

efficacy of fluid warmers and rapid infusion devices.

In the final section, "New Horizons in Synthetic Blood Substitutes," Drs. Como and Malangoni review the complex issues surrounding the use of hemoglobin solutions in trauma in their article on hemoglobin-based oxygen carriers. They report on the experience with PolyHeme (human hemoglobin-based temporary red cell substitute), the only hemoglobin-based oxygen carrier that has been evaluated in severely injured patients in the United States. Final results of the PolyHeme study, if favorable, may herald the introduction of hemoglobin-based oxygen carriers to patient care. Dr. Schubert concludes this issue by examining the potential clinical uses and effectiveness of hemoglobin-based oxygen carriers and perfluorocarbons. The long shelf life, long circulation half-life, and

good oxygen-carrying capacity and tissue oxygen delivery make these compounds particularly attractive in patients with high blood loss, that is, trauma patients. In his article, Dr. Schubert evaluates the different hemoglobin solutions and the pitfalls associated with their clinical use.

As editors and principle organizers of this special issue, we have attempted to provide a concise, up-to-date reference on massive transfusion and management of hemorrhage in the trauma patient, a reference that integrates both basic science and clinical practice. We sincerely hope that you, the reader, will obtain essential knowledge from this publication that will enable you improve your clinical practice when caring for trauma patients.

## SECTION I. ETIOLOGY AND PATHOPHYSIOLOGY

### Trauma, A Disease of Bleeding

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**Learning Objectives:** 1) To describe alternatives to the use of vital signs in determining depth of shock. 2) To define a newer resuscitation scheme that may limit the blood loss. 3) To describe the role activated factor VIIa may have as an adjunctive hemostasis agent.

#### Abstract

Acute blood loss is the most common life-threatening problem immediately after injury. Diagnosis is obvious in some patients but can be far more subtle in others. Vital signs often underestimate the degree of hemorrhage. Other parameters such as measuring the degree of metabolic acidosis can be helpful. In addition, newer technology can noninvasively measure the adequacy of perfusion by measuring blood flow in vascular beds that are particularly sensitive to blood loss. Certainly some patient populations, such as the elderly, are more sensitive than others to loss of circulating blood volume. Rapid diagnoses are essential in these patients to avoid cardiovascular collapse. Resuscitation strategies have changed recently as well. Limited fluid resuscitation may be better than large-volume crystalloid resuscitation. Transfusion therapies have evolved with more liberal use of fresh-frozen plasma. Finally, factor VIIa can be extremely helpful as adjunctive homeostasis. These issues will continue to require refinement in order to provide optimum care.

Acute blood loss is a very common problem following injury. Rapid recognition and restoration of homeostasis is the cornerstone of the initial care of any badly injured patient. Untreated, hemorrhage robs the cardiovascular system of the preload necessary to ensure adequate cardiac output and peripheral oxygen delivery. Inadequate perfusion, even if it is not associated with overt hypotension, can set off the neurohumoral cascade, ultimately leading to sequential organ failure.<sup>1</sup> This is especially important, as the mortality from established organ failure has not changed since it was first described almost 25 years ago.<sup>2</sup> Thus, it is imperative that hemorrhage is recognized and treated early.

The recognition of acute hemorrhage can be difficult. The American College of Surgeons has developed the classification scheme for hemorrhage, stratifying blood loss from stage 1 (<15% of total circulating blood volume) to stage 4 (>40% of total circulating blood volume).<sup>3</sup> Changes in various physiologic parameters as hemorrhage volume increases are listed in Table 1. Unfortunately, many of these signs and symptoms are nonspecific. In addition, a number of other parameters will affect the patient's vital signs and physical findings. For instance, the rapidity of volume loss may be as important as the total volume of hemorrhage.<sup>3</sup> Underlying cardiovascular reserve also plays a role. Young people with very compliant blood vessels may compensate extremely well for large-volume blood loss, even as much as 40% to 50% of total circulating blood volume.<sup>4</sup> They then develop sudden cardiovascular compromise when compensatory mechanisms fail. Elderly people, on the other hand, will develop cardiovascular insufficiency and hypotension with much smaller blood loss.<sup>5</sup> Prescription medication and/or illicit drugs will also influence the cardiovascular response to injury.<sup>6,7</sup> The amount of resuscitation, if any, the patient received in the field will affect cardiovascular response as well.<sup>4</sup>

