AV, Kheirabadi BS, Fruchterman TM, Scherer M, Cortez D, Wade CE, Dubick MA, Holcomb JB. A novel biologic hemostatic dressing (fibrin patch) reduces blood loss and resuscitation volume and improves survival in hypothermic, coagulopathic Swine with grade V liver injury. J Trauma. 2008 Jan;64(1):75-80. PMID: 18188102

207. Jesty J, Wieland M, Niemiec J. Assessment in vitro of the active hemostatic properties of wound dressings. J Biomed Mater Res B Appl Biomater. 2009 May;89(2):536-42. PMID: 18985792

208. Xie H, Khajanchee YS, Teach JS, Shaffer BS. Use of a chitosan-based hemostatic dressing in laparoscopic partial nephrectomy. J Biomed Mater Res B Appl Biomater. 2008 Apr;85(1):267-71. PMID: 17932955

209. Erdogan D, van Gulik TM. Evolution of fibrinogen-coated collagen patch for use as a topical hemostatic agent. J Biomed Mater Res B Appl Biomater. 2008 Apr;85(1):272-8. PMID: 17806107

210. Zhang M-X, Chen Z-H, Li J, Yang C-Y, Xie Z-G, Chen G-J. Hemostatic effect and biocompatibility of RT-Q medical biomembrane. J Clin Rehabil Tiss Eng Res. 2008 Jan 01;12(1):175-9.

211. Franz MG, Steed DL, Robson MC. Optimizing healing of the acute wound by minimizing complications. Curr Probl Surg. 2007 Nov;44(11):691-763. PMID: 18036992

212. Chaby G, Senet P, Vaneau M, Martel P, Guillaume JC, Meaume S, Teot L, Debure C, Dompmartin A, Bachelet H, Carsin H, Matz V, Richard JL, Rochet JM, Sales-Aussias N, Zagnoli A, Denis C, Guillot B, Chosidow O. Dressings for acute and chronic wounds: a systematic review. Arch Dermatol. 2007 Oct;143(10):1297-304. PMID: 17938344

213. Almogy G, Rivkind AI. Terror in the 21st century: milestones and prospects-part II. Curr Probl Surg. 2007 Sep;44(9):566-619.

214. Honsik KA, Romeo MW, Hawley CJ, Romeo SJ, Romeo JP. Sideline skin and wound care for acute injuries. Curr Sports Med Rep. 2007 Jun;6(3):147-154.

215. Hirshberg A, Hoyt DB, Mattox KL. From "Leaky Buckets" to vascular injuries: understanding models of uncontrolled hemorrhage. J Am Coll Surg. 2007 Apr;204(4):665-672.

216. Kauvar DS, Baer DG, Walters TJ. Influence of systemic hypotension on skeletal muscle ischemia-reperfusion injury after 4-hour tourniquet application. J Surg Educ. 2007 Sep-Oct;64(5):273-7. PMID: 17961884

217. Rattanatayarom W, Wattanasirichaigoon S. Evaluation of dermal irritancy potential of Carboxymethyl-chitosan hydrogel and poly-(acrylic acid) chitin hydrogel. J Med Assoc Thai. 2007 Apr;90(4):724-9. PMID: 17487127

218. Sheikh BY. Efficacy of acrylate tissue adhesive as vascular repair and hemostatic material. Ann Vasc Surg. 2007 Jan;21(1):56-60. PMID: 17349337

219. Kheirabadi BS, Acheson EM, Deguzman R, Crissey JM, Delgado AV, Estep SJ, Holcomb JB. The potential utility of fibrin sealant dressing in repair of vascular injury in swine. J Trauma. 2007 Jan;62(1):94-103. PMID: 17215739

220. Roy SC, Paulose M, Grimes CA. The effect of TiO2 nanotubes in the enhancement of blood clotting for the control of hemorrhage. Biomaterials. 2007 Nov;28(31):4667-72. PMID: 17692372

221. Bjorses K, Holst J. Various local hemostatic agents with different modes of action; an in vivo comparative randomized vascular surgical experimental study. Eur J Vasc Endovasc Surg. 2007 Mar;33(3):363-370.

222. Aballay AM, Recio P, Slater H, Goldfarb IW, Tolchin E, Papasavas P, Caushaj PF. The use of esmarch exsanguination for the treatment of extremity wound burns. Ann Burns Fire Disasters. 2007 Mar 31;20(1):22-4. PMID: 21991062

223. Vertrees A, Kellicut D, Ottman S, Peoples G, Shriver C. Early definitive abdominal closure using serial closure technique on injured soldiers returning from Afghanistan and Iraq. J Am Coll Surg. 2006 May;202(5):762-72. PMID: 16648016

224. Pursifull NF, Morris MS, Harris RA, Morey AF. Damage control management of experimental grade 5 renal injuries: further evaluation of FloSeal gelatin matrix. J Trauma. 2006 Feb;60(2):346-50. PMID: 16508494

225. Higgins TF, Swanson ER. Pelvic antishock sheeting. Air Med J. 2006 Mar-Apr;25(2):88-90. PMID: 16516121

226. Hunt PA, Greaves I, Owens WA. Emergency thoracotomy in thoracic trauma-a review. Injury. 2006 Jan;37(1):1-19. PMID: 16410079

227. Nzewi O, Slight RD, Zamvar V. Management of blunt thoracic aortic injury. Eur J Vasc Endovasc Surg. 2006 Jan;31(1):18-27. PMID: 16226902

228. Voinchet V, Vasseur P, Kern J. Efficacy and safety of hyaluronic acid in the management of acute wounds. Am J Clin Dermatol. 2006;7(6):353-7.

229. Schecter WP, Ivatury RR, Rotondo MF, Hirshberg A. Open abdomen after trauma and abdominal sepsis: a strategy for management. J Am Coll Surg. 2006 Sep;203(3):390-6.

230. Jurgens C, Schulz AP, Porte T, Faschingbauer M, Seide K. Biodegradable films in trauma and orthopedic surgery. Eur J Trauma. 2006 Apr;32(2):160-171.

231. De Alwis W. Fingertip injuries. Emerg Med Australas. June 2006;18(3):229-237.

232. Klemcke HG. Evaluation of FloSeal as a potential intracavitary hemostatic agent. J Trauma. 2006 Feb;60(2):385-9. PMID: 16508500

233. Wang X, Yan Y, Zhang R. A comparison of chitosan and collagen sponges as hemostatic dressings. 2006 Jan;21(1):39-54.

234. Schreiber MA. Coagulopathy in the trauma patient. Curr Opin Crit Care. 2005 Dec;11(6):590-7. PMID: 16292065

235. Pope LE, Hobbs CG. Epistaxis: an update on current management. Postgrad Med J. 2005 May;81(955):309-14. PMID: 15879044

236. Kataoka Y, Maekawa K, Nishimaki H, Yamamoto S, Soma K. Iliac vein injuries in hemodynamically unstable patients with pelvic fracture caused by blunt trauma. J Trauma. 2005 Apr;58(4):704-8; discussion 708-10. PMID: 15824645

237. Tiemann AH, Bohme J, Josten C. Emergency treatment of multiply injured patients with unstable disruption of the posterior pelvic ring by using the "C-clamp": analysis of 28 consecutive cases. Eur J Trauma. 2005 Jun 2005;31(3):244-251.

238. Brandenburg MA, Hawkins L, Quick G. Hand injuries, part 2: when nerves, vasculature, tendons, or ligaments are traumatized. Consultant. 2005 Mar;45(3):361-8.

239. Sagerman PJ. Wounds. Pediatr Rev. 2005 Feb 2005;26(2):43-9.

240. Degiannis E, Bowley DM, Westaby S. Penetrating cardiac injury. Ann R Coll Surg Engl. 2005 Jan;87(1):61-3.

241. Rothwell SW, Reid TJ, Dorsey J, Flournoy WS, Bodo M, Janmey PA, Sawyer E. A salmon thrombin-fibrin bandage controls arterial bleeding in a swine aortotomy model. J Trauma. 2005 Jul;59(1):143-9. PMID: 16096554

242. Kheirabadi BS, Acheson EM, Deguzman R, Sondeen JL, Ryan KL, Delgado A, Dick EJ Jr, Holcomb JB. Hemostatic efficacy of two advanced dressings in an aortic hemorrhage model in Swine. J Trauma. 2005 Jul;59(1):25-34; discussion 34-5. PMID: 16096535

243. Cihan A, Yilmaz E, Yenidunya S, Ucan BH. Medical haemostasis in acute hepatocyte injury and experimental liver trauma. ANZ J Surg. 2005 Apr;75(4):239-43. PMID: 15839974

244. Hick EJ, Morey AF, Harris RA, Morris MS. Gelatin matrix treatment of complex renal injuries in a porcine model. J Urol. 2005 May;173(5):1801-4. PMID: 15821591

245. Laurence S, Bareille R, Baquey C, Fricain JC. Development of a resorbable macroporous cellulosic material used as hemostatic in an osseous environment. J Biomed Mater Res A. 2005 Jun 15;73(4):422-9. PMID: 15880722

246. Bochicchio G, Dunne J, Bochicchio K, Scalea T. The combination of platelet-enriched autologous plasma with bovine collagen and thrombin decreases the need for multiple blood transfusions in trauma patients with retroperitoneal bleeding. J Trauma. 2004 Jan;56(1):76-9. PMID: 14749569

247. Kopp J, Jeschke MG, Bach AD, Kneser U, Horch RE. Applied tissue engineering in the closure of severe burns and chronic wounds using cultured human autologous keratinocytes in a natural fibrin matrix. Cell Tissue Bank. 2004;5(2):89-96.

248. Borowik S, Popko J, Ladny R, Slowinski K. [External stabilization in the treatment of unstable pelvis fractures combined with additional injuries of internal organs]. Pol Przegl Chir. 2004;76(3):285-95.

249. King DR, Cohn SM, Proctor KG, Miami Clinical Trials Group. Modified rapid deployment hemostat bandage terminates bleeding in coagulopathic patients with severe visceral injuries. J Trauma. 2004 Oct;57(4):756-9. PMID: 15514529

250. Gansslen A, Krettek C, Pohlemann T. Die temporare Stabilisierung des Beckenrings mit der sog. Notfallbeckenzwinge. Oper Orthop Traumatol. 2004 Jun;16(2):192-204.

251. Giannoudis PV, Pape HC. Damage control orthopaedics in unstable pelvic ring injuries. Injury. 2004 Jul;35(7):671-7.

252. Ang CY, Samsudin AR, Karima AM, Nizam A. Locally produced bovine bone sponge as a haemostatic agent. Med J Malaysia. 2004 May;59 Suppl B:149-50. PMID: 15468862

253. Pusateri AE, Delgado AV, Dick EJ Jr, Martinez RS, Holcomb JB, Ryan KL. Application of a granular mineral-based hemostatic agent (QuikClot) to reduce blood loss after grade V liver injury in swine. J Trauma. 2004 Sep;57(3):555-62; discussion 562. PMID: 15454802

254. Schwaitzberg SD, Chan MW, Cole DJ, Read M, Nichols T, Bellinger D, Connolly RJ. Comparison of poly-N-acetyl glucosamine with commercially available topical hemostats for achieving hemostasis in coagulopathic models of splenic hemorrhage. J Trauma. 2004 Jul;57(1 Suppl):S29-32. PMID: 15280748

255. Krishnan LK, Mohanty M, Umashankar PR, Lal AV. Comparative evaluation of absorbable hemostats: advantages of fibrin-based sheets. Biomaterials. 2004 Nov;25(24):5557-63. PMID: 15142738

256. Griffith BC, Morey AF, Rozanski TA, Harris R, Dalton SR, Torgerson SJ, Partyka SR. Central renal stab wounds: treatment with augmented fibrin sealant in a porcine model. J Urol. 2004 Jan;171(1):445-7. PMID: 14665952

257. Doillon CJ, Dion Y-M. Comparison of a plasma-based composite biologic sealant with fibrin glue (Tisseel) for vascular anastomoses. Surg Laparosc Endosc Percutan Tech. 2004 Dec;14(6):335-9.

258. Vournakis JN, Demcheva M, Whitson A, Guirca R, Pariser ER. Isolation, purification, and characterization of poly-N-acetyl glucosamine use as a hemostatic agent. J Trauma. 2004 Jul;57(1 Suppl):S2-6.

259. Underhill S, Crumplin MKH. A high price for victory: the management of pain and transport of the sick and wounded in the Napoleonic Wars (1793-1815). CPD Anaesth. 2003;5(3):144-151.

260. Starr AJ. Immediate management of pelvic fractures. Oper Tech Orthop. 2003 Apr;13(2):73-8.

261. Donelan S. Teaching wound care and bandaging: an historical perspective. Wilderness Environ Med. 2003;14(1):47-56.

262. Salehian O, Teoh K, Mulji A. Blunt and penetrating cardiac trauma: a review. Can J Cardiol. 2003 Aug;19(9):1054-9.

263. Pusateri AE, Modrow HE, Harris RA, Holcomb JB, Hess JR, Mosebar RH, Reid TJ, Nelson JH, Goodwin CW Jr, Fitzpatrick GM, McManus AT, Zolock DT, Sondeen JL, Cornum RL, Martinez RS. Advanced hemostatic dressing development program: animal model selection criteria and results of a study of nine hemostatic dressings in a model of severe large venous hemorrhage and hepatic injury in Swine. J Trauma. 2003 Sep;55(3):518-26. PMID: 14501897

264. Vournakis JN, Demcheva M, Whitson AB, Finkielsztein S, Connolly RJ. The RDH bandage: hemostasis and survival in a lethal aortotomy hemorrhage model. J Surg Res. 2003 Jul;113(1):1-5. PMID: 12943803

265. Jewelewicz DD, Cohn SM, Crookes BA, Proctor KG. Modified rapid deployment hemostat bandage reduces blood loss and mortality in coagulopathic pigs with severe liver injury.[Erratum appears in J Trauma. 2003 Oct;55(4):621. J Trauma. 2003 Aug;55(2):275-80; discussion 280-1. PMID: 12913637

266. Singer AJ, Nable M, Cameau P, Singer DD, McClain SA. Evaluation of a new liquid occlusive dressing for excisional wounds. Wound Repair Regen. 2003 May-Jun;11(3):181-7. PMID: 12753599

267. Schreiber MA, Holcomb JB, Hedner U, Brundage SI, Macaitis JM, Aoki N, Meng ZH, Tweardy DJ, Hoots K. The effect of recombinant factor VIIa on noncoagulopathic pigs with grade V liver injuries. J Am Coll Surg. 2003 May;196(5):691-7. PMID: 12742197

268. Sondeen JL, Pusateri AE, Coppes VG, Gaddy CE, Holcomb JB. Comparison of 10 different hemostatic dressings in an aortic injury. J Trauma. 2003 Feb;54(2):280-5. PMID: 12579052

269. Pusateri AE, McCarthy SJ, Gregory KW, Harris RA, Cardenas L, McManus AT, Goodwin CW Jr. Effect of a chitosan-based hemostatic dressing on blood loss and survival in a model of severe venous hemorrhage and hepatic injury in swine. J Trauma. 2003 Jan;54(1):177-82. PMID: 12544915

270. Peng Y, Ye C, Zou H, Liang P. Investigation of features of hemostasis sponge of collagen and chitosan compound. Chin J Clin Rehab. 2003 Jan;7(2):342.

271. Chiu J, Ketchum LH, Reid TJ. Transfusion-sparing hemostatic agents. Curr Opin Hematol. 2002 Nov;9(6):544-50. PMID: 12394180

272. Rennie M. Trauma, immobility and undernutrition, the harbingers of insulin resistance. Br J Intensive Care. 2002;12(2):29.

273. O'Mara MS, Goel A, Recio P, Slater H, Goldfarb IW, Tolchin E, Caushaj PF. The use of tourniquets in the excision of unexsanguinated extremity burn wounds. Burns. 2002 Nov;28(7):684-7.

274. Schreiber MA, Holcomb JB, Hedner U, Brundage SI, Macaitis JM, Hoots K. The effect of recombinant factor VIIa on coagulopathic pigs with grade V liver injuries. J Trauma. 2002 Aug;53(2):252-7; discussion 257-9. PMID: 12169930

275. Kheirabadi BS, Field-Ridley A, Pearson R, MacPhee M, Drohan W, Tuthill D. Comparative study of the efficacy of the common topical hemostatic agents with fibrin sealant in a rabbit aortic anastomosis model. J Surg Res. 2002 Jul;106(1):99-107. PMID: 12127814

276. Kheirabadi BS, Pearson R, Tuthill D, Rudnicka K, Holcomb JB, Drohan W, MacPhee MJ. Comparative study of the hemostatic efficacy of a new human fibrin sealant: is an antifibrinolytic agent necessary?. J Trauma. 2002 Jun;52(6):1107-15. PMID: 12045638

277. Turner AS, Parker D, Egbert B, Maroney M, Armstrong R, Powers N. Evaluation of a novel hemostatic device in an ovine parenchymal organ bleeding model of normal and impaired hemostasis. J Biomed Mater Res. 2002;63(1):37-47. PMID: 11787027

278. Ishihara M, Nakanishi K, Ono K, Sato M, Kikuchi M, Saito Y, Yura H, Matsui T, Hattori H, Uenoyama M, Kurita A. Photocrosslinkable chitosan as a dressing for wound occlusion and accelerator in healing process. Biomaterials. 2002 Feb;23(3):833-40. PMID: 11771703

279. Anema JG, Morey AF, Harris R, MacPhee M, Cornum RL. Potential uses of absorbable fibrin adhesive bandage for genitourinary trauma. World J Surg. 2001 Dec;25(12):1573-7. PMID: 11775194

280. Klobucar H, Delinar D, Korzinek M, Korzinek K. CMC external fixator. Acta Chir Orthop Traumatol Cech. 2001;68(1):55-8. PMID: 11706716

281. Ertel W, Keel M, Eid K, Platz A, Trentz O. Control of severe hemorrhage using C-clamp and pelvic packing in multiply injured patients with pelvic ring disruption. J Orthop Trauma. 2001 Sep-Oct;15(7):468-74. PMID: 11602828

282. Tyburski JG, Wilson RF, Dente C, Steffes C, Carlin AM. Factors affecting mortality rates in patients with abdominal vascular injuries. J Trauma. 2001 Jun;50(6):1020-6. PMID: 11426115

283. Edlich RF, Reddy VR. 5th Annual David R. Boyd, MD Lecture: revolutionary advances in wound repair in emergency medicine during the last three decades. A view toward the new millennium. J Emerg Med. 2001 Feb;20(2):167-93. PMID: 11207414

284. Djurickovic S, Snelling CFT, Boyle JC. Tourniquet and subcutaneous epinephrine reduce blood loss during burn excision and immediate autografting. J Burn Care Rehabil. 2001;22(1):1-5.

285. Ono K, Ishihara M, Ozeki Y, Deguchi H, Sato M, Saito Y, Yura H, Sato M, Kikuchi M, Kurita A, Maehara T. Experimental evaluation of photocrosslinkable chitosan as a biologic adhesive with surgical applications. Surgery. 2001 Nov;130(5):844-50. PMID: 11685194

286. Davis SC, Eaglstein WH, Cazzaniga AL, Mertz PM. An octyl-2-cyanoacrylate formulation speeds healing of partial-thickness wounds. Dermatol Surg. 2001 Sep;27(9):783-8. PMID: 11553164

287. Barbolt TA, Odin M, Leger M, Kangas L. Pre-clinical subdural tissue reaction and absorption study of absorbable hemostatic devices. Neurol Res. 2001 Jul;23(5):537-42. PMID: 11474811

288. Martinowitz U, Holcomb JB, Pusateri AE, Stein M, Onaca N, Freidman M, Macaitis JM, Castel D, Hedner U, Hess JR. Intravenous rFVIIa administered for hemorrhage control in hypothermic coagulopathic swine with grade V liver injuries. J Trauma. 2001 Apr;50(4):721-9. PMID: 11303171

289. Pusateri AE, Holcomb JB, Harris RA, MacPhee MJ, Charles NC, Beall LD, Hess JR. Effect of fibrin bandage fibrinogen concentration on blood loss after grade V liver injury in swine. Mil Med. 2001 Mar;166(3):217-22. PMID: 11263022

290. Morey AF, Anema JG, Harris R, Gresham V, Daniels R, Knight RW, Beall D, Macphee M, Cornum RL. Treatment of grade 4 renal stab wounds with absorbable fibrin adhesive bandage in a porcine model. J Urol. 2001 Mar;165(3):955-8. PMID: 11176521

291. Hill A, Estridge TD, Maroney M, Monnet E, Egbert B, Cruise G, Coker GT. Treatment of suture line bleeding with a novel synthetic surgical sealant in a canine iliac PTFE graft model. J Biomed Mater Res. 2001 May 1;58(3):308-12. PMID: 11319746

292. Clumpner BR, Polston RW, Kragh JF Jr, Westmoreland T, Harcke HT, Jones JA, Dubick MA, Baer DG, Blackbourne LH. Single versus double routing of the band in the combat application tourniquet. J Spec Oper Med. 2013;13(1):34-41. PMID: 23526320

293. Barlow BT, Kuhn KM. Limb salvage compared with amputation in the acute setting: criteria used on the battlefield. Curr Orthop Pract. 2013 Mar-Apr;24(2):153-7.

294. Sorensen B, Fries D. Emerging treatment strategies for trauma-induced coagulopathy. Br J Surg. 2012 Jan;99 Suppl 1:40-50. PMID: 22441854

295. Orman JA, Eastridge BJ, Baer DG, Gerhardt RT, Rasmussen TE, Blackbourne LH. The impact of 10 years of war on combat casualty care research: a citation analysis. J Trauma Acute Care Surg. 2012 Dec;73(6 Suppl 5):S403-8.

296. Brown KV, Guthrie HC, Ramasamy A, Kendrew JM, Clasper J. Modern military surgery: lessons from Iraq and Afghanistan. J Bone Joint Surg Br. 2012 Apr;94B(4):536-43.

