Outcomes of patients with subarachnoid haemorrhage admitted to Australian and New Zealand intensive care units following a cardiac arrest

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ABSTRACT

Objectives: To describe the characteristics and outcomes of adults with a subarachnoid haemorrhage (SAH) admitted to Australian and New Zealand intensive care units (ICUs) with a cardiac arrest in the preceding 24 hours.
Design: Retrospective cohort study.
Setting: Study data from 144 Australian and New Zealand ICUs were obtained from the Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation Adult Patient Database.
Participants: A total of 439 of 11 047 (3.9%) patients admitted to an ICU with a SAH had a documented cardiac arrest in the 24 hours preceding their ICU admission. The mean age of patients with SAH and a preceding cardiac arrest was 55.3 years (SD, 13.7) and 251 of 439 (57.2%) were female.
Main outcome measures: The primary outcome of interest was in-hospital mortality. Key secondary outcomes were ICU mortality, ICU and hospital lengths of stay, the proportion of patients discharged home.
Results: SAH patients with a history of cardiac arrest preceding ICU admission had a higher mortality rate (81.5% *v* 23.3%; $P < 0.0001$) and a lower rate of discharge home (4.6% *v* 37.0%; $P < 0.0001$) compared with patients with SAH who did not have a cardiac arrest. Among patients with SAH who had a cardiac arrest and survived, 20 of 81 (24.7%) were discharged home. In SAH patients with cardiac arrest, having a GCS of 3, the Australian and New Zealand Risk of Death score, and being admitted to ICU for palliative care or organ donation were significant predictors of in-hospital death.
Conclusions: Almost one in five SAH patients who had a documented cardiac arrest in the 24 hours preceding ICU admission to an Australian and New Zealand ICU survived to hospital discharge, with around a quarter of these survivors discharged home. The neurological outcomes of these patients are uncertain, and understanding the burden of disability in survivors is an important area for further research.

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Subarachnoid haemorrhage (SAH) is a relatively common intensive care unit (ICU) admission diagnosis in patients who have sustained a cardiac arrest before ICU admission, representing a readily identifiable patient subgroup. Cardiac arrest secondary to SAH is associated with larger volume bleeds[1] and is caused by myocardial stunning and subendocardial ischaemia resulting from the massive catecholamine release which accompanies the rapid rise in intracranial pressure in these patients.

Between 3% and 11% of patients with SAH experience a cardiac arrest,[2] with survival to hospital discharge rates of between 0% and 6% reported in Asian, European and North American centres in this patient subgroup.[2,3] The survival rates for patients with SAH who are admitted to Australian and New Zealand ICUs after a cardiac arrest have not been reported. Such locally obtained data may be useful for Australian and New Zealand clinicians, both to guide decision making about the appropriateness of neurosurgical intervention and to provide relevant information to communicate to families.

Accordingly, the primary aim of our study was to describe the characteristics and outcomes of adults with SAH who sustained a cardiac arrest before admission to an Australian and New Zealand ICU between 2008 and 2019 and to compare them with those of patients with a SAH who did not have a cardiac arrest before ICU admission. The secondary aim of this study was to describe temporal trends in in-hospital mortality in these patients over the same period. We hypothesised that, consistent with the experience elsewhere,[2,3] the proportion of Australian and New Zealand patients with SAH and cardiac arrest who survived to hospital discharge would be 6% or lower, and that few, if any, patients would be discharged home.

Methods

Study design

We performed a retrospective cohort study using data from the Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database (APD), a clinical quality registry run by the ANZICS Centre for Outcome and Resource Evaluation, which contains over 2.5 million ICU records from more than 190 ICUs since 1993, and presently receives over 180 000 ICU records every year from ICUs in both Australia and New Zealand. The Alfred Hospital Human Research Ethics Committee (Melbourne, VIC, Australia) approved the study (HRED ref: 409/17), with waiver of individual patient consent.

Study population

All patients admitted to an Australian and New Zealand ICU from January 2008 to June 2019 were evaluated. The following diagnostic codes were used to identify patients with SAH:

- 402 (subarachnoid haemorrhage/arteriovenous malformation/intracranial aneurysm); or
- 1503 (subarachnoid haemorrhage/arteriovenous malformation/intracranial aneurysm, surgery for).

We excluded patients who were aged less than 16 years, elective admissions, readmissions, admissions from another ICU, and patients for whom in-hospital mortality data were missing.

