Airway and ventilation management strategies for hemorrhagic shock. To tube, or not to tube, that is the question!

Anthony J. Hudson, MA, Geir Strandenes, MD, Christopher K. Bjerkvig, MD, Marius Svanevik, MD, *and* **Elon Glassberg, MD, MHA**, *Devon, UK*

ABSTRACT: Many standard trauma management guidelines advocate the early use of endotracheal intubation (ETI) and positive pressure ventilation as key treatment interventions in hemorrhagic shock. The evidence for using these airway and ventilation strategies to manage a circulation problem is unclear. The potentially harmful effects of drug-assisted intubation and positive pressure ventilation include reduced cardiac output, apnea, hypoxia, hypocapnea (due to inadvertent hyperventilation), and unnecessarily prolonged on-scene times. Conversely, the beneficial effects of spontaneous negative pressure ventilation on cardiac output are well described. Few studies, however, have attempted to explore the potential advantages of a strategy of delayed intubation and ventilation (together with a policy of aggressive volume replacement) in shocked trauma patients. Given the lack of evidence, the decision making around how, when, and where to subject shocked trauma patients to intubation and positive pressure ventilation remains complex. If providers choose to delay intubation, they must have the appropriate skills to safely manage the airway and recognize the need for subsequent intervention. If they decide to perform intubation and positive pressure ventilation, they must understand the potential risks and how best to minimize them. We suggest that for patients with hemorrhagic shock who do not have a compromised airway and who are able to maintain adequate oxygen saturation (or mentation if monitoring is unreliable), a strategy of delayed intubation should be strongly encouraged. (*J Trauma Acute Care Surg.* 2018;84: S77–S82. Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved.)

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The presurgical management of life-threatening hemorrhage is one of the greatest challenges in the treatment of patients with traumatic injuries. During the initial assessment, providers must identify and treat time-critical life or limb-threatening injuries in order of priority. A structured approach is widely used in which airway management comes second only to the management of visible catastrophic hemorrhage. At this stage of resuscitation care, many providers resort to the "known": intubation and positive pressure ventilation to secure the airway and manage ventilation of patients in hemorrhagic shock. This would seem to be treating a "C" (circulatory) problem with an "A" (airway) solution. We describe the reasoning behind using these advanced airway and ventilation management techniques to treat patients with hemorrhagic shock and discuss whether these interventions may have an adverse impact on patient outcomes.

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From the Department of Emergency Medicine (A.J.H.), Royal Devon & Exeter NHS Foundation Trust, Exeter, Devon, UK; Department of War Surgery and Emergency Medicine (G.S.), Norwegian Armed Forces Medical Services; Department of Immunology and Transfusion Medicine (G.S.), Haukeland University Hospital, Bergen, Norway; Norwegian Special Operations Commando (C.K.B.), Rena, Norway; Norwegian Naval Special Operations Commando, Norwegian Armed Forces (M.S.), Bergen, Norway; Department of Anaesthesia and Intensive care (C.K.B.), Haukeland University Hospital, Bergen, Norway; Department of Gastrointestinal Surgery (M.S.), Vestfold Hospital Trust, Tønsberg, Norway; Israel Defense Forces Medical Corps (E.G.), Ramat Gan, Israel; Faculty of Medicine in the Galilee (E.G.), Bar-Ilan University, Safed, Israel; and Department of Surgery (E.G.), Uniformed Services, University of the Health Sciences, Bethesda, Maryland.

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Address for reprints: Tony Hudson, MA, MBBS, FRCPEd, FRCEM, Emergency Department, Royal Devon & Exeter NHS Foundation Trust, Barrack Road, Exeter EX2 5DW, Devon, UK; email: anthony.hudson1@nhs.net.

