Past and present role of extracorporeal membrane oxygenation in combat casualty care: How far will we go?

Jeremy W. Cannon, MD, Phillip E. Mason, MD, *and* **Andriy I. Batchinsky, MD***, Philadelphia, Pennsylvania*

ABSTRACT: Advanced extracorporeal therapies have been successfully applied in the austere environment of combat casualty care over the previous decade. In this review, we describe the historic underpinnings of extracorporeal membrane oxygenation, review the recent experience with both partial and full lung support during combat operations, and critically assess both the current status of the Department of Defense extracorporeal membrane oxygenation program and the way forward to establish long-range lung rescue therapy as a routine capability for combat casualty care. (*J Trauma Acute Care Surg.* 2018;84: S63–S68. Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved.)

KEY WORDS: Extracorporeal membrane oxygenation; acute respiratory distress syndrome; combat casualty care.

Extracorporeal membrane oxygenation (ECMO) has gained wider acceptance in the management of critically ill adults over the past decade leading to increased ECMO case volumes and more ECMO centers.[1] Multiple factors have contributed, including improved equipment and evidence, supporting its use leading to better patient selection.[2–4] Over this same period, the use of ECMO for combat casualty care has been explored.[5] By adding this additional level of advanced care to the options available for managing severely injured casualties in remote, austere locations, multiple lives have been saved that undoubtedly would have been lost in previous conflicts.[5,6] Now, the questions of sustainment and delivery to even more remote locations must be addressed. The following review defines the scope of this discussion and outlines the current pathway for using advanced lung rescue techniques in austere battlefield conditions as a matter of routine combat casualty care.

DEFINITIONS AND INDICATIONS

Extracorporeal life support (ECLS) is the general, blanket term used to include multiple forms of extracorporeal rescue therapies. This article will focus exclusively on the use of ECLS for pulmonary indications. These indications include both hypoxemic and hypercarbic respiratory failures, with the former being the more common indication for ECLS initiation. The ECLS support for hypoxemia is typically provided with venovenous ECMO (VV ECMO) in which deoxygenated blood is drained from a large central vein and pumped through a gas exchange membrane before being returned to the central venous circulation.[2,3] In this configuration, the pulmonary circulation is not bypassed, and the heart does not see any significant change in either preload or afterload.[7] Another approach, which has been applied typically in Europe for hypercarbic respiratory failure is arteriovenous pumpless support, so-called pumpless extracorporeal lung assist (PECLA). In this configuration, relatively hypoxemic and hypercarbic blood is drained from a femoral artery and passed through a gas exchange membrane and back into a femoral vein with the patient's blood pressure.[8–10] However, this approach limits the patient's mobility, has a 21% cannulation site complication rate, and there are currently no Food and Drug Administration (FDA)-approved devices for this technique available in the United States. This article will not address venoarterial ECMO (VA ECMO) for resuscitation[11] or deep hypothermic arrest for salvage after exsanguination,[12] which have not been used for combat casualty care to date.

HISTORIC CONTEXT

Extracorporeal membrane oxygenation has been used for severe respiratory failure in adult trauma patients for decades.[13] In recent years, concerns over postinjury hemorrhage have been addressed with nuanced management of anticoagulation, and improved survival in trauma patients with severe acute respiratory distress syndrome (ARDS) has been demonstrated.[14]

The first interfacility ECMO transport was performed by Bartlett and colleagues[15,16] for a 17-year-old female with pulmonary hemorrhage from Goodpasture syndrome in 1977. They transported her from Albuquerque, NM to Orange County Medical Center (now UC Irvine Medical Center) on a US Air Force C-130 with bread-truck type ambulances used for the ground portions of the transfer between each hospital and the airfield.

Submitted: January 2, 2018, Revised: January 30, 2018, Accepted: February 5, 2018, Published online: February 13, 2018.

From the Division of Traumatology, Surgical Critical Care & Emergency Surgery (J.W.C.), Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania; Uniformed Services University of the Health Sciences (J.W.C.), Bethesda, Maryland; Department of Surgery (P.E.M.), San Antonio Military Medical Center; US Army Institute of Surgical Research (A.I.B.), Joint Base San Antonio-Fort Sam Houston, Texas; and the Geneva Foundation, Tacoma, Washington (A.I.B.).

Disclaimer: The views expressed herein are those of the authors and do not reflect the official policy or position of the US Air Force, the US Army Medical Department, the US Army Office of the Surgeon General, the Department of the Army, the Department of Defense, or the US Government.

