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Control of severe, life-threatening external bleeding in the out-of-hospital setting: a systematic review

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Abstract

Objective: Trauma, with resultant bleeding, is a significant cause of morbidity and mortality throughout the world, however the best possible method of bleeding control by immediate responders is unknown. We performed a systematic review of the effectiveness of treatment modalities for severe, life-threatening external bleeding in the out-of-hospital first aid setting. **Methods:** We followed the Cochrane Handbook for Systematic Reviews of Interventions methodology and report results according to PRISMA guidelines. We included randomized controlled trials, non-randomized comparative studies and case series investigating adults and children with severe, life-threatening external bleeding who were treated with therapies potentially suitable for first aid providers. We assessed the certainty of the evidence and risk of bias. Outcomes were prioritized by first aid specialists based on importance for patients and decision-makers and included mortality due to bleeding, all-cause mortality, cessation of bleeding, time to cessation of bleeding, a decrease in bleeding and complications/adverse effects. Results were reported in Evidence Profiles. **Results:** Of the 1,051 full-text articles screened, 107 were included for analysis including 22,798 patients. The primary methods of bleeding control were tourniquets (n=49), hemostatic dressings (n=34), hemostatic devices (n= 14), pressure dressings/bandages/devices (n=8), pressure points (n=4), including two studies that reported multiple hemorrhage control methods. Overall, certainty of evidence was very low and often relied on indirect evidence and poorly controlled studies. Tourniquets were associated with a

decrease in mortality when compared with direct manual pressure. Hemostatic dressings resulted in a shorter time to hemostasis than direct manual pressure using standard dressings. Direct manual compression resulted in a shorter time to hemostasis than pressure dressings/devices. Conclusion: Overall, data regarding the control of life-threatening bleeding is of very low certainty, making it difficult to draw robust conclusions for treatment by immediate responders. While more robust data is needed on first aid treatments of life-threatening bleeding, this systematic review aggregates the most comprehensive to date to help guide recommendations.

Keywords: bleeding; hemorrhage; tourniquet; hemostatic dressing; direct pressure

Introduction

Trauma is the leading cause of injury-related morbidity and mortality throughout the world, resulting in millions of deaths and hospitalizations each year, and uncontrolled bleeding is the primary cause of death in 35% of trauma patients (1–3). As victims of trauma can exsanguinate in as little as five minutes, before the arrival of emergency medical services, the rapid control of bleeding by immediate responders is essential to help prevent injury-related morbidity and mortality (4–6). While management of external bleeding in the out-of-hospital setting includes the use of a wide range of techniques, current international immediate responder guidelines advocate the use of direct manual pressure as the initial method for control of bleeding, with use of tourniquets and/or hemostatic dressings when direct manual compression is not possible or fails to control bleeding (7,8).

The Stop the Bleed (STB) campaign in the United States (US), launched in 2015, aims to translate battlefield medicine successes to the civilian prehospital sector by empowering the public to use tourniquets and pressure to control life-threatening bleeding (9). Numerous educational courses have since emerged in the US and are spreading globally as a result of the STB campaign in an attempt to educate immediate responders on the proper techniques of immediate bleeding control. Emergence of military and civilian data can assist in translating these life-saving military practices to civilian lay providers and inform developing of bleeding control guidelines for immediate responders and the STB campaign. This systematic review was

designed to be a comprehensive analysis of the scientific literature to assess the effectiveness of modalities that can be potentially applied by an immediate responder in the civilian setting to control severe, life-threatening external bleeding.

Methods

We performed a systematic review according to the Cochrane Handbook for Systematic Reviews of Interventions (<http://handbook-5-1.cochrane.org>) and the results are reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Our review was registered in PROSPERO (CRD42018091326).

Search strategy

The search strategy was developed in collaboration with two medical librarians (RC, IK) to identify studies that evaluated interventions for the management of severe, life-threatening external bleeding (Appendix A). An initial search revealed no comprehensive systematic reviews that could be updated for our purposes, but among 3,207 screened citations we identified 41 systematic and narrative reviews that served as sources for search terms and individual studies. We searched for original studies in the following electronic databases with no age, language or time restrictions: Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library), MEDLINE (Ovid interface), Embase (Ovid interface), Cumulative Index to Nursing and Allied Health Literature (CINAHL). We also searched selected journals from ProQuest and EBSCO military sections (International Journal of Disaster Risk Science, Disaster and Military Medicine, Studies in Conflict & Terrorism, Occupational Health & Safety) as well as ClinicalTrials.gov to identify any ongoing or unpublished studies. An initial search was conducted November 9th, 2017; to capture additional studies published during the course of the

review, two follow up searches were conducted on November 12th, 2018 and November 7th, 2019.

Selection criteria

We used the following *a priori* criteria:

Population: Adults and children with severe, life-threatening external bleeding in an out-of-hospital setting. Bleeding from both compressible and non-compressible external sites were included. Nasal and oral bleeding were excluded.

Intervention: All bleeding control methods applicable for use by trained or untrained first aid providers including manufactured or improvised tourniquets, hemostatic dressings or agents, cryotherapy, direct manual pressure, pressure points, pressure dressings or bandages or elevation of the injured area.

Comparisons: Direct manual pressure alone or any other management technique listed in Intervention, if a comparison was available.

Outcomes: Outcomes were prioritized for importance *a priori*, as per the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach (Table 1).

Study Designs: Randomised controlled trials (RCTs) and non-randomized comparative studies were included. If there were no or limited comparative studies, then case series of four or more subjects and simulation studies were also included. Conference abstracts and trial protocols were excluded. All languages were included where an English abstract was available.

Study selection

Pairs of trained reviewers independently screened titles and abstracts of identified citations using the selection criteria and guidance from experts in prehospital and emergency medicine (AB, AS, KB, MD, ML, RN). Subsequently, two trained reviewers used a standardized form to screen the full-text of potentially eligible studies (JS, NC). Disagreements were resolved through consensus, or by a third reviewer.

We searched for studies assessing the effect of interventions of interest in civilian and military subjects (direct evidence), followed by the indirect evidence of hospitalized subjects, healthy volunteers, and simulation studies, if required.

Data extraction

One reviewer extracted data using a pre-piloted form, which was checked by a second reviewer (AB, AS, JB, KB, MD, ML, RN).

Risk of bias and certainty of evidence assessment

We summarized the available evidence for each comparison of interest in Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) evidence profiles (EP). The certainty of the evidence for each comparison and outcome was assessed by reviewers experienced in applying the GRADE methodology (AD, JB, NS, RN, SK). Risk of bias was assessed using the Cochrane risk of bias tool for RCTs and the Newcastle-Ottawa scale for comparative non-randomized studies. Single-arm studies and simulation studies were classified as very low certainty as they have the highest risk of bias.

Data analysis

GRADEPro software (Guideline Development Tool [Software], McMaster University, gradepro.org) was used to create Evidence Profiles (EPs) for reporting summary of findings and certainty of the evidence per comparison and outcome. Dichotomous outcomes were reported as

relative risk (RR), odds ratio (OR) or risk difference (RD). If a measure of association was not reported, the authors calculated an unadjusted RR for the study using MedCalc for Windows Version 19.07 (MedCalc Software, Ostend, Belgium). When presented in the primary study, adjusted ORs (aOR) and adjusted RRs (aRR) were also reported. Continuous outcomes were reported as mean difference (MD) and standardized mean difference (SMD), if available. For single arm studies, we reported results as published (means or proportions), and provided the median among all included studies, or in some studies, when limited data was available, reported minimum and maximum.

Results

Results of the search

We identified 18,116 unique references, of which 1,051 were included for full-text screening. A total of 107 studies (22,718 patients) met eligibility criteria and were included for analysis; 20 RCTs (3,909 patients) and 87 observational studies (18,809 patients) (Figure 1).

Study Characteristics

Studies evaluated the use of pressure dressings/bandages/devices (n=8), (10–17) pressure points (n=4), (18–21) tourniquets (n=49), (22–70) hemostatic dressings (n=34), (29,71–103) and hemostatic devices (n= 14) (19,104–116), including two studies that reported multiple hemorrhage control methods. Study characteristics are provided in Tables 2a-d. No studies included cryotherapy or elevation of the injured body part, therefore, no data could be reported for these pre-specified interventions. Most studies had a moderate to high risk of bias (Table 3), and overall the certainty of the evidence was very low with a few exceptions. Certainty downgrades were typically due to risk of bias, indirectness and/or imprecision. We attempted to

assess publication bias, but there were not enough studies for any comparison to allow for formal evaluation. All results of included studies can be found in the online EPs.

Study findings

Results are reported with a focus on critical outcomes and comparative studies, which are felt to be most important for guidelines development. Full results, including case series and simulation studies can be found in the online EPs.

Tourniquets reported by comparison and published outcomes for each comparison

The results from 49 studies were summarized per outcome, and for all outcomes the certainty of the evidence was very low (*link to the Evidence Profile*). Characteristics of studies reporting the effect of tourniquets are presented in Table 2a.

Tourniquets compared with direct manual pressure reported by outcome

Mortality due to bleeding:

Among four civilian cohort studies, one reported an association with increased risk for mortality due to bleeding if tourniquet placement was delayed until arrival at hospital (aOR, 4.5; 95% CI, 1.23-16.4; $p = 0.02$) (22), however no association with a higher-risk for mortality due to bleeding was reported in the other three studies that did not perform adjusted analysis (very low certainty evidence) (23–25).

Bleeding Cessation Rates

In the military setting, one cohort study of 70 participants reported that a higher rate of bleeding cessation was associated with use of a tourniquet compared with direct pressure alone (83.3% vs

60.7%; $p=0.033$)(32), while in another cohort study all 6 patients in both groups achieved cessation of bleeding (very low certainty evidence) (31).