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PRESURGICAL INTUBATION AND VENTILATION IN HEMORRHAGIC SHOCK

Hemorrhage is known to be the greatest single cause of potentially preventable death on the battlefield.[1] The increased awareness of the role of hemorrhage control in battlefield trauma management has had a profound effect on doctrine, training, and equipment with consequent impact on survival rates.[2] Providers are taught to focus on the rapid control of hemorrhage and to manage the airway by conventional means, including securing a definitive airway by surgical techniques (cricothyroidotomy) or ETI.[3,4] Many treatment guidelines suggest that the placement of an endotracheal tube by rapid intubation is a key component of the management of hemorrhagic shock in trauma.[5] The perils of using anesthesia in shocked trauma patients have been known for many years, with one author even suggesting in 1943 that in war surgery, "intravenous anaesthesia is also an ideal method of euthanasia".[6] While the accuracy of Halford's data has subsequently been questioned, it does highlight that there have been concerns for many years about the risks of using drug-assisted intubation and positive pressure ventilation in patients with hemorrhagic shock.[7]

Why Do We Want to Intubate Patients?

In patients with direct airway injury or obstruction, there is clearly an urgent need to open and maintain the airway. This can safely be provided in most cases using simple airway opening maneuvers and adjuncts. When these strategies fail, or there is significant airway injury, many civilian emergency medicine service (EMS) providers resort to drug-assisted intubation to secure the airway. In the military environment, there is good evidence that prehospital providers have high success rates with securing a definitive airway using surgical techniques at this stage of airway care.[8–10] When, however, advanced providers and resources are available far forward (usually on evacuation platforms or at Role 2 hospital facilities), then patients may also undergo drug-assisted ETI for a number of other indications. One of the most common reasons to perform intubation is the theoretical concern that patients with a reduced level of consciousness may be unable to protect their own airway. The evidence behind the widely accepted standard that patients with a Glasgow Coma Score (GCS)of 8 or less must be intubated is poor.[11] Emergency airway interventions are also routinely performed in the prehospital arena for significant breathing problems (respiratory distress), circulation problems (hemorrhagic shock), disability problems (low GCS or combative, agitated head-injured patients), and other reasons such as pain management (multiple distressing injuries and amputations). Reviews of recent practice describe the many perceived indications to perform intubation but not the evidence behind them.[12,13] Whatever the indications, the potential negative impact on a patient with hemorrhagic shock must not be forgotten.

The decision when to undertake this potentially dangerous intervention in these challenging and sometimes hostile environments requires experience, skill, and judgment; and there is evidence that outcomes are influenced by the level of experience of the provider.[14] As in many other areas of medicine, it is maybe harder to decide when not to perform an intervention than it is to actually undertake that intervention. Deciding not to perform intubation and ventilation in the presence of hemorrhagic shock requires the associated skills to safely manage such patients by using alternative strategies. These may include management of agitated patients with the safe use of sedation agents such as ketamine, or even placement of surgical airways to allow spontaneous ventilation (using local anesthetic techniques in conscious patients with significant airway injury).

In shocked trauma patients, ETI represents an attempt to maintain a patent airway and maximize the tissue delivery of oxygen to the tissues. Below a critical level of oxygen delivery, an incurred oxygen debt begins to accumulate with associated rise in lactate and eventual irreversible cellular damage.[15] Fick's equation (Fig. 1) demonstrates that oxygen delivery is directly proportional to hemoglobin concentration, oxygen saturation, and cardiac output; and hence, all efforts must be made to maximize these values during resuscitation. This is especially true when delays in definitive surgical control of hemorrhage are involved. Indeed, hemoglobin must be retained and losses replaced. Intubation and positive pressure ventilation represent an attempt to maximize oxygen saturation but at what cost to cardiac output and hence oxygen delivery?

Adverse Effects of Drug-Assisted Intubation and Positive Pressure Ventilation

Drug-assisted intubation and subsequent positive pressure ventilation carry many well-described risks, especially to the patient in shock. In a retrospective database review of 444 trauma patients undergoing intubation on arrival in a Canadian tertiary trauma center over a 15-year period, 161 patients (36.3%) experienced postintubation hypotension, suggesting that this procedure is not without risk of impact on cardiac output.[16] Another study of 2,403 patients who underwent emergency tracheal intubation in the emergency department found that 41 patients (1.7%) had a postintubation cardiac arrest within 10 minutes of the procedure. Systolic hypotension before intubation, defined as a systolic blood pressure of 90 mm Hg or less, was independently associated with postintubation cardiac arrest (odds ratio, 3.67 [95% confidence interval, 1.58–8.55], $p = 0.01$).[17] This highlights the importance of volume resuscitation for these patients. It also emphasizes the fact that airway interventions and positive pressure ventilation should not be the standard response for these patients, but instead treating the shock state with blood product replacement and hemostasis.

