

Tsuei BJ, Kearney PA

Hypothermia in the trauma patient

Injury 2004; **35**: 7-15

Hypothermia is a common finding in severely injured patients. Historically described as a consequence of wartime casualties where cold exposure was common, this topic has resurfaced in the trauma literature because of the increasing recognition of the morbidity and mortality associated with hypothermia. Hypothermia, along with acidosis and coagulopathy, has been identified as a component of the "lethal triad" in injured patients, and has been shown to contribute to increased mortality in these patients. Decreases in core temperature during the

course of initial evaluation and resuscitation are common, and can contribute to poor outcomes in the injured patient. As induced hypothermia has been shown to be beneficial in some clinical situations, recent animal studies have attempted to investigate whether hypothermia in the trauma patient has any beneficial effects. This review examines the incidence and pathophysiology of hypothermia, and discusses mechanisms of heat loss and rewarming techniques that can be utilized in the trauma patient.

Comment: This is a thorough review of the present knowledge of the effects of hypothermia in the trauma victim. Physiological effects, causes as well as management of hypothermia is discussed in detail. The authors conclude their review by this statement: "Thus, although hypothermia may be protective by decreasing oxygen consumption, the effect of prolonged hypothermia during resuscitation after haemorrhagic shock is as yet unclear. Given these findings, the current generally accepted practice of simultaneous aggressive rewarming with fluid resuscitation may be the best practice until further studies indicate otherwise."

Hildebrand F, Giannoudis PV, van Griensven M, Chawda M, Pape HC

Pathophysiologic changes and effects of hypothermia on outcome in elective surgery and trauma patients

Am J Surg 2004; **187**: 363-71

Generally, hypothermia is defined as a core temperature <35°C. In elective surgery, induced hypothermia has beneficial effects. It is recommended to diminish complications attributable to ischemia reperfusion injury. Experimental studies have shown that hypothermia during hemorrhagic shock has beneficial effects on outcome. In contrast, clinical experience with hypothermia in trauma patients has shown accidental hypothermia to be a cause of posttraumatic complications. The different etiology of hypothermia might be one reason for this disparity because induced therapeutic hypothermia, with induction of poikilothermia and shivering prevention, is quite different from accidental hypothermia, which results in

physiological stress. Other studies have shown evidence that this contradictory effect is related to the plasma concentration of high-energy phosphates (e.g., adenosine triphosphate [ATP]). Induced hypothermia preserves ATP storage, whereas accidental hypothermia causes depletion. Hypothermia also has an impact on the immunologic response after trauma and elective surgery by decreasing the inflammatory response. This might have a beneficial effect on outcome. Nevertheless, posttraumatic infectious complications may be higher because of an immunosuppressive profile. Further studies are needed to investigate the impact of induced hypothermia on outcome in trauma patients.

Comment: As the previous study, this is a review of the effects of hypothermia on trauma victims. The authors detailed discuss the seemingly contradictory findings between experimentally induced hypothermia and real life findings. Again, the authors conclude their review: "The available current literature supports the view that further clinical and experimental studies in polytraumatized patients are necessary to examine whether therapeutic controlled hypothermia could contribute to an improved posttraumatic outcome. The potentially negative aspects should be considered before prospective randomized trials in trauma patients are designed and undertaken".

Vaagenes P, Gundersen Y, Opstad PK

Rapid rewarming after mild hypothermia accentuates the inflammatory response after acute volume controlled haemorrhage in spontaneously breathing rats

Resuscitation 2003; **58**: 103-112.