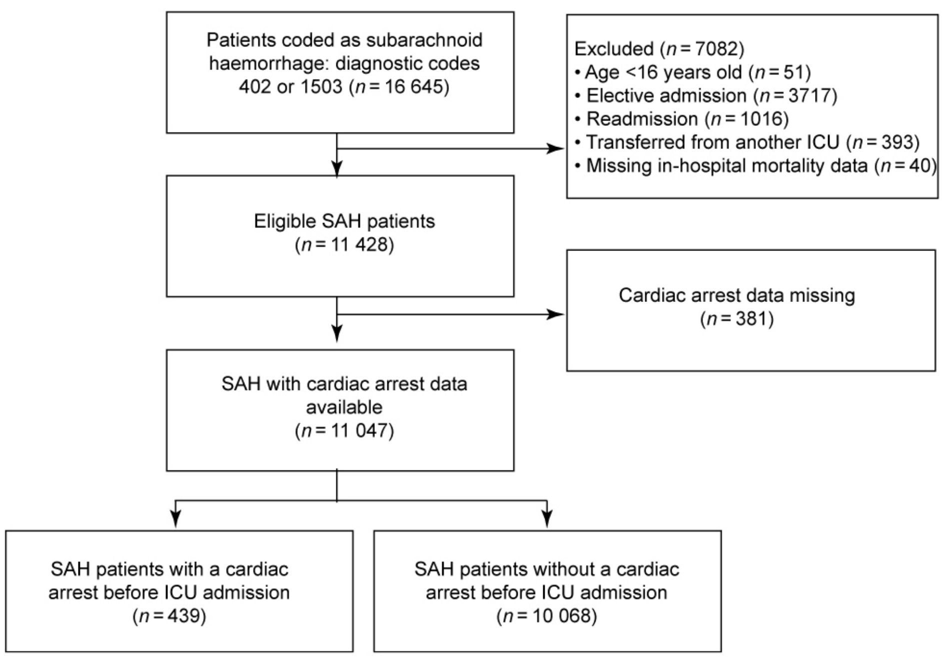
We divided the study cohort into those patients who experienced a cardiac arrest before ICU admission and those patients who did not. Cardiac arrest before ICU was defined as a cessation or sudden reduction in cardiac output leading to loss of effective circulation in the 24 hours before ICU admission.

Study data

Patient demographics (age and gender), illness severity scores, the Glasgow Coma Score (GCS), the ICU admission source (operating theatre/recovery, emergency department, ward, or other hospital), the pre-ICU hospital admission time, and the ventilation status (whether the patient was invasively mechanically ventilated on day 1) were recorded. Illness severity was determined using both the Acute Physiology and Chronic Health Evaluation (APACHE) III and the Australian and New Zealand Risk of Death (ANZROD). ANZROD is a locally derived mortality prediction model which uses components of the APACHE scoring system and locally collected variables to provide highly discriminatory (area under the receiver operating characteristic > 0.9) risk adjustment for ICU admissions in Australia and New Zealand.[4,5] The recorded GCS was the best GCS score in the first 24 hours in the ICU or, for sedated patients, as the best GCS score before sedation for purposes of mechanical ventilation.

The primary outcome of interest was in-hospital mortality. Secondary outcomes were ICU mortality, ICU and hospital length of stay, the proportion of patients discharged to a chronic care/rehabilitation facility, and the proportion of patients discharged home.

Figure 1. Study cohort selection



ICU = intensive care unit; SAH: subarachnoid haemorrhage.

Statistical analyses

All data were initially assessed for normality. We did not impute for missing data. We report categorical variables as *n* (%) and continuous variables as means ± standard deviations (SDs) or medians (interquartile ranges [IQRs]) as appropriate. Comparisons between groups (cardiac arrest *v* no cardiac arrest and hospital mortality [Yes/No]) were made using χ^2 tests for equal proportions, Student *t*-tests for normally distributed data and Wilcoxon rank sum tests otherwise, with results reported as *n* with percentages,

Table 1. Characteristics and outcomes of subarachnoid patients with and without a cardiac arrest in the 24 hours before intensive care unit (ICU) admission

