Increased Hospital Morbidity Among Trauma Patients With Diabetes Mellitus Compared With Age- and Injury Severity Score–Matched Control Subjects

Rehan Ahmad, DO; Robert A. Cherry, MD; Irina Lendel, MD; David T. Mauger, PhD; Sara L. Service, RN, BSN, CEN; Lindsay J. Texter, BS; Robert A. Gabbay, MD, PhD

Hypothesis: We hypothesized that patients with diabetes mellitus (DM) have worse outcomes following trauma compared with patients without a history of DM.

Design: Retrospective data analysis of the Pennsylvania Trauma Systems Foundation database that compiles data from 27 accredited trauma centers in Pennsylvania.

Setting: We used the Pennsylvania Trauma Systems Foundation database of 295,561 patients to compare outcomes in patients with DM vs those in patients who did not have DM.

Patients: A total of 12,489 patients with DM from January 1984 to December 2002 were matched by sex, age, and Injury Severity Score with 12,489 patients who did not have DM.

Main Outcome Measures: Differences in the length of hospital stay, intensive care unit stay, ventilatory assistance days, complications, and mortality rates.

Results: Patients with DM spent more days in the intensive care unit and receiving ventilator support. They were more likely to have a complication (23.0% in the DM group vs 14.0% in the non-DM group [odds ratio, 1.80; 95% confidence interval, 1.69-1.92]). No difference in mortality rates or length of hospital stay was noted.

Conclusion: Patients with DM exposed to trauma have greater hospital morbidity resulting from longer intensive care unit stay, increased ventilator support, and more complications.

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Diabetes mellitus (DM) is reaching near epidemic proportions in the United States. There are approximately 17 million Americans with DM, and one-third remain undiagnosed.1 This represents a significant health care burden, as patients with DM develop complications more frequently compared with those who do not have DM. Patients with DM have worse outcomes in the setting of acute illness regardless of the severity of the initial illness.2-4 Findings from studies2-8 among patients with DM hospitalized for acute stroke, myocardial infarction, and cardiothoracic surgery indicate higher complication rates compared with patients who do not have DM. Little is known about outcomes of trauma patients with DM. The aim of this study was to determine whether patients with DM have a difference in the length of hospital stay, intensive care unit (ICU) stay, days receiving ventilatory assistance, and other complications when involved in trauma.

Methods

We used the Pennsylvania Trauma Outcome Study database, a statewide registry maintained by the Pennsylvania Trauma Systems Foundation, to determine outcomes of patients with DM hospitalized for trauma. The Pennsylvania Trauma Outcome Study compiles data from 27 accredited trauma centers in Pennsylvania and provides information with respect to patient demographics; mechanism of injury; injury descriptors; and prehospital, emergency department, and inpatient hospital care and patient outcomes. Records were obtained from the Pennsylvania Trauma Systems Foundation for 310,795 patients entered in the registry between January 1984 and December 2002. Entries that recorded sex; discharge status; and total number of ICU days, stepdown unit days, and hospital days were used in the analysis. Each patient admission recorded in the database is assigned a unique identifier.
identifier number, which precluded data from any successive hospital admission of a patient. Of 310,795 entries in the database, 295,561 (95.1%) met our criteria for completeness (age, sex, diabetic status, and Injury Severity Score [ISS]) and were included in the preliminary analysis. Data were extracted from the database for age; sex; systolic blood pressure on admission; pulse rate on admission; Glasgow Coma Scale score on admission; ISS; revised trauma score; and the total number of hospital days, ICU days, stepdown days, ventilatory assistance days; and occurrence of cardiac, pulmonary, infectious, and renal complications. The registry identified patients based on insulin use before admission and not by type of DM.

Unmatched data analyses compared the outcomes of patients with DM and those of patients who did not have DM. Because there were significant differences between the DM and non-DM groups for age and ISS, matched analyses were carried out. This was accomplished by generating a matched data set in which each patient with DM was matched with a patient who did not have DM randomly selected from all of those who were of the same sex and age and had the same ISS as the matching patient with DM. Therefore, the matched data set allowed a comparison of DM and non-DM groups unconfounded by age, sex, and ISS.

