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Long-term mortality trends in functionally-dependent adults following severe traumatic-brain injury

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Abstract

Primary objective: To investigate mortality trends in functionally dependent adults following traumatic brain injury (TBI).
Methods: Data for 966 consecutive admissions to a specialist TBI rehabilitation service were reviewed. Details for 69 subjects who were functionally dependent at rehabilitation discharge were cross-referenced against the State Government Death Register. The observed mortality rate was compared to an equivalent population sample derived from Australian Life Tables.
Results: Twenty-five subjects (36%) were deceased at an average 10.5 years post-injury (SD 5 years; range 1.7–18.8 years). The observed numbers of deaths far exceeded the expected population figure (1.9) for the same period (1989–2007) yielding a standardized mortality rate of 13.2. Mortality trends suggested a bimodal distribution, with more deaths in the first 5 years post-injury followed by no further deaths until 9 years post-injury.
Conclusions: Mortality in this functionally-dependent group was significantly associated with age, male sex and degree of disability at discharge. The bimodal distribution of mortality data suggests different contributory mechanisms to early vs. late mortality in this group.

Keywords: *Mortality, life expectancy, brain injury, severe disability*

Introduction

Traumatic brain injury (TBI) is a significant cause of death and long-term disability worldwide. An estimated 1.4 million people sustain a TBI in the US per year, of whom 17% require hospital admission [1]. Approximately 30–35% of patients admitted with moderate-to-severe TBI die within the first 30 days following the injury [2–4], a rate 5.2-times that of mild TBI [2], either due to the initial brain injury or from related trauma [5].

The literature regarding mortality after this first 30 day period presents a more complex picture. Authors have presented data from mixed TBI cohorts, combining acute with post-acute samples and/or mixing injury severity, age groups, mode of injury, physical outcome and so on. Unsurprisingly, the heterogeneity of these samples produces variability in the details of research findings. However, despite the differences in methodologies, almost all studies have identified that mortality rates in adult populations following TBI are higher than that expected in a non-injured, matched sample. By comparing TBI data to age- and sex-matched population samples, standardized mortality rates (SMR) following TBI have been reported to increase by a factor between 1.1–4.0 [2, 5–9]. Where reported, moderate-to-severe TBI produces a reduction in life expectancy of 3–9 years [5, 9, 10].

A common, but not universal, pattern to emerge from these papers is a tendency for the greatest proportion of deaths to occur in the early years post-discharge [2, 6, 9, 11]. Others report no such tendency for deaths to cluster in the years immediately following discharge [7]. Furthermore, the

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mortality rate of males has been suggested to be marginally higher than females [2, 9], although a mechanism for this finding has not been suggested.

Studies that have stratified results to account for the effect of severe disability following TBI report an even greater mortality rate than the mixed severity findings above. Indicators of disability such as reduced mobility, cognition, communication and swallowing have consistently been associated with increased mortality [5, 6, 9, 11–14]. The earliest studies found post-TBI mortality rates of 100% at 10 years [15] and 96% at 15 years [16] in the most dependent subjects. However, other studies show better long-term mortality. In Locked-In Syndrome, a syndrome that could be considered analogous to the most poorly functioning TBI subjects, debate has recently resurfaced as to whether the 20-year survival is 31 or 40% [17–19]. In addition there are a considerable number of incidental case reports where such physically disabled TBI survivors have lived in excess of 15 years post-injury [20, 21]. This begs the question as to what other features may modify the survival of these individuals.

The question of determining the life expectancy of an individual with severe disability following TBI is an important one. In some jurisdictions, legal processes determine costs of care and compensation based on life expectancy around this limited literature base [19]. As a consequence, the aim of this study was to examine the influence of sex, age, discharge destination and time post-injury on the long-term mortality rate of people surviving severe TBI who were functionally dependent at discharge from rehabilitation.

