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Factors Associated With In-Hospital Death among Elderly Patients Sustaining a Traumatic Subdural Haemorrhage

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Abstract

Objective: To identify factors associated with in-hospital mortality amongst elderly patients with traumatic Subdural Haemorrhage [SDH], and to determine the association between mortality and exposure to anti-platelet/anti-coagulant drugs at the time of injury.

Methods: This was a retrospective chart review of consecutive patients with SDH between August 2006 and January 2010. Clinical characteristics associated with death were determined using logistic regression. The association between death and use of anti-coagulant/anti-platelet drugs (asprin, clopidogrel, warfarin) was analysed using the Mantel-Haenszel test for trend, and further evaluated using logistic regression to control for confounding.

Results: The most common injury mechanism was a fall from standing [67%], and 66% of all patients were on antiplatelet/anticoagulant medication. Patients who died were more severely injured, had a lower GCS on arrival, larger SDH with greater mass effect, and more associated intra-cranial traumatic pathologies. Mortality increased with the bleeding tendency of the anti-platelet/anti-coagulant drug, and the severity of the injury mechanism. In contrast, age, blood pressure, pre-morbid level of function, time from injury to arrival, operative management and the presence of a focal neurological deficit had no association with death.

After controlling for confounding effects, warfarin use, the number of associated intra-cranial pathologies, injury severity score and degree of midline shift were found to be independent predictors of death. Taking an anti-platelet/anti-coagulant drug was associated with death [$p<0.05$], the probability of which increased with potency of the anti-coagulant/anti-platelet drug [$p<0.05$]. After controlling for confounders this trend persisted, although only the association with warfarin remained statistically significant.

Conclusion: In elderly patients sustaining a traumatic SDH, warfarin use, the number of associated intra-cranial pathologies, ISS and degree of midline shift were found to be predictive of death.

Keywords: Elderly; Subdural haemorrhage; Trauma; Mortality; Risk factors

Introduction

As the population ages, traumatic head injuries in older patients are an increasingly common presentation to emergency departments [1]. It is not uncommon for these patients to be taking some form of anti-coagulant or anti-platelet therapy, which may put this group of patients at greater risk for a poor outcome [2,3]. The optimal treatment for acute traumatic Subdural Haemorrhage [SDH] in the elderly can be uncertain, as high levels of co-morbid disease or drugs such as anti-coagulant and anti-platelet therapies may render the risks of neurosurgery too high, while the benefits of neurosurgery may be negligible in patients with particularly severe injuries or poor pre-morbid quality of life. Conservative therapy may be an appropriate treatment option in selected cases. Knowledge of prognostic factors after SDH aids decisions on choice of optimal treatment.

There are a variety of studies looking at prognostic factors associated with SDH, although a portion of these focus on patients with chronic SDH [4-7]. The associations found in these patients may not extrapolate to an elderly population with acute traumatic SDH. There are only a few studies focusing on patients with acute traumatic SDH [8-12](11)(11). The variables of prognostic value include increasing age, low GCS, Coagulopathy, APACHE III score, pupil abnormalities, raised ICP, other associated intra-cranial injuries such as brain contusion or subarachnoid haemorrhage, and greater thickness of the SDH or greater midline shift all of which were associated with poor outcomes. Reduced mortality was associated with surgical evacuation.

Only two of these studies focused specifically on the elderly population [10,12]. Variables associated with a poor outcome included a low GCS, pupil abnormalities, the presence of contusions and subarachnoid haemorrhage, greater thickness of the SDH and midline shift, and elevated intra-cranial pressure.

SDH frequently occurs with other intracranial injuries such as skull fractures, brain contusions, and subarachnoid haemorrhage. Few studies have included these other injuries as potential predictors of outcome. One study of particular interest which evaluated these associated injuries [10], found contusion and subarachnoid haemorrhage to be of prognostic value. This current study contributes further to this data-poor area of the literature.

The aim of this study was to identify factors associated with in-hospital mortality amongst elderly patients with a traumatic SDH. A secondary aim was to determine the association between mortality and exposure to an anti-platelet/anti-coagulant drug at the time of injury.

