Meeting Proceedings

OTA ORTHOPAEDIC TRAUMA ASSOCIATION

OTA INTERNATIONAL THE OPEN ACCESS JOURNAL OF ORTHOPAEDIC TRAUMA

OPEN

The polytrauma patient: Current concepts and evolving care

Christopher Lee, MD[a], Todd E. Rasmussen, MD[b], Hans-Christoph Pape, MD[c], Joshua L. Gary, MD[d], James P. Stannard, MD[e], Justin M. Haller, MD[f]

Abstract

Principles of care in the polytraumatized patient have continued to evolve with advancements in technology. Although hemorrhage has remained a primary cause of morbidity and mortality in acute trauma, emerging strategies that can be applied pre-medical facility as well as in-hospital have continued to improve care. Exo-vascular modalities, including the use of devices to address torso hemorrhage and areas not amenable to traditional tourniquets, have revolutionized prehospital treatment. Endovascular advancements including the resuscitative endovascular balloon occlusion of the aorta (REBOA), have led to dramatic improvements in systolic blood pressure, although not without their own unique complications. Although novel treatment options have continued to emerge, so too have concepts regarding optimal time frames for intervention. Though prior care has focused on Injury Severity Score (ISS) as a marker to determine timing of intervention, current consensus contends that unnecessary delays in fracture care should be avoided, while respecting the complex physiology of certain patient groups that may remain at increased risk for complications. Thromboelastography (TEG) has been one technique that focuses on the unique pathophysiology of each patient, providing guidance for resuscitation in addition to providing information in recognizing the at-risk patient for venous thromboembolism. Negative pressure wound therapy (NPWT) has emerged as a therapeutic adjuvant for select trauma patients with significant soft tissue defects and open wounds. With significant advancements in medical technology and improved understanding of patient physiology, the optimal approach to the polytrauma patient continues to evolve.

Keywords: hemorrhage control, polytrauma patient, thromboelastography

1. Hemorrhage control

Severe trauma results in the death of over 5 million persons annually, and is projected to surpass 8 million annually by 2020.[1] Hemorrhage accounts for up to 35% of these traumatic injuries, second only to central nervous system injuries.[2] The lethality of various bleeding patterns was emphasized from the wars in Iraq and Afghanistan. In the study by Eastridge et al, 976 of the 4596 premedical treatment facility battlefield fatalities were classified as potentially survivable, with 90.9% of those deaths associated with hemorrhage. They concluded that strategies to mitigate hemorrhage must be implemented to combat casualties with potentially survivable injuries.[3] Furthermore, a 7-year analysis of vascular injury from the war in Afghanistan showed an 18% rate of vascular injury, more than 5 times that of past wars.[4]

The strategies to combat hemorrhage can largely be stratified into two approaches: (1) the exo-vascular, and (2) the endovascular. The use of tourniquets in preventing combat casualties was studied by Kragh Jr. et al,[5] who found that tourniquet-use was strongly associated with survival if shock was absent, and prehospital use was associated with fewer deaths than ED usage. Furthermore, they concluded that speed of successful application was vital and the morbidity risks minimal.[5] New external devices for hemorrhage control have been developed for military and civilian use. These include the Junctional Emergency Treatment Tool (JETT™, Greer, SC), an external device that wraps around the pelvis and can apply external pressure to the thigh and groin in regions where tourniquets cannot be placed. The Combat Ready Clamp (CRoC™, Harriburg, NC) is an additional device that can apply direct pressure over regions not amenable to tourniquet use, including the axilla and neck. In a study by Theodoridis et al, the JETT and CRoC were applied in 37 and 29 s, respectively, and were able to occlude arterial flow in a mean of 54 s.[6] Other devices such as the XSTAT (Wilsonville, OR) provide hemorrhage control through injecting rapidly expanding sponges into a wound cavity. Similarly, the development of ResQFOAM™ (Waltham, MA), an in-situ forming polymeric foam that rapidly expands through actively flowing blood and compresses the injury, has gained widespread interest. This material can be removed at the time of definitive surgical repair, and is currently undergoing a multicenter clinical trial (REVIVE).[7]

Source of Funding: Nil.

This study was deemed exempt from Institutional Review Board and Animal Use Committee Review.

There is no section to this effect. No IRB is needed as this is not a summary and review article of prior research and no patient information was utilized.

The authors have no funding and no conflicts of interest to disclose.