Method

Sample

Approval for the project was obtained from the local institutional ethics committee. A rehabilitation database and medical file audit of all first-injury admissions to an inpatient brain injury rehabilitation service during the calendar years 1989–2006 (inclusive) was conducted. Nine hundred and sixty-six consecutive admissions were screened for potential inclusion into the study according to the following criteria: age 16–70 years, principal diagnosis of hypoxic or traumatic brain injury and classified as 'dependent' at discharge from rehabilitation. In this context, dependency at discharge was operationally defined as scoring $\leq$54 on the Functional Independence Measure (FIM^{TM}). This represents an average score of $\leq$3 on each item. A score of '3' is defined by the FIM^{TM} as 'Requiring Moderate Assistance'. Medical records of individual admissions were excluded on the basis of age ($n=51$), scoring $\geq$55 on discharge FIM^{TM} ($n=767$) or unknown discharge FIM^{TM} ($n=74$), short admission for assessment purposes only ($n=4$) or diagnosis of stroke ($n=1$). A sample of 69 subjects (7.1%) met inclusion criteria and further data collection was undertaken. The sample characteristics are summarized in Table I.

Table I. Pre-morbid history and injury-related differences between surviving and deceased groups.

	Alive ($n=44$)	Deceased ($n=25$)	p
Age at injury years: *M* (SD)	29.7 (11.5)	36.8 (15.0)	0.05
Sex: *n* (%)			
Male	31 (70)	23 (95)	0.04
Female	13 (30)	2 (5)	
Type of injury: *n* (%)			
Closed HI	39 (89)	21 (84)	
Open HI	2 (4)	2 (8)	
Hypoxic	3 (7)	2 (8)	
Mode of injury: *n* (%)			
MV-related	25 (57)	14 (56)	
Fall	6 (14)	4 (16)	
Assault	5 (11)	4 (16)	
GSW	0 (0)	1 (4)	
Hypoxia	3 (7)	2 (8)	
Other	5 (11)	0 (0)	
GCS [best in 1st 24 hours]: *M* (SD)	4 (2)	5 (4)	
Compensation status: *n* (%)			
Public patient	30 (68)	17 (68)	
Motor vehicle insurance	11 (25)	6 (24)	
Workers compensation	3 (7)	2 (8)	
Prior medical history: *n* (%)			
Head injury	3 (7)	4 (16)	
Epilepsy	0 (0)	3 (12)	
Psychiatric illness	5 (11)	5 (20)	
Substance abuse	4 (9)	8 (32)	
Alcohol abuse	5 (11)	8 (32)	

HI = head injury, MV = motor vehicle, GSW = gunshot wound, GSC = Glasgow Coma Scale.

Data collection

Demographic data including age, sex, history of pre-injury alcohol and/or drug use, psychiatric illness, previous TBI and/or a diagnosis of epilepsy were collected for all 69 subjects. Injury-related details including GCS, admission FIM^{TM}, length of stay (LOS), occurrence of in-hospital aspiration pneumonia, insertion of a tracheostomy tube or percutaneous endoscopic gastrostomy (PEG) tube during admission and discharge swallowing status (scored on Functional Assessment Measure [22]) were extracted from the medical record of each participant. Level of function was determined at the time of discharge from inpatient rehabilitation using the FIM^{TM} total, motor and cognitive sub-scale scores.

The survival status of subjects was determined at the anchor point of 16 August 2007; allowing a 12-month period to elapse between the last discharged subject in the sample (17 August 2006) and the anchor point. Participant information was forwarded to the New South Wales Department of Births, Deaths and Marriages. Requests to four additional states and territories of Australia occurred in cases known to have relocated out-of-state after discharge. Information regarding the cause and date of death were obtained for deceased subjects.

Analysis

Using Life Expectancy (LE) tables [23], a population-based control sample was first constructed based on the sex and age of each TBI subject corresponding to each year the subjects were enrolled in the study. The cumulative risk of death was calculated for the modelled control sample and compared with actual sample mortality rates. Furthermore, a sub-analysis of the modelled and actual LE data examined the impact of sex-adjusted mortality rates. Descriptive statistics were undertaken on cause of death data as small category sizes prevented inferential analysis.

Differences between the living and deceased groups were measured on several demographic and injury-related variables using independent sample *t*-tests or Mann-Whitney U-tests for non-parametric analyses (SPSS v.15.0). Chi-square analyses were used to compare between-group differences on categorical variables. Differences were considered statistically significant when $p \leq 0.05$.

