

Mortality associated with withdrawal of life-sustaining therapy for patients with severe traumatic brain injury: a Canadian multicentre cohort study

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ABSTRACT

Background: Severe traumatic brain injury often leads to death from withdrawal of life-sustaining therapy, although prognosis is difficult to determine.

Methods: To evaluate variation in mortality following the withdrawal of life-sustaining therapy and hospital mortality in patients with critical illness and severe traumatic brain injury, we conducted a two-year multicentre retrospective cohort study in six Canadian level-one trauma centres. The effect of centre on hospital mortality and withdrawal of life-sustaining therapy was evaluated using multivariable logistic regression adjusted for baseline patient-level covariates (sex, age, pupillary reactivity and score on the Glasgow coma scale).

Results: We randomly selected 720 patients with traumatic brain injury for our study. The overall hospital mortality among these patients was 228/720 (31.7%, 95% confidence interval [CI] 28.4%–35.2%) and ranged from 10.8% to 44.2% across centres (χ^2 test for overall difference, $p < 0.001$). Most deaths

(70.2% [160/228], 95% CI 63.9%–75.7%) were associated with withdrawal of life-sustaining therapy, ranging from 45.0% (18/40) to 86.8% (46/53) (χ^2 test for overall difference, $p < 0.001$) across centres. Adjusted odd ratios (ORs) for the effect of centre on hospital mortality ranged from 0.61 to 1.55 ($p < 0.001$). The incidence of withdrawal of life-sustaining therapy varied by centre, with ORs ranging from 0.42 to 2.40 ($p = 0.001$). About one half of deaths that occurred following the withdrawal of life-sustaining therapies happened within the first three days of care.

Interpretation: We observed significant variation in mortality across centres. This may be explained in part by regional variations in physician, family or community approaches to the withdrawal of life-sustaining therapy. Considering the high proportion of early deaths associated with the withdrawal of life-sustaining therapy and the limited accuracy of current prognostic indicators, caution should be used regarding early withdrawal of life-sustaining therapy following severe traumatic brain injury.

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Traumatic brain injury is the leading cause of death and disability among patients younger than 45 years of age, with mortality rates ranging from 30% to 40%.^{1–3} Moreover, the impact of traumatic brain injury on quality of life among survivors is tremendous, with up to 30% of patients acquiring major neurologic sequelae.

Although few studies have compared mortality among centres in global trauma populations,^{4,5} overall mortality and variation in mortality, specifically for patients with critical

illness and traumatic brain injury, are less well described. Because patients with severe traumatic brain injury lack capacity for making medical decisions, relatives and medical teams must frequently estimate patients' preferences for treatment, including life support. Decisions to withdraw life-sustaining therapies are usually based on perceptions of unfavourable prognosis for meaningful neurologic recovery.^{6–8} However, there are relatively few accurate and useful prediction tools to inform such estimates of prognosis. Therefore, prognostication is often

based on clinicians' impressions and past experiences. The subjective nature of neuroprognostication may lead to variability in the incidence of death associated with the withdrawal of life-sustaining therapy. With the recent advent of programs for organ donation following cardiovascular death, potential variability in mortality and withdrawal of life-sustaining therapy among patients with severe traumatic brain injury would be of major importance from a medicolegal perspective. The ethical debate surrounding organ donation following cardiovascular death having recently reached a public hearing⁹ highlights the need to improve our understanding of withdrawal of life-sustaining therapy for this specific population of patients.

We hypothesized that hospital mortality varies across centres and that this may be explained, at least in part, by variability in the rate of withdrawal of life-sustaining therapy. We conducted a multicentre cohort study in six Canadian level-one trauma centres to investigate and compare rates of death associated with withdrawal of life-sustaining therapy among patients with severe traumatic brain injury.