297. Mamczak CN, Born CT, Obremskey WT, Dromsky DM, Extremity War Injuries VII Acute Care Panel. Evolution of acute orthopaedic care. J Am Acad Orthop Surg. 2012;20 Suppl 1:S70-3. PMID: 22865142

298. Rasmussen TE, Dubose JJ, Asensio JA, Feliciano DV, Fox CJ, Nunez TC, Sise MJ, Military Liaison Committee of the American Association for the Surgery of Trauma. Tourniquets, vascular shunts, and endovascular technologies: esoteric or essential? A report from the 2011 AAST Military Liaison Panel. J Trauma Acute Care Surg. 2012 Jul;73(1):282-5. PMID: 22743396

299. Jorgensen HO, Heier-Madsen K, Stokkebye JE. Casualty rates among Danish soldiers in Iraq and Afghanistan. J R Army Med Corps. 2012 Mar;158(1):10-3. PMID: 22545367

300. Mishwani AH, Ghaffar A, Janjua S. Combat related vascular trauma. J Coll Physicians Surg Pak. 2012 Apr;22(4):213-7. PMID: 22482375

301. Swan KG, Swan KG Jr, Ahearn M. Tourniquets, pressure points, and extremity hemorrhage. Mil Med. 2012 Jan;177(1):6-7. PMID: 22338970

302. Titley P. A topical subject. EBR Eur Biopharm Rev. 2012 Oct;(AUTUMN):56-60.

303. Kheirabadi BS, Terrazas IB, Williams JF, Hanson MA, Dubick MA, Blackbourne LH. Negative-pressure wound therapy: a hemostatic adjunct for control of coagulopathic hemorrhage in large soft tissue wounds. J Trauma Acute Care Surg. 2012 Nov;73(5):1188-94. PMID: 23117379

304. Pasquier P, Renner J, Merat S. Infections and tourniquet application in severe open tibia fractures from combat. J Trauma Acute Care Surg. 2012 Oct;73(4):1033. PMID: 23026921

305. Polk T, Sims C. Rollover car crash almost costs driver his life, limb. JEMS. 2012 Sep;37(9):30-1. PMID: 23342696

306. Jacobs N, Rourke K, Rutherford J, Hicks A, Smith SR, Templeton P, Adams SA, Jansen JO. Lower limb injuries caused by improvised explosive devices: proposed 'Bastion classification' and prospective validation. Injury. 2012 May 19:Epub ahead of print. PMID: 22613453

307. Francesko A, Tzanov T. Chitin, chitosan and derivatives for wound healing and tissue engineering. Adv Biochem Eng Biotechnol. 2011;125:1-27. PMID: 21072697

308. Parker P, Limb Trauma Working Group. Consensus statement on decision making in junctional trauma care. J R Army Med Corps. 2011 Sep;157(3 Suppl 1):S293-5. PMID: 22053391

309. King DR. Thirty consecutive uses of a hemostatic bandage at a US Army combat support hospital and forward surgical team in Operation Iraqi Freedom. J Trauma. 2011 Dec;71(6):1775-8. PMID: 22182888

310. Waibel KH, Haney B, Moore M, Whisman B, Gomez R. Safety of chitosan bandages in shellfish allergic patients. Mil Med. 2011 Oct;176(10):1153-6. PMID: 22128651

311. Rich NM. Vascular trauma historical notes. Perspect Vasc Surg Endovasc Ther. 2011 Mar;23(1):7-12. PMID: 21502112

312. Pohlemann T, Stengel D, Tosounidis G, Reilmann H, Stuby F, Stockle U, Seekamp A, Schmal H, Thannheimer A, Holmenschlager F, Gansslen A, Rommens PM, Fuchs T, Baumgartel F, Marintschev I, Krischak G, Wunder S, Tscherne H, Culemann U. Survival trends and predictors of mortality in severe pelvic trauma: estimates from the German Pelvic Trauma Registry Initiative. Injury. 2011 Oct;42(10):997-1002. PMID: 21513936

313. Metcalfe AJ, Davies K, Ramesh B, O'Kelly A, Rajagopal R. Haemorrhage control in pelvic fractures--a survey of surgical capabilities. Injury. 2011 Oct;42(10):1008-11. PMID: 21247559

314. Yin H, He H, Arbon P, Zhu J. A survey of the practice of nurses' skills in Wenchuan earthquake disaster sites: implications for disaster training. J Adv Nurs. 2011 Oct;67(10):2231-8. PMID: 21615462

315. Dai T, Tanaka M, Huang YY, Hamblin MR. Chitosan preparations for wounds and burns: antimicrobial and wound-healing effects. Expert Rev Anti Infect Ther. 2011 Jul;9(7):857-79. PMID: 21810057

316. Tourtier JP, Jault P, Tazarourte K, Borne M, Bargues L. Tourniquets on the battlefield: could N-acetylcysteine be useful?. J Trauma. 2011 Jul;71(1):264. PMID: 21818040

317. Fox CJ, Perkins JG, Kragh JF Jr, Singh NN, Patel B, Ficke JR. Popliteal artery repair in massively transfused military trauma casualties: a pursuit to save life and limb. J Trauma. 2010 Jul;69 Suppl 1:S123-34. PMID: 20622606

318. Crossley B. Tourniquet systems pose challenges. Biomed Instrum Technol. 2010 Jan-Feb;44(1):34-5. PMID: 20374118

319. Katoch BR, Gambhir CRPS. Warfare vascular injuries. Med J Armed Forces India. 2010 Oct;66(4):338-341.

320. Duncan NS, Moran C. (i) Initial resuscitation of the trauma victim. Orthop Trauma. 2010 Feb;24(1):1-8.

321. Davenport R, Tai N, Walsh M. Vascular trauma. Surgery (Oxford). 2009 Aug;27(8):331-6.

322. Franco P. Alert--watch for "look alike" Combat Application Tourniquet (C.A.T.). J Spec Oper Med. 2009;9(2):136-7. PMID: 19813525

323. von Tersch R, Birch H, Gupta R, Tyner CF. Examining technologies to control hemorrhage by using modeling and simulation to simulate casualties and treatment. Mil Med. 2009 Feb;174(2):109-18. PMID: 19317189

324. Shipman N, Lessard CS. Pressure applied by the emergency/Israeli bandage. Mil Med. 2009 Jan;174(1):86-92. PMID: 19216303

325. Rush Jr RM, Beekley AC, Puttler EG, Kjorstad RJ. The mangled extremity. Curr Probl Surg. 2009 Nov;46(11):851-926.

326. Parker P. Emergency tourniquet use. Ann Surg. 2009 Sep;250(3):496-7. PMID: 19730182

327. Fludger S, Bell A. Tourniquet application in a rural Queensland HEMS environment. Air Med J. 2009 Nov-Dec;28(6):291-3. PMID: 19896580

328. Mullins J, Harrahill M. Use of a tourniquet after a gunshot wound to the thigh. J Emerg Nurs. 2009 Jun;35(3):265-7; quiz 271. Epub 2009 Mar 27. PMID: 19446140

329. Moore FA. Tourniquets: another adjunct in damage control? Ann Surg. 2009 Jan;249(1):8-9. PMID: 19106668

330. Fox CJ, Gillespie DL, Cox ED, Kragh JF Jr, Mehta SG, Salinas J, Holcomb JB. Damage control resuscitation for vascular surgery in a combat support hospital. J Trauma. 2008 Jul;65(1):1-9. PMID: 18580508

331. Gwinn DE, Keeling J, Froehner JW, McGuigan FX, Andersen R. Perioperative differences between bone bridging and non-bone bridging transtibial amputations for wartime lower extremity trauma. Foot Ankle Int. 2008 Aug;29(8):787-93. PMID: 18752776

332. Recinos G, Inaba K, Dubose J, Demetriades D, Rhee P. Local and systemic hemostatics in trauma: a review. Ulus Travma Acil Cerrahi Derg. 2008;14(3):175-81.

333. Blackbourne LH, Mabry R, Sebesta J, Holcomb JB. Joseph Lister, noncompressible arterial hemorrhage, and the next generation of "tourniquets"?. US Army Med Dept J. 2008 Jan-Mar:56-9. PMID: 20091974

334. Perkins JG, Cap AP, Weiss BM, Reid TJ, Bolan CD. Massive transfusion and nonsurgical hemostatic agents. Crit Care Med. 2008 Jul;36(7 Suppl):S325-39. PMID: 18594260

335. Mackenzie CF, Shander A. What to do if no blood is available but the patient is bleeding?. South Afr J Anaesth Analges. 2008 Jan-Feb;14(1):39-43.

336. Nelson TJ, Clark T, Stedje-Larsen ET, Lewis CT, Grueskin JM, Echols EL, Wall DB, Felger EA, Bohman HR. Close proximity blast injury patterns from improvised explosive devices in iraq: a report of 18 cases. J Trauma. J2008 Jul;65(1):212-7.

337. Fan Y, Sun H, Pei G, Ruan C. Haemostatic efficacy of an ethyl-2-cyanoacrylate-based aerosol in combination with tourniquet application in a large wound model with an arterial injury. Injury. 2008 Jan;39(1):61-6. PMID: 18155219

338. Li Z, Zhou G-H, Liu C, Mei Y-J, Ning Z-S, Lu S-M. A multifunctional tourniquet attachment system. J Clin Rehabil Tiss Eng Res. 2008 Feb 22;12(4):794-6.

339. Fox CJ, Starnes BW. Vascular surgery on the modern battlefield. Surg Clin North Am. 2007 Oct;87(5):1193-211. PMID: 17936482

340. Moorhouse I, Thurgood A, Walker N, Cooper B, Mahoney PF, Hodgetts TJ. A realistic model for catastrophic external haemorrhage training. J R Army Med Corps. 2007 Jun;153(2):99-101. PMID: 17896537

341. Bulger EM, Maier RV. Prehospital care of the injured: what's new. Surg Clin North Am. 2007 Feb;87(1):37-53.

342. Kragh JF Jr, Baer DG, Walters TJ. Extended (16-hour) tourniquet application after combat wounds: a case report and review of the current literature. J Orthop Trauma. 2007 Apr;21(4):274-8. PMID: 17414556

343. McManus J, Hurtado T, Pusateri A, Knoop KJ. A case series describing thermal injury resulting from zeolite use for hemorrhage control in combat operations. Prehosp Emerg Care. 2007 Jan 1;11(1):67-71.

344. Laskowski-Jones L. First aid for bleeding wounds. Nursing. 2006 Sep;36(9):50-1. PMID: 16951621

345. Mucciarone JJ, Llewellyn CH, Wightman JM. Tactical combat casualty care in the assault on Punta Paitilla Airfield. Mil Med. 2006 Aug;171(8):687-90. PMID: 16933806

346. Esmarch F. Historical article. J Hand Surg [Br]. 2006 Aug;31(4):390-6.

347. Beekley AC. United States military surgical response to modern large-scale conflicts: the ongoing evolution of a trauma system. Surg Clin North Am. 2006 Jun;86(3):689-709.

348. Ostomel TA, Stoimenov PK, Holden PA, Alam HB, Stucky GD. Host-guest composites for induced hemostasis and therapeutic healing in traumatic injuries. J Thromb Thrombolysis. 2006 Aug;22(1):55-67. PMID: 16786234

349. Owens BD, Wenke JC, Svoboda SJ, White DW. Extremity trauma research in the United States Army. J Am Acad Orthop Surg. 2006;14(10 Spec No.):S37-40. PMID: 17003204

350. Walters TJ, Wenke JC, Greydanus DJ, Kauvar DS, Baer DG. Laboratory evaluation of battlefield tourniquets in human volunteers. Fort Sam Houston (TX): United States Army Institute of Surgical Research; 2005 Sep. 34 p.

351. Hodgetts TJ, Russell RJ, Mahoney PF, Russell MQ, Kenward G. Evaluation of clinician attitudes to the implementation of novel haemostatic techniques. J R Army Med Corps. 2005 Sep;151(3):176-8. PMID: 16440961

352. Holcomb JB. Methods for improved hemorrhage control. Crit Care. 2004 Jun;8 Suppl 2:S57-60. PMID: 15196327

353. Kulkarni R. Alternative and topical approaches to treating the massively bleeding patient. Clin Adv Hematol Oncol. 2004 Jul;2(7):428. PMID: 16163216

354. Guyver PM, Lambert AW. Vascular access on the front line. J Vasc Access Devices. 2004 Sep 21;9(3):142-4.

355. Gansslen A, Giannoudis P, Pape HC. Hemorrhage in pelvic fracture: who needs angiography?. Curr Opin Crit Care. 2003 Dec;9(6):515-23. PMID: 14639072

356. Porter K, Greaves I. Crush injury and crush syndrome: a consensus statement. Emerg Nurse. 2003 Oct;11(6):26-30. PMID: 14603647

357. Becker C. Bloodless coup. Funded by the Army, Oregon researchers turn to the sea to develop a revolutionary bandage that stanches heavy bleeding. Mod Healthc. 2003 Jul 14;33(28):30-1. PMID: 12884716

358. McEwen JA, Kelly DL, Jardanowski T, Inkpen K. Tourniquet safety in lower leg applications. Orthop Nurs. 2002 Sep-Oct;21(5):55-62. PMID: 12432700

359. Scalea T. What's new in trauma in the past 10 years. Int Anesthesiol Clin. 2002;40(3):1-17.

360. Strong DP, Edwards AT. Vascular trauma. Trauma. 2002;4(1):39-63.

361. Blackwood M. Royal Army Medical Corps, 3rd Corps Medical Society. Treatment of wounds from fire trench to field ambulance. 1916. J R Army Med Corps. 2001 Jun;147(2):230-5; discussion 229. PMID: 11469225

362. Rich NM, Rhee P. An historical tour of vascular injury management: from its inception to the new millennium. Surg Clin North Am. 2001;81(6):1199-1215.

363. Yong H, Jianning L. The design and the clinical application of the mini-tourniquet. Eur J Plastic Surg. 2001;24(2):100-1.

364. Sena MJ, Douglas G, Gerlach T, Grayson JK, Pichakron KO, Zierold D. A pilot study of the use of kaolin-impregnated gauze (Combat Gauze) for packing high-grade hepatic injuries in a hypothermic coagulopathic swine model. J Surg Res. 2013 Aug;183(2):704-9. Epub 2013 Mar 13. PMID: 23541814

365. Martin MJ. Editorial to accompany "A pilot study of the use of kaolin-impregnated gauze (Combat Gauze) for packing high-grade hepatic injuries in a hypothermic coagulopathic swine model (JSURGRES-D-12-01536R1). J Surg Res. 2013 Mar 22. pii: S0022-4804(13)00208-4. [Epub ahead of print]. PMID: 23535115

366. Floyd CT, Rothwell SW, Martin R, Risdahl J, Olson CE. A salmon thrombin-fibrinogen dressing controls hemorrhage in a swine model compared to standard kaolin-coated gauze. J Spec Oper Med. 2012 Spring;12(1):49-55. PMID: 22427049

367. Mueller GR, Pineda TJ, Xie HX, Teach JS, Barofsky AD, Schmid JR, Gregory KW. A novel sponge-based wound stasis dressing to treat lethal noncompressible hemorrhage. J Trauma Acute Care Surg. 2012 Aug;73(2 Suppl 1):S134-9. PMID: 22847084

368. De Castro GP, Dowling MB, Kilbourne M, Keledjian K, Driscoll IR, Raghavan SR, Hess JR, Scalea TM, Bochicchio GV. Determination of efficacy of novel modified chitosan sponge dressing in a lethal arterial injury model in swine. J Trauma Acute Care Surg. 2012 Apr;72(4):899-907. PMID: 22491602

369. Charbonneau S, Lemarie CA, Peng HT, Ganopolsky JG, Shek PN, Blostein MD. Surface-attached amphipathic peptides reduce hemorrhage in vivo. J Trauma Acute Care Surg. Jan 2012;72(1):136-42. PMID: 22027883

370. Shukla A, Fang JC, Puranam S, Jensen FR, Hammond PT. Hemostatic multilayer coatings. Adv Mater. 2012 Jan 24;24(4):492-6. PMID: 22223363

371. Seetharaman S, Natesan S, Stowers RS, Mullens C, Baer DG, Suggs LJ, Christy RJ. A PEGylated fibrin-based wound dressing with antimicrobial and angiogenic activity. Acta Biomater. 2011 Jul;7(7):2787-96. PMID: 21515420

372. Dowling MB, Kumar R, Keibler MA, Hess JR, Bochicchio GV, Raghavan SR. A self-assembling hydrophobically modified chitosan capable of reversible hemostatic action. Biomaterials. 2011 May;32(13):3351-7. PMID: 21296412

373. Bowman PD, Wang X, Meledeo MA, Dubick MA, Kheirabadi BS. Toxicity of aluminum silicates used in hemostatic dressings toward human umbilical veins endothelial cells, HeLa cells, and RAW267.4 mouse macrophages. J Trauma. 2011 Sep;71(3):727-732. PMID: 21768911

374. Hirst H, Brinkman J, Beasley A, Crocker R, O'Sullivan J. The effects of blood pressure on rebleeding when using ExcelArrest in a porcine model of lethal femoral injury. J Emerg Trauma Shock. 2011 Apr;4(2):207-11. PMID: 21769207

375. Naimer SA. New era of transparent compression to control bleeding from traumatic wounds: removing the blindfold. Clin Res Regul Affair. 2010 Sep;27(3):82-6.

376. Kranokpiraksa P, Pavcnik D, Kakizawa H, Uchida BT, Jeromel M, Keller FS, Rosch J. Hemostatic efficacy of chitosan-based bandage for closure of percutaneous arterial access sites: An experimental study in heparinized sheep model. Radiol Oncol. 2010 Jun 1;44(2):86-91.

377. Gegel BT, Burgert JM, Lockhart C, Austin R 3rd, Davila A, Deeds J, Hodges L, Hover A, Roy J, Simpson G, Weaver S, Wolfe W, Johnson D. Effects of Celox and TraumaDEX on hemorrhage control in a porcine model. AANA J. 2010 Apr;78(2):115-20. PMID: 20583456

378. Velmahos GC, Tabbara M, Spaniolas K, Duggan M, Alam HB, Serra M, Sun L, de Luis J. Self-expanding hemostatic polymer for control of exsanguinating extremity bleeding. J Trauma. 2009 Apr;66(4):984-8. PMID: 19359903

379. Li J, Yan W, Jing L, Xueyong L, Yuejun L, Wangzhou L, Shaozong C. Addition of an alginate to a modified zeolite improves hemostatic performance in a swine model of lethal groin injury. J Trauma. 2009 Mar;66(3):612-20. PMID: 19276728

380. Walters T, Baer DG, Kauvar DS. A large animal fatal extremity hemorrhage model and evaluation of a polymeric dressing (fatal extremity hemorrhage). J Trauma. 2006 Nov;61(5):1107-12. PMID: 17099515

381. Pusateri AE, Kheirabadi BS, Delgado AV, Doyle JW, Kanellos J, Uscilowicz JM, Martinez RS, Holcomb JB, Modrow HE. Structural design of the dry fibrin sealant dressing and its impact on the hemostatic efficacy of the product. J Biomed Mater Res B Appl Biomater. 2004 Jul 15;70(1):114-21. PMID: 15199591

382. Fischer TH, Connolly R, Thatte HS, Schwaitzberg SS. Comparison of structural and hemostatic properties of the poly-N-acetyl glucosamine Syvek Patch with products containing chitosan. Microsc Res Tech. 2004 Feb 15;63(3):168-74. PMID: 14755604

383. Jewelewicz DD, Cohn SM, Crookes BA, Proctor KG. Erratum to Modified rapid deployment hemostat bandage reduces blood loss and mortality in coagulopathic pigs with severe liver injury (J Trauma Inj Infect Crit Care 2003:55;275-281) J Trauma Inj Infect Crit Care. 2003 Oct;55(4):621.

384. Rothwell SW, Fudge JM, Reid TJ, Krishnamurti C. Epsilon-amino caproic acid additive decreases fibrin bandage performance in a swine arterial bleeding model. Thromb Res Suppl. 2002 Dec 15;108(5-6):341-5. PMID: 12676196

385. Rothwell SW, Fudge JM, Chen WK, Reid TJ, Krishnamurti C. Addition of a propyl gallate-based procoagulant to a fibrin bandage improves hemostatic performance in a swine arterial bleeding model. Thromb Res Suppl. 2002 Dec 15;108(5-6):335-40. PMID: 12676195

386. Gustafson SB, Fulkerson P, Bildfell R, Aguilera L, Hazzard TM. Chitosan dressing provides hemostasis in swine femoral arterial injury model. Prehosp Emerg Care. 2007 Apr-Jun;11(2):172-8. PMID: 17454803

387. Carraway JW, Kent D, Young K, Cole A, Friedman R, Ward KR. Comparison of a new mineral based hemostatic agent to a commercially available granular zeolite agent for hemostasis in a swine model of lethal extremity arterial hemorrhage. Resuscitation. 2008 Aug;78(2):230-5. PMID: 18485561

388. Zhang R, Shen L, Xie Y, Gen L, Li X, Ji Q. Effect of morphine-induced postconditioning in corrections of tetralogy of fallot. J Cardiothorac Surg. 2013 Apr 11;8(1):76. PMID: 23577699

389. MacIntyre AD, Quick JA, Barnes SL. Hemostatic dressings reduce tourniquet time while maintaining hemorrhage control. Am Surg. 2011 Feb;77(2):162-5. PMID: 21337872

390. Devlin JJ, Kircher S, Kozen BG, Littlejohn LF, Johnson AS. Comparison of ChitoFlex, CELOXTM, and QuikClot in control of hemorrhage. J Emerg Med. 2011 Sep;41(3):237-45. PMID: 19345045

391. Littlejohn LF, Devlin JJ, Kircher SS, Lueken R, Melia MR, Johnson AS. Comparison of Celox-A, ChitoFlex, WoundStat, and combat gauze hemostatic agents versus standard gauze dressing in control of hemorrhage in a swine model of penetrating trauma. Acad Emerg Med. 2011 Apr;18(4):340-50. PMID: 21496135

392. Watters JM, Van PY, Hamilton GJ, Sambasivan C, Differding JA, Schreiber MA. Advanced hemostatic dressings are not superior to gauze for care under fire scenarios. J Trauma. 2011 Jun;70(6):1413-9. PMID: 21817978

393. Kheirabadi BS, Mace JE, Terrazas IB, Fedyk CG, Valdez KK, MacPhee MJ, Beall D, Estep JS, Dubick MA, Blackbourne LH. Clot-inducing minerals versus plasma protein dressing for topical treatment of external bleeding in the presence of coagulopathy. J Trauma. 2010 Nov;69(5):1062-72; discussion 1072-. PMID: 21068612

394. Kilbourne M, Keledjian K, Hess JR, Scalea T, Bochicchio GV. Hemostatic efficacy of modified amylopectin powder in a lethal porcine model of extremity arterial injury. Ann Emerg Med. 2009 Jun;53(6):804-10. PMID: 19321227

395. Connolly RJ. Application of the poly-N-acetyl glucosamine-derived rapid deployment hemostat trauma dressing in severe/lethal Swine hemorrhage trauma models. J Trauma. 2004 Jul;57(1 Suppl):S26-8. PMID: 15280747

396. Arnaud F, Parreno-Sadalan D, Tomori T, Delima MG, Teranishi K, Carr W, McNamee G, McKeague A, Govindaraj K, Beadling C, Lutz C, Sharp T, Mog S, Burris D, McCarron R. Comparison of 10 hemostatic dressings in a groin transection model in swine. J Trauma. 2009 Oct;67(4):848-55. PMID: 19820595

397. Arnaud F, Tomori T, Carr W, McKeague A, Teranishi K, Prusaczyk K, McCarron R. Exothermic reaction in zeolite hemostatic dressings: QuikClot ACS and ACS+. Ann Biomed Eng. 2008 Oct;36(10):1708-13. PMID: 18712606

398. Nowshad N, Saghafinia M, Panahi F, Bolandparvaz S, Tanideh N. Comparison of the efficacy of two local haemostatic agents. Trauma Monthly. 2011 Dec;16(4):188-90.

399. Burgert J, Gegel B, Neal AR, Kammer KE, Paul ME, Schwartz DJ, Loughren M, Johnson A. The effects of arterial blood pressure on rebleeding when BleedArrest, Celox and TraumaDex are used in a porcine model of lethal femoral injury. Mil Med. 2012 Mar;177(3):340-4. PMID: 22479924

400. Gegel B, Burgert J, Cooley B, MacGregor J, Myers J, Calder S, Luellen R, Loughren M, Johnson D. The effects of BleedArrest, Celox, and TraumaDex on hemorrhage control in a porcine model. J Surg Res. 2010 Nov;164(1):e125-9. PMID: 20863522

401. Gegel B, Burgert J, Loughren M, Johnson D. The effects of BleedArrest on hemorrhage control in a porcine model. US Army Med Dept J. 2012 Oct-Dec;:31-5. PMID: 23007934

402. Burgert JM, Gegel BT, Austin R 3rd, Davila A, Deeds J, Hodges L, Hover A, Lockhart C, Roy J, Simpson G, Weaver S, Wolfe W, Johnson D. Effects of arterial blood pressure on rebleeding using Celox and TraumaDEX in a porcine model of lethal femoral injury. AANA J. 2010 Jun;78(3):230-6. PMID: 20572410

403. Lyon M, Shiver SA, Greenfield EM, Reynolds BZ, Lerner EB, Wedmore IS, Schwartz RB. Use of a novel abdominal aortic tourniquet to reduce or eliminate flow in the common femoral artery in human subjects. J Trauma Acute Care Surg. 2012 Aug;73(2 Suppl 1):S103-5. PMID: 22847077

404. Koller H, Keil P, Seibert F. Individual and team training with first time users of the Pelvic C-Clamp: do they remember or will we need refresher trainings?. Arch Orthop Trauma Surg. 2013 Mar;133(3):343-9. PMID: 23229458

405. Koller H, Balogh ZJ. Single training session for first time pelvic C-clamp users: correct pin placement and frame assembly. Injury. 2012 Apr;43(4):436-9. PMID: 21733509

Appendix A. Methods of Identifying the Literature

ECRI Institute information specialists searched the following databases for relevant information.

Table A.1. Resources to be searched

Name	Date Limits	Platform/Provider
Bibliographic Databases		
The Cochrane Central Register of Controlled Trials (CENTRAL)	2001 through 2013	Wiley
The Cochrane Health Technology Assessment Database	2001 through 2013	Wiley
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	2001 through 2013	Wiley
Cochrane Database of Abstracts of Reviews of Effectiveness (DARE)	2001 through 2013	Wiley
Cumulative Index of Nursing and Allied Health Literature (CINAHL)	2001 through 2013	EBSCOhost
EMBASE (Excerpta Medica)	2001 through 2013	OVIDSP
MEDLINE	2001 through 2013	OVIDSP
PUBMED (PreMEDLINE)	2013	NLM
U.K. National Health Service Economic Evaluation Database (NHS EED)	2001 through 2013	Wiley
Gray Literature Resources		
ClinicalTrials.gov	Through 2013	NIH
ECRI Institute Library Catalog	2001 through 2013	ECRI Institute
Health Devices	2001 through 2013	ECRI Institute
Healthcare Standards	2001 through 2013	ECRI Institute
Internet	2001 through 2013	Google
Manufacturer Web sites:	2013	
Medscape	Through 2013	WebMD
National Guideline Clearinghouse (NGC)	Through 2013	AHRQ
U.S. Food and Drug Administration (FDA), including Medical Device databases/Drugs@FDA	Through 2013	FDA

Hand Searches of Journal and Gray Literature

Journals and supplements maintained in ECRI Institute's collections were reviewed. Nonjournal publications and conference proceedings from professional organizations, private agencies, and government agencies were also be screened. Other mechanisms used to retrieve additional relevant information include review of bibliographies/reference lists from peer-reviewed and gray literature. (Gray literature consists of reports, studies, articles, and monographs produced by Federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations. These documents do not appear in the peer-reviewed journal literature.)