Descriptive statistics, including mean, median, standard deviation, minimum and maximum values, and frequency tables were calculated for all outcome measures. The 2-tailed, 2-sample t test was used to assess group differences for continuous outcome measures, and Pearson χ² test was used to assess group differences for binary outcome measures. The continuous variables were checked for normality and variance equality before conducting the tests. Odds ratios and 95% confidence intervals (CIs) associated with group differences in the frequency of complications were also constructed. P < .05 was taken to indicate significance.

Approval for this study was obtained from the institutional review board at Penn State College of Medicine, Hershey, Pennsylvania. Consents were waived because patient privacy was maintained by using the unique identifiers assigned within the Pennsylvania Trauma Outcome Study registry database.

### RESULTS

Of 295,561 entries, 65.1% were male and 34.9% were female (Table 1). A total of 12,658 patients (4.3%) were identified as having a history of DM on admission. The mean age was 65 years for the group with DM vs 39 years for the group without DM. The mean ISS was lower for the DM group compared with the non-DM group (11.44 vs 12.56, P < .001). Although a similar percentage of patients in each group required ICU level of care (38.6% in the DM group vs 39.2% in the non-DM group, P = .18), among patients who had at least 1 day of ICU care, patients with DM had a longer ICU stay (7.6 vs 5.0 days, P < .001). Twenty-one percent of patients in the DM group and 17.5% of the non-DM group required stepdown level of care (P = .001). The number of days in a stepdown unit was greater in the DM group (4.42 vs 3.68 days, P < .001). The number of days of ventilatory support was added to the registry beginning in 1998. Between 1998 and 2002, of 90,487 patients entered in the database, 17,899 required ventilator support. Nineteen percent of patients in the DM group and 19.8% of patients in the non-DM group required ventilatory support (P = .10). Among the patients who required ventilator support, the number of days receiving ventilatory assistance was greater for the patients with DM (10.7 vs 6.7 days, P < .001). Patients with DM also had increased mortality rates compared with those who did not have DM (8.1% vs 6.8%, P < .001).

Patients with DM were then matched by the same values for sex, age, and ISS to patients who did not have DM to allow comparisons of similar groups, resulting in 12,489 patients in the DM group and 12,489 in the non-DM group (Table 2). Of these patients in both groups, 52.0% were male and 48.0% were female. Greater proportion of patients in the DM group required ICU care (38.4% in the DM group vs 35.9% in the non-DM group, P < .001). Those with DM had a longer ICU stay compared with those who did not have DM (7.6 vs 6.1 days, P < .001) (Figure 1). The proportion of patients requiring ventilator support throughout the hospital stay was similar in both groups (18.8% in the DM group vs 18.1% in the non-DM group, P = .33). However, the amount of time receiving ventilatory assistance among patients requiring ventilator support was longer for the group with DM (10.8 vs 8.4 days,

### Table 1. Unmatched Analyses of Characteristics and Outcomes of Patients With Diabetes Mellitus (DM) Involved in Trauma

<table>
<thead>
<tr>
<th>Variable</th>
<th>DM Group (n = 12,658)</th>
<th>Non-DM Group (n = 282,903)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>6584 (52.0)</td>
<td>185,934 (65.7)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Age, y</td>
<td>65 ± 16.6</td>
<td>39 ± 23.7</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Injury Severity Score</td>
<td>11.44 ± 9.7</td>
<td>12.56 ± 11.3</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Patients requiring ICU level of care</td>
<td>4882 (38.6)</td>
<td>110,766 (39.2)</td>
<td>.18</td>
</tr>
<tr>
<td>ICU duration, d&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.6 ± 13.7</td>
<td>5.0 ± 9.2</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Patients requiring stepdown level of care</td>
<td>2660 (21.1)</td>
<td>49,468 (17.5)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Stepdown duration, d&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.42 ± 6.1</td>
<td>3.68 ± 6.1</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Patients requiring ventilatory support</td>
<td>1259/6627 (19.0)</td>
<td>16,630/83,860 (19.8)</td>
<td>.10</td>
</tr>
<tr>
<td>Ventilatory support duration, d&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>10.7 ± 17.5</td>
<td>6.7 ± 11.4</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Mortality</td>
<td>1026 (8.1)</td>
<td>19,237 (6.8)</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

Abbreviation: ICU, intensive care unit.