Accidental hypothermia is a common companion of trauma/haemorrhage, and several clinical studies have identified

reduced body temperature as an independent risk predisposing to increased morbidity and mortality. Accordingly, the

majority of trauma care guidelines prescribe early and aggressive rewarming of hypothermic patients. Enzyme reactions are generally downregulated at temperatures below 37°C, including most of those responsible for the inflammatory response. The rationale for adhering to these recommendations uncritically may therefore be questioned. In a rat model of mild hypothermia and haemorrhagic shock we wanted to compare the influence of rapid rewarming with persistently reduced temperature on the synthesis of early inflammatory mediators and organ function. Thirty-four male albino Sprague–Dawley rats were studied. Withdrawal of 2.5 ml blood/100 g body weight was performed over 10 min, with simultaneous reduction of body temperature to 32.5–33.5 °C. Seventy-five minutes after initiation of bleeding, two-thirds of the shed blood was retransfused. One group (n=17) was rewarmed to normothermia, the other (n=17) was kept

hypothermic. The study was terminated after an observation period of 2 h. At the end of the study the rewarmed animals had a significantly lower mean arterial pressure, higher heart rate, higher synthesis of reactive oxygen species from peritoneal phagocytes, increased circulating levels of nitric oxide, and higher values of the organ markers aspartate aminotransferase and urea. The pro-inflammatory cytokines TNF- α and IL-6, the anti-inflammatory cytokine IL-10, the organ markers alanine aminotransferase, γ -glutathione S-transferase and creatinine, as well as organ injury scores were equal in both groups. Three rewarmed rats died prematurely, versus one hypothermic animal. In conclusion, the results suggest that during the early stages after haemorrhagic shock, rapid rewarming from mild hypothermia may have unfavourable effects both on basic haemodynamic variables, and on the internal inflammatory environment of cells and tissues.

Comment: *This is a carefully performed experimental study in a series where the authors have studied the effects of hemorrhage and hypothermia in a rat model. A previous study from the same group showed beneficial effects of maintained hypothermia in the resuscitative phase when considering inflammatory response and organ injury (1). The intention in the present study was to evaluate early inflammatory response and organ function as a function of rewarming strategy, “mimicking the clinical situation as far as possible”. And here I think we are at the clou, as the experimental design did not contain any tissue injury. Does a situation with controlled bleeding and retransfusion resemble the multiply injured patient with extensive tissue injury? This may be part of the explanation for the lack of benefit from hypothermia in the clinical setting with injured, hypovolemic patients.*

Janczyk RJ, Howells GA, Bair HA, Huang R, Bendick PJ, Zelenock GB

Hypothermia is an independent predictor of mortality in ruptured abdominal aortic aneurysms

Vasc Endovascular Surg 2004; **38**: 37-42

Hypothermia is known to significantly increase mortality in trauma patients, but the effect of hypothermia on outcomes in ruptured abdominal aortic aneurysms (RAAA) has not been evaluated. The authors reviewed their experience from 1990 to 1999 in 100 consecutive patients who presented with RAAA and survived at least to the operating room for surgical treatment. There were 70 men and 30 women, with a mean overall age of 74 +/-8 years. Overall mortality was 47%. Univariate ANOVA (analysis of variants) showed significant correlation with mortality for decreased intraoperative temperature, decreased intraoperative systolic blood pressure, increased intraoperative base deficit, increased blood volume transfused, increased crystalloid volume (all $p < 0.001$); decreased preoperative hemoglobin ($p = 0.015$); and increased age ($p = 0.026$). Patient sex, initial preoperative temperature, preoperative systolic blood pressure, and operating room time were not correlated with mortality in the univariate analysis. Using these same clinical variables, multiple logistic regression analysis showed only 2 factors independently

correlated with mortality: lowest intraoperative temperature ($p = 0.006$) and intraoperative base deficit ($p = 0.009$). The mean lowest temperature for survivors was 35 +/-1 degrees C and for nonsurvivors 33 +/-2 degrees C ($p < 0.001$). When patients were grouped by lowest intraoperative temperature, those whose temperature was < 32 degrees C ($n = 15$) had a mortality rate of 91%, whereas patients with a temperature between 32 and 35 degrees C ($n = 50$) had a mortality rate of 60%. In the group that remained at or > 35 degrees C ($n = 35$) the mortality rate was only 9%. A nomogram of predicted mortality versus temperature was constructed from these data and showed that for temperatures of 36, 34, and 32 degrees C the predicted mortality was 15%, 49%, and 84%, respectively. The authors conclude that hypothermia is a strong independent contributor to mortality in patients with ruptured abdominal aortic aneurysms and that very aggressive measures to prevent hypothermia are warranted during the resuscitation and treatment of these patients.

