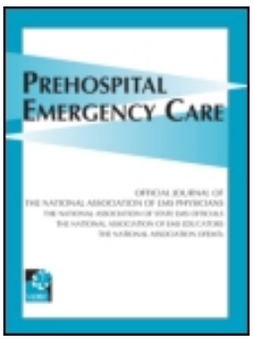

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An Evidence-based Prehospital Guideline for External Hemorrhage Control: American College of Surgeons Committee on Trauma

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SPECIAL CONTRIBUTION

AN EVIDENCE-BASED PREHOSPITAL GUIDELINE FOR EXTERNAL HEMORRHAGE CONTROL: AMERICAN COLLEGE OF SURGEONS COMMITTEE ON TRAUMA

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ABSTRACT

This report describes the development of an evidence-based guideline for external hemorrhage control in the prehospital setting. This project included a systematic review of the literature regarding the use of tourniquets and hemostatic agents for management of life-threatening extremity and junctional hemorrhage. Using the GRADE methodology to define the key clinical questions, an expert panel then reviewed the results of the literature review, established the quality of the evidence and made recommendations for EMS care. A clinical care guideline is proposed for adoption by EMS systems.
Key words: tourniquet; hemostatic agents; external hemorrhage

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INTRODUCTION

External hemorrhage has been increasingly recognized as a major cause of potentially preventable death following severe injury. This issue has been thoroughly addressed by the U.S. military Tactical Combat Casualty Care Committee (TCCC) in response to the increase in life-threatening external hemorrhage seen in the conflicts in Iraq and Afghanistan (www.health.mil/Education_And_Training/TCCC.aspx). Implementation of the TCCC guidelines for tourniquet use has been associated with a significant reduction in the number of combat deaths attributed to extremity hemorrhage.[1] Lessons learned from the military management of these injuries are beginning to be adopted in the civilian community and the recent Boston marathon bombing event highlighted this issue.[2] A report from the National Trauma databank suggests that mortality for patients with isolated lower extremity trauma with an arterial injury is 2.8%, with a 6.5% amputation rate.[3]

The use of tourniquets and hemostatic agents in the civilian EMS community is not widespread.[4,5] While there is increasing interest in the use of these agents by civilian EMS agencies, the differences between the civilian and military populations may be important. These considerations, not well addressed in the published military experience, include the use of these modalities in elderly and pediatric patients and the impact of medical comorbidities on outcome. Even as recently as 2011, the Guidelines for Field Triage of Injured Patients does not include a recommendation for tourniquet use as a trauma triage criteria 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."[6] However, the National EMS Scope of Practice Model published in 2007 lists tourniquet use as part of the minimum psychomotor skill set for emergency trauma care for emergency medical technicians. In addition, tourniquets have been included as required basic life support (BLS) equipment in the Joint Policy Statement: Equipment for Ambulances.[7] Topical hemostatic agents are listed as optional basic equipment. The recent Hartford consensus conference also encourages wider civilian use of tourniquets for management of hemorrhage in active shooter events.[8]

The purpose of this project was to develop evidence-based guidelines for the use of tourniquets and hemostatic dressings in the U.S. civilian prehospital setting. The recommendations were based on a systematic review of the current literature and were developed using the GRADE methodology.[9] External hemorrhage is defined as blood loss originating from a ruptured blood vessel and appearing on the body surface. For the purposes of our review, this includes extremity hemorrhage and junctional hemorrhage. Junctional hemorrhage includes the groin proximal to the inguinal ligament, the buttocks, the gluteal and pelvic areas, the perineum, the axilla and shoulder girdle, and the base of the neck.[10]

APPROACH

Expert Panel

An expert panel was convened by the American College of Surgeons Committee on Trauma EMS Committee to include nationally recognized experts in prehospital trauma care. Representatives were included from the military's Tactical Casualty Combat Care Committee, Prehospital Trauma Life Support, civilian State EMS directors, trauma surgeons, emergency physicians, a pediatric surgeon, an EMS researcher, a GRADE methodologist, and a paramedic. Representatives were from both the United States and Canada. Panelists provided input to the formulations of the PICOTS (populations, interventions, comparators, outcomes, timing, and settings) questions prior to the initiation of the literature review. For the PICOTS questions, the population of interest was defined to be individuals with extremity hemorrhages; the interventions were commercially available tourniquets and hemostatic dressings; comparators were external wound pressure and nontourniquet or nonhemostatic interventions; outcomes of interest were limb salvage, hypovolemic shock, survival, and adverse effects. Because timing and setting were considered to be key aspects of the investigation the PICO format was expanded to include both immediate and long-term outcomes and the setting for the intervention was defined as the prehospital environment, before any procedures are performed in the hospital emergency department or operating theater. Following the completion of the systematic literature review, the panel met to review the literature in a full day meeting in Washington DC, October 2013. An expert in the application of the GRADE methodology facilitated the meeting and the panel used this approach to develop recommendations for each PICOTS question.