Presentations: This work was presented in part at the 2017 Remote Damage Control Resuscitation (RDCR) Symposium, June 26–28, 2017, in Bergen, Norway.

Address for reprints: Jeremy W. Cannon, MD, Division of Trauma, Surgical Critical Care and Emergency Surgery, 51N., 39th St, MOB Suite 120, Philadelphia, PA 19104; email: jeremy.cannon@uphs.upenn.edu.

DOI: 10.1097/TA.0000000000001846

ECMO transport programs were subsequently established by the US Air Force at Wilford Hall Medical Center[17] and at several civilian institutions, including the University of Michigan[18] and Arkansas Children's Hospital.[19] These programs demonstrated the safety of long-range ECMO transport and set an important precedent for centralizing ECMO care in high-volume centers.

EARLY COMBAT CASUALTY EXPERIENCE

Severely injured combat casualties who survive to surgical care often require a massive resuscitation in the course of their initial management. If the sources of bleeding and contamination can be controlled, the expected survival is excellent. However, we now know that about 8% of combat casualties who survive to surgical care go on to die a preventable death from multiple organ failure.[20] In this same population, approximately 3% of intubated casualties manifest ARDS in their hospital course, and this is independently associated with increased mortality.[21,22] In mechanically ventilated burned casualties, ARDS is even more common at 33%, and those with severe ARDS have a 43% mortality.[23] Still, others with severe pulmonary or tracheal injuries require advanced ventilator management and may also require aggressive surgical interventions, such as pneumonectomy. These patients consume tremendous medical resources on the ground and also outstrip the ability of the standard transport ventilator, thereby precluding safe evacuation (Fig. 1). Recognition of these challenging and potentially life-threatening situations in otherwise salvageable patients prompted the establishment of the Acute Lung Rescue Team (ALRT) based at the Level IV combat facility in Landsthuhl Regional Medical Center (LRMC) in November 2005.[24,25]

The ALRT launched from LRMC in response to requests for advance lung support in the combat theaters of both Iraq (Operation Iraqi Freedom [OIF]) and Afghanistan (Operation Enduring Freedom [OEF]). Additional interventions for ARDS provided by this team included advanced ventilators with additional modes of ventilation (e.g., the percussive VDR ventilator), inhaled pulmonary vasodilation therapy, and eventually extracorporeal support first with PECLA in 2005 (Fig. 2) and ultimately full VV ECMO as of October 2010 (Fig. 3).[5,26] Patients managed with ECLS included those with blast injury and traumatic brain injury often with relative contraindications to anticoagulation wherein the bleeding risk was mitigated by either holding or targeting very low levels of anticoagulation. The results reported by this team were exceptional with 90% survival in US casualties managed with extracorporeal support, reflecting both very good patient selection and robust patient substrate.[5]

Figure 1. Double lumen endotracheal tube for independent lung ventilation during transport. Reproduced from Cannon, JW and McNeil JD. Critical Care for War-Related Thoracic Injuries. In: Sellke F, Del Nido P & Swanson S. eds. Sabiston and Spencer Surgery of the Chest, 9th ed. Philadelphia, PA: Elsevier; 2015:61.1-61.13, with permission.

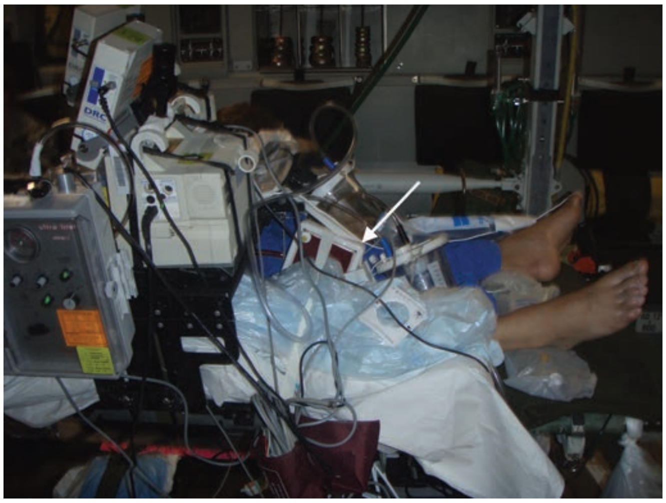

Figure 2. AV partial lung support with an early generation Novalung Interventional Lung Assist (iLA) (Xenios AG, Heilbronn, Germany) gas exchange membrane (*arrow*). Photo courtesy of Erik C. Osborn, MD.