Topic-specific Search Terms

The search strategies employ combinations of free-text keywords as well as controlled vocabulary terms including, but not limited to, the following concepts. Strategies for EMBASE and MEDLINE bibliographic database follow this table.

Table A.2. Medical Subject Headings (MeSH), EMTREE, CINAHL, and keywords*

Concept	Controlled Vocabulary	Keywords
Pre-hospital emergency setting or population (combat, disaster, vehicle accident, military, first responders)	**MEDLINE (MeSH)** accidents/ accidents, traffic/ disasters/ advanced trauma life support care/ emergency medical services/ exp emergency responders/ exp emergency treatment/ emergencies/ field hospitals/ military medicine/ triage/ military personnel/ war/ veterans/ veterans health/ **EMBASE (EMTREE)** exp accident/ air force/ ambulance/ army/ disaster medicine/ exp emergency care/ emergency health service/ exp emergency treatment/ field hospital/ military medicine/ navy/ rescue personnel/ soldier/ traffic accident/ veteran/ veterans health/ exp war/ **CINAHL** MH "accidents, traffic" MH "Aeromedical Transport" MH "Ambulances" MH "Emergency Medical Services+" MH "Emergency Service+" MH "Emergency Patients" MH "War+" MH "Hospitals, Military" MH "Military Medicine" MH "Military Personnel+"	accident$ ((afghan OR Afghanistan OR Iraq$) and (war or conflict)) air force ambulance$ armed forces army battle$ ((car OR auto OR automobile OR vehicle) adj2 (crash$ or accident$)) casualt$ "care under fire" combat disaster$ emergency medical services EMT emergency medical technician$ emergency responder$ "in the field" "field triage" firefight$ first responder$ "Iraq war" "Iraqi freedom" life support marines medic medics military naval navy "pre hospital" "pre-hospital" "prehospital" police$ rescue soldier$ "tactical combat casualty care" trauma triage veteran$ victim victims war

Concept	Controlled Vocabulary	Keywords
	MH "Military Services+" MH "Military Nursing" MH "Veterans+" MH "Victims" MH "Disasters+" MH "Police" MH "Firefighters" MH "Prehospital Care"	
Hemorrhage	**MEDLINE (MESH)** blast injuries/ exp hemorrhage/ lacerations/ multiple trauma/ exp Wounds and injuries/ wounds, penetrating/ wounds, stab/ wounds, gunshot/ **EMBASE (EMTREE)** Exp bleeding/ exp injury perforation/ penetrating trauma/ stab wound/ gunshot injury/ crush trauma/ laceration/ **CINAHL** MH "Hemorrhage+" MH "Trauma+" MH "Wounds and Injuries+" MH "Wounds, penetrating" MH "wounds, stab" MH "wounds, gunshot" MH "tears and lacerations" MH "multiple trauma"	bleed$ exsanguinat$ haemorrhag$ hemorrhag$ injury injuries injured wound$ gunshot$ lacerat$
Tourniquet	**MEDLINE (MESH)** tourniquets/ **EMBASE (EMTREE)** tourniquet/ **CINAHL** MH "Tourniquets"	"combat application tourniquet" "combat application tourniquets" "combat ready clamp" "croc" "junctional hemorrhage control" clamp* "SOFTT" "SOF tactical tourniquet" "soft t" "soft-t" "sof t" "sof-t" "TK4" "TK-4" "TK 4" "Tourni kwik" "tourni-kwik" tourniquet$

Concept	Controlled Vocabulary	Keywords
Dressings	**MEDLINE (MESH)** Exp bandages/ **EMBASE (EMTREE)** exp "bandages and dressings"/ **CINAHL** MH "Bandages and Dressings+" MH "Tapes+"	bandag$ dressing$ gauze$ sponge sponges tape tapes taping
Hemostasis	**MEDLINE (MESH)** exp blood coagulation factors/ fibrin tissue adhesive/ exp hemostasis/ exp hemostatics/ exp hemostatic techniques **EMBASE (EMTREE)** exp blood clotting/ Exp hemostatic agent/ hemostasis/ **CINAHL** MH "Hemostasis+" MH "Hemostatics+"	chitosan chito$ clot clotting clots coagulat$ fibrinolysis (fibrin AND (seal OR adhesive)) hemostas$ hemostat$ stasis staunch$
Hemostatic Dressings (product names)		BioHemostat CELOX$ "Combat Gauze" Chitogauze "chito gauze" HemCon "modified rapid deployment hemostat" "MRDH" QuikCLot TraumaDEX Woundstat

*Exp or + = “explodes” controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary’s hierarchy)

/ or MH = denotes a controlled subject heading

$ = truncation

Search Strategy

Table A.3. Embase/MEDLINE (presented in OVID syntax)

Set #	Concept	Search Statement
1	Prehospital (emergency, combat, disaster, trauma) – Controlled Terms	accidents/ OR accidents, traffic/ OR disasters/ OR advanced trauma life support care/ OR emergency medical services/ OR exp emergency responders/ OR exp emergency treatment/ OR emergencies/ OR field hospitals/ OR military medicine/ OR triage/ OR military personnel/ OR war/ OR veterans/ OR veterans health/ OR exp accident/ OR air force/ OR ambulance/ OR army/ OR disaster medicine/ OR exp emergency care/ OR emergency health service/ OR exp emergency treatment/ OR field hospital/ OR military medicine/ OR navy/ OR rescue personnel/ OR soldier/ OR traffic accident/ OR veteran/ OR veterans health/ OR exp war/
2	Prehospital (emergency, combat, disaster, trauma) – keywords	accident$ OR ((afghan OR Afghanistan OR Iraq$) and (war or conflict)) OR air force OR ambulance$ OR armed forces OR army OR battle$ OR ((car OR auto OR automobile OR vehicle) adj2 (crash$ or accident$)) OR casualt$ OR "care under fire" OR combat OR disaster$ OR emergency medical services OR EMT OR emergency medical technician$ OR emergency responder$ OR "in the field" OR "field triage" OR firefight$ OR first responder$ OR "Iraq war" OR "Iraqi freedom" OR life support OR marines OR medic OR medics OR military OR naval OR navy OR "pre hospital" OR "pre-hospital" OR "prehospital" OR police$ OR rescue OR soldier$ OR "tactical combat casuality care" OR trauma OR triage OR veteran$ OR victim OR victims OR war
3	Combine sets – prehospital setting	1 OR 2
4	Hemorrhage (due to injury) – Controlled terms	blast injuries/ OR exp hemorrhage/ OR lacerations/ OR multiple trauma/ OR exp Wounds and injuries/ OR wounds, penetrating/ OR wounds, stab/ OR wounds, gunshot/ OR Exp bleeding/ OR exp injury OR perforation/ OR penetrating trauma/ OR stab wound/ OR gunshot injury/ OR crush trauma/ OR laceration/
5	Hemorrhage (due to injury) – Keywords	bleed$ OR exsanguinat$ OR haemorrhag$ OR hemorrhag$ OR injury OR injuries OR injured OR wound$ OR gunshot$ OR lacerat$
6	Combine sets - Hemorrhage	4 OR 5
7	Tourniquets - controlled terms and keywords	tourniquets/ OR tourniquet/ OR "combat application tourniquet" OR "combat application tourniquets" OR "combat ready clamp" OR "croc" OR "junctional hemorrhage control" OR clamp* OR "SOFTT" OR "SOF tactical tourniquet" OR "soft t" OR "soft-t" OR "sof t" OR "sof-t" OR "TK4" OR "TK-4" OR "TK 4" OR "Tourni kwik" OR "tourni-kwik" OR tourniquet$
8	Hemostatic dressings – controlled terms and keywords	(exp bandages/ OR exp "bandages and dressings"/ OR bandag$ OR dressing$ OR gauze$ OR tape OR tapes OR taping OR sponge OR sponges) AND (exp hemostasis/ OR exp hemostatics/ OR exp hemostatic techniques OR fibrin tissue adhesive/ OR exp blood coagulation factors/ OR exp hemostatic agent/ OR exp blood clotting/ OR chitosan OR chito$ OR clot OR clotting OR clots OR coagulat$ OR fibrinolysis OR (fibrin AND (seal OR adhesive)) OR hemostat$ OR hemostas$ OR stasis OR staunch$)
9	Hemostatic dressings – product names	BioHemostat OR celox$ OR "Combat Gauze" OR Chitogauze OR “chito gauze” OR HemCon OR “modified rapid deployment hemostat” OR "MRDH" OR quikclot OR traumadex OR woundstat
10	Combine sets - Hemostatic dressings	8 OR 9
11	Combine sets	3 AND 6 AND (7 OR 10)
12	Limit to English language	Limit 11 to English language
13	Limit to publication year	Limit 12 to yr="2001-Current"

Set #	Concept	Search Statement
14	Exclude unwanted publication types	13 NOT (book/ OR edited book/ OR case report/ OR case reports/ OR comment/ OR conference abstract/ OR conference paper/ OR conference review/ OR editorial/ OR letter/ OR news/ OR note/ OR proceeding/ OR (book OR edited book OR case report OR case reports OR comment OR conference OR editorial OR letter OR news OR note OR proceeding).pt.)
		Additional terms were added as necessary to restrict retrieval to specific study designs (human, animal, controlled trials, systematic reviews, guidelines, etc.)

OVID SYNTAX

$ or * = truncation character (wildcard)

ADJ*n* = search terms within a specified number (*n*) of words from each other in any order

/ = search as a subject heading (note that terms preceded by an asterisk are searched as a major subject headings)

exp = "explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)

.de. = limit controlled vocabulary heading

.fs. = floating subheading

.hw. = limit to heading word

.mp. = combined search fields (default if no fields are specified)

.pt. = publication type

.ti. = limit to title

.tw. = limit to title and abstract fields

Appendix B. Excluded Articles

Table B.1. Articles excluded at the abstract level

Reference	Year of Publication	Authors	Title of Article
[102]	2013	Zentai, C., Grottke, O., Spahn, D. R., and Rossaint, R.	Nonsurgical Techniques to Control Massive Bleeding
[103]	2013	Moriwaki, Y., Toyoda, H., Harunari, N., Iwashita, M., Kosuge, T., Arata, S., and Suzuki, N.	Gauze packing as damage control for uncontrollable haemorrhage in severe thoracic trauma
[104]	2013	Fitzpatrick, G. M., Cliff, R., and Tandon, N.	Thrombosomes: a platelet-derived hemostatic agent for control of noncompressible hemorrhage
[105]	2013	Riha, G. A. and Schreiber, M. A.	Update and new developments in the management of the exsanguinating patient
[106]	2013	Adkins, C. L.	Wound care dressings and choices for care of wounds in the home
[107]	2013	Abrassart, S., Stern, R., and Peter, R.	Unstable pelvic ring injury with hemodynamic instability: what seems the best procedure choice and sequence in the initial management
[108]	2013	Inaba, K., Branco, B. C., Rhee, P., Putty, B., Okoye, O., Barmparas, G., Talving, P., and Demetriades, D.	Long-term preclinical evaluation of the intracorporeal use of advanced local hemostatics in a damage-control swine model of grade IV liver injury
[109]	2013	Phaneuf, M. D., Bide, M. J., Hannel, S. L., Platek, M. J., Monahan, T. S., Contreras, M. A., Phaneuf, T. M., and LoGerfo, F. W.	Development of an infection-resistant, bioactive wound dressing surface
[110]	2013	Nitecki, S. S., Karram, T., Ofer, A., Engel, A., and Hoffman, A.	Management of combat vascular injuries using modern imaging: Are we getting better?
[111]	2013	Muthukumar, T., Senthil, R., and Sastry, T. P.	Synthesis and characterization of biosheet impregnated with Macrotyloma uniflorum extract for burn/wound dressings
[112]	2013	Sellei, R. M., Schandelmaier, P., Kobbe, P., Knobe, M., and Pape, H. C.	Can a Modified Anterior External Fixator Provide Posterior Compression of AP Compression Type III Pelvic Injuries
[113]	2013	Carr, D., Kieser, J., Mabbott, A., Mott, C., Champion, S., and Girvan, E.	Damage to apparel layers and underlying tissue due to hand-gun bullets
[114]	2013	Metsemakers, W. J., Vanderschot, P., Jennes, E., Nijs, S., Heye, S., and Maleux, G.	Transcatheter embolotherapy after external surgical stabilization is a valuable treatment algorithm for patients with persistent haemorrhage from unstable pelvic fractures: Outcomes of a single centre experience
[115]	2013	Boonkong, W., Petsom, A., and Thongchul, N.	Rapidly stopping hemorrhage by enhancing blood clotting at an opened wound using chitosan/polylactic acid/polycaprolactone wound dressing device
[116]	2013	Wu, J., Lemarie, C. A., Barralet, J., and Blostein, M. D.	Amphiphilic peptide-loaded nanofibrous calcium phosphate microspheres promote hemostasis in vivo
[117]	2012	Pavic, R. and Margetic, P.	Emergency treatment for clinically unstable patients with pelvic fracture and haemorrhage
[118]	2012	Gansslen, A., Hildebrand, F., and Pohlemann, T.	Management of hemodynamic unstable patients "in extremis" with pelvic ring fractures

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[119]	2012	Hauschild, O., Aghayev, E., von, Heyden J., Strohm, P. C., Culemann, U., Pohlemann, T., Suedkamp, N. P., and Schmal, H.	Angioembolization for pelvic hemorrhage control: results from the German pelvic injury register
[120]	2012	Pohlemann, T., Culemann, U., and Holstein, J. H.	Initial experience using a pelvic emergency simulator to train reduction in blood loss
[121]	2012	Daruwalla, Z. J., Rowan, F., Finnegan, M., Fennell, J., and Neligan, M.	Exsanguinators and tourniquets: do we need to change our practice?
[122]	2012	Percival, T. J. and Rasmussen, T. E.	Reperfusion strategies in the management of extremity vascular injury with ischaemia
[123]	2012	Gruen, R. L., Brohi, K., Schreiber, M., Balogh, Z. J., Pitt, V., Narayan, M., and Maier, R. V.	Haemorrhage control in severely injured patients
[124]	2012	Palmier, B.	[Conditions for the survival of combat casualties in overseas operations: procedure and experience from the Afghan out-of-hospital theater]
[125]	2012	Travers, S., Dubourg, O., Ribeiro, Parenti L., Lefort, H., Albarello, S., and Domanski, L.	[Prehospital use of haemostatic dressing QuikClot ACS+ for hemorrhage control of a perineal trauma]
[126]	2012	Yang, J. H., Lim, H., Yoon, J. R., and Jeong, H. I.	Tourniquet associated chemical burn
[127]	2012	Du, L., Tong, L., Jin, Y., Jia, J., Liu, Y., Su, C., Yu, S., and Li, X.	A multifunctional in situ-forming hydrogel for wound healing
[128]	2012	Hu, G., Xiao, L., Tong, P., Bi, D., Wang, H., Ma, H., Zhu, G., and Liu, H.	Antibacterial hemostatic dressings with nanoporous bioglass containing silver
[129]	2012	Morrison, J. J., Percival, T. J., Markov, N. P., Villamaria, C., Scott, D. J., Saches, K. A., Spencer, J. R., and Rasmussen, T. E.	Aortic balloon occlusion is effective in controlling pelvic hemorrhage
[130]	2012	Korkmaz, T., Sarikas, N. G., Kilicgun, A., Serin, E., and Boran, C.	The mechanism of activity of ankaferd blood stopper in the control of arterial bleeding and in the process of wound healing
[127]	2012	Du, L., Tong, L., Jin, Y., Jia, J., Liu, Y., Su, C., Yu, S., and Li, X.	A multifunctional in situforming hydrogel for wound healing
[131]	2012	Xie, H., Lucchesi, L., Teach, J. S., and Virmani, R.	Long-term outcomes of a chitosan hemostatic dressing in laparoscopic partial nephrectomy
[132]	2012	Shoffstall, A. J., Atkins, K. T., Groynom, R. E., Varley, M. E., Everhart, L. M., Lashof-Sullivan, M. M., Martyn-Dow, B., Butler, R. S., Ustin, J. S., and Lavik, E. B.	Intravenous hemostatic nanoparticles increase survival following blunt trauma injury
[133]	2011	Hansen, A., McMillan, L., Morrison, A., Petrik, J., and Bradley, M.	Polymers for the rapid and effective activation and aggregation of platelets
[134]	2011	Wigginton, J. G., Roppolo, L., and Pepe, P. E.	Advances in resuscitative trauma care

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[135]	2011	Rtshiladze, M. A., Andersen, S. P., Nguyen, D. Q., Grabs, A., and Ho, K.	The 2009 Sydney shark attacks: case series and literature review
[136]	2011	Kubiak, B. D., Albert, S. P., Gatto, L. A., Vieau, C. J., Roy, S. K., Snyder, K. P., Maier, K. G., and Nieman, G. F.	A clinically applicable porcine model of septic and ischemia/reperfusion-induced shock and multiple organ injury
[137]	2011	Clamp, J. A. and Moran, C. G.	Haemorrhage control in pelvic trauma
[138]	2011	Lustenberger, T., Meier, C., Benninger, E., Lenzlinger, P. M., and Keel, M. J.	C-clamp and pelvic packing for control of hemorrhage in patients with pelvic ring disruption
[139]	2011	Razavi, S., Ardakani, H. Z., Rajai, S., Hollisaz, M., Sadeghipoor, H., Farshad, A., Shojaeezadeh, D., and Khodai, G.	Trends in Prevalent Injuries among Iranian Pilgrims in Hajj
[140]	2011	Dregelid, E. B. and Pedersen, G.	Treatment of major vein injury with the hemostatic fleece TachoSil by interposing a peritoneal patch to avoid vein thrombosis: A feasibility study in pigs
[141]	2011	Valentine, R., Boase, S., Jervis-Bardy, J., Dones Cabral, J. D., Robinson, S., and Wormald, P. J.	The efficacy of hemostatic techniques in the sheep model of carotid artery injury
[142]	2011	Inaba, K., Rhee, P., Teixeira, P. G., Barmparas, G., Putty, B., Branco, B. C., Cohn, S., and Demetriades, D.	Intracorporeal use of advanced local hemostatics in a damage control swine model of grade IV liver injury
[143]	2011	White, J. M., Cannon, J. W., Stannard, A., Burkhardt, G. E., Spencer, J. R., Williams, K., Oh, J. S., and Rasmussen, T. E.	Direct vascular control results in less physiologic derangement than proximal aortic clamping in a porcine model of noncompressible extrathoracic torso hemorrhage
[144]	2011	Grottke, O., Braunschweig, T., Daheim, N., Coburn, M., Grieb, G., Rossaint, R., and Tolba, R.	Effect of TachoSil in a coagulopathic pig model with blunt liver injuries
[145]	2011	De Castro, G. P., MacPhee, M. J., Driscoll, I. R., Beall, D., Hsu, J., Zhu, S., Hess, J. R., Scalea, T. M., and Bochicchio, G. V.	New hemostatic dressing (FAST Dressing) reduces blood loss and improves survival in a grade V liver injury model in noncoagulopathic swine
[146]	2011	White, J. M., Cannon, J. W., Stannard, A., Spencer, J. R., Hancock, H., Williams, K., Oh, J. S., and Rasmussen, T. E.	A porcine model for evaluating the management of noncompressible torso hemorrhage
[147]	2011	Schnuriger, B., Inaba, K., Barmparas, G., Rhee, P., Putty, B., Branco, B. C., Talving, P., and Demetriades, D.	A new survivable damage control model including hypothermia, hemodilution, and liver injury
[148]	2011	Spector, D., Perry, Z., Konobeck, T., Mooradian, D., and Shikora, S.	Comparison of hemostatic properties between collagen and synthetic buttress materials used in staple line reinforcement in a swine splenic hemorrhage model

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[149]	2011	Pick, D. L., Kolla, S. B., Mucksavage, P., Louie, M. K., Sountoulides, P., Kaufmann, O., Olamendi, S., Kaplan, A., Huynh, V., Ortiz-Vanderdys, C., Truong, H. P., Said, S. A., Andrade, L., Tongson-Ignacio, J., McDougall, E. M., and Clayman, R. V.	Sprayed fibrin sealant as the sole hemostatic agent for porcine laparoscopic partial nephrectomy
[150]	2011	Anilkumar, T. V., Muhamed, J., Jose, A., Jyothi, A., Mohanan, P. V., and Krishnan, L. K.	Advantages of hyaluronic acid as a component of fibrin sheet for care of acute wound
[151]	2011	Hutchinson, R. W., Broughton, D., Barbolt, T. A., Poandl, T., Muench, T., Rockar, R., Johnson, M., and Hart, J.	Hemostatic effectiveness of Fibrin pad after partial nephrectomy in swine
[152]	2011	Lu, C.-R., Chen, L., Chen, W.-B., Dou, C.-Q., Liu, R., and Huang, Z.-Q.	Absorbable bandage wrapping in treatment of severe blast liver injury: A miniature swine model
[153]	2010	Jagodzinski, N. A., Weerasinghe, C., and Porter, K.	Crush injuries and crush syndrome - A review. Part 1: The systemic injury
[154]	2010	Williams-Johnson, J., Williams, E., and Watson, H.	Management and Treatment of Pelvic and Hip Injuries
[155]	2010	Feliciano, D. V.	Management of peripheral arterial injury
[156]	2010	Kheirabadi, B. S., Mace, J. E., Terrazas, I. B., Fedyk, C. G., Estep, J. S., Dubick, M. A., and Blackbourne, L. H.	Safety evaluation of new hemostatic agents, smectite granules, and kaolin-coated gauze in a vascular injury wound model in swine
[157]	2010	Estrera, A. L., Gochnour, D. C., Azizzadeh, A., Miller, C. C., III, Coogan, S., Charlton-Ouw, K., Holcomb, J. B., and Safi, H. J.	Progress in the treatment of blunt thoracic aortic injury: 12-year single-institution experience
[158]	2010	Pollak, A. N., Powell, E. T., Fang, R., Cooper, E. O., Ficke, J. R., and Flaherty, S. F.	Use of negative pressure wound therapy during aeromedical evacuation of patients with combat-related blast injuries
[159]	2010		Silver dressings - Do they work?
[160]	2010	Sinha, C. V. K. and Anand, L. C. S.	Extremity and orthopaedic injuries
[161]	2010	Dubose, J., Inaba, K., Barmparas, G., Teixeira, P. G., Schnuriger, B., Talving, P., Salim, A., and Demetriades, D.	Bilateral internal iliac artery ligation as a damage control approach in massive retroperitoneal bleeding after pelvic fracture
[162]	2010	Khashayar, P., Amoli, H. A., Tavakoli, H., and Panahi, F.	Efficacy of prehospital care in trauma patients in Iran
[163]	2010	Mylankal, K. J. and Wyatt, M. G.	Control of major haemorrhage
[164]	2010	Peng, H. T. and Shek, P. N.	Novel wound sealants: Biomaterials and applications
[165]	2010	Ahmad, Z.	Playing with fire and getting burnt-A retrospective analysis of injuries presenting to the emergency department during 'firework season'
[166]	2010	Rich, P. B., Douillet, C., Buchholz, V., Overby, D. W., Jones, S. W., and Cairns, B. A.	Use of the novel hemostatic textile Stasilon(R) to arrest refractory retroperitoneal hemorrhage: a case report