[a] Department of Orthopaedic Surgery, University of California – Los Angeles, Los Angeles, CA, [b] Department of General Surgery, F. Edward Hebert School of Medicine at the Uniformed Services University, Bethesda, MD, [c] Department of Trauma Surgery, University of Zurich, Zurich, Switzerland, [d] Department of Orthopaedic Surgery, University of Texas Health Science Center at Houston, Houston, TX, [e] Department of Orthopaedic Surgery, University of Missouri, Columbia, MO, [f] Department of Orthopaedic Surgery, University of Utah, Salt Lake City, UT

Corresponding author. Address: University of California Los Angeles, Department of Orthopaedic Surgery, 10833 Le Conte Ave, Los Angeles, California 90095. Tel: +310-825-7077; Fax: +310-825-1311;
E-mail address: Christopherlee@mednet.ucla.edu.

OTA (2021) e108

Published online 15 April 2021

http://dx.doi.org/10.1097/OI9.0000000000000108

Endovascular techniques were initially focused on age-related disease and not applied to the trauma setting until the 1970s.[8–10] In 2008, the first report on diagnostic and therapeutic endovascular capabilities in the management of acute wartime injury was published, demonstrating high success rates with minimal complications (3%).[11] As the clinical applicability of endovascular techniques evolved, the emergence of the resuscitative endovascular balloon occlusion of the aorta (REBOA) gained widespread use. First reported in the Korean War, this technique gained broader applicability in the early 2010s for torso hemorrhage.[12] In a systematic review by Morrison et al, pooled analysis demonstrated an increase in mean systolic pressure by 53 mm Hg following REBOA use.[13] However, several studies have reported episodes of device-related morbidity, femoral arterial complications, and balloon-related embolic events. Overall, the morbidity rate in the literature has been reported at 3.7%, with overall procedure-related arterial injury, amputation, and non-fatal embolic events rates at 2.9%, 0.8%, and 0.5%, respectively.[13] This remains an exciting technique that may continue to gain widespread utility with increased experience and advancing technology.

2. Timing of surgery

Fracture fixation strategies continue to evolve with an improved understanding of patient physiology. Prior to early staged management,[14] it was believed that with Injury Severity Scores (ISS) of 40 and above, early fixation of long bones would improve outcomes.[15] Additionally, it was unclear whether the method of definitive fixation or injury pattern played an important role (Table 1).[16–18] The literature appeared to suggest two options: (1) fix all major fractures acutely,[19] or (2) use external fixators in up to 40% of patients.[20] Currently, there is general consensus that unnecessary delays in fracture care should be avoided, while respecting that some patients may be at increased risk for complications. However, the vast majority of studies published after Scalea et al's recommendations[14] continue to respect ISS, with higher ISS patients selected for delayed definitive fixation. As previously discussed,[21] this trend seems to be independent from the conclusion made by the given author and the particular approach (Table 1). In a recent study, a group of improving borderline patients that had initial definitive surgeries developed complications attributable to the injuries, which underscores the need for a higher awareness of patient condition.[22]

Multiple attempts have been made to improve patient assessment before surgery. O'Toole et al. were among the first to describe the value of a defined resuscitation protocol. They suggested a defined endpoint of resuscitation (admission lactate level of 2.5 mmol/L),[23] similar to previous recommendations.[24] Vallier et al. were the first to utilize a database to develop a score.[25] Although multiple scores for perioperative assessment have been developed, only 4 are applicable prior to initial surgical care. The first includes 5 cascade systems (coagulopathy, acid-base changes, indicators of acute hemorrhage, body temperature, and soft tissue injuries) with different thresholds. This system was not substantiated by a database[23] and was later modified by a different group.[25] An additional score used three different parameters indicative of the acid–base status (pH <7.25, base excess <5.5, lactate >4 mmol/l).[26] The final assessment utilized a nationwide trauma registry whereby a deductive calculation revealed admission BP<90 mm Hg, NISS of >50 points, or mass transfusion (pRBC >15) to be predictive of complications. However, none of these scales were validated in patient groups outside of their respective studies, but have been recently evaluated in a separate database (n=3668, ISS >16). The Receiver Operating Characteristic (ROC) analysis revealed a difference in the prediction for early (e.g., death from hemorrhage) versus late complications (e.g., sepsis). For early complications, the combination of shock, coagulation, and soft tissue injuries (area under the curve [AUC] 0.77) was superior to acid–base changes alone (AUC 0.67; Fig. 1). Late complications were predicted reliably when a similar combination was used. Acid–base changes alone, however, had no predictive value. It appears that early clinical assessment may predict both early and late complications if the score uses multiple functional pathways.[27] Interestingly, general surgeons found a similar result, though this may be of limited use to orthopaedists as their study included penetrating trauma patients without fractures and head injured patients.[28]

These advances have led to a more flexible approach to fracture management (Table 2). The intraoperative reassessment in the

Table 1

Adaptation of patient selection according to the Injury Severity Score before and after 2000.