Data from the past 15 years strongly suggest that normally followed vital signs are a very poor indication of the depth of hemorrhage.<sup>8</sup> In particular, blood pressure and pulse rate, the two vital signs often used in the emergency department to gauge hemorrhage, are tremendously nonspecific. Central venous oxygen saturation and mixed venous oxygen saturation are far more sensitive and reliable measurements of acute volume loss.<sup>8,9</sup> Degree of metabolic acidosis, as measured by the base deficit from an arterial blood gas, is also extremely helpful in gauging the degree of shock.<sup>10</sup> Base deficit has been shown to correlate with transfusion

**Table 1. American College of Surgeons Classification of Acute Hemorrhage\***

	<b>Class I</b>	<b>Class II</b>	<b>Class III</b>	<b>Class IV</b>
Blood loss (mL)	<750	750–1,500	1,500–2,000	≥2,000
% Blood volume lost	<15	15–30	30–40	≥40
Pulse rate	<100	>100	>120	≥140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure (mm Hg)	Normal or increased	Decreased	Decreased	Decreased
Capillary refill	Normal	Delayed	Delayed	Delayed
Respiratory rate	14–20	20–30	30–40	>35
Urine output	>30	20–30	5–15	Negligible
Mental status	Slightly anxious	Mildly anxious	Anxious, confused	Confused, lethargic
Recommended fluid replacement	0.9% saline, 3:1	0.9% saline, 3:1	0.9% saline + red cells	0.9% saline + red cells

\*Adapted from the American College of Surgeons Committee on Trauma. *Advanced Trauma Life Support Program for Physicians, Student and Instructor Manual*. Chicago: American College of Surgeons, 1993.  
Amounts are based on the patient's initial presentation. Assumes 70-kg male with a blood volume of approximately 70 mL/kg.

requirements, intensive care unit (ICU) stay, and ultimate outcome.<sup>11,12</sup> During initial resuscitation, base deficit should also correlate with serum lactate level. The ability to clear lactate to normal is one of the most important predictors of survival following hemorrhage and injury.<sup>13,14</sup>

Once the clinician has made the diagnosis of acute blood loss, several issues become important. Traditional dogma suggests that restoration of forward flow by crystalloid resuscitation followed by blood is optimal therapy. However, increases in blood pressure produced by fluid may, in fact, increase blood loss by displacing the hemostatic clot that was formed at the time of hypotension.<sup>15</sup> However, there are now data to suggest that sustained hypotension produces a more injurious shock insult than do multiple episodes of shock and resuscitation.<sup>16</sup> Thus, the clinician must estimate the degree of hemorrhage, the depth of shock, and the time to definitive hemostasis when making a decision.

Regardless of the resuscitation decision, patients who demonstrate ongoing bleeding require definitive hemostasis. Serial blood gas determinations and/or central venous oxygen saturation determination may be very helpful in determining whether blood loss is continuing.<sup>8,9</sup> Unfortunately, the relationship between blood loss and physiologic parameters may be different after resuscitation than they were during hemorrhage. For instance, approximately 12 to 16 hours following resuscitation, the relationship changes between base deficit and anion gap versus serum lactate, and anion gap and base deficit no longer correlate with lactate.<sup>17</sup> During this time, one must directly measure serum lactate as it cannot be inferred from either of the other two measurements. When resuscitation decisions are based on these parameters, therapy will be inappropriate almost 50% of the time.