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[167]	2010	Takacs, I., Wegmann, J., Horvath, S., Ferencz, A., Ferencz, S., Javor, S., Odermatt, E., Roth, E., and Weber, G.	Efficacy of different hemostatic devices for severe liver bleeding: a randomized controlled animal study
[168]	2010	Rothwell, S. W., Settle, T., Wallace, S., Dorsey, J., Simpson, D., Bowman, J. R., Janmey, P., and Sawyer, E.	The long term immunological response of swine after two exposures to a salmon thrombin and fibrinogen hemostatic bandage
[169]	2010	Millner, R., Lockhart, A. S., and Marr, R.	Chitosan arrests bleeding in major hepatic injuries with clotting dysfunction: an in vivo experimental study in a model of hepatic injury in the presence of moderate systemic heparinisation
[170]	2010	Bochicchio, G. V., Kilbourne, M. J., Keledjian, K., Hess, J., and Scalea, T.	Evaluation of a new hemostatic agent in a porcine grade V liver injury model
[171]	2010	Grottke, O., Braunschweig, T., Philippen, B., Gatzweiler, K. H., Gronloh, N., Staat, M., Rossaint, R., and Tolba, R.	A new model for blunt liver injuries in the swine
[172]	2010	Gu, R., Sun, W., Zhou, H., Wu, Z., Meng, Z., Zhu, X., Tang, Q., Dong, J., and Dou, G.	The performance of a fly-larva shell-derived chitosan sponge as an absorbable surgical hemostatic agent
[173]	2010	Hammes, C., Moersdorf, G., Refeidi, A., Post, S., and Kaehler, G.	Endoscopic application of hemostatic thrombin-gelatin matrix (FloSeal) in anticoagulated pigs
[174]	2010	Stratos, I., Graff, J., Rotter, R., Mittlmeier, T., and Vollmar, B.	Open blunt crush injury of different severity determines nature and extent of local tissue regeneration and repair
[175]	2010	Aysan, E., Bektas, H., Ersoz, F., Sari, S., Kaygusuz, A., and Huq, G. E.	Ability of the ankaferd blood stopper to prevent parenchymal bleeding in an experimental hepatic trauma model
[176]	2010	Spiro, D. M., Zonfrillo, M. R., and Meckler, G. D.	Wounds
[177]	2009	du-Frimpong, J.	Genitourinary Trauma in Boys
[178]	2009	Claudet, I., Pasian, N., Debuisson, C., Salanne, S., and Rekhroukh, H.	Tourniquet syndrome: interest of a systematic analysis of families' social conditions to detect neglect situations
[179]	2009	Van Natta, T. L., Smith, B. R., Bricker, S. D., and Putnam, B. A.	Hilar control in penetrating chest trauma: a simplified approach to an underutilized maneuver
[180]	2009	Richard, M. J. and Tornetta, P., III	Emergent management of APC-2 pelvic ring injuries with an anteriorly placed C-clamp
[181]	2009	Chalkias, A. F.	Prehospital emergency thoracotomy: When to do it?
[182]	2009	Berend, K. and Levi, M.	Management of Adult Jehovah's Witness Patients with Acute Bleeding
[183]	2009	Barnard, A. R. and Allison, K.	The classification and principles of management of wounds in trauma
[184]	2009	Bochicchio, G., Kilbourne, M., Kuehn, R., Keledjian, K., Hess, J., and Scalea, T.	Use of a modified chitosan dressing in a hypothermic coagulopathic grade V liver injury model
[185]	2009	Wang, Y. and Lu, W.	[The study and clinical application of absorbable hemostatic agent]

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[186]	2009	Clay, J. G., Zierold, D., Grayson, K., and Battistella, F. D.	Dextran polymer hemostatic dressing improves survival in liver injury model
[187]	2009	Adams, G. L., Manson, R. J., Hasselblad, V., Shaw, L. K., and Lawson, J. H.	Acute in-vivo evaluation of bleeding with Gelfoam plus saline and Gelfoam plus human thrombin using a liver square lesion model in swine
[188]	2009	Xie, H., Teach, J. S., Burke, A. P., Lucchesi, L. D., Wu, P. C., and Sarao, R. C.	Laparoscopic repair of inferior vena caval injury using a chitosan-based hemostatic dressing
[189]	2009	Bjorses, K. and Holst, J.	Topical haemostatics in renal trauma--an evaluation of four different substances in an experimental setting
[190]	2009	Bilgili, H., Kosar, A., Kurt, M., Onal, I. K., Goker, H., Captug, O., Shorbagi, A., Turgut, M., Kekilli, M., Kurt, O. K., Kirazli, S., Aksu, S., and Haznedaroglu, I. C.	Hemostatic efficacy of ankaferd blood stopper in a swine bleeding model
[191]	2009	Bertram, J. P., Williams, C. A., Robinson, R., Segal, S. S., Flynn, N. T., and Lavik, E. B.	Intravenous hemostat: nanotechnology to halt bleeding
[192]	2009	Fischer, T. H., Vournakis, J. N., Manning, J. E., McCurdy, S. L., Rich, P. B., Nichols, T. C., Scull, C. M., McCord, M. G., Decorta, J. A., Johnson, P. C., and Smith, C. J.	The design and testing of a dual fiber textile matrix for accelerating surface hemostasis
[193]	2009	Liu, Y., Kopelman, D., Wu, L. Q., Hijji, K., Attar, I., Preiss-Bloom, O., and Payne, G. F.	Biomimetic sealant based on gelatin and microbial transglutaminase: an initial in vivo investigation
[194]	2008	Kheirabadi, B. S., Sieber, J., Bukhari, T., Rudnicka, K., Murcin, L. A., and Tuthill, D.	High-pressure fibrin sealant foam: an effective hemostatic agent for treating severe parenchymal hemorrhage
[195]	2008	Chirinos, F. S.	Local doctor creates clothing with tourniquets for troops
[196]	2008	Shokrollahi, K., Sharma, H., and Gakhar, H.	A technique for temporary control of hemorrhage
[197]	2008	Hong, J. P., Kim, Y. W., Lee, S. K., Kim, S. H., and Min, K. H.	The effect of continuous release of recombinant human epidermal growth factor (rh-EGF) in chitosan film on full thickness excisional porcine wounds
[198]	2008	Cuschieri, J., Freeman, B., O'Keefe, G., Harbrecht, B. G., Bankey, P., Johnson, J. L., Minei, J. P., Sperry, J., West, M., Nathens, A., Moore, E. E., and Maier, R. V.	Inflammation and the host response to injury a large-scale collaborative project: Patient-oriented research core standard operating procedure for clinical care x. guidelines for venous thromboembolism prophylaxis in the trauma patient
[199]	2008	Degiannis, E. and Zinn, R. J.	Pitfalls in penetrating thoracic trauma (lessons we learned the hard way...)
[200]	2008	Bastos, R., Baisden, C. E., Harker, L., and Calhoon, J. H.	Penetrating Thoracic Trauma
[201]	2008	Kaneko, N., Kobayashi, Y., and Okada, Y.	Anatomic variations of the renal vessels pertinent to transperitoneal vascular control in the management of trauma
[202]	2008	Ong, S. Y., Wu, J., Moochhala, S. M., Tan, M. H., and Lu, J.	Development of a chitosan-based wound dressing with improved hemostatic and antimicrobial properties

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[203]	2008	Sanghi, P., Virmani, R., Do, D., Erikson, J., Elliott, J., Cilingiroglu, M., Matthews, H., Kazi, M., Ricker, R., and Bailey, S. R.	A comparative evaluation of arterial blood flow and the healing response after femoral artery closure using angio-seal STS Plus and StarClose in a porcine model
[204]	2008	Xie, H., Khajanchee, Y. S., and Shaffer, B. S.	Chitosan hemostatic dressing for renal parenchymal wound sealing in a porcine model: implications for laparoscopic partial nephrectomy technique
[205]	2008	Leixnering, M., Reichetseder, J., Schultz, A., Figl, M., Wassermann, E., Thurnher, M., and Redl, H.	Gelatin thrombin granules for hemostasis in a severe traumatic liver and spleen rupture model in swine
[206]	2008	Delgado, A. V., Kheirabadi, B. S., Fruchterman, T. M., Scherer, M., Cortez, D., Wade, C. E., Dubick, M. A., and Holcomb, J. B.	A novel biologic hemostatic dressing (fibrin patch) reduces blood loss and resuscitation volume and improves survival in hypothermic, coagulopathic Swine with grade V liver injury
[207]	2008	Jesty, J., Wieland, M., and Niemiec, J.	Assessment in vitro of the active hemostatic properties of wound dressings
[208]	2008	Xie, H., Khajanchee, Y. S., Teach, J. S., and Shaffer, B. S.	Use of a chitosan-based hemostatic dressing in laparoscopic partial nephrectomy
[209]	2008	Erdogan, D. and van Gulik, T. M.	Evolution of fibrinogen-coated collagen patch for use as a topical hemostatic agent
[210]	2008	Zhang, M.-X., Chen, Z.-H., Li, J., Yang, C.-Y., Xie, Z.-G., and Chen, G.-J.	Hemostatic effect and biocompatibility of RT-Q medical biomembrane
[211]	2007	Franz, M. G., Steed, D. L., and Robson, M. C.	Optimizing Healing of the Acute Wound by Minimizing Complications
[212]	2007	Chaby, G., Senet, P., Vaneau, M., Martel, P., Guillaume, J. C., Meaume, S., Teot, L., Debure, C., Dompmartin, A., Bachelet, H., Carsin, H., Matz, V., Richard, J. L., Rochet, J. M., Sales-Aussias, N., Zagnoli, A., Denis, C., Guillot, B., and Chosidow, O.	Dressings for acute and chronic wounds: a systematic review
[213]	2007	Almogy, G. and Rivkind, A. I.	Terror in the 21st Century: Milestones and Prospects-Part II
[214]	2007	Honsik, K. A., Romeo, M. W., Hawley, C. J., Romeo, S. J., and Romeo, J. P.	Sideline skin and wound care for acute injuries
[215]	2007	Hirshberg, A., Hoyt, D. B., and Mattox, K. L.	From "Leaky Buckets" to Vascular Injuries: Understanding Models of Uncontrolled Hemorrhage
[216]	2007	Kauvar, D. S., Baer, D. G., and Walters, T. J.	Influence of systemic hypotension on skeletal muscle ischemia-reperfusion injury after 4-hour tourniquet application
[217]	2007	Rattanatayarom, W. and Wattanasirichaigoon, S.	Evaluation of dermal irritancy potential of Carboxymethyl-chitosan hydrogel and poly-(acrylic acid) chitin hydrogel
[218]	2007	Sheikh, B. Y.	Efficacy of acrylate tissue adhesive as vascular repair and hemostatic material

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[219]	2007	Kheirabadi, B. S., Acheson, E. M., Deguzman, R., Crissey, J. M., Delgado, A. V., Estep, S. J., and Holcomb, J. B.	The potential utility of fibrin sealant dressing in repair of vascular injury in swine
[220]	2007	Roy, S. C., Paulose, M., and Grimes, C. A.	The effect of TiO2 nanotubes in the enhancement of blood clotting for the control of hemorrhage
[221]	2007	Bjorses, K. and Holst, J.	Various Local Hemostatic Agents with Different Modes of Action; an in vivo Comparative Randomized Vascular Surgical Experimental Study
[222]	2007	Aballay, A. M., Recio, P., Slater, H., Goldfarb, I. W., Tolchin, E., Papasavas, P., and Caushaj, P. F.	The use of esmarch exsanguination for the treatment of extremity wound burns
[223]	2006	Vertrees, A., Kellicut, D., Ottman, S., Peoples, G., and Shriver, C.	Early Definitive Abdominal Closure Using Serial Closure Technique on Injured Soldiers Returning from Afghanistan and Iraq
[224]	2006	Pursifull, N. F., Morris, M. S., Harris, R. A., and Morey, A. F.	Damage control management of experimental grade 5 renal injuries: further evaluation of FloSeal gelatin matrix
[225]	2006	Higgins, T. F. and Swanson, E. R.	Pelvic antishock sheeting
[226]	2006	Hunt, P. A., Greaves, I., and Owens, W. A.	Emergency thoracotomy in thoracic trauma-a review
[227]	2006	Nzewi, O., Slight, R. D., and Zamvar, V.	Management of blunt thoracic aortic injury
[228]	2006	Voinchet, V., Vasseur, P., and Kern, J.	Efficacy and safety of hyaluronic acid in the management of acute wounds
[229]	2006	Schecter, W. P., Ivatury, R. R., Rotondo, M. F., and Hirshberg, A.	Open Abdomen after Trauma and Abdominal Sepsis: A Strategy for Management
[230]	2006	Jurgens, C., Schulz, A. P., Porte, T., Faschingbauer, M., and Seide, K.	Biodegradable films in trauma and orthopedic surgery
[231]	2006	De, Alwis W.	Fingertip injuries
[232]	2006	Klemcke, H. G.	Evaluation of FloSeal as a potential intracavitary hemostatic agent
[233]	2006	Wang, X., Yan, Y., and Zhang, R.	A comparison of chitosan and collagen sponges as hemostatic dressings
[234]	2005	Schreiber, M. A.	Coagulopathy in the trauma patient
[235]	2005	Pope, L. E. and Hobbs, C. G.	Epistaxis: an update on current management
[236]	2005	Kataoka, Y., Maekawa, K., Nishimaki, H., Yamamoto, S., and Soma, K.	Iliac vein injuries in hemodynamically unstable patients with pelvic fracture caused by blunt trauma
[237]	2005	Tiemann, A. H., Bohme, J., and Josten, C.	Emergency treatment of multiply injured patients with unstable disruption of the posterior pelvic ring by using the "C-clamp": Analysis of 28 consecutive cases
[238]	2005	Brandenburg, M. A., Hawkins, L., and Quick, G.	Hand injuries, part 2: When nerves, vasculature, tendons, or ligaments are traumatized
[239]	2005	Sagerman, P. J.	Wounds
[240]	2005	Degiannis, E., Bowley, D. M., and Westaby, S.	Penetrating cardiac injury

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[241]	2005	Rothwell, S. W., Reid, T. J., Dorsey, J., Flournoy, W. S., Bodo, M., Janmey, P. A., and Sawyer, E.	A salmon thrombin-fibrin bandage controls arterial bleeding in a swine aortotomy model
[242]	2005	Kheirabadi, B. S., Acheson, E. M., Deguzman, R., Sondeen, J. L., Ryan, K. L., Delgado, A., Dick, E. J., Jr., and Holcomb, J. B.	Hemostatic efficacy of two advanced dressings in an aortic hemorrhage model in Swine
[243]	2005	Cihan, A., Yilmaz, E., Yenidunya, S., and Ucan, B. H.	Medical haemostasis in acute hepatocyte injury and experimental liver trauma
[244]	2005	Hick, E. J., Morey, A. F., Harris, R. A., and Morris, M. S.	Gelatin matrix treatment of complex renal injuries in a porcine model
[245]	2005	Laurence, S., Bareille, R., Baquey, C., and Fricain, J. C.	Development of a resorbable macroporous cellulosic material used as hemostatic in an osseous environment
[246]	2004	Bochicchio, G., Dunne, J., Bochicchio, K., and Scalea, T.	The combination of platelet-enriched autologous plasma with bovine collagen and thrombin decreases the need for multiple blood transfusions in trauma patients with retroperitoneal bleeding
[247]	2004	Kopp, J., Jeschke, M. G., Bach, A. D., Kneser, U., and Horch, R. E.	Applied tissue engineering in the closure of severe burns and chronic wounds using cultured human autologous keratinocytes in a natural fibrin matrix
[248]	2004	Borowik, S., Popko, J., Ladny, R., and Slowinski, K.	[External stabilization in the treatment of unstable pelvis fractures combined with additional injuries of internal organs]
[249]	2004	King, D. R., Cohn, S. M., Proctor, K. G., and Miami Clinical Trials Group	Modified rapid deployment hemostat bandage terminates bleeding in coagulopathic patients with severe visceral injuries
[250]	2004	Gansslen, A., Krettek, C., and Pohlemann, T.	Die temporare Stabilisierung des Beckenrings mit der sog. Notfallbeckenzwinge
[251]	2004	Giannoudis, P. V. and Pape, H. C.	Damage control orthopaedics in unstable pelvic ring injuries
[252]	2004	Ang, C. Y., Samsudin, A. R., Karima, A. M., and Nizam, A.	Locally produced bovine bone sponge as a haemostatic agent
[253]	2004	Pusateri, A. E., Delgado, A. V., Dick, E. J., Jr., Martinez, R. S., Holcomb, J. B., and Ryan, K. L.	Application of a granular mineral-based hemostatic agent (QuikClot) to reduce blood loss after grade V liver injury in swine
[254]	2004	Schwaitzberg, S. D., Chan, M. W., Cole, D. J., Read, M., Nichols, T., Bellinger, D., and Connolly, R. J.	Comparison of poly-N-acetyl glucosamine with commercially available topical hemostats for achieving hemostasis in coagulopathic models of splenic hemorrhage
[255]	2004	Krishnan, L. K., Mohanty, M., Umashankar, P. R., and Lal, A. V.	Comparative evaluation of absorbable hemostats: advantages of fibrin-based sheets
[256]	2004	Griffith, B. C., Morey, A. F., Rozanski, T. A., Harris, R., Dalton, S. R., Torgerson, S. J., and Partyka, S. R.	Central renal stab wounds: treatment with augmented fibrin sealant in a porcine model
[257]	2004	Doillon, C. J. and Dion, Y.-M.	Comparison of a plasma-based composite biologic sealant with fibrin glue (Tisseel) for vascular anastomoses
[258]	2004	Vournakis, J. N., Demcheva, M., Whitson, A., Guirca, R., and Pariser, E. R.	Isolation, purification, and characterization of poly-N-acetyl glucosamine use as a hemostatic agent

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[259]	2003	Underhill, S. and Crumplin, M. K. H.	A high price for victory: The management of pain and transport of the sick and wounded in the Napoleonic Wars (1793-1815)
[260]	2003	Starr, A. J.	Immediate management of pelvic fractures
[261]	2003	Donelan, S.	Teaching wound care and bandaging: An historical perspective
[262]	2003	Salehian, O., Teoh, K., and Mulji, A.	Blunt and penetrating cardiac trauma: A review
[263]	2003	Pusateri, A. E., Modrow, H. E., Harris, R. A., Holcomb, J. B., Hess, J. R., Mosebar, R. H., Reid, T. J., Nelson, J. H., Goodwin, C. W., Jr., Fitzpatrick, G. M., McManus, A. T., Zolock, D. T., Sondeen, J. L., Cornum, R. L., and Martinez, R. S.	Advanced hemostatic dressing development program: animal model selection criteria and results of a study of nine hemostatic dressings in a model of severe large venous hemorrhage and hepatic injury in Swine
[264]	2003	Vournakis, J. N., Demcheva, M., Whitson, A. B., Finkielsztein, S., and Connolly, R. J.	The RDH bandage: hemostasis and survival in a lethal aortotomy hemorrhage model
[265]	2003	Jewelewicz, D. D., Cohn, S. M., Crookes, B. A., and Proctor, K. G.	Modified rapid deployment hemostat bandage reduces blood loss and mortality in coagulopathic pigs with severe liver injury.[Erratum appears in J Trauma. 2003 Oct;55(4):621
[266]	2003	Singer, A. J., Nable, M., Cameau, P., Singer, D. D., and McClain, S. A.	Evaluation of a new liquid occlusive dressing for excisional wounds
[267]	2003	Schreiber, M. A., Holcomb, J. B., Hedner, U., Brundage, S. I., Macaitis, J. M., Aoki, N., Meng, Z. H., Tweardy, D. J., and Hoots, K.	The effect of recombinant factor VIIa on noncoagulopathic pigs with grade V liver injuries
[268]	2003	Sondeen, J. L., Pusateri, A. E., Coppes, V. G., Gaddy, C. E., and Holcomb, J. B.	Comparison of 10 different hemostatic dressings in an aortic injury
[269]	2003	Pusateri, A. E., McCarthy, S. J., Gregory, K. W., Harris, R. A., Cardenas, L., McManus, A. T., and Goodwin, C. W., Jr.	Effect of a chitosan-based hemostatic dressing on blood loss and survival in a model of severe venous hemorrhage and hepatic injury in swine
[270]	2003	Peng, Y., Ye, C., Zou, H., and Liang, P.	Investigation of features of hemostasis sponge of collagen and chitosan compound
[271]	2002	Chiu, J., Ketchum, L. H., and Reid, T. J.	Transfusion-sparing hemostatic agents
[272]	2002	Rennie, M.	Trauma, immobility and under nutrition, the harbingers of insulin resistance
[273]	2002	O'Mara, M. S., Goel, A., Recio, P., Slater, H., Goldfarb, I. W., Tolchin, E., and Caushaj, P. F.	The use of tourniquets in the excision of unexsanguinated extremity burn wounds
[274]	2002	Schreiber, M. A., Holcomb, J. B., Hedner, U., Brundage, S. I., Macaitis, J. M., and Hoots, K.	The effect of recombinant factor VIIa on coagulopathic pigs with grade V liver injuries
[275]	2002	Kheirabadi, B. S., Field-Ridley, A., Pearson, R., MacPhee, M., Drohan, W., and Tuthill, D.	Comparative study of the efficacy of the common topical hemostatic agents with fibrin sealant in a rabbit aortic anastomosis model

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[276]	2002	Kheirabadi, B. S., Pearson, R., Tuthill, D., Rudnicka, K., Holcomb, J. B., Drohan, W., and MacPhee, M. J.	Comparative study of the hemostatic efficacy of a new human fibrin sealant: is an antifibrinolytic agent necessary?
[277]	2002	Turner, A. S., Parker, D., Egbert, B., Maroney, M., Armstrong, R., and Powers, N.	Evaluation of a novel hemostatic device in an ovine parenchymal organ bleeding model of normal and impaired hemostasis
[278]	2002	Ishihara, M., Nakanishi, K., Ono, K., Sato, M., Kikuchi, M., Saito, Y., Yura, H., Matsui, T., Hattori, H., Uenoyama, M., and Kurita, A.	Photocrosslinkable chitosan as a dressing for wound occlusion and accelerator in healing process
[279]	2001	Anema, J. G., Morey, A. F., Harris, R., MacPhee, M., and Cornum, R. L.	Potential uses of absorbable fibrin adhesive bandage for genitourinary trauma
[280]	2001	Klobucar, H., Delinar, D., Korzinek, M., and Korzinek, K.	CMC external fixator
[281]	2001	Ertel, W., Keel, M., Eid, K., Platz, A., and Trentz, O.	Control of severe hemorrhage using C-clamp and pelvic packing in multiply injured patients with pelvic ring disruption
[282]	2001	Tyburski, J. G., Wilson, R. F., Dente, C., Steffes, C., and Carlin, A. M.	Factors affecting mortality rates in patients with abdominal vascular injuries
[283]	2001	Edlich, R. F. and Reddy, V. R.	5th Annual David R. Boyd, MD Lecture: Revolutionary advances in wound repair in emergency medicine during the last three decades. A view toward the new millennium
[284]	2001	Djurickovic, S., Snelling, C. F. T., and Boyle, J. C.	Tourniquet and subcutaneous epinephrine reduce blood loss during burn excision and immediate autografting
[285]	2001	Ono, K., Ishihara, M., Ozeki, Y., Deguchi, H., Sato, M., Saito, Y., Yura, H., Sato, M., Kikuchi, M., Kurita, A., and Maehara, T.	Experimental evaluation of photocrosslinkable chitosan as a biologic adhesive with surgical applications
[286]	2001	Davis, S. C., Eaglstein, W. H., Cazzaniga, A. L., and Mertz, P. M.	An octyl-2-cyanoacrylate formulation speeds healing of partial-thickness wounds
[287]	2001	Barbolt, T. A., Odin, M., Leger, M., and Kangas, L.	Pre-clinical subdural tissue reaction and absorption study of absorbable hemostatic devices
[288]	2001	Martinowitz, U., Holcomb, J. B., Pusateri, A. E., Stein, M., Onaca, N., Freidman, M., Macaitis, J. M., Castel, D., Hedner, U., and Hess, J. R.	Intravenous rFVIIa administered for hemorrhage control in hypothermic coagulopathic swine with grade V liver injuries
[289]	2001	Pusateri, A. E., Holcomb, J. B., Harris, R. A., MacPhee, M. J., Charles, N. C., Beall, L. D., and Hess, J. R.	Effect of fibrin bandage fibrinogen concentration on blood loss after grade V liver injury in swine
[290]	2001	Morey, A. F., Anema, J. G., Harris, R., Gresham, V., Daniels, R., Knight, R. W., Beall, D., MacPhee, M., and Cornum, R. L.	Treatment of grade 4 renal stab wounds with absorbable fibrin adhesive bandage in a porcine model

Table B.1. Articles excluded at the abstract level (continued)

Reference	Year of Publication	Authors	Title of Article
[291]	2001	Hill, A., Estridge, T. D., Maroney, M., Monnet, E., Egbert, B., Cruise, G., and Coker, G. T.	Treatment of suture line bleeding with a novel synthetic surgical sealant in a canine iliac PTFE graft model