Author year	Mean ISS (points) Definitive surgery <24h ETC/EAC	Mean ISS (points) Definitive surgery>24 h DCO/SDS.	Comment
Johnson, 1985	49	53	subgroup analysis: patients with ISS >40
Bone,1989	31.8	31.3	randomized study
Charash, 1994	25/27	24/29	compares chest / no chest injury, ISS
Bosse,1997	n.a.	n.a.	compares nail vs plate
Bone,1998	n.a.	n.a.	compares nail vs plate
Carlson, 1998	n.a.	n.a.	compares reamed vs unreamed nailing
Scalea,2000	*16,8*	*26,8*	*Introduction of staged management concepts*
Nowotarsky, 2000	n.a.	n.a.	29 (range, 13 to 43)
Taeger 2005	30.4	37.3	ISS difference: 6.9 points
Pape,2007	23.3	29	ISS difference: 5.7 points
Morshed, 2009	27.2	32.3	ISS difference: 5.1 points
O'Toole, 2009	27.4	36.2	ISS difference:8.8 points
Nahm, 2011.	28.8	36.4	ISS difference:7.6 points
Steinhausen, 2014	23.5	31.1	ISS difference: 7.6 points
Dukan, 2019	n.a	n.a.	focus on Patients with ISS 16–25 (borderline)

DCO = damage control orthopaedics, EAC = early appropriate care, ETC = early total care, n.a. = not available, SDS = safe definitive orthopaedic surgery.