Methods

Consecutive mechanically ventilated patients with severe traumatic brain injury admitted to six level one trauma centres from three Canadian provinces (Centre hospitalier affilié universitaire de Québec–Hôpital de l'Enfant-Jésus and Hôpital du Sacré-Coeur de Montréal, Quebec; Hamilton General Hospital, Sunnybrook Health Sciences Centre and St-Michael's Hospital, Ontario; and Foothills Medical Centre, Alberta) over a 24-month period (January 2005–December 2006) were considered for inclusion in the study. Severe traumatic brain injury was defined as a score of 8 or lower on the Glasgow coma scale, either in the emergency department or upon admission to the intensive care unit (ICU). We excluded patients younger than 16 years of age or patients with penetrating brain injuries.

The primary outcome was the unadjusted and adjusted proportion of patients dying following the withdrawal of life-sustaining therapy. Sec-

ondary outcomes of interest were unadjusted and adjusted hospital mortality, the proportions of early deaths associated with withdrawal of life-sustaining therapy (within the first three days) and the factors that motivated the decision to withdraw life-sustaining therapy. We obtained approval from the Research Ethics Board of the Centre hospitalier affilié universitaire de Québec–Hôpital de l'Enfant-Jésus and from each participating institution.

Identification of patients

We retrospectively identified patients from trauma registries and/or discharge databases at all centres using the *International Statistical Classification of Diseases and Related Health Problems*, 10th revision (codes for traumatic brain injury: S06.0–S06.9). Patients with no record of admission to an ICU were excluded. Data abstractors reviewed individual patient charts to confirm eligibility for the study.

Sample size

To obtain representative patients from both calendar years and to avoid seasonality, we randomly selected 60 patients per year at each centre ($n = 120$), for a total sample size of 720 patients. The size of this sample provided sufficient power to generate 95% confidence intervals (CIs) with $\pm 10\%$ precision for proportion of death associated with withdrawal of life-sustaining therapy and hospital mortality. Considering an incidence of withdrawal of life-sustaining therapy among nonsurvivors of 70%, with a hospital mortality of 30%, we had sufficient power to estimate the hospital effect in a logistic regression model including 16 variables, according to the rule of thumb of 8–10 events per independent variable.¹⁰

Developing the case report form

The standardized case report form was designed by critical care physicians, researchers and research nurses with experience reviewing charts. Research personnel pretested the case report form in two centres (Hôpital de l'Enfant-Jésus and Hamilton General Hospital). We performed duplicate data abstraction in one centre, analyzed the reasons for discordant data retrieval and modified the forms accordingly. An operations manual was developed to ensure the uniform collection of data.

Data collection

Qualified and trained research assistants with nursing or medical backgrounds retrieved data in each centre. The principal investigator provided clarification on data collection as needed. The

To promote transparency, *CMAJ* publishes the names of public institutions in research papers that compare their performance or quality of care with other institutions. The authors of this paper have not linked individual institutions to outcome data. We decided to publish this paper without this information, as we felt that it was more important to communicate the finding that variation exists between institutions in decisions about the withdrawal of life-sustaining therapy than to insist on transparency.
—Editor, *CMAJ*

data collected included patient age and sex, mechanism of trauma, severity of illness scores (Glasgow coma scale, injury severity score), pupillary reactivity on admission to the ICU and initial computed tomodensitometry of the head. Documentation concerning prognosis and end-of-life decision-making was collected up to the time of discharge from hospital. Withdrawal of life-sustaining therapy was labeled whenever therapies such as mechanical ventilation, inotropes, vasopressors or renal replacement therapy were withdrawn without the expectation of survival. Reasons for withdrawal of life-sustaining therapy were collected. More than one reason motivating the decision to withdraw life-sustaining therapy could be collected for each patient.

Statistical analysis

We described continuous variables using means and standard deviations (SDs) or medians and interquartile ranges (IQRs). We compared groups using Student *t* tests, one-way analysis of variance, Wilcoxon rank sum or Kruskal–Wallis tests, as appropriate. Associations between categorical variables were evaluated using Pearson χ^2 or Fisher exact tests. We tabulated Wilson confidence intervals for binomial proportions.