There is a wide choice of sedating agents used to assist performing presurgical ETI, but for patients with significant traumatic injury, many providers opt for ketamine given its safety profile and proven efficacy in remote and austere settings.[18] Etomidate is also widely used in the United States, as it has a favorable hemodynamic profile in shocked patients, but has been withdrawn from use in many countries owing to concerns about adrenal suppression. While many other sedating agents are available, almost all carry a significant risk of provoking hypotension in the presence of hemorrhagic shock.[19] Although ketamine is widely used as the first-line sedation agent for shocked patients, there have been case reports of deaths with its use.[20] In vitro, ketamine has a negatively inotropic effect; but in vivo, this is thought to be outweighed by endogenous catecholamine release.[21,22] It is postulated that the deaths associated with ketamine administration for induction in these patients may have occurred due to pre-existing catecholamine depletion, although the adverse effects of positive pressure ventilation may have also contributed. One study of the potential hypotensive effects of ketamine in patients undergoing prehospital rapid sequence intubation (RSI) demonstrated that while only 2% of patients with a low shock index (<0.9) became hypotensive following ketamine administration, a far larger proportion of patients (26%) with a high shock index (≥0.9) developed hypotension.[23]

Neuromuscular blocking agents are routinely given as part of the regime of agents for RSI, and these also carry significant

$$DO_2 = 1.34 \times Hb \times SaO_2 \times CO$$

DO_2 (oxygen delivery), Hb (haemoglobin concentration), SaO_2 (oxygen saturation), CO (cardiac output)

Figure 1. Fick's Equation.

risks in patients with hemorrhagic shock. Paralysis renders the patient apneic, which will cause the partial pressure of carbon dioxide (Pco_2) to rise until the patient is ventilated. The resulting respiratory acidosis will exacerbate any existing metabolic acidosis due to the hemorrhagic shock state. Furthermore, any patient who becomes apneic is at immediate risk of hypoxemia until ventilation is re-established. Studies have shown that intubation and repeated laryngoscopy attempts can carry significant risk of hypoxemia and cardiac arrest.[24,25]

Positive pressure ventilation has long been known to decrease cardiac output.[26] Raised intrathoracic pressure during inspiration associated with the positive pressure of ventilation reduces the already compromised venous return, right ventricular output, and pulmonary blood flow and hence reduces cardiac output.[27] In expiration, the intrathoracic pressure decreases toward zero, allowing an increase of venous return unless positive end expiratory pressure is applied. Although this is well described, the impact of positive pressure ventilation on cardiac output in shocked trauma patients is perhaps not always fully appreciated when providers are striving to manage time critical injuries in distressed, multiply injured patients. Drug-assisted intubation and then positive pressure ventilation represent a rapid and decisive intervention that seemingly brings order to a chaotic situation but in doing so may cause significant harm.

Hyperventilation by EMS providers following drug-assisted intubation is a further potential threat to patients with hemorrhagic shock, particularly in the presence of associated traumatic brain injury (TBI). Hyperventilation reduces Pco_2, which in turn causes cerebral vasoconstriction, hence reducing cerebral perfusion. Furthermore, there is evidence from animal studies that in the presence of hemorrhagic shock, hyperventilation is not only unnecessary but also contributes to a reduction in cardiac output.[28]

A further, often unrecognized complication of intubation in the presence of hemorrhagic shock is the time that it takes to prepare for and deliver this intervention. Patients with life-threatening hemorrhage that has not been successfully managed by direct compression have a time critical need for damage control surgery (or other interventions) that require urgent transport to an appropriate medical treatment facility. Intubation may delay that process.

These potentially harmful effects of drug-assisted intubation and positive pressure ventilation are summarized in Table 1.

