Co-morbid factors in trauma patients

T D Wardle

Medical Directorate, Countess of Chester Hospital, Chester, UK

A variety of factors influence the survival of trauma patients including the severity and site of injury, and the timing and quality of care. However, host factors including age and gender have also been reported as independent risk factors that adversely influence outcome. In addition, the presence of co-morbid or pre-existing factors has been shown to increase mortality and morbidity after trauma. This chapter reviews the evidence for these associations and considers their impact on assessment and management of the trauma patient.

Most trauma victims are young, but the consequences of injury are evident at all ages, with at least two surviving with serious permanent disabilities for every person killed. In those over the age of 65 years, a death rate of 86 per 100,000 was reported in 1984, twice the rate for all ages.

A variety of factors affect the survival of these patients. These include the severity and site of injury, and the timing and quality of care. However, host factors including age and gender have also been reported as independent risk factors that adversely influence outcome. In addition, the presence of co-morbid or pre-existing factors has been shown to increase mortality and morbidity after trauma.

Host factors

Age

The relationship between age and survival has been clearly described in trauma patients. Mortality increases in proportion to the severity of injury for all ages, but there has been a marked discrepancy in reported morbidity and mortality. The consensus is that survival is directly related to both severity and site of injury. This is most notable in abdominal trauma where mortality rises by a factor of three in elderly patients compared with younger people.

The increase in both morbidity and mortality in elderly patients following trauma is not surprising. Nevertheless, why should this occur? One factor that is likely to influence the response to trauma is aging.
This process is manifested by a decrease in the number of functional cells culminating in changes in anatomy, physiology and biochemistry. The significance of cardiovascular compromise associated with increasing age and the associated effect on outcome is well described in the literature\(^{16,17}\). Another, more plausible explanation is that the elderly may have an increased number of pre-existing conditions. Both of these suggestions are likely to influence the elderly patient’s response to trauma. In addition, the elderly are more likely to develop complications following trauma\(^{2,11,12}\) and the presence and number of such problems increase mortality\(^{11}\). Pulmonary and infective complications are not age specific but cardiovascular complications occur in significantly greater numbers in the elderly\(^{18}\).

**Gender**

While males are more likely to suffer trauma, especially the penetrating variety\(^3\), no significant difference in mortality was shown when examining the effect of gender in patients under the age of 40 years\(^9\). In contrast, older males have a significant increase in mortality. The only exception is female road traffic accident victims aged between 15 and 45 years who have an increased risk of death (25%) when compared with males, controlled for age and severity of impact\(^10\). Although there is no statistically significant association between age and pre-injury psychopathology\(^19\) there is an interesting variation in symptom profile. Females reported predominantly somatic features with headaches, illness caused by worry and fainting spells being common complaints. In contrast, men related mood or neurotic symptoms expressed by feeling isolated, worthless, unmotivated and manifested by increased alcohol use\(^19\).

**Co-morbid or pre-existing factors**

Another host factor that has recently received increasing attention is pre-injury illness. In North America, 4.8–19% of trauma victims had one or more pre-existing medical conditions (PEMCs)\(^8,20,21\) which were more prevalent with advancing age. Moreover, these conditions adversely influenced outcome\(^8\) and as the numbers of PEMCs rose\(^20,21\), the mortality increased. Of all the conditions reported, the presence of either renal and/or hepatic disease had the greatest impact on mortality. Furthermore, the effect of PEMCs on death was most marked in those patients who had mild injury\(^8\). Mortality doubled in the severely injured younger patients with the presence of a PEMC, but for the elderly it was not affected. It is likely that these patients are already at an increased risk of dying by virtue
of their advanced age and injury severity. Thus it would appear that outcome is affected by age and not the presence of a PEMC.