CURRENT STATUS OF ECMO FOR WORLDWIDE COMBAT CASUALTY CARE

Providing consistent care for a complex clinical problem, like ARDS, over many years with a high turnover in providers

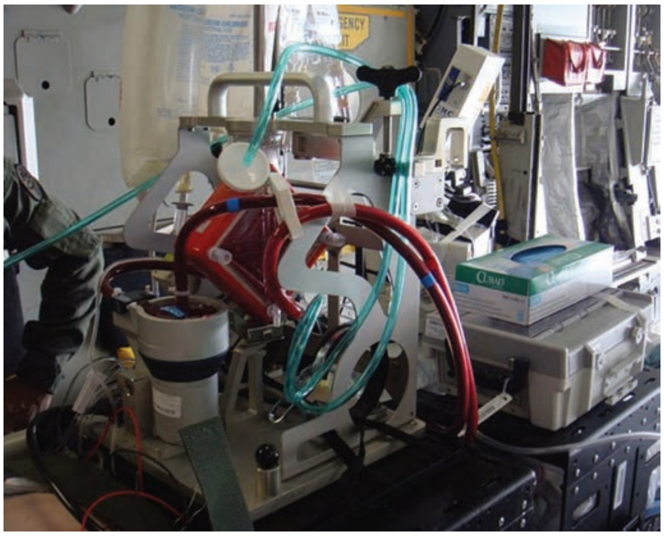

Figure 3. First ECMO transport. Reproduced from Cannon, JW and McNeil JD. Critical Care for War-Related Thoracic Injuries. In: Sellke F, Del Nido P & Swanson S. eds. Sabiston and Spencer Surgery of the Chest, 9th ed. Philadelphia, PA: Elsevier; 2015:61.1-61.13, with permission.

© 2018 Wolters Kluwer Health, Inc. All rights reserved.

and support personnel is a major challenge for combat casualty care. As seen in the variable availability and application of renal replacement therapies from Korea to Vietnam and then throughout OIF and OEF, the institutional knowledge for delivering advanced therapies is unfortunately extinguishable.[27] To mitigate this risk with advanced lung rescue and ECMO support, a multidimensional effort was undertaken starting in 2010. These efforts proceeded in parallel and included the following elements: (1) creation of an ARDS clinical practice guideline (CPG), (2) establishment of a fixed based of operations for adult ECMO support in the Department of Defense (DOD), (3) development of a translational ECMO research agenda, (4) creation of a leadership pipeline for the ECMO program with an ECMO fellowship pathway, and (5) establishing ECMO as a core capability in combat casualty care doctrine.

The Joint Trauma System is responsible for developing and maintaining a number of CPGs on all aspects of clinical care from wound management and antibiotic selection to the care of ocular injuries in the combat theater. In April 2014, the first version of the Acute Respiratory Failure CPG was published with a recent update posted in January 2017.[28] This guideline seeks to standardize the care of all patients with any level of ARDS severity and also provides guidance on obtaining expert consultation for possible extracorporeal support. The latter is of paramount importance because early recognition of both the presence of ARDS and the need for advanced care by an experienced ECMO team are central to optimizing survival.[29,30]

San Antonio Military Medical Center (SAMMC) is a Level I trauma center designated by the state of Texas and verified by the American College of Surgeons. It is co-located with the US Army Institute of Surgical Research Burn Unit, which is approved by the American Burn Association. Finally, it is designated a Level V combat casualty care facility. With these resources and the history of pediatric and neonatal ECMO transport at Wilford Hall Medical Center (which merged its inpatient mission with Brooke Army Medical Center in 2011), this seemed to be the ideal location for establishing a permanent DOD adult ECMO program. After many years of preparation to include hosting an Extracorporeal Life Support Organization adult ECMO training course and securing buy-in and approval from the DOD medical leadership, this program began operations in September 2012. Since that time, this team has managed 69 patients over 800 inpatient ECMO days with a 65% survival to discharge which compares very favorably to the 66% survival reported by Extracorporeal Life Support Organization.[1] These patients include both military as well as civilian patients using a special approval process designed to maintain critical skills and to support an appropriate ECMO clinical volume in keeping with recommended standards.[30] In addition, this team has been involved in 45 ECMO transports on both ground and fixed-wing platforms including multiple international transports from Afghanistan, Colombia, Germany, Honduras, Iraq, and Japan. The most recent ECMO transport was arranged from Baghdad, Iraq, to SAMMC for a critically injured combat casualty using the Cardiohelp system (Maquet Cardiovascular, Wayne, NJ), a very compact ECMO system specifically designed for transport (Fig. 4).