OUTCOMES

We are not aware of any published randomized controlled trials comparing intubation against conservative airway management strategies for the presurgical management of trauma patients with hemorrhagic shock. Available evidence is based largely on retrospective database reviews that seek to review the recorded outcomes in patients who received intubation and compare with those patients who did not receive the intervention (or extrapolation from other scenarios and medical conditions). Some studies include patients who underwent ETI without the use of drugs, while others include drug-assisted or RSI. One retrospective database review compared trauma patients who underwent ETI before arrival in hospital with those who were intubated upon arrival in the emergency department (ED).[29] Patients with a GCS of less than 8 and an injury severity score of greater than 16 were included, these being considered as surrogates for inability to maintain an airway or being more likely to be hypovolemic. Patients who were intubated in the field were reported to be more likely to be hypotensive upon arrival in ED and had worse survival, but the cause of this was unclear. Prehospital vital signs were not recorded. While the authors concluded that this showed an association between prehospital ETI and poor outcomes, it is clear that this association may be due to the fundamental differences between the two population groups compared. Patients who can be intubated in the field by paramedics without the use of drugs were more likely to be more severely injured and hence have worse outcomes. A recent systematic review and meta-analysis comparing mortality rates of adult trauma patients undergoing prehospital ETI to those undergoing ED ETI showed higher mortality rates after prehospital ETI (although the authors noted that the overall quality of evidence is very low).[30] A further retrospective database review has also suggested an association between field intubation and higher mortality specifically for trauma patients with hemorrhagic shock.[31] In this study, the authors identified 552 adult trauma patients who received massive transfusion on arrival at hospital. Sixty-three of these patients (11%) underwent field intubation before arrival in hospital, with the remaining 489 (89%) not undergoing intubation before hospital. The group that underwent field intubation had lower GCS, lower median systolic blood pressure, and higher median injury severity score. While it would seem that the two groups were fundamentally different, the authors attempted to control for this with the use of multivariate regression analysis and concluded that field intubation may be associated with higher mortality in this group of patients with hemorrhagic shock requiring massive transfusion. Critics suggest, however, that the statistical methods used are unlikely to control for the significant differences between the two groups and that from these data, it is impossible to attribute the higher mortality to the effect of intubation and positive pressure ventilation alone.[32]

These findings suggest that it may be impossible in retrospective studies to decide whether poor outcomes are due to the intubation and ventilation process itself or the injuries for which the providers decided that the patient required this intervention. Suggestion of harm is found in one review of moderately injured patients who underwent intubation but who at subsequent review were felt not to have required that intervention.[33] In this retrospective trauma registry review, patients who were intubated but who were only moderately injured (GCS ≥ 13, maximum Abbreviated Injury Scale score for any one region ≤3, no packed cells given in ED) were matched with similarly injured patients who were not intubated. The results demonstrated that the intubated

TABLE 1. Potential Pitfalls of Drug-Assisted Intubation and Positive Pressure Ventilation in Hemorrhagic Shock

Intervention	Potential Adverse Effect
Neuromuscular blocking agents	Apnea, hypoxemia, respiratory acidosis
Sedation agents	Hypotension, respiratory depression, hypoxemia
Intubation attempts	Hypoxemia, unrecognized oesophageal placement of endotracheal tube
Positive pressure ventilation	Reduced cardiac output, hypothermia,
Inadvertent hyperventilation	Cerebral vasoconstriction

patients spent longer at scene, had more volume replacement, more coagulation derangement and lower hemoglobin concentrations than the nonintubated patients. With all its limitations, this may be one of the few publications that address the negative effect of unnecessary intubations.

Animal studies currently provide the only available prospective evidence for comparison of airway and ventilation management strategies in hemorrhagic shock. One study used a swine model of exsanguinating hemorrhage to explore the potential benefits of spontaneous ventilation compared with positive pressure ventilation in the presence of hemorrhagic shock.[34] This study found that spontaneously ventilating subjects maintained cardiac output and body temperature at higher levels than those receiving positive pressure ventilation. Such studies would seem to suggest that in hemorrhagic shock, a strategy of conservative airway management that allows spontaneous ventilation might protect patients from the risks of impaired cardiac output associated with positive pressure ventilation, provided that the airway is patent and the patient is not managed with any sedation agents that cause respiratory depression.