Methods

Study design and setting

This retrospective cohort study was undertaken at a major trauma centre located in Sydney, New South Wales, Australia. The Hospital admits over 50,000 patients annually and is the trauma referral hospital for south eastern Sydney, a geographic zone of approximately 1.5 million inhabitants. About 25% of trauma admissions to SGH are aged over 65 years. The SGH trauma service collects comprehensive clinical and treatment data on all trauma presentations. Permission for the study was granted by the hospital's human research ethics committee.

Selection of participants

Consecutive patients presenting between August 2006 and January 2010 were identified from two sources: the trauma database and the hospital clinical information database. The inclusion criteria were age ≥65, a traumatic SDH, and time between injury and presentation within two weeks. We defined an elderly population as ≥65 years based on evidence that trauma patients over this age have higher mortality following all forms of trauma, independent of their pre-existing co-morbid diseases or the region of injury **[13]**. Other studies on SDH have also used this age to define an elderly population **[5-7]**.

Patients with SDH were identified from two sources; the trauma database using abbreviated injury severity codes for SDH **[14]**, and the clinical information database using ICD-10 codes. Demographic and hospital length-of-stay data were also extracted.

Data collection

After duplicates were removed and results limited to ages ≥65, a medical record review was performed by two of the authors [SEA, JK]. Each record was screened for inclusion criteria. A standardised template for data extraction was created and refined through several trials on a small sample of medical records. Each data point was explicitly defined and the section of the medical record from which the data item was to be obtained specified. The data collected from the medical record included anti-platelet/anti-coagulant drug use at the time of injury, time of injury, pre-morbid level of function, Glasgow Coma Score [GCS] and systolic blood pressure on arrival, focal neurological deficit on arrival, mechanism of injury, operative treatment of intra-cranial injuries, and in-hospital mortality. Radiographic data from the first CT brain performed in the hospital was obtained from the reports in the radiology database. The following data was obtained: maximal thickness of the SDH, bilateral/unilateral distribution, degree of midline shift, and the presence of the following pathologies: subarachnoid haemorrhage, extra-dural haemorrhage, brain contusion, intra-cerebral haemorrhage, intra-ventricular blood, hydrocephalus, herniation, skull fracture. Injury Severity Scores [ISS] were calculated based on these reports and medical documentation.

Analysis

The sample size estimate was based on a previous study on SDH [8]. The mortality in coagulopathic patients was 25% compared with 8% with normal coagulation. With a power of 90% to demonstrate a similar difference in mortality at an alpha level of 0.05, and assuming differing group sizes in the same proportion as this study, 209 patients were required.

Demographic and clinical characteristics were first compared according to whether the patient was dead or alive at hospital discharge. Categorical variables were presented as proportions and compared using the chi-square test. Continuous, non-normally distributed data were presented as medians with IQR, and compared using the Mann-Whitney-U test, while normally distributed data were presented as means with SD and compared using student's t-test.

For the primary analysis, the association between death and all variables of interest were analysed using logistic regression. Variables considered as potential confounders were selected by clinical opinion and previous research [5,10,15,16]. These were age, sex, anti-platelet/anti-coagulant drug use, time from injury to arrival, pre-morbid level of function, GCS, systolic blood pressure, focal neurological deficit, mechanism of injury, operative treatment, ISS, thickness of the SDH, degree of midline shift, skull fracture, and the number of additional intracranial pathologies (extra-dural/subarachnoid/intra-cerebral/intra-ventricular haemorrhage, brain contusion, hydrocephalus, herniation). The univariate association between death and each variable was first explored using simple linear regression. Those variables whose association had $p<0.25$ were included in the multivariate model. Using stepwise backward elimination, variables were removed until only variables with $p<0.05$ remained in the model. Using the values of the intercept and the coefficients of each of the significant explanatory variables from the multivariate model, a predictive model was derived to estimate the probability of death for a given individual.