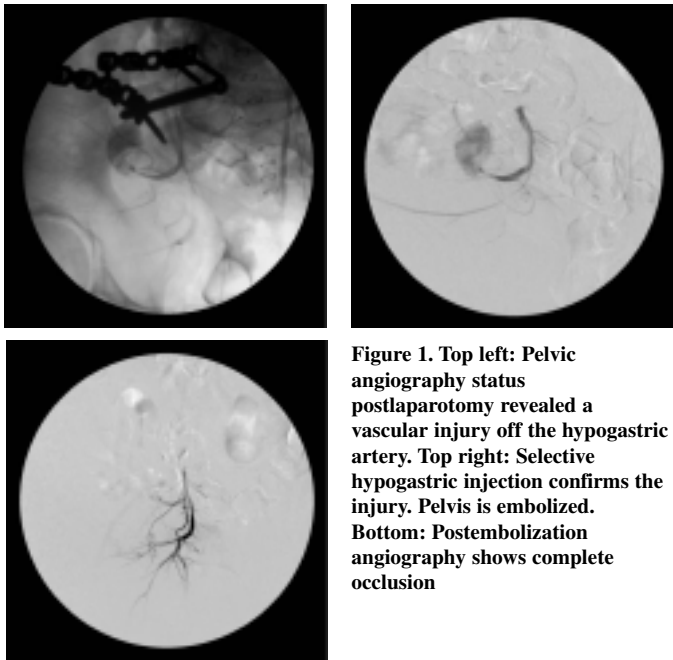
Elderly patients with poor underlying cardiovascular reserve often require invasive monitoring to precisely measure the physiologic deficits and to guide therapy. In fact, in high-risk elderly patients (Table 2), monitoring must be instituted extremely early, within 2 to 3 hours of injury, if possible. There is a statistically significant decrease in survival when monitoring is delayed as long as 6 hours.<sup>5</sup> Even young people may have inadequate cardiovascular response to substantial injuries. A surprising percentage of young patients with either blunt or penetrating trauma benefit from invasive monitoring and require volume and pharmacologic therapy to support cardiovascular performance and clear lactate.<sup>18,1</sup>

Clearly, achieving hemostasis is the most important part of resuscitating the trauma victim. Resuscitation efforts will not be successful until blood loss is arrested. Substantial hemorrhage usually requires operative therapy. Recently, however, other techniques have emerged and should be considered, even in patients with hypotension. The diagnosis of ongoing blood loss with angiography and hemostasis with transcatheter embolization is a real alternative to standard operative therapy.<sup>20</sup> This has been a mainstay of therapy for many years in patients bleeding from blunt pelvic injury (Fig. 1). Retroperitoneal exploration in these patients is fraught with danger, and embolization is far preferable in almost every case. These techniques have been extended to other areas of the body. More recently, transcatheter embolization has been used for nonoperative management of solid visceral injuries within the abdomen. Treatment algorithms using splenic artery embolization in patients managed nonoperatively have resulted in a greater than 90% rate of splenic salvage<sup>21</sup> (Fig. 2).

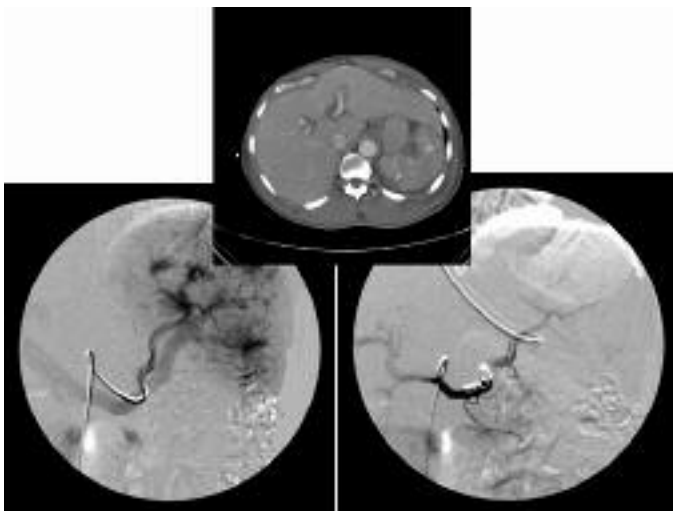
Table 3 depicts our guidelines for nonoperative management of pelvic injuries. This is far higher than any series using observation and/or operation alone. In addition, embolotherapy may be extremely helpful in patients with vascular injuries in relatively inaccessible areas. Exposure of the carotid artery in Zone 3 of the neck is extremely difficult. Embolotherapy has a real role in managing these injuries. Temporary hemostasis can be achieved with percutaneous balloons used at the time of diagnostic angiography. This temporary control of bleeding allows further imaging, ongoing resuscitative efforts, and time to plan definitive therapy. In addition to its usefulness in Zone 3 of the neck, angiographic hemostasis has great utility in injuries to the thoracic outlet and deep within the pelvis.