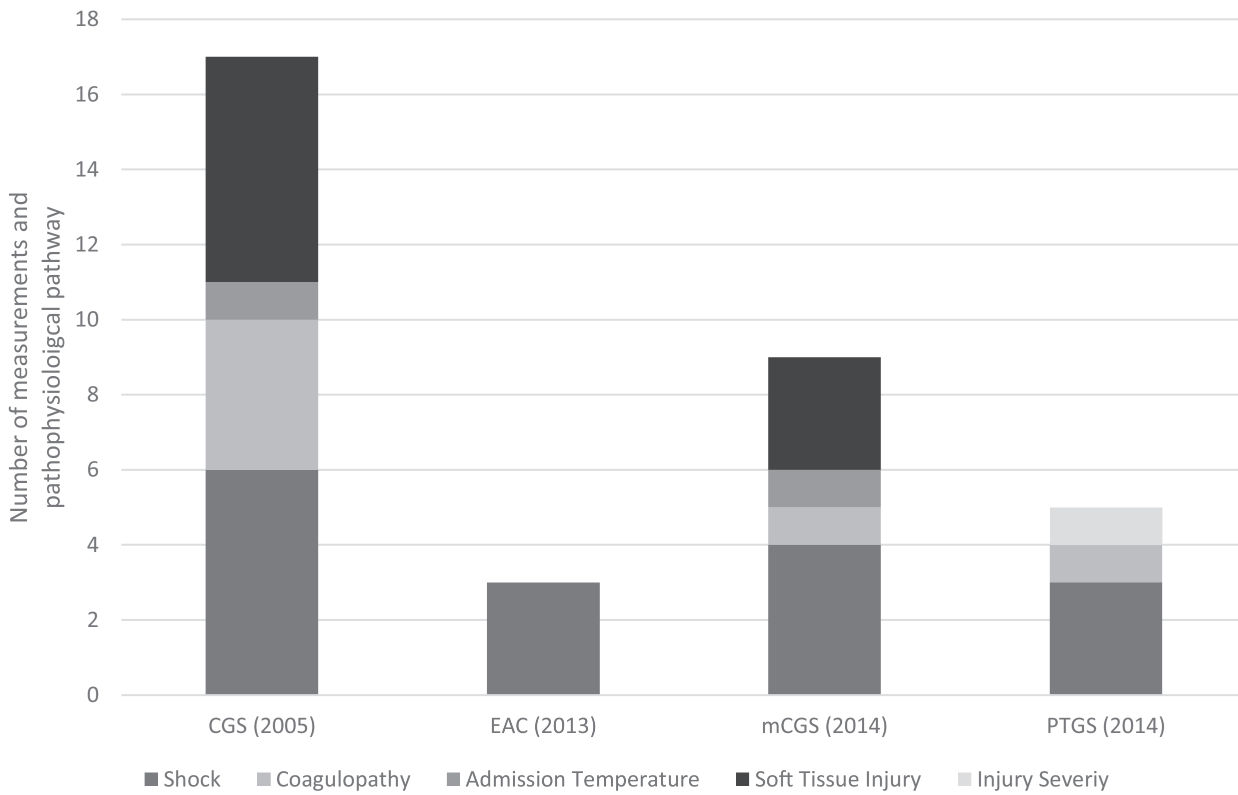

Figure 1. Comparison of different published scoring systems. The colors mark different pathophysiological pathways within the scoring systems. The size of the bar in each color marks the number of parameters that were listed for each given scoring system. CGS = Clinical Grading Scale, EAC = Early Appropriate Care, mCGS = modified Clinical Grading Scale, PTGS = Polytrauma Grading Scale.

presence of multiple fractures[29] has also been discussed and appears to be widely used. Although previous recommendations were strictly based on phases following certain time frames from injury ("window of opportunity" during day one surgery[30]), currently, the patient‘s response to resuscitation is assessed and included in the decision making and the selection of techniques for early fracture fixation.

3. Spectrum of coagulopathy in trauma: Acute trauma-induced coagulopathy vs. venous thromboembolism?

Traumatic injury is the leading cause of mortality worldwide and continues to increase with each passing decade.[31,32] Hemorrhagic shock and traumatic brain injury remain the most common killers for the traumatized patient,[33] but venous thromboembolic events (VTE) can result in death in hospital or subacutely after hospital discharge.[34,35] The spectrum of coagulopathy demands dynamic management from time of injury to full recovery as providers must address hypocoagulability in a bleeding patient and limit hypercoagulability in a resuscitated patient at risk for life-threatening VTE. Historically, the international normalized ratio (INR) measured hypocoagulability (>1.0) and hypercoagulability (<1.0) and platelet levels $>$ 100,000/μL indicated clotting could occur.

Thromboelastography (TEG) was introduced in the mid-20th century[36] and creates a graphical representation of the coagulation cascade including clot initiation, formation,

Table 2

A static (window or opportunity) to a dynamic surgical approach.

Static approach: Pre-2005			
Three surgical phases	Surgery (day-1) Life/limb saving proceedures Unstable pelvis Major extremity fractures	Intermediate (days 2–4) Avoid fixations	Reconstructive (days 5–15) Conversion to definitive fixation
Dynamic approach: 2020			
Three surgical phases	Surgery (day-1) Less time dependent constraints Completion of resuscitation Life/limb saving procedures Perform fixations according to physiological reserve	Intermediate (days 2–4) Physiology based decision-making Day-2 and thereafter Complete initial temporary fixations	Reconstructive (days 5–15)