There may also be a potential beneficial role of negative pressure created by inspiratory resistance. One study of human volunteers subjected to an artificial shock state demonstrated that the use of an impedance threshold device in spontaneously breathing subjects delayed the onset of cardiovascular collapse.[35] This would seem to support that a strategy of deferring intubation and positive pressure ventilation in hemorrhagic shock states may have a protective effect on cardiac output.

Head Injury

The initial care of patients with both hemorrhagic shock and head injury presents particular challenges in the presurgical environment. It may be impossible to discern whether a patient has a low GCS as a result of direct brain injury or as a consequence of hemorrhagic shock. Hence, strategies to manage the critically injured patient with hemorrhagic shock and a reduced GCS must ensure the optimum management of any potential associated brain injury. Any advanced airway interventions must have a minimal effect on cerebral perfusion and intracranial pressure and must not cause unnecessary delays in the transport of the patient. The use of drug-assisted intubation and positive pressure ventilation has significant potential to do harm in the presence of TBI. It has been shown that a single excursion of blood pressure below 90 mm Hg systolic is independently associated with a more than doubling of mortality in TBI with repeated episodes associated with an up to eightfold increase in mortality.[36] A single episode of oxygen saturation below 90% was also reported to be independently associated with at least doubling of mortality in TBI, while the combination of both hypoxia and hypotension has been described as associated with a sixfold increase in mortality in TBI.[37,38] Endotracheal intubation can be extremely challenging in the prehospital environment; and in this stressful situation, EMS providers have frequently been observed to hyperventilate patients following intubation.[39] This is known to cause hypocapnea, which in turn produces potentially harmful vasoconstriction in the brain. Hyperventilation in patients with TBI following RSI has been shown to more than double mortality.[40] However, for patients who do have severe TBI, there is some evidence that prehospital RSI may be associated with improved neurological outcome.[41]

DISCUSSION

While the use of presurgical intubation and positive pressure ventilation in the management of patients with hemorrhagic shock is widespread, the evidence behind the use of these airway and breathing interventions to address a circulation problem is unclear. Furthermore, the adverse effects of intubation, particularly in patients with hemorrhagic shock, have a sound physiological basis and are well described. Hence, although there is often certainty that a given patient with hemorrhagic shock will need to be intubated to achieve surgical control of hemorrhage, the timing of this procedure is unclear. An important analogy is the deliberate delay in the induction of anesthesia for the patient with a leaking abdominal aortic aneurysm until appropriate hemostatic resources are available. Although few vascular anesthetists would ever contemplate initiating positive pressure ventilation in the prehospital setting or even the ED for a shocked patient with a leaking abdominal aortic aneurysm, trauma patients with similar hemodynamic compromise are often subjected to intubation and positive pressure ventilation in these settings, with occasionally lethal results.[42] The timing and location of intubation for all patients with hemorrhagic shock must be carefully considered. Delivering rapid intubation skills into the prehospital arena, where most preventable deaths occur, requires significant investment in training, equipment, and skills to manage the very few patients who may succumb to airway obstruction and who are already often managed successfully by relatively inexperienced providers using basic airway techniques and surgical cricothyroidotomy. It must not be forgotten that most preventable trauma deaths occur owing to hemorrhage and that damage control resuscitation teams must put the management of hemorrhage at sufficiently high priority that complex, time-consuming, and potentially dangerous solutions to airway problems are not used when far simpler strategies are likely to be effective. If indicated, intubation under such circumstances should be performed in conjunction with aggressive blood product administration to mitigate the considerable risks of the procedure.