All-Cause Mortality

Of twelve cohort studies in the out-of-hospital and military setting (22–25,31,32,38,39,43–46), one reported an association with a higher risk for all-cause mortality for patients treated with direct pressure compared with the use of a tourniquet in adjusted analysis (aOR, 5.86; 95% CI, 1.41-24.47)(38). However, a second study reported an association with a higher risk for all-cause mortality with use of a tourniquet compared direct pressure (very low certainty evidence) (unadjusted RR=2.17, 95% CI: 1.67-2.81; $p<0.001$)(45). Each of the ten remaining studies failed to demonstrate a statistically significant difference in all-cause mortality with use of a tourniquet compared with direct pressure alone (22–25,31,32,39,43,44,46).

Complication Rates

Complications including compartment syndrome, fasciotomy, nerve palsy and thromboembolic complications were similar between groups as assessed in three cohort studies in the civilian out-of-hospital setting (very low certainty evidence)(23,38,39). Rates of amputation were also similar in 6 cohort studies in the civilian out-of-hospital setting (very low certainty evidence) (22,23,32,38,39,53).

Tourniquets compared with hemostatic dressings reported by outcome

Mortality Due to Bleeding

One cohort study in the military setting reported no statistical difference in mortality due to bleeding with use of a tourniquet compared with use of hemostatic dressings (68). However, tourniquet use was associated with a decreased all-cause mortality rate compared with

hemostatic dressings in unadjusted analysis (4/66 (6.1%) vs 9/30 (30.0%) [RD, 24 fewer per 100 participants; 95% CI, from 12 fewer to 28 fewer]) (68).

Manufactured Tourniquets compared with improvised tourniquets

We did not identify any randomized prehospital studies comparing the use of manufactured with improvised tourniquets for the management of severe, life-threatening external bleeding. We summarized the findings from three simulation studies with healthy volunteers and one study using manikins ([link to the Evidence Profile](#))(60,65–67).

Windlass tourniquet compared with other tourniquet designs

We did not identify any randomized prehospital studies comparing the use of windlass with other tourniquet designs for the management of severe, life-threatening external bleeding. We summarized the findings from six simulation studies with healthy volunteers and four simulation studies in manikin models ([link to the Evidence Profile](#)) (55–63,70).

Hemostatic dressings reported by comparison and published outcomes for each comparison

The results from 34 studies were summarized per outcome, and for all outcomes the certainty of the evidence was very low ([link to the Evidence Profile](#)). Characteristics of studies reporting the effect of hemostatic dressings are presented in Table 2b.

Hemostatic dressings compared with direct manual pressure reported by outcome

Cessation of Bleeding Rate

Cessation of bleeding at any time following the injury was reported as 100% with both a hemostatic dressing and direct pressure alone in one RCT in the in-hospital civilian trauma setting (very low certainty evidence) ([link to the Evidence Profile](#)) (71). Cessation of bleeding at

any time following an in-hospital endovascular procedure was comparable in two RCTs and one observational study (very low certainty evidence for both) (79,80).

One in-hospital RCT with civilian trauma casualties reported that cessation of bleeding was achieved within 5 minutes of initiating treatment in 41/80 (51.2%) patients receiving chitosan-coated hemostatic gauze compared with 26/80 (32.5%) receiving pressure dressings (RR, 1.58; 95% CI, 1.08-2.31) (low certainty evidence) (71). The reported range of mean differences in bleeding cessation from treatment initiation from 14 in-hospital RCTs following endovascular procedures varied from 2 minutes (95% CI, 0.46-3.54) to 32 minutes (95% CI, 28.03-35.97) favouring hemostatic gauze (low certainty evidence) (79,80,83–86,88–95).

All-Cause Mortality

Evidence from two in-hospital RCTs following arterial puncture wounds for endovascular procedures and one cohort study from a military setting reported no statistical difference in all-cause mortality between patients treated with hemostatic dressings compared with direct pressure alone (very low certainty evidence for both) (85,87,96).

Complications

Regarding complications, reported re-bleeding rates (nine in-hospital RCTs) and major complications (four in-hospital RCTs) were comparable between hemostatic dressing and direct pressure groups (very low certainty evidence for both) (79,80,84–88,90,93,103). Greater subject discomfort was reported with hemostatic dressings in one in-hospital RCT and comparable with direct pressure in two in-hospital cohort studies following endovascular procedures (very low certainty evidence for both) (81,93,95).

Hemostatic dressings compared with another type of hemostatic dressing reported by outcomes

Time to Bleeding Cessation

Three in-hospital RCTs following arterial puncture wounds for endovascular procedures reported no significant difference in time to bleeding cessation (moderate certainty evidence) (85,88,91).

All-Cause Mortality

One in-hospital RCT following arterial puncture wounds for endovascular procedures reported no difference in all-cause mortality (very low certainty evidence) when using one type of hemostatic dressing compared with another (*link to the Evidence Profile*)(88).

Complications

Two in-hospital RCTs reported no significant difference in major re-bleeding complications between different types of hemostatic dressings (very low certainty evidence)(85,88).

Pressure dressings/bandages/devices and pressure points reported by comparison

The results from 8 studies were summarized per outcome, and for all outcomes the certainty of the evidence was very low (*link to the Evidence Profile*). Characteristics of studies reporting the effect of pressure dressings/bandages/devices and pressure points are presented in Table 2c.

Pressure dressings/bandages/devices compared with direct manual pressure reported by outcome

Bleeding Cessation Rate

One in-hospital RCT following arterial puncture wounds for endovascular procedures reported a bleeding cessation rate of 73% with pneumatic compression and 100% with the combined groups of clamp compression and manual compression (individual group data not reported) (very low certainty evidence) (17). One cohort study of in-hospital patients with arterio-venous fistula puncture for hemodialysis reported 47% and 44% bleeding cessation rates, respectively, with

manual compression at two different test periods and 82% with a compressive bandage (very low certainty of the evidence) (11).

Time to Bleeding Cessation

Three in-hospital RCTs following arterial puncture wounds for endovascular procedures demonstrated a longer time to bleeding cessation with the use of pneumatic or mechanical pressure devices when compared with manual compression (very low certainty evidence)(12,13,17). Two in-hospital cohort studies found conflicting results, with one reporting a longer and the other a shorter time to hemostasis with use of mechanical pressure devices compared with manual compression following in-hospital endovascular procedures (very low certainty evidence) (14,15).

Complications

Six studies all with in-hospital subjects with either an arterio-venous fistula puncture or endovascular procedure reported varying complication/adverse effect rates, with one RCT reporting a higher complication rate in the pressure dressings/bandages/device group, (12) two RCTs and two observational studies reporting similar rates (11,13,14,17), and one observational study reported a lower rate with pressure dressings/bandages/devices (very low certainty evidence)(15). A higher re-bleeding rate was reported with use of a pneumatic compression device compared with a clamp or manual compression in one RCT (17), however, three cohort studies did not find a significant difference in re-bleeding rates associated with use of compression bandages/devices compared with manual compression (11,14,16).

Pressure points compared with direct manual pressure

We did not identify any studies comparing the use of pressure points with direct manual pressure for the management of severe, life-threatening external bleeding, but we have summarized the findings from different pressure point applications from four simulation studies (*link to the Evidence Profile*).

Hemostatic devices reported by comparison and published outcomes for each comparison

The results from 14 studies were summarized per outcome, and for all outcomes the certainty of the evidence was very low (*link to the Evidence Profile*). Characteristics of studies reporting the effect of hemostatic devices are presented in Table 2d.

Junctional tourniquets compared with direct manual pressure

We did not identify any human studies comparing the use of junctional tourniquets with direct pressure for the management of severe, life-threatening external bleeding, but we have summarized the findings from 12 simulation studies (*link to the Evidence Profile*) (19,104–114)

Wound clamps compared with direct manual pressure

We did not identify any studies comparing wound clamps with direct pressure for the management of severe, life-threatening external bleeding, but we report the findings from two case series (*link to the Evidence Profile*) (115,116).

Discussion

Our systematic review identified 107 studies reporting outcomes of interest for various available methods for the immediate responder management of severe, life-threatening bleeding. While high quality studies comparing first aid modalities for the control of bleeding are generally lacking, our systematic review summarizes the best available data for the creation of guidelines

for immediate responders, specifically evaluating evidence for the use of direct manual pressure, tourniquets, hemostatic dressings, and pressure devices.

Civilian trials evaluating tourniquets and hemostatic dressing are emerging and based on adjusted data analysis, reported an association with decreased mortality with use of tourniquets compared with no tourniquet application (22,38). For tourniquet use, however, data from the prehospital civilian setting is limited, confined to observational studies, and often confounded by multiple factors, limiting our confidence in the estimates of effect of the intervention. Two adjusted analysis suggested that the use of a tourniquet for limb bleeding was superior to the application of direct manual pressure alone to prevent mortality from life-threatening bleeding, with a low associated incidence of adverse effects (22,38). However other unadjusted observational studies failed to demonstrate a survival benefit (23–25). A recent systematic review of tourniquets in the prehospital civilian setting found similar results (117). While a greater amount of data is available in the military setting, it is difficult to extrapolate these results to the civilian setting due to potential differences in injury patterns and settings, and more studies are needed to further define the role of tourniquets in the civilian prehospital setting.

We did not identify any randomized prehospital trials comparing windlass tourniquets with other tourniquet designs, such as elastic or ratcheting. Further research is needed to determine what tourniquet design is ideal for hemorrhage control. While one study suggested that tourniquets are associated with lower rates of all-cause mortality when compared to hemostatic dressings (68), it is unclear if injuries were comparable and it is therefore difficult to draw a conclusion.

We identified studies from the in-hospital setting demonstrating that use of hemostatic dressings resulted in a decreased time to hemostasis compared with direct manual pressure alone,

suggesting a benefit for use in life-threatening bleeding (71,79,80,83–93). However, given the limited direct comparisons, it is unclear if one type of hemostatic dressing is superior to another.

