

Survival Trends after Surgery for Acute Subdural Hematoma in Adults over a 20-Year Period

Original study - observational

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MINI-ABSTRACT

Acute subdural hematomas are considered the most lethal type of traumatic brain injury. Using the Trauma Audit and Research Network database, we analyzed 2,498 surgically-treated cases. Prognostic factors were age, GCS, ISS and pupil reactivity. A significantly increased survival was identified over the last 20 years.

STRUCTURED ABSTRACT

Objective – We sought to determine 30-day survival trends and prognostic factors following surgery for acute subdural hematomas (ASDH) in England and Wales over a 20 year period.

Summary Background Data – Acute subdural hematomas are still considered the most lethal type of traumatic brain injury. It remains unclear whether the adjusted odds of survival have improved significantly over time.

Methods – Using the Trauma Audit and Research Network (TARN) database, we analyzed ASDH cases in the adult population (>16 years) treated surgically between 1994 and 2013. 2,498 eligible cases were identified. Univariable and multiple logistic regression analyses were performed, using multiple imputation for missing data.

Results – The cohort was 74% male with a median age of 48.9 years. Over half of patients were comatose at presentation (53%). Mechanism of injury was due to a fall (<2m 34%, >2m 24%), road traffic collision (25%), and other (17%). 36% of patients presented with polytrauma. Gross survival increased from 59% in 1994-1998 to 73% in 2009-2013. Under multivariable analysis, variables independently associated with survival were: year of injury, Glasgow Coma Scale, Injury Severity Score, age and pupil reactivity. The time interval from injury to craniotomy and direct admission to a neurosurgical unit were not found to be significant prognostic factors.

Conclusions – A significant improvement in survival over the last 20 years was observed after controlling for multiple prognostic factors. Prospective trials and cohort studies are expected to elucidate the distribution of functional outcome in survivors.

INTRODUCTION

Trauma is the most common cause of death for those under the age of 45. Traumatic brain injury (TBI) remains the cause of approximately half of the deaths secondary to trauma.¹ One of the important early sequelae of TBI is the development of intracranial hematomas. These can be extradural, subdural, intraparenchymal or a combination thereof. It has long been recognized that acute subdural hematomas (ASDH) are often associated with intraparenchymal injuries and brain swelling. Hence, outcomes have historically been worse for patients with ASDH with mortality rates as high as 68%.²

Temporal evidence from the 1990s suggested that outcome following head injury had failed to improve to the same degree as other trauma.³⁻⁵ As a result, the UK National Institute for Health and Care Excellence (NICE) introduced guidelines for the management of head injury in 2003, subsequently revised in January 2014 (NICE CG176).⁶ Indeed, a study presenting data from 2003 to 2009 identified a reduction in the odds of death following head injury.⁷ There was, however, no specific analysis performed for ASDH, the focus of this study. Research utilizing the Nationwide Inpatient Sample in the USA identified an improvement in traumatic subdural hematoma mortality from 16.4% in 1996 to 11.6% in 2006.⁸ However, the authors did not distinguish acute versus chronic subdural hematomas, as it was based on ICD-9 codes. As the pathophysiology, patient populations, management strategies and outcomes differ significantly between acute and chronic subdural hematomas, the findings of this study cannot be extrapolated to ASDH.⁸

Previous retrospective cohort studies have found age, Glasgow Coma Scale (GCS), Injury Severity Scale (ISS) and pupil reactivity as independent prognostic factors.⁹⁻¹¹ Following research from the 1980s investigating the effect of time to surgery on outcome after ASDH,¹² and studies supporting this finding thereafter,¹³ it has been advised that “*life-saving decompressive surgery must be available within four hours*”.¹⁴ However, more recent studies have challenged this conclusion.^{9,11,15-19}

The aim of this study therefore was to identify trends in survival for surgical management of ASDH across England and Wales, leveraging multiple logistic regression analysis to control for case mix changes over the last 20 years. Through this we also sought to identify prognostic factors relating to outcome in ASDH and examine the relationship between time interval from injury to craniotomy and survival.

METHODS

Study Design

This is an observational cohort study with retrospective analysis of prospectively recorded data. The study is reported in accordance with the STROBE statement for cohort studies. We analyzed anonymized data on all patients with a diagnosis of subdural hematoma from the Trauma Audit and Research Network (TARN) database over a twenty-year period (1994-2013). A twenty-year period starting in 1994 was selected to provide data ten years before and after the introduction of 2003 NICE head injury guidelines. The TARN database was established in 1989. The objective of TARN is to support trauma service development and inform the research agenda by collecting information on patients admitted with major trauma.²⁰ The TARN database is now one of the largest trauma registries in Europe, with more than 500,000 cases. Initially covering 13 hospitals, the database now covers 100% of trauma receiving hospitals in England and Wales.