To examine the impact of functional dependency at rehabilitation discharge, the data from this study was compared to data previously collected at the same facility, reported in 2000 [9]. The 2000 study evaluated 476 subjects, on average 5.3 years post-injury. The earlier sample included all discharges during the calendar years 1986–1996 and was largely unstratified for level of functional dependency. The overlap between studies meant data from 30 subjects are present in both data sets.

Results

Time from injury to the anchor-point ranged from 1.7–18.8 years. Survival status was determined on average 10.5 years post-injury (SD 5 years). From this sample of 69 subjects, 25 were deceased at the anchor point, representing 36% of the sample (Poisson exact 95% CI 0.234–0.535). In contrast, only 1.9 deaths (2.8%, Poisson exact 95% CI 0.003–0.103) were expected in an equivalent modelled sample from the general population. The absence of overlap in the 95% confidence interval suggests that

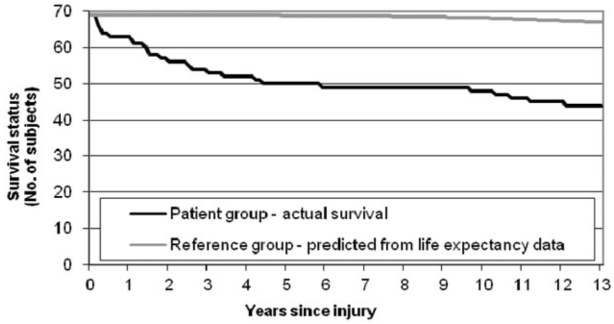

Figure 1. Survival status of predicted and actual sample.

the mortality rates between the two groups were significantly different. Differences between observed and expected mortality rate yield an SMR = 13.2.

Mean interval from injury to death was 3.6 years (range 2 months to 12 years). The greatest mortality rate was evident during the first 4 years post-injury (see Figure 1). One death occurred during the 5^{th} post-injury year. A plateau occurred during years 6–9, during which time no deaths took place. Five late deaths occurred during years 9–12 post-injury. Approximately half the sample (55%, 38 subjects) had sustained their injury more than 10 years prior to the anchor date, of whom 50% ($n = 19$) were deceased when followed-up. In comparison, 18 subjects (26% of total sample) had sustained their injuries 15 years prior to the anchor point, of whom seven (39%) were deceased.

Differences between surviving and deceased groups

Table I outlines demographic and injury-related differences between the deceased and living groups. The deceased group were significantly older at the time of injury ($t = -2.03$; $p = 0.05$), by an average of 7 years, and included proportionally more males than the living group ($\chi^2 = 4.4$; $p = 0.04$). The observed ratio of male:female deaths in the TBI sample was 11.5 : 1. This contrasts to a predicted ratio of male : female deaths of 9.5 : 1 in the equivalent modelled population sample, equating to a 21% over-representation of male deaths in the TBI sample. Differences between groups based on injury type, initial GCS and compensation status were not statistically significant. Pre-injury variables such as drug and alcohol abuse, psychiatric illness, epilepsy and prior head injury may be associated with increased risk of death, however in this sample small numbers prevented further analysis.

The course of rehabilitation differed between individuals who later died or survived to follow-up (see Table II). While FIM^{TM} scores were not different between groups on admission to rehabilitation, by discharge the group who subsequently died

Table II. In-hospital medical and outcome differences between living and deceased groups.

	Alive ($n=44$)	Deceased ($n=25$)	p
LOS days: M (SD)	363 (223)	256 (184)	0.05
FIM scores: M (SD)			
Admission total	20 (5)	20 (6)	
Discharge total	30 (10)	24 (8)	0.01
Discharge score = 18: n (%)	6 (14)	9 (24)	
Discharge score 19–36: n (%)	26 (62)	8 (40)	
Discharge score 37–54: n (%)	10 (24)	3 (15)	
Discharge motor sub-scale: M (SD)	20 (8)	17 (6)	0.06
Discharge cognitive sub-scale: M (SD)	10 (5)	7 (3)	0.01
Tracheostomy: n (%)	39 (89)	16 (64)	
PEG tube: n (%)	36 (82)	17 (68)	
Swallow achieved at discharge (FAM score $\geq$ 6): n (%) from $n=61$	6 (15)	4 (20)	
Post-TBI epilepsy: n (%)			
Early (1st 2 days)	5 (11)	3 (12)	
Late	9 (20)	6 (24)	
In-hospital aspiration pneumonia: n (%)	17 (39)	10 (42)	
Initial discharge destination: n (%)			
In-hospital	6 (14)	6 (24)	
Nursing home	16 (36)	14 (56)	
Rehabilitation facility	8 (8)	1 (2)	
Private dwelling	14 (32)	4 (16)	