The effect of centre on overall mortality and mortality associated with withdrawal of life-sustaining therapy was estimated at 28 days and over the entire stay in hospital using adjusted odds ratios (ORs). These ORs were risk-adjusted using baseline patient-level covariates that have high accuracy for predicting outcome after traumatic brain injury (age, motor score on the Glasgow coma scale and pupillary reactivity)^{11–13} and sex, using a hierarchical regression model to account for clustering within centres. We assessed for the presence of multicollinearity between covariates. Fixed effects using Nagelkerke R^2 were used to estimate the influence of centres versus baseline risk factors on the systematic variation. These ORs represent the odds of death (overall) or the odds of withdrawal of life-sustaining therapy in a specific hospital compared with an average hospital (mean). An OR different than 1 therefore indicates a centre effect on the rates of death associated with withdrawal of life-sustaining therapy.

All tests were two-tailed and the type 1 error rate was set at 5.0%. Statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, North Carolina).

Results

Data from 720 patients were collected from the six participating centres. Sixteen patients were missing

scores on the Glasgow coma scale; we included data from 704 patients in our regression analysis.

Patient characteristics

The baseline characteristics of patients according to hospital mortality and death associated with the withdrawal of life-sustaining therapy among nonsurvivors are presented in Table 1. Most patients were male (77.1%), with a mean age of 42.4 (SD 20.5) years. The most common cause of trauma was motor vehicle collision (55.5%), followed by fall (29.7%) and assault (7.5%). Hospital mortality was 228/720 (31.7%, 95% CI 28.4%–35.2%) and ranged from 10.8% to 44.1% across centres (data not shown). Most deaths (70.2%, 95% CI 63.9%–75.7%) were associated with the withdrawal of life-sustaining therapy, the rate of which varied from 45.0% to 86.8% across centres (data not shown). Median length of stay in hospital was 16 days (IQR 5–38 d), and the median length of stay in the ICU was 6 days (IQR 2–13 d). We found a significant difference between centres ($p < 0.0001$) in terms of median length of stay for both the hospital (11–23 d) and the ICU (3–9 d) (data not shown). Among the survivors who were discharged from hospital, most were subsequently admitted to a rehabilitation centre ($n = 197$), another hospital ($n = 103$), a nursing home ($n = 12$), another ICU ($n = 5$) or sent home ($n = 141$). The fates of 18 patients postdischarge were unknown.

Mortality

Overall adjusted mortality varied by centre for 28-day mortality ($p < 0.0001$) and hospital mortality ($p < 0.0001$) (Table 2, Figure 1). A significant deviation from average mortality was observed for two centres; one centre had higher than average mortality (OR 1.57, 95% CI 1.07–2.30), whereas another centre had lower than average mortality (OR 0.61, 95% CI 0.40–0.94) (Table 2).

Withdrawal of life-sustaining therapy among nonsurvivors

No patient survived the withdrawal of life-sustaining therapy. A significant centre effect on the incidence of death following withdrawal of life-sustaining therapy was found after risk adjustment when considering both the first 28 days ($p < 0.001$) and the whole length of the stay in hospital ($p = 0.001$; Table 3, Figure 2). The adjusted ORs for death associated with the withdrawal of life-sustaining therapy while staying in hospital showed a marked deviation from the average rate of withdrawal of life-sustaining therapy (range of effects across centres, OR 0.42, 95% CI 0.23–0.74, to OR 2.42, 95% CI 1.31–4.45; Table 3). The systematic variation

explained by statistical models of hospital withdrawal of life-sustaining therapy, estimated by Nagelkerke R^2 , was 0.0924 in the model with baseline risk factors only (sex, age, pupillary reactivity and motor score on the Glasgow coma scale) and 0.2190 for the model including centres as a fixed effect. These results indicate that baseline risk factors account for little variation in the incidence of withdrawal of life-sustaining therapy and that centre accounts for more systematic variation than baseline risk factors.