Thus, although decision making is complex, providers must know when not to deploy this skill as much as when they should use it. The possible time delays that this intervention may cause must be acknowledged. Advanced providers must be trained not only in the techniques of intubation and positive pressure ventilation but also in the other measures that may allow safe deferral of these interventions. The importance of simple airway management techniques must be emphasized and strategies taught to avoid premature use of neuromuscular blocking agents and positive pressure ventilation. Providers must be taught the clinical skills and provided with appropriate equipment (pulse oximetry and capnography) to monitor nonintubated patients and facilitate early identification of airway or ventilatory failure. Even when advanced providers and equipment are available either in the field or on arrival in a medical treatment facility, these providers must then be fully aware of the hazards of drug-assisted intubation and positive pressure ventilation, particularly for patients with hemorrhagic shock. Knowledge of the hypotensive effects of induction agents, risks of respiratory acidosis due to apnea during laryngoscopy, dangers of multiple intubation attempts, impairment of cardiac output resulting from positive pressure ventilation, and effects of hyperventilation, particularly in patients who may have TBI, must be emphasized. Providers must be prepared to consider other management strategies that minimize these risks, including rapid evacuation of the casualty (with or without using simple airway management techniques) while monitoring the casualty and the oxygen saturation.

CONCLUSION

There is no good quality prospective evidence to support the use of prehospital intubation for the management of patients with hemorrhagic shock. Available evidence even includes evidence of harm for such patients who were intubated and for those who did not need ETI (or when the intervention could have been postponed until the arrival to the hospital) but received this treatment. Similarly, there is a paucity of evidence of the effects of not intubating patients with severe hemorrhagic shock who traditionally have been considered to warrant this intervention. Animal studies confirm the physiologic advantages of not performing positive pressure ventilation in the presence of hemorrhagic shock and, where feasible, spontaneous ventilation should be considered to maintain cardiac output and hence maximize tissue oxygen delivery and negative pressure ventilation. This will require adaptation of the clinical practice guidelines, education, and training, but mostly requires appreciation of the substantial detrimental effects that intubation and positive pressure ventilation have in bleeding casualties. Whenever possible, spontaneous ventilation should be preferred over drug-assisted intubation and positive pressure ventilation. We suggest that for patients with hemorrhagic shock who do not have a significant airway injury and who are able to maintain adequate oxygen saturation (or mentation, in absence of reliable monitoring), a strategy of delayed intubation should be strongly encouraged.

AUTHORSHIP

G.S. suggested the review. A.J.H. undertook the initial literature review and wrote the first draft of the manuscript. E.G. created the initial outline, assisted with the first draft, and oversaw subsequent critical revisions of the manuscript. All authors contributed equally to further literature review, critical revisions, and writing of the final manuscript.