Evidence Review

A systematic review of the literature was conducted by the ECRI Institute, one of the eleven Evidenced-Based Practice Centers designated by the U.S. Agency for Healthcare Research and Quality. Their systematic literature review and evidence tables were used by the expert panel to develop these recommendations. A summary of the findings is included in this manuscript; the full ECRI report will be simultaneously published by the National Highway Traffic Safety Administration (NHTSA) and will be available at www.ems.gov. The PICOTS questions used to guide the literature review were developed with input from the multidisciplinary expert panel.

Literature search included 13 external and internal electronic databases, including CINAHL, EMBASE, and Medline, from 2001 to the present for fully published, primary, clinical studies. The Cochrane Database of Systematic Reviews (Cochrane Reviews), Database of Abstracts of Reviews of Effects (DARE), and Health Technology Assessment and Database (HTA) were also searched for secondary reviews. Additional search steps included manual search of bibliographies listed in fully published studies; search and written inquiry to regulatory agencies, including the U.S. Food and Drug Administration; and search of www.ClinicalTrials.gov and www.controlled-trials.com for ongoing clinical trials. Publications were also suggested for inclusion by expert panel members who commented on the draft report.

The criteria for inclusion in the systematic review were studies published in English that reported on traumatic hemorrhage treated by EMS personnel in the prehospital setting with tourniquets or hemostatic dressings currently available in U.S. commercial markets. In addition, the studies reported findings on at least one of the outcomes identified in the PICOTS questions and included at least 5 patients per treatment group; results for extremity and junctional hemorrhage were considered separately. To avoid duplication, when several sequential reports from the same study center were available, only findings from the largest, most recent, or most complete report was used. Because of the paucity of published studies on hemostatic dressings, for these questions the inclusion criteria were expanded to include animal studies of FDA-cleared or approved hemostatic dressings using either a swine or goat model of extremity bleeding. Risk of bias and other indicators of strength of evidence were assessed and reported.

The absolute risk differences and relative risk (RR) with 95% confidence intervals for the primarily dichotomous outcomes were calculated for individual studies. In cases in which meta-analyses was possible a summary odds ratio (OR) was calculated using a random effects model. Studies were combined using meta-analysis when populations and interventions were similar. Given the nature of the populations examined in this report, military populations were separated from civilian populations and data from children (younger than 18 years of age) was also examined independently. Statistical heterogeneity was examined using I^2, but the small number of studies in the comparisons limited our confidence in measures of heterogeneity.

PICOTS Questions

1) In trauma patients with extremity hemorrhage (excludes junctional hemorrhage) who are treated in the prehospital setting, 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?
2) In trauma patients with junctional hemorrhage who are treated in the prehospital setting, what is the effect of junctional hemorrhage control device use with or without external wound pressure on limb salvage, hypovolemic shock, survival, and adverse effects compared with external pressure alone.
3) In trauma patients with extremity hemorrhage (excludes junctional hemorrhage) who are treated in the prehospital setting, do different brands or models of tourniquets differ from each other in their effect on limb salvage, hypovolemic shock, survival, and adverse effects?
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 hemorrhage control devices differ from each other in their effect on limb salvage, hypovolemic shock, survival, and adverse effects?
5) In trauma patients with external hemorrhage (excludes junctional hemorrhage) who are treated in the prehospital setting 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?
6) In trauma patients with external hemorrhage (hemorrhage from any body surface) who are treated in the prehospital setting, what is the effect of hemostatic dressings with or without external wound pressure on, control of hemorrhage, limb salvage (if an extremity involved), hypovolemic shock, survival, and adverse effects compared with using non-hemostatic gauze with or without external wound pressure?
7) In trauma patients with external hemorrhage (hemorrhage from any body surface) who are treated in the prehospital setting, do different brands or types of hemostatic dressings differ from each other in their effect on, hemorrhage control, limb salvage (if an extremity is involved), hypovolemic shock, survival, and adverse effects?

GRADE Methodology

The panel used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology to guide the process of PICOTS question formulation, evidence appraisal, and to designate the strength of recommendations. The process also adhered to the National Prehospital Evidence-Based Guideline (EBG) Model Process approved by the Federal Interagency Council for EMS and the National EMS Advisory Council.[11,12] Panel members received an introduction to the GRADE methodology and reviewed the evidence for structured clinical questions using the PICO framework. After reading and discussing the systematic review of the evidence, the panel drafted graded recommendations. The recommendations were graded strong or weak, based on the balance between risk, benefit, burden, and cost, while the quality of evidence was appraised as high, moderate, low, or very low.[13–18] Although the initial assignment of a strength of evidence rating is based on

study design, GRADE allows the evidence appraisal to be upgraded or downgraded, depending on such factors as the size and consistency of the reported effect or the presence of a dose response.[19] Using the GRADE terminology, strong recommendations begin with the words "we recommend" and indicate that the panel believes that the benefits clearly outweigh any risks associated with the treatment and that nearly all informed patients would want the recommended treatment. Weak recommendations begin with the words "we suggest," which indicates that the panel had a higher level of uncertainty about estimated benefits of the treatment the balance between benefits and risks.

RESULTS

Summary of Evidence Review

Our searches identified 1,599 potential citations for evaluation and full review identified 23 clinical studies that met our inclusion criteria (Figure 1). While not the focus of this review we also reviewed 39 animal model studies, which compared efficacy of the topical hemostatic agents. Nine studies were identified that used only human volunteers and these were excluded.