A longstanding research program in respiratory rescue technologies for severely burned patients at the US Army Institute of Surgical Research was expanded to include protocols evaluating extracorporeal techniques in 2003.[31–36] Indeed, this research platform created a fertile environment for establishing the clinical ECMO program, with a strong translational emphasis. The subsequent reciprocal exchange between the research and clinical programs has mutually benefitted both programs, which continue to explore innovative approaches to management of combat casualties with ARDS and multiple organ failure using various ECLS technologies.[32,37–42]

Figure 4. Recent ECMO transport from Baghdad to SAMMC.

In 2013, the US Air Force approved a salaried position for fellowship training in ECMO management. This advanced training is to be undertaken in a high-volume ECMO center in which the trainee learns all aspects of ECMO patient management and program administration through didactics and hands-on experience in both VV and VA adult ECMO. This fellowship position enabled a year of intensive training for the current DOD ECMO Medical Director (PEM) and will ensure a continuous supply of ECMO-trained critical care physicians who can lead the DOD ECMO program going forward. Furthermore, significant progress has been made in cementing ECMO care into the DOD's combat casualty care doctrine given the initial success of this program. Future combat operations should be continuously supported by these and other innovative advanced care capabilities.

PLANNING FOR THE FUTURE

The principal challenges for routinely providing ECMO support downrange include the time it currently takes from ECMO team activation to initiation and the education and training required to sustain an ECMO program during the ebbs and flows of the operational tempo. To address these challenges going forward, some instructive examples now exist in the civilian realm. Extracorporeal membrane oxygenation has been initiated in a prehospital setting by trained personnel in Paris, France, and Regensburg, Germany, for cases of cardiac arrest.[43–45] In all of these cases, a well-trained ECMO team has launched from a nearby hospital. Once on scene, this ECMO team has directed the cardiopulmonary resuscitation, cannulated the patient and then transported the patient to the hospital for ongoing ECMO care. Although some of the lessons learned from these experiences can inform preparations for firmly establishing VV ECMO support for combat casualty care, there are some important differences in these situations. First, these teams initiating out-

© 2018 Wolters Kluwer Health, Inc. All rights reserved.

of-hospital ECMO have worked together in their home institutions and have significant experience with initiating ECMO in pulseless patients, where the ability or inability to cannulate determines success or failure of the approach. Furthermore, they are working in close proximity to their home institution where the patient will be managed following ECMO initiation.

In OIF/OEF, ECLS capability was provided by the ALRT DOD transport team based at LRMC (Level IV). Patients had ECLS (five PECLA, five VV ECMO) initiated at Level III by ALRT providers before transport or at LRMC after transport from the combat zone. All inpatient ECMO care was then provided at University Hospital Regensburg.[5] With the decrease in operational tempo, this capability has been pulled back to the continental US making the current minimum time from ECMO consultation to cannulation in the CENTCOM area of operations 24 hours to 48 hours.

Opportunities for growth of this program are detailed in Table 1. To maintain an ECMO capability that can be initiated within hours of the recognized need for this level of support, a sustained education effort on the appropriate triggers for ECMO consultation and initiation must be undertaken. Using the "focused empiricism" which has successfully bridged multiple gaps in combat casualty care,[46] a new paradigm in lung rescue for combat casualties must be developed. We recommend that two complementary courses of action be pursued to address this gap.

One approach would be to initiate partial lung extracorporeal support using a less complex system early after injury.[32,37] The DOD has significant research experience with these devices that resemble modern renal replacement systems routinely used in both civilian critical care and combat casualty management.[47] Because the blood flow rates for these systems is relatively low (e.g., 500–1,000 mL/min as compared to 5 L/min for full ECMO), the vascular access catheter resembles a double lumen dialysis catheter. A general surgeon, emergency medicine physician, or critical care physician can easily place these access catheters using standard ultrasound-guided Seldinger technique. Furthermore, these systems all have an intuitive user interface. Both of these factors simplify the initial training and the skills maintenance aspects of initiating extracorporeal lung support. From a patient management standpoint, this partial extracorporeal approach would also allow reduction in the ventilator settings which would both mitigate the ongoing barotrauma and volutrauma to the lungs while also improving the hemodynamic status of the patient until the team with full ECMO and ECMO transport capability arrives.[6,32]