Outcome was recorded as a dichotomous variable (alive or dead) based on assessment at 30 days or at discharge if the latter happened before 30 days. This will be referred to as 30-day survival for economy of words. No further outcome measures were collected for identification of neurological sequelae or other disability following injury. Cases over the age of 16 whom underwent craniotomy within 48 hours of injury were selected, in order to focus on acute operative cases in the adult.

Statistical Analysis

Descriptive statistics were performed based on five-year intervals (1994-1998, 1998-2003, 2004-2008, 2009-2013). We investigated 30-day survival as a dependent variable. Variables hypothesized

to be related to survival were modeled using univariate logistic regression, retained as continuous variables where possible to maximize statistical utility.^{21,22} The date of injury was converted to a decimal, such that the exact point in the year in which the injury occurred could be retained. Subdural hematoma severity was coded using the Abbreviated Injury Scale (AIS), ranging from 4 (Severe) to 5 (Critical) in this study. Additional injuries were combined with the subdural hematoma AIS to create the Injury Severity Score (ISS).²³ Other variables analyzed included GCS, age, sex, day of the week of injury, time interval from injury to craniotomy, location of admission, presence of polytrauma, pupil reactivity and mechanism of injury. Pupil reactivity and GCS were recorded on arrival in the emergency department; the values at the scene of the accident were recorded for patients arriving intubated. This is a commonly employed approach in the TBI literature. Variables were progressed into a multiple logistic regression model. Interaction terms were tested and included if significant. Non-linear variables in this study were all modeled using restricted cubic splines.

Following selection of operative cases in adults within 48 hours, where pupil reactivity data were missing but GCS was 14 or 15, we assumed that no significant brainstem compression / uncal herniation would exist and pupils were considered to be both reactive. Multiple imputation was then applied in the updated dataset. Sensitivity was tested under multiple logistic regression analysis in three ways. Firstly, using an offset ranging between the maximum and minimum of the variable in question, with restrictions such that any imputed data did not exceed the highest and lowest possible values.^{24,25} For example, with an offset of +12 on GCS (ranging from 3 to 15), all imputed values would be 15 regardless of their initial value. Secondly, multiple logistic regression was repeated using only original sites to account for bias as a result of the addition of new sites over time. Finally, we performed propensity score matching as a further sensitivity test of modifiable risk factors found to be significant in the multivariable logistic regression model. Propensity score matching involves the construction of a conditional probability for a patient chosen at random to be exposed to the risk factor in question, after controlling for other known risk factors. This methodology was undertaken to minimise bias as a result of non-randomisation, and was performed through a one-to-one nearest neighbour method matching process.²⁶

A single p-value was obtained by computing a Wald χ^2 pooled statistic of all coefficients of the variable of interest. Significance threshold for all variables and interaction terms was set at $p < 0.05$. All analyses were performed using package *rms* in R, version 2.15.2.^{27,28} Logistic regression output was converted to a probability of survival for graphical presentation. Graphical production was completed using the *ggplot2* package in R, version 2.15.2.²⁹ Further details to the statistical methodology can be found in the Supplemental Digital Content.

Ethics

The UK Department of Health's Patient Information Advisory Group governs the use of patient information and has given ethical approval for research using anonymized TARN data.

RESULTS

Sample Characteristics

A total of 29,643 cases were identified between 1994 and 2013. Figure 1 demonstrates the process for selection of the final sample of 2,498 patients (8.4% of total sample). Sample descriptive statistics through five-year intervals and for the total cohort are shown in Table 1.

The number of patients in the database increased dramatically over the 20 year period, such that 61% presented in the period 2009-2013 (Supplemental Digital Content Figure S1). The age and sex of the patient was stable throughout, as was the Injury Severity Score (ISS) at presentation (Table 1). GCS was categorized in accordance with the Head Injury National Institute for Health and Care Excellence Guideline CG176 (Figure 2).⁶ The most common GCS at presentation was 3 (20%), followed by 15 (12%). The most common mechanism of injury for patients aged 16-45 was a road traffic collision (RTC, 37%), compared to a fall of less than 2 meters in patients aged over 45 (47%) (Supplemental Digital Content Figure S2).

Statistical Analyses

Results from univariate logistic regressions for all variables are shown in the Supplemental Digital Content. Restricted cubic splines were fitted to model the year of the injury, time interval from injury to craniotomy, age, GCS and the ISS. Pupil reactivity was modeled as a multinomial variable. All variables demonstrated significant associations to 30-day survival with the exception of sex and the day of the week of the injury (Supplemental Digital Content Tables S1 and S2).