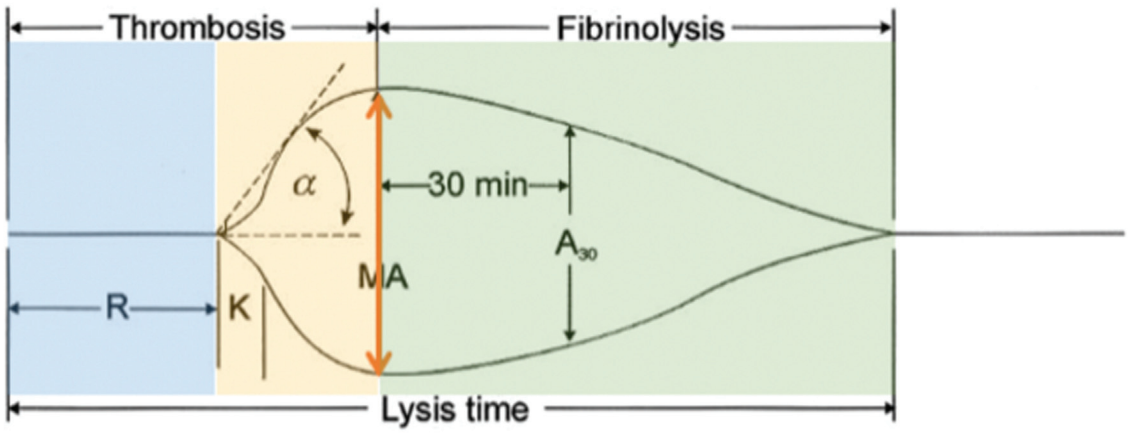

Figure 2. Sample TEG tracing. The R-value reflects clotting factor activation via initial fibrin formation. The K value is a time interval from the R until a predetermined level of clot firmness is reached and represented contributions of both fibrinogen and platelets. The Alpha Angle is generated by a tangential line from horizontal *x*-axis to the point when cross-linking occurs as the tracing begins to flatten out. A larger angle indicates larger clot formation as the angle reflects the amount of fibrinogen being converted to fibrin. The maximum amplitude simulates the platelet contribution to the final point of coagulation. The LY-30 is the percent of the clot that has lysed at 30 min.

strength, and eventual fibrinolysis (Fig. 2). Rapid thromboelastography (r-TEG) provides results within 20 min with only a small blood sample and allows for guided transfusion of blood products in the acute resuscitative phase. A series of almost 2000 trauma patients demonstrated that r-TEG could replace traditional laboratory tests including prothrombin time (PT), partial thromboplastin time (PTT), INR, platelet count, and fibrinogen levels.[37] A single-center, randomized, prospective trial of resuscitation guided by traditional lab values versus TEG-guided transfusion demonstrated 20% mortality in the TEG-guided group compared to 36% mortality by conventional lab tests; TEG-guided resuscitation resulted in less use of fresh frozen plasma (FFP) and platelets.[38] TEG-guided resuscitation for forty patients with severe pelvic injuries changed the ratio of packed red blood cells (PRBCs) to FFP to platelets from 1:1:1 to 2.5:1:2.8.[39]

As the patient transitions from the resuscitation phase into the treatment and recovery phases of trauma, focus generally shifts to VTE prevention and hypercoagulable states. Elevated TEG mA values greater than 65 on hospital admission have been associated with increased odds of VTE and the odds ratio further increases in a stepwise fashion when TEG mA values exceed 69 and 72.[40] For patients who underwent massive transfusion protocol on arrival in the prospective PROPPR trial, a 13% VTE rate was documented with early (<12 days) and late (>12 days) events. For early VTE, most occurred within 72 h of admission and increased risk was seen with transfusion of plasma or cryoprecipitate, development of sepsis, or associated pelvic or femur fracture. Late VTE was more common with increasing age and use of dialysis.[41] The effects of surgical treatments in the early phase after trauma may also impact coagulability as the intraoperative blood losses and perioperative repletion alter the coagulation factors. In a prospective study of patients with pelvic and acetabular fractures, TEG mA values increased at 24 h for patients undergoing closed reduction techniques compared to those patients who required open surgical approaches, with thought that increased surgical blood losses may protect from postoperative hypercoagulability.[42]

The knowledge and experience surrounding TEG now provides a rapid assessment of the patient's coagulable state. TEG has become a new standard to guide resuscitation and elevated mA values on admission have been associated with increased risk for VTE. Prospective studies evaluating serial TEG values beyond admission and in the resuscitative phase may provide more insight into the prediction of VTE events.

4. Negative pressure wound therapy in polytrauma patients

Negative pressure wound therapy (NPWT) has become a staple treatment in polytrauma patients with severe soft tissue injuries. Although the mechanism of action is not universally agreed upon, proposals include: (1) angiogenesis to promote wound healing; (2) the removal of excess interstitial fluid or edema; (3) mechanical stress to tissues enhancing tissue growth and expansion; and (4) increasing the tensile strength of wounds to prevent dehiscence. In addition to other studies analyzing skin blood flow, Timmers et al[43] reported marked increases in cutaneous blood flow to intact skin treated with NPWT. Suh et al performed a swine study that demonstrated that NPWT can be remarkably effective in dealing with dead space.[44] The data demonstrated a significant decrease in wound drainage and a significant increase in skin perfusion. They also demonstrated an increase in the tensile strength of the wound at both 7 and 21 days, which may explain the significant decrease in wound dehiscence following NPWT use in high risk fractures.[45]