**Table 2. Geriatric Patients**

- Initial systolic blood pressure <130 mm Hg
- Closed-head injury
- Multiple long-bone fractures
- Metabolic acidosis
- Pedestrian–motor vehicle mechanism



**Figure 1.** Top left: Pelvic angiography status postlaparotomy revealed a vascular injury off the hypogastric artery. Top right: Selective hypogastric injection confirms the injury. Pelvis is embolized. Bottom: Postembolization angiography shows complete occlusion



**Figure 2.** Computed tomography scan reveals splenic injury. Angiography demonstrates multiple pseudoaneurysms, which are treated with proximal coil embolization

Embolization techniques can be combined with surgery, allowing the patient to benefit from both techniques. Ideally, this should be done in the operating room and, in some centers, biplanar angiography is available. Patients who may benefit from this technology are those with a combination of intra-abdominal blood loss and pelvic blood loss. The pelvic blood loss can be embolized while intra-abdominal blood loss is treated directly via surgery. Some patients are too profoundly ill to allow definitive surgery. Damage control techniques should then be employed. In these settings, major vascular injuries are repaired and gastrointestinal contamination controlled. The patient is then packed with laparotomy pads and taken to the ICU for ongoing resuscitation and warming techniques. Once patients are resuscitated, they can return to the operating room for unpacking, gastrointestinal reconstruction, and any other procedures necessary. Angiographic embolotherapy has a role in

**Table 3. Nonoperative Management of Splenic Injuries and Splenic Injury Grading Scale**

- A. Hemodynamic stability:** Nonoperative management of splenic injury can be considered when all of the following conditions have been met:
1. Diagnosis of splenic injury on computed tomography (CT) scan
  2. Hemodynamically normal patient (to be determined by the trauma attending)
    - a. Lack of hypotension
    - b. Systolic blood pressure >100 mm Hg
    - c. Less than 2 liters of crystalloid resuscitation and/or an appropriate response to resuscitation in a patient with multiple injuries in which the bleeding is attributed to other sources
- B. Management and Grade Injury** (see below for definitions of grade of injury)
1. **Grade I injuries:**  
The patient should be admitted and serial hemoglobin/hematocrits and abdominal examinations should be performed; if hemoglobin/hematocrits and abdominal examinations are stable, then the patient may be discharged the following day. No repeat CT scan is necessary unless the abdominal examination changes, or there is an unexplained drop in hemoglobin/hematocrit.
  2. **Grade II injuries:**
    - a. CT scanning with serial hemoglobin/hematocrits and abdominal examinations until two stable examinations and hematocrits are obtained. Then the patient may be transferred to a regular, nontelemetry floor.
    - b. Repeat CT scanning should be performed at 24–48 hours with discharge following a CT scan demonstrating no evidence of vascular injury.
  3. **Grade III injuries and no evidence of vascular injury:**
    - a. Undergo angiographic evaluation and embolism as appropriate **during daylight angiography hours** (i.e., nighttime admissions can be performed as first case the following day). Those admitted during the day should undergo their angiography during the day at next available IR slot.
    - b. Repeat CT scan at 48–72 hours
    - c. Discharge following a CT demonstrating no delayed pseudoaneurysm or bleed if otherwise appropriate.
  4. **Grades IV and V injuries:**
    - a. Require **immediate** evaluation and angioembolization.
    - b. Should undergo repeat CT scan at 48–72 hours
    - c. Consider admitting to intermediate or intensive care unit following angiography: monitor hourly vital signs, bed rest, nothing by mouth, and serial hemoglobin/hematocrits q8hr until stable.
    - d. Discharge following a CT demonstrating no delayed pseudoaneurysm or bleed if otherwise appropriate.
  5. **Pseudoaneurysm/vascular injury present:**  
Patients with **any grade injury** with evidence of pseudoaneurysm or contrast blush require immediate evaluation and angioembolization.

