Updates on the clinical practice of emergency medicine

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Massive transfusion during early trauma resuscitation

Uncontrolled hemorrhage after both civilian and combat traumatic injury is the most common cause of potentially preventable death. These patients will often require massive transfusion to complement rapid surgical or angiographic hemostasis in an effort to save lives. Massive transfusion is defined as greater than or equal to ten units of packed red blood cells given within 24 h. Massive transfusion patients account for less than 3% of civilian hospital admissions, yet have a 30–60% mortality rate [1].

Current resuscitation algorithms, as presented in the Advanced Trauma Life Support Manual, 8th edition [2], support the sequential use of crystalloids followed by red blood cells, and then plasma and platelet transfusions. Civilian guidelines for massive transfusion have typically recommended a 1:3 ratio of plasma to red blood cells. Optimal platelet:red blood cell ratios are unknown.

Military data demonstrate that a plasma:red blood cell ratio approaching 1:1 improves long-term outcome in massive-transfusion combat casualties. Recently, the damage-control resuscitation strategy, which is focused on halting and/or preventing the lethal triad of coagulopathy, acidosis and hypothermia, has challenged traditional thinking on early resuscitation strategies [1].

During his presentation highlighting recent updates in the trauma literature, Dr Michael Rotondo, Chairman of Surgery at East Carolina's Pitt County Memorial Hospital (NC, USA) points out that damage-control resuscitation advocates are transfusing earlier, and increased amounts of plasma and platelets are given along with the first units of red blood cells, while simultaneously minimizing crystalloid use in patients who are predicted to require massive transfusion [1].

He discussed the results of Dr John Holcomb's study from the United States Army Institute of Surgical Research (TX, USA). This was a study of 466 massively transfused civilian trauma patients, the largest from level-one trauma centers, in which the overall survival rate was 60%. The overall survival rates were improved from 41 to 71% by transfusing increased amounts of plasma and platelets. The results were similar to data from combat causalities (92% penetrating injury), demonstrating improved survival (35–81%) associated with increased plasma ratios. The survival benefit was predominantly in patients with truncal hemorrhage, with most improvement seen as early as 6 h [1].

Dr Rotondo expressed his support of a more balanced approach to initial trauma resuscitation, stressing that a ratio of 1:1:1 of plasma:packed red blood cells:platelets has already appeared in many civilian trauma centers and will likely become more prevalent in the future, especially in patients requiring massive transfusions. The success of a massive transfusion protocol relies heavily on the coordination of the blood bank in minimizing administrative paperwork and ensuring the delivery of a predetermined fixed ratio of plasma, platelets and red blood cells to the bedside.

These data represent a significant shift in trauma resuscitation. After World War II, it was recognized that hemorrhagic shock was optimally treated with whole blood replacement. In 1976 it was felt that optimal resuscitation consisted of 1–2 l of lactated ringers, accompanied by whole blood transfusion. Whole blood is difficult to store, expensive and causes significant antigenic reactions. By the mid 1980s, plasma, platelets and cryoprecipitate had been removed from cells. Despite this, resuscitation strategies focused on rapid infusion of warm crystalloid and red blood cells to maintain blood pressure and ensure oxygen delivery to tissues. The proposed current strategies are an attempt to give back some of the components of whole blood earlier with the hope of fewer complications [1].

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Tourniquets

Hemorrhage from extremity injuries has been recognized in wars throughout history as one of the leading causes of potentially preventable death on the battlefield. However, relatively few clinical series specifically analyzing the effectiveness of tourniquets on hemorrhage control and casualty outcome have been published [3]. Until recently, the most modern series was published by Lakstein *et al.* in 2003, in which 110 tourniquets were applied to 91 patients from the Israeli defense force's prehospital experience, and demonstrated that the combination of aggressive tourniquet use training, guidelines with a rapid evacuation and trauma care system could prevent deaths from extremity hemorrhage with a low tourniquet complication rate [3,4].

Dr Rotondo points out that in the study by Beekley *et al.*, published in the *Journal of Trauma* (prehospital tourniquet use in Operation Iraqi Freedom: effect on hemorrhage control and outcomes), the placement of prehospital tourniquets in 67 patients resulted in significantly improved hemorrhage control, and there were no adverse outcomes related to its use. A total of 98 patients had severe extremity injuries but no prehospital tourniquets [3]. Analysis revealed that four of the seven deaths, or 57%, could have potentially been prevented with prehospital tourniquet placement.

