A Brief Episode of Hypotension Increases Mortality in Critically Ill Trauma Patients

Mazen S. Zenati, MD, Timothy R. Billiar, MD, Ricard N. Townsend, MD, Andrew B. Peitzman, MD, and Brian G. Harbrecht, MD

Objective: Hypotension is associated with increased mortality, however previous studies have failed to account for the depth and duration of hypotension. We evaluated the effect of the duration of hypotension on outcome in injured patients.

Methods: Trauma patients admitted to the intensive care unit (ICU) from 1999 to 2000 were prospectively evaluated. Patients transferred to a ward ≤ 48 hours after admission were excluded. The lowest systolic blood pressure and duration of all episodes of systolic blood pressure below 90 mm Hg were recorded along with the total ICU length of stay and discharge status. The Kruskal-Wallis test, Pearson χ², and test for trend were used for analysis.

Results: Patients with hypotension during the first 24 hours of ICU care had an increased mortality rate. A brief (≤ 10 minutes) episode of hypotension was associated with increased mortality that increased with duration of hypotension (p = 0.0001). ICU length of stay also increased with duration of hypotension (p = 0.0001).

Conclusion: Brief episodes of hypotension are associated with an increased risk of death in patients requiring admission to the ICU after injury and a longer ICU recovery for those who survive.


Trauma represents the leading cause of death for adults in their most productive years, and incurs substantial short- and long-term disability. The development of multiple organ dysfunction syndrome (MODS) contributes significantly to the morbidity and mortality of traumatic injury and is the leading cause of late deaths after injury. A number of risk factors for the development of MODS and for trauma-related mortality have been identified. The presence of hypotension and shock are frequently implicated in the development of complications and MODS after injury. Prehospital hypotension has been considered a clinical predictor of severe injury and a marker of substantial blood loss even in the face of normal emergency department (ED) systolic blood pressure (SBP). Hypotension was one of the admission variables associated with highest relative risk of death in geriatric blunt trauma patients. Patients with prehospital or emergency department hypotension had an early mortality rate of 12% and a late mortality rate of 32%, suggesting that prehospital hypotension is a valid criterion for trauma team activation.

It is intuitive that the presence of hypotension will be associated with increased mortality and morbidity. However, many previous studies evaluating the effect of hypotension have included substantial numbers of moribund patients that died early from exsanguinating injuries despite sound and timely care. Furthermore, these studies have typically noted the presence or absence of hypotension but have failed to account for the magnitude of the shock insult, which may be reflected in the depth or duration of hypotension. Experimental studies in animal models of shock have demonstrated that magnitude of the physiologic insult after hemorrhage, the degree of tissue injury, the level of oxygen deficit, and the survival rate all correlate with the severity (degree and duration) of hypotension. Conversely, no evaluation of the degree and duration of hypotension in injured patients has been performed.

We hypothesized that an increased duration of hypotension would be associated with increased mortality and morbidity in severely injured patients. Our data demonstrate that even brief periods of hypotension in the intensive care unit (ICU) are associated with significantly increased mortality and length of stay (LOS).

PATIENTS AND METHODS

All injured patients admitted to the intensive care unit at the University of Pittsburgh Medical Center from 1999 to 2000 were prospectively reviewed. Patients who were transferred to a ward within 48 hours of admission were excluded. The medical records of all remaining eligible patients were examined for demographic information, emergency department data, information on vital signs, laboratory test results, and hemodynamic measurements. Injury severity, prehospital admission history, hospital course, and outcome were obtained from the computerized trauma registry. Hypotension was defined as SBP ≤ 90 mm Hg. Duration was defined as the elapsed time in minutes (on the basis of data entry in the hospital or emergency department hypotension had an early...
ICU records) from the initial SBP of ≤ 90 until the next recorded SBP > 90 mm Hg. The lowest SBP and the duration in minutes of all episodes of SBP ≤ 90 mm Hg were retrieved from the computerized ICU record during the first 48 hours of ICU care. Preterminal episodes of SBP of ≤ 90 mm Hg were excluded. The total ICU LOS, total hospital LOS, and death/discharge status for each patient were recorded.