Table B.2. Documents that were retrieved and then excluded

Reference	Year of Publication	Authors	Title of Article	Reason for Exclusion
[292]	2013	Clumpner, B. R., Polston, R. W., Kragh, J. F., Jr., Westmoreland, T., Harcke, H. T., Jones, J. A., Dubick, M. A., Baer, D. G., and Blackbourne, L. H.	Single versus Double Routing of the Band in the Combat Application Tourniquet	Clinical study with fewer than 5 subjects
[293]	2013	Barlow, B. T. and Kuhn, K. M.	Limb salvage compared with amputation in the acute setting: Criteria used on the battlefield	Focus is not prehospital control of bleeding
[294]	2012	Sorensen, B. and Fries, D.	Emerging treatment strategies for trauma-induced coagulopathy	Narrative review not focused on prehospital bleeding
[295]	2012	Orman, J. A., Eastridge, B. J., Baer, D. G., Gerhardt, R. T., Rasmussen, T. E., and Blackbourne, L. H.	The impact of 10 years of war on combat casualty care research: A citation analysis	Addresses topics other than hemostatic dressings and tourniquets
[296]	2012	Brown, K. V., Guthrie, H. C., Ramasamy, A., Kendrew, J. M., and Clasper, J.	Modern military surgery: Lessons from Iraq and Afghanistan	Focus is not prehospital control of bleeding
[297]	2012	Mamczak, C. N., Born, C. T., Obremskey, W. T., Dromsky, D. M., and Extremity War Injuries VII Acute Care Panel	Evolution of acute orthopaedic care	Review is not exclusive to prehospital control of bleeding
[298]	2012	Rasmussen, T. E., Dubose, J. J., Asensio, J. A., Feliciano, D. V., Fox, C. J., Nunez, T. C., Sise, M. J., and Military Liaison Committee of the American Association for the Surgery of Trauma	Tourniquets, vascular shunts, and endovascular technologies: esoteric or essential? A report from the 2011 AAST Military Liaison Panel	Not a clinical study
[299]	2012	Jorgensen, H. O., Heier-Madsen, K., and Stokkebye, J. E.	Casualty rates among Danish soldiers in Iraq and Afghanistan	Clinical study does not address tourniquet or hemostatic dressing use
[300]	2012	Mishwani, A. H., Ghaffar, A., and Janjua, S.	Combat related vascular trauma	Clinical study had too few patients using tourniquets
[301]	2012	Swan, K. G., Swan, K. G., Jr., and Ahearn, M.	Tourniquets, pressure points, and extremity hemorrhage	Editorial
[302]	2012	Titley, P.	A topical subject	Insufficient information to use as background reference
[303]	2012	Kheirabadi, B. S., Terrazas, I. B., Williams, J. F., Hanson, M. A., Dubick, M. A., and Blackbourne, L. H.	Negative-pressure wound therapy: a hemostatic adjunct for control of coagulopathic hemorrhage in large soft tissue wounds	Not a prehospital treatment for bleeding
[304]	2012	Pasquier, P., Renner, J., and Merat, S.	Infections and tourniquet application in severe open tibia fractures from combat	Letter to the editor

Table B.2. Documents that were retrieved and then excluded (continued)

Reference	Year of Publication	Authors	Title of Article	Reason for Exclusion
[305]	2012	Polk, T. and Sims, C.	Life & limb: tourniquet saves man severely injured in vehicle crash	Case report
[306]	2012	Jacobs, N., Rourke, K., Rutherford, J., Hicks, A., Smith, S. R., Templeton, P., Adams, S. A., and Jansen, J. O.	Lower limb injuries caused by improvised explosive devices: Proposed 'Bastion classification' and prospective validation	Not a prehospital clinical study
[307]	2011	Francesko, A. and Tzanov, T.	Chitin, chitosan and derivatives for wound healing and tissue engineering	Review does not cover hemostasis
[308]	2011	Parker, P. and Limb Trauma Working Group	Consensus statement on decision making in junctional trauma care	Does not contain prehospital background information
[309]	2011	King, D. R.	Thirty consecutive uses of a hemostatic bandage at a US Army combat support hospital and forward surgical team in Operation Iraqi Freedom	Not a prehospital application of hemostatic dressing
[310]	2011	Waibel, K. H., Haney, B., Moore, M., Whisman, B., and Gomez, R.	Safety of chitosan bandages in shellfish allergic patients	Not a clinical study of bleeding
[311]	2011	Rich, N. M.	Vascular trauma historical notes	Background reference not specific to prehospital hemostasis
[312]	2011	Pohlemann, T., Stengel, D., Tosounidis, G., Reilmann, H., Stuby, F., Stockle, U., Seekamp, A., Schmal, H., Thannheimer, A., Holmenschlager, F., Gansslen, A., Rommens, P. M., Fuchs, T., Baumgartel, F., Marintschev, I., Krischak, G., Wunder, S., Tscherne, H., and Culemann, U.	Survival trends and predictors of mortality in severe pelvic trauma: estimates from the German Pelvic Trauma Registry Initiative	Not a prehospital clinical study
[313]	2011	Metcalfe, A. J., Davies, K., Ramesh, B., O'Kelly, A., and Rajagopal, R.	Haemorrhage control in pelvic fractures--a survey of surgical capabilities	Not a prehospital clinical study
[314]	2011	Yin, H., He, H., Arbon, P., and Zhu, J.	A survey of the practice of nurses' skills in Wenchuan earthquake disaster sites: implications for disaster training	Not a clinical study focused on bleeding
[315]	2011	Dai, T., Tanaka, M., Huang, Y. Y., and Hamblin, M. R.	Chitosan preparations for wounds and burns: antimicrobial and wound-healing effects	Review, not related to bleeding or hemostasis
[316]	2011	Tourtier, J. P., Jault, P., Tazarourte, K., Borne, M., and Bargues, L.	Tourniquets on the battlefield: could N-acetylcysteine be useful?	Letter to the editor
[317]	2010	Fox, C. J., Perkins, J. G., Kragh, J. F., Jr., Singh, N. N., Patel, B., and Ficke, J. R.	Popliteal artery repair in massively transfused military trauma casualties: a pursuit to save life and limb	Not a prehospital clinical study
[318]	2010	Crossley, B.	Tourniquet systems pose challenges	Cover tourniquets used in surgery

Table B.2. Documents that were retrieved and then excluded (continued)

Reference	Year of Publication	Authors	Title of Article	Reason for Exclusion
[319]	2010	Katoch, B. R. and Gambhir, C. R. P. S.	Warfare vascular injuries	Does not provide sufficient prehospital information to use as a background reference.
[320]	2010	Duncan, N. S. and Moran, C.	(i) Initial resuscitation of the trauma victim	Not specific to prehospital treatment
[321]	2009	Davenport, R., Tai, N., and Walsh, M.	Vascular trauma	Not a prehospital background reference
[322]	2009	Franco, P.	Alert--watch for "look alike" Combat Application Tourniquet (C.A.T.)	Not related to clinical tourniquet use
[323]	2009	von, Tersch R., Birch, H., Gupta, R., and Tyner, C. F.	Examining technologies to control hemorrhage by using modeling and simulation to simulate casualties and treatment	Not a clinical study. Used modeling and stimulation
[324]	2009	Shipman, N. and Lessard, C. S.	Pressure applied by the emergency/Israeli bandage	Not a clinical study. Simulation.
[325]	2009	Rush Jr, R. M., Beekley, A. C., Puttler, E. G., and Kjorstad, R. J.	The Mangled Extremity	Focus is not prehospital control of bleeding
[326]	2009	Parker, P.	Emergency tourniquet use	Letter to the editor
[327]	2009	Fludger, S. and Bell, A.	Tourniquet application in a rural Queensland HEMS environment	Case report
[328]	2009	Mullins, J. and Harrahill, M.	Use of a tourniquet after a gunshot wound to the thigh	Case report
[329]	2009	Moore, F. A.	Tourniquets: another adjunct in damage control?	Editorial
[330]	2008	Fox, C. J., Gillespie, D. L., Cox, E. D., Kragh, J. F., Jr., Mehta, S. G., Salinas, J., and Holcomb, J. B.	Damage control resuscitation for vascular surgery in a combat support hospital	Does not address any of the key questions
[331]	2008	Gwinn, D. E., Keeling, J., Froehner, J. W., McGuigan, F. X., and Andersen, R.	Perioperative differences between bone bridging and non-bone bridging transtibial amputations for wartime lower extremity trauma	Not a prehospital clinical study
[332]	2008	Recinos, G., Inaba, K., Dubose, J., Demetriades, D., and Rhee, P.	Local and systemic hemostatics in trauma: A review	Narrative review with sparse information on hemostatic dressings
[333]	2008	Blackbourne, L. H., Mabry, R., Sebesta, J., and Holcomb, J. B.	Joseph Lister, noncompressible arterial hemorrhage, and the next generation of "tourniquets"?	Historical account of tourniquet use
[334]	2008	Perkins, J. G., Cap, A. P., Weiss, B. M., Reid, T. J., and Bolan, C. D.	Massive transfusion and nonsurgical hemostatic agents	Review article is not focused on prehospital control of bleeding
[335]	2008	Mackenzie, C. F. and Shander, A.	What to do if no blood is available but the patient is bleeding?	Insufficient prehospital background information to use as reference

Table B.2. Documents that were retrieved and then excluded (continued)

Reference	Year of Publication	Authors	Title of Article	Reason for Exclusion
[336]	2008	Nelson, T. J., Clark, T., Stedje-Larsen, E. T., Lewis, C. T., Grueskin, J. M., Echols, E. L., Wall, D. B., Felger, E. A., and Bohman, H. R.	Close proximity blast injury patterns from improvised explosive devices in Iraq: A report of 18 cases	Too few patients with tourniquets or hemostatic dressing to use
[337]	2008	Fan, Y., Sun, H., Pei, G., and Ruan, C.	Haemostatic efficacy of an ethyl-2-cyanoacrylate-based aerosol in combination with tourniquet application in a large wound model with an arterial injury	Not a hemostatic dressing, type of tourniquet not report
[338]	2008	Li, Z., Zhou, G.-H., Liu, C., Mei, Y.-J., Ning, Z.-S., and Lu, S.-M.	A multifunctional tourniquet attachment system	Not related to commercially available tourniquet use
[339]	2007	Fox, C. J. and Starnes, B. W.	Vascular surgery on the modern battlefield	Background reference does not emphasize prehospital procedures
[340]	2007	Moorhouse, I., Thurgood, A., Walker, N., Cooper, B., Mahoney, P. F., and Hodgetts, T. J.	A realistic model for catastrophic external haemorrhage training	Describes a model and does not present patient data
[341]	2007	Bulger, E. M. and Maier, R. V.	Prehospital Care of the Injured: What's New	Focus is not prehospital control of bleeding
[342]	2007	Kragh, J. F., Jr., Baer, D. G., and Walters, T. J.	Extended (16-hour) tourniquet application after combat wounds: a case report and review of the current literature	Case report
[343]	2007	McManus, J., Hurtado, T., Pusateri, A., and Knoop, K. J.	A case series describing thermal injury resulting from zeolite use for hemorrhage control in combat operations	Case reports
[344]	2006	Laskowski-Jones, L.	First aid for bleeding wounds	Not a clinical study or suitable background reference
[345]	2006	Mucciarone, J. J., Llewellyn, C. H., and Wightman, J. M.	Tactical combat casualty care in the assault on Punta Paitilla Airfield	Clinical study with too few subjects
[346]	2006	Esmarch, F.	Historical Article	Not related to extremity hemorrhage control
[347]	2006	Beekley, A. C.	United States Military Surgical Response to Modern Large-Scale Conflicts: The Ongoing Evolution of a Trauma System	Background reference not focused on prehospital procedures
[348]	2006	Ostomel, T. A., Stoimenov, P. K., Holden, P. A., Alam, H. B., and Stucky, G. D.	Host-guest composites for induced hemostasis and therapeutic healing in traumatic injuries	Study does not involve human or animal subjects
[349]	2006	Owens, B. D., Wenke, J. C., Svoboda, S. J., and White, D. W.	Extremity trauma research in the United States Army	Background reference not specific to prehospital treatment
[350]	2005		Laboratory evaluation of battlefield tourniquets in human volunteers	Not published in a peer reviewed journal / manuscript copy

Table B.2. Documents that were retrieved and then excluded (continued)

Reference	Year of Publication	Authors	Title of Article	Reason for Exclusion
[351]	2005	Hodgetts, T. J., Russell, R. J., Mahoney, P. F., Russell, M. Q., and Kenward, G.	Evaluation of clinician attitudes to the implementation of novel haemostatic techniques	Survey, no clinical prehospital data related to evidence report
[5]	2005	Dorlac, W. C., DeBakey, M. E., Holcomb, J. B., Fagan, S. P., Kwong, K. L., Dorlac, G. R., Schreiber, M. A., Persse, D. E., Moore, F. A., and Mattox, K. L.	Mortality from isolated civilian penetrating extremity injury	Clinical study, did not use tourniquets or hemostatic dressings
[352]	2004	Holcomb, J. B.	Methods for improved hemorrhage control	Narrative review with no information on prehospital care
[353]	2004	Kulkarni, R.	Alternative and topical approaches to treating the massively bleeding patient	Background information already available in more complete references
[354]	2004	Guyver, P. M. and Lambert, A. W.	Vascular access on the front line	Focus is not prehospital control of bleeding
[355]	2003	Gansslen, A., Giannoudis, P., and Pape, H. C.	Hemorrhage in pelvic fracture: who needs angiography?	Background reference not specific to prehospital treatments for external bleeding
[356]	2003	Porter, K. and Greaves, I.	Crush injury and crush syndrome: a consensus statement	Not related to extremity hemorrhage control
[357]	2003	Becker, C.	Bloodless coup. Funded by the Army, Oregon researchers turn to the sea to develop a revolutionary bandage that stanches heavy bleeding	Narrative review does not contain information needed for this evidence report
[358]	2002	McEwen, J. A., Kelly, D. L., Jardanowski, T., and Inkpen, K.	Tourniquet safety in lower leg applications	Not related to extremity hemorrhage control
[359]	2002	Scalea, T.	What's new in trauma in the past 10 years	Focus is not prehospital control of bleeding
[360]	2002	Strong, D. P. and Edwards, A. T.	Vascular trauma	Focus is not prehospital control of bleeding
[361]	2001	Blackwood, M.	Royal Army Medical Corps, 3rd Corps Medical Society. Treatment of wounds from fire trench to field ambulance. 1916	Background reference not related to focus of the evidence report
[362]	2001	Rich, N. M. and Rhee, P.	An historical tour of vascular injury management: From its inception to the new millennium	Focus is not prehospital control of bleeding
[363]	2001	Yong, H. and Jianning, L.	The design and the clinical application of the mini-tourniquet	The device is not intended for prehospital use.

Table B.3. Excluded animal model nonclinical studies

Reference	Year of Publication	Authors	Title of Article	Reason for Exclusion
[364]	2013	Sena, M. J., Douglas, G., Gerlach, T., Grayson, J. K., Pichakron, K. O., and Zierold, D.	A pilot study of the use of kaolin-impregnated gauze (Combat Gauze) for packing high-grade hepatic injuries in a hypothermic coagulopathic swine model	Hepatic injury animal model
[365]	2013	Martin, M. J.	Editorial to accompany "A pilot study of the use of kaolin-impregnated gauze (Combat Gauze) for packing high-grade hepatic injuries in a hypothermic coagulopathic swine model	Hepatic injury animal model
[366]	2012	Floyd, C. T., Rothwell, S. W., Martin, R., Risdahl, J., and Olson, C. E.	A salmon thrombin-fibrinogen dressing controls hemorrhage in a swine model compared to standard kaolin-coated gauze	Test dressing is not commercially available
[367]	2012	Mueller, G. R., Pineda, T. J., Xie, H. X., Teach, J. S., Barofsky, A. D., Schmid, J. R., and Gregory, K. W.	A novel sponge-based wound stasis dressing to treat lethal noncompressible hemorrhage	Investigational hemostatic dressing
[368]	2012	De Castro, G. P., Dowling, M. B., Kilbourne, M., Keledjian, K., Driscoll, I. R., Raghavan, S. R., Hess, J. R., Scalea, T. M., and Bochicchio, G. V.	Determination of efficacy of novel modified chitosan sponge dressing in a lethal arterial injury model in swine	The hemostatic dressings is not a commercially available product
[369]	2012	Charbonneau, S., Lemarie, C. A., Peng, H. T., Ganopolsky, J. G., Shek, P. N., and Blostein, M. D.	Surface-attached amphipathic peptides reduce hemorrhage in vivo	Not appropriate external hemorrhage animal model
[370]	2012	Shukla, A., Fang, J. C., Puranam, S., Jensen, F. R., and Hammond, P. T.	Hemostatic multilayer coatings	Technical discussion of development and creation of a hemostatic dressing
[371]	2011	Seetharaman, S., Natesan, S., Stowers, R. S., Mullens, C., Baer, D. G., Suggs, L. J., and Christy, R. J.	A PEGylated fibrin-based wound dressing with antimicrobial and angiogenic activity	In vitro study only
[372]	2011	Dowling, M. B., Kumar, R., Keibler, M. A., Hess, J. R., Bochicchio, G. V., and Raghavan, S. R.	A self-assembling hydrophobically modified chitosan capable of reversible hemostatic action	In vitro study
[373]	2011	Bowman, P. D., Wang, X., Meledeo, M. A., Dubick, M. A., and Kheirabadi, B. S.	Toxicity of aluminum silicates used in hemostatic dressings toward human umbilical veins endothelial cells, HeLa cells, and RAW267.4 mouse macrophages	Not a clinical study. Used cell cultures
[374]	2011	Hirst, H., Brinkman, J., Beasley, A., Crocker, R., and O'Sullivan, J.	The effects of blood pressure on rebleeding when using ExcelArrest in a porcine model of lethal femoral injury	No outcomes of interest

Table B.3. Excluded animal model nonclinical studies (continued)

Reference	Year of Publication	Authors	Title of Article	Reason for Exclusion
[375]	2010	Naimer, S. A.	New era of transparent compression to control bleeding from traumatic wounds: Removing the blindfold	Product is not commercially available
[376]	2010	Kranokpiraksa, P., Pavcnik, D., Kakizawa, H., Uchida, B. T., Jeromel, M., Keller, F. S., and Rosch, J.	Hemostatic efficacy of chitosan-based bandage for closure of percutaneous arterial access sites: An experimental study in heparinized sheep model	Not related to extremity hemorrhage wounds
[377]	2010	Gegel, B. T., Burgert, J. M., Lockhart, C., Austin, R., III, Davila, A., Deeds, J., Hodges, L., Hover, A., Roy, J., Simpson, G., Weaver, S., Wolfe, W., and Johnson, D.	Effects of Celox and TraumaDEX on hemorrhage control in a porcine model	Contains data already published in another publication
[378]	2009	Velmahos, G. C., Tabbara, M., Spaniolas, K., Duggan, M., Alam, H. B., Serra, M., Sun, L., and de, Luis J.	Self-expanding hemostatic polymer for control of exsanguinating extremity bleeding	Not a commercially available product
[379]	2009	Li, J., Yan, W., Jing, L., Xueyong, L., Yuejun, L., Wangzhou, L., and Shaozong, C.	Addition of an alginate to a modified zeolite improves hemostatic performance in a swine model of lethal groin injury	Not a commercially available product
[380]	2006	Walters, T., Baer, D. G., and Kauvar, D. S.	A large animal fatal extremity hemorrhage model and evaluation of a polymeric dressing (fatal extremity hemorrhage)	BioFoam is not commercially available in the U.S.
[381]	2004	Pusateri, A. E., Kheirabadi, B. S., Delgado, A. V., Doyle, J. W., Kanellos, J., Uscilowicz, J. M., Martinez, R. S., Holcomb, J. B., and Modrow, H. E.	Structural design of the dry fibrin sealant dressing and its impact on the hemostatic efficacy of the product	Not a model of extremity hemorrhage
[382]	2004	Fischer, T. H., Connolly, R., Thatte, H. S., and Schwaitzberg, S. S.	Comparison of structural and hemostatic properties of the poly-N-acetyl glucosamine Syvek Patch with products containing chitosan	Not an animal study of extremity bleeding
[383]	2003	Jewelewicz, D. D., Cohn, S. M., Crookes, B. A., and Proctor, K. G.	Erratum: Modified Rapid Deployment Hemostat Bandage Reduces Blood Loss and Mortality in Coagulopathic Pigs with Severe Liver Injury	Not related to extremity hemorrhage control
[384]	2002	Rothwell, S. W., Fudge, J. M., Reid, T. J., and Krishnamurti, C.	Epsilon-amino caproic acid additive decreases fibrin bandage performance in a swine arterial bleeding model	No comparisons of interest, no standard gauze control
[385]	2002	Rothwell, S. W., Fudge, J. M., Chen, W. K., Reid, T. J., and Krishnamurti, C.	Addition of a propyl gallate-based procoagulant to a fibrin bandage improves hemostatic performance in a swine arterial bleeding model	No comparisons of interest, no standard gauze control

Appendix C. Evidence Tables for Indirect Evidence: Animal, Volunteer and Simulation Studies

Animal Studies

Animal studies using 5 seconds or less of free bleeding

Two of the studies using 5 seconds or less free bleeding time were designed to test hemostasis rates at 4 minutes after application when trained military personnel were using the hemostatic dressings. Satterly et al.[82] reported that QuikClot Combat Gauze had a 83% hemostasis rate compared with 53% for HemCon but the difference was not statistically significant. However military personnel improved the hemostasis rate by 20% compared with nonmedical personnel; the increase was statistically significant. Military personnel also rated QuikClot Combat Gauze the easiest to use.

The other study using trained military personnel examined various versions of HemCon and reported the best results with the double-sided bandage; hemostasis with this dressing was 76% at 4 minutes and was significantly better than standard gauze.[83] Military personnel preferred the double-sided HemCon bandage.

Gustafson et al.[386] reported that application of HemCon Bandages after 5 seconds of free bleeding achieved significant hemostasis (100% at 30 minutes). Wright et al.[84] specifically looked at tissue damage and wound healing when using QuikClot granules. Extensive tissue burns, necrosis, and impaired wound healing were noted in animals treated with QuikClot granules.

Table C.1. Animal studies using 5 seconds or less of free bleeding time

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Satterly et al. 2013[82]	Assess employment and efficacy of multiple hemostatic bandages by the actual personnel administering care at the front lines as well as a subjective evaluation of both the training and the ease of use of the various hemostatic products. Military personnel were trained prior to deployment. Celox, ChitoGauze, QuikClot Combat Gauze, and HemCon were examined. Femoral and axillary artery injury in a goat model. Free bleeding for 5 seconds. Dressings were applied and then manual pressure for 2 minutes. Bleeding was evaluated and then manual pressure reapplied for 4 minutes.	Hemostasis at 4 minutes: QuikClot Combat Gauze 83%, Celox 75%, ChitoGauze 69%, and HemCon 53%; differences were not statistically significant.	Not reported	Not reported	QuikClot Combat Gauze was rated easiest to use by the soldiers, the difference was statistically significant. When compared to nonmedical personnel, active duty soldiers with prior medical training improved hemostasis at 4 minutes by 20%, the difference was statistically significant.	"There is no significant difference in hemostasis between hemostatic bandages for proximal arterial hemorrhage. Hemostasis significantly improves between 2 and 4 minutes using direct pressure and hemostatic agents. Prior medical training leads to 20% greater efficacy when using hemostatic dressings."
Sohn et al. 2009[83]	Evaluate the efficacy of 3 chitosan-based hemostatic dressings (HemCon: 1-sided (OS), 2-sided (DS), and powder (CP)) compared with standard gauze when applied to a standardized femoral artery partial transection in a goat model. All dressings were applied by U.S. Army combat medics with previous training on how to use the dressings. Femoral artery injury. No free bleeding period. Applied dressings and manual pressure for 2 minutes. Dressings could be reapplied if bleeding continued after 1st application. 123 active bleeding arterial injuries were created in 62 goats.	Standard gauze failed to achieve hemostasis in 99% of the injuries. At 2 minutes hemostasis was: OS 36%, DS 44%, CP 38%. At 4 minutes hemostasis was: OS 53%, DS 76%, CP 69%. Differences were not statistically significant.	—	—	Medics preferred the DS dressing.	"Chitosan based bandages are significantly more effective at hemorrhage control compared to standard gauze field dressings. The dual-sided chitosan dressing demonstrated better hemorrhage control than the one-sided dressing and the chitosan powder, and was less likely to fail despite application errors."