However, this bridge approach remains untested in the management of patients with multiple injuries with severe ARDS, and none of the devices are FDA approved at this point. Furthermore, if the ARDS is rapidly progressive, these low flow systems would be unlikely to provide enough gas exchange to permit a significant change in the patient's ventilator settings. Thus, another approach would be to establish and maintain ECMO initiation and management skills among teams at Levels III and IV facilities as an initial proof of concept followed by potential expansion to Level II facilities in time. A simplified management approach using existing, FDA-approved equipment (albeit use beyond 6 hours is technically off-label) could be developed and paired with teleconsultation for patient selection, circuit preparation, and cannula insertion. Training for ECMO initiation and early management could easily be incorporated into predeployment training for critical care physicians, nurses, and respiratory therapists. This approach offers significant patient benefit by providing full extracorporeal lung support at the outset thereby permitting complete lung rest while awaiting transport.

We recommend pursuing both of these options in parallel while increasing exposure of DOD physicians, nurses, and respiratory therapists to the full spectrum of extracorporeal support. This exposure and training should be achieved by continuing to support ECMO operations at SAMMC while also seeking appropriate civilian partners to aid in this mission. This approach is in keeping with the recommendations by the National Academies of Science, Engineering and Medicine for sustained military excellence in trauma care as we seek to reduce the number of preventable deaths from all injuries, including those sustained in combat operations, to zero.[46]

TABLE 1. Current Capability Gaps in Global ECMO Support and Proposed Solutions

Gap	Solutions	Potential Barriers
Knowledge of ECMO indications and triggers for ECMO consultation	Widely disseminate respiratory failure CPG; provide education on additional indications for VV ECMO including pneumonectomy and tracheobronchial injury	Personnel turnover; low operational tempo
ECMO cannulation and patient management currently limited to cardiothoracic surgeons and trained intensivists (e.g., trauma surgeons, emergency medicine/critical care, internal medicine/critical care)	Train deployment-eligible surgeons, emergency medicine, and critical care physicians on cannulation techniques; provide both real-world and simulation training (live tissue and model-based) for cannulation and patient management	Limited exposure to ECMO in primary specialty training; skills maintenance; availability of high-fidelity live tissue and model-based simulators
Full ECMO support and ECMO transport limited to Level V combat facilities based in the United States (minimum time from consult to on-site cannulation is currently 24–48 h)	Initiate extracorporeal lung support at Level III and IV facilities while awaiting ECMO transport	Lack of leadership support for expanded ECMO training; gaining and maintaining skills for ECMO initiation and short-term management among all Level III and IV personnel
Need for ongoing ECMO training for both transport and routine ECMO care	Expand Level V ECMO capability to include both VV and VA ECMO; ensure adequate case volume through designee programs permitting civilian care in military treatment facilities; seek civilian partners for expanded ECMO training	Lack of leadership support for expanded ECMO training

© 2018 Wolters Kluwer Health, Inc. All rights reserved.

CONCLUSION

Current evidence supports ECMO as a lifesaving intervention that can be safely used in the management of severely injured trauma patients with severe respiratory failure. This capability has been applied successfully in the management of combat casualties over the past decade. To maintain this capability during periods of lower operational tempo (i.e., low level conflicts or peacetime with few combat casualties), multiple gaps must be addressed as enumerated above including logistical support planning; ongoing education of military ECMO personnel including respiratory therapists, intensive care unit nurses, perfusionists and physicians; and incubation of these personnel in high-volume civilian and/or military ECMO centers for skills retention. Going forward, plans should also be made to enable initiation of extracorporeal lung support routinely at Levels III and IV facilities to save even more casualties in future conflicts. This capability is well within reach with either partial extracorporeal lung support as a "bridge" solution or even full ECMO support, paired with early activation of the transport team. Future efforts should be focused on further development and evaluation of partial lung support, on translational efforts to field such a device for routine combat casualty care use, and on exploring the possibility of training downrange teams to provide short-term full ECMO support.

AUTHORSHIP

J.W.C. and A.I.B. conceived this report. J.W.C. drafted the initial article. All authors contributed to and critically revised the final article.

DISCLOSURE

The authors received no funding for this work. A.I.B. reported travel and speaking expenses paid by Maquet Cardiovascular. The other authors declared no conflicts of interest.