Data are presented as the mean ± SD. Categorical variables were analyzed by the χ² test. A value of p < 0.05 was used to designate statistical significance. To characterize and comprehend the relation between hypotension duration during the initial 24 hours of ICU care and the outcome, we used the test for trend. To perform the test for trend, we ranked both death and ICU LOS along a time frame of early versus late in a manner that corresponded to previous work by other investigators.20–23 The ranking used in this analysis was as follows: died early (≤ 2 days), died within 3 to 7 days, died late (> 7 days), survived and was discharged from the ICU late (> 7 days), and survived and was discharged early (≤ 7 days). The Kruskal-Wallis test was used to determine the effect of depth and duration of hypotension on the ICU LOS for both survivors and patients who died.

RESULTS

From 1999 to 2000, there were 783 patients admitted to the ICU after injury. Of these patients, 247 were discharged from the ICU less than 48 hours after admission and were therefore excluded, leaving 536 patients for analysis. There were 370 men (69%) and 166 women (31%). We could not gather complete data for eight patients as a result of transfer to other facilities for insurance purposes. One patient was excluded when he was found to have an aortic dissection and no acute injury as the cause of admission. In the remaining 528 patients, 145 (28%) died during the course of hospitalization and 383 (72%) survived. The average age of all patients was 48.6 ± 22.8 years. The average ICU and hospital LOS for the entire group was 5.6 ± 8.6 days and 15.4 ± 14.9 days, respectively. The average Injury Severity Score (ISS) was 26 ± 12. Examining the differences of the average age and average ISS, we found that those who died after 48 hours were older and more severely injured (age, 64 ± 22.6 years; ISS, 30 ± 17) than those who were discharged from the ICU alive after 48 hours (age, 49 ± 22 years; ISS, 25 ± 12).

In the initial 24 hours after ICU admission, 245 patients (46%) had at least one episode of hypotension and 288 (54%) did not. Of the 245 patients with SBP ≤ 90 mm Hg, there were 85 patients (35%) whose lowest SBP was < 70 mm Hg, 75 patients (30%) whose lowest SBP was between 71 and 80 mm Hg, and 85 patients (35%) whose lowest SBP was between 81 and 90 mm Hg. Of the remaining 288 patients, 75 (26%) had their lowest SBP between 91 and 100 mm Hg and 213 (74%) had their lowest SBP above 100 mm Hg. We tabulated the total duration of hypotension in minutes and categorized duration as brief (1–10 minutes), moderate (11–60 minutes), long (61–120 minutes), and prolonged (> 120 minutes). The duration of hypotension in patients with SBP ≤ 90 mm Hg was brief in 27 patients, moderate in 91 patients, long in 53 patients, and prolonged in 75 patients.

Figure 1 illustrates the overall mortality rate for patients who were and were not hypotensive during the first 24 hours of ICU care. Patients who had an episode of SBP ≤ 90 mm Hg had a significantly increased mortality compared with those that did not. Figure 2 demonstrates the total LOS and survival of all patients according to their lowest measured SBP during the first 24 hours in ICU care. When the mortality rate was calculated after stratifying patients according to depth of hypotension, we found that mortality increased as the severity of hypotension increased, with statistically significant differences for all SBP categories (p < 0.005) (Fig. 3).

We next examined the duration of hypotension during the first 24 hours of ICU care. We found that mortality rate...
increased as the duration of hypotension increased (Fig. 4). When we examined ICU LOS in patients that were discharged from the ICU, we found that ICU LOS increased as the depth and duration of hypotension increased (Figs. 5 and 6). In contrast, the length of stay for those who died in the ICU decreased as the depth and duration of hypotension increased (Figs. 5 and 6). Using the Kruskal-Wallis test to compare length of stay with duration and depth of hypotension, a statistically significant relationship was observed ($p < 0.0001$).