Table C.1. Animal studies using 5 seconds or less of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Gustafson et al. 2007[386]	Test efficacy of HemCon Bandage (HC) to standard gauze, 48-ply (48PG). Both femoral arteries were injured. Free bleeding for 5 seconds, then wound was packed with standard gauze and removed after 1 minute, allowed to bleed for another 5 seconds and then treatment dressings applied. Random assignment of dressing between arteries. 3 minutes of manual pressure. If the dressing failed in the first 30 minutes, a 2nd application was allowed. If the 2nd application failed, the alternative dressing was applied, again for up to 2 applications.	Chronic hemostasis was considered maintenance of hemostasis for 4 hours. Acute hemostasis (30 minutes: PG48, 3 of 14 (21%); HC, 14 of 14 (100%); differences were significant. 11 rescue HCs were acutely successful. Chronic hemostasis: 48PG ,1 of 14 (7%); HC, 21 of 25 (84%); differences were significant.	—	—	No dressing-related tissue damage was noted during histologically examination.	"Chitosan acetate hemorrhage control dressings provided superior hemostasis to 48 ply gauze in high inguinal femoral arterial injuries. Chitosan-based dressings may provide prehospital treatment options for hemostasis in patients with severe hemorrhagic arterial injuries."
Wright et al. 2004[84]	This study reports on injuries related to the use of QuikClot granules. Wounds were created in skin, semitendinosus muscle, liver, spleen, femoral artery, and femoral vein. None of the wounds were life threatening. FloSeal, FastAct, and granular QuikClot hemostatic dressings were used. N=8 per group. Three of the animals were allowed to recover to monitor wound healing.	Artery wound time to hemostasis in minutes, mean (SD): No agent 158 (123), QuikClot 145 (144); not significantly different.	No deaths	QuikClot caused extensive tissue burns and interfered with proper wound healing. The femoral arteries suffered thermal injuries resulting in necrosis.	Blood loss: QuikClot significantly lowered bleeding in vein wounds but not artery wounds, compared with no-agent controls.	"Topical administration of a granular mineral hemostatic agent to a variety of wounds in an experimental swine model resulted in thermal tissue injury and necrosis. Suggestions for reducing the extent of injury with this product are offered."

Animal studies using 30 or 45 seconds of free bleeding time

Only hemostatic dressings tested in three or more studies or in models of special physiologic conditions are discussed here. All studies using 30 to 45 seconds of free bleeding time are summarized in a table in Appendix C.

QuikClot zeolite/kaolin clay-based dressing comes in granule, powder, and sponge form. These dressings were examined in six studies and showed poor hemostasis and survival properties.[74,75,78-80,387]

- Kheirabadi et al. 2009a[74] reported that the QuikClot advanced clotting sponge (ACS) failed to achieve hemostasis in any animals leading to animal deaths from exsanguination and therefore discontinued use of this dressing in the experiment.
- Two studies reported that QuikClot ACS was better than standard gauze:
    - Clay et al.[80] reported that 50% of QuikClot ACS treated animals survived, which was better than standard gauze (all animals died).
    - Arnaud et al.[75] compared QuikClot ACS with HemCon, WoundStat, Celox, and standard gauze and reported that the hemostatic dressings were significantly better than standard gauze for hemostasis and animal survival with WoundStat and Celox being the most effective (85% survival compared with 60% for ACS, 25% for HemCon, and 13% for standard gauze).
- One study reported that QuikClot powder and standard gauze had similar, but very poor hemostasis rates: Acheson et al.[79] compared QuikClot powder, HemCon, and standard gauze. Hemostasis was poor (0% for standard gauze and QuikClot, 7% for HemCon) and no animals survived when treated with these dressings.
- QuikClot granules were inferior to WoundStat in two studies:
    - Carraway[387] reported that QuikClot granules were inferior to WoundStat for hemostasis and survival (0% for QuikClot vs. 100% for WoundStat for both outcomes).
    - Ward et al.[78] compared QuikClot granules, QuikClot ACS, HemCon, and WoundStat with standard gauze. WoundStat showed better hemostasis and survival (100% for WoundStat vs. 0% for standard gauze, QuikClot Granules, and QuikClot ACS, and 20% for HemCon).

All the studies using QuikClot granules reported that a large amount of heat was generated in the wound.

QuikClot Combat Gauze (zeolite/kaolin-based dressing) was examined in three studies and showed good hemostasis and survival properties.[71-73]

- Rall et al.[71] reported that QuikClot Combat Gauze and Combat Gauze XL both provided effective hemostasis at 3 minutes (30% and 80%, respectively) and survival (60% and 70%, respectively) while creating no significant tissue damage.
- Schwartz et al.[72] found no difference comparing QuikClot Combat Gauze with ChitoGauze (HemCon) in hemostasis (all greater than 50%) or survival (all animals survived).
- Kheirabadi et al. 2009b[73] reported that QuikClot Combat Gauze was superior to both the HemCon bandage and Celox-D. This study compared QuikClot Combat Gauze with an advanced HemCon bandage, Celox-D, and standard gauze, and QuikClot Combat Gauze achieved 30% hemostasis compared with 0% for the HemCon bandage and Celox-D and 80% survival for QuikClot Combat Gauze compared with 0% survival for other two. The

authors recommended that QuikClot Combat Gauze replace HemCon bandages on the battlefield, based on their study results.

HemCon (chitosan-based dressing) was examined in 10 studies and showed broadly divergent results for hemostasis and survival: some studies reported 0% survival while others reported 100% survival.[71-80]

Kheirabadi et al. 2009a[74] reported that HemCon achieved 60% initial hemostasis but 9 of 10 animals died. As noted above, Acheson et al.[79] reported that hemostasis with HemCon was poor (7% for HemCon and 0% for standard gauze and QuikClot granules) and no animals survived when treated with these dressings. But another study noted much better survival: Rall et al.[71] reported that HemCon ChitoGauze provided 60% hemostasis and 70% survival with no significant tissue damage.

Two studies differed in their comparison of HemCon with QuikClot Combat Gauze:

- As noted above Schwartz et al.[72] reported that ChitoGauze (HemCon) and QuikClot Combat Gauze and were equally effective at hemostasis and preventing deaths.
- But Kheirabadi et al. 2009b[73] reported (as noted above) that HemCon bandage had worse results than QuikClot Combat Gauze.

Two studies reported that HemCon performed better than standard gauze:

- Clay et al.[80] reported that HemCon performed better, with 67% of HemCon-treated animals surviving compared with 0% for standard gauze–treated animals.
- Arnaud et al.[75] reported that HemCon was similar to QuikClot ACS and WoundStat and significantly better than standard gauze.

Three studies reported that HemCon had results similar to standard gauze:

- Sambasivan et al.[388] reported that ChitoFlex (HemCon) was similar to standard gauze for hemostasis (14% vs. 50%) and survival (70% vs. 100%).
- Englehart et al.[77] also reported that HemCon was similar to standard gauze for hemostasis (20% versus 50%) and survival (70% versus 90%).

As noted above, Ward et al.[78] reported that HemCon was similar to standard gauze, QuikClot granules, and QuikClot ACS, but inferior to WoundStat.

Celox (chitosan-based dressing) was examined in five studies and showed good hemostasis and survival properties except for one study.[71,73-75,80]

- Kheirabadi et al. 2009a[74] reported that Celox achieved 70% initial hemostasis and 60% of the animals survived.
- Rall et al.[71] reported that Celox produced 70% hemostasis and 90% survival.
- Clay et al.[80] reported that 83% of Celox-treated animals survived compared with 0% for standard gauze–treated animals.
- As noted above Arnaud et al.[75] reported that Celox was significantly better than standard gauze for hemostasis and animal survival, with WoundStat and Celox being the most effective with 85% survival.
- The outlier was the Kheirabadi et al. 2009b[73] study that, as noted above, reported that QuikClot Combat Gauze (80% survival) was superior to Celox-D (0% survival).

WoundStat (smectite/nonmetallic clay-based dressing) was examined in five studies and showed consistently good results for hemostasis and survival.[74,75,78,80,387]

- Kheirabadi et al.[74] reported that WoundStat prevented death in all 10 animals tested and was more effective than HemCon or QuikClot ACS in preventing death. However the authors noted that WoundStat produced moderate to severe endothelial injuries and multifocal vein necrosis.

- Clay et al.[80] reported that 100% of WoundStat treated animals survived compared with 0% for standard gauze–treated animals.
- Arnaud et al.[75] reported that WoundStat was similar to ACS and HemCon and significantly better than standard gauze.
- As mentioned above, Carraway[387] reported that WoundStat was superior to QuikClot granules.
- Also as noted above, Ward et al.[78] reported that WoundStat was superior to QuikClot granules, QuikClot ACS, HemCon, and standard gauze.

Despite the favorable hemostasis and survival results reported in studies of WoundStat, it is not used by the U.S. Military because of its high potential for tissue injury. Gerlach et al.[34] evaluated the extent of tissue damage induced by WoundStat compared with standard gauze in a study designed to allow all animals to survive the initial 45 seconds of blood loss. At each of five time points after surgery—1, 2, 3, 4, and 5 weeks—three animals that had been treated with WoundStat were euthanized. Examination of the tissues showed poor wound healing with extensive fibrosis, inflammation, and endothelial degeneration and necrosis. The results of this study lead to the discontinuation of WoundStat by the U.S. Military.

The 30- or 45-second free bleeding periods were used in several studies with unique designs and procedures intended to test hemostatic dressings in special situations. MacIntyre et al.[389] combined a tourniquet with standard gauze, HemCon, QuikClot granules, and Celox. After the tourniquet and direct pressure were released, standard gauze did not achieve hemostasis while effective hemostasis was found using HemCon (100%), QuikClot granules (80%), and Celox (60%). Two studies used a complete severing of the femoral artery and vein to produce a wound to "simulate the ragged, lacerated muscle of the cavity associated with high-velocity projectile tracts." Devlin et al.[390] used this model to compare QuikClot ACS, HemCon ChitoFlex, Celox, and standard gauze. All dressings were effective at stopping initial hemorrhage and 83% of the test animals survived when using standard gauze, QuikClot ACS, or HemCon ChitoFlex; 75% survived when using Celox. Littlejohn et al.[391] used this model to compare standard gauze with WoundStat, Celox, and QuikClot Combat Gauze. All the dressings, including standard gauze, were effective at producing initial hemostasis and differences in survival were not statistically significant, except that Celox (88% survival) was significantly better than WoundStat (56% survival). The authors suggested that proper wound packing and pressure may be more important than the use of hemostatic dressings in these types of wounds.

Watters et al.[392] used a study design with no external pressure to replicate care under fire. The study compared QuikClot Combat Gauze with Celox Gauze and standard gauze and reported that all animals survived with no differences in hemostasis. The authors concluded that advanced hemostatic dressings did not outperform standard gauze in a care-under-fire scenario.

Kheirabadi et al.[393] tested WoundStat, QuikClot Combat Gauze, and standard gauze in a model of hypothermia and dilution coagulopathy. WoundStat was ineffective in this model (bleeding stopped in 2 of 15 animals) while QuikClot Combat Gauze was only partially effective (bleeding stopped in 5 of 15 animals), although most animals survived the experiment.

Table C.2. Studies using 30 or 45 seconds of free bleeding

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Rall et al. 2013[71]	Determine the efficacy of novel hemostatic gauze products as compared to the current Committee on Tactical Combat Casualty Care standard, QuikClot Combat Gauze (QCG). QuikClot Combat Gauze XL (QCX), Celox Gauze (CEL), Celox Trauma Gauze (CTG), and HemCon ChitoGauze (HCG). N=10 per group. Femoral artery injury. Free bleeding for 45 seconds. Manual pressure for 3 minutes. 500 mL Hextend. Observed for 150 minutes.	Hemostasis after 3 minutes: QCG 30%, CTG 30%, QCX 80%, CEL 70%, HCG 60%; QCX was significantly different from QCG and CTG.	Survival: QCG 60%, CEL 90%, QCX 70%, HCG 70%, CTG 50%; differences were not significant.	No significant damage was observed in any of the tissues. CEL left particles in the tissue.	Blood loss was lowest in the QCX and CEL groups, but differences were not significant. All dressings retained hemostasis with leg movement. Free bleeding occurred with all dressings when gently removed, suggesting the gauze must remain in place to be continually effective.	"These results suggest that the novel hemostatic devices perform at least as well as the current Committee on Tactical Combat Casualty Care standard for point-of-injury hemorrhage control. Despite their different compositions and sizes, the lack of clear superiority of any agent suggests that contemporary hemostatic dressing technology has potentially reached a plateau for efficacy."
Watters et al. 2011[392]	The goal of this study was to determine whether these advanced dressings are superior to standard gauze in an animal model that replicates care-under-fire scenarios. Packing with standard gauze (SG), QuikClot Combat Gauze (CG), or Celox Gauze (XG) without external pressure. N=8 per group. Femoral artery injury. Free bleeding for 30 seconds, then dressing was applied through a pool of blood into the wound. Observed for 120 minutes.	Dressing failure: XG 50%, CG 25%, SG 0%; differences were not significant. Time to failure mean and (SE) in seconds: XG 200.0 (200.0), CG 416.3 (118.2); no significant differences.	All animals survived the test after 120 minutes before being euthanized.	Inflammation, necrosis, or deposition of dressing particles in vessel walls was not observed. No histologic or ultrastructural differences were found between any of the study dressings.	SG dressings packed significantly faster than either CG or XG.	"Advanced hemostatic dressings do not perform better than conventional gauze in an injury and application model similar to a care under fire scenario."

Table C.2. Studies using 30 or 45 seconds of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
MacIntyre et al. 2011[389]	Examine the combination of a tourniquet along with Standard gauze, QuikClot, HemCon, and Celox. Femoral artery and vein injury. Free bleeding for 30 seconds then tourniquet applied to stop bleeding. The dressing was applied with manual pressure for 3 minutes. The tourniquet and direct pressure were released. If bleeding occurred the procedure was considered a failure. N=10 per group.	Hemostasis (n of 10 for each): Standard gauze 0%, Celox 60%, QuikClot 80%, HemCon 100%.	All animals survived, but the study did not have a lengthy observation period.	No apparent complications during the study. QuikClot generated a large amount of heat.	—	"Use of hemostatic dressings in conjunction with a tourniquet may reduce tourniquet times and improve outcomes in peripheral vascular injury and warrants further study."
Devlin et al. 2011[390]	Compare ChitoFlex bandage (CF), QuikClot ACS dressing (QC), CELOX free granule formulation (CX) and standard gauze (SD) in their effectiveness to control arterial bleeding from a lethal non-cavitary groin wound. A groin injury was created to simulate the ragged, lacerated muscle of the cavity associated with high-velocity projectile tracts. Femoral artery and vein were completely severed. Free bleeding for 30 seconds. Dressings were applied with 3 minutes of manual pressure. Followed by application of a pressure bandage. Observed for 180 minutes. N=12 per group.	All hemostatic agents and standard gauze were effective at stopping initial hemorrhage.	Survival rate: 10 of 12 (83%) SD animals, 10 of 12 (83%) CF animals, 10 of 12 (83%) QC animals, and 9 of 12 (75%) CX animals; there was no significant difference.	—	Mean total blood loss: 31.8 mL/kg for SD (range 10.1–52.7 mL/kg), 27.4 mL/kg for CF (range 16.3–48.4 mL/kg), 32.0 mL/kg for QC (range 12.6–49.6 mL/kg), and 34.0 mL/kg for CX (range 17.5–52.1 mL/kg); differences were not statistically significant.	"In our study of limited-access extremity bleeding, ChitoFlex performed equally well in mitigating blood loss and promoting survival. The ChitoFlex dressing is an equally effective alternative to currently available hemostatic agents. However, no agents were superior to standard gauze in our model of limited access."

Table C.2. Studies using 30 or 45 seconds of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Schwartz et al. 2011[72]	Compare the effectiveness of ChitoGauze (HemCon) and QuikClot Combat Gauze. Femoral artery injury. Free bleeding for 45 seconds. Then dressings applied followed by compression with 75-lb dumbbell for 2 minutes. Pressure was released and dressings left in place for 180 minutes. Hextend 500 mL. Standard gauze with compression was not studied.	Hemostasis was defined as no residual blood pooling or seepage around the dressing. Immediate hemostasis: 4 of 7 QuikClot Combat Gauze, 5 of 7 ChitoGauze; difference was not statistically significant. Time to hemostasis, mean: QuikClot Combat Gauze 32.4 minutes, ChitoGauze 13.1 minutes; not statistically different.	All animals survived.	—	Dressing application was considered a failure if the animal died before 180 minutes, pCO_2 was less than 15 mm Hg, or mean arterial pressure dropped below 20 mm Hg. Blood loss and saline use were similar.	"ChitoGauze and Combat Gauze appear to be equally efficacious in their hemostatic properties, as demonstrated in a porcine hemorrhage model."
Littlejohn et al. 2011[391]	Examine 4 hemostatic agents, granular agents WoundStat (WS), Celox-A (CA), rolled QuikClot Combat Gauze (CG), and flexible rolled bandage Chitoflex (CF) to standard gauze (SG) in a model specifically designed to simulate the ragged, lacerated muscle of the cavity associated with high-velocity projectile tracts and the complete severing of the femoral artery and vein. Free bleed for 45 seconds with no application of a pressure dressing after applying the hemostatic dressing. Direct manual pressure was applied for 5 minutes then released. Observed for 180 minutes. N=16 per group.	Any bleeding that occurred in the first 5 minutes after release of manual pressure was considered a failure of initial hemostasis. CA, 16 of 16; CF, 13 of 16; CG, 15 of 16; SG, 13 of 16; WS, 11 of 16; WS was significantly different from CA.	Deaths: CA, 2 of 16; CF, 3 of 16; CG, 4 of 16; SG, 3 of 16; WS, 7 of 16; WS was significantly different from CA. Survival: CA 88%, CF 81%, CG 75%, SG 81%, WS 56%.	—	—	In this swine model of uncontrolled penetrating hemorrhage, SG dressing performed similarly to the hemostatic agents tested. This supports the concept that proper wound packing and pressure may be more important than the use of a hemostatic agent in small penetrating wounds with severe vascular trauma.

Table C.2. Studies using 30 or 45 seconds of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Kheirabadi et al. 2010[393]	Compare WoundStat (WS) with QuikClot Combat Gauze (CG) and control gauze (GZ) in coagulopathic subjects and assess the risk/benefit in trauma patients with acquired coagulopathy. Also examined FAST, a biological dressing. Spleens were removed. Hypothermia and dilutional coagulopathy were induced. 60% of the circulating blood volume was withdrawn and replaced with an equal volume of Hextend solution. Femoral artery injury followed by 30 seconds free bleeding. Dressings were applied followed by 2 minutes of direct manual pressure (except for FAST which received 3 minutes). Dressing could be reapplied 3 minutes after compression was stopped. Hemostasis was observed for the next 180 minutes. N was 12 to 15 per group.	Stable hemostasis: GZ, 1 of 12; WS, 2 of 15; CG, 5 of 15; FAST, 10 of 13; FAST was significantly different from GZ and WS. Total time bleeding stopped in minutes, mean (SEM): GZ 13.7 (8.9), WS 28.2 (16.2), CG 75.8 (21.6), FAST 113.3 (25); FAST was significantly different from GZ and WS.	GZ, 11 of 12; WS, 13 of 15; CG, 9 of 15; FAST, 3 of 13; FAST was significantly different from GZ and WS.	—	—	"The tissue sealant property of WS is apparently mediated by clot formation in the wound; therefore, it was ineffective under coagulopathic conditions. CG was partially effective in maintaining blood pressure up to 1 hour after application. FAST dressing showed the highest efficacy because of the exogenous delivery of concentrated fibrinogen and thrombin to the wound, which bypasses coagulopathy and secures hemostasis."
Clay et al. 2010[80]	Compare Enhanced HemCon (HC), QuikClot ACS+ (advanced clotting sponge), Celox (CX), and WoundStat (WS), with a standard army field dressing (AFD). Spleen was removed. Femoral artery and vein injury. Free bleed 45 seconds then dressings applied followed by manual pressure for up to 6 minutes. Pressure released and animals observed for 120 minutes. N=6 per group.	—	WS, 100%; CX, 83%; HC, 67%; ACS+, 50%; AFD. 0%; WS was significantly different from ACS+, all dressing were different from control.	—	Blood loss mL/Kg, mean (SD): HC, 10.0 (3.6); ACS+, 15.8 (3.6); CX, 12.9 (4.9); WS, 4.6 (2.3); AFD, 27.0 (2.7); WS was significantly different from ACS+, all dressings were different from control.	"All hemostatic dressings result in significantly less blood loss and improved survival over standard gauze dressing."

Table C.2. Studies using 30 or 45 seconds of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Gerlach et al. 2010[34]	Compare WoundStat (WS) with plain gauze in a severe extremity artery injury to determine extent of tissue damage and ability for wound healing and survival up to 5 weeks after surgery. Femoral artery injury. N=18 WS and n=3 gauze. 45 seconds free bleeding. Manual pressure for 3 minutes followed by compression from a sandbag for 1 hour. 500 mL Hextend. Reapplication allowed if rebleeding occurred during the 1-hour period. Gauze control group had manual pressure for 1 hour. WS and gauze were removed from the wounds after 1 hour and the wounds were irrigated with saline. Arteries were repaired with a saphenous vein patch. At each time point of baseline and 1, 2, 3, 4, and 5 weeks after surgery, 3 WS animals were euthanized.	All animals achieved hemostasis.	All animals survived.	WS particles were visible in treated wounds and were surrounded by fibrous tissue. Sections of the femoral artery from the injured legs in the WS group had multifocal to diffuse, moderate to severe, and chronic fibrogranulomatous inflammation except at baseline. Variable amounts of endothelial degeneration and necrosis were seen. Femoral nerves in WS group showed abundant perineural fibrogranulomatous inflammation with mild-to-moderate axonal degeneration. Given these histological findings the authors recommend not using WS assuming other options are available.	WS was moderately difficult to remove from the wound.	"Although an effective hemostatic agent, WS use was associated with a substantial local inflammatory response and neurovascular changes up to 5 weeks postinjury."

Table C.2. Studies using 30 or 45 seconds of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Kheirabadi et al. 2009a[74]	Determine the efficacy and acute safety of 3 new hemostatic products in granular/powder form. Enhanced HemCon bandage (HC), QuikClot advanced clotting sponge plus (ACS), WoundStat (WS), super quick relief (SQR), and Celox (CX). HC was considered the control. Spleens were removed. Femoral artery injury. Free bleeding for 45 seconds then dressing applied. 500 mL Hextend. The compression or packing and compression were stopped after 2 minutes and hemostasis was observed for 3 minutes without removing the laparotomy gauze. Dressings could be applied a second time. Observed for 180 minutes. N=10 per group.	ACS treatment failed to produce hemostasis in 6 consecutive experiments, resulting in hemorrhage and exsanguination of 5 animals. Therefore, further testing of this material was discontinued and the related data were excluded for statistical analysis. Initial hemostasis: HC, 60%; WS, 60%; CX, 70%; SQR, 90%; not significantly different. Initial hemostasis was considered to occur when bleeding was stopped for at least 3 minutes after compression.	Deaths: HC, 9 of 10 died; WS, none died; CX, 4 died; SQR, 3 died; WS and SQR were significantly different from the others.	WS, CX, and SQR produced moderate to severe endothelial injuries along with moderate vascular and perivascular changes, including multifocal vein necrosis. SQR was considered the most damaging. The interaction of SQR with blood produces significant heat with persistent high temperatures causing significant damage to underlying tissues including nerve structures. The granular hemostatic products, particularly those with procoagulant activities (WS and SQR) may pose a potential risk for thromboembolism that should be further investigated in survival studies.	Total time bleeding stopped in minutes, mean (SD): ACS, 10.6 (10); HC, 2 (18); CX, 108.6 (29); SQR, 125.5 (24); WS, 166.0 (7.5); CX, SQR, WS were significantly different from ACS and HC. The most difficult agent to remove was SQR. Some particles that formed a scab to stop the bleeding were essentially embedded into the tissues.	"The new hemostatic agents are significantly more effective in treating arterial hemorrhage than currently deployed products [HemCon dressing or QuikClot granular products]. Among them, WS granules appear to be most efficacious, followed by SQR and CX powders. The clinical significance of tissue damage caused by these agents and any potential risk of embolism with procoagulant granular/powder products are unknown and warrant survival studies."