For the secondary analysis the association between death and use of anti-coagulant/anti-platelet drugs was first analysed using the Mantel-Haenszel test for trend to assess for evidence of an increasing proportion of death from the first to the last category [nothing, asprin, clopidogrel, warfarin]. This ranking of drugs was based on evidence suggesting an ordered increasing intra-cranial haemorrhage risk associated with these drugs [17]. Where the trend was confirmed this was tested for significant departures from the observed trend. The association was further evaluated using logistic regression to control for confounding. Variables were defined as either potential confounders or intervening variables. Intervening variables are those on the causal pathway between the exposure [anti-coagulant/anti-platelet drug] and the outcome [death], and cannot be included in a regression analysis. The associated intra-cranial pathologies [extra-dural/subarachnoid/intra-cerebral/intra-ventricular haemorrhage, brain contusion, hydrocephalus and herniation] were considered intervening variables: anti-coagulant/anti-platelet drugs are likely to cause bleeding following head trauma which contribute to the development of associated pathologies which in turn contribute to death. Similarly the SDH thickness, midline-shift, presence of bilateral SDH and GCS were considered intervening variables.

This analysis was conducted using SAS statistical software version 9.3 [SAS Institute, Cary, NC, USA].

Results

Two hundred and sixty-six patients ≥ 65 were identified. The files for 27 could not be located, and 19 did not satisfy the inclusion criteria providing 220 patients for analysis.

While the inclusion criteria allowed for the time between injury and presentation of up to two weeks, the majority presented very soon after the injury with a median time of 2.3 hours [IQR 1.0-12.0]. The most common injury mechanism was a fall from standing [67%], 66% of all patients were on antiplatelet/anticoagulant medication, and 15% of all patients were dependent, living in institutional care. Demographic and clinical characteristics of participants according to vital status are presented in Table 1. Patients who died were more severely injured, had a lower GCS on arrival to hospital, larger SDH with greater mass effect, and more associated intra-cranial traumatic pathologies. Mortality increased with the bleeding tendency of the anti-platelet/anti-coagulant drug, and the severity of the injury mechanism. In contrast, age, blood pressure, pre-morbid level of function, time from injury to arrival, operative management and the presence of a focal neurological deficit had no association with death. For those taking warfarin, the INR was identical for both groups (dead or alive).

Category	**Vital status**		
	Dead	Alive	
n [%]	43 [19.5]	177 [80.5]	Total 220
	Mean [SD]	Mean [SD]	p
Age	81 [8]	82 [7]	0.63
Systolic BP [hospital arrival]	150 [42]	155 [27]	0.35
	Median [IQR]	Median [IQR]	p
Glasgow Coma Score [hospital arrival]	11 [4-14]	15 [14-15]	<0.001
Injury Severity Score	26 [25-30]	17 [14-25]	<0.001
INR: Patients on warfarin [n=42]	2.3 [1.9-2.9]	2.3 [1.9-2.8]	0.74
All patients	1.3 [1.1-2.2]	1.1 [1.0-1.2]	<0.001
SDH thickness [mm]	11 [6-17]	7 [4-10]	<0.001
Midline shift [mm]	5 [0-16]	0 [0-0]	<0.001
Number of additional intra-cranial traumatic pathologies:	2 [0-3]	0 [0-1]	<0.001
Time from injury to arrival [hrs]	2.1 [0.8-10.8]	2.3 [1.0-12.1]	0.43
Hospital length of stay [days]	5 [1-11]	12 [6-22.5]	<0.001
	n [column%]	n [column%]	p
Male	27 [62.8]	81 [45.8]	0.05
SDH: Unilateral	29 [85.3]	150 [90.4]	0.38*
Bilateral	5 [14.7]	16 [9.6]	
Subarachnoid haemorrhage	25 [58.1]	46 [26.0]	<0.001
Brain contusion:	17 [39.5]	32 [18.1]	0.002
Intra-cerebral haemorrhage	7 [16.3]	11 [6.2]	0.03
Extra-dural haemorrhage	3 [7.0]	4 [2.3]	0.11
Intra-ventricular blood	7 [16.3]	10 [5.6]	0.02
Herniation	10 [23.3]	9 [5.1]	<0.001
Hydrocephalus	8 [18.6]	6 [3.4]	<0.001
Skull fracture	16 [37.2]	21 [11.9]	<0.001
Operative treatment	7 [16.3]	38 [21.5]	0.45