these patients as well and can be used postoperatively to supplement surgical hemostasis. Injuries deep within the substance of the liver, in the retroperitoneum, or in the pelvis may be more easily controlled via embolization than surgery.

There are several new advances in the diagnosis of shock and therapy for hemorrhage that may provide new options for the clinician at the bedside in the near future. We have known for some time that blood flow does not fall equally in all vascular beds following hemorrhage. Certainly one of the most important compensatory mechanisms following hemorrhage is vasoconstriction limiting blood flow to skin and skeletal muscle, preserving flow to the more central organs. The splanchnic circulation is also very sensitive to acute blood loss and blood flow falls early after hemorrhage. Until recently, this has not been measurable at the bedside.

In 1982, Fiddian-Green et al<sup>22</sup> described the method to measure intracellular pH in the stomach. Gastric tonometry then became commercially available. The technique involves placing a tube in the stomach that has a balloon attached to the tip. The balloon is semipermeable and is filled with saline. Gastric acid must be neutralized for this technique to work. The balloon must be in contact with the gastric mucosa. The saline in the balloon equilibrates with the gastric mucosa cells and the saline can be withdrawn. The pH of the mucosal cells can be calculated using the Henderson-Hasselbach equation.

Although this technology has gained some favor in the ICU, it is cumbersome and time-consuming, thus it has little utility in the emergency department. Sato et al<sup>23</sup> and Nakagawa et al,<sup>24</sup> however, have demonstrated that all cells in the foregut behave the same as the stomach, including the oral mucosa. They have developed a sublingual capnometer that calculates PCO<sub>2</sub> of the oral mucosal cell (Fig. 3). They have also demonstrated that this correlates with serum lactate in the ICU.<sup>25</sup> Recently, we have demonstrated that sublingual capnometry is a sensitive measure of acute hemorrhage.<sup>26</sup> The clinical utility of this device remains to be elucidated.

Factor VIIa is a recombinant product that is approved by the Food and Drug Administration for use in hemophiliacs. As early as 1999, antidotal reports appeared describing the use of factor VIIa in hemorrhaging trauma patients who developed coagulopathy from massive transfusion.<sup>27,28</sup> Factor VIIa, when used in doses of 90 to 110 mcg/kg, is extremely expensive and may cost between \$7,000 and \$10,000 per dose, lessening enthusiasm for its use. There is a single randomized perspective trial in Europe examining the utility of factor VIIa.<sup>29</sup> In the study, patients were randomized after receiving eight units of blood. The study demonstrated no statistically difference in mortality but there were fewer transfusions in patients who received factor VIIa.



**Figure 3. Sublingual capnometry measures sublingual PCO<sub>2</sub>, which correlates with a gastric intracellular pH.**

**Table 4. Guidelines for Use of Factor VIIa**

- “Off-label” use requested by attending physician
- Gatekeeper approval required
  - Life-threatening hemorrhage
  - Coagulopathy
  - Failure of conventional therapy
  - Nonfutile

The Shock Trauma Center in Baltimore has the largest single institutional experience in North America. Table 4 depicts our guidelines for factor VIIa line. In our experience 20% of patients did not respond.<sup>30</sup> The survival rate in the 80% of patients who did respond was 50%. In addition, we have defined patients in whom factor VIIa use would appear to be futile.<sup>31</sup> We have recently begun using much smaller doses of factor VIIa in patients with moderate coagulopathy (D. Stein, personal communication, 2007). We currently use 1.2 mg in such patients, the smallest dose commercially available. The cost for this dose is approximately \$900, which is equal to four units of fresh-frozen plasma in our hospital. The results from minidose factor VIIa use have been quite good. The United States military has a liberal policy and use factor VIIa as part of their resuscitation scheme. They have also been able to demonstrate fewer transfusions in patients who have received factor VIIa early.<sup>32</sup>