Table C.2. Studies using 30 or 45 seconds of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Kheirabadi et al. 2009b[73]	Evaluate QuikClot Combat Gauze (CG), TraumaStat (TS), Celox-D (CXb), advanced HemCon bandage (HCs), and placebo gauze (PG). Spleen was removed. Femoral artery injury. Free bleeding for 45 seconds, dressings applied, manual pressure for 2 minutes with 500 mL Hextend, if rebleeding occurred after release of manual pressure dressings were reapplied. 2 more minutes of manual compression. Observed for 180 minutes.	Hemostasis defined as secure hemostasis for at least 3 minutes immediately after treatment. HCs and CXb had 0% hemostasis; CG, 30%; TS, 10%; PG, 17%. The HC and CXb groups were discontinued and not included in any statistically analysis.	HCs and CXb had 0% survival, n=6 for each group. TS, 2 of 10, (20%); CG, 8 of 10, (80%); PG, 2 of 6, (33%). CG was significantly different from TS and PG.	Complete removal of CXb particles from the wound required more effort than other dressings and pieces of the bags (undissolved), and some dry chitosan material were often found in the wound.	—	"CG was the most effective dressing tested in this arterial hemorrhage model. The hemostatic property of CG is attributed to its raw material (nonwoven Rayon and polyester blend), kaolin coating, and the large surface area (3 inch / 4 yd) of this absorbent sponge. CG is now recommended as the first line of treatment for life-threatening hemorrhage on the battlefield, replacing HC."
Arnaud et al. 2009[75]	Evaluate hemostatic dressings in a severe vascular puncture injury model: QuikClot ACS+, Celox (CEL), Instaclot (IC), WoundStat (WS), Alpha Bandage (AB), BloodStop (BLS), X-Sponge (XS), Chitoflex (CHI), HemCon (HC), Polymem FP-21 (FP-21), standard gauze (SD). N=8 per group. Femoral artery injury. Free bleeding for 45 seconds then applied test dressing. Manual pressure for 5 minutes. At 15 minutes given 500 mL Hextend. Observed for 180 minutes.	Rebleeding: Bleeding upon the release of manual compression ranged from 50% to 62.5% for XS, WS, CEL, and ACS, and 75% to 100% for all other dressings.	Survival rate: SD, 13%; WS, 85%; CEL, 85%; XS, 70%; ACS+, 60%; IC, 50%; AB, 50%; CHI, 25%; FP-21, 25%; HC, 25%; BLS, 25%. All dressing were significantly better than SD. WS, CEL, XS, and ACS+ were significantly better than other dressings.	—	—	"The findings indicated that the efficacy of Woundstat, Celox, X-Sponge, and ACS+ were similar and superior in improving survival, hemostasis, and maintenance of mean arterial pressure in an actively bleeding wound caused in this severe vascular injury model."

Table C.2. Studies using 30 or 45 seconds of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Kilbourne et al. 2009[394]	Evaluate the hemostatic efficacy of a newly modified amylopectin powder (Hemostasis, LLC, St. Paul, MN) compared with standard gauze. Femoral artery injury, free bleeding for 45 seconds, then dressings were applied. Manual compression for 3 minutes. Dressings could be applied a second time with 3 minutes additional manual pressure. 180 minute observation period. N=6 per group.	Hemostasis: gauze, 0%; powder, 100%. 9 minutes for the powder. Gauze group did not achieve hemostasis.	All animals in the gauze group died. All survived in the powder group.	—	Median post-treatment blood loss: powder 275 mL, gauze 1,312 mL.	"Modified amylopectin powder demonstrates the ability to control major vascular bleeding in a lethal arterial injury model during a 3-hour period."
Sambasivan et al. 2009[76]	Compare TraumaStat with Chitoflex (HemCon, Inc.), a chitosan dressing and standard gauze, with a 30-second application time to better reflect the time available to apply a dressing in a tactical combat scenario. Femoral artery and vein injury. Free bleeding for 30 seconds. Dressings applied and held for 30 seconds. Observed for 120 minutes. N=8 per group.	TraumaStat, 8 of 8 (100%); Chitoflex, 1 of 7 (14%); standard gauze, 4 of 8 (50%). TraumStat was significantly different from other dressings.	TraumaStat: no deaths. Chitoflex: 3 of 7 died. Standard gauze: no deaths. Differences were not statistically significant.	—	—	"TraumaStat performed significantly better than Chitoflex and standard gauze in controlling hemorrhage from a severe groin injury in swine."
Englehart et al. 2008[77]	Compare the hemostatic properties of TraumaStat to HemCon and gauze dressing in a lethal groin injury model of severe uncontrolled hemorrhage in swine. Femoral artery and vein injury. Free bleeding for 30 seconds. Dressings were applied and pressure held for 5 minutes. Observed for 120 minutes. N=10 per group.	Dressing failures: TraumaStat, 1 of 10; HemCon, 8 of 10; gauze, 5 of 10. TraumaStat was significantly different from HemCon.	Deaths: TraumaStat, 1 of 10; HemCon, 3 of 10; gauze, 1 of 10. Differences were not significant.	—	Blood loss after treatment, median: TraumaStat, 117 mL; HemCon, 774 mL; gauze dressing, 268 mL. TraumaStat was significantly different from HemCon and gauze.	"TraumaStat was superior to HemCon and gauze dressings in controlling bleeding from a severe groin injury. TraumaStat may be a better hemostatic dressing for control of active hemorrhage than current standards of care."

Table C.2. Studies using 30 or 45 seconds of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Carraway 2008[387]	Compare WoundStat (WS) to QuikClot granules (QCG). Femoral artery injury. Free bleeding for 45 seconds then dressings applied. Manual pressure for 3 minutes. 500 mL Hextend. A second dressing application was allowed if rebleeding occurred. Observed for 120 minutes.	All WS animals achieved hemostasis with no second application. All QCG animals needed a 2nd application, but hemostasis was not achieved in any animal.	All WS animals survived but no QCG animals survived; difference was statistically significant.	QCG animals showed a significantly higher wound temperature: mean 64 °C vs. 33 °C.	—	"WS consisting of just the smectite mineral was superior to QCG tested in this model. Additional study is warranted to determine its potential for use in combat and civilian trauma."
Ward et al. 2007[78]	Evaluate WoundStat (WS) (a granular blend of smectite mineral and a super absorbent polymer) compared to Army gauze field bandage (AFB), QuikClot granules (QCG), QuikClot Advanced Clotting Sponge (ACS), HemCon chitosan Dressing (HC), N=5 per group. Spleen was removed. Femoral artery injury. Free bleeding for 45 seconds then dressings were applied. 200 mm Hg pressure applied for 3 minutes. Application was repeated if rebleeding occurred. 500 mL Hextend. Observed for 180 minutes. N=5 for all groups.	WS achieved complete hemostasis in all animals with no second application. All other dressings needed a second application.	All WS animals survived, 100%; AFB, 0%; QCG, 0%; ACS, 0%; HC, 20%, WS was significantly different from all other dressings.	Temperatures were significantly higher for the QCG and ACS groups immediately after application.	WS had significantly less blood loss than the other dressings.	"WS was superior to the other hemostatic agents tested in this study of lethal arterial vascular injury. Additional study is warranted on this agent to determine its potential for use in combat and civilian trauma."

Table C.2. Studies using 30 or 45 seconds of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Acheson et al. 2005[79]	Compare QuikClot powder (QC), chitosan dressing Hemcon (CD), and fibrin sealant dressing (FSD) with standard gauze control Army Field Bandage (AFB). Spleen was removed. Femoral artery injury. Free bleeding for 45 seconds then dressings applied. Manual pressure for 3 minutes. 500 mL Hextend. Observed for 180 minutes. N=15 per group.	Hemostasis: AFB, 0%; QC, 0%; CD, 7%; FSD, 67%; FSD significantly different from other dressings.	Survival: AFB, 0%; QC, 0%; CD, 0%; FSD, 67%; FSD significantly different from other dressings.	QC produced markedly higher maximum temperatures with an average of 70.8 °C; temperature for other dressings was 37 °C; the difference was statistically significant. Tissue damage was seen primarily in QC treated animals.	—	"FSD was superior to other currently utilized hemostatic products in controlling lethal arterial hemorrhage in this model of a fatal extremity wound. CD showed some hemostatic benefit. The exothermic reaction of QC was significant and resulted in gross and histologic tissue changes of unknown clinical significance. Controlled human studies with the promising products are required."
Connolly 2004[395]	Compare the hemostatic capabilities of the Rapid Deployment Hemostat (RDH) Bandage (n=6) with a gauze pad (n=5). Femoral artery injury. Tibia was fractured. Free bleeding for 30 seconds. Dressings applied followed by 5 minutes manual pressure.	—	—	—	Blood loss after 30 minutes, mean (SD): RDH, 14% (9); gauze pad, 35% (14); difference was significantly different.	"The RDH Bandage was demonstrated to be an effective hemostatic agent capable of rapidly stopping arterial hemorrhage with the potential to decrease trauma bleeding mortality."

Animal studies using 1 or 2 minutes of free bleeding

QuikClot granules/powder/sponge were examined in three studies and showed good hemostatic and survival properties.[396-398]

- Arnaud et al.[396] compared QuikClot ACS, Celox, WoundStat, HemCon, and several other hemostatic dressings with standard gauze. All dressings were significantly better than standard gauze for survival (37% for gauze, 60% for HemCon, 70% for ACS, 90% for Celox and WoundStat). QuikClot ACS was noted to have caused some mild burn injuries.
- Arnaud et al.[397] also noted that QuikClot ACS was an effective hemostatic agent and that a different formulation of the sponge could reduce the amount of heat generated.
- Nowshad et al.[398] used a brachial artery injury in a goat model to compare QuikClot and Chitohem powders and reported that QuikClot was the better agent.

QuikClot Combat Gauze was examined in three studies and showed good results for hemostasis and survival.[85-87] Two of these studies, examining differing outcomes, reported that QuikClot Combat Gauze was significantly better than standard gauze:

- Gegel et al.[85] reported that QuikClot Combat Gauze was significantly better than standard gauze at controlling blood loss and preventing further bleeding when the limb was vigorously moved.
- Causey et al.[86] reported that hemostasis using QuikClot Combat Gauze was significantly better than standard gauze when used in conditions of severe acidosis and coagulopathy.

In the third study, Arnaud et al.[87] compared QuikClot Combat Gauze with TraumaStat and reported that both dressings were effective hemostatic agents and protected most animals from dying (QuikClot Combat Gauze, 88% survival; TraumaStat, 50% survival).

TraumaDex (microporous polysaccharide hemospheres) was examined in two studies and showed good results for hemostasis and survival.[399,400] One of the studies looked at rebleeding and found not only TraumaDex but also other hemostatic dressings were better than standard gauze for preventing rebleeding:

- Burgert et al.[399] tested TraumaDex, BleedArrest, Celox, and standard gauze in a model intended to determine the arterial blood pressure at which rebleeding would occur. All of the hemostatic dressings were effective at hemostasis (BleedArrest and TraumaDex 100%, Celox 80%) but standard gauze failed to achieve hemostasis. All of the hemostatic dressings were effective at preventing rebleeding while blood pressure was raised pharmacologically.
- The second study, Gegle et al.,[400] compared blood loss among TraumaDex, Celox, BleedArrest, and standard gauze. All of the hemostatic dressings were significantly better at preventing blood loss than standard gauze but no differences were found among the hemostatic dressings.

Table C.3. Studies using 1 or 2 minutes of free bleeding

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Gegel et al. 2012[85]	The purpose of this study was to examine the effectiveness of QuikClot Combat Gauze (QCG) compared to a control group and the effect of movement on hemorrhage control when QCG is employed. Femoral artery and vein injury. Free bleeding for 1 minute then dressings applied. Firm manual pressure of 25 lb per square inch was applied for 5 minutes. 10-pound sandbag was applied to the wound for an additional 30 minutes. N=11 per group.	Hemostasis was defined as a clot formation with oozing of no more than 2% of the swine's total blood volume over a 5-minute period. Data on number of animals to achieve hemostasis were not reported.	—	—	5 minute hemorrhage amounts, mean (SD): QC, 50±154 mL; control, 351±354 mL; difference was statistically significant. Movement caused significantly more rebleeding in the control group.	"QCG is statistically and clinically superior at controlling hemorrhage compared to the standard pressure dressing control group. Furthermore, it produces a more robust clot that can withstand significant movement. These movements were severe and should be avoided in patients with an inguinal injury. However, the investigators wanted reproducible movements that would test the robustness of a newly formed clot. Based on this study and the requirements outlined by Pusateri, QCG is an effective hemostatic agent for use in civilian and military trauma management."
Gegel et al. 2012[401]	BleedArrest (Hemostasis LLC, Saint Paul, MN) compared to standard compression. Uncontrolled hemorrhage model. N=10 per group. Femoral artery and vein were injured. Bleeding for 1 minute. Manual 25 psi pressure applied for 5 minutes after application of dressings followed by pressure dressing of rolled gauze and 10 pound sandbag, left in place for 30 minutes.	—	—	No exothermic heat product with BleedArrest and no signs of tissue damage.	Blood loss mean (SD): BloodArrest, 72 mL (72); control, 317 mL (112); the difference was statistically significant.	"BleedArrest is statistically and clinically superior at controlling hemorrhage compared to the standard pressure dressing control group. In conclusion, BleedArrest is an effective hemostatic agent for use in civilian and military trauma management."

Table C.3. Studies using 1 or 2 minutes of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Causey et al. 2012[86]	Test QuikClot Combat Gauze (CG) and standard gauze (SG) under conditions of severe acidosis and coagulopathy. Used an ischemia-reperfusion swine model to produce a clinically significant metabolic (lactic) acidosis and dilutional coagulopathy. Femoral artery was injured and allowed to bleed freely for 2 minutes. Dressings were applied, followed by 2 minutes of compression, followed by a 5 minutes period to watch for rebleeding. If rebleeding occurred, the old dressing was removed and new dressings were reapplied. The study end point was hemostasis or 2 failed attempts.	Hemostasis success rate: CG, n=9, 89% after first application and 100% after second; SG, n=8, 0% after first application and 3% after second application; difference was statistically significant.	—	—	—	"Combat Gauze significantly outperforms standard gauze dressings in a model of major vascular hemorrhage in acidotic and coagulopathic conditions. This effect appears to result from a decreased time lag between activation and first detectable clotting. Combat Gauze appears to maintain its efficacy even in the setting of severe acidosis and coagulopathy for the control of hemorrhage from vascular injury."

Table C.3. Studies using 1 or 2 minutes of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Burgert et al. 2012[399]	Determine and compare the arterial blood pressures at which rebleeding occurred when the hemostatic agents (BleedArrest, Celox, and TraumaDex) were used to control hemorrhage compared with rebleeding with standard pressure dressing. Femoral artery and vein injury. Free bleeding for 1 minute. Manual pressure (25 psi) was applied for 5 minutes. A standard pressure dressing was then applied and maintained for 30 minutes under a 10 lb sandbag. After hemostasis was achieved, phenylephrine was used for arterial pressure manipulation. N=5 per group.	Hemostasis: BleedArrest, 100%; TraumaDex, 100%; Celox, 80%; standard gauze, 0%.	—	—	All of the hemostatic dressings were significantly better than standard gauze at preventing rebleeding at increased blood pressure.	"The results of the current study suggest that when BleedArrest, Celox, and TraumaDex are used, the clots are stronger compared to clots formed in the control group and may provide an extra margin of safety in the presence of elevated blood pressures. This study only investigated the effects of arterial blood pressure on rebleeding when hemostatic agents were used. Future studies should investigate the effects of hemodilution on rebleeding."

Table C.3. Studies using 1 or 2 minutes of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Arnaud et al. 2011[87]	Compare QuikClot Combat Gauze (CBG) to TraumaStat (TMS). Tested with both full femoral transection (including artery and vein) and a femoral artery puncture injury models. Full femoral transection: n=6 for each dressing, 2 minute free bleeding. Artery puncture: n=8 for each dressing, 45 second free bleeding. Followed by dressing application and 5 minutes of manual compression. Dressings stayed in place for 180 minutes.	Rebleeding was defined as blood oozing from the dressings (post-treatment blood loss) and requiring aspiration as opposed to no bleeding or bleeding controlled by the dressing (blood retained in the dressing and no need for aspiration). After compression: transection model CBG, 0%; TMS, 17%; puncture model CBG, 63%; TMS, 75%; difference was not statistically significant.	Transection: all animals survived for 180 minutes. Puncture: CBG. 7 of 8 survived; TMS, 4 of 8 survived; difference was not statistically significant.	—	Blood loss was significantly greater in the transection model. Both dressings were easy to use and remove from the wound.	"These findings indicated that CBG and TMS were similarly effective in improving hemostasis. These two fabric-like dressings showed easy application and removal, leaving a clean wound for surgical repair."
Gegel et al. 2010[400]	Examine the effectiveness of BleedArrest, TraumaDex, Celox, and control. N=5 for each group. Femoral artery and vein injury. Free bleeding for 1 minute then dressing applied. Manual pressure of 25 lb per square inch applied for 5 minutes. Followed by pressure wrap for 30 minutes. 500 mL of Hextend. Pressure wrap removed. No further observation period.	Hemostasis was defined as clot formation with oozing of no more than 2% of the swine's total blood volume over a 5-minute period. No data were reported on rates of hemostasis.	—	—	Blood loss for 5 minutes, mean (SD): BleedArrest, 21.0 (36.6) mL; TraumaDex, 68.0 (103.5) mL; Celox, 18.2 (41.6) mL; control, 230 (154) mL; all hemostatic dressings were significantly different from control but not from each other.	"BleedArrest, Celox, and TraumaDex were statistically and clinically superior at controlling hemorrhage compared with the standard pressure dressing in the control group."

Table C.3. Studies using 1 or 2 minutes of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Burgert et al. 2010[402]	Determine the arterial blood pressures at which rebleeding occurs when Celox and TraumaDEX are used to control hemorrhage compared with a standard pressure dressing. N=5 per group. Femoral artery and vein injury. Free bleeding for 1 minute, application of hemostatic dressing, 5 minutes 25 psi manual pressure, then standard pressure dressing for 30 minutes. Blood pressure was raised using phenylephrine infusion.	Hemostasis was defined as clot formation with blood loss of no more than 2% of the swine's total blood volume over 5 minutes.	—	—	Rebleeding systolic blood pressure mm Hg, mean (SD): Celox, 166.40 (40.92); TraumaDEX group, 152.20 (59.05); control, 88.25 (2.80); Celox and TraumaDEX were significantly different from control but not each other.	"Celox and TraumaDEX effectively prevent rebleeding compared with standard dressing."
Arnaud et al. 2009[396]	Evaluate 10 different hemostatic dressings: Advanced Clotting Sponge ACS+, Celox (CEL), Instaclot (IC), WoundStat (WS), Alpha bandage (AB), BloodStop (BLS), X-sponge (XS), Chitoflex (CHI), HemCon (HC), Polymem FP-21 (FP-21). Femoral artery and vein injury. N=8 per group. Free bleeding for 2 minutes, then dressings applied with standard gauze dressing placed over the dressings, pressure applied for 5 minutes, 500 mL Hextend at 15 minutes, observed for 180 minutes.	Rebleeding: XS, WS, CEL, and IC, were significantly better with less than a 40% rate.	Survival rate (extrapolated from figure): ACS+, 70%; CEL, 90%; IC, 60%; WS, 90%; AB, 50%; BLS, 50%; XS, 90%; CHI, 50%; HC, 60%; FP-21, 50%; standard gauze, 37%; all dressings were significantly different from standard gauze.	ACS+ caused a rise of 7.2 °C and 8.7 °C between 2 and 4 minutes after application. ACS+ animals had more edema-like changes with the greatest depth in the muscle layer that could be attributed to a mild burn injury.	Blood loss was lowest in IC, CEL, XS, and WS and were significantly different from HC, BS, FP-21, and CHI.	"Celox, QuikClot ACS, WoundStat, and X-Sponge ranked superior in terms of low incidence of rebleeding, volume of blood loss, maintenance of mean arterial pressure >40 mm Hg, and survival."

Table C.3. Studies using 1 or 2 minutes of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Arnaud et al. 2008[397]	Compare the temperature change and the hemostatic efficacy of Advanced Clotting Sponge ACS+ to ACS in the groin hemorrhage model; compared to standard gauze. Femoral artery and vein injury. Free bleeding for 2 minutes (40% estimated blood volume). Dressings were applied, then manual pressure for 5 minutes. Observation for 180 minutes while wound remained covered. 500 mL Hextend at 15 minutes. 2 studies were conducted, 1 with blood in the wound and 1 with blood removed from the wound.	Rebleeding occurred in 50% of both ACS groups in no-blood-present study.	Survival rate (no blood present): ACS+, 63.6% (7 of 11); and ACS, 100% (4 of 4); both higher than standard dressing (12.5%, 1 of 8). ACS groups were not significantly different but both were significantly different from gauze. Survival rate (blood present): ACS, 67% (4 of 6); gauze, 25% (1 of 4).	—	Wound temperature with no blood present before dressing application: significantly lower with ACS+ treatment compared with ACS treatment (40.3±1.8 °C vs. 61.4±10.7 °C; significantly different). Temperature was higher by 3.2±1.6 °C in ACS+ group than rectal temperature (significantly different). With blood present, ACS temperature was significantly lower than with no blood present.	"The lower heat release with ACS+ compared to ACS was confirmed in an animal model and ACS+ had similar efficacy in arresting bleeding when compared to Standard Dressing."
Nowshad et al. 2011[398]	Compare the effectiveness of QuikClot powder and Chitohem powder for control of bleeding. Brachial artery injury in a goat model. Free bleeding for 60 seconds then dressing applied. Animals were stabilized with intravenous fluid. Incisions were closed using silk sutures. Observation for 120 minutes. Animals were allowed to recover.	Hemostasis achieved: Chitohem 15 of 20 stopped bleeding, results not presented for QuikClot but were significantly better than Chitohem.	—	—	Blood loss: QuikClot 51.1±4.48 cc, Chitohem 63.3±12.04 cc; differences was significantly different.	"In this study, it seems that activity of 'Quikclot' in cessation of bleeding of large arterial vessels was slightly better than 'Chitohem.' Due to limitations which we had in this study, further studies are necessary to show the actual differences between these agents and their side effects."

Animal studies using 3 or more minutes of free bleeding

QuikClot was compared to various hemostatic agents and standard gauze in all five studies using 3 or more minutes of free bleeding.[69,70,88-90] In these studies of severe bleeding, QuikClot was effective at promoting hemostasis and survival.

Kozen et al.[88] compared QuikClot granules to Celox, HemCon, and standard gauze to determine the extent of rebleeding after animals are resuscitated after severe blood loss (66% of blood volume). Each of the hemostatic dressings was effective at preventing rebleeding compared with rebleeding with standard gauze. Survival was only 50% for the standard gauze group compared with 100% for Celox, 92% for QuikClot, and 67% for HemCon. A significant increase in wound temperature was noted in QuikClot animals.

Arnaud et al.[89] compared QuikClot granules and ACS (bagged QuikClot) with standard gauze and no treatment. All animals that received no treatment died, compared with a survival rate of 12.5% for gauze and 75% for both forms of QuikClot. Both forms of QuikClot significantly raised wound temperature.

Ahuja et al.[90] reported on survival in animals treated with various reformulations of QuikClot compared with QuikClot granules in a bag, HemCon, standard gauze, and no treatment. All animals that received no treatment died, compared with a survival rate of 50% for gauze, 75% for HemCon, and 90% for QuikClot granules in a bag. Only QuikClot granules in a bag was significantly different from gauze. Tissue damage was also reduced with bagged QuikClot granules.

Alam et al.[69] compared QuikClot granules with HemCon, TraumaDex, other hemostatic agents, standard gauze, and no treatment. All nontreated animals died as well as 57% of gauze-treated animals. No QuikClot-treated animals died compared with a survival rate of 74% for HemCon-treated animals and 67% for TraumaDex-treated animals.

Alam et al.[70] compared QuikClot granules with Rapid Deployment Hemostat (poly-N-acetylglucosamine derived from algae), TraumaDex, standard gauze, and no treatment. QuikClot treated animals had the lowest blood loss and no deaths. No treatment resulted in 17% survival, Rapid Deployment Hemostat in 33% survival, and standard gauze and TraumaDex both resulted in 67% survival.