We stratified all patients who died according to time of death and examined these patients with reference to the duration of hypotension (Fig. 7). There were 96 patients who died early (≤ 48 hours), 22 patients who died within 3 to 7 days, and 27 patients who died late (> 7 days). As anticipated, patients who had prolonged and long periods of hypotension predominantly died early (≤ 48 hours). However, a substantial group of patients with brief and moderate periods of hypotension also died early. Interestingly, in patients who died late (> 7 day), the largest group of deaths was present in those patients with brief (1–10 minutes) and moderate (11–60 minutes) periods of hypotension. When duration of hypotension was examined in patients who survived and were discharged from the ICU, patients who were discharged late (> 7 day) more frequently experienced episodes of hypotension than those discharged early (≤ 7 days) (Fig. 8). The test for trend and Person $\chi^2$ using the duration of hypotension categories and the range of outcome described above demonstrated a statistically significant association between duration of hypotension and outcome ($p = 0.0001$).
DISCUSSION

Hypotension was identified as a significant clinical event after injury in the early 20th century and as a risk factor of early death and the development of MODS. It is intuitive that the presence of shock and hypotension may have significant adverse consequences. Franklin et al. demonstrated that patients who experience hypotension in the ED or in a prehospital setting frequently required operative treatment and had a high mortality rate. This high mortality rate associated with shock has been seen by other investigators as well. These studies, however, included many patients who were unsalvageable because of fatal exsanguinating injuries. Therefore, whether the effect of hypotension remains as profound in patients surviving their initial evaluation and resuscitation is less clear. Several authors have noted that the presence of hypotension is significantly associated with subsequent development of MODS. With fewer patients dying with MODS and with the outcome from MODS potentially improving, the effect of hypotension on mortality remains a viable question.

Most studies that have evaluated the contribution of hypotension to outcome after injury have examined hypotension as a categorical variable (i.e., it is present or not). Few studies have attempted to quantify the magnitude of the shock insult in trauma patients according to the degree and duration of shock. We know that duration of shock directly contributes to the pathophysiologic sequelae after hemorrhage and subsequent mortality in animal models of hemorrhage. Our data suggest that a similar relationship also exists in trauma victims.

In this study, we quantified the depth and duration of all episodes of SBP ≤ 90 mm Hg in a group of severely injured patients admitted to the ICU within a period of 2 years. Our data demonstrate significant increases in the mortality rate and morbidity (defined as ICU length of stay); even for brief episodes of SBP ≤ 90 mm Hg, mortality and morbidity increase as the depth and duration of hypotension increases.

In this study, we excluded patients who died of exsanguinating injuries in the emergency department or in the operating room. We also excluded patients who were admitted to the ICU because of prehospital intubation, slow recovery from anesthesia, or other reasons, but were minimally injured and able to be transferred to a regular ward within 48 hours. The remaining patients represent a group of severely injured trauma victims (average ISS, 26) who were in the ICU for 5.6 days and with an expectation of potential recovery from their injuries. Our data suggest that hypotension in the ICU in this group of patients has significant effects on morbidity and mortality.

Although the findings of this study are straightforward, our analysis does have limitations. We did not quantify the presence of hypotension in the emergency department resuscitation bay, operating room (OR), or before patients arrived to the ICU. It is not clear whether the results of this analysis can be extrapolated to hypotension that occurs in these areas before ICU admission. We did not evaluate how many patients may have had an episode of SBP ≤ 90 mm Hg in the ED and OR and were never admitted to an ICU. Whether duration of hypotension in the ED and OR has a similar relationship to outcome as that which occurs in the ICU will require further study. In addition, SBP measurements of this study were obtained from the ICU record as documented by the ICU nursing staff. The accuracy of the SBP measurements and estimates of duration of hypotension therefore depend on the accuracy of the information entered into the medical record. Continuous real-time SBP measurements for patients with arterial lines that have a continuous readout included as part of the medical record are not yet available.
Whether these limitations would substantially alter the results of the current analysis is unclear.

Despite the limitations noted above, our results do have clinical relevance. These data suggest that any episode of hypotension may have significant clinical impact. These results emphasize the fact that hypotension not only should be aggressively prevented. This fact is particularly relevant as the nonoperative treatment of solid organ injuries continue to be refined. Development of hypotension is an indication of failure of nonoperative management for blunt abdominal injuries. Our data suggest that a consideration of the potential for a patient to become hypotensive, with its attendant contribution to mortality and morbidity, should be weighed carefully when treatment options are considered.