Variable	No documented cardiac arrest	Documented cardiac arrest	*P*
Total number of patients	10 608	439	
Patient characteristics			
Age (years), mean (SD)	56.7 ± 14.3	55.3 ± 13.7	0.08
Female gender	6525 (61.5%)	251 (57.1%)	0.07
ICU admission source			
OT/recovery	2987 (28.2%)	67 (15.3%)	< 0.0001
Emergency department	4153 (39.1%)	283 (64.5%)	< 0.0001
Ward	967 (9.1%)	25 (5.7%)	0.014
Other hospital	2494 (23.5%)	63 (14.4%)	< 0.0001
Hours in hospital before ICU admission, median (IQR)*	4.5 (1.83–10.6)	2.83 (1.35–4.97)	< 0.0001
APACHE III, mean (SD)†	53.6 ± 28.2	97.9 ± 26.6	< 0.0001
ANZROD (%), median (IQR)†	18.3% (9.1–32.4%)	58.5% (36.8–78.3%)	< 0.0001
GCS, mean (SD)‡	10.3 ± 4.72	4.19 ± 3.11	< 0.0001
GCS 15	2858/10 441 (27.4%)	19/425 (4.5%)	< 0.0001
GCS 13–14	2327/10 441 (22.3%)	8/425 (1.9%)	< 0.0001
GCS 7–12	2335/10 441 (22.4%)	24/425 (5.6%)	< 0.0001
GCS 3–6	2921/10 441 (28.0%)	374/425 (88.0%)	< 0.0001
Admitted to ICU for palliative care	142 (1.3%)	37 (8.4%)	< 0.0001
Admitted to ICU to facilitate organ donation	180 (1.7%)	68 (15.5%)	< 0.0001
Process of care measures			
Mechanically ventilated in the first 24 hours in ICU	6324 (59.6%)	339 (90.9%)	< 0.0001
Length of stay in ICU (hours), median (IQR)	96.2 (38.4–244)	28.5 (15.3–65.2)	< 0.0001
Length of stay in hospital (hours), median (IQR)	353 (142–599)	32 (15.5–107)	< 0.0001
Patient outcomes			
ICU mortality§	1910/10 553 (18.1%)	338/437 (77.3%)	< 0.0001
In-hospital mortality	3193 (24.4%)	430 (80.7%)	< 0.0001
Discharged to chronic care facility or rehabilitation	1567 (14.8%)	18 (4.1%)	< 0.0001
Discharged home	3920 (37.0%)	20 (4.6%)	< 0.0001

APACHE III = Acute Physiology and Chronic Health Evaluation III; ANZROD = Australian and New Zealand Risk of Death; GCS = Glasgow Coma Score; IQR = interquartile range; OT = operating theatre; SD = standard deviation.* Hours in hospital before ICU admission data were missing for 1891 patients. † Illness severity data (APACHE III and ANZROD) were missing for 32 patients. ‡ GCS data were missing for 181 patients. § ICU mortality data were missing for 57 patients.

mean ± SDs or median (IQRs) respectively. We reported annualised in-hospital mortality rates for SAH patients with and without a cardiac arrest before ICU admission, along with corresponding 95% confidence intervals (CIs), which were determined using the Clopper–Pearson method. We evaluated trends in in-hospital mortality over time using the Cochran–Armitage trend test. For patients who had sustained a cardiac arrest, we performed a multivariable analysis using logistic regression with in-hospital mortality as the dependent variable. Variables with $P < 0.05$ on univariable analyses or those deemed clinically significant were considered for inclusion in a hierarchical regression model to identify the independent predictors of death for these patients.

All calculated *P* values were two-tailed. A $P < 0.05$ was chosen to indicate statistical significance. No adjustment for multiplicity of comparisons was undertaken. All analyses were performed with SAS software version 9.4 (SAS Institute, Cary, NC, USA).

Results

Patients

A total of 16 645 patients were admitted to an Australian and New Zealand ICU with a SAH between January 2008 and June 2019 of which 5217 met an exclusion criterion. Cardiac arrest status data were missing for 381 participants. Of the remaining patients, 439 of 11 047 (4.0%) had a documented cardiac arrest before ICU admission (Figure 1).