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DISCLOSURE

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REFERENCES

1. Eastridge BJ, Mabry RL, Seguin P, Cantrell J, Tops T, Uribe P, Mallett O, Zubko T, Oetjen-Gerdes L, Rasmussen TE, et al. Death on the battlefield (2001–2011): implications for the future of combat casualty care. *J Trauma Acute Care Surg*. 2012;73(6 Suppl 5):S431–S437.
2. Kotwal RS, Montgomery HR, Kotwal BM, Champion HR, Butler FK Jr, Mabry RL, Cain JS, Blackbourne LH, Mechler KK, Holcomb JB. Eliminating preventable death on the battlefield. *Arch Surg*. 2011;146(12):1350–1358.
3. Care CoTCC. Tactical Combat Casualty Care Guidelines for Medical Personnel. Available at: http://www.cotccc.com/. [Available from: http://www.cotccc.com/. Accessed October 1, 2017.
4. ATLS Subcommittee; American College of Surgeons' Committee on Trauma; International ATLS working group. Advanced trauma life support (ATLS®): the ninth edition. *J Trauma Acute Care Surg*. 2013;74(5):1363–1366.
5. Rossaint R, Bouillon B, Cerny V, Coats TJ, Duranteau J, Fernandez-Mondejar E, Filipescu D, Hunt BJ, Komadina R, Nardi G, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition. *Crit Care*. 2016;20:100.
6. Halford FJ. A critique of intravenous anesthesia in war surgery. *Anesthesiology*. 1943;4:67–69.
7. Bennetts FE. Thiopentone anaesthesia at Pearl Harbor. *Br J Anaesth*. 1995; 75(3):366–368.
8. Barnard EB, Ervin AT, Mabry RL, Bebarta VS. Prehospital and en route cricothyrotomy performed in the combat setting: a prospective, multicenter, observational study. *J Spec Oper Med*. 2014;14(4):35–39.
9. Katzenell U, Lipsky AM, Abramovich A, Huberman D, Sergeev I, Deckel A, Kreiss Y, Glassberg E. Prehospital intubation success rates among Israel Defense Forces providers: epidemiologic analysis and effect on doctrine. *J Trauma Acute Care Surg*. 2013;75(2 Suppl 2):S178–S183.
10. Kyle T, le Clerc S, Thomas A, Greaves I, Whittaker V, Smith JE. The success of battlefield surgical airway insertion in severely injured military patients: a UK perspective. *J R Army Med Corps*. 2016;162(6):460–464.
11. Mayglothling J, Duane TM, Gibbs M, McCunn M, Legome E, Eastman AL, Whelan J, Shah KH. Eastern Association for the Surgery of Trauma. Emergency tracheal intubation immediately following traumatic injury: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg*. 2012;73(5 Suppl 4):S333–S340.
12. Adams BD, Cuniowski PA, Muck A, De Lorenzo RA. Registry of emergency airways arriving at combat hospitals. *J Trauma*. 2008;64(6):1548–1554.
13. Haldane AG. Advanced airway management—a medical emergency response team perspective. *J R Army Med Corps*. 2010;156(3):159–161.
14. Bossers SM, Schwarte LA, Loer SA, Twisk JW, Boer C, Schober P. Experience in prehospital endotracheal intubation significantly influences mortality of patients with severe traumatic brain injury: a systematic review and meta-analysis. *PLoS One*. 2015;10(10):e0141034.
15. Barbee RW, Reynolds PS, Ward KR. Assessing shock resuscitation strategies by oxygen debt repayment. *Shock*. 2010;33(2):113–122.
16. Green RS, Butler MB, Erdogan M. Increased mortality in trauma patients who develop postintubation hypotension. *J Trauma Acute Care Surg*. 2017; 83:569–574.
17. Kim WY, Kwak MK, Ko BS, Yoon JC, Sohn CH, Lim KS, Andersen LW, Donnino MW. Factors associated with the occurrence of cardiac arrest after emergency tracheal intubation in the emergency department. *PLoS One*. 2014;9(11):e112779.
18. Morris C, Perris A, Klein J, Mahoney P. Anaesthesia in haemodynamically compromised emergency patients: does ketamine represent the best choice of induction agent? *Anaesthesia*. 2009;64(5):532–539.
19. Shafer SL. Shock values. *Anesthesiology*. 2004;101(3):567–568.
20. Dewhirst E, Frazier WJ, Leder M, Fraser DD, Tobias JD. Cardiac arrest following ketamine administration for rapid sequence intubation. *J Intensive Care Med*. 2013;28(6):375–379.
21. Gelissen HP, Epema AH, Henning RH, Krijnen HJ, Hennis PJ, den Hertog A. Inotropic effects of propofol, thiopental, midazolam, etomidate, and ketamine on isolated human atrial muscle. *Anesthesiology*. 1996;84(2):397–403.
22. Chernow B, Lake CR, Cruess D, Coyle J, Hughes P, Balestrieri F, Casey L, Rainey TG, Fletcher JR. Plasma, urine, and CSF catecholamine concentrations during and after ketamine anesthesia. *Crit Care Med*. 1982;10(9):600–603.
23. Miller M, Kruit N, Heldreich C, Ware S, Habig K, Reid C, Burns B. Hemodynamic response after rapid sequence induction with ketamine in out-of-hospital patients at risk of shock as defined by the shock index. *Ann Emerg Med*. 2016;68(2):181–188.e2.
24. Dunford JV, Davis DP, Ochs M, Doney M, Hoyt DB. Incidence of transient hypoxia and pulse rate reactivity during paramedic rapid sequence intubation. *Ann Emerg Med*. 2003;42(6):721–728.