Surprisingly, evidence for use of direct manual pressure, long considered the traditional ‘gold standard’ for immediate control of bleeding in the first aid setting, comes primarily from in-hospital studies following either an arterio-venous fistula puncture or endovascular procedure. In-hospital studies demonstrated a longer time to hemostasis with the use of mechanical pressure devices when compared with manual compression alone. (12,13,17). However indirect this evidence may be for first responders, these studies suggested that direct manual pressure is associated with better control of bleeding when compared with pressure devices.

Finally, no comparative studies were found regarding the effect of pressure points, junctional tourniquets, wound clamps, cryotherapy or limb elevation to support their use by immediate responders for treatment of life-threatening bleeding.

Additional research is needed to further define algorithms for the sequence of treatment of life-threatening external bleeding. Tourniquets are becoming a standard for life-threatening limb bleeding and it is unlikely that any future RCT’s will be conducted comparing them to direct manual pressure alone. However, additional studies could further define tourniquet indications in the prehospital setting and the ability of lay providers to utilize tourniquets in a real-world setting. Further studies are needed to define the role of hemostatic dressings and direct manual pressure on life-threatening limb bleeding. These studies could compare use of tourniquets to hemostatic dressing either for primary hemorrhage control or in comparison to placing a second tourniquet after an initial tourniquet fails to stop bleeding. Additional studies are also needed to evaluate the optimal types of hemostatic dressings for use in the prehospital setting. As

hemostatic dressings represent an additional purchase cost and training and therefore may not be available in every situation, methods of applying adequate direct manual pressure while minimizing fatigue should continue to be evaluated as it will remain a mainstay of hemorrhage control.

Limitations

The identified evidence was generally of very low certainty, primarily due to serious risk of bias, indirectness and imprecision, which precluded consistent conclusions. Randomized controlled trials are lacking as they are difficult to perform in the populations and settings of interest. Non-randomized studies were too heterogeneous in study design, setting, population, type of injuries, and measurements to allow pooling in meta-analysis. Most non-randomized comparative studies were at high risk of bias as they typically did not adjust for potential confounders. An important concern was confounding by indication; different interventions were applied in different types of injuries (e.g. limb versus junctional or torso bleeding) causing uncertainty whether any observed differences were due to the intervention or the type of injury. It is important to note that for many studies included in this review the types and locations of wounds treated by each intervention were unclear (e.g. limb, junctional, or core) and, therefore, it is unknown if the injuries are comparable among interventions. In addition, certain wound characteristics, such as the depth of the wound, may affect the ideal type of hemorrhage control. No study found in this review addressed this factor. In this systematic review military studies were considered direct evidence as these injuries occurred in the prehospital setting and were applied by soldiers who often receive training in first aid, including tourniquets and hemostatic dressings, but have no formal medical training. However, injuries in the military setting may not be similar to civilian injuries,

which would result in lower certainty of effect. Inclusion of studies in hospitalized patients, healthy volunteers, or simulation models replaced or supplemented direct evidence from the out-of-hospital and military settings for several comparisons, but this increased indirectness of the evidence. For most outcomes, there was a lack of power with small numbers of participants and outcomes across studies, which led to imprecision of the effect estimates. For several outcomes, we also included case series, to estimate outcome event rates when applying an intervention in consecutive patients, but as such studies lack a comparator group this evidence cannot be used to answer the outcome questions. Additional well-designed prospective, randomized studies in the population and setting of interest are needed to directly compare specific types of bleeding control techniques.

Conclusion

A summary of the available literature suggests that commercial tourniquets are superior to the application of direct manual pressure or hemostatic dressings for the treatment of life-threatening limb bleeding. In addition, hemostatic dressings decrease the time to hemostasis over the application of direct manual pressure with standard dressings alone and the application of direct manual pressure is superior to the use of pressure dressings or devices when stopping life-threatening bleeding. Well-designed, sufficiently powered studies that directly evaluate the population of interest are lacking. Additional studies are needed that are to increase the certainty of the overall body of evidence regarding the best treatments by immediate responders for severe, life-threatening bleeding.

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Competing Interests

The authors have no conflicts of interest relevant to this article to disclose.

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Figure 1. Flowchart of search and selection process

Table 1. Defined outcomes of importance as predetermined by the Task Force.

Outcome	Definition	Importance Rating
Mortality due to bleeding	Mortality specifically due to bleeding	Critical
Mortality from any cause	Mortality from any cause	Critical
Cessation of bleeding / achieving hemostasis	Dichotomous variable of whether or not initial bleeding was controlled	Critical
Time to achieving hemostasis	Time at which initial bleeding was controlled	Critical
Decrease in bleeding	Reduction in initial bleeding related to the intervention	Important
Complications / adverse effects	Reported complications or adverse events related to the intervention	Important

Table 2a. Characteristics of Included Studies - Tourniquets

Study	Study design	Intervention	Comparison	Participants	Setting	Key Results
Tourniquets compared with direct pressure						
Smith 2019	Cohort	Major extremity injury with a tourniquet placed. (n=127)	Major extremity injury amenable to a tourniquet but no tourniquet placed. (n=77)	Adult patients with penetrating major extremity trauma amenable to tourniquet use (major vascular trauma, traumatic amputation and near-amputation)	Level 1 trauma center at the University Medical Center in New Orleans (UMCNO)	All-cause mortality 9/127 (7.1%) vs 10/77 (13.0%; unadjusted RR=0.55, 95% CI: 0.23-1.28; p=0.16. Lower rate of secondary amputation with tourniquet vs no tourniquet (1/127 [0.8%] vs 7/77 [9.1%]; RR=0.09, 95% CI: 0.01-0.69; p=0.005)
Kauvar 2018	Cohort	Tourniquet (n=254)	No tourniquet (n=201)	Patients with at least one arterial injury to the common, superficial or deep femoral, popliteal, or tibial arteries.	US military casualties during Operations Iraqi and Enduring Freedom	Limb amputation rate 63/254 (25%) with a tourniquet vs 40/201 (20%) without a tourniquet (p=0.22). All-cause

						mortality 8/254 (3.2%) vs 8/201 (4%) for tourniquet vs no tourniquet respectively (p=NS).
Teixeira 2018	Cohort	Tourniquet use in the prehospital setting (n=181)	No prehospital tourniquet use (n=845)	Patients with traumatic peripheral vascular injuries admitted to 11 participating Level I trauma centers	Multicenter retrospective study of patients sustaining peripheral vascular injuries admitted to 11 Level I trauma centers	Higher risk for all-cause mortality without tourniquet compared with tourniquet (5.2 vs 3.9%; univariable OR = 1.36, 95% CI: 0.60-1.65; p=0.452) which was significant in multivariable analysis (adjusted OR = 5.86, 95% CI: 1.41-24.47; p=0.015).
Scerbo 2017	Cohort	Prehospital tourniquet (n=252)	Trauma center tourniquet (n=29)	Trauma patients with injuries to upper and lower extremities, with indicated tourniquet	Trauma, USA	There was a 4.5 fold increased risk of death from hemorrhagic shock if tourniquet placement was

						delayed until arrival at the hospital (OR=4.5, 95% CI: 1.23-16.4; p=0.02)
King 2015	Cohort	Tourniquet (n=27 extremities) All tourniquets were improvised	No tourniquet (n=9 extremities)	Patients with severely bleeding extremity injuries treated in the prehospital setting following the Boston Marathon bombing	Boston trauma center, USA	No mortality due to bleeding in either group (0/27 vs 0/2 [unadjusted RR=0.10, 95% CI: 0.00-4.49; p=1.0])
Kragh, Nam 2015	Cohort	Tourniquet (n=720)	No tourniquet (n=693)	Patients with major limb trauma, transfusion	US military registry, active duty casualties in Iraq or Afghanistan	All-cause mortality 88/720 (12.2%) with a tourniquet vs 79/693 without a tourniquet (11.4%; unadjusted RR=1.07, 95% CI: 0.81-1.43; p=0.63)
Kragh, Dubick 2015	Cohort	Tourniquet (n=1,272)	No tourniquet (n=3,025)	Patients with major limb trauma (the extremity Abbreviated Injury Scale (AIS) severity suffix 3 or higher)	US military registry, active duty casualties in Iraq or Afghanistan	All-cause mortality 102/1272 (8.0%) with a tourniquet vs 112/3025 without (3.7%; unadjusted RR=2.17, 95%

						CI: 1.67-2.81; p<0.001)
Ode 2015	Cohort	Tourniquet (n=24; 25 tourniquets) 20 Combat Application Tourniquets 5 improvised tourniquets	No tourniquet (n=32) Patients received trauma dressings and/or direct pressure	Patients with prehospital emergency tourniquet or prehospital documentation of active uncontrolled extremity hemorrhage, penetrating extremity trauma, open fracture with active bleeding, or traumatic extremity amputation (excluding amputations of the foot or hand).	Trauma, USA	Mortality due to bleeding was 1/24 with a tourniquet vs 0/32 without a tourniquet (unadjusted RR=3.96, 95% CI: 0.17-93.17; p=0.43)
Passos 2014	Cohort	Tourniquet (n=4) All 4 tourniquets were improvised	No tourniquet (n=186) 4 patients received a tourniquet within the first hour after arrival in the trauma bay	Adult patients with arterial injuries from extremity trauma	Two large Level 1 Trauma Centres, Canada	Mortality due to bleeding 0/4 in those with a tourniquet vs 6/186 without a tourniquet; unadjusted RR=2.88, 95% CI: 0.19-44.37; p=1.0.
Gerhardt 2011	Cohort	Tourniquets (n=8)	Tourniquet indicated but not applied (n=9)	Military personnel wounded in action and treated at a combat field hospital	US military personnel wounded in battle in Iraq	All-cause mortality 2/8 (25.0%) with a tourniquet vs 2/9 (22.2%) without; unadjusted