Focal deficit present [hospital arrival]	7 [17.5]	27 [15.5]	0.77
	n [row%]	n [row%]	p*
Anticoagulant type:			
Nothing	10 [13.3]	65 [86.7]	0.004
Asprin	7 [17.1]	59 [89.4]	
Clopidogrel	9 [25.7]	26 [74.3]	
Warfarin	15 [35.7]	27 [64.3]	
Premorbid level of function:			
Independent	26 [20.2]	103 [79.8]	0.98
Assistance with ADL	11 [19.3]	46 [80.7]	
Dependent	6 [18.8]	26 [81.3]	
Injury mechanism			
Fall from standing	20 [13.6]	127 [86.4]	0.005
Fall 1-5m	15 [28.8]	37 [71.2]	
Other high energy mechanism	8 [38.1]	13 [61.9]	

Table 1: Baseline characteristics of patients with SDH according to vital status

* Overall p-value for the category; ADL activities of daily living (washing, dressing, toilet, cooking, etc.)

Variables whose associations with death in the univariate analysis were <0.25 are presented in Table 2. After controlling for confounding effects, warfarin use, the number of associated intra-cranial pathologies, ISS and degree of midline shift were found to be independent predictors of death (Table 3).

Category	OR	95% CI	p
GCS	0.8	0.7 – 0.8	<0.001
SDH depth (for a 1mm increase)	1.1	1.0 – 1.1	<0.001
Bilateral versus unilateral	2.1	1.3 – 6.0	0.01
Number of additional intra-cranial traumatic pathologies:	2.2	1.7 – 3.0	<0.001
Subarachnoid haemorrhage	4	2.0 – 7.9	<0.001
Brain contusion	3	1.4 – 6.1	0.004
Intra-cerebral haemorrhage	2.9	1.1 – 8.1	0.05
Extra-dural haemorrhage	3.2	0.7 – 15.1	0.15
Intra-ventricular blood	3.2	1.2 – 9.1	0.03
Skull fracture	4.4	2.0 – 9.5	0.0002
Herniation	5.7	2.1 – 15	0.0007
Hydrocephalus	6.5	2.1 – 19.9	0.001
Sex (female vs male)	0.5	0.3 – 1.0	0.04
Anticoagulant type:			
Nothing	1.0†		0.006*
Asprin	0.8	0.3 – 2.2	

Clopidogrel	2.3	0.8 – 6.2	
Warfarin	3.6	1.4 – 9.0	
Injury mechanism			
Fall from standing	1.0†		0.007*
Fall 1-5m	2.6	1.2 – 5.5	
Other high energy mechanism	3.9	1.4 – 10.6	
Injury severity score	1.1	1.1 – 1.2	<0.001
INR (all patients)	2.1	1.3 – 3.2	0.002
Midline shift	1.2	1.1 – 1.3	<0.001

Table 2: Univariate associations with in-hospital death, Only those variables whose association with death was <0.25 are displayed.

† Reference category; *Overall p-value for the category

Category	OR	95% CI	p
Warfarin	2.9	1.1 – 7.3	0.03
Number of additional intra-cranial traumatic pathologies	1.7*	1.2 – 2.4	0.004
Injury severity score	1.1*	1.1 – 1.2	<0.001
Midline shift (mm)	1.1*	1.0 – 1.2	0.001

Table 3: Multivariate analysis: variables associated with in-hospital death.

† Reference category; *Odds ratio for a 1 unit increase in the parameter

The association between death and anti-platelet/anti-coagulant drug use at the time of injury was first assessed without controlling for any confounders. Being on an anti-platelet/anti-coagulant agent was associated with death [p=0.004], the probability of which increased with potency16 of the anti-coagulant/anti-platelet drug [p=0.001]. Departures from this trend were insignificant [p=0.23]. After controlling for confounders this trend persisted, although only the association with warfarin remained statistically significant (Table 4).