<sup>a</sup>Data are given as number (percentage) or as mean ± SD unless otherwise indicated.

<sup>b</sup>For ICU days, stepdown days, and ventilator support days, the computation of days was performed only on those requiring the respective level of care.

<sup>c</sup>Ventilator support days were added to the Pennsylvania Trauma Systems Foundation database beginning in 1998.

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Similar numbers of patients in both groups required stepdown level of care (20.9% in the DM group vs 19.5% in the non-DM group, P = .006). The differences in the total number of hospital days and the total number of stepdown days between the groups were not statistically significant (P = .69). The difference in mortality between the groups (995 patients [8.0%] with DM vs 982 patients [7.9%] who did not have DM) was not statistically significant (P = .76) (Table 2).

Significant differences in complication rates were noted between the 2 groups (Figure 2 and Table 3). Patients with DM (23.0%) were more likely to experience a complication in the setting of acute trauma compared with patients without DM (14.0%) (odds ratio, 1.80; 95% CI, 1.69–1.92; P < .001). Infectious complications were among the most common in both groups; however, patients with DM had a greater tendency to develop an infection (11.3% vs 6.3% [odds ratio, 1.90; 95% CI, 1.73–2.08]). Urinary tract infection was the most common infectious complication in both groups; however, patients with DM had a greater tendency to develop a urinary tract infection compared with those who did not have DM. Decubitus ulcers were 2.36 (95% CI, 1.91–2.92) times and sepsis was 2.17 (95% CI, 1.71–2.76) times more likely to occur in patients with DM. Single and multiple pulmonary complications were more frequent in patients with DM compared with patients who did not have DM. Of the pulmonary complications, pneumonia was the most common among both groups and was more frequent in the group with DM. Cardiovascular complications were more common in the group with DM, with the most common being major arrhythmia. Myocardial infarction and deep vein thrombosis were also more likely to occur in patients with DM. The only renal complication recorded in the registry was acute renal failure (ARF), which was seen more commonly among patients with DM. The use of insulin before admission was not predictive of clinical outcomes.

The results of this study indicate that patients with DM involved in trauma have greater inhospital morbidity from infectious and noninfectious complications after matching for age, sex, and ISS. They also require longer ICU care; however, hospital days and mortality rates are not different. Patients with DM were less likely to be discharged to home and were more likely to require skilled nursing care after discharge compared with patients who did not have DM. This may have accounted for the similarity in overall hospital length of stay between the DM and non-DM groups. In addition, improved DM treatment modalities and advances in critical care and trauma resuscitation likely contributed to comparable mortality rates between the 2 groups, despite the greater morbidity associated with having DM. The excess morbidity of patients with DM in the setting of trauma might be attributable to alterations in the immune system, level of glycemic control, or preexisting comorbidities.

The effect of DM on the immune system has been studied extensively. Hyperglycemia has been linked to impairments in chemotaxis, adherence, oxidative burst, the killing potential of polymorphonuclear cells, and the ability to fight infection. Impairment in macrophage chemotaxis and phagocytosis has also been described in patients with DM. Results from this study confirm that patients with DM are at higher risk for developing an infectious complication, despite matching for sex, age, and the severity of injury. It is possible that other comorbidities that were not controlled for in our analysis alter the susceptibility to infection.

Moss et al showed that patients with DM who develop septic shock have a lower incidence of acute respiratory distress syndrome (ARDS). They hypothesized...
this was in part secondary to decreased polymorphonuclear cell activity, limiting the inflammatory lung injury encountered in ARDS. However, our data suggest that ARDS is more common among patients with DM involved in trauma, although we did not analyze the subpopulations of those with ARDS and concurrent septic shock vs those who had ARDS secondary to other causes.