						RR=1.13, 95% CI: 0.20-6.24; p=1.0
Kragh, Littrel 2011	Cohort	Tourniquet (pre-hospital) (n=228 patients)	No pre-hospital tourniquet (n=38 patients)	War casualties	Military hospital (10th & 28th Combat Support Hospitals, US Army, Ibn Sina Hospital, International Zone, Baghdad, Iraq)	All-cause mortality 26/228 (11.4%) vs 8/38 (21.1%); unadjusted RR=0.54, 95% CI: 0.27-1.11; p=0.09)
Beekley 2008	Cohort	Tourniquet (n=67)	No tourniquet (n=98)	Patients in whom tourniquet was used, or had traumatic extremity amputations (excluding partial amputations of foot, hand, or digits), or had extremity vascular injuries (named vessel)	US military casualties in Operation Iraqi Freedom, before transfer to combat support hospital	Absence of bleeding on arrival with tourniquet (83.3% vs 60.7%; p=0.033). All-cause mortality 3/67 (4.5%) with a tourniquet vs 4/98 (4.1%) without; unadjusted RR=1.10, 95% CI: 0.25-4.74; p=1.0)
Mucciaron e 2006	Cohort	Tourniquet (n=2)	Pressure dressing (n=4)	Casualties with bleeding, treated before evacuation to medical center	US military casualties during Operation Just Cause, Panama	Bleeding cessation in 2/2 patients with and 4/4 patients without a

						tourniquet. All-cause mortality 0/2 vs 0/3, for tourniquet vs no tourniquet respectively.
Romanoff 1977	Cohort	Tourniquet (n=14)	No tourniquet (n=42)	<p>Patients with vascular injuries</p> <p>For 17 patients tourniquet status on admission was not recorded</p>	Trauma, Israel	<p>Limb amputation rate 5/14 (35.7%) with a tourniquet vs 10/42 (23.8% without; unadjusted RR=1.50, 95% CI: 0.62-3.64; p=0.37)</p>
Shlaifer 2017	Case series	Tourniquets (n=119) in 90 casualties	NA	Casualties treated by the Israel Defense Forces Medical Corps	Casualties wounding during Operation Protective Edge	All-cause mortality 11/90 (12.2%)
Dunn 2016	Case series	Tourniquets (n=24)	NA	Military personnel wounded in action with a field tourniquet applied	US military personnel wounded in battle in Iraq	All-cause mortality 1/24 (4.2%)
El Sayed 2016	Case series	Tourniquet (n=2,048)	NA	Patients with EMS activation for out-of-hospital trauma	U.S. National Emergency Medical Services Information System Database	All-cause mortality 14/2048 (0.7%)
Leonard 2016	Case series	<p>Combat Application tourniquet (n=61)</p> <p>Tourniquet was</p>	Kaolin-based hemostatic pad (QuikClot Combat Gauze) (n=40)	Patients with out-of-hospital traumatic or nontraumatic bleeding	10 medical institutions, USA	The rate of nerve palsy was in the tourniquet group was, 0/61 (0%)

		applied if direct pressure failed and the injury was amenable to tourniquet use	6 patients also received a tourniquet QuikClot was applied if direct pressure failed and the injury was not amenable to tourniquet use			
Scerbo 2016	Case series	Tourniquet, prehospital or in ED (n=105)	NA	Patients with major limb trauma of any etiology	Level-1 trauma center, USA	All-cause mortality was 7/105 (14%)
Callaway 2015	Case series	Combat Application Tourniquet (n=4)	NA	Civilian victims of violent trauma	Law enforcement officers, prior to EMS arrival, USA	All-cause mortality 0/4 (0%).
Inaba 2015	Case series	Tourniquet (n=44) 30 Combat Application Tourniquets 7 pneumatic tourniquets 7 other tourniquets	NA	Patients with out-of-hospital injury/trauma	Urban medical center, USA	Authors reported one limb loss likely to be caused by the use of a tourniquet.
Kue 2015	Case series	Tourniquet (n=98) 94 standard surgical latex tubing tourniquets	NA	Patients with traumatic or non-traumatic injury	EMS, USA	Of available data bleeding cessation occurred in 87/95, (95% CI: 85.9–97.3%)

		4 improvised tourniquets Some patients also received hemostatic gauze (HemCon ChitoGauze)				patients. The rate of nerve palsy was 1/95 (1.1%)
Schroll 2015	Case series	Tourniquet (n= 197)	NA	Adult trauma patients with out-of-hospital bleeding	Nine urban Level 1 trauma centers, USA	Bleeding cessation occurred in 175/197 (89%) patients. Nerve palsy occurred in 12/197 (6.1%)
Zietlow 2015	Case series	Tourniquet (Combat Application Tourniquet) (n=73; 77 tourniquets) 3 tourniquets were improvised. 7 patients also received hemostatic gauze, after standard compression bandages were unsuccessful	Kaolin-based dressing (QuickClot Combat Gauze) (n=52; 62 gauzes)	Patients with blunt trauma, penetrating wounds, or other mechanisms of injury	Gold Cross Ambulance and the Mayo One Medical Transport service, USA	Bleeding cessation occurred in 76/77 (99%) of tourniquet uses
Kragh	Case series	Tourniquet, pre-	NA	War casualties	Military hospital (10th	262/277 (94.5%)

2013		<p>hospital</p> <ul style="list-style-type: none"> - Mar 2006 – Oct 2006 (n=232 patients) - Nov 2006 – Feb 2007 (n=267 patients) - Mar 2007 – Jun 2007 (n=228 patients) 			<p>& 28th Combat Support Hospitals, US Army, Ibn Sina Hospital, International Zone, Baghdad, Iraq)</p> <p>Significant overlap with Kragh 2011 studies</p>	limbs bled less after tourniquet application
King 2012	Case series	<p>Tourniquet (n=54; 79 tourniquets on 65 limbs)</p> <p>The tourniquets identified were 90% Combat Application Tourniquets (CAT, 71/79), 5% Special Operations Forces Tactical Tourniquets (SOFTT, 4/79), 2.5% ratchet-type tourniquets (2/79), and 2.5% improvised</p>	NA	War casualties with signs of life such as a palpably detectable pulse with tourniquet use, evacuated directly from point-of-injury to the forward surgical team	US military, Afghanistan	Of available data 5/14 (35.7%) patients had no palpable pulse distal to the tourniquet.

		tourniquets (2/79)				
Kragh 2012	Case series	Tourniquet (n=88)	NA	Pediatric casualties with extremity bleeding treated at a combat support hospital	Pediatric casualties treated at US military hospitals	All-cause mortality was 7/88 (8.0%)
Kragh, O'Neill 2011	Case series	Tourniquet (n = 499)	NA	Minor and major limb trauma bleeding occurring out of hospital among US service persons during current war	US Joint Theater Trauma Registry, war casualty data at the Landstuhl Regional Medical Center (Germany)	All-cause mortality was 65/499 (13.0%)
Brodie 2009	Case series	Tourniquet (n=70) casualties	NA	Casualties with field tourniquet use presenting to a field hospital for treatment	Casualties treated at UK field hospitals in Iran and Afghanistan	All-cause mortality 9/70 (12.9%)
Kragh 2009	Case series	Tourniquet (n=194)	NA	Casualties with extremity bleeding treated at a combat support hospital	Casualties treated at a US military hospital in Iraq Significant overlap with Kragh 2008	All-cause mortality was 22/194 (11.3%)
Dayan 2008	Case series	Tourniquet (n=5)	NA	Five casualties with prolonged tourniquet periods presenting to a field hospital.	Casualties of armed conflict in Lebanon	All-cause mortality was 0/5 (0%)
Kalish 2008	Case series	Tourniquet (n=11)	NA	Patients with penetrating extremity wounds who were brought to the ED after the application of a prehospital tourniquet	Level 1 trauma center, USA	All-cause mortality 1/11 (9.1%)

Kragh 2008	Case series	Tourniquet (n=194)	NA	Casualties with extremity bleeding treated at a combat support hospital	Casualties treated at a US military hospital in Iraq Significant overlap with Kragh 2009	All-cause mortality was 22/194 (11.3%)
Lakstein 2003	Case series	Tourniquets (n=91 patients with 110 tourniquets)	NA	Military personnel wounded in action with a field tourniquet applied	Israeli Defense Force personnel wounded in action and treated by medical providers in the prehospital setting	107/110 (97.3%) tourniquet applications did not have ongoing bleeding at arrival to the hospital
Tourniquets compared with hemostatic dressings						
Kotwal 2011	Cohort	Tourniquet (n=66 patients; 89 tourniquets) Primarily Combat Application Tourniquet	Hemostatic dressing (n=30 patients; 37 dressings) Primarily HemCon bandages and Combat Gauze	Members of the 75th Ranger Regiment who sustained battle injuries	Military, Iraq and Afghanistan	Mortality due to bleeding was 0/66 (0.0%) with tourniquets vs 0/30 (0.0%) with hemostatic dressings. All-cause mortality was 4/66 (6.1%) with tourniquets vs 9/30 (30.0%) with hemostatic dressings
Manufactured tourniquets compared with Improvised tourniquets						
Heldenberg 2015	Simulation	Comparison of 3 tourniquets: 1. Improvised "Russian" tourniquet (IRT). 2. Combat Application Tourniquets		23 operators from the Israeli Naval Unit were divided into two groups according to	Laboratory setting	A 23% failure rate occurred with manufactured