Table C.4. Studies using 3 minutes or more of free bleeding

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Filips et al. 2013[35]	Compare the iTClamp to standard gauze. N=5 per group. Four study groups according to bleeding time: control (no treatment), Early iTClamp (clamp applied after 10 seconds of free bleeding), Late iTClamp (applied after 3 minutes of free bleeding), and standard gauze (applied after 3 minutes of free bleeding). Observed for 180 minutes.	—	Survival: Control 0%, standard gauze 60%, Early iTClamp 100%, Late iTClamp 100%.	No adverse events reported	The mean external blood loss was significantly lower in the iTClamp groups compared to control animals. Early iTClamp but not Late iTClamp had significantly less blood loss than standard gauze.	"The iTClamp showed statistically significant improvement in survival, survival time, and estimated blood loss when compared to no treatment. This proof-of-concept study demonstrates the potential of the iTClamp to control severe bleeding and prevent blood loss."
Kozen et al. 2008[88]	Compare the Celox (CX), HemCon (HC), and QuikClot granules (QC) dressings to standard gauze dressing (SD). N=12 per group. Femoral artery and vein injury. Free bleeding for 3 minutes then dressing applied. Manual pressure for 5 minutes followed by a compression dressing. 500 mL Hextend. Observed for 180 minutes. Mean initial blood loss was more than 66% of blood volume.	Initial hemostasis was achieved in all animals but rebleeding occurred in 10 of 12 in the SD group with 6 of 12 achieving a second hemostasis. Rebleeding: CX, 0%; HC, 33%; QC, 8%; all were significantly different from SD.	Survival: CX, 100%; SD, 50%; HC, 67%; QC, 92%; CX was significantly different from SD. Some animals died before dressing application and were excluded from the study.	Mean maximum temperature in wounds treated with QC was 61.0 °C and statistically different from 37.6 °C in CX, 38.2 °C in HC, and 38.8 °C in SD.	Blood loss, mean (SD): SD, 54.0±7.2 mL/kg; CX, 46.4±5.2; HC, 50.1±11.0; QC, 46.5±4.9	"In this porcine model of uncontrolled hemorrhage, CX improved hemorrhage control and survival. CELOX is a viable alternative for the treatment of severe hemorrhage."

Table C.4. Studies using 3 minutes or more of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Arnaud et al. 2007[89]	Compare the modified "bagged" QuikClot (ACS) with the original granular QC, standard gauze (SD) and no treatment (NONE). Femoral artery and vein injury. Free bleeding for 3 minutes then dressings were applied. Manual pressure for 5 minutes. 500 mL Hextend. Observed for 240 minutes. N=8 per group.	—	Survival: NONE, 0%; SD, 12.5%; QC, 75%; ACS, 75%.	Wound temperature, mean (SD): maximum of 58.1(4.5) °C for QC and 58.2 (5.3) °C for ACS; significantly higher than SD, 37.8 (0.4) °C; and NONE, 37.5 (0.7) °C.	Blood loss: ACS-treated animals (10.3% estimated blood volume [EBV]) and SD-treated animals (22.3% EBV), significantly lower than the blood loss in NONE-treated animals (31.5% EBV).	"ACS was as efficacious as original granular QC in inducing hemostasis and improving survival as compared with the efficacy of SD. Easier and more rapid application and complete removal of ACS may offer a distinct advantage in battlefield resuscitation efforts to enhance a clean wound site and eventual surgical repair."
Ahuja et al. 2006[90]	Compare new varieties of ion exchange zeolites, and the new generation of chitosan dressing (HemCon), with standard gauze and QuikClot granules in a bag. Femoral artery and vein injury. Free bleeding for 3 minutes followed by dressing application and 5 minutes of manual pressure. 500 mL Hextend. Observed for 180 minutes.	—	All animals in the control (no dressing) group died, n=9. Standard dressing group had 50% mortality, n=10. QuikClot granules, 10% mortality, n=10; HemCon, 25%, n=8; only QuikClot was significantly different from standard gauze.	—	Bagged-QuikClot was considered easier to apply and remove. The bags conformed to the contours of the wound on packing. Removal was extremely easy and quick. This version was superior to the original used in a previous study. The zeolite formulas including bagged QuikClot all produced heat but necrosis was absent in all of the artery sections examined.	"The use of zeolite hemostat can control hemorrhage and dramatically reduce mortality from a lethal groin wound. Modifications of zeolite hemostat can decrease the exothermic reaction and attenuate tissue damage."

Table C.4. Studies using 3 minutes or more of free bleeding (continued)

Reference	Methods	% Hemostasis	Survival	Adverse Events	Other Outcomes	Author's Conclusions
Alam et al. 2004[69]	Compare no dressing (ND) n=8, standard gauze (SD) n=7, QuikClot granules n=7 (1% residual moisture [RM] zeolite hemostat 3.5 oz), HemCon (HC) n=7, Quick Relief n=8, Fast Act (FA) n=6, TraumaDex (TDex) n=7. QuikClot in a bag was tested in 5 animals. Femoral artery and vein injury. Free bleeding for 3 minutes. Treatment dressings were applied followed by manual compression for 5 minutes. 500 mL Hextend. Observed for 180 minutes.	QuikClot stopped bleeding in all animals. HC stopped bleeding in 5 animals but failed completely in 2 animals.	Mortality: All ND animals died. SD, 57%; QuikClot, 0%; HC, 28.6%; FA, 83.3%; TDex, 42.9%; Quick Relief, 75%; only QuikClot was significantly different from ND and SD. QuikClot in bag 40%.	QuikClot and Quick Relief showed temperature increases in the wound and tissue damage.	QuikClot had the lowest volume of blood loss.	"The use of zeolite hemostatic agent (1% residual moisture, 3.5 oz) can control hemorrhage and dramatically reduce mortality from a lethal groin wound."
Alam et al. 2003[70]	Define a clinically relevant animal model of lethal hemorrhage from a complex groin wound and compare the efficacy of different hemostatic agents to standard dressing (SD) and no dressing (ND) for control of bleeding and improvement of early survival. Rapid Deployment Hemostat (RDH) bandage, QuikClot hemostatic agent (QC), and TraumaDEX (TDEX). Femoral artery and vein injury. Free bleeding for 5 minutes. 1,000 mL normal saline. Observed for 180 minutes. N=6 per group.	—	Mortality: ND, 83%; SD, 33.4%; QuikClot, 0%; RDH, 66.6%; TDEX, 33.4%; QuikClot was significantly different from ND.	—	QC had the lowest blood loss but it was not statistically different from the ND control.	"Of the hemostatic agents tested, QuikClot improved survival and decreased bleeding in a swine model of lethal vascular and soft tissue injury."

Volunteer Studies

Table C.5. Studies testing tourniquets with volunteers

Reference	Type of Tourniquet Tested, Purpose and Methods	Outcomes	Author's Conclusions
Wall et al. 2013[91]	Combat Application Tourniquet (CAT) and Stretch, Wrap, and Tuck Tourniquet (SWAT-T) Collect occlusion and completion pressures of tourniquets with different widths and styles designed for tactical environments. Test if arterial occlusion pressures are lower with wider designs and if tourniquet completion pressures with the stretch and wrap design (SWAT-T) and the windlass design (CAT) are higher than the pressure required for arterial occlusion. Occlusion pressures were recorded with distal arterial Doppler pulse signal. Tourniquet appliers trained with the adult blood pressure cuffs with a certified Emergency Medical Technician. Volunteers trained with the SWAT-T and CAT with the manufacturer's printed instructions, PowerPoint slides from the manufacturer's Web site (CAT), and training videos posted on the internet (SWAT-T and CAT). 6 male and 11 female volunteers. Median age 22 years. 64 applications per tourniquet: 16 each at self-Thigh, Nonself-Thigh, Self-Arm, and Nonself-Arm.	Ease of Use: Mostly rated as Easy. CAT applications exhibited significantly greater discomfort than SWAT-T and only ones with severe ratings. CAT: No discomfort 1, little 20, moderate 32, severe 11; SWAT-T No discomfort 12, little 24, moderate 28, severe 0. Occlusion: Reached occlusion- Self-thigh CAT 15 of 16, SWAT-T 15 of 16; Nonself-Thigh CAT 15 of 16, SWAT-T 14 of 16; Self-Arm CAT 16 of 16, SWAT-T 16 of 16; Nonself-Arm CAT 15 of 16, SWAT-T 16 of 16. Fewer arm than thigh CAT and SWAT-T applications lost occlusion. "Arterial occlusion pressures were lower with the wider SWAT-T and pneumatic blood pressure cuffs than with the CAT, and completion pressures with the SWAT-T and CAT were higher than arterial occlusion pressures." Other: Completion pressures with the CAT and SWAT-T were generally higher than occlusion pressures (differences were significant). Two CAT thigh applications were halted due to pain.	"Limb circumference/tourniquet width occlusion pressure predictions are not good substitutes for measurements. The wider SWAT-T has lower occlusion and completion pressures than the CAT. Decreases in muscle tension lead to decreases in tourniquet pressure, especially with the nonelastic CAT, which can lead to occlusion loss."
Lyon et al. 2012[403]	Abdominal Aortic Tourniquet (AAT) The AAT is a pneumatic belt designed for constant delivery of pressure. Study was designed to determine in human volunteers if AAT results in cessation of common femoral artery (CFA) blood flow. Prospective observational study. Nine subjects, all male, were enrolled. The AAT was applied by a single provider. Blood flow was measured with pulse wave Doppler. A 10 point pain scale was used to measure patient discomfort.	Ease of Use: AAT was applied in less than 1 minute. Occlusion: Flow stopped in 7 subjects at a median pressure of 180 mm Hg (150-230 mm Hg). One subject seemed to show no blood flow response with increasing pressure. Other: Median patient discomfort was 7, range 3-10. Pain resolved after device was released	"The AAT device was effective at reducing flow in the CFA and ceased flow in most of the subjects. Application of the device was associated with discomfort varying from moderate to severe and resolving with device removal."

Table C.5. Studies testing tourniquets with volunteers (continued)

Reference	Type of Tourniquet Tested, Purpose and Methods	Outcomes	Author's Conclusions
Wall et al. 2012[95]	Stretch, Wrap, and Tuck Tourniquet (SWAT-T) The SWAT-T is wider than the Combat Application Tourniquet. Determine if the SWAT-T is easily to apply with little prior training and can stop arterial blood flow through each extremity location. 15 volunteer tourniquet appliers and 15 volunteer recipients. The applier group watched 19 seconds of a thigh application video 3 times. Occlusion pressures were the manometer pressures of the pneumatic blood pressure cuffs (arm or thigh) when the distal arterial Doppler pulse signal became inaudible (wrist radial artery or ankle posterior tibial artery). Tourniquets were tried high, mid, and just above and below joint on both leg and arm. Volunteers were healthy undergraduate men and women in their 20s.	Ease of Use: 150 tourniquet applications were evaluated. Minimal training- 101 applications were rated Easy. Among 96 Doppler successes 85% Easy, 13% Challenging, 2% Difficult; Among 54 Doppler failures 35% Easy, 46% Challenging, 19% Difficult. Discomfort 53 None, 62 Little, 34 Moderate, 1 Severe. Doppler failure was significantly associated with rating of "None." Doppler success 24% None, Doppler failure 56% None. Properly stretched tourniquets were significantly associated with some discomfort (20% None vs. 51% None). Application of tourniquet took less than 40 seconds. Additional training provided some improvements especially with increased discomfort while still being easy to apply. Occlusion: Doppler signal was lost within 16 seconds when applications was successful. Doppler success was significantly more frequent on arms than legs. Tourniquet placement high on the thigh had the lowest Doppler success rate (3 of 15); when Doppler successful had the longest times to loss of the Doppler signal.	"Proper application of the SWAT-T is easy and can stop extremity arterial flow but requires some training for many appliers."
Childers et al. 2011[92]	Combat Application Tourniquet (CAT) Determine whether direct exposure to the Afghanistan environment decreases efficacy or increases breakdown of CATs and determine the average number of turns of the tourniquet windlass necessary to stop the distal pulse. Exposed CATs were compared to unexposed CATs on the thighs of volunteers (active duty male military members). 166 human subjects and 332 tourniquets were used in the study. A CAT was efficacious if it terminated the distal pulse (dorsalis pedis artery) for at least 30 seconds (measured using a Doppler stethoscope) without causing intolerable pain—regardless of tourniquet breakage.	Ease of Use: Not part of study Occlusion: Efficacy of exposed tourniquets was lower than unexposed: 63% vs. 91%, statistically significant difference. 8% of the exposed tourniquets broke compared to none of the unexposed. Other: 59% of the CATs required three turns to be effective, median number of turns was 2.0, same whether exposed or unexposed.	"Environmental exposure of military tourniquets is associated with decreased efficacy and increased breakage. In most cases, tourniquets require three turns to stop the distal lower extremity pulse."

Table C.5. Studies testing tourniquets with volunteers (continued)

Reference	Type of Tourniquet Tested, Purpose and Methods	Outcomes	Author's Conclusions
Guo et al. 2011[96]	5 types: bladder tourniquet, windlass tourniquet, cargo-strap tourniquet, rubber tube, and improvised tourniquet (canvas military belts). Evaluate currently available tourniquets in China for prehospital use. Enrolled 20 young soldiers (20-27 years old), 12 males, 8 females. Participants were given training and repeatedly practiced self-placement of the tourniquets until they were successful. Vascular Doppler Ultrasound was used to monitor the blood flow in the brachial artery and popliteal artery. Absence of a blood flow signal was considered a successful application.	Ease of Use: Application time for Cargo-strap tourniquet was the shortest, 7.22±2.30 seconds in the upper extremities and 6.48±2.40 seconds in the lower extremities. The application time for bladder tourniquet was the longest, and the time in the upper extremities (25.78±7.87) was greater than in lower extremities (19.59±7.52). Occlusion: The bladder tourniquet and windlass tourniquet had the best outcomes: bladder tourniquet was 75% in upper extremities and 100% in the lower extremities; windlass was 80% upper and 100% lower; cargo strap was 70% upper and 85% lower; rubber tubing was 60% upper and 75% lower; and improvised tourniquet 45% upper and 60% lower. Other: Pain (zero to three scale, none to very painful): rubber tube 2.40, improvised 1.90, cargo-strap 1.50, windlass 1.25, bladder 0.95. The bladder tourniquet was considered the least portable.	"The bladder tourniquet and the windlass tourniquet are efficient tourniquets, although the windlass is superior with respect to portability and pain. The Cargo-strap and rubber tourniquets have several disadvantages that reduce their suitability for field use. The improvised tourniquet is not recommended because of low efficiency and severe pain during implementation."
Taylor et al. 2011[93]	Combat Application Tourniquet (CAT) and Emergency and Military Tourniquet (EMT) Evaluate whether the currently issued tourniquet (CAT) was physically able to adequately occlude arterial flow when applied at mid-thigh level, first when self-applied and then when applied to the patient by a trained caregiver. The pneumatic EMT tourniquet was applied to the first thigh and inflated by the lead researcher to a maximum pressure possible (not self-applied). Participants were currently serving military personnel. Blood flow in the popliteal artery was detected by Doppler ultrasound. Success was defined as the complete eradication of detectable popliteal blood flow. 24 participants were enrolled.	Ease of Use: not part of study. Occlusion: The self-applied CAT occluded popliteal flow in only 4 subjects (16.6%). The CAT applied by a researcher occluded popliteal flow in 2 subjects (8.3%). The EMT prevented popliteal flow in 18 subjects (75%). The differences were statistically significant.	"This study demonstrates that the CAT tourniquet is ineffective in controlling arterial blood flow when applied at mid-thigh level. The EMT was successful in a significantly larger number of participants."

Table C.5. Studies testing tourniquets with volunteers (continued)

Reference	Type of Tourniquet Tested, Purpose and Methods	Outcomes	Author's Conclusions
Swan et al. 2009[97]	Three common non-commercial tourniquets: the sphygmomanometer (Propper, Rankin Biomedical, Holly, MI), the half inch rubber tubing and the cloth with windlass. Objectives: Determine the simplest technique for tourniquet control of extremity arterial hemorrhage. Determine if a tourniquet, placed on the forearm or the leg, arrests distal hemorrhage. Determine if tourniquet-induced pain is an important consideration in tourniquet use. Enrolled 10 healthy volunteers, mean age 36.5 years. Doppler ultrasound was used to determine stoppage of blood flow. Tourniquets were applied sequentially to arm, forearm, thigh, and leg.	Ease of Use: Sphygmomanometer much easier to use on arm than thigh. Rubber tubing easier to use on arm than leg. Cloth and windlass easiest to use on arm and leg. Occlusion: Sphygmomanometer- 38 out of 40 successful except to two thighs that were too large for the cuff. Pressure needed to stop flow was about 30 mm Hg higher for the thigh than arm, 163 mm Hg vs. 133 mm Hg. Rubber tubing- was successful on all applications except for pain in lower extremity resulted in one failure. Cloth and windlass- one failure due to severe pain in thigh. Tourniquets on arm or thigh that readily eliminate arterial blood flow, based on distal Doppler pulse cessation, accomplish the same objective when placed below the elbow or below the knee. Other: Sphygmomanometer moderate discomfort on leg. Rubber tubing some pain including one severe. Cloth and windlass one severe pain.	"Our data indicate that all tourniquets can be used successfully below the knee or elbow. The cloth and windlass is the easiest to apply. It is probably the most readily available or simplest to procure/improvise. Pain is irrelevant. "Pressure Point Control" of extremity arterial hemorrhage is a euphemistic misnomer."

Table C.5. Studies testing tourniquets with volunteers (continued)

Reference	Type of Tourniquet Tested, Purpose and Methods	Outcomes	Author's Conclusions
King et al. 2006[94]	Five tourniquet systems: Self Applied Tourniquet System (SATS); One-Handed Tourniquet (OHT); tie & cravat Improvised Tourniquet (IT); pneumatic Emergency Medical Tourniquet (EMT); and latex surgical tubing (ST). Evaluate currently available tourniquets for future operational use by Canadian Forces. Study focused on tourniquets that had not been previously evaluated by medics in simulated operational conditions and that were readily available. 10 volunteer junior medics from 1 Field Ambulance, part of 1 Canadian Mechanized Brigade Group in Edmonton, Alberta, Canada. Each given a 20 minute briefing on use of tourniquets. Five groups of 2 each worked together, one applying the tourniquet and the other acting as patient, then switching places. Vascular Doppler was used by a surgeon to judge stoppage of pulse. Each team tested all 5 tourniquet systems. One application series used thicker winter clothing. Only the lower limb was tested.	Ease of Use: ST mean application time was 24 seconds, others 30 seconds or more, difference was significant. Occlusion: ST was the most successful with 90% success, EMT 80%, and others less than 50%, OHT did not work on any attempt. Nearly same results with winter clothing. Other: EMT use had the lowest average pain scores (0.9 out of 5), averaging minor discomfort. ST average pain was 3.7. ST was considered most portable. Overall, volunteers clearly preferred the EMT followed by the ST by a significant margin. However, the medics believed that the EMT was too bulky and prone to durability issues to be given to soldiers.	"The most effective tourniquets were the EMT and ST. The ST is also the lightest, fastest, easiest to learn, and the cheapest but it causes a lot of pain and presumably, local tissue damage. ST can be issued to every soldier with a minimum of training and used effectively in the "Care Under Fire" phase. The EMT, which causes the least pain and is equally effective, can be applied during the "Tactical Field Care" phase by the medic to replace the surgical tubing. Fine adjustments can be made to the EMT, which allows the medic to safely deflate the device, assess the wound, determine if a tourniquet is required, and re-inflate quickly if necessary."

Table C.5. Studies testing tourniquets with volunteers (continued)

Reference	Type of Tourniquet Tested, Purpose and Methods	Outcomes	Author's Conclusions
Walters et al. 2005[28]	Combat application tourniquet (CAT), Self-Applied Tourniquet System (SATS), Mechanical Advantage Tourniquet (MAT), Special Operations Forces Tactical Tourniquet (SOFTT), One-Handed Tourniquet (H-Dyne), Last Resort Tourniquet (LRT), Emergency & Military Tourniquet (EMT), London Bridge Tourniquet (LBT), K2 Tactical Tourniquet (K2). U.S. Army Institute of Surgical Research evaluated commercially available tourniquets for efficacy in stopping blood flow. Study design was prospective with a randomized crossover design. Experiments were performed at the proximal femur and the proximal humerus. 20 healthy men and women ages 23 to 47 were enrolled, 18 leg and 12 arm. Doppler ultrasound confirmed blood flow stoppage. Volunteers applied own tourniquets until Doppler confirmed stoppage or pain prevented further tightening. U.S. Armed Forces considered devices effective if distal arterial flow in the thigh was occluded in at least 80% of patients.	Ease of Use: Not reported. Occlusion: CAT, EMT, and SOFTT were 100% effective in stopping blood flow in the leg. MAT was 88% effective. The LRT, SATS, and H-Dyne did not reach 80%. CAT, EMT, and SOFTT were 100% effective in stopping blood flow in the arm. The MAT was 75%. Other: The 3 tourniquets that were not effective all produced pain some of which stopped their use. The MAT failed the arm test because of intolerable pinching pain.	"Some commercially available tourniquets do not reliably occlude arterial blood flow and may not be successful in preventing extremity exsanguination in a trauma patient. Potential purchasers of such devices should bear this in mind when selecting a device for clinical use."

Simulation Studies

Table C.6. Studies testing abdominal clamps with simulation models

Reference	Type of Tourniquet Tested, Purpose and Methods	Outcomes	Author's Conclusions
Koller et al. 2013[404]	Pelvic C-Clamp Determine if a single training period could adequately educate physicians to place the Pelvic C-Clamp safely on a model in a reasonable time and that this knowledge would be retained at the follow-up evaluation session. The study used a two-step training program with an oral presentation including detailed description of the Pelvic C-Clamp and its indications and contra-indications, its assembly and the different possible pin placement sites. In the second phase each participant assembled and placed the clamp onto a prepared pelvic model. Time needed and the accuracy of pin placement were then evaluated. The participants' skills were reevaluated 12 months later. 32 participants with various experience in pelvic surgery.	Ease of Use: First evaluation- time needed for assembly 60.66 ±21.25 (range 28–112) seconds. The placement task was finished within 148.34 ±41.31 (range 54–267) seconds. Average total time was 214.47 ±77.72 (range 71–531) seconds. 12 month evaluation- only 18 participated. Time needed for assembly 77.39 ±35.37 (range 37–154) seconds. The placement task was accomplished in an average of 223.89 ±81.86 (range 110–379) seconds. Average total time of 301.28 ±101.20 (range 175–466) to assemble and place the clamp. Significant average increase of 107.56 seconds (55.52 %) to complete the positioning task. Occlusion: not part of study. Other: Pin placement at first evaluation: 57/64 pins (89.15%) were placed inside the safe area. 12 month evaluation: 75% of all pins were safely placed.	"The majority of 57 pins were placed in the safe area within 6 min after one single training session. This reproduces the Australian data and supports the theory that adequately educated and skilled physicians should be able to handle the device properly. The data from the re-evaluation suggest that repeating the training session with the device improves performance."

Table C.6. Studies testing abdominal clamps with simulation models (continued)

Reference	Type of Tourniquet Tested, Purpose and Methods	Outcomes	Author's Conclusions
Mann-Salinas et al. 2013[29]	Combat Ready Clamp (CRoC) Determine whether CRoC user performance to stop simulated bleeding varied by casualty positioning surface (hard and flat, soft and flat, or soft and curved) and assess time to control bleeding and some indices of device safety. Enrolled 6 experienced medical researchers trained in using the CRoC. Experiments were conducted on a specially designed manikin to evaluate the CRoC; simulated proximal right thigh through-and-through high-velocity gunshot wound to the right common femoral artery.	Ease of Use: Time to completion was slowest on the litter (soft curved surface) mean 65 seconds compared to soft flat 55 seconds, and hard flat 58 seconds. Time to assemble CRoC averaged 33 seconds. Occlusion: 100% hemorrhage control by all users on all three surfaces. Other: Estimated blood loss averaged 581 ±148 ml.	"These findings indicate that training was effective and that training of other users is plausible, feasible, and practical within the scope of the present evidence."
Koller and Balogh 2012[405]	Pelvic C-clamp Examine training effect on ability to assemble and correctly place the pelvis C-clamp. Assembly was on an anatomic pelvic model specifically developed for pelvic trauma training. Each participant was evaluated approximately 11 days after training. 27 participants were trained and evaluated. Nine participants had previous experience in pelvic surgery.	Ease of Use: Clamp assembly completed in 99.7 +/- 39.7 (range: 35–182) seconds, application performed in 133.9 +/- 74 (range: 34–279) seconds. Total time to assemble and apply was 228.6 +/- 97.7 (range: 82–409) seconds. 14 participants were able to position both pins of the clamp inside the safe area (51.9%). 18.5% of pins were placed in the dangerous area, 11.1% on target, and 70.4% inside the safe area. Occlusion: not part of study.	"The majority of pins were placed into the safe zone on a training model within 4 min after one training session. 18.5% dangerous pin placement within 11 days of the training requires careful consideration (risk/benefit) in the context of a critically injured dying patient."

DOT HS 811 999b
May 2014

U.S. Department of Transportation
National Highway Traffic Safety Administration

www.nhtsa.gov

10048a-051514-v3a