Early deaths and withdrawal of life-sustaining therapy

On average, 50.0% (114/228) of deaths occurred within the first three days of admittance to an ICU (Table 4). Among these deaths, most (64.0%) were associated with withdrawal of life-sustaining therapy, but this proportion varied from 30.4% to 92.9% across centres (Table 4). When considering only deaths due to withdrawal of life-sustaining therapy, the proportion of these deaths that occurred within the first three days

Table 1: Baseline characteristics of 720 patients admitted to intensive care with severe traumatic brain injury

Characteristic	Total (n = 720)	Overall			Nonsurvivors		
		Survivors (n = 492)	Nonsurvivors (n = 228)	p value	WLST (n = 160)	No WLST (n = 68)	p value
Age, yr, mean (SD)	42.4 (20.5)	38.6 (18.7)	50.7 (21.7)	< 0.01	53.9 (21.2)	43.0 (21.1)	< 0.01
> 55, no. (%)	214 (29.7)	103 (20.9)	111 (48.7)	< 0.01	88 (55.0)	23 (33.8)	< 0.01
Male sex, no. (%)	555 (77.1)	395 (80.3)	160 (70.2)	< 0.01	110 (68.8)	50 (73.5)	0.51
Cause of trauma, no. (%)				< 0.01			< 0.01
Motor vehicle collision	400 (55.5)	293 (59.5)	107 (46.9)		67 (41.9)	40 (58.8)	
Assault	54 (7.5)	42 (8.5)	12 (5.2)		5 (3.1)	7 (10.3)	
Fall	214 (29.7)	120 (24.4)	94 (41.2)		74 (46.3)	20 (29.4)	
Other	31 (4.3)	20 (4.2)	11 (4.8)		10 (6.3)	1 (1.5)	
Unknown	21 (2.9)	17 (3.5)	4 (1.7)		4 (2.5)	0 (0.0)	
Severity scores, median (IQR)							
Glasgow coma scale							
Total score	3.0 (3.0–6.0)	6.0 (3.0–7.0)	3.0 (3.0–4.0)	< 0.01	3.0 (3.0–4.0)	3.0 (3.0–3.0)	< 0.01
Motor scale score	1.5 (1.0–4.0)	4.0 (1.0–5.0)	1.0 (1.0–2.0)	< 0.01	1.0 (1.0–3.0)	1.0 (1.0–1.0)	< 0.01
Injury severity scale	30.0 (25.0–41.0)	29.0 (25.0–41.0)	34.0 (25.0–42.5)	0.17	29.0 (25.0–41.0)	35.5 (26.0–45.0)	0.03
Abbreviated injury scale — head	5.0 (4.0–5.0)	5.0 (4.0–5.0)	5.0 (5.0–5.0)	< 0.01	5.0 (5.0–5.0)	5.0 (5.0–5.0)	0.32
Absence of pupillary reactivity, no. (%)	155 (21.5)	25 (5.1)	130 (57.0)	< 0.01	84 (52.5)	46 (67.7)	0.03
Initial head CT scan							
Delay, h, median (IQR)	2.8 (1.7–5.5)	3.0 (1.8–6.4)	2.4 (1.7–4.5)	< 0.01	2.3 (1.7–4.5)	24. (1.7–4.1)	0.78
Type of intracranial injuries, no. (%)							
Epidural hematoma/hemorrhage	76 (10.6)	55 (11.2)	21 (9.2)	0.42	12 (7.5)	9 (13.2)	0.21
Subdural hematoma/hemorrhage	329 (45.7)	201 (40.9)	128 (56.1)	< 0.01	93 (58.1)	35 (51.5)	0.38
Brain/intracranial contusion/hemorrhage	409 (56.8)	285 (57.9)	124 (54.4)	0.37	91 (56.9)	33 (48.5)	0.31
Intraventricular hemorrhage	175 (24.3)	103 (20.9)	72 (31.6)	< 0.01	51 (31.9)	21 (30.9)	0.88
Subarachnoid hemorrhage	388 (53.9)	252 (51.2)	136 (59.6)	0.03	101 (63.1)	35 (51.5)	0.11
Cerebral edema	125 (17.4)	51 (10.4)	74 (32.5)	< 0.01	52 (32.5)	22 (32.4)	0.98
Diffuse brain injury	94 (13.1)	61 (12.4)	33 (14.5)	0.44	23 (14.4)	10 (14.7)	0.94
Herniation	83 (11.5)	29 (5.9)	54 (23.7)	< 0.01	42 (26.3)	12 (17.6)	0.16
Shift of the median line, mm, mean (SE)	10.5 (0.9)	8.0 (0.6)	12.8 (1.5)	< 0.01	9.0 (0.75)	14.8 (2.2)	0.01

Note: CT = computed tomography, IQR = interquartile range, SD = standard deviation, SE = standard error, WLST = withdrawal of life-sustaining therapy.