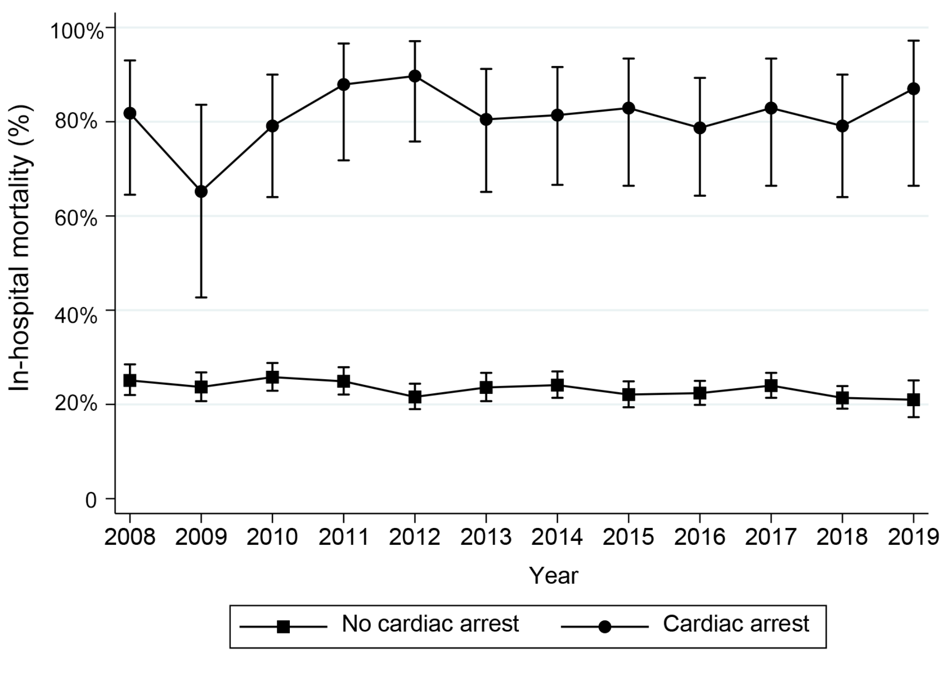
The mean age of eligible patients with SAH was 56.7 years (SD, 14.3), and of 11 047 patients, 6776 (61.3%) were female.

The age of patients with SAH was similar for those who did and did not have a cardiac arrest before ICU admission. Among those patients with cardiac arrest data available, patients with SAH who had a cardiac arrest before ICU admission were less likely to be female and had higher illness severity scores and a lower GCS (Table 1).

Patient outcomes and process of care measures

A total of 358 of 439 (81.5%) of patients with SAH who had a cardiac arrest before ICU admission died in hospital compared with 2471 of 10 608 (23.3%) who did not have a cardiac arrest ($P < 0.0001$). In the cardiac arrest group, 20 of 439 (4.6%) were discharged home compared with 3920 of 10 608 (37.0%) who did not have a cardiac arrest ($P < 0.0001$). Trends in in-hospital mortality of patients with SAH over time are shown in Figure 2. There was a significant decline in in-hospital mortality over time (25.1%

Figure 2. In-hospital mortality rates in patients with subarachnoid haemorrhage admitted to Australian and New Zealand intensive care units over time



Error bars represent 95% confidence intervals.

Table 2. Characteristics and mortality outcomes for subarachnoid patients with a history of cardiac arrest preceding intensive care unit (ICU) admission

Variable	Died in hospital	Discharged from hospital alive	*P*
Total number of patients	358	81	
Patient characteristics			
Age (years), mean (SD)	55 ± 14.3	56.6 ± 10.5	0.35
Female gender	203 (57.7%)	48 (59.3%)	0.68
ICU admission source			
OT/recovery	52 (14.5%)	15 (18.5%)	0.37
Emergency department	238 (66.5%)	45 (55.6%)	0.06
Ward	19 (5.3%)	6 (7.4%)	0.46
Other hospital	48 (13.4%)	15 (18.5%)	0.24
Hours in hospital before ICU admission, median (IQR)*	2.77 (1.42–4.62)	3.18 (1.15–6.7)	0.45
APACHE III, mean (SD)†	104 ± 21.5	69.6 ± 28	< 0.0001
ANZROD, median (IQR)†	62.6% (45.8–79.6%)	29.7% (18.5–47.6%)	< 0.0001
GCS, median (IQR)‡	3 (3–3)	6.5 (3–13)	< 0.0001
GCS 15	5/347 (1.4%)	14/78 (17.9%)	< 0.0001
GCS 13–14	1/347 (0.29%)	7/78 (9%)	< 0.0001
GCS 7–12	6/347 (1.7%)	18/78 (23.1%)	< 0.0001
GCS 3–6	335/347 (96.5%)	39/78 (50%)	< 0.0001
GCS motor score, median (IQR)	1 (1–1)	4 (1–6)	< 0.0001
Admitted to ICU for palliative care	36 (10.1%)	1 (1.2%)	0.01
Admitted to ICU to facilitate organ donation	67 (18.7%)	1 (1.2%)	< 0.0001
Process of care measures			
Mechanically ventilated in the first 24 hours in ICU	333 (93.0%)	66 (81.5%)	< 0.0001
Length of stay in ICU (hours), median (IQR)	25.4 (14.2–47.1)	120 (38.4–279)	< 0.0001
Length of stay in hospital (hours), median (IQR)	26.4 (14–52.9)	466 (163–850)	< 0.0001
Patient outcomes			
ICU mortality §	338/356 (94.9%)	0	< 0.0001
Discharged to a chronic care facility/ rehabilitation	na	18 (22.2%)	na
Discharged home	na	20 (24.7%)	na