Category	OR	95% CI	p
Anticoagulant type:			
Nothing	1.0†		
Asprin	0.9	0.3 – 2.9	0.8
Clopidogrel	2.5	0.8 – 8.2	0.1
Warfarin	4.7	1.6 – 13.7	0.005

Table 4: Multivariate analysis of the association of anticoagulant/antiplatelet drug use with in-hospital death

† Reference category

Discussion

In this study we found that warfarin use, the number of associated intra-cranial pathologies, ISS and degree of midline shift to be independent predictors of death among patients sustaining a traumatic SDH.

With regard to other intra-cranial pathologies, due to the sample size we were unable to specifically assess associations for each individual intra- cranial pathology in the adjusted analysis. The unadjusted analysis is, therefore, worth commenting on. The presence of subarachnoid haemorrhage and brain contusion had a strong association with death, an association noted in one other study with a similar study population [10]. In addition intra-cerebral/intra-ventricular blood, herniation, hydrocephalus and skull fracture were associated with death. The combined effect of other intra-cranial pathologies is likely to be very useful for predicting outcome in this population, and future research should focus on determining the relative value of these pathologies in studies with larger sample sizes.

Our findings have some similarities to previous predictive studies which identified less favourable outcomes with midline shift [10,11], width of hematoma [10,11], coagulopathy[8], and APACE III score[8]. In contrast we did not find any association with operative treatment [8,15], or the presence of focal neurology [10]. GCS has also been shown to be a useful predictor of outcome for a variety of types of traumatic head injuries [9-11,18], and this also appeared to be the case in the unadjusted comparison in this study. However, this association disappeared in the multivariate analysis after controlling for confounders. A reason that GCS in this study is not an independent predictor is likely due to the inclusion of the variable 'additional intra-cranial pathologies' which would be expected to correlate with GCS but may be a better predictor in this age group where many patients with dementia or other pre-existing chronic neurologic disease had an altered baseline GCS.

There was also evidence to suggest a trend of increasing mortality with the use of anti-platelet/anti-coagulant drugs with greater propensity to cause bleeding [17], although after controlling for confounding only warfarin had a statistically significant association similar to other research [3]. In contrast, one previous study of elderly patients with acute traumatic SDH did not find any association between anti-platelet/anti-coagulant use and mortality [16].

The mechanism of the injury in the majority of cases in this study was a fall from standing height. It is recognised in a number of other studies that traumatic SDH amongst the elderly is most commonly due to this low energy mechanism [1,5,7,16,18]. Indeed, amongst elderly people who died after falling from standing, SDH was the most common traumatic lesion found [19]. However, the assumption of cause and effect is a limitation of all these studies as a spontaneous SDH may have occurred, which then caused the fall/motor vehicle accident/etc. This scenario is all the more likely in patients taking anti-coagulant/anti-platelet agents.

There are several other limitations to this study. Data were collected retrospectively from the medical record, and the accuracy of this information was dependent on how reliably this information was originally documented in the medical record. Those performing the chart reviews were not blinded to the objectives of the study. All patients with SDH may not have been captured with our methods, as this relies on correct codes having been recorded for the injuries sustained. An important confounder in observational studies where we are looking for predictive variables for the outcome of death is that the natural history of the disease is altered by treatment, most importantly the decision to perform surgery. While a variable may well be very predictive of death, no association may be found because clinicians had recognised this and took a course of action that prevented death thus removing any association. While we can attempt to control for this in the analysis, the interplay of variables that contribute to making these decisions are complex and it is unlikely that bias from this variable can be adequately controlled simply by introducing surgery as a binary variable in a regression model.

Conclusion

In elderly patients sustaining a traumatic subdural haemorrhage, warfarin use, the number of associated intra-cranial pathologies, ISS and degree of midline shift were found to be predictive of death.

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