(overall 45.6%, 95% CI 38.1%–53.4%) also varied widely across centres (range 22.2%–59.1%). An association between withdrawal of life-sustaining therapy and death within the first three days of admittance to an ICU is apparent (χ^2 test for overall difference, $p = 0.043$).

Reasons to justify withdrawal of life-sustaining therapy

The most common reason to withdraw life-sustaining therapy was a poor chance of survival (according to the medical team) (54.4%, 95% CI 46.7%–61.9%), followed by a prognosis incompatible with the patient's wishes (as indicated by the next of kin) (33.8%, 95% CI 26.9%–41.43%) and a poor long-term neurologic prognosis (as indicated by the medical team) (28.5%, 95% CI 21.2%–34.9%) (data not shown). Overall, the differences between reasons motivating the decision to withdraw life-sustaining therapy were statistically significant between centres (χ^2 test for overall difference, $p < 0.0001$).

Interpretation

In this Canadian multicentre cohort study, we saw that most deaths after severe traumatic brain injury occurred after withdrawal of life-sustaining therapy and that the rate of withdrawal of life-sustaining therapy varied significantly across level one trauma centres. Moreover, a significant proportion of deaths following withdrawal of life-sustaining therapy occurred within the first three days of acute care. We also saw considerable variability in overall hospital mortality that persisted after risk adjustment. This raises the concern that differences in mortality between centres may be partly due to variation in physicians' perceptions of long-term prognosis and physicians' practice patterns for recommending withdrawal of life-sustaining therapy.

In a large observational study on the determinants of withdrawal from mechanical ventilation among patients with critical illness, Cook and colleagues saw that one of the three strongest predictors was the presence of any disease of the central nervous system.¹⁴ Among trauma patients, the decision to withdraw life-sustaining therapy was shown to be high among nonsurvivors and was associated with concomitant traumatic brain injury.¹⁵

Although evidence suggests that the prevalence of "do not resuscitate" orders following trauma varies across centres,^{16,17} variation in the proportion of deaths following the withdrawal of life-sustaining therapy has not been previously reported for the population of patients with traumatic brain injuries. Most studies evaluating differences across centres caring for such patients have focused on comparing the impact of specific management interventions, specific factors or the designation of the trauma centre on outcomes.^{18–21}

In our study, variation in mortality following withdrawal of life-sustaining therapy is of great clinical relevance when one considers that people who acquire a severe traumatic brain injury are often young and have few or no comorbidities. Furthermore, in this specific population of patients, the decision to withdraw life-sustaining therapy made by patients' relatives and medical teams is mainly based on prognostic information. Our findings are particularly concerning because many decisions to withdraw life-sustaining therapy were made early; in our study, 64% of patients who died within three days of admission to an ICU had life-sustaining therapy withdrawn. In some instances, this may be too early for accurate neuroprognostication.

The observed variation in patterns of withdrawing life-sustaining therapy among centres may be explained by differing treatment modalities.

Table 2: Unadjusted and adjusted odds ratios by centre for mortality in hospital and after 28 days

Centre	Hospital mortality			28-day mortality		
	Unadjusted OR	Adjusted OR* (95% CI)	<i>p</i> value	Unadjusted OR	Adjusted OR* (95% CI)	<i>p</i> value
A	0.88 (0.62–1.25)	0.95 (0.65–1.41)	0.82	0.83 (0.58–1.19)	0.95 (0.65–1.39)	0.80
B	1.72 (1.25–2.39)	1.31 (0.90–1.92)	0.16	1.67 (1.20–2.31)	1.24 (0.86–1.81)	0.25
C	0.34 (0.22–0.53)	0.61 (0.40–0.94)	0.02	0.34 (0.22–0.53)	0.63 (0.42–0.96)	0.03
D	1.72 (1.25–2.39)	1.57 (1.07–2.30)	0.02	1.72 (1.24–2.38)	1.53 (1.05–2.23)	0.03
E	1.13 (0.81–1.58)	0.93 (0.62–1.38)	0.71	1.17 (0.83–1.65)	0.93 (0.63–1.36)	0.70
F	0.98 (0.70–1.38)	0.77 (0.42–1.39)	0.38	1.04 (0.74–1.48)	0.69 (0.37–1.29)	0.25