Diabetes mellitus has not been shown to be an independent risk factor for developing community-acquired pneumonia. However, patients with DM who develop lower respiratory tract infections requiring hospitalization have a higher mortality rate and are more likely to develop nosocomial pneumonia. In our study, pneumonia occurred with the second highest frequency among all types of infections. Patients with DM were 1.82 times more likely to develop pneumonia than age- and ISS-matched patients who did not have DM (Table 3). Acute respiratory failure, the number of days receiving ventilatory assistance, and length of ICU stay were greater in the group with DM, which may have been a result of the higher rates of pneumonia seen among these patients.

Stress hyperglycemia has been shown in other studies to be a marker of poor outcome. A recent study by Yendamuri et al. did not distinguish patients with DM, suggested that admission hyperglycemia (defined by a plasma glucose level of greater than 135 mg/dL [to convert to millimoles per liter, multiply by 0.0555]) was an independent predictor of mortality, length of ICU stay, and days receiving ventilatory support.

Table 3. Matched Analyses Demonstrating That Patients With Diabetes Mellitus (DM) Involved in Trauma Are More Likely to Have Complications Than Patients Without DM

<table>
<thead>
<tr>
<th>Variable</th>
<th>DM Group (n = 12,489)</th>
<th>Non-DM Group (n = 12,489)</th>
<th>Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All infectious complications b</td>
<td>1411 (11.3)</td>
<td>786 (6.3)</td>
<td>1.90 (1.73-2.08)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>212 (1.7)</td>
<td>99 (0.8)</td>
<td>2.17 (1.71-2.76)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>834 (6.7)</td>
<td>472 (3.8)</td>
<td>1.82 (1.62-2.05)</td>
</tr>
<tr>
<td>Wound infection</td>
<td>130 (1.0)</td>
<td>70 (0.6)</td>
<td>1.86 (1.39-2.50)</td>
</tr>
<tr>
<td>Decubitus ulcer</td>
<td>282 (2.3)</td>
<td>124 (1.0)</td>
<td>2.36 (1.91-2.92)</td>
</tr>
<tr>
<td>Pulmonary complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All pulmonary complications</td>
<td>1261 (10.1)</td>
<td>769 (6.2)</td>
<td>1.71 (1.56-1.88)</td>
</tr>
<tr>
<td>Acute respiratory distress syndrome</td>
<td>196 (1.6)</td>
<td>87 (0.7)</td>
<td>2.24 (1.74-2.89)</td>
</tr>
<tr>
<td>Acute respiratory failure</td>
<td>578 (4.6)</td>
<td>351 (2.8)</td>
<td>1.68 (1.47-1.92)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>633 (5.1)</td>
<td>357 (2.9)</td>
<td>1.82 (1.59-2.07)</td>
</tr>
<tr>
<td>Cardiovascular complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cardiovascular complications</td>
<td>781 (6.3)</td>
<td>427 (3.4)</td>
<td>1.88 (1.67-2.12)</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>240 (1.9)</td>
<td>125 (1.0)</td>
<td>1.94 (1.56-2.41)</td>
</tr>
<tr>
<td>Major arrhythmia</td>
<td>416 (3.3)</td>
<td>240 (1.9)</td>
<td>1.76 (1.50-2.06)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>152 (1.2)</td>
<td>57 (0.5)</td>
<td>2.68 (1.96-3.60)</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>274 (2.2)</td>
<td>94 (0.8)</td>
<td>2.95 (2.33-3.74)</td>
</tr>
<tr>
<td>Overall complication rate</td>
<td>2872 (23.0)</td>
<td>1748 (14.0)</td>
<td>1.80 (1.69-1.92)</td>
</tr>
</tbody>
</table>

a Data are given as number (percentage) unless otherwise indicated. P<.01 or better for all the complications listed.
b Includes the total number of patients who had 1 of the complications or more listed in each category.
stay, hospital stay, and infectious complications in patients admitted for trauma. Although our study did not include admission glucose levels, DM was an independent risk factor for complications, length of ICU stay, and number of days receiving ventilatory assistance.