		(CAT) 3. Special Operations Force Tactical Tourniquets (SOFTT)	their medical training (11 operators trained as first-responders; 12 operators as medics)- 23 healthy males, combat teams members, aged 19-23		tourniquets and a 38% failure rate occurred with improvised tourniquets. Pain rating was 4.1 with manufactured tourniquets vs 1.3 with improvised, scale 1 to 5 whereby score 5 is 'no pain') (p values not given)
Lyles 2015	Simulation	Comparison of: 1. Improvised tourniquet – bandage 2. Improvised tourniquet – bandana 3. Commercial Combat Application Tourniquet	Two users testing the tourniquets on a laboratory manikin (HapMed™ Leg Tourniquet Trainer) that was designed to train users by providing feedback on user performance.	Laboratory setting	Hemorrhage ceased in 100% of manikins using manufactured CAT, 40% using improvised bandage, and 10% using improvised bandana. Effectiveness of the CAT exceeded effectiveness of both the bandage and bandana

					tourniquets (p<0.001).
Guo 2011	Simulation	<p>Comparison of:</p> <ol style="list-style-type: none"> 1. Windlass tourniquet 2. Cargo-strap tourniquet 3. Rubber tube 4. Improvised tourniquet 	Providers and study population: healthy young soldiers (male and female aged 20-27 years old)	Laboratory setting	<p>Reported 85-100% rate of abolishing pulses with manufactured but 60-75% with improvised tourniquets. Cessation of distal pulses occurred in 36/40 (90%) with a windlass tourniquet compared with 66/80 (82.5%) with a non-windlass tourniquet (p= 0.2936). Pain with manufactured tourniquets 0.95-1.5 vs improvised tourniquets 1.9-2.4, on a scale of 0-3 whereby score 3 = very painful) (p values not</p>

King 2006	Simulation	<p>Comparison of:</p> <ol style="list-style-type: none"> 1. Self Applied Tourniquet System (SATS) 2. One-Handed Tourniquet (OHT) 3. Tie & cravat Improvised Tourniquet (IT) 4. Pneumatic Emergency Medical Tourniquet (EMT) 5. Latex surgical tubing (ST). 	Providers and models: junior medics from 1 Field Ambulance with less than 10 years of experience within the medical branch	Laboratory setting	<p>given).</p> <p>Pulse cessation occurred in 80% with pneumatic tourniquet, 30% with tie/cravat, and 90% with surgical tubing.</p> <p>Mean pain was 3 or less with manufactured, but from 3.7 - 3.9 with the improvised tourniquet (scale 0-5 whereby score 5 = could not tolerate) (p values not given).</p>
Windlass style manufactured tourniquets compared with other manufactured tourniquet designs					
Glick 2018	Simulation	<p>Combat Application Tourniquet (CAT) windlass tourniquet (n=78)</p>	<p>Israeli Silicone Tourniquet (IST) (n=78)</p>	<p>78 military personnel applying both tourniquets to a laboratory mannequin (HapMed™ Leg Tourniquet Trainer)</p>	<p>Laboratory</p> <p>Effective occlusion (applied pressure reached at least 200 mmHg) occurred in 57/78 (73.1%) and 71/78 (91%) with the CAT and IST</p>

						<p>respectively (p=0.007).</p> <p>Time to effective occlusion (among effective attempts) was 27 seconds (range 11-90) and 33 (range 5-74) with the CAT and IST respectively (p=0.58)</p>
Beaven 2017	Simulation	Tactical mechanical tourniquet windlass design	Tactical pneumatic tourniquet	The tourniquets were tightened by the same single researcher to health military volunteers	Laboratory setting	Time to pulse occlusion in the mechanical tourniquet was 16.0 secs (IQR 12-20) and 11.0 secs (IQR 7-12) for the pneumatic tourniquet
Bequette 2017	Simulation	<p>Comparison of 4 tourniquets:</p> <ol style="list-style-type: none"> 1. Tourni-belt, strap-and-windlass design 2. TourniquetBelt, strap-and-windlass design 3. ParaBelt, ratchet design 4. BattleBuddy, pulley design. 		Two volunteers with first aid experience applied 20 tests with each model to a laboratory manikin (HapMed™ Leg Tourniquet Trainer)	Laboratory setting	Average time to hemostasis ranged from 56 to 80 seconds. No difference was observed between the

					systems, except for a shorter time to hemostasis with ParaBelt compared to Tourniquet Belt (p=0.048).
Walters 2005	Simulation	<p>Comparison of:</p> <ol style="list-style-type: none"> 1. Combat Application Tourniquet (CAT) 2. Emergency & Military Tourniquet (EMT) 3. Special Operations Forces Tactical Tourniquet (SOFTT) 4. Mechanical Advantage Tourniquet (MAT) 5. The Last Resort Tourniquet, One-Handed Tourniquet 6. The Self-Applied Tourniquet System 	Healthy, normotensive men and women ranging in age from 23 to 47 years	Laboratory setting	Windlass tourniquets (CAT, SOFTT) were 100% effective, while other types of tourniquet had success rates ranging from 22% to 100%.
O'Connor 2017	Simulation	<p>Comparison of 3 tourniquets:</p> <ol style="list-style-type: none"> 1. Special Operations Forces Tactical Tourniquet ((SOFTT-W; Tactical Medical Solutions) 2. Ratcheting Medical Tourniquet ((RMT) 3. Generation 6 version of the Combat Application Tourniquet (CAT) 	Two users testing the tourniquets on a laboratory manikin (HapMed™ Leg Tourniquet Trainer) for a total of 300 iterations	Laboratory setting	Cessation of pulses occurred in 185/200 (92.5%) with windlass tourniquets vs 94/100 (94%) with the ratcheting tourniquet. Time to hemostasis

						was 21 secs for the CAT, 29 secs for the SOFTT-W and 34 secs for the RMT (p<0.001).
Gibson, Aden 2016	Simulation	Combat Application Tourniquet (CAT) of a strap-and-windlass design.	Emergency and Military Tourniquet (EMT) and two Tactical Pneumatic Tourniquet (TPT) models differing in width: 2 in. (50.8mm; TPT2) and 3 in. (76.2mm; TPT3)	Two users testing the tourniquets on a laboratory manikin (HapMed™ Leg Tourniquet Trainer) for a total of 80 iterations	Laboratory setting	Time to cessation of bleeding was not significantly different from the pneumatic models and the CAT
Gibson, Housler 2016	Simulation	Windlass tourniquets 1. Combat Application Tourniquet (CAT). 2. Tactical Mechanical Tourniquet (TMT)	Rapid Application Tourniquet System (RATS)	Two users testing the tourniquets on a manikin (HapMed™ Leg Tourniquet Trainer) for a total of 60 iterations.	Laboratory setting	Pulse cessation occurs in 20/20 (100%) of non-windlass design and in 39/40 (97.5%) of the windlass design (p=NS). The time to cessation of pulses was reported to be longer in the RATS than either the CAT or TMT (p<0.001 and 0.006, respectively).

Peponis 2016	Simulation	Combat Application Tourniquet (CAT) windlass tourniquet	Pneumatic tourniquet	Healthy volunteers between 18 and 50 years old who were wearing a hazardous material suit.	Laboratory setting	Distal pulses were abolished in 2020 (100%) of those with a pneumatic tourniquet and 20/20 (100%) of those with a CAT applied
Wall 2013	Simulation	Combat Application Tourniquet (CAT) windlass tourniquet	Stretch, Wrap, and Tuck Tourniquet (SWAT-T)	Sixteen volunteers self-applied and had tourniquets applied to their thighs and arms	Laboratory setting	61/64 (95.3%) of CAT vs 61/64 (95.3%) of SWAT-T applications had initial arterial occlusion (p=NS)
Taylor 2011	Simulation	Combat Application Tourniquet (CAT) (a windlass tourniquet)	Emergency and Military Tourniquet (EMT) (a pneumatic tourniquet)	Volunteers: Patients attending Orthopaedic Outpatient Clinic. All invited participants were currently serving military personnel	Laboratory setting	8.3% of applications by the researcher and 16.6% of self-applications were successful with windlass tourniquet, while 75% were successful with a pneumatic tourniquet (p<0.001)

Table 2b. Characteristics of Included Studies – Hemostatic Dressings

Study	Study design	Intervention	Comparison	Participants	Setting	Key Results
Hemostatic dressings compared with direct pressure						
Kang 2017	RCT	Hemostatic pad (chitosan based) with compression device (n=59)	Compression device (n=36)	Patients who underwent elective or urgent coronary angiography or interventions with radial access	In hospital endovascular procedures	29/59 (49.2%) for those with a hemostatic dressing vs 1/36 (2.8%) with a compression device alone achieved hemostatic within 5 minutes (p<0.001)
Dai 2015	RCT	Hemostatic pad (chitosan-based) plus manual pressure and elastic bandage (n=300)	Radial compression device (n=300)	Patients who had undergone transradial coronary intervention	In hospital endovascular procedures	No major complications occurred in either the hemostatic dressing group (0/300) or the group with the compression device (0/300).
Hatamabadi 2015	RCT	Chitosan-coated (CeloX) gauze (n=80)	Simple pressure dressing (n=80)	Patients who presented to the emergency department penetrating limb trauma	Level 1 urban trauma center in Tehran, Iran	Cessation of bleeding occurred in all patients in the hemostatic dressing group (80/80) and the pressure dressing group (80/80).