Several studies have demonstrated that NPWT can decrease the infection rate following severe open fractures. In a prospective randomized trial of significant open fractures, Stannard et al demonstrated that NPWT for a short period of time and then obtaining closure or coverage of the wound showed significant improvements regarding infection rates. NPWT for long periods in an attempt to avoid the use of flap coverage did not show an improvement in infection rates.[46] Parrett et al demonstrated the infection rate was unchanged by the use of NPWT following Type IIIB tibia fractures. However, they documented a decrease in the use of free flaps from 42% to 11%.[47] An additional prospective randomized trial showed a decrease in infection when used as incisional NPWT following high risk fractures.[45] A recent meta-analysis demonstrated a decrease in infections, hospital stays, and amputations with NPWT use.[48] Grant-Freemantle et al demonstrated a decreased likelihood of deep infection and less flap failure in the NPWT group compared to conventional dressings for open fracture treatment.[49]

Although NPWT is promising, some studies have failed to demonstrate a clinical benefit. In a multicenter, randomized controlled trial of conflict-related extremity wounds, Alga et al[50] failed to demonstrate quicker wound closure or a reduction in wound complications with NPWT. In a multicenter, prospective randomized clinical trial of centers in the UK, the WOLLF trial failed to demonstrate a significantly better Disability Rating Index or fewer deep surgical site infections with NPWT as compared to standard dressings for open lower extremity fractures.[51] Similarly, a multicenter, randomized investigation comparing incisional NPWT with standard dressing for lower extremity fracture did not demonstrate fewer infections at 30 or 90 days postsurgery between groups.[52]

Polytrauma patients often have severe soft tissue injuries as well as many other challenges that make infection and wound healing challenges a major problem. NPWT has become a key weapon in the battle to overcome these. However, the literature does not currently support the routine use of NPWT or incisional NPWT, and NPWT should be appropriately utilized for patients with high-risk soft tissue injuries.

5. Conclusions

Polytraumatized patients represent a unique, challenging cohort of patients to treat. The introduction of novel external and internal modalities for hemorrhage control, in addition to the expanding use of NPWT has provided new therapeutic adjuvants. Additionally, evolving concepts on timing of intervention coupled with the use of methods including TEG to assess the unique pathophysiology of this cohort of patients have contributed to continued progress in the principles used to guide treatment.