Tourniquet Use

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.,[20] Gerhardt et al.,[21] Kragh et al.,[22] Kragh et al.[23] In two instances, the same study population was assessed in two separate publications. Kragh et al.[24] and Kragh et al.[25] used the same set of 499 patients and Kragh et al.[26] and Kragh et al.[27] used the same set of 232 patients. The 16 included publications are listed in Table 1 along with the setting in which the data on tourniquet

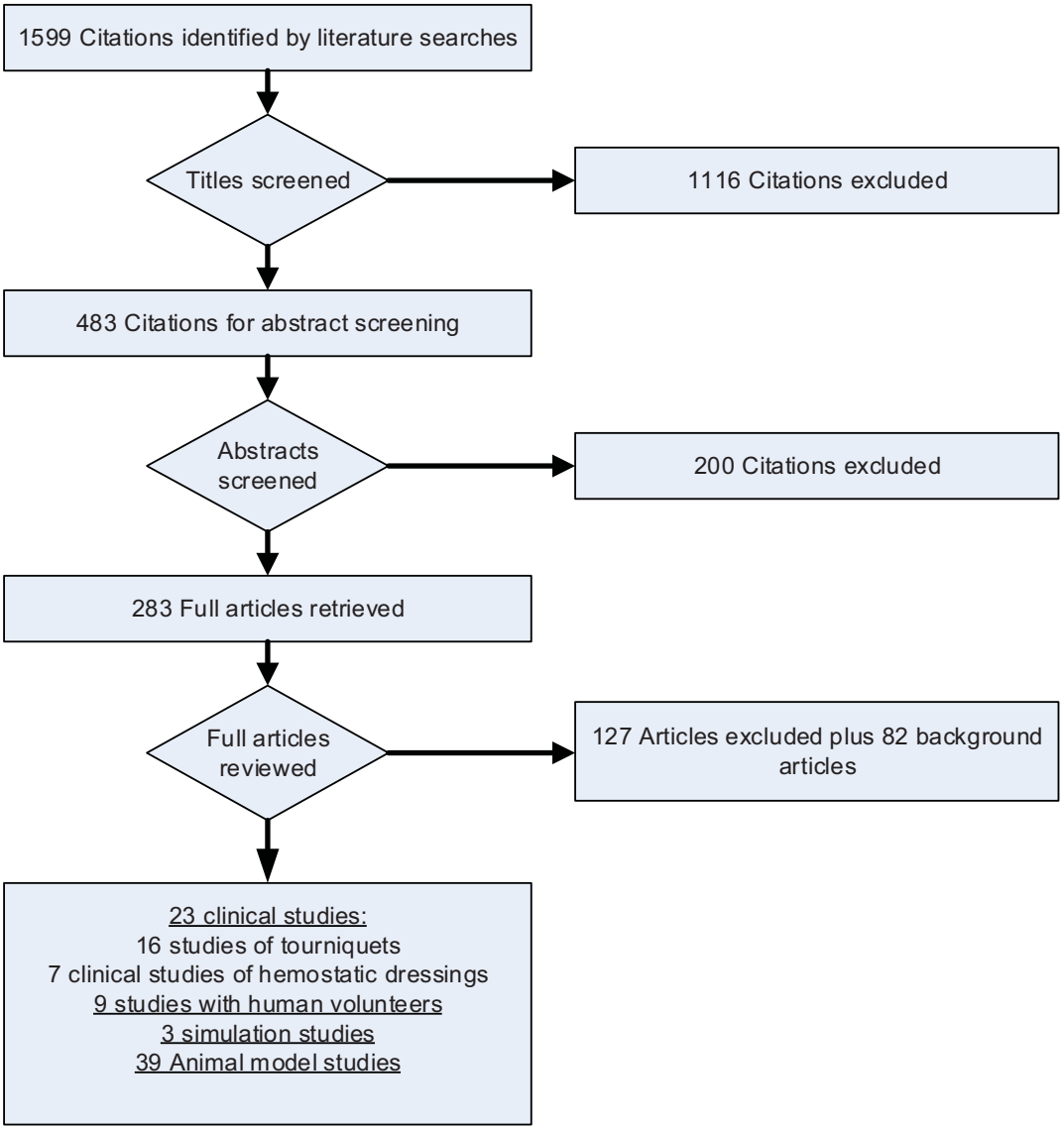

FIGURE 1. Summary of literature review.