						<p>Hemostasis within 5 minutes occurred in 41/80 (51.2%) of the hemostatic dressing group and 26/80 (32.5%) of the pressure dressing group. (RR, 1.58; 95% CI, 1.08-2.31) (p=0.02). Hemostatic dressings had an average of 0.43 few blood soaked gauze than pressure dressings (95% CI, 0.85 to 0.01 fewer)</p>
Kordestani 2012	RCT	Hemostatic dressing (ChitoHem powder) (n=62)	Manual Compression (n=62)	Patients receiving femoral artery puncture for endovascular procedures	In hospital endovascular procedures	<p>Time to hemostasis was 4.6 ± 1.3 min in the hemostatic dressing group vs 12.4 ± 4.4 min in the manual compression group (p<0.001).</p>
Trabattoni 2011	RCT	Kaolin-based hemostatic dressing	Manual compression (n=100)	Patients undergoing angiography or PCI via a femoral approach	In hospital endovascular procedures	<p>Mean time to haemostasis was 5.4 ± 1.5 min the</p>

		(QuikClot) (n=100)				hemostatic dressing group vs. 25 ± 15 min with standard manual compression ($p < 0.001$). 2/100 (2.0%) major bleeding complications in the hemostatic dressing group compared with 4/100 (4.0%) in the manual pressure group (RR=0.50, 95% CI: 0.09-2.67; $p=0.68$)
Arbel 2011	RCT	Hemostatic dressing (HemCon pad) (n=70)	Manual Compression (n=66)	Patients with femoral artery puncture for PCI	In hospital endovascular procedures	Time to hemostasis was 5.6 ± 2.1 in the hemostatic dressing group compared with 8.4 ± 3.5 in the manual compression group ($p < 0.001$). Patient satisfaction using a 1-10 scale for hemostatic

						dressings and manual compression was 9.7% (SD 0.5) vs. 9.4% (SD 1.0); p=0.4
Politi 2011	RCT	Hemostatic pad (QuikClot) (n=50)	Compression bandage (n=50)	Patients with radial artery puncture for endovascular procedures	In hospital endovascular procedures	All-cause mortality was 0/50 with hemostatic dressings compared with 0/50 for direct pressure (RR=1.00, 95% CI: 0.02-49.44; p=1.0). No major bleeding complications occurred in either group: 0/50 vs 0/50 (RR=1.00, 95% CI: 0.02-49.44; p=1.0).
Sairaku 2011	RCT	Manual compression with kaolin-impregnated pad (QuikClot) (n=59)	Manual compression (n=59)	Patients with femoral venous access for atrial fibrillation ablation	In hospital endovascular procedures	Time to hemostasis was 6.1±2.3 min in those treated with a hemostatic dressing compared to 14.5±4.0 min for those treated with

						manual compression (p<0.0001).
Waragai 2011	RCT	Microporous polysaccharide hemospheres (MPH) hemostasis bandage (n=8)	Manual compression (n=13)	Children undergoing cardiac catheterization through femoral artery	In hospital endovascular procedures	Hemostasis was achieved in 8/8 (100%) patients with hemostatic dressings and 13/13 (100%) with manual compression. Time to hemostasis was 8.3±6.0 min for hemostatic dressing and 17.2±10.9 min for manual compression (p=0.048)
Zhu 2010	RCT	Hemostatic dressing (V+PAD – chitosan based) (n=40)	Manual Compression (n=40)	Patients with femoral artery puncture for endovascular procedure	In hospital endovascular procedures	Time to hemostasis was 7.9±0.5 min in the hemostatic dressing group compared with 19.8±5.1 min in the manual compression group (p<0.001).
Behler 2009	RCT	Hemostatic dressing (n=9)	Manual Compression (n=10)	Patients with femoral artery puncture for endovascular procedure	In hospital endovascular procedures	Time to hemostasis was 9.44±3.09 for the

						hemostatic dressing group vs 13.00 ± 1.56 for manual compression. ($p = 0.0065$)
Balzer 2007	RCT	Hemostatic Clo-Sur PAD (n=60)	Manual Compression (n=60)	Patients with femoral artery puncture for endovascular procedure	In hospital endovascular procedures	Hemostasis was achieved in 57/60 (95%) with a hemostatic dressing compared with 60/60 (100%) with manual compression ($p=0.24$). Time to hemostasis was 10.15 ± 1.96 min in the hemostatic dressing group vs 16.20 ± 1.79 min in the manual compression group ($p<0.0001$). No major complications occurred in either group (RR=1.00, 95% CI: 0.02-49.60; $p=1.0$)
Narins 2008	RCT	Hemostatic dressing (SafeSeal)	Manual compression	Patients undergoing coronary or peripheral	In hospital endovascular	Time to hemostasis was

		Patch) (n=75)	(n=75)	intervention through the femoral artery	procedures	11.8 ± 3.6 min in the hemostasis dressing group vs. 13.8 ± 5.8 min with manual compression (p=0.023).
Mlekusch 2006	RCT	Hemostatic dressing (Clo-Sur PAD™) (n=104)	Manual compression (n=105)	Patients with femoral artery puncture for endovascular procedures	In hospital endovascular procedures	The average time to hemostasis with a hemostatic dressing was 13.6 min vs 20.3 min with manual compression (p.0.001)
Schauer 2017	Cohort	Kaolin-based hemostatic pad (QuikClot Combat Gauze) (n=28)	Patients without a hemostatic gauze (n=162)	Patients listed in Prehospital Trauma Registry with available outcome data	Military prehospital setting, Afghanistan	Of those with available data, all-cause mortality was 11% (3/28) mortality in those receiving hemostatic gauze and 6% (9/162) in those who did not (unadjusted RR=1.93, 95% CI: 0.56-6.69; p=0.39). Of total hemostatic dressing applications

						103/141 (88.3%) achieved hemorrhage control.
Tjong 2012	Cohort	Hemostatic dressing (n=50)	Manual Compression (n=38)	Patients with femoral artery puncture for endovascular procedure	In hospital endovascular procedures	Hemostasis occurred in 50/50 in the hemostatic dressing group and 38/38 with manual compression. There was no significant difference in pain scores between the manual and hemostatic patch groups (data not given).
Warriner 2018	Case series	XSTAT [®] expandable minisponge hemostatic device (n=10)	NA	Patients presenting with penetrating trauma	US level 1 trauma center	Cessation of bleeding occurred in 10/10 patients. All-cause mortality was 0/10. 1/10 cases had the complication of retained sponges requiring wound extension and retrieval.
te Grotenhuis	Case series	Chitosan-based dressing (HemCon	NA	Patients of civilian emergency medical	Netherlands emergency	Hemostasis occurred in 46/66

2016		ChitoGauze) (n=66)		services with out-of-hospital massive traumatic external haemorrhage	medical services	(70%) of patients. Median time to hemostasis was 1 min (IQR: 0 to 3 minutes). 0/66 patients experienced adverse events.
Travers 2016	Case series	Kaolin-based dressing (QuikClot Combat Gauze) (n=30)	NA	<p>Patients with out-of-hospital hemorrhagic open wounds</p> <p>QuikClot used in cases where other techniques were ineffective, or bleeding occurred in an inaccessible area for pressure or tourniquet</p>	Paris fire brigade, France	All-cause mortality was 6/30 (20%). Bleeding cessation occurred in 22/30 (73.3%) patients. A decrease in bleeding occurred in 6/30 (20%) cases. 0/30 patients experienced adverse events.
Wedmore 2016	Case series	Chitosan-based hemostatic dressing (HemCon) (n=64 patients)	NA	<p>Combat casualties</p> <p>In 42 (66%) of the cases, the HemCon dressings were used after failure of traditional dressings. In the remaining 22 cases, it was unclear if any methods had been tried before HemCon application</p>	US military in Iraq or Afghanistan	Bleeding cessation occurred in 62/64 (96.8%) patients. 0/64 patients experienced adverse events.
Shina 2015	Case	Kaolin-based	NA	Traumatic casualties	Prehospital	All-cause

	series	hemostatic pad (QuikClot Combat Gauze) (n=122)		registered in IDF Trauma Registry (ITR)	military, Israel	mortality was 7/122 (5.7%) Of available data, a decrease or cessation in bleeding occurred in 31/37 (83.7%) cases of junctional hemorrhage.
Peters 2014	Case series	Chitosan-based dressing (HemCon) (n=24)	NA	Patients with bleedings suspected to be difficult to control with conventional bandages, or with unsuccessful use of conventional bandages	Helicopter trauma medical team, The Netherlands	Bleeding cessation occurred in 18/24 (75.0%) of patients. 6/24 (25%) patients experienced a decrease in bleeding. 0/18 patients with available data were reported to have adverse events.
Weppner, 2013	Case series	Kaolin-based hemostatic pad (QuickClot Combat Gauze) plus direct pressure (n=35 patients)	NA	Persistent hemorrhage caused by penetrating neck or maxillofacial trauma	Operation Enduring Freedom in Afghanistan	Cessation of bleeding was achieved in 31/35 (88.6%) patients. All-cause mortality was 8/35 (22.8%).
Pozza, 2011	Case	Chitosan-based	NA	Soldiers suffering from	Military patients	Hemostasis was

	series	hemostatic dressing (CeloX) (n=6 patients)		gunshot wounds	received treatment at a ROLE 2 (Enhanced Care) Facility in Afghanistan	achieved in 6/6 (100%) patients. All-cause mortality was 0/6 patients.
Brown 2010	Case series	HemCon (n=25 patients)	NA	Civilians suffering from external hemorrhage in which direct pressure with a traditional gauze bandage failed to control the bleeding.	UK military, Iraq and Afghanistan	Cessation of bleeding occurred in 19/25 (76%) patients. Time to hemostasis was within 1 minute in 35% of patients, within 3 minutes in 74%, within 10 minutes in 79%, and within 10 minutes or longer in 100%. 0/25 patients experienced adverse events.
Ran 2010	Case series	QuikClot Combat Gauze (n=14 patients)	NA	Treated military personnel were wounded with various penetrating and blast mechanism injuries	Israel Defense Force casualties in Gaza strip	Cessation of bleeding occurred in 11/14 (78.6%) patients. All-cause mortality was 1/14 (7.1%). No adverse events were reported (0/14).
Cox 2009	Case	QuikClot or	NA	Military casualties treated	Prehospital and	42/44 (95.5%)

	series	<p>HemCon hemostatic bandages (n=44 patients)</p> <p>40 HemCon 3 QuikClot 1 HemCon and QuikClot</p>		with hemostatic dressings prehospital (n=8) or in the combat support hospital (n=36)	Level III combat support hospital, USA	<p>patients had an overall cessation or decrease in bleeding. All-cause mortality was 2/44 (4.5%). 2/4 (50%) patients that received QuikClot zeolite-based granules experienced superficial burns in the soft tissues and at the wound edges.</p>
Rhee 2008	Case series	<p>QuikClot (zeolite) (n=14 civilian pre-hospital) (n=69 military)</p>	NA	Trauma cases where QuikClot was used as submitted by users or identified through interview with users	US military or civilian personnel	<p>Cessation of bleeding occurred in 14/14 civilian patients and 65/69 (94.2%) of military patients. All-cause mortality was 0/14. 25% of patients experienced mild to severe pain and discomfort and 3/83 (3.6%) experienced burns for an exothermic</p>

						reaction.
Kragh 2015	Simulation	XSTAT expandable minisponge hemostatic device (n=10)	Standard gauze	A model of penetrating groin injury was packed with XSTAT gauze and standard gauze 10 times each and packing parameters were measured.	Laboratory setting	Cessation of bleeding was achieved in 50% (5/10) of mini cellulose sponge injector applications compared with 10% (1/10) with regular dressing. Simulated blood loss was 93ml with the minisponges and 113ml with the bandage roll.
Kragh 2014	Simulation	QuikClot Combat gauze (n=4)	No gauze	A single user applied QuikClot Combat gauze with the use of pressure and an overwrap compared with no gauze to a model of penetrating groin injury. Each test was done 4 times.	Laboratory setting	4/16 iterations showed reduced bleeding, as measured by liquid loss from the manikin, with full application of the QuikClot Combat Gauze compared to no use of the gauze
One hemostatic dressing type compared with another hemostatic dressing type						
McConnell 2012	RCT	Comparison of three methods of hemostasis: 1. Manual compression alone (n=26)		Patients receiving femoral artery puncture for endovascular procedures	In hospital endovascular procedures	Time to hemostasis: manual pressure 22.3±1.2 min,