Clearly there are some complications associated with factor VIIa, although the rate of complications has not been clearly demonstrated in trauma patients. Recent work from our institution demonstrates that 8.7% of patients who receive factor VIIa have thromboembolic complications (R. P. Dutton, personal communication, 2007). This is not to say that all complications are related to factor VIIa. As with any other drug, analysis of the risk/benefit ratio is important when making a decision to use any therapy.

Traditional resuscitative schemes involve using crystalloid in the red blood cells as the initial choice. Como et al<sup>33</sup> recently demonstrated that patients who received massive transfusions, defined as more than 10 units of blood, ultimately receive a unit of fresh-frozen plasma for every unit of red cells transfused. We have modified our transfusion scheme and now use red cells and plasma in a 1:1 ratio early on in patients who have large-scale transfusion needs. Holcomb et al (personal communication, 2007) have also demonstrated better survival in military with more liberal use of plasma.

Hypoperfusion is a common complication after injury. Early recognition of bleeding is key to the optimal care of trauma patients. Normally followed vital signs underestimate the degree of physiologic deficit. Limited crystalloid resuscitation is prudent initially, at least until blood loss is controlled. New technology may soon be available to help with the diagnosis of hemorrhage. Early use of fresh-frozen plasma is probably wise in patients with severe hemorrhage using blood and plasma in a 1:1 ratio. The use of factor VIIa requires further work before its role is clearly elucidated. It can be lifesaving in selected patients.