Comment: *A seemingly carefully controlled retrospective study indicating a separate strong predictive value of the development of hypothermia during major vascular surgery.*

Is hypothermia in the victim of major trauma protective or harmful?

A randomized, prospective study.

Ann Surg 1997; **226**: 439-447

Objective: The purpose of this randomized, prospective clinical trial was to determine whether hypothermia during resuscitation is protective or harmful to critically injured trauma patients.

Summary background data: Hypothermia has both protective and harmful clinical effects. Retrospective studies show higher mortality in patients with hypothermia; however, hypothermia is more common in more severely injured patients, which makes it difficult to determine whether hypothermia contributes to mortality independently of injury severity. There are no randomized, prospective treatment studies to assess hypothermia's impact as an independent variable.

Methods: Fifty-seven hypothermic ($T \leq 34.5$ C), critically injured patients requiring a pulmonary artery catheter were randomized to a rapid rewarming protocol using continuous arteriovenous rewarming (CAVR) or to a standard rewarming (SR) control group. The primary outcome of interest was first 24-hour blood product and fluid resuscitation requirements.

Other comparative analyses included coagulation assays, hemodynamic and oxygen transport measurements, length of stay, and mortality.

Results: The two groups were well matched for demographic and injury severity characteristics. CAVR rewarmed significantly faster than did SR ($p < 0.01$), producing two groups with different amounts of hypothermia exposure. The patients who underwent CAVR required less fluid during resuscitation to the same hemodynamic goals (24,702 mL vs. 32,540 mL, $p = 0.05$) and were significantly more likely to rewarm ($p = 0.002$). Only 2 (7%) of 29 patients who underwent CAVR failed to warm to 36 C and both died, whereas 12 (43%) of 28 patients who underwent SR failed to reach 36 C, and all 12 died. Patients who underwent CAVR had significantly less early mortality ($p = 0.047$).

Conclusion: Hypothermia increases fluid requirements and independently increases acute mortality after major trauma.

Comment: *This study is one of the few randomised studies evaluating rewarming strategies in victims of severe trauma. See further general comments below.*

General comments:

The last issue of this journal focused on the beneficial effects of hypothermia after global cerebral ischemia. It would be tempting to consider deliberate hypothermia in the trauma patient as well. If hypothermia works in the experimental setting, why shouldn't it work in clinical practice? First, the clinical setting differs from the experimental setting because the amount of tissue injury in the experimental setting generally is less and has less physiological impact as compared to the trauma-related hypothermia. Secondly, Hildebrand and co-workers speculate about the order of events - if hypothermia precedes hemorrhage the plasma concentration of ATP will remain unchanged, while in severe tissue injury the decrease in ATP correlates to an anaerobic metabolic state that is related to less heat production. As the origin of hypothermia is different, so will the outcome be. We are probably comparing two different clinical entities, of which we only know a little. The overwhelming amount of clinical evidence indicates a strong correlation between temperature and survival in the traumatized patient.

Non-intended hypothermia in trauma victims is common, and occurs early during the resuscitative phase, according to Tsuei. We're probably all guilty in paying too little attention to this. Especially in the patients with reduced consciousness - not to mention those in anaesthesia - heat loss is fast and asymptomatic. But it seems that hypothermia is easily preventable. In a study of 170 patients in Northern Iraq and Cambodia (2) we found a significantly reduced frequency of hypothermia in the intervention group after an average prehospital transportation of 6.6 hours - with only basic interventions to reduce heat loss and warming of infusions.

In conclusion, although there seem to be evidence that active cooling after global cerebral ischemia reduces morbidity and mortality, we should still continue to strive to maintain normothermia in trauma victims until good research - in this group of patients or comparable animal settings - indicates benefit from deliberate hypothermia.