		2. Hemostatic dressing SyvekPatch with manual compression (n=26) 3. Hemostatic dressing D-Stat Dry plus manual compression (n=28)				SyvekPatch 17.8±1.3 min (p=0.008), D-Stat Dry 17.5±1.4 min (p =0.010).
Schwarz 2009	RCT	Hemostatic dressing with calcium ion releasing device and compression bandage (Neptune-PAD) (n=303)	Hemostatic dressing with thrombin covered pad and compression bandage (D-Stat-Dry-PAD) (n=303)	Patients undergoing diagnostic or therapeutic procedures via a 5 or 6 F femoral sheath	In hospital endovascular procedures	Time to hemostasis was 11.5±8.0 min for the Neptune-PAD and 12.4±6.7 min for D-Stat Dry (p value not given). There was a lower rate of minor bleeding following use of Neptune-PAD (20/303 [6.6%]) compared with the hemostatic thrombin covered bandage D-Stat Dry (37/303 [12.2%]) (RR=0.54, 95% CI: 0.32-0.91; p=0.02)
Nguyen 2007	RCT	Comparison of three methods of hemostasis: 1. Manual compression alone (n=45) 2. Hemostatic pad Chito-Seal		Patients with femoral artery puncture for endovascular procedures	In hospital endovascular procedures	Time to hemostasis: manual compression 19.3±7.8 min,

		(n=47) 3. Hemostatic pad Clo-Sur PAD (n=43)			Chito-Seal 16.2±4.9 min, Clo-Sur PAD 16.0±5.3 min (p=0.027)
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Table 2c. Characteristics of Included Studies – Pressure dressings, bandages, devices or proximal pressure

Study	Study design	Intervention	Comparison	Participants	Setting	Key Results
Pressure dressings/bandages/devices compared with direct manual pressure						
Chlan, 2005	RCT	External compression devices 1. Pneumatic compression (FemoStop) (n=99) 2. C-clamp (n=108)	Manual compression (n=99)	Patients with femoral artery puncture for endovascular procedure	In hospital endovascular procedures	Mean time to hemostasis was: Femostop 40.2 ± 23.2 , C-clamp 32.6 ± 9.8 and manual 27.5 ± 6.3 minutes ($p < 0.0001$). The rate of adverse events in the pressure device group was 94/207 (45.4%) vs. 56/99 (56.6%) in the manual compression group (RR=0.80, 95% CI: 0.64-1.01; $p=0.06$).
Walker 2001	RCT	Pneumatic (FemoStop) external compression device (n=116)	Manual compression (n=143)	Patients undergoing coronary angioplasty and coronary stent placement through femoral artery puncture	In hospital endovascular procedures	Mean time to hemostasis in the Femostop group was 35.2 ± 12.3 minutes compared with the manual compression time of 12.9 ± 12.4 minutes ($p < 0.001$). Adverse events were reported in 18.1% (21/116) of the pressure devices group and 9.0% (13/143) of the manual pressure group. (RR=1.99, 95% CI: 1.04-3.80; $p=0.04$)
Lehmann 1999	RCT	External compression devices	Manual compression (n=152)	Patients with femoral artery puncture for	In hospital endovascular procedures	The mean time to hemostasis was: pneumatic device 15.6 ± 4.81 min, c-

		<ol style="list-style-type: none"> 1. C-clamp (n=143) 2. Pneumatic compression (FemoStop) (n=102) 		endovascular procedures		clamp 14.5 ± 4.5 min, manual compression 13.9 ± 3.5 min (overall $p=0.006$). There was a comparable rate of adverse events for pneumatic compression (25%), clamp compression (30%), and manual compression (26%) (p =value not reported).
Neto, 2015	Cohort	TR band or RadiStop external radial artery compression device (n=112)	Compressive Dressing (n=416)	Patients with radial artery puncture for endovascular procedures	In hospital endovascular procedures	Re-bleeding after initial hemostasis occurred in 0/112 (0%) with a wristband device compared with 8/416 (1.9%) for manual compression and compressive dressing ($p=0.21$).
Boulanger, 2014	Cohort	IRIS compression bandage (n=64)	Manual compression (n=128)	64 patients undergoing post hemodialysis with arteriovenous fistula puncture site bleeding treated with manual compression twice and the IRIS bandage once on alternative weeks over the course of	In hospital hemodialysis treatments	Hemostasis was achieved in 47% and 44% with manual compression in the first and third week of the study design, while 82% had bleeding cessation with the IRIS bandage in the second week of the study ($p<0.05$)

				three weeks. Only data from the arterial side was included.		
Sulzbach-Hoke, 2010	Cohort	C-clamp external compression device (n=223)	Manual Compression (n=105)	Patients undergoing percutaneous coronary intervention through the femoral artery	In hospital endovascular procedures	C-clamp had a higher median compression time to achieve hemostasis than the use of direct manual compression (median [min-max]: 35 min [10-110] vs 20 min [10-45]; p<0.001)
Semler, 1985	Cohort	C-clamp External mechanical compression (n=2250)	Manual Compression (n=1005)	Patients with femoral artery puncture for endovascular procedures	In hospital endovascular procedures	A mechanical clamp had a time to hemostasis of 19.9 minutes compared with 33.5 minutes for the use of direct manual pressure (p values not reported). There was a lower rate of complications in the mechanical clamp group compared to the manual pressure group (2% vs 6%; p<0.001).
Naimer, 2006	Case series	Compression dressing with ELAD (elastic adhesive dressing) (n=62)	NA	Trauma victims wounded out-of-hospital by firearms, explosives, or accidents presenting with actively bleeding wounds	Trauma teams including physicians, paramedic and volunteer first aid providers in Israel	54/62 (87.1%) of patients achieved bleeding cessation with the ELAD pressure dressing and additional 7/62 (11.3%) achieved a decrease in bleeding with the ELAD pressure dressing.
Pressure points compared with direct manual pressure						

Slevin 2019	Simulation	Jiu-Jitsu knee mount position pressure points <ol style="list-style-type: none"> 1. Brachial artery (shoulder) (n=11) 2. Femoral artery (groin) (n=11) 3. Aorta (abdomen) (n=11) 		11 healthy adult volunteers with multiple iterations of each method	Laboratory	<p>Complete vessel occlusion, as measured by mean arterial blood flow velocity (MAV), occurred 73% (8/11) of the time with brachial compression, 55% (6/11) of the time with femoral compression and 9% (1/11) of the time with aortic compression.</p> <p>100% of brachial [mean - 97.5 (-100% to -94%)] and femoral [-78% (-100% to -56%)] artery pressure decreased MAV greater than 20%, which was deemed to be the clinically relevant value.</p> <p>The mean MAV decrease with aortic compression was -35% (-57% to -12%).</p>
Garrick, 2016	Simulation	Doppler ultrasound probe use to compress the popliteal artery to occlude blood flow (n=27)	NA	27 healthy human volunteers	Laboratory	Distal pulse cessation occurred 25/27 (93%) participants.
Kragh, 2013	Simulation	Inguinal pressure point compression <ol style="list-style-type: none"> 1. Digital compression 2. Manual compression (palm of 		Mannequin model of groin hemorrhage with	Laboratory	All modalities stopped simulated bleeding as measured by wound flow

		hand) 3. Knee compression 4. Kettle bell compression 5. Medical junctional compression devices	multiple iterations of each method		and femoral arterial pressure (120/120). Average times to bleeding cessation: Digital compression 9 secs, Manual compression 27 secs, knee compression 40 secs, kettlebell, 29 secs, junctional devices 60 secs.
Swan, 2009	Simulation	Pressure points 1. Brachial artery a. Arm (n=10) b. Cubital fossa (n=10) 2. Femoral artery (n=10) 3. Popliteal artery (n=10)	10 healthy adult volunteers with multiple iterations for each method.	Laboratory	Ablation of distal pulse occurred in 1/10 for the brachial artery at the arm, 4/10 for the brachial artery at the cubital fossa, 1/10 for femoral artery and 6/10 of popliteal artery.