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References

1. Dantzer D. Oxygen delivery and utilization in sepsis. *Crit Care Clin* 1989;5:81-98.
2. Scalea TM, Henry SM. Inotropes in the intensive care unit. In: *Advances in Trauma and Critical Care*, vol. 7. St. Louis: Mosby, 1992.
3. Committee on Trauma, American College of Surgeons. *The Advanced Trauma Life Support Program, Instructors Manual*. Chicago: American College of Surgeons, 1988;59-62.
4. Lewis FR. Prehospital intravenous fluid therapy: a physiologic computerized model. *J Trauma* 1986;26:804-11.
5. Scalea TM, Simon HM, Duncan AL, et al. Geriatric blunt trauma: improved survival with early invasive monitoring. *J Trauma* 1990;30:129-36.
6. Horton JW. Ethanol impairs cardiocirculatory function in treated canine hemorrhagic shock. *Surgery* 1986;100:520-30.
7. Sloan EP, Zalenski RJ, Smith RF, et al. Toxicology screening in urban trauma patients: drug prevalence and its relationship to trauma severity and management. *J Trauma* 1989;29:1647-53.
8. Scalea TM, Holman M, Fuortes M, et al. Central venous blood oxygen saturation: an early accurate measurement of volume during hemorrhage. *J Trauma* 1988;28:725-32.
9. Scalea TM, Hartnett RW, Duncan AO, et al. Central venous oxygen saturation: a useful clinical tool in trauma patients. *J Trauma* 1990;30:1529-44.
10. Rutherford EJ, Morris JA Jr, Reed GW, Hall KS. Base deficit stratifies mortality and determines therapy. *J Trauma* 1992;33:417-23.
11. Davis JW, Shackford SR, MacKersie RC, Hoyt DB. Base deficit as a guide to volume resuscitation. *J Trauma* 1988;28:1464-7.
12. Davis JW, Parks SN, Kaups KL, et al. Admission base deficit predicts transfusion requirements and risk of complications. *J Trauma* 1996;41:769-74.
13. Iberti TJ, Leibowitz AB, Papdakos PJ, Fischer EP. Low cardiac sensitivity of the anion gap as a screen to detect hyperlactatemia in critically ill patients. *Crit Care Med* 1990;18:275-7.
14. Abramson D, Scalea TM, Hitchcock D, et al. Lactate clearance and survival following injury. *J Trauma* 1993;35:584-9.
15. Shaftan GW, Chui C, Dennis C, et al. Fundamentals of physiologic control of arterial hemorrhage. *Surgery* 1965;58:851.
16. Sinha HA, Baron BJ, Buckley MC, et al. Fluid restriction versus early resuscitation in hemorrhagic shock. *J Trauma* 1994;37:1015.
17. Mikulaschek A, Henry SM, Donovan R, Scalea TM. Serum lactate is not predicted by anion gap or base excess after trauma resuscitation. *J Trauma* 1996;40:218-24.
18. Abou-Khalil B, Scalea TM, Trooskin SZ. Hemodynamic responses to shock in trauma patients: the need for invasive monitoring. *Crit Care Med* 1994;22:633-9.
19. Scalea TM, Maltz S, Yelon J, et al. Resuscitation of multiple trauma and head injuries: role of crystalloid fluid and inotropes. *Crit Care Med* 1994;22:1610-5.
20. Panetta T, Sclafani SJA, Goldstein AJ, Phillips TF, Shaftan GW. Percutaneous transcatheter embolization for massive bleeding from pelvic fractures. *J Trauma* 1985;25:1021-9.
21. Sclafani SJA, Scalea TM, Herskowitz M, et al. Salvage of CT-diagnosed splenic injuries: utilization of angiography for triage and embolization for hemostasis. *J Trauma* 1995;39:818-27.
22. Fiddian-Green RH, Pittenger G, Whitehouse WM. Back diffusion of CO<sub>2</sub> and its influence on the intramucosal pH in gastric mucosa. *J Surg Res* 1982;33:39-48.
23. Sato Y, Weil MH, Tang W, et al. Esophageal pCO<sub>2</sub> as a monitor of perfusion failure during hemorrhagic shock. *J Appl Physiol* 1997;82:558-62.
24. Nakagawa Y, Weil MH, Tang W, et al. Sublingual capnometry for diagnosis and quantification of circulatory shock. *Am J Respir Crit Care Med* 1998;157:1838-43.
25. Weil MH, Nakagawa Y, Tang W, et al. Sublingual capnometry: a new noninvasive measurement for diagnosis and quantitation of severity of circulatory shock. *Crit Care Med* 1999;27:1225-9.
26. Baron BJ, Sinert R, Zehtabchi S, Stavile KL, Scalea TM. Diagnostic utility of sublingual Pco<sub>2</sub> detecting hemorrhage in penetrating trauma patients. *J Trauma* 2004;57:69-74.
27. Martinowitz U, Kenet G, Segal E, et al. Recombinant activated factor VII for adjunctive hemorrhage control in trauma. *J Trauma* 2001;51:431-9.
28. O'Neill PA, Bluth M, Gloster ES, et al. Successful use of factor VII for trauma associated hemorrhage in a patient without preexisting coagulopathy. *J Trauma* 2002;52:400-5.
29. Boffard KD, Riou B, Warren B, et al. Recombinant factor VIIa as adjunctive therapy for bleeding control in severely injured trauma patients: two parallel randomized, placebo-controlled, double-blind clinical trials. *J Trauma* 2005;59:8-18.
30. Dutton RP, McCunn M, Hyder M, et al. Factor VIIa for correction of traumatic coagulopathy. *J Trauma* 2005;57:709-19.
31. Stein DM, Dutton RP, O'Connor JV, Alexander M, Scalea TM. Determinants of futility in administration of recombinant factor VIIa in trauma. *J Trauma* 2005;59:609-15.
32. Perkins JG, Schneider MA, Wade CE, Holbrook JB. Early versus late recombinant factor VIIa in trauma patients requiring massive transfusion. *J Trauma* 2007;62:1095-101.
33. Como JJ, Dutton RP, Scalea TM, Edelman BB, Hess JR. Blood transfusion rates in the care of acute trauma. *Transfusion* 2004;44:809-13