LOS = length of stay in hospital, FIM = Functional Independence Measure, PEG = percutaneous endoscopic gastrostomy, FAM = Functional Assessment Measure.

had achieved significantly lower FIM^{TM} scores ($t=2.57$; $p=0.013$) and were discharged after a significantly shorter period of time ($t=2.14$; $p=0.047$). Differences in scores achieved on the cognitive sub-scale of the FIM^{TM} primarily contributed to the difference in functional ability at discharge ($z=-2.47, p=0.014$), while differences on the motor sub-scale approached statistical significance ($z=-1.88, p=0.060$).

Although fewer people in the deceased group had tracheostomy or PEG tubes placed, the differences, whilst clinically important, did not reach statistical significance in this sample (refer to Table II). Other factors reported to be associated with increased risk of death in people with severe disability, such as aspiration pneumonia during rehabilitation, unsafe swallow at discharge and post-TBI epilepsy, were not significantly different between the deceased and living groups. A large proportion of the deceased group were discharged to nursing home facilities or were transferred from rehabilitation back to acute management and later died in hospital.

Causes of death

Infection was the primary cause of death in 36% of this sample (Table 3). Pneumonia was cited as a primary or contributory factor in all of these cases. The proportion of deaths due to infection in the current sample was higher than the 2000 sample. Deaths due to carcinoma and cerebrovascular accident (CVA) occurred in this later sample (2008) but not in the earlier sample (2000).

Discussion

This study examined mortality rate in a stratified sample of adults surviving TBI with a high degree of residual disability at rehabilitation discharge, an average of 10.5 years post-injury. At this point over one-third (36%) of the sample were deceased, yielding an SMR of 13.2. This represents a considerably higher value than reported in studies unstratified for functional dependency at discharge, but is consistent with literature suggesting an association between increased dependency and reduced life expectancy [5, 6, 8, 9, 11]. Thirty-eight of the study group were more than 10 years post-injury and 18 subjects more than 15 years post-injury. Fifty per cent and 39% of these groups were deceased, respectively. This result compares favourably to mortality rates of 96–100% for these time-frames in some earlier studies [15, 16] and is broadly compatible with mortality rates observed in Locked-In Syndrome [17].

Multiple factors known to reduce life expectancy in people with disabilities [12, 24] were present in this sample. All subjects were functionally dependent at the time of hospital discharge in both motor and

Table III. Causes of death—comparison between 2008 and 2000 sample.

	2008 sample ($n=69$)		2000 sample ($n=426$)	
Cause of death	*n*	%	*n*	%
Infection—pneumonia/sepsis	9	36	6	22
Cardiorespiratory arrest	5	20	8	30
Haemorrhage	2	8	4	14
Renal	1	4	1	4
Accidental	1	4	2	7
Substance abuse/overdose	1	4	1	4
Epilepsy	0	0	1	4
Suicide	0	0	1	4
Insufficient information/other				
–insufficient information on death cert	3	12	3	11
–carcinoma	2	8		
–cerebral-vascular accident	1	4		
Total	25	100	27	100

Note: Data sets are inter-related (30 subjects appear in both samples).

cognitive arenas and less than half had achieved the ability to swallow independently. The deceased group were generally older at the time of their injury and there was a 21% over-representation of males (age- and sex-matched) amongst the deceased. This latter finding supports previously reported sex differences in mortality in adults [2, 9] and in children and adolescents [25].

Limited ability or opportunity to mobilize may contribute to circulatory and respiratory related causes of death. Infection/pneumonia and cardio-respiratory arrest were the highest-ranking causes of death in this sample, consistent with earlier findings by this group [9] and others. Harrison-Felix et al. [26] identified circulatory conditions, external causes and respiratory conditions as the top three ranking causes of death in adults following TBI who survived the initial 12-month post-injury period. In another large cohort study from Glasgow [11], circulatory disorders, neoplasms, respiratory disorders and digestive disorders led to the greatest number of deaths in adults with TBI who had survived the initial 12-month period post-injury.