TABLE 1. Studies of prehospital tourniquet use

Reference	Setting	Period of data collection	*N*	Patient characteristics	Outcomes reported
Eastridge et al., 2012[1]	U.S. military Iraq/Afghanistan	Oct 2001 to June 2011	976	Not reported	Deaths
King et al., 2012[40]	U.S. military Afghanistan	Aug 2011 to Nov 2011	54	Not reported	Deaths, adverse events
Kragh et al., 2012[28]	U.S. military Iraq/Afghanistan pediatric casualties	May 2003 to Dec 2009	88 (pediatric)	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%.	Deaths
Kotwal et al., 2011[29]	U.S. military Iraq/Afghanistan	Oct 2001 to March 2010	460 (66 w/tourniquet)	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%.	Deaths, amputations
Kragh et al., 2011[25]	U.S. military Iraq	March 2006 to March 2007	499	96% male, average age 29 years, 16 were children and 5 elderly. Injury: explosion 75%.	Deaths, adverse events
Kragh et al., 2011[24] (same study as Kragh et al., 2011[25] but reporting morbidities)	U.S. military Iraq	March 2006 to March 2007	499	96% male, average age 29 years, 16 were children and 5 elderly. Injury: explosion 75%.	Adverse events
Brown et al., 2010[41]	U.K. military Iraq/Afghanistan	Aug 2003 to May 2008	23	Median age 26 years, range 18–42 years, not specific to tourniquet patients. Injuries for entire patient pool: explosion 62%, gunshot 38%.	Adverse events
Brodie et al., 2009[42]	U.K. military Iraq/Afghanistan	Feb 2003 to Sept 2007	70	Gender and age data not reported. Injuries: explosion 86%, gunshot 14%.	Deaths, amputations, adverse events
Clasper et al., 2009[31]	U.K. military Iraq/Afghanistan	Dec 2003 to May 20008	44 (22 w/tourniquet)	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%.	Amputations, adverse events
Kragh et al., 2009[26] (reassessment of data from Kragh et al., 2008[27])	U.S. military Iraq	March to Oct 2006	232 (194 w/tourniquet)	95% male, mean age of 29 years, range 4–70 years, 9 children and 1 elderly. Injuries: explosion 63%, gunshot 23%.	Deaths, amputations, adverse events
Tien et al., 2009[43]	Canadian military Afghanistan	Feb 2006 to May 2006	134??	Entire study examined 134 patients, 96% male, mean age of 26 years. Injuries: explosion 34%, gunshot 32%, blunt 22%.	Deaths
Beekley et al., 2008[30]	U.S. military Iraq	Jan 2004 to Dec 2004	165 (67 w/ tourniquet)	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%.	Deaths, amputations, adverse events
Dayan et al., 2008[32]	Israeli military	2006	5 (prolonged tourniquet use)	All males, 20–22 years old. Injuries: explosion = 1, gunshot. = 4.	Deaths, amputations, adverse events
Kalish et al., 2008[44]	U.S. civilian	Jan 1999 to April 2006	11	All males, mean age of 27 years, gunshot wounds 55%, stab wounds 27%, lacerations 18%.	Deaths and adverse events
Kragh et al., 2008[27]	U.S. military Iraq	March 2006 to Oct 2006	232 (194 w/tourniquet)	95% male, mean age of 29 years, range 4–70 years, 9 children and 1 elderly. Injuries: explosion 63%, gunshot 23%.	Deaths, amputations, adverse events
Lakstein et al., 2003[33]	Israeli military	Jan 1997 to Jan 2001	91 (improvised tourniquets)	Gender and mean age not reported. Injuries: explosion 73%, gunshot 27%.	Deaths, amputations, adverse events

use were collected and the outcomes reported by each study. The large majority of studies were conducted by the U.S. military in Iraq and Afghanistan (8 studies) with 3 studies from the U.K. military, 2 from the Israeli military, and 1 from Canadian military. Only 1 study was conducted in a civilian setting. One study used data on pediatric casualties described in the Joint Theater Trauma Registry and collected during the wars in Iraq and Afghanistan.[28] 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.

Eight of the studies used prospective data collection. Most of the studies provided some information on how the tourniquets were to be used, but only a few were specific about the instructions. However, the studies from the U.S. military were using TCCC practices when data were collected after 2005 and tourniquets were likely used aggressively as a first option for traumatic extremity hemorrhage.

Comparisons between casualties treated with a tourniquet and similar casualties not treated with a tourniquet were attempted by only a few studies. Kotwal et al.[29] reported the number of casualties treated with compression dressings but did not report outcomes for this group. Beekley et al.[30] reported outcome data for tourniquet- and nontourniquet-treated casualties but did not report what prehospital treatments the nontourniquet group received. Clasper et al.[31] matched surviving tourniquet-treated casualties with surviving nontourniquet-treated casualties to examine the rate of adverse events. These authors note, however, that "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."[31]

Meta-analysis of the 9 studies reporting survival for adult military casualties treated with tourniquets demonstrated a summary effect size estimate for survival rate of 92% with 95% confidence intervals of 88–95%. Findings in the study of children were similar (92%, with CI 84–96%). The study of a civilian population was small (11 cases), so the confidence interval was wide, but the survival rate similar (91%, CI 56–99%). A similar analysis for 6 studies reporting amputation rates demonstrated a summary effect size estimate of 19% with a 95% confidence interval from 16–23%. These amputations are presumably primarily associated with the severity of the extremity injury, as they are not described as complications of tourniquet use. The overall quality of the evidence for PICOTS Question 1 was rated using the GRADE system as Moderate for survival based on upgrading due to the large effect size and Very Low for amputation rate (Table 2).