In response, the US army implemented a design, testing, training and fielding program for battlefield tourniquets, resulting in a policy that all military personnel carry tourniquets. As a result of this and several other efforts, tourniquets are now common on the battlefields of Iraq and Afghanistan, both in the hands of medical and nonmedical personnel. With the assistance of the Tactical Combat Casualty Care initiative, over 400,000 field tourniquets have been placed into the combat zone [3].

As a result of this, and in an effort to save lives, Kraugh *et al.*, from the US Army institute of Surgical Research (TX, USA) recently published the largest series to date demonstrating the lifesaving capability of tourniquets [5]. In this study, 428 tourniquets were applied to 309 injured limbs among 2838 injured with a mean age of 29 years [5].

Tourniquets, when applied early within 10 min and before shock was present, were associated with survival of 90 versus 10%. The prehospital application of the tourniquets was associated with a 50% reduction in deaths when compared with the emergency department application of the tourniquet (11 vs 24% mortality) [5]. No limbs were lost because of tourniquet use, and no amputations resulted solely from tourniquet use.

The five casualties indicated for tourniquets, but those who had not had them applied had a survival rate of 0 versus 87% for those casualties with tourniquets used [5]. The body of the article describes that in these cases, when a tourniquet is indicated, it should be placed before extrication and transport. The scoop-and-go decision is contrary to the doctrine that hemorrhage control should occur first with tourniquets, and may have saved the lives of these five patients.

Kraugh *et al.* describe that before their study, "the only first-aid device carried by medics that shows data on improved survival in limb-injured patients was the Thomas splint. This splint was felt to decrease mortality by controlling hemorrhage in prehospital causalities in World War I, which makes the splint and the tourniquet analogous. Similar to Thomas splints, the use of tourniquets improved prehospital survival, and prehospital use is required to prevent shock onset."

Currently, there is no better temporary measure to stop bleeding available on the battlefield, and tourniquets should be applied quickly before shock ensues to save lives. This is a specific combat casualty setting, and a population that may hamper generalization to the civilian trauma population [5].

Dr Rotondo took a moment of silence in memory of his dear friend and colleague, Dr John Pryor, who was killed while on duty in Iraq. John was bravely serving his country and brought state-of-the-art trauma care to the battlefield.

Ischemic stroke

Summary of update presented

In the early 1990s, it was not uncommon for emergency medicine physicians to receive presumed ischemic stroke patients and move them to the back of the emergency department so that they could attend to more urgent patients. Recently, a 40-year-old female who sustained a devastating ischemic stroke to her dominant hemisphere went on to develop increasing cerebral edema, slipped into a coma and died 72 h after the initial presentation, despite aggressive management with intravenous thrombolytics. The initial presentation in this case was not as dramatic as a gunshot wound to the chest, but the end result was tragic and helps to emphasize that this disease should not be underestimated.

National mortality rates for penetrating trauma remain less than 5% and overall stroke mortality rates remain at greater than 20% [6–10]. National

level-one trauma centers are widely supported, and have the resources and infrastructure to have in-house expert trauma teams and operating rooms available 24 h a day. The development and implementation of designated comprehensive and primary stroke centers, whose goal is to focus on stroke care and reduce morbidity and mortality, is becoming increasingly important [7–10].

How could one approach ischemic stroke in the clinical arena?

Ischemic stroke is a devastating disease, with the only US FDA-approved treatment being intravenous thrombolytics administered at less than 3 h from the time the patient was last seen normal [7]. The MERCI© clot-retrieval system is also an FDA-approved device that can be used for up to 8 h after the patient was last seen normal by a trained interventional neuroradiologist and neurosurgeons to aid stroke treatment [7,11]. An unenhanced CT scan is used for inclusion criteria and to rule out hemorrhage. With all ischemic strokes, hemorrhagic risk is increased with time and the sooner patients are treated the better their chance of a good outcome.