References.

1. Gundersen Y, Vaagenes P, Pharo A, Valø ET, Opstad PK. Moderate hypothermia blunts the inflammatory response and reduces organ injury after acute haemorrhage. *Acta Anaesthesiol Scand* 2001; **45**: 994-1001
2. Husum H, Olsen T, Murad M, Heng YV, Wisborg T, Gilbert M. Preventing post-injury hypothermia during prolonged prehospital evacuation. *Prehosp Disast Med* 2002; **17**: 23-26

Montazeri A

Road-traffic-related mortality in Iran: a descriptive study

Public Health 2004; **118**: 110-113

Road traffic accidents are considered to be the second highest cause of mortality in Iran. A study was conducted to describe road-traffic-related mortality data in Iran in a given period. All Iranian mortality data on road traffic accidents between March 1999 and 2000 (one complete Iranian calendar year) were obtained. The main variables studied were deceased's gender, age, education level, status (i.e. driver, car occupant, etc.), cause and place of death. A total of 15482 individuals died from road traffic accidents in Iran in the study period. A disproportionate number of deceased individuals were male

(79%), mostly aged 40 years or less (65%), and who were pedestrians or car occupants (62%). Head injury was the most common cause of road-traffic-related mortality (66%) in males and females of all ages. Following road traffic accidents, 57% of deaths occurred pre-hospital. Head injury is the most common single cause of mortality attributable to road traffic accidents in Iran, and since most deaths occur pre-hospital, it seems many are preventable. To overcome this major public health problem, there is an urgent need to develop a comprehensive injury control policy and strategy in Iran.

Zafarghandi MR, Modagheh MHS, Roudsari BS

Preventable Trauma Death in Tehran: An Estimate of Trauma Care Quality in Teaching Hospitals

J Trauma 2003; **55**: 459-465

Objective : The purpose of this study was estimate the number of preventable trauma deaths in teaching hospitals in Tehran.

Methods: We evaluated the complete prehospital, hospital, and postmortem data of 70 trauma patients who had died during a 1-year period in two of the largest university hospitals in Tehran with a multidisciplinary panel of experts.

Results: Panel members identified 26% of all trauma deaths as preventable deaths. From 31 non-central nervous system-related deaths, 17 and 6 cases were identified as surely

preventable and probably preventable, respectively. In central nervous system-related deaths, 5% of the deaths overall (2 of 38 cases) were identified as surely preventable or probably preventable. Sixty-four cases of medical errors were identified in 31 trauma deaths and 80% of these errors were directly related to the death of the patients.

Conclusion: The high preventable trauma death rate in our teaching hospitals indicates that a relatively significant percentage of trauma fatalities could have been prevented by improving prehospital and in-hospital trauma care.

Moini M, Rezaishiraz H, Zafarghandi MR

Characteristics and Outcome of Injured Patients Treated in Urban Trauma Centers in Iran

J Trauma 2000; **48**: 503-507

Comments: These three papers are from Iran, the two latter from a very active research unit in the Sina Medical Center in Tehran. More than one million persons die each year from road traffic injuries. 88 percent of these deaths are in low- and middle- income countries (3). These injuries does not hit indiscriminately. Not only are the lowest developed countries hit hardest, but also the poor inhabitants in these countries are at greatest risk. These countries are however aware of the situation, and able to describe it with a precision and quality that leaves many of our hospitals and countries far behind. Basic first responder care for victims may have a tremendous effect in these settings, and if combined with structural, political and economical changes may improve survival and reduce morbidity. Keep an eye on medical development in the third world. Not only will you personally learn a lot about your own life – and theirs, but also the major breakthrough in trauma care for the majority of the world's population will appear there. *Injury*, *Journal of Trauma* and also the major general medical journals are publishing an increasing number of high quality papers from the third world. Look out!

Reference:

3. Peden MM, Krug E, Mohan D et al. Five-year WHO strategy on road traffic injury prevention. Geneva: World health Organization; 2001.