There were no studies available that directly addressed PICOTS questions 2, 3, and 4. These included the efficacy of junctional hemorrhage control devices or the comparison of different brand or models of tourniquets. Regarding PICOTS question 5, there were 4 studies that correlated duration of tourniquet use with adverse events but specifics were not provided on the timing and setting of tourniquet removal.[27,30,32,33] Thus, the grade of evidence for PICOTS question 5 was rated as Low.

Hemostatic Agents

Seven studies were reviewed that reported on the prehospital use of hemostatic dressings (Table 3). Five were conducted in a military setting. One was civilian and 1 included both military and civilian data. The products tested included HemCon (3 studies), Celox (1 study), QuickClot granules (2 studies), and QuickClot Gauze (1 study). One study did not report the type of hemostatic dressings used. Only 1 study reported mortality and 4 studies reported on adverse events. No studies provided a direct comparison between the use of hemostatic dressings and simply applying direct pressure to the wound. The primary adverse event noted was pain and discomfort associated with an exothermic reaction to QuickClot granules.

The primary outcome for 5 studies was cessation of bleeding. The study by Brown et al.[34] 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.[35] is confounded because 7 of the 8 patients treated with hemostatic dressings in the field were also treated with a tourniquet. The study by Pozza and Millner[36] 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.[37] reported that QuickClot gauze successfully stopped bleeding in 11 out of 14 cases of extremity and truncal hemorrhage. The study by Rhee et al.[38] reported that QuickClot granules were 100% effective in stopping bleeding. In the study by Wedmore et al.,[39] 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. 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 graded as Low using the GRADE system.

TABLE 2. Key Question 1: Strength of evidence grades for survival rate and amputation rate with prehospital tourniquet use

					Decrease GRADE					Increase GRADE			
Outcome	# Studies (total N)	Type of studies	Findings	Starting GRADE	Study limitations	Consistency	Directness	Precision	Publication bias	Large magnitude of effect	Dose-response	Confounders	GRADE of evidence for outcome
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

Table 3. Studies of prehospital hemostatic dressings

Reference	Setting	Period of data collection	Number of casualties treated	Patient characteristics
Brown et al., 2009[34]	U.S. civilian	June 2006 to Aug 2006	HemCon $n = 34$	53% extremity wounds, 68% male, mean age of 51.5 years, range of 16–91 years.
Cox et al., 2009[35]	U.S. military Iraq	April 2006 to Oct 2006	HemCon $n = 5$, QuikClot granules $n = 3$	7 of 8 extremity wounds, other data not reported.
Lairet et al., 2012[20]	U.S. military Afghanistan	Nov 2009 to Nov 2011	Not specified $n = 23$, 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.
Pozza and Millner, 2010[36]	U.S. military Afghanistan	April 2008 to April 2008	Celox = 21	All gunshot wounds. All male between ages of 18 and 45 years.
Ran et al., 2010[37]	Israel military	2009	Quikclot Combat Gauze n = 14	Injuries: blast = 7, gunshot = 6, stab = 1. Other data not reported.
Rhee et al., 2008[38]	U.S. civilian and U.S. military Iraq	Not specified, but study was completed in 2006	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%.
Wedmore et al., 2006[39]	U.S. military Iraq/Afghanistan	2003 to 2004	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.

In regard to PICOTS Question 7, there were no patient studies that directly compared the different hemostatic dressings. The U.S. military has developed a standardized swine model, which involves a femoral artery injury with a standard period of free bleeding. This literature was summarized and reviewed by the expert panel. For the details of this review please see the full ECRI Institute report. These data factored into the recommendation by the panel for the use of a gauze format product that could be packed into the wound. The panel also supported the use of this standardized model for comparison of different products.

RECOMMENDATIONS BY EXPERT PANEL

The recommendations of the panel for management of external hemorrhage are summarized in Figure 2.

Tourniquets

Recommendation 1: We recommend the use of tourniquets in the prehospital setting for the control of significant extremity hemorrhage if direct pressure is ineffective or impractical.

Strength of Recommendation: Strong
Quality of Evidence: Moderate. The overall quality of the evidence for survival benefits of tourniquet use was upgraded from Low to Moderate, based on the large effect size. The evidence for preventing amputation was very low, due to a smaller effect size and issues relating to confounding (see Table 2).
Remarks: The panel believes that tourniquets used to treat severe extremity hemorrhage have a clear survival benefit, demonstrated by a large and consistent effect size across several studies. The panel discussed that direct pressure may be ineffective in the setting of major arterial injury or impractical in circumstances with limited manpower, unsecure scene, or when complex extrication or extraction is required.

Recommendation 2: We suggest using commercially produced windlass, pneumatic, or ratcheting devices that have been demonstrated to occlude arterial flow.

Strength of Recommendation: Weak
Quality of Evidence: Low
Remarks: The panel discussed the military experience with varying types of tourniquets and felt that tourniquet selection should be based on proven effectiveness at arterial occlusion. Tourniquets that impede venous return without adequate arterial occlusion may only worsen hemorrhage and increase complications.

Recommendation 3: We suggest against the use of narrow, elastic, or bungee-type devices.