25. Mort TC. Emergency tracheal intubation: complications associated with repeated laryngoscopic attempts. *Anesth Analg*. 2004;99(2):607–613, table of contents.
26. Cournand A, Motley HL, et al. Physiological studies of the effects of intermittent positive pressure breathing on cardiac output in man. *Am J Physiol*. 1948;152(1):162–174.
27. Pepe PE, Roppolo LP, Fowler RL. The detrimental effects of ventilation during low-blood-flow states. *Curr Opin Crit Care*. 2005;11(3):212–218.
28. Pepe PE, Lurie KG, Wigginton JG, Raedler C, Idris AH. Detrimental hemodynamic effects of assisted ventilation in hemorrhagic states. *Crit Care Med*. 2004;32(9 Suppl):S414–S420.
29. Shafi S, Gentilello L. Pre-hospital endotracheal intubation and positive pressure ventilation is associated with hypotension and decreased survival in hypovolemic trauma patients: an analysis of the National Trauma Data Bank. *J Trauma*. 2005;59(5):1140–1145; discussion 5–7.
30. Fevang E, Perkins Z, Lockey D, Jeppesen E, Lossius HM. A systematic review and meta-analysis comparing mortality in pre-hospital tracheal intubation to emergency department intubation in trauma patients. *Crit Care*. 2017; 21(1):192.
31. Chou D, Harada MY, Barmparas G, Ko A, Ley EJ, Margulies DR, Alban RF. Field intubation in civilian patients with hemorrhagic shock is associated with higher mortality. *J Trauma Acute Care Surg*. 2016;80(2):278–282.
32. Floccare DJ, Galvagno SM Jr. Field intubation for hemorrhagic shock: a flawed syllogism. *J Trauma Acute Care Surg*. 2016;81(3):615.
33. Hussmann B, Lefering R, Waydhas C, Ruchholtz S, Wafaisade A, Kauther MD, Lendemans S. Prehospital intubation of the moderately injured patient: a cause of morbidity? A matched-pairs analysis of 1,200 patients from the DGU Trauma Registry. *Crit Care*. 2011;15(5):R207.
34. Taghavi S, Jayarajan SN, Ferrer LM, Vora H, McKee C, Milner RE, Gaughan JP, Dujon J, Sjoholm LO, Pathak A, et al. “Permissive hypoventilation” in a swine model of hemorrhagic shock. *J Trauma Acute Care Surg*. 2014;77(1):14–19.
35. Convertino VA, Ryan KL, Rickards CA, Cooke WH, Idris AH, Metzger A, Holcomb JB, Adams BD, Lurie KG. Inspiratory resistance maintains arterial pressure during central hypovolemia: implications for treatment of patients with severe hemorrhage. *Crit Care Med*. 2007;35(4):1145–1152.
36. Manley G, Knudson MM, Morabito D, Damron S, Erickson V, Pitts L. Hypotension, hypoxia, and head injury: frequency, duration, and consequences. *Arch Surg*. 2001;136(10):1118–1123.
37. Chesnut RM, Marshall LF, Klauber MR, Blunt BA, Baldwin N, Eisenberg HM, Jane JA, Marmarou A, Foulkes MA. The role of secondary brain injury in determining outcome from severe head injury. *J Trauma*. 1993;34(2):216–222.
38. Spaite DW, Hu C, Bobrow BJ, Chikani V, Barnhart B, Gaither JB, Denninghoff KR, Adelson PD, Keim SM, Viscusi C, et al. The effect of combined out-of-hospital hypotension and hypoxia on mortality in major traumatic brain injury. *Ann Emerg Med*. 2017;69(1):62–72.
39. Davis DP, Heister R, Poste JC, Hoyt DB, Ochs M, Dunford JV. Ventilation patterns in patients with severe traumatic brain injury following paramedic rapid sequence intubation. *Neurocrit Care*. 2005;2(2):165–171.
40. Denninghoff KR, Griffin MJ, Bartolucci AA, Lobello SG, Fine PR. Emergent endotracheal intubation and mortality in traumatic brain injury. *West J Emerg Med*. 2008;9(4):184–189.
41. Bernard SA, Nguyen V, Cameron P, Masci K, Fitzgerald M, Cooper DJ, Walker T, Std BP, Myles P, Murray L, et al. Prehospital rapid sequence intubation improves functional outcome for patients with severe traumatic brain injury: a randomized controlled trial. *Ann Surg*. 2010;252(6):959–965.
42. Ellard L, Djaiani G. Anaesthesia for vascular emergencies. *Anaesthesia*. 2013;68(Suppl 1):72–83.