Unfortunately, because of the different methods used in these studies, further comparisons were precluded. In addition, the results were also influenced by difficulties in defining, scoring and reporting PEMCs. These points were exemplified in the study by Morris et al., where the authors acknowledged that their analyses were restricted by using in-patient deaths and anatomical indices of injury severity. To overcome these problems, alternative PEMC categorisations were sought. However, similar difficulties occurred with inadequate classification using ICD-9-CM and gross under reporting in medical discharge summaries. Similarly, the use of a limited component of physiological severity affected the study by Miltzman and colleagues, which was also uncontrolled and used a self-devised classification of PEMCs. In contrast, Sacco et al. used APACHE II and ASCOT scoring, respectively, to define pre-injury conditions and provide a better physiological assessment of severity. Their analyses were influenced by patient age. As 91% of the study population was less than 55 years old, they were unlikely to have an associated medical problem. Most of the remaining patients aged 55 years and over had evidence of PEMC. Further bias was introduced as data from inpatient deaths resulted in under reporting of pathology. This was exacerbated by the controversial use of APACHE II that does not include many disease categories.

Some drugs, in particular benzodiazepines, increase the risk of having an accident and the severity of injury. The presence of these sedatives in trauma patients varies from 0.5% in Sweden to 12.4% in Canada (UK = 6.8%). Similarly, tricyclic drugs adversely affect driving safety but it is not clear whether this effect is due to the drug, the underlying psychiatric condition or a combination of these factors. However, the link between tricyclic antidepressants and falls in the elderly is well established. The combination of drugs and alcohol is common in trauma with 55–72% of patients having a positive toxicology screen. This comprised alcohol and drugs (35%), drugs without alcohol 45% and alcohol alone in 20%.

The final host factors that could influence survival in trauma patients are alcohol use and smoking. The effect of alcohol is well documented, especially with regards to road traffic accidents. However, acute alcohol intoxication has no effect on mortality. In contrast, chronic alcohol consumption was associated with an increase in post traumatic complications, in particular pneumonia. Smoking can be responsible for starting a fire that could result in a spectrum of injuries including burns and the sequelae to inhalation of hot gases and particles of incomplete combustion. Furthermore, smoking is a major risk factor for cardiovascular and respiratory diseases that can influence outcome following major trauma.
Pre-existing medical conditions in UK trauma victims

One of the major problems affecting the assessment of PEMCs and their effect on outcome has been the difficulty in defining what exactly constitutes a pre-existing medical condition. A variety of systems have been used, including specific chronic conditions coded as secondary diagnoses from discharge data\(^8\), a self-devised classification based on laboratory and clinical findings\(^20\) and Apache II\(^21\), as discussed earlier.

Much of the early work relating to pre-injury health was done in North America. The remainder of this chapter will focus on the UK perspective as described mainly by Wardle \(et\ al\)\(^40-43\). This work has used data from both the UK Trauma, Audit and Research Network (UK TARN: formerly the UK Major Trauma Outcome Study UK MTOS) and Hope Hospital, Salford.

**Definition**

To eliminate the problems of disease categorisation and recording, PEMCs were defined as any condition diagnosed, with or without treatment, before major trauma.

**Number of pre-existing medical conditions**

Pre-existing medical problems are common, occurring in 38.8% of UK trauma victims\(^40\). However, although the UK TARN data base contained information from 33,497 patients, only 13,198 had complete records. This study population had the following age distribution: 54% (7121) were less than 45 years, 21.4% (2826) were between the ages of 45–65 years and 24.7% (3,251) were greater than 65 years old (Table 1). The number of patients with at least one PEMC was 5,129 (38.8%). The number of conditions increased with age affecting 21% (1553) of patients less than 45 years, 47% (1350) were between the ages of 45–65 years and 68.7% (2226) were greater than 65 years old (Table 1).

Similar data were obtained from randomly selected records of 1471 trauma victims from Hope Hospital\(^20-21\). Of these patients, 664 (45.1%) had at least one PEMC; the majority (73.6%) had two, or less (Fig. 1).

It was not surprising, therefore, that the number of PEMCs increased as the definition was changed and expanded. If, however, psychiatric conditions were excluded from analyses in this study the incidence of ‘at least one PEMC’ falls to 28.1%. Thus, when comparing studies, the difference in definition will account for some, but not all, of the variability in PEMC incidence. Therefore in major trauma victim’s PEMCs are
### Table 1  The relationship between the age, number of patients and pre-existing medical conditions

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Number of patients with no PEMC</th>
<th>Number of patients with PEMCs</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 45</td>
<td>5568 (162)</td>
<td>1553 (47)</td>
<td>7121 (209)</td>
</tr>
<tr>
<td>45–65</td>
<td>1476 (40)</td>
<td>1350 (68)</td>
<td>2826 (108)</td>
</tr>
<tr>
<td>&gt; 65</td>
<td>8069 (238)</td>
<td>5129 (404)</td>
<td>13198 (642)</td>
</tr>
</tbody>
</table>

Figures in brackets show the number of deaths.

common. They were present in 38.8% of patients in the UK MTOS and 45.1% of patients from Hope Hospital. This is a marked increase when compared with results from North America (4.8–19%).