APACHE III = Acute Physiology and Chronic Health Evaluation III; ANZROD = Australian and New Zealand Risk of Death; GCS = Glasgow Coma Score; IQR = interquartile range; na = not applicable; OT = operating theatre; SD = standard deviation.* Hours in hospital before ICU admission data were missing for 53 patients. † Illness severity data (APACHE III) were missing for four patients. ‡ GCS data were missing for 14 patients. § ICU mortality data were missing for two patients.

Table 3. Multivariable analysis for predictors of in-hospital death among subarachnoid haemorrhage (SAH) patients with preceding history of cardiac arrest before ICU admission*

Variable	Odds ratio (95% CI)	P
Age	1.02 (0.99-1.04)	0.19
ICU admission source		
OT/recovery	Reference category	
Emergency department	0.30 (0.12–0.78)	0.01
Ward	0.28 (0.07–1.16)	0.08
Other hospital	0.38 (0.13–1.14)	0.08
ANZROD†	1.06 (1.04–1.08)	< 0.0001
GCS		
GCS 15	Reference category	
GCS 13–14	0.71 (0.06–8.20)	0.78
GCS 7–12	0.78 (0.15–3.91)	0.19
GCS 3–6	12.01 (3.30–43.68)	0.0002
Mechanically ventilated in the first 24 hours in ICU	0.23 (0.06–0.88)	0.03
Admitted to ICU for palliative care or organ donation	12.36 (2.58–59.15)	0.002

ANZROD = Australian and New Zealand Risk of Death; GCS = Glasgow Coma Score; ICU = intensive care unit; OT = operating theatre. * An odds ratio of less than one suggests that the variable is associated with a decreased risk of in-hospital mortality. † For the purposes of the regression analyses, ANZROD was calculated with the age, admission source, and GCS components removed. Hosmer and Lemeshow goodness of fit test, $P = 0.59$ (suggests good fit); area under the receiver operating characteristic = 0.89 (95% CI, 0.85–0.93), suggesting good discrimination for the model.

in 2008 *v* 20.6% in 2019) for patients with SAH who had no cardiac arrest (*P* value for trend = 0.015); however, no such trend was seen (81.8% in 2008 *v* 87% in 2019) for patients with SAH who had a cardiac arrest before ICU admission (*P* value for trend = 0.65).

Data on the use of invasive ventilation in the first 24 hours in the ICU and the ICU and hospital lengths of stay are shown in Table 1, with patients with SAH who suffered a cardiac arrest being more likely to be invasively mechanically ventilated and having shorter ICU and hospital lengths of stay.

Patients with SAH who suffered a cardiac arrest were more likely to be admitted to the ICU for palliative care or to facilitate organ donation, with a total of 37 of 439 of such patients (8.4%) admitted to the ICU for palliative care and 68 of 349 (15.5%) admitted to the ICU to facilitate organ donation (Table 1).

Characteristics of survivors versus non-survivors among patients who had a cardiac arrest before ICU admission

The characteristics of survivors versus non-survivors among patients with SAH admitted to the ICU following a recent cardiac arrest are shown in Table 2. The median ICU length of stay for patients who had a cardiac arrest and died was 25.4 hours (IQR, 14.2–47.1 hours) compared with 120 hours (IQR, 38.4–279 hours) for patients who survived ($P < 0.0001$). Among patients who had a cardiac arrest and survived, 20 of 81 (24.7%) were discharged home. Among patients with SAH who had a cardiac arrest, non-survivors had statistically significantly lower GCS and correspondingly lower motor scores compared with those who survived. In the multivariable regression, among patients with SAH who had a preceding history of cardiac arrest, a GCS of 3 and admission to the ICU for palliative care or organ donation were the strongest predictors of in-hospital death (Table 3).