References

1. Spahn D, Bouillon B, Cerny V, et al. Management of bleeding and coagulopathy following major trauma: an updated european guideline. Crit Care. 2013;17:R76.
2. Kauvar D, Lefering R, Wade C. Impact of hemorrhage on trauma outcome: an overview of epidemiology, clinical presentations, and therapeutic considerations. J Trauma. 2006;60 (suppl 6):S3–S11.
3. Eastbridge B, Mabry R, Seguin P, et al. Death on the battlefield (2001-2011): implications for the future of combat casualty care. J Trauma Acute Care Surg. 2012;73 (suppl 1):S431–S437.
4. Patel J, White J, White P, et al. A contemporary, 7-year analysis of vascular injury from the war in afghanistan. J Vasc Surg. 2018;68:1872–1879.
5. Kragh JJr, Walters T, Baer D, et al. Survival with emergency tourniquet use to stop bleeding in major limb trauma. Annals of Surgery. 2009;249:1–7.
6. Theodoridis C, Kafka K, Perez A, et al. Evaluation and testing of junctional tourniquets by special operation forces personnel: a comparison of the combat ready clamp and the junctional emergency treatment tool. J Spec Oper Med. 2016;16:44–50.
7. Chang J, Holloway B, Zamisch M, et al. ResQFOAM for the treatment of non-compressible hemorrhage on the front line. Mil Med. 2015; 180:932–933.
8. Ring E, Athansoulis C, Waltman A, et al. Arteriographic management of hemorrhage following pelvic fracture. Radiology. 1973;109:65–70.
9. Barlow B, Rottenberg R, Santulli T. Angiographic diagnosis and treatment of bleeding by selective embolization following pelvic fracture in children. J Pediatr Surg. 1975;10:939–942.
10. Chuang V, Reuter S. Selective arterial embolization for the control of traumatic splenic bleeding. Invest Radiol. 1975;10:18–24.
11. Rasmussten T, Clouse W, Peck M, et al. Development and implementation of endovascular capabilities in wartime. J Trauma. 2008;64:1169–1176.
12. Stannard A, Eliason J, Rasumussen T. Resuscitative endovascular balloon occlusion of the aorta (REBOA) as an adjunct for hemorrhagic shock. J Trauma. 2011;71:1869–1872.
13. Morrison J, Galgon R, Jansen J, et al. A systematic review of the use of resuscitative endovascular balloon occlusion of the aorta in the management of hemorrhagic shock. J Trauma. 2016;80:324–334.
14. Scalea T, Boswell S, Scott J, et al. External fixation as a bridge to intramedullary nailing for patients with multiple injuries and with femur fractures: damage control orthopaedics. J Trauma. 2000;48:613–623.
15. Johnson K, Cadambi A, Seibert B. Incidence of adult respiratory distress syndrome in patients with multiple musculoskeletal injuries: effect of early operative stabilization of fractures. J Trauma. 1985;25:375–381.
16. Carlson D, Rodman GJr, Kaehr D, et al. Femur fractures in chest-injured patients: is reaming contraindicated? J Orthop Trauma. 1998;12: 164–168.
17. Bosse M, MacKenzie E, Riemer B, et al. Adult respiratory distress syndrome, pneumonia, and mortality following thoracic injury and a femoral fracture treated either with intramedullary nailing with reaming or with a plate. A comparative study. J Bone Joint Surg Am. 1997; 79:799–809.
18. Charash W, Fabian T, Croce M. Delayed surgical fixation of femur fractures is a risk factor for pulmonary failure independent of thoracic trauma. J Trauma. 1994;37:667–672.
19. Bone L, Anders M, Rohrbacher B. Treatment of femoral fractures in the multiply injured patient with thoracic injury. Clin Orthop Relat Res. 1998;347:57–61.
20. Rixen D, Grass G, Sauerland S, et al. Polytrauma study group of the german trauma society evaluation of criteria for temporary external fixation in risk-adapted damage control orthopedic surgery of femur shaft fractures in multiple trauma patients: "evidence-based medicine" versus "reality" in the trauma registry of the German Trauma Society. J Trauma. 2005;59:1375–1394.
21. Pape H, Halvachizadeh S, Leenen L, et al. Timing of major fracture care in polytrauma patients - an update on principles, parameters and strategies for 2020. Injury. 2019;50:1656–1670.
22. Dukan R, Trousselier M, Briand S, et al. What are the differences in outcomes between simple and complicated FSF managed by early IMN? Arch Orthop Trauma Surg Published online. 2020;140:1037–1045.
23. O'Toole R, O'Brien M, Scalea T, et al. Resuscitation before stabilization of femoral fractures limits acute respiratory distress syndrome in patients with multiple traumatic injuries despite low use of damage control orthopedics. J Trauma. 2009;67:1013–1021.
24. Pape H, Giannoudis P, Krettek C, et al. Timing of fixation of major fractures in blunt polytrauma: role of conventional indicators in clinical decision making. J Orthop Trauma. 2005;19:551–562.
25. Nahm N, Moore T, Vallier H. Use of two grading systems in determining risks associated with timing of fracture fixation. J Trauma Acute Care Surg. 2014;77:268–279.
26. Vallier H, Wang X, Moore T, et al. Timing of orthopaedic surgery in multiple trauma patients: development of a protocol for early appropriate care. J Orthop Trauma. 2013;27:543–551.
27. Halvachizadeh S, Baradaran L, Cinelli P, et al. How to detect a polytrauma patient at risk of complications: a validation and database analysis of four published scales. PLoS One. 2020;15:e0228082.
28. Dezman Z, Comer A, Smith G, et al. Failure to clear elevated lactate predicts 24-hour mortality in trauma patients. J Trauma Acute Care Surg. 2015;79:580–585.
29. Pape HC, Giannoudis P, Krettek C. The timing of fracture treatment in polytrauma patients. Am J Surg. 2002;183:622–629.
30. Ertel W, Trentz O. Polytrauma and multi-organ failure syndrome. Definition–pathophysiology–therapy. Zentralbl Chir. 1994;119:159–167.
31. Injuries and violence: the facts. Geneva: World Health Organization; 2010.
32. Rhee P, Joseph B, Pandit V, et al. Increasing trauma deaths in the United States. Ann Surg. 2014;260:13–21.
33. Tisherman S, Schmicker R, Brasel K, et al. Detailed description of all deaths in both the shock and traumatic brain injury hypertonic saline trials of the resuscitation outcomes consortium. Ann Surg. 2015;261: 586–590.
34. Geerts W, Code K, Jay R, et al. A prospective study of venous thromboembolism after major trauma. NEJM. 1994;331: 1601–1606.