Table 2d. Characteristics of Included Studies –Hemostatic devices

Study	Study design	Intervention	Comparison	Participants	Setting	Key Results
Junctional tourniquets compared with direct pressure						
Gaspary 2018	Simulation	Junction tourniquets: 1. Combat Ready Clamp (CRoC) (Combat Medical Systems) 2. Junctional Emergency Treatment Tool (JETT) (North American Rescue) 3. SAM Junctional Tourniquet (SJT) (SAM Medical Products, Inc.)		49 military personnel who applied each of the tourniquets to each other in succession	Simulation study in healthy human participants	Elimination of distal pulses occurred in 84% for the CRoC, 82% for the JETT and 82% for the SJT (p=0.95).
Chen 2016	Simulation	Junction tourniquets: 1. Combat Ready Clamp (CRoC) (Combat Medical Systems) 2. Abdominal Aortic and Junctional Tourniquet (AAJT, Compression Works, Hoover, AL). 3. Junctional Emergency Treatment Tool (JETT) (North American Rescue) 4. SAM Junctional Tourniquet (SJT) (SAM Medical Products, Inc.)		14 military medics who applied each of the four models to the groin	Simulation study in healthy human participants	Overall effectiveness in eliminating distal pulses was 161/186 (86.6%).
Kragh	Simulation	Junction tourniquets:		30 military medical personnel who	Simulation	Devices were

2016		<ol style="list-style-type: none"> 1. Combat Ready Clamp (CRoC) (Combat Medical Systems) 2. Junctional Emergency Treatment Tool (JETT) (North American Rescue) 3. SAM Junctional Tourniquet (SJT) (SAM Medical Products, Inc.) 		applied each device to a mannequin	study on mannequin model of groin bleeding	successful in controlling simulated bleeding 270/270 (100%) iterations.
Meusnier 2016	Simulation	Combat Ready Clamp (CRoC) (Combat Medical Systems) (n=36)	SAM Junctional Tourniquet (SJT) (SAM Medical Products, Inc.) (n=38)	4 military medical personnel who applied junction tourniquets to 74 healthy military personnel	Simulation study in healthy human participants	The CRoC eliminated distal pulses 91.7% of the time whereas the SJT eliminated distal pulses 86.9% of the time.
Theodoris 2016	Simulation	Combat Ready Clamp (CRoC) (Combat Medical Systems) (n=33)	Junctional Emergency Treatment Tool (JETT) (North American Rescue) (n=33)	33 military personnel who applied both junctional tourniquets to each other	Simulation study in healthy human participants	The CRoC eliminated distal pulses 33/33 times vs 30/33 for the JETT (p=0.192). Mean application time from the CRoC was 70.24 secs vs 54.79 secs for the JETT (p<0.001)
Kragh 2015	Simulation	Junction tourniquets: <ol style="list-style-type: none"> 1. Combat Ready Clamp (CRoC) (Combat Medical Systems) 2. Junctional Emergency Treatment Tool (JETT) (North American 		10 participants with a total of 120 applications of the four devices by two study personnel.	Simulation study in healthy human participants	Junctional tourniquets were effective in eliminating distal pulses 27-97% of the time. When excluding the AAJT

		Rescue) 3. SAMVR Junctional Tourniquet (SJT) (SAM Medical Products, Inc.) 4. Abdominal Aortic and Junctional Tourniquet (AAJT, Compression Works, Hoover, AL).				they were effective 77-97% of the time.
Lyon 2015	Simulation	Abdominal Aortic and Junctional Tourniquet (AAJT, Compression Works, Hoover, AL).		Study personnel applied the AAJT to 13 healthy male participants at both the axillae and groin	Simulation study human participants	The AAJT was effective at eliminated pulses 26/26 (100%) times.
Gates 2014	Simulation	Junctional Emergency Treatment Tool (JETT) (North American Rescue)	Combat Ready Clamp (CRoC) (Combat Medical Systems)	8 applications of both the JETT and CRoC to a cadaver model by study personnel	Simulation study in perfused human cadavers	Both the JETT and the CRoC resulted in elimination of simulated blood flow 8/8 (100%) times.
Kragh 2014	Simulation	Junction tourniquets: 1. Combat Ready Clamp (CRoC) (Combat Medical Systems) 2. Abdominal Aortic and Junctional Tourniquet (AAJT, Compression Works, Hoover, AL). 3. Junctional Emergency Treatment Tool (JETT) (North American Rescue) 4. SAMVR Junctional Tourniquet (SJT) (SAM Medical Products, Inc.)		9 military personnel who applied each of the four devices on one another for a total of 72 tests	Simulation study in healthy human participants	The SJT and CRoC eliminated distal pulses 100% and 95% of the time, respectively (p=0.187). Both the SJT and CRoC were more effective than the JETT and AAJT, which eliminated distal pulses 89% and 11% of the time, respectively (p<0.001).

Cotte 2013	Simulation	Combat Ready Clamp (CRoC) (Combat Medical Systems)	Study personnel applied the junctional tourniquet to 30 healthy military participants	Simulation study in healthy human participants	Cessation of distal pulses occurred in 29/30 (96.7%) of participants.
Kragh, 2013	Simulation	<p>Inguinal pressure point compression</p> <ol style="list-style-type: none"> 4. Digital compression 5. Manual compression (palm of hand) 6. Knee compression 7. Kettle bell compression 8. Combat Ready Clamp (CRoC) (Combat Medical Systems) 9. Abdominal Aortic and Junctional Tourniquet (AAJT, Compression Works, Hoover, AL). 10. Junctional Emergency Treatment Tool (JETT) (North American Rescue) 11. SAMVR Junctional Tourniquet (SJT) (SAM Medical Products, Inc.) 	Mannequin model of groin hemorrhage with multiple iterations of each method	Laboratory	<p>All modalities stopped simulated bleeding as measured by wound flow and femoral arterial pressure (120/120). Average times to bleeding cessation [Avg(min-max)]: Digital compression 9 (5-17) secs, Manual compression 27 (17-41) secs, knee compression 40 (34-50) secs, kettlebell, 29 (26-34) secs, CRoC 59 (40-102) secs, SAM 26 (25-29) secs, JETT 41 (21-80) secs, AAJT 102 (87-117) secs. Average simulated blood loss was [Avg(min-max)]: digital compression 96 (60-155) mL, Manual compression 239 (160-300) mL, knee compression 251</p>

						(155-520) mL, kettlebell 140 (115-240) mL, CRoC 581 (400-1150) mL, SAM 35 (21-80) mL, JETT 342 (50-1380) mL, AAJT 787 (435-1070) mL
Taylor 2013	Simulation	Abdominal Aortic and Junctional Tourniquet (AAJT, Compression Works, Hoover, AL).		Study personnel applied the junctional tourniquet to 16 healthy military participants	Simulation study human participants	Cessation of distal blood flow occurred in 15/16 (93.8%) of participants.
Wound clamps compared with direct pressure						
McKee 2018	Case series	iTClamp (n=245)	NA	Patients with iTClamp applied	Prehospital and in-hospital environments globally	Hemorrhage was adequately controlled in 198/245 (81%) of cases.
Tan, 2016	Case series	iTClamp (n=10)	NA	Severe trauma patients with iTClamp applied after unsuccessful use of bandages, or for bleedings suspected of being difficult to control	Helicopter emergency medical service, The Netherlands	Mortality due to bleeding occurred in 0/10 (0.0%). A decrease in bleeding occurred in 9/10 (90.0%). Average time to achieve hemostasis was 11 minutes (95% CI: 5 to 16).

Table 3a. Risk of Bias for Randomized Studies: Cochrane RoB 2 tool

Study	Design	Allocation: Generation	Allocation: Concealment	Blinding: Participants	Blinding: Personnel/Assessors	Outcome: Complete	Outcome: Selective	Other Bias
Arbel 2011	RCT	Unclear	Unclear	Low	High	Low	Low	High
Balzer 2007	RCT	Low	Low	Low	High	Low	Low	Low
Behler 2009	RCT	Unclear	Unclear	Low	Low	Low	Low	Low
Chlan 2005	RCT	Low	Low	High	High	Low	Low	Low
Dai 2015	RCT	Low	Low	Low	Low	Low	Low	Low
Hatamabadi 2015	RCT	Low	Unclear	Low	High	Low	Low	Low
Kang 2017	RCT	Low	Low	Low	High	Low	Low	Low
Kordestani 2012	RCT	Low	Unclear	Unclear	High	Low	Low	Low
Lehmann 1999	RCT	Low	Low	Low	Low	Low	Low	Low
McConnell 2012	RCT	Low	Unclear	Low	High	Low	Low	Low
Mlekusch 2006	RCT	Low	Low	High	Low	Low	Low	Low
Narins 2008	RCT	Low	Unclear	Low	High	Low	Low	Low
Nguyen 2007	RCT	Unclear	Unclear	Low	High	Low	Low	Low
Politi 2011	RCT	Low	Unclear	Low	Low	Low	Low	Low
Sairaku 2011	RCT	Low	Low	Low	High	Low	Low	Low
Schwarz 2009	RCT	Unclear	Unclear	Low	Low	Low	Low	Low
Trabattoni 2011	RCT	Unclear	Unclear	Low	High	Low	Low	Low
Walker 2001	RCT	Unclear	Low	Low	High	Low	Low	Low
Waragai 2011	RCT	High	High	Low	High	Low	Low	Low
Zhu 2010	RCT	Unclear	Unclear	Low	High	Low	Unclear	Low

Table 3b. Risk of Bias for Cohort Studies: Newcastle-Ottawa scale

Study	Selection (maximum 4★)	Comparability (maximum 2★)	Outcome (maximum 3★)
Beekley 2008	★★★★	-	★★
Boulanger 2014	★★★★	-	★★★
Gerhardt 2011	★★★★	-	★★
Kauvar 2018	★★★★	-	★★
King 2015	★★★★	-	★
Kragh 2011 (J Emerg Med)	★★★★	-	★★
Kragh, Nam 2015 (Ann Emerg Med)	★★★★	★	★★
Kragh, Dubick 2015 (PEC)	★★★★	-	★★
Mucciarone 2006	★★	-	★
Neto 2015	★★★★	-	★★
Ode 2015	★★★★	-	★★
Passos 2014	★★★★	-	★★
Romanoff 1977	★★★★	-	★
Scerbo 2017	★★★★	★	★★
Schauer 2017	★★★★	-	★
Semler 1985	★★★★	-	★
Smith 2018	★★★★	★	★★
Sulzbach-Hoke 2010	★★★★	-	★★
Teixeira 2018	★★★★	★	★★
Tjiong 2012	★★★★	-	★