This difference is likely to reflect either age differences within the populations studied, or diverging definitions of PEMC, or the increased incidence of penetrating trauma in North America, or a combination of these. Furthermore, younger patients are more likely to incur penetrating trauma and less likely to have pre-existing medical problems. The poor quality of health in the Salford community may also account, in part, for the fact that out of the 664 patients, 349 (45.1%) had more than one PEMC and that the number of conditions increased with increasing age. Furthermore patients with PEMCs were older than their counterparts, although the difference was not statistically significant — unlike the results reported by Miltzman and colleagues.

Fig. 1 Pre-existing medical problems by age. 'Other' includes rheumatoid disease, malignancy, anaemia, psychiatric; 'Res' is respiratory disease; 'Met' is metabolic including hepatic and renal failure, and diabetes mellitus; 'CVS' is cardiovascular disease; 'Neu' is neurological.
Age

In the UK MTOS data, different PEMCs were present at different ages, in particular cardiovascular disease increased markedly from patients who were less than 45 years to those who were more than 65 years (Fig. 1). In contrast, there was diametrically opposite reduction in respiratory disease. While these findings may reflect the high overall morbidity from cardiovascular disease and an increase in both chronic respiratory pathology and associated mortality in the younger population, firm conclusions cannot be drawn from such a heterogeneous population. Therefore further information is required to establish the precise reason behind these findings.

Although the number of patients in the Hope Hospital study was small (1471), there was a distinct advantage in that the number of co-morbid factors was recorded as part of the comprehensive data base. This information was extracted from notes within the emergency department, medical records and primary care files. Despite this undertaking, insufficient numbers of individual conditions were available for analysis. Similarly, the diversity and frequency of PEMCs from UK TARN data prevented accurate comparison. Unfortunately, as with previous studies, PEMCs had to be grouped to facilitate analysis.

The relationship between the type of PEMC and the patient’s age, from UK TARN data, is shown in Figure 2. The PEMCs grouped as ‘other’ occurred most frequently affecting 44% of patients less than 45 years of age, compared with 42% and 40% in the 45–65 year and more than 65 year age groups, respectively. In the same sequence of age groups, respiratory disease fell from 33% to 16% and 11% but there was a marked increase in cardiovascular disease 6%, 22% and 35%, respectively. In contrast, there was minimal difference in metabolic disease (13%, 18%, 10%) and neurological disease (4%, 2%, 4%).

Type of pre-existing medical conditions

A more detailed assessment of PEMC type was provided by the comprehensive data base from Hope Hospital. This enabled the PEMC groups to be refined (Fig. 3). A total of 1130 conditions were identified in the 664 trauma victims. Cardiovascular disease was the commonest group accounting for 218 or 20% of all conditions (Fig. 2). However, this also meant that of the 664 patients with PEMCs, 218 or 33% had cardiovascular disease. Similarly the 205 psychiatric conditions represented 18% of PEMCs and affected 30% of patients. These data are virtually identical to previous reports. However, pre-injury psychopathology was diagnosed in 88% of patients with penetrating trauma, 47% of those with...
blunt trauma and 75% of people who were intoxicated\textsuperscript{19}. This marked increase is likely to reflect the use of a psychiatric assessment index.

Of the remaining conditions, respiratory, abdominal and neurological comprised 13%, 12% and 11% of the total and affected 23%, 21% and 19% of patients, respectively. Thus, cardiovascular, psychiatric and respiratory conditions accounted for 51% of all PEMCs. The age related distribution of pre-injury problems (data not shown) virtually mirrored the UK data (Fig. 2) with only significant changes in cardiovascular and respiratory disease.