35. Godat L, Kobayashi L, Chang D, et al. Can we ever stop worrying about venous thromboembolism after trauma? J Trauma Acute Care Surg. 2015;78:475–481.
36. Hartert H. Blutgerinnung studien mit der thromboelastographie, einen neuen untersuchingsverfahren [Translation: Blood coagulation studies with thrombelastography, a new investigation procedure]. Klinische Wochenschrift. 1948;26:577–583.
37. Holcomb J, Minei K, Scerbo M, et al. Admission rapid thrombelastography can replace conventional coagulation tests in the emergency department: experience with 1974 consecutive trauma patients. Ann Surg. 2012;256:476–486.
38. Gonzalez E, Moore E, Moore H, et al. Goal-directed hemostatic resuscitation of trauma-induced coagulopathy: a pragmatic randomized clinical trial comparing a viscoelastic assay to conventional coagulation assays. Ann Surg. 2016;263:1051–1059.
39. Mamczak C, Maloney M, Fritz B, et al. Thromboelastography in orthopaedic trauma acute pelvic fracture resuscitation: a descriptive pilot study. J Orthop Trauma. 2016;30:299–305.
40. Gary J, Schneider P, Galpin M, et al. Can thrombelastography predict venous thromboembolic events in patients with severe extremity trauma? J Orthop Trauma. 2016;30:294–298.
41. Myers S, Brown J, Leeper C, et al. Early versus late venous thromboembolism: a secondary analysis of data from the PROPPR trial. Surgery. 2019;166:416–422.
42. Byrd Z, Davis E, Schneider P, et al. Does reduction technique for pelvic and acetabular injuries associated with changes in trauma-induced coagulopathy? A prospective cohort study [abstract]. Presented at the Annual Meeting of the Orthopaedic Trauma Association; 2017 Oct 11-14; Vancouver, Canada.
43. Timmers M, Cessie S, Banwell P, et al. The effects of varying degrees of pressure delivered by negative-pressure wound therapy on skin perfusion. Ann Plast Surg. 2005;55:665–671.
44. Suh H, Lee A, Park E, et al. Negative pressure wound therapy on closed surgical wounds with dead space: animal study using a swine model. Ann Plast Surg. 2016;76:717–722.
45. Stannard J, Volgas D, McGwin GIII, et al. Incisional negative pressure wound therapy following high-risk lower extremity fractures. J Orthop Trauma. 2012;26:37–42.
46. Stannard J, Volgas D, Stewart R, et al. Negative pressure wound therapy (NPWT) after severe open fractures: a prospective randomized study. J Orthop Trauma. 2009;23:552–557.
47. Parrett B, Matros E, Pribaz J, et al. Lower extremity trauma: trends in the management of soft-tissue reconstruction of open tibia-fibula fractures. Plas Reconst Surg. 2006;117:1315–1322.
48. Liu X, Zhang H, Cen S, et al. Negative pressure wound therapy versus conventional wound dressings in treatment of open fractures: a systematic review and meta-analysis. Int J Surg. 2018;53:72–79.
49. Grant-Freemantle M, Ryan E, Flynn S, et al. The effectiveness of negative pressure wound therapy versus conventional dressing in the treatment of open fractures: a systematic review and meta-analysis. J Orthop Trauma. 2020;34:223–230.
50. Älgå A, Haweizy R, Bashaireh K, et al. Negative pressure wound therapy versus standard treatment in patients with acute conflict-related extremity wounds: a pragmatic, multisite, randomised controlled trial. Lancet Glob Health. 2020;8:E423–E429.
51. Costa M, Achten J, Bruce J, et al. Effect of negative pressure wound therapy vs standard wound management on 12-month disability among adults with severe open fracture of the lower limb: the WOLLF randomized clinical trial. JAMA. 2018;319:2280–2288.
52. Costa M, Achten J, Knight R, et al. Effect of incisional negative pressure wound therapy vs standard wound dressing on deep surgical site infection after surgery for lower limb fractures aAssociated with major trauma: the WHIST randomized clinical trial. JAMA. 2020; 323:519–526.