Note: CI = confidence interval, OR = odds ratios.
*Adjusted for sex, age, pupillary reactivity and score on the Glasgow coma motor scale. The reference group was the average for all hospitals.

ties, variation in the determination of prognoses and how or to what extent this information is provided to families by the medical team. In

addition, reluctance or willingness to withdraw life-sustaining therapies may be influenced by the spiritual and/or religious beliefs of the

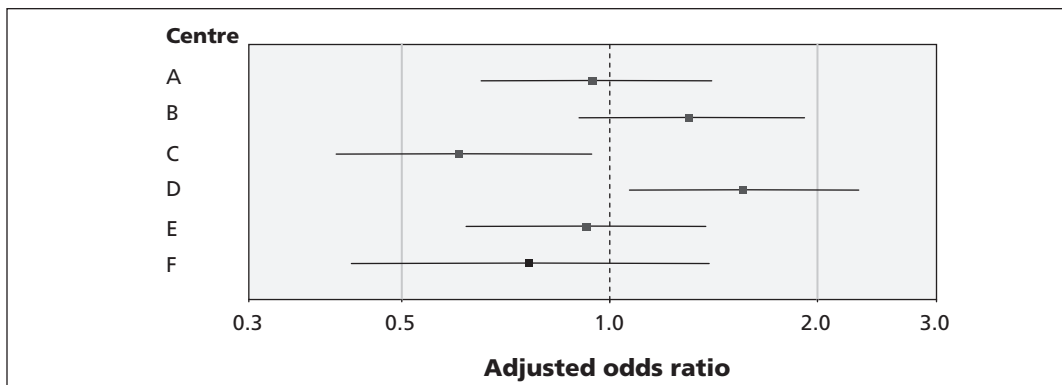


Figure 1: Adjusted odds ratios for hospital mortality by centre. Odds ratios were adjusted for sex, age, pupillary reactivity and patients' scores on the Glasgow coma scale. An odds ratio greater than 1.00 is associated with greater odds of death; an odds ratio of less than 1.00 is associated with lower odds of death. Error bars indicate 95% confidence intervals.

Table 3: Unadjusted and adjusted odds ratios by centre for mortality in hospital and after 28 days following the withdrawal of life-sustaining therapy

Centre	Hospital mortality following withdrawal			28-day mortality following withdrawal		
	Unadjusted OR	Adjusted OR* (95% CI)	p value	Unadjusted OR	Adjusted OR* (95% CI)	p value
A	1.37 (0.74-2.55)	1.27 (0.65-2.45)	0.48	1.22 (0.62-2.40)	1.18 (0.58-2.40)	0.65
B	2.12 (1.19-3.79)	2.42 (1.31-4.45)	< 0.01	3.13 (1.58-6.23)	3.58 (1.74-7.36)	< 0.01
C	0.97 (0.45-2.10)	0.85 (0.37-1.96)	0.70	0.89 (0.38-2.07)	0.75 (0.30-1.92)	0.55
D	1.14 (0.67-1.93)	1.21 (0.70-2.09)	0.50	1.17 (0.67-2.06)	1.21 (0.67-2.18)	0.52
E	0.43 (0.25-0.72)	0.42 (0.23-0.74)	< 0.01	0.39 (0.22-0.69)	0.38 (0.20-0.70)	< 0.01
F	0.73 (0.42-1.27)	0.77 (0.42-1.39)	0.38	0.64 (0.35-1.17)	0.69 (0.37-1.29)	0.25

Note: CI = confidence interval, OR = odds ratios.
 *Adjusted for sex, age, pupillary reactivity and score on the Glasgow coma motor scale. The reference group was the average for all hospitals.