All variables were included for multiple logistic regression. Despite a significant increase in GCS over the 20-year period, the interaction between these terms was not significant ($\chi^2 = 4.33$, $p = 0.8885$). All other interactions were also not found to be significant ($p > 0.05$) and were thus omitted. Full multiple logistic regression results were calculated with odds ratios for pupil reactivity, mechanism of injury and day of the week given relative to their respective modal values (pupil reactivity was both reactive pupils; mechanism was a fall of less than two meters; weekday was Sunday) (Tables 2 and 3). Median variables of continuous variables and mode values of discrete variables were imputed to produce plots of the results from the model.

The multiple logistic regression results demonstrated a significant improvement in survival following surgery for ASDH between 1994 and 2013 ($\chi^2 = 16.19$, $p = 0.0010$). Age ($\chi^2 = 63.44$, $p < 0.0001$), pupil reactivity ($\chi^2 = 169.21$, $p < 0.0001$), ISS ($\chi^2 = 34.68$, $p < 0.0001$) and GCS ($\chi^2 = 10.31$, $p = 0.0161$) were also significant under multivariable analysis. Median values of continuous variables and modal values of discrete variables were imputed to produce plots of the results from the model for an example patient by year of injury, age, time interval from injury to craniotomy, GCS and ISS (Figures 3 and 4). The patient imputed was a 48.9 year old male whom suffered a grade 5 SDH after a fall of less than 2 meters, without polytrauma, presenting to a hospital without a dedicated neurosciences unit on a Sunday with both reactive pupils, an ISS of 25 and GCS of 8.

With regards to age, the greatest fall in probability of survival was seen in the age range 45-70 years (45 years 30-day survival probability = 0.86 95% CI 0.78-0.91, 70 years 30-day survival probability = 0.71 95% CI 0.59-0.80), in contrast to a steady decline elsewhere (Figure 3). The time from injury to craniotomy showed no significant increase in probability of survival the earlier the procedure was performed ($\chi^2 = 3.90$, $p = 0.4203$). In addition, mechanism of injury ($\chi^2 = 9.14$, $p = 0.0577$), direct admission to NSU ($\chi^2 = 2.59$, $p = 0.1078$), presence of polytrauma ($\chi^2 = 2.57$, $p = 0.1088$), SDH severity ($\chi^2 = 0.17$, $p = 0.6837$), sex ($\chi^2 = 3.12$, $p = 0.0772$) and day of the week ($\chi^2 = 6.67$, $p = 0.3527$) were not found to be significant.

With regards to sensitivity analysis, a range of offset values were added to the imputed data separately for pupil reactivity and GCS. The multiple logistic regression was repeated and probability of survival re-calculated with 95% confidence intervals at the median and mode values for all continuous and discrete variables respectively. The probability of survival did not statistically significantly change with any offset of either variable (Supplemental Digital Content Figures S3 and S4). Furthermore, significant improvement in survival over time was observed in additional sensitivity analysis of original sites ($\chi^2 = 9.47$, $p = 0.0088$) and propensity score analysis of matched cohorts ($\chi^2 = 21.63$, $p < 0.0001$) at the beginning and end of the 20 year period (Supplemental Digital Content Tables S3 and S4).

DISCUSSION

The descriptive statistics identified a substantial improvement in survival following ASDH in England and Wales from 59% in 1994-1998 to 73% in 2009-2013. Furthermore, multiple logistic regression analysis showed a significantly improved survival over that period after controlling for all identified prognostic factors. This improvement in survival is consistent with other studies of TBI published from the TARN database.^{7,30} The significant improvement in gross survival may have been a consequence of improvements in pre-hospital and neuro-intensive care management of head-injured patients. The observed increase in baseline GCS over the 20 year period points towards improved pre-hospital management. However, one also needs to take into account that the introduction of the NICE

head injury guidelines in 2003 has led to cranial CT imaging more often being performed in patients with higher GCS in recent years.⁶

Time interval from injury to craniotomy was not found to be predictive of survival under multivariable logistic regression analysis. These results are consistent with cohort studies from Canada, Poland, the USA and the UK finding the time from injury to operative management was not predictive of outcome.^{15,16,18,19} Two studies have paradoxically found that increasing time to surgery had a significant effect in decreasing mortality. Dent et al. evaluated 211 patients, finding a strong trend towards reduced survival for patients with hematoma evacuated within 4 hours ($p = 0.07$).⁹ Walcott et al. identified a greater mortality associated with faster time to surgery, but the study was limited to patients with ASDH but limited additional structural brain injury.¹¹ A 2006 systematic review by Bullock et al. found that most studies focusing on the time between injury and surgery did not show a correlation with outcome but also noted that “the relationship between time from injury to operation and outcome is difficult to study because patients who are operated on soon after TBI tend to have more severe injuries than those who undergo delayed surgery”.²