Discussion

Statement of principal findings

In this multicentre retrospective cohort study evaluating the outcomes of patients with SAH admitted to Australian and New Zealand ICUs between 2008 and 2019, we found that almost one in five patients with SAH who had a documented cardiac arrest in the 24 hours preceding ICU admission survived to hospital discharge and around a quarter of these survivors were discharged home.

Relationship to previous studies

The rates of survival that we observed among SAH patients with a preceding history of cardiac arrest in our series were higher than previously reported.[2,3,6] There are a number of potential explanations for these findings. First, we only included patients who survived to ICU admission compared with some other studies that also included patients who died before ICU admission.[2,7] Second, in our study, although patients who were transferred from one hospital to another were categorised as alive at hospital discharge, some of these patients may be have been transferred from a neurosurgical centre to a peripheral hospital for withdrawal of active treatment and palliative care. Third, we included patients with bleeding from arteriovenous malformations, and it is possible that these patients have a different risk profile from patients who have aneurysmal bleeds. Fourth, we relied on registry data to determine whether or not patients had a cardiac arrest. It is possible that some patients who were categorised as having a cardiac arrest, particularly those who had cardiac arrests in hospital, had very transient periods of low cardiac output. These kinds of patients may not have been included in previous reports and would potentially have a better prognosis than patients with more prolonged cardiac arrest episodes.[2] Finally, it is possible that despite all of the above considerations, the outcomes of Australian and New Zealand patients with SAH and cardiac arrest are somewhat better than elsewhere. Our finding that around a quarter of patients who had a cardiac arrest and survived were discharged home suggests that a favourable outcome may be possible for these patients. However, we cannot exclude the possibility that some patients were discharged home for palliative care in the community.

To our knowledge, this is the largest sample size of patients in whom outcomes following subarachnoid haemorrhage with cardiac arrest have been reported. Furthermore, our data was prospectively collected at multiple centres across Australia and New Zealand, and represented more than 90% of all relevant ICU admissions, providing a degree of generalisability in the study findings, at least for Australian and New Zealand clinicians.

Limitations

Our study has a number of limitations. First, we did not obtain data on the degree of neurological recovery and cannot preclude the possibility that all patients who survived were severely neurologically impaired, although the number of patients discharged home suggests this is unlikely. Second, we did not collect specific details related to the cardiac arrest event or to the computed tomography or clinical grade of the SAH, which are likely to be important determinants of patient outcomes.[1] Third, because we relied on registry data, we cannot preclude the possibility that the cardiac arrest status was incorrectly recorded in some patients or that other errors were present in the dataset. Fourth, a total of 3717 patients were excluded because they were coded as elective admissions. However, it is possible that some of these patients had a SAH and went on to have surgical treatment during the same hospital admission. Fourth, organ donation rates have increased since 2008, and it is possible associated differences in ICU admission practices over time for patients with cardiac arrest and SAH in particular may confound the interpretation of temporal trends on mortality rates in these patients.

Implications for clinical practice

Our findings suggest that the clinical outcomes of patients with SAH and a history of cardiac arrest preceding ICU admission to an Australian and New Zealand ICU may not be uniformly poor. The burden placed on ICU resources from the care of SAH patients with cardiac arrest who died was relatively small, as patients who died typically had short ICU lengths of stay. Having a GCS of 3 or being admitted to an ICU for palliative care or organ donation were significant predictors of death in such patients. A number of patients with SAH who had suffered a cardiac arrest were admitted to facilitate organ donation and one patient who was admitted for this reason survived. Admitting such patients may allow more accurate prognostication and potentially provides an opportunity to offer end-of-life care in an environment that can facilitate patient and family wishes about organ donation.[8]

Conclusions

Almost one in five patients with SAH who had a documented cardiac arrest in the 24 hours preceding ICU admission to an Australian and New Zealand ICU survived to hospital discharge, with more than a quarter of these survivors discharged home. The neurological outcomes of these patients are not clear, and understanding the burden of disability of this cohort of patients is an important area for further research.

Competing interests

This research was conducted during the tenure of a Clinical Practitioner Research Fellowship from the Health Research Council held by Paul Young. The Medical Research Institute of New Zealand is supported by independent research organisation funding from the Health Research Council of New Zealand.

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