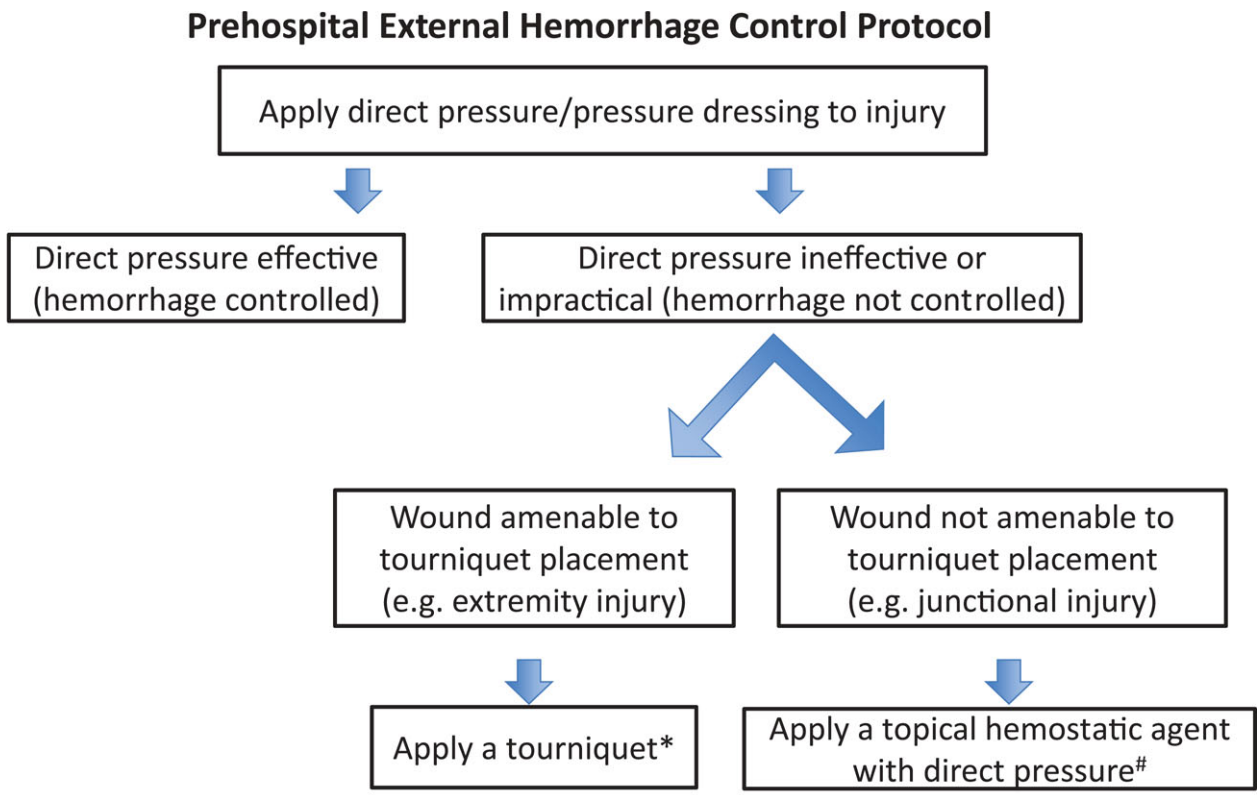

Figure 2. Protocol for prehospital external hemorrhage control.

Strength of Recommendation: Weak
Quality of Evidence: Low
Remarks: The panel discussed the military experience with varying types of tourniquets and felt that tourniquet selection should be based on proven effectiveness at arterial occlusion. Tourniquets that impede venous return without adequate arterial occlusion may only worsen hemorrhage and increase complications.

Recommendation 4: We suggest that improvised tourniquets be applied only if no commercial device is available.

Strength of Recommendation: Weak
Quality of Evidence: Low
Remarks: The panel discussed the military experience with varying types of tourniquets and felt that tourniquet selection should be based on proven effectiveness at arterial occlusion. Tourniquets that impeded venous return without adequate arterial occlusion may only worsen hemorrhage and increase complications. Commercially available tourniquets are favored over improvised tourniquets unless there is no other option.

Recommendation 5: We suggest against releasing a tourniquet that has been properly applied in the prehospital setting until the patient has reached definitive care.

Strength of Recommendation: Weak
Quality of Evidence: Low
Remarks: Given the relatively short transport times for most civilian EMS agencies, the committee felt the safest option was to leave a tourniquet that had been placed in the field in place until the patient can be assessed in the hospital. There may be exceptions to this approach for prolonged transport times or austere environments. In these circumstances, prehospital providers should consult direct (online) physician medical direction.

Junctional Hemorrhage Devices

Regarding the questions related to junctional hemorrhage devices, we believe this is an important area for

further study, but did not find sufficient evidence to make a recommendation at this time.

Topical Hemostatic Agents

Recommendation 1: We suggest the use of topical hemostatic agents, in combination with direct pressure, for the control of significant hemorrhage in the prehospital setting in anatomic areas where tourniquets cannot be applied and where sustained direct pressure alone is ineffective or impractical.

Strength of Recommendation: Weak
Quality of Evidence: Low
Remarks: While the evidence was low, there are consistent data from animal models, suggesting reduced hemorrhage with these agents compared to standard gauze and the committee felt that junctional hemorrhage and torso wounds may benefit from the combination of direct pressure and hemostatic dressings.