Intensive insulin treatment in critically ill patients has been shown to reduce morbidity and mortality in patients with DM and in patients who do not have DM. Van den Bergh et al\(^2\) demonstrated a decrease in incidence of infection, sepsis, ARF, days receiving ventilatory assistance, and critical illness polyneuropathy in patients treated with an intensive insulin infusion to maintain glucose levels below 110 mg/dL. In a follow-up study, achievement of glycemic control rather than the amount of insulin infused correlated with an improvement in all outcomes except ARF. A recent study by Finney et al\(^3\) confirmed that finding.

Renal disease in the patient with DM is typically a slow progressing disease resulting from microvascular changes. Patients involved in trauma are at risk for renal failure due to a decrease in circulatory volume, myoglobinuria resulting from muscle injury, and exposure to ionic contrast for radiographic studies or other nephrotoxic agents. Burn patients typically develop early ARF from hypovolemia and myoglobinuria, whereas late renal failure correlates with development of sepsis and drug toxicity. The likelihood of development of ARF in patients with DM was almost 3 times higher in our study. Whether this increased risk among the patients with DM was due to multiorgan system failure, an isolated insult to the kidney, or preexisting diabetic nephropathy was not analyzed in this study.

Although the size of the registry used in the analysis is a strength of the study, there are several limitations that must be acknowledged. This was a retrospective analysis of data gathered from institutions across the state. Although data were matched for sex, age, and ISS, there may be other unidentified factors contributing to the differences in outcome. The analysis was based on the assumption that ISS represents the severity of injury equally across this spectrum of patients. Although many of the changes were instituted due to multiorgan system failure, an isolated insult to the kidney, or preexisting diabetic nephropathy was not analyzed in this study. The Pennsylvania Trauma Systems Foundation database only provides information about whether a patient was using insulin before admission. Generally, more than 90% of patients with DM admitted with trauma have type 2 DM. It is reasonable to suggest that patients with longer duration of type 2 DM are more likely to be treated with insulin and would be at higher risk for DM-related comorbidities and complications of trauma. However, our analyses showed no difference in clinical outcomes between the patients with a history of insulin use before admission and those who did not have a history. The limitations of the database also include lack of information on glycohemoglobin level, admission glucose level, DM-related comorbidities, body mass index, medication compliance, and duration of DM.

Studies that control for other comorbidities may be helpful in further explaining the increase in morbidity seen in patients with DM. Factors such as chronic glycemic control, preexisting cardiopulmonary disease, and hypertension may also play a role in outcomes in these patients.

Many changes in trauma care have occurred during the 19-year span of the study, including advances in trauma resuscitation, critical care, and infectious diseases, as well as evolving definitions, classifications, and therapies for DM. An evaluation of the effect of many of these innovations in trauma care over time would be of interest. However, many of the changes were instituted across trauma centers at various times. Therefore, it would be difficult to ascertain which changes might have affected trauma outcomes and to evaluate the temporal effects of changes in trauma care on relative outcomes of patients who have DM vs patients who do not have DM. The objective of the present study was to evaluate whether DM is a marker of poor outcome. Future studies are needed to determine if therapeutic changes in trauma care may have caused relative differences in outcomes between the DM and non-DM groups.

Patients with DM have a higher incidence of developing complications when hospitalized for trauma. They also require a higher level of care, which adds to the cost of hospitalization. Future studies are needed to evaluate the effect of improved glycemic control on hospitalized patients with DM involved in trauma.

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Correspondence: Robert A. Cherry MD, Department of Trauma and Critical Care, Penn State College of Medicine, Milton S. Hershey Medical Center, MC H075, 500 University Dr, Hershey, PA 17033.

Author Contributions: Dr Cherry had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Ahmad, Cherry, and Gabbay. Acquisition of data: Ahmad, Cherry, and Service. Analysis and interpretation of data: Ahmad, Cherry, Lendel, Mauger, Service, and Gabbay. Drafting of the manuscript: Ahmad, Lendel, Mauger, Service, and Gabbay. Critical revision of the manuscript for important intellectual content: Ahmad, Cherry, Lendel, and Gabbay. Statistical analysis: Mauger. Administrative, technical, and material support: Ahmad, Cherry, Lendel, and Service. Study supervision: Cherry and Gabbay.

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REFERENCES