REFERENCES

1. ECLS. *Registry Report International Summary.* Available at: https://www.elso.org/Registry/Statistics/InternationalSummary.aspx. Accessed Dec 5, 2017.
2. Brodie D, Bacchetta M. Extracorporeal membrane oxygenation for ARDS in adults. *N Engl J Med*. 2011;365(20):1905–1914.
3. Cannon JW, Gutsche JT, Brodie D. Optimal strategies for severe acute respiratory distress syndrome. *Crit Care Clin*. 2017;33(2):259–275.
4. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, Hibbert CL, Truesdale A, Clemens F, Cooper N, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet*. 2009;374(9698):1351–1363.
5. Bein T, Zonies D, Philipp A, Zimmermann M, Osborn EC, Allan PF, Nerlich M, Graf BM, Fang R. Transportable extracorporeal lung support for rescue of severe respiratory failure in combat casualties. *J Trauma Acute Care Surg*. 2012;73(6):1450–1456.
6. Neff LP, Cannon JW, Stewart IJ, Batchinsky AI, Zonies DH, Pamplin JC, Chung KK. Extracorporeal organ support following trauma: the dawn of a new era in combat casualty critical care. *J Trauma Acute Care Surg*. 2013; 75(2 Suppl 2):S120–S129.
7. Hou X, Guo L, Zhan Q, Jia X, Mi Y, Li B, Sun B, Hao X, Li H. Extracorporeal membrane oxygenation for critically ill patients with 2009 influenza A (H1N1)-related acute respiratory distress syndrome: preliminary experience from a single center. *Artif Organs*. 2012;36(9):780–786.
8. Bein T, Scherer MN, Philipp A, Weber F, Woertgen C. Pumpless extracorporeal lung assist (pECLA) in patients with acute respiratory distress syndrome and severe brain injury. *J Trauma*. 2005;58(6):1294–1297.
9. Bein T, Weber F, Philipp A, Prasser C, Pfeifer M, Schmid F-X, Butz B, Birnbaum D, Taeger K, Schlitt HJ. A new pumpless extracorporeal interventional lung assist in critical hypoxemia/hypercapnia. *Crit Care Med*. 2006;34(5):1372–1377.
10. McKinlay J, Chapman G, Elliot S, Mallick A. Pre-emptive Novalung-assisted carbon dioxide removal in a patient with chest, head and abdominal injury. *Anaesthesia*. 2008;63(7):767–770.
11. Arlt M, Philipp A, Voelkel S, Rupprecht L, Mueller T, Hilker M, Graf BM, Schmid C. Extracorporeal membrane oxygenation in severe trauma patients with bleeding shock. *Resuscitation*. 2010;81(7):804–809.
12. Tisherman SA, Alam HB, Rhee PM, Scalea TM, Drabek T, Forsythe RM, Kochanek PM. Development of the emergency preservation and resuscitation for cardiac arrest from trauma clinical trial. *J Trauma Acute Care Surg*. 2017;83(5):803–809.
13. Hill JD, O'Brien TG, Murray JJ, Dontigny L, Bramson ML, Osborn JJ, Gerbode F. Prolonged extracorporeal oxygenation for acute post-traumatic respiratory failure (shock-lung syndrome). Use of the Bramson membrane lung. *N Engl J Med*. 1972;286(12):629–634.
14. Guirand DM, Okoye OT, Schmidt BS, Mansfield NJ, Aden JK, Martin RS, Cestero RF, Hines MH, Pranikoff T, Inaba K, et al. Venovenous extracorporeal life support improves survival in adult trauma patients with acute hypoxemic respiratory failure: a multicenter retrospective cohort study. *J Trauma Acute Care Surg*. 2014;76(5):1275–1281.