Similar to the approach in Walcott et al., our model controlled for ISS, GCS and pupil reactivity.¹¹ The current study also presents 2,498 cases, in excess of the maximum of 211 patients previously published on this topic.⁹ Whilst it is still feasible that more severely injured people were operated on sooner, thus creating a selection bias, the design of this study significantly reduces this likelihood. However, perhaps the time interval that can have an impact on outcome is the one from the time of neurological deterioration (deterioration in GCS or new pupil abnormality), as previously suggested.²

The significance of age, GCS, ISS and pupil reactivity identified in multiple logistic regression analysis are consistent with previous findings.⁹⁻¹¹ In light of the aging population, our results suggest that the age range of 45-70 is a critical range with a significant reduction in the probability of survival above the age of 70.

The proportion of patients presenting to neurosurgical units on initial admission (33%) is consistent with the literature.^{6,7,9} Several studies in TBI literature have provided conflicting results of the effect of NSU direct admission. Raj et al. identified no significant difference in 6-month mortality for direct and indirect admission to a neurosurgical trauma centre.³¹ However, Härtl et al. identified a 50% higher risk of mortality for patients transported indirectly to a centre with neurosurgical services.³² This study did not find a significant association between direct NSU admission and survival ($\chi^2 = 2.59, p = 0.1078$). Interaction terms between direct NSU admission and mechanism of injury, GCS, ISS and pupil reactivity were also not found to be significant, suggesting direct NSU admission is also not associated with more severely injured patients or improved pre-operative resuscitation and stabilization.

LIMITATIONS

There are some limitations to the results presented here. Firstly, we defined an acute subdural hematoma as a subdural hematoma requiring a craniotomy within 48 hours of the injury. Radiological diagnosis of ASDH was not available. Our results may have therefore excluded some cases. However, overall we feel that the cut-off of 48 hours is reasonable, as this paper aimed to focus on the more severe end of the spectrum of ASDH following acute trauma.

Secondly, the model did not adjust for comorbidities due to limited data in the TARN database in early years. However as comorbidities are likely to be more prevalent with increasing age and the mean age increased over the study period, the improvement in risk-adjusted mortality over time may have been underestimated. Over the 20-year period there was also a substantial increase in the number of hospitals covered in the TARN database. Sensitivity analysis of sites present throughout the 20 year period provided consistent results to the total cohort. Whilst the case mix of patients was controlled, their location and hence potential disparities in their management was not. However, none of the NSUs were outliers on TARN mortality monitoring over the time period studied.

Furthermore, there was a substantial proportion of data with missing values as previously identified in Table 1. This is particularly pertinent for pupil reactivity which was missing throughout the period 1994-2003. Where pupil reactivity data were missing but GCS was 14 or 15, we assumed that no significant brainstem compression / uncal herniation would exist and pupils were considered to be both reactive. This way, the number of missing pupils was further reduced. Multiple imputation was then applied in the updated dataset, with statistical methods employed to minimize the potential risk to internal validity.³³

Finally, the available data do not allow us to investigate the role of primary decompressive craniectomy in the management of ASDH.³⁴ This is clearly an important aspect of surgical management and will hopefully be answered by an ongoing randomised trial (RESCUE-ASDH).³⁵

CONCLUSION

This study has reviewed TARN data of 20 years of operative management of acute subdural hematoma in England and Wales from 1994-2013. A significant improvement of survival was observed over the 20-year period after controlling for all identified prognostic factors. The analysis identified several prognostic factors of survival consistent with previously published data, notably age, GCS, ISS and pupil reactivity. Direct admission to a hospital with an on-site neurosurgical unit and a shorter time interval from injury to craniotomy were not associated with improved survival. Prospective trials and cohort studies are expected to elucidate the distribution of functional outcome in survivors.

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FIGURE LEGENDS

Figure 1 – Process for selection of final sample

Figure 2 – GCS category for ASDH across 5-Year Intervals. Values were missing in 14% of cases.

Figure 3 – Effect of year of injury, age and time interval from injury to craniotomy on probability of survival following ASDH after controlling for mechanism of injury, location of admission, GCS, ISS, pupil reactivity, severity of SDH, existence of other trauma, sex and day of the week. Shaded area represents a 95% confidence interval for the trend.

Figure 4 – Effect of ISS and GCS on probability of survival following ASDH after controlling for year of injury, age, time interval from injury to craniotomy, mechanism of injury, location of admission, pupil reactivity, severity of SDH, existence of other trauma, sex and day of the week. Error bars represent a 95% confidence interval for the trend.