**Outcome**

Although PEMCs are common in UK trauma victims\textsuperscript{40}, the most interesting aspect is whether they influence outcome. Of the 8,074 patients without pre-injury problems, only 238 (2.94%) died. In this control group, age did not influence outcome. In contrast, death occurred in 380 (7.3%) of the 5,129 patients having one or more PEMCs. Furthermore, mortality increased with advancing age from 3% (47 patients) aged less than 45 years to 5% (68 patients) between 45–65 years and 13% patients (289) greater than 65 years (Table 1). Although these data are not controlled for gender and injury severity, they show that the major factor...
Co-morbid factors in trauma patients

Fig. 3 A detailed assessment of the types of pre-existing medical condition from the comprehensive data base from Hope Hospital. 'CVS' cardiovascular; 'psy' psychology; 'res' respiratory; 'abd' abdominal, 'neu' neurological; 'Other' includes rheumatoid disease and malignancy; 'P.inf.' previous infection in particular meningitis or peritonitis; 'met' metabolic including diabetes mellitus, renal and hepatic failure; 'S.PMH' significant previous medical history in particular surgery to the head, thorax or abdomen.

influencing outcome is the presence of PEMCs rather than age. Therefore, to investigate these findings further, the following study was controlled for ISS, RTS and age\textsuperscript{21,22}. There were 121 deaths in the study population of 1471 patients. In patients without PEMCs the mortality was 6.2%. This increased to 10.7% with at least one pre-injury condition. Furthermore, the number of PEMCs also influenced mortality (Table 2) which increased from 5.2% with no conditions, to 9.3% for one and 12.2% for two or more conditions. Not surprisingly, therefore, the risk of death rose as the number of PEMCs increased. In comparison with patients grouped as having either none or one PEMC, the presence of two to four PEMCs approximately doubled the risk of death (odds ratio = 2.18: 95% CI = 0.87, 5.48: \(P = 0.0097\)). Moreover, with greater than 4 PEMCs the risk of death was approximately 7-fold (odds ratio = 6.76: 95% CI = 1.95, 23.4: \(P = 0.026\)).

Table 2 The relationship between number of pre-existing conditions and mortality

<table>
<thead>
<tr>
<th>PEMC number</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5.2</td>
</tr>
<tr>
<td>1</td>
<td>9.3</td>
</tr>
<tr>
<td>2</td>
<td>15.2</td>
</tr>
<tr>
<td>3</td>
<td>23.7</td>
</tr>
<tr>
<td>&gt; 4</td>
<td>42.2</td>
</tr>
</tbody>
</table>
Although this information is of interest, more details were required to examine the impact of specific conditions on outcome. Unfortunately, for the reasons previously described, this was not possible. However, analysis of UK TARN group showed that the mortality of 7.3% for all PEMCs, increased 14% with cardiovascular disease, 24% for renal pathology and 32% for liver disease. In a smaller, but controlled study cardiovascular disease was responsible for a 3-fold increase in mortality (odds ratio = 3.37: 95% CI 1.28, 8.88: $P = 0.00139$) but this was increased even further, to almost 6-fold, in patients with pre-existing renal or liver (odds ratio = 5.69: 95% CI 1.75, 18.5: $P = 0.0039$).

The effect of these conditions has been investigated further by examining the influence of injury severity, age and PEMC on mortality (Fig. 4). These data clearly show that as the severity of injury increases so does the mortality in patients aged between 45 and 65 years. In addition, mortality is increased further, for each index of injury severity, if pre-existing cardiovascular disease is present. Similar data (not shown) were obtained for all ages. However, the changes were less marked in patients under 45 years and more dramatic in those over 65 years. Furthermore, virtually identical results were obtained in patients with metabolic conditions (mainly renal and liver disease). The prevalence of individual conditions in these studies will be influenced by variations in geography, culture and socio-economic status. This point was exemplified by the results from Hope Hospital where cardiovascular disease was the most prevalent condition and had the greatest impact on mortality. This finding was not surprising as the hospital catchment area, Salford, has one of the highest incidences of cardiovascular disease in the UK.  