15. Bartlett RH, Gazzaniga AB, Fong SW, Jefferies MR, Roohk HV, Haiduc N. Extracorporeal membrane oxygenator support for cardiopulmonary failure. Experience in 28 cases. *J Thorac Cardiovasc Surg*. 1977;73(3):375–386.
16. Cannon J, Allan PF, Osborn EC, Phillip A, Arlt M, Tyree MM. Transport of the ECMO Patient from Concept to Implementation. In: *Extracorporeal cardiopulmonary support in critical care*. 4th ed. Ann Arbor, MI: ELSO; 2012.
17. Coppola CP, Tyree M, Larry K, DiGeronimo R. A 22-year experience in global transport extracorporeal membrane oxygenation. *J Pediatr Surg*. 2008;43(1):46–52; discussion 52.
18. Foley DS, Pranikoff T, Younger JG, Swaniker F, Hemmila MR, Remenapp RA, Copenhaver W, Landis D, Hirschl RB, Bartlett RH. A review of 100 patients transported on extracorporeal life support. *ASAIO J*. 2002; 48(6):612–619.
19. Heulitt MJ, Taylor BJ, Faulkner SC, Baker LL, Chipman CW, Harrell JH, VanDevanter SH. Inter-hospital transport of neonatal patients on extracorporeal membrane oxygenation: mobile-ECMO. *Pediatrics*. 1995;95(4):562–566.
20. Eastridge BJ, Hardin M, Cantrell J, Oetjen-Gerdes L, Zubko T, Mallak C, Wade CE, Simmons J, Mace J, Mabry R, et al. Died of wounds on the battlefield: causation and implications for improving combat casualty care. *J Trauma*. 2011;71(Suppl 1):S4–S8.
21. Park PK, Cannon JW, Ye W, Blackbourne LH, Holcomb JB, Beninati W, Napolitano LM. Transfusion strategies and development of acute respiratory distress syndrome in combat casualty care. *J Trauma Acute Care Surg*. 2013; 75(2 Suppl 2):S238–S246.
22. Park PK, Cannon JW, Ye W, Blackbourne LH, Holcomb JB, Beninati W, Napolitano LM. Incidence, risk factors, and mortality associated with acute respiratory distress syndrome in combat casualty care. *J Trauma Acute Care Surg*. 2016;81(5 Suppl 2 Proceedings of the 2015 Military Health System Research Symposium):S150–S156.
23. Belenkiy SM, Buel AR, Cannon JW, Sine CR, Aden JK, Henderson JL, Liu NT, Lundy JB, Renz EM, Batchinsky AI, et al. Acute respiratory distress syndrome in wartime military burns: application of the Berlin criteria. *J Trauma Acute Care Surg*. 2014;76(3):821–827.
24. Dorlac GR, Fang R, Pruitt VM, Marco PA, Stewart HM, Barnes SL, Dorlac WC. Air transport of patients with severe lung injury: development and utilization of the Acute Lung Rescue Team. *J Trauma*. 2009; 66(Suppl 4):S164–S171.
25. Fang R, Allan PF, Womble SG, Porter MT, Sierra-Nunez J, Russ RS, Dorlac GR, Benson C, Oh JS, Wanek SM, et al. Closing the "care in the air" capability gap for severe lung injury: the Landstuhl Acute Lung Rescue Team and extracorporeal lung support. *J Trauma*. 2011;71(Suppl 1):S91–S97.
26. Zimmermann M, Philipp A, Schmid FX, Dorlac W, Arlt M, Bein T. From Baghdad to Germany: use of a new pumpless extracorporeal lung assist system in two severely injured US soldiers. *ASAIO J*. 2007;53(3):e4–e6.
27. Chung KK, Perkins RM, Oliver JD 3rd. Renal replacement therapy in support of combat operations. *Crit Care Med*. 2008;36(Suppl 7):S365–S369.