Data from this study suggests that the relationship between time post-injury and death for dependent patients is not linear, having separate early and late components. The mortality rate appeared to follow a bimodal distribution, with more deaths in the first 5 years post-injury and then a relative plateauing of mortality rate. A similar bi-modal distribution was observed by Ratcliff et al. [7], with a high mortality rate during the first 3 years post-discharge, followed by a slowing in mortality and a second increase during years 7 and 8 post-discharge. This finding would appear to suggest that separate mechanisms contribute to early vs. late deaths in these individuals.

In this regard, one difficulty in interpreting the published life expectancy data is the potential effect of so-called 'passive euthanasia' in severely disabled adults with TBI [27, 28]. While the findings from the current study cannot confirm the existence of such a practice, they do not oppose it either, particularly given that the most common cause of death in this study was infection. This represents a problem, in that if end of life decisions are being made but not recorded, this invalidates the accuracy of predicted life expectancy based on current data sets. Available published data suggests that other subjective factors including ongoing quality of care and environmental setting [12, 24] may also impact on life expectancy. Harrison-Felix et al. [5] found the relative risk of death after TBI for individuals discharged to a nursing home or adult home environment vs. discharge to a private residence to be 1.9 (95% CI 1.2–3.1, 95% CI 0.9–3.9, respectively). The comparable relative risk value in the current study was 2.1, parallelling the trend in the earlier study. Although open to multiple interpretations, these various observations serve to highlight the issue of potential and currently uninvestigated, confounding variables in mortality rates in highly dependent individuals.

By way of example, a published letter detailed the calculation of life tables for individuals following TBI [14] utilising the Disability Rating Scale (DRS) scores from a previously published sample [5]. This model predicts that individuals with a DRS of 19 would exhibit a 50% reduction in life expectancy, but also stated that due to small sample size 'extrapolation of these results to scores above 19 should be viewed with caution' [14]. These data did not evaluate unrecorded end of life decisions or potentially preventable causes of early mortality (e.g. infection, malnutrition, pressure areas and so on).

Any of these factors have the potential to skew the interpretation of data for low functioning patients. This is not to say that it is inappropriate for clinicians to be involved in making end-of-life decisions. In a situation where there is a proven absence of cognition, an earlier death may be considered a not unreasonable outcome. However, this is not the accepted community standard in a situation where a person has the potential to interact with his or her environment and, as such, may attain a modified but positive quality of life.

The present study is also not without limitations. While the number of subjects in this study is small and from a single centre, the sample ($n = 69$) represents all functionally dependent subjects from a consecutive series of 966 discharges (i.e. 7%). Future research is required to replicate these findings in a larger, multi-centre study. Secondly, Australia does not have a Federal register of deaths. Some subjects may have moved interstate without the knowledge of the rehabilitation service, potentially leading to an under-estimate of the number of deaths. However, such unrecorded interstate mobility is not typically observed in this subject cohort and all recorded interstate moves were followed up. Thirdly, limitations exist when determining cause of death, as this relies on the accuracy of death certificates, for which there is no validation mechanism. Finally, this study has identified risk of death associated with functional status at rehabilitation discharge. Social and medical variables occurring prior to injury or during the period of time between discharge and follow-up could not be accounted for when determining risk of death.

Conclusion

The standardized mortality rate for highly-dependent adults following TBI was 13.2-times higher than an age- and sex-matched population sample. This figure represents a much greater relative risk of death following TBI than reported in functionally non-stratified studies (SMR range 1.1–4.0). The relative risk of death associated with TBI was higher for adults who sustained their injury at an older age, were male and for those who experience greater disability as a consequence of TBI. Mortality in this highly-dependent group appeared to follow a bimodal distribution, suggesting different contributory mechanisms to early vs. late mortality in this group. The debate around life expectancy continues due to the lack of adequately powered, well-designed studies that account for the various potential confounding factors. This is particularly true in those individuals with the lowest functional abilities post-injury.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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