Do We Know **Enough?**

Better Evidence for Combat Casualty Care

You never know what is enough unless you know what is more than enough.

— William Blake

Why clinical trials are essential to the Joint Trauma System's continuing efforts to improve combat casualty care.

By CDR James V. Lawler
Deputy Director, JC2RT

Barely twenty years old, evidence-based medicine (EBM) has transformed medical practice and improved outcomes in patient care. Gordon Guyatt, who coined the term, described EBM this way: "Evidence-based medicine de-emphasizes intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research." The DoD Joint Trauma System (JTS) embraced the concept of EBM in the development of its Clinical Practice Guidelines (CPGs), the introduction of which has significantly improved survival of combat casualties in the Iraq and Afghanistan theaters.

As JTS builds on its successes, the time has come to take evidence-based combat casualty care to the next level. The effectiveness of EBM hinges on the quality of the evidence. We need a higher level of confidence in what we know and what we don't know to be certain that we are delivering the right care at the right time.

The Quality of Evidence Matters

DoD possesses unparalleled expertise in the care of combat wounded, but EBM teaches that expertise alone is insufficient for determining optimal clinical management. In fact, EBM is based upon the principle that experts are frequently wrong. The history of medicine and surgery is replete with testament to this principle. The Cardiac Arrhythmia Suppression Trial (CAST, 1989: post-MI anti-arrhythmic use actually increased deaths by 3.6 times), the Strategies for Management of Antiretroviral Therapy trial (SMART 1, 2006: structured treatment interruption for HIV resulted in 80 percent higher mortality), and the Normoglycemia in Intensive Care Evaluation–Survival Using Glucose Algorithm Regulation trial (NICE-SUGAR, 2009: tight glucose control for critically ill patients in the ICU actually increased mortality by 10 percent) are but three of many examples where conventional wisdom, supported by the best available evidence and expert opinion, was definitively refuted by large randomized clinical trials (RCTs).

In the above instances, evidence supporting the accepted best-practice included observational clinical studies in addition to in vitro and animal research. The evidence upon which experts made their (ultimately misguided) recommendations was good. It just wasn't good enough. In an effort to avoid similar errors in current practice guidelines, most medical professional societies now accompany their recommendations with some grade or rating of the supporting evidence. Most prominent grading systems—for instance, Grading of Recommendations Assessment, Development and Evaluation, or GRADE—impart the highest confidence rating only to evidence that is supported by well-designed RCTs. Observational studies are generally given moderate grades for evidence, with anecdotal reports and animal data receiving even less confidence.

Unfortunately, almost none of the evidence available in the combat casualty care literature would be considered high grade. Clinical research performed in theater is largely observational and retrospective, and it often employs historical-, unmatched-, or no controls. Any RCT data related to the management of blast or penetrating trauma is from civilian trauma systems, the applicability of which is debatable. The reader should not interpret these observations as criticism of our combat casualty care researchers or their work to date; indeed, given the constraints of the combat environment, resource limitations, and policy restrictions, DoD's combat casualty care research enterprise has produced remarkably good data. But is it good enough?

A Surmountable Challenge

To answer the above question, and to continue improving patient outcome in the military combat casualty care system, we need better evidence. We know that our current practices work better than our old, but we don't know which parts contribute what. This uncertainty also confounds analysis of future

U.S. Marine Corps Lance Cpl. Cameron W. Stevie, right, and U.S. Navy Hospital Corpsman 3rd Class Geoffrey C. Pierce, left, with 3rd Battalion, 7th Marine Regiment, Regimental Combat Team 6 carry an Afghan National Army soldier into the battalion aid station on Forward Operating Base Jackson, Sangin, Helmand province, Afghanistan 5 February 2012. The soldier was treated for injuries sustained during a vehicle collision outside of the FOB. (U.S. Marine Corps photo by Cpl. Armando Mendoza/Released)

interventions. As our results continue to improve, effect sizes of new interventions will likely shrink, amplifying the effect of confounders. As we strive to understand the best pre-hospital care and appropriate application of new drugs and adjunctive interventions, larger, rigorously designed prospective observational studies and RCTs will be essential to insuring the fidelity of our CPGs.

The complexity of performing such rigorous prospective studies and RCTs in combat trauma is daunting but not insurmountable. The civilian trauma research community has performed numerous such large trials, many of them influential studies on prehospital care. Ethics committees do approve well-designed intervention trials where consent is not possible, and investigators have used creative approaches to inform citizens and gain support for such trials within communities. With well over 100,000 patients entered in the DoD Trauma Registry, the Department has encountered ample patients to conduct numerous large trials during these last 12 years of operations abroad.

Next steps

Obviously, the time to conduct large prospective trials in Afghanistan has passed. However, when the next large conflict arises, we will likely be asking the same questions with no prospect of finding definitive answers unless we act now. DoD should commit to the execution of large prospective studies (preferably RCTs when possible) in combat casualty care. In order to do this, combat casualty care research will require significantly better supporting infrastructure in theater. Such support should include additional dedicated clinical research specialists, information technology staff, and data management support. Human subject research oversight also will need to be addressed, including clarification or revision of DoD policy regarding the waiver of informed consent as outlined in DoD Instruction 3216.02. Such an effort will require a streamlined but thorough review process.

Our wounded warriors deserve the best evidence-based care we can give them, and in order to deliver, we must develop the best evidence. If the combat casualty care enterprise were to pick the four to eight most pressing questions in combat casualty care and develop pre-packaged prospective studies that we could implement at the outset of the next major conflict, we could make tremendous strides in producing evidence with a high degree of confidence. These questions would not be difficult to identify, as many of them are asked on a daily basis in the battlefield and our role two and three hospitals: What is the appropriate use of tranexamic acid? Is ketamine a more effective analgesic than opiates in the field? Is transfusion capability in medevac worth the effort and potential delay? There are certainly many more. Only through better evidence can we be confident that we are delivering the right care at the right time.

The opinions or assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. ■