© 2018 Wolters Kluwer Health, Inc. All rights reserved.

28. Cannon JW, Pamplin JC, Zonies DH, Mason PH, Sine CR, Cancio LC, Mcneil JD, Colombo C, Osborn EC, Allan PF, et al. Acute Respiratory Failure (CPG ID: 6). Available at: http://www.usaisr.amedd.army.mil/cpgs/Acute_Resp_Failure_23_Jan_2017.pdf. Accessed Dec 5, 2017.
29. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, Gattinoni L, van Haren F, Larsson A, McAuley DF, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA*. 2016;315(8):788.
30. Combes A, Brodie D, Bartlett R, Brochard L, Brower R, Conrad S, De Backer D, Fan E, Ferguson N, Fortenberry J, et al. Position paper for the organization of extracorporeal membrane oxygenation programs for acute respiratory failure in adult patients. *Am J Respir Crit Care Med*. 2014; 190(5):488–496.
31. Cancio LC. Building on the legacy of Dr. Basil A. Pruitt, Jr., at the US Army Institute of Surgical Research during the wars in Iraq and Afghanistan. *J Trauma Acute Care Surg*. 2017;83(5):755–760.
32. Batchinsky AI, Jordan BS, Regn D, Necsoiu C, Federspiel WJ, Morris MJ, Cancio LC. Respiratory dialysis: reduction in dependence on mechanical ventilation by venovenous extracorporeal CO2 removal. *Crit Care Med*. 2011;39(6):1382–1387.
33. Batchinsky AI, Martini DK, Jordan BS, Dick EJ, Fudge J, Baird CA, Hardin DE, Cancio LC. Acute respiratory distress syndrome secondary to inhalation of chlorine gas in sheep. *J Trauma*. 2006;60(5):944–956; discussion 956-7.
34. Batchinsky AI, Weiss WB, Jordan BS, Dick EJ Jr, Cancelada DA, Cancio LC. Ventilation-perfusion relationships following experimental pulmonary contusion. *J Appl Physiol (1985)*. 2007;103(3):895–902.
35. Cancio LC, Batchinsky AI, Dubick MA, Park MS, Black IH, Gómez R, Faulkner JA, Pfannenstiel TJ, Wolf SE. Inhalation injury: pathophysiology and clinical care proceedings of a symposium conducted at the Trauma Institute of San Antonio, San Antonio, TX, USA on 28 March 2006. *Burns*. 2007;33(6):681–692.
36. Batchinsky AI, Jordan BS, Necsoiu C, Dubick MA, Cancio LC. Dynamic changes in shunt and ventilation-perfusion mismatch following experimental pulmonary contusion. *Shock*. 2010;33(4):419–425.
37. Langer T, Vecchi V, Belenkiy SM, Cannon JW, Chung KK, Cancio LC, Gattinoni L, Batchinsky AI. Extracorporeal gas exchange and spontaneous breathing for the treatment of acute respiratory distress syndrome: an alternative to mechanical ventilation?*. *Crit Care Med*. 2014;42(3): e211–e220.
38. Scaravilli V, Kreyer S, Linden K, Belenkiy S, Jordan B, Pesenti A, Zanella A, Chung K, Cannon J, Cancio LC, et al. Modular extracorporeal life support: effects of ultrafiltrate recirculation on the performance of an extracorporeal carbon dioxide removal device. *ASAIO*. 2014;60(3):335–341.
39. Kreyer S, Scaravilli V, Linden K, Belenkiy SM, Necsoiu C, Li Y, Putensen C, Chung KK, Batchinsky AI, Cancio LC. Early utilization of extracorporeal CO2 removal for treatment of acute respiratory distress syndrome due to smoke inhalation and burns in sheep. *Shock*. 2016;45(1):65–72.
40. Linden K, Scaravilli V, Kreyer SF, Belenkiy SM, Stewart IJ, Chung KK, Cancio LC, Batchinsky AI. Evaluation of the Cytosorb™ hemoadsorptive column in a pig model of severe smoke and burn injury. *Shock*. 2015; 44(5):487–495.
41. Scaravilli V, Kreyer S, Belenkiy S, Linden K, Zanella A, Li Y, Dubick MA, Cancio LC, Pesenti A, Batchinsky AI. Extracorporeal carbon dioxide removal enhanced by lactic acid infusion in spontaneously breathing conscious sheep. *Anesthesiology*. 2016;124(3):674–682.
42. Scaravilli V, Kreyer S, Linden K, Belenkiy S, Pesenti A, Zanella A, Cancio LC, Batchinsky AI. Enhanced extracorporeal CO2 removal by regional blood acidification: effect of infusion of three metabolizable acids. *ASAIO J*. 2015;61(5):533–539.
43. Ried M, Bein T, Philipp A, Müller T, Graf B, Schmid C, Zonies D, Diez C, Hofmann HS. Extracorporeal lung support in trauma patients with severe chest injury and acute lung failure: a 10-year institutional experience. *Crit Care*. 2013;17(3):R110.
44. Lamhaut L, Hutin A, Deutsch J, Raphalen JH, Jouffroy R, Orsini JP, Baud F, Carli P. Extracorporeal Cardiopulmonary Resuscitation (ECPR) in the prehospital setting: an illustrative case of ECPR performed in the Louvre Museum. *Prehosp Emerg Care*. 2017;21(3):386–389.
45. Richardson AS, Schmidt M, Bailey M, Pellegrino VA, Rycus PT, Pilcher DV. ECMO Cardio-Pulmonary Resuscitation (ECPR), trends in survival from an international multicentre cohort study over 12-years. *Resuscitation*. 2017; 112:34–40.
46. National Academies of Sciences, Engineering, and Medicine. *A national trauma care system: integrating military and civilian trauma systems to achieve zero preventable deaths after injury*. Washington, DC: National Academies Press; 2016.
47. Zonies D, DuBose J, Elterman J, Bruno T, Benjamin C, Cannon J, Chung KK. Early implementation of continuous renal replacement therapy optimizes casualty evacuation for combat-related acute kidney injury. *J Trauma Acute Care Surg*. 2013;75(2):S210–S214.

© 2018 Wolters Kluwer Health, Inc. All rights reserved.