Recommendation 2: We suggest that topical hemostatic agents be delivered in a gauze format that supports wound packing.

Strength of Recommendation: Weak
Quality of Evidence: Low
Remarks: This recommendation was based on the military experience and the animal studies suggesting that products that allow packing of the wound have superior hemorrhage control.

Recommendation 3: Only products determined effective and safe in a standardized laboratory injury model should be used.

Strength of Recommendation: Weak
Quality of Evidence: Low
Remarks: The U.S. Army Institute for Surgical Research has developed a standardized large animal model for comparison of hemostatic dressings. The committee felt that all new products should be subject to this testing.

Additional Training Recommendations

- We advise that tourniquets and topical hemostatic agents be used under clinical practice guidelines and following product specific training.
- We advise that hemostatic agent training for prehospital personnel include proper wound packing and pressure application techniques.
- We advise that tourniquets and topical hemostatic agents use be expanded to include all prehospital personnel, including emergency medical responders (in concordance with the Hartford Consensus Statement[8]).

Need for Additional Research

While the military data were convincing that the use of tourniquets to control severe extremity hemorrhage is life saving, there remain several unanswered questions regarding the logistics of hemorrhage control in the civilian EMS community. The evidence available to assess many of the practical issues surrounding the use of tourniquets and hemostatic agents in the civilian community is very limited. There were insufficient data to make any recommendations regarding the newly developed devices for junctional hemorrhage control. There were insufficient data to make any specific recommendations regarding application in the extremes of age including pediatric and elderly patients. Future research should focus on these gaps in knowledge to further guide clinicians in the civilian application of these products.

References

1. Eastridge BJ, Mabry RL, Seguin P, Cantrell J, Tops T, Uribe P, Mallett O, Zubko T, Oetjen-Gerdes L, Rasmussem 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;73(6 Suppl 5):S431–7.
2. Walls RM, Zinner MJ. The Boston Marathon response: why did it work so well? JAMA. 2013;309(23):2441–2.
3. Kauvar DS, Sarfati MR, Kraiss LW. National trauma databank analysis of mortality and limb loss in isolated lower extremity vascular trauma. J Vascular Surg. 2011;53(11):1598–1603.
4. Lee C, Porter KM, Hodgetts TJ. Tourniquet use in the civilian prehospital setting. Emerg Med J. 2007;24(8):584–7.
5. Doyle GS, Taillac PP. Tourniquets: a review of current use with proposals for expanded prehospital use. Prehosp Emerg Care. 2008;12(2):241–56.
6. Sasser SM, Hunt RC, Faul M, Sugarman D, Pearson WS, Dulski T, Wald MM, Newgard CD, Lerner EB. Guidelines for field triage of injured patients: recommendations of the National Expert Panel on Field Triage, 2011. MMWR Recommendations and reports: Morbidity and mortality weekly report Recommendations and reports / Centers for Disease Control. 2012;61(RR-1):1–20.
7. American Academy of Pediatrics, American College of Emergency Physicians, American College of Surgeons Committee on Trauma, et al. Equipment for ground ambulances. Prehosp Emerg Care. 2014;18(1):92–97.
8. Jacobs LM, McSwain NE, Rotondo MF, Wade D, Fabbri W, Eastman A, Butler FK, Sinclair J; Joint Committee to Create a National Policy to Enhance Survivability from Mass Casualty Shooting Events. Improving survival from active shooter events: the Hartford Consensus. J Trauma Acute Care Surg. 2013; 74:1399–400.
9. Kerwin AJ, Haut ER, Elliot R, Burns J, Bracken DO, Como JJ, Haider A, Stassen N, Dahm P. The Eastern Association of the Surgery of Trauma approach to practice management guideline development using Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology. J Trauma Acute Care Surg. 2012;73(5 Suppl 4):S283–7.
10. Kragh JF, Murphy C, Dubick MA, Baer DG, Johnson J, Blackbourne LH. New tourniquet device concepts for battlefield hemorrhage control. US Army Med Dept J. 2011:38–48.
11. Brown KM, Macias CG, Dayan PS, Shah MI, Welk TS, Wright JL, Lang ES. The development of evidence-based prehospital