In conclusion, our data demonstrate that depth and duration of hypotension in the ICU correlate with morbidity and mortality after traumatic injury. They suggest that any episode of hypotension, no matter how brief, may have significant clinical impact.

REFERENCES

1. Trunkey DD. Trauma: accidental and intentional injuries account for more years of life lost in the U.S. than cancer and heart disease—among the prescribed remedies are improved preventive efforts, speedier surgery and further research. Sci Am. 1983;249:28–35.


DISCUSSION

Dr. Michael B. Shapiro (Philadelphia, Pennsylvania): Dr. Zenati and colleagues reviewed 528 records to assess the impact of hypotension in injured patients in the intensive care unit. I can draw several conclusions from the authors’ data: first, hypotension may lead to death; second, greater degrees of hypotension suggest that death may be more imminent; and third, patients who die sooner spend less time in the ICU.

I believe that the authors have simply begged the question and then answered it. All patients who die are, at some point, hypotensive.

August 2002

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.
It is both intuitive and defined in the literature that the more hypotensive they are, the more likely they are to die. The question needs to be, Are the patients dying because they are hypotensive or hypotensive because they are dying? For that, you need information that relates injury severity to hypotension and outcome and considers the response to treatment.

Unfortunately, this information is absent from the article. It is perhaps notable in the Results section that a period of hypotension of as little as 1 to 10 minutes seems to have been associated with increased mortality in this population, although if I were the patient, I would prefer not to have this held against me. This finding really depends on the validity of the data collection and interpretation.

There’s not enough time here to consider all the questions that this article raises, but I would like to ask five. First, almost one third of the eligible patients were transferred out of the ICU in less than 48 hours and, therefore, are excluded from the analysis. Why? Were there no patients in this group who had even brief episodes of hypotension? The exclusion of these patients in any such events obviously skews the data and, given the size of this subset, potentially skews it a lot. What about the patients who were hypotensive before arrival in the ICU?

Second, since the entire analysis depends on measurements of blood pressure, it is a critical failure that there is no protocol for standardization of how this was measured or how frequently. How are discordant values arbitrated? In the absence of a protocol, the data are dependent on what are essentially random pattern measurements.

Third, is all hypotension alike and does the response to treatment matter? A patient whose thoracic epidural catheter is overdosed shouldn’t be in the same category as an under-resuscitated damage control patient. The physiology is different and the outcome should be too. Where’s the ISS data?

Fourth, data are recorded for 48 hours but only analyzed for 24 hours in the article. Is it okay to be hypotensive in the second 24 hours?

Finally, with all the recent discussion of endpoints of resuscitation and the limitations of blood pressure therein, isn’t it strange that we’re talking about blood pressure at all? Sure, hypotension is intuitively a bad thing, and it should be corrected and avoided, but we didn’t really need 528 more patients to tell us that. Estimating its clinical significance for a patient or a population, I submit, remains an elusive target.

I’d like to thank the organization for the privilege of discussing this article.

Dr. Mazen S. Zenati (closing): It is, indeed, intuitive to know that hypotension is a risk factor for mortality and morbidity in trauma patients, but the matter here is to quantify that risk. In other words, are a couple of minutes or so an important risk at all and when is that risk very high?

Regarding the exclusion of those patients who stayed less than 48 hours in the ICU, those patients were different subset in their criteria. Their average ICU length of stay was 1 day, or to be more precise 0.9 days. There were substantial differences in their average ISS compared with the remaining population of our study. That difference exceeded, on average, 11 points across the board on the ISS. Most of those excluded patients were intubated at the scene of the accident for altered consciousness and may have been intoxicated but were quickly found to not have life-threatening injuries and were discharged from the ICU. Actually we did not want to “contaminate” our data with patients who did not require intensive care. This study targeted the critically ill trauma patients.

With respect to patient grouping and outcome, we put patients into groups according to their first 24 hours ICU stay hypotension severity and outcome. Thus we started with those who died during the first 48 hours, then those who died between 3 and 7 days, and so on, until those who were discharged alive in less than 7 days. Here we are not saying merely that those patients who were hypotensive died quickly and did not stay long in the ICU. Those patients who suffered even a brief period of hypotension died more frequently, even late in their hospitalization, or required a significantly longer stay in the ICU.