**Fig. 4** The influence of injury severity, age and pre-existing medical condition on mortality. 'ISS' Injury Severity Score, 'cvd' cardiovascular; 'rts' revised trauma score
Table 3. The effect of pre-existing medical conditions on length of stay in hospital

<table>
<thead>
<tr>
<th>PEMC</th>
<th>Mean stay (days)</th>
<th>95% Confidence intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>9.1</td>
<td>8.8, 9.7</td>
</tr>
<tr>
<td>Any</td>
<td>11.7</td>
<td>10.9, 12.5*</td>
</tr>
<tr>
<td>Neurological</td>
<td>13.4</td>
<td>11.5, 15.6*</td>
</tr>
</tbody>
</table>

*P < 0.001 compared with none (i.e. no PEMC)

Pre-existing medical conditions have a profound effect on outcome following major trauma even after controlling for ISS, RTS and age. This is an important fact when taking into consideration the incidence of such problems in the UK. Although, similar findings were noted by Sacco et al they concluded that the relatively low incidence of PEMCs in their sample (4.8%) did not strongly influence outcome as measured by z + W values. In contrast, Miltzman and colleagues using multi-variate regression showed that PEMCs were significant, independent, factors influencing mortality. Thus, data from North America and from the UK show that PEMCs are an independent risk factor adversely influencing outcome despite varying patient populations, methods and results.

Another pertinent measure of outcome is the duration of hospital treatment. The presence of pre-injury pathology significantly increases the length of stay in hospital (Table 3). This difference was most marked when previous neurological problems were present. Similar findings were reported by Mackenzie, but only for patients aged less than 55 years. It is interesting to speculate that this finding is most likely to reflect either a longer duration of rehabilitation, or greater time required to arrange for the complex-care-needs to ensure safe and appropriate discharge. Furthermore, patients with PEMCs are more likely to develop complications, may have less immunological and physiological reserve, and require greater treatment not only for their injuries but also the underlying diseases.

Of the remaining host factors, there was no effect on outcome when assessing the effects of the number and type of prescribed drugs, smoking and alcohol. Of interest was the fact that although heavy drinkers (greater than or equal to 200 units/week) had more serious injuries, increased alcohol use was not an independent risk factor influencing outcome.

The patient’s age is a renowned factor that affects survival. These studies challenge this assumption and assert the alternative explanation that PEMCs, rather than age, influence outcome – especially as these conditions increase with increasing age. The previously described data from the UK TARN study support this hypothesis, as do the findings from a more recent study controlled for injury severity (Fig. 5). Mortality following trauma was approximately 4% for all age groups. This figure was significantly increased by a factor of 2.25-fold for patients under 60.
Pre-existing medical conditions rather than age influence mortality in those over 79 years old and nearly 4-fold for those less than 79 years. However, it is of interest that there was no significant difference between these figures. In contrast, patients over the age of 79 years have a significant increase in mortality. Thus, age is not an independent risk factor affecting outcome unless the patient is 79 years or older.

**Clinical relevance**

Pre-existing medical conditions have a profound effect on trauma patient survival even after controlling for age and indices of anatomical and physiological severity. These conditions are common within the UK and they not only increase with age but also increase mortality. They may influence both initial assessment and the patient’s response to resuscitation. Thus, an accurate medical history is essential to identify such conditions.

The possibility of a PEMC should be considered in a trauma patient if: (i) the physical signs seem inappropriate for the mechanism and/or severity of injury; or (ii) the patient does not respond to treatment as expected. Most medical problems can be managed along conventional guidelines, in particular during the resuscitation phase\(^49\). However, early liaison with a physician is advised.

**The future**

An internationally agreed definition of PEMC is needed to: (i) ensure the recruitment of sufficient numbers of patients, into future studies, to
examine the effects of individual diseases; (ii) facilitate comparison between studies; (iii) develop an individual scoring system that will allow detailed examination of specific PEMCs; and (iv) decide which conditions should be recorded if more than one is present, for example, in a diabetic patient should the associated ischaemic heart disease (IHD) and chronic renal failure be considered as separate conditions to the underlying diabetes mellitus? Ideally the PEMCs should indicate the primary pathology e.g.: IHD. However, sequelae due to either the disease (left ventricular failure secondary to IHD) or drug therapy (gout caused by diuretics used to treat pulmonary oedema) should be recorded to produce subgroups of valuable data for analysis.

Pre-existing conditions will continue to assume greater importance in the management of trauma. However, considerable research in this context is required to assess the effect of individual diseases. This will facilitate the development of appropriate care pathways to reduce the morbidity and mortality associated with these conditions.

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