guidelines using a GRADE-based methodology. Prehosp Emerg Care. 2014;18(Suppl 1):3–14.
12. Lang ES, Spaite DW, Oliver ZJ, Gotschall CS, Swor RA, Dawson D, Hunt RC. A national model for developing, implementing, and evaluating evidence-based guidelines for prehospital care. Acad Emerg Med. 2012;19(2):201–9.
13. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, Norris S, Falck-Yiter 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;64(4):383–94.
14. Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, Alderson P, Glasziou P, Falck-Yiter Y, Schunemann HJ. GRADE guidelines, 2: framing the question and deciding on important outcomes. J Clin Epidemiol. 2011;64(4):395–400.
15. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, Vist G, Falck-Yiter Y, Meerpohl J, Norris S, Guyatt GH. GRADE guidelines, 3: rating the quality of evidence. J Clin Epidemiol. 2011;64(4):401–6.
16. Guyatt GH, Oxman AD, Santesso N, Helfand M, Vist G, Kunz R, Brozek J, Norris S, Meerpohl J, Djuibegovic 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;66(2):158–72.
17. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Yiter Y, Nasse M, Meerpohl J, Post PN, Kunz R, Brozek J, Vist G, Rind D, Akl EA, Schunemann HJ. GRADE guidelines, 14: going from evidence to recommendations – the significance and presentation of recommendations. J Clin Epidemiol. 2013;66(7):719–25.
18. Andrews JC, Schünemann HJ, Oxman AD, Pottie K, Meerpohl J, Alonso-Coello P, Rind D, Monton VM, Brito JP, Norris S, Elbarbary M, Post P, Nasser M, Shukla V, Jaeschke R, Brozek J, Djulbegovic B, Guyatt G. GRADE guidelines, 15: going from evidence to recommendation – determinants of a recommendation's direction and strength. J Clin Epidemiol. 2013;66(7):726–35.
19. Guyatt GH, Oxman AD, Sultan S, Glasziou P, Akl EA, Alonso-Coello P, Atkins D, Kunz R, Brozek J, Monton V, Jaeschke R, Rind D, Dahm P, Meerpohl J, Vist G, Berliner E, Norris S, Falck-Yiter Y, Murad MH, Schunemann HJ. GRADE guidelines, 9: rating up the quality of evidence. J Clin Epidemiol. 2011;64(12):1311–6.
20. 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;73(2 Suppl 1):S38–42.
21. Gerhardt RT, Berry JA, Blackbourne LH. Analysis of life-saving interventions performed by out-of-hospital combat medical personnel. J Trauma. 2011;71(1 Suppl):S109–13.
22. Kragh JF, 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;25(3):134–9.
23. Kragh JF, 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. Military Med. 2011;176(10):1144–52.
24. Kragh JF, O'Neill ML, Walters TJ, Jones JA, Baer DG, Gersham 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. Military Med. 2011;176(7):817–23.
25. Kragh JF, 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;41(6):590–7.
26. Kragh JF, 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;249(1):1–7.
27. Kragh JFJ, 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;64(2 Suppl):S38–49; discussion S49–50.
28. Kragh JF, Cooper A, Aden JK, Dubick MA, Baer DG, Wade CE, Blackbourne LH. Survey of trauma registry data on tourniquet use in pediatric war casualties. Pediatric Emerg Care. 2012;28(12):1361–5.
29. Kotwal RS, Montgomery HR, Kotwal BM, Champion HR, Butler FK, Mabry RL, Cain JS, Blackbourne LH, Mechler KK, Holcomb JB. Eliminating preventable death on the battlefield. Arch Surg. 2011;146(12):1350–8.
30. Beekley AC, Sebesta JA, Blackbourne LH, Herbert GS, Kauvar DS, Baer DG, Walters TJ, Mullenix PS, Holcomb JB. Prehospital tourniquet use in Operation Iraqi Freedom: effect on hemorrhage control and outcomes. J Trauma. 2008;64(2 Suppl):S28–37; discussion S37.
31. Clasper JC, Brown KV, Hill P. Limb complications following pre-hospital tourniquet use. J R Army Med Corps. 2009;155(3):200–2.
32. Dayan L, Zinmann C, Stahl S, Norman D. Complications associated with prolonged tourniquet application on the battlefield. Military Med. 2008;173(1):63–6.
33. 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;54(5 Suppl):S221–5.
34. Brown MA, Daya MR, Worley JA. Experience with chitosan dressings in a civilian EMS system. J Emerg Med. 2009;37(1):1–7.
35. Cox ED, Schreiber MA, McManus J, Wade CE, Holcomb JB. New hemostatic agents in the combat setting. Transfusion. 2009;49 Suppl 5:248S–55S.
36. Pozza M, Millner RWJ. Celox (chitosan) for haemostasis in massive traumatic bleeding: experience in Afghanistan. Eur J Emerg Med. 2011;18(1):31–33.
37. Ran Y, Hadad E, Daher S, Ganor O, Kohn J, Yegorov Y, Bartal C, Ash N, Hirschhom 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;25(6):584–8.
38. 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;64(4):1093–9.
39. 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;60(3):655–8.
40. King DR, van der Wilden G, Kragh JF, Blackbourne LH. Forward assessment of 79 prehospital battlefield tourniquets used in the current war. J Spec Operations Med. 2012;12(4):33–8.
41. Brown KV, Murray CK, Clasper JC. Infectious complications of combat-related mangled extremity injuries in the British military. J Trauma. 2010;69 (Suppl 1):S109–15.
42. Brodie S, Hodgetts TJ, Ollerton J, McLeod J, Lambert P, Mahoney P. Tourniquet use in combat trauma: U.K. military experience. J Spec Operations Med. 2009;9(1):74–7.
43. Tien HC, Jung V, Rizoli SB, Acharya SV, MacDonald JC. An evaluation of tactical combat casualty care interventions in a combat environment. J Spec Operations Med. 2009;9(1):65–8.
44. 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;33(8):44–6, 49–50, 52–4.