Tissue plasminogen activator (TPA, specifically alteplase) for acute ischemic stroke has been studied for more than 12 years. The original article that was published in the *New England Journal of Medicine* in 1995 [12] by The National Institute of Neurological Disorders and Stroke (NINDS), rt-PA study group [3–9], demonstrated that there was no immediate improvement in patient outcome. The results of the NINDS part 2 demonstrated good clinical results at 3 months in 333 patients. The magnitude of the clinical improvement that was observed in this trial was recently revalidated in the third European Cooperative Acute Stroke Study (ECASS-III) and published in the *New England Journal of Medicine* in 2008 [7–13].

Patients who met all the outcome scores of a Barthel index greater than 95, modified Rankin scale less than 1, Glasgow outcome scale equal to 1, and NIHSS less than 1 look clinically normal, and therefore have had a dramatic outcome despite facing a potentially life-threatening stroke.

The results of the studies show that patients treated with TPA were at least 30% more likely to have minimal or no disability at 3 months as measured by these outcome scales. What this translates into in the clinical arena is the following: for patients who have sustained an ischemic stroke, approximately one out of three stay the same, one out of three progress and die, and one out of three will improve.

TPA increases the likelihood of improvement to 40–50% and yet, while the risk of hemorrhage is greater in treated patients, mortality rates are similar. This may occur because perfusion to the area of the ischemic penumbra may be more important than the subsequent reperfusion injury sometimes manifested as intracranial hemorrhage.

It becomes important to explain as much of this information to patients and their families as possible to help guide and assist them through treatment options. The recent ECASS-III trial results suggest that the window may be extended to 4.5 h after the onset of stroke symptoms, with the only caveat being that for intravenous TPA the sooner treatment is given, the better. Having more time does not mean we should be allowed to take more time. Community hospitals can also safely administer intravenous TPA if strict NINDS protocols are followed [14].

At the recent International Stroke Conference 2009 (17–20 February, CA, USA), it was noted that stroke neurologists are looking for reasons to treat patients with TPA, instead of reasons not to treat. This is a significant shift in the approach to the treatment of this potentially devastating and life-threatening condition [7–13,15].

More TPA is currently being used for stroke patients, and angioedema has become a more well-recognized but rare complication [7]. It is a reaction that presents with oral and pharyngeal swelling, along with tongue edema similar to ACE inhibitor reactions. Prompt recognition of this reaction is essential in order to prevent increased morbidity and mortality. Airway protection, cessation of the drug's administration and antihistamines with steroids should be administered.

The MERCI clot-retrieval system is an effective mechanical embolectomy device that has demonstrated good recanalization rates of up to 57% in the multi-MERCI trial. It is important to note that in this study the primary end point was recanalization of the target vessel. Among patients who experienced recanalization, there was a twofold survival advantage and a significantly higher proportion of patients who lived without significant disability [16,17].

The trial was unable to conclusively demonstrate that thrombectomy actually improves stroke outcome, but the absolute difference of a 27% reduction in mortality between recanalizers and nonrecanalizers is proof that the device works, and by allowing perfusion appears to improve mortality rates. Further studies of the device are needed to provide more conclusive evidence that its use can improve stroke outcomes.

There are other factors helping ischemic stroke patients to recover and survive. The application of standing order sets, early mobilization and rehabilitation, along with deep vein thrombosis prophylaxis and assessment of swallowing before feeding, have been added to the 2007 stroke guidelines for this reason. Dedicated stroke units, along with defining an acute stroke rapid-response team, are also improving patient outcomes, and various successful models exist throughout the country [7–13].

An important target blood pressure is 185/110 mmHg for entry into acute treatment protocols. Rapid drops in blood pressure and overcorrection can result in a poor outcome. The target blood pressure advised calls for a moderate reduction in blood pressure, not normal blood pressure. It is important to note that the clinician can lower the initial blood pressure to bring the patient in range for the administration of TPA.

Modern ischemic stroke care is evolving. Intravenous TPA and the MERCI clot-retrieval system should be considered in all eligible patients. In order to help aid our patients, revised stroke guidelines and blood pressure recommendations should be followed. Acute rapid stroke teams also help to facilitate treatment.

The sooner a patient is treated the better. Look for reasons to treat with these modalities, instead of reasons not to treat [7–16].

Dynamic CT, MRI scanning and telemedicine are currently being utilized and studied at multiple stroke centers throughout the world, and will have a profound effect on shaping the future of modern stroke care.

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