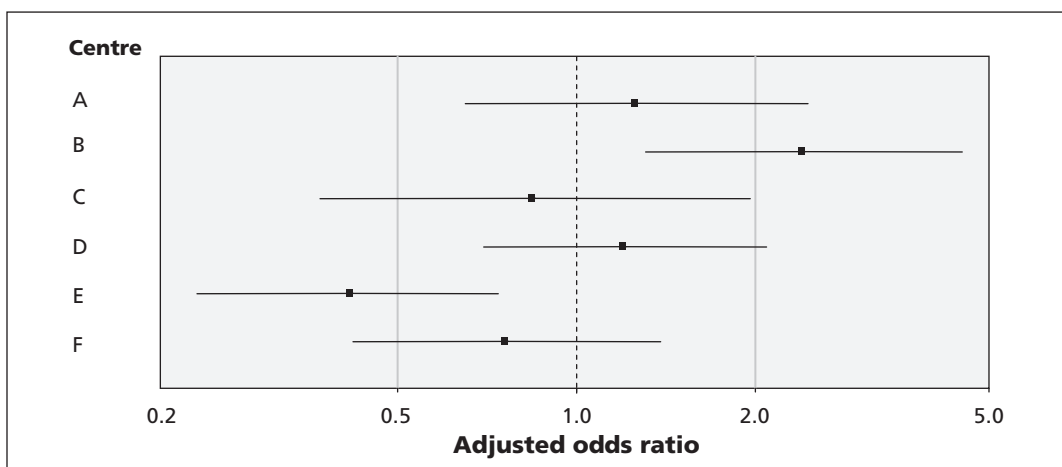


Figure 2: Adjusted odds ratios for hospital mortality following withdrawal of life-sustaining therapy by centre. Odds ratios were adjusted for sex, age, pupillary reactivity and patients' scores on the Glasgow coma scale. An odds ratio greater than 1.00 is associated with greater odds of death; an odds ratio of less than 1.00 is associated with lower odds of death. Error bars indicate 95% confidence intervals.

patients, their families and the medical teams, which may vary by region.²²

Strengths and limitations

First, the retrospective design of our study precluded the evaluation of functional and long-term outcome measures.²³ However, mortality at 12 months is likely to be comparable with hospital mortality among patients with critical illness and traumatic brain injury. Second, our study was not designed to assess the effect of potential referral bias, which might have affected mortality across centres. Indeed, there may be differences in referral patterns or case mix across centres. Third, despite using the best available predictors of mortality for risk adjustment, including sex, we cannot exclude the possibility of residual confounding. Fourth, our reliance on data from patients' medical records may have underestimated the incidence of withdrawal of life-sustaining therapy, which in turn may have provided misleading information on what drove these decisions. Nonetheless, underestimation would only reinforce our observations and concerns. Finally, we did not collect information on ethnicity, religious faith, spiritual beliefs or other factors not written in medical records, which may have had an impact on decisions surrounding withdrawal of life-sustaining therapy and consequent mortality.

Our study has several strengths. We randomly identified patients using the same strictly defined criteria at each centre, thereby enabling broad and accurate representation of practice in each centre. The size of our sample permitted accept-

able accuracy for observed estimates, and our methods allowed for the collection of high-quality, accurate, standardized data and its abstraction. Point estimates were adjusted for the three strongest prognostic indicators of death in this population,¹¹⁻¹³ and shrinkage estimates thus minimized the risk of overinflated estimates.

Conclusion

The high proportion of deaths in all centres following withdrawal of life-sustaining therapy, specifically in the early phase of care, is concerning when placed in the context of limited ability to accurately determine prognosis for patients with severe traumatic brain injury. Our study highlights the need for high-quality research to better inform decisions to stop life-sustaining treatments for these patients. However, our study was not intended to compare the quality of hospitals based on differences in care practices and mortality after traumatic brain injury. We therefore have not publicly linked hospital names to outcome data to avoid the potential for drawing spurious inferences about the quality of care.²⁴

Despite our robust analysis, observed differences in adjusted mortality across centres may still represent residual confounding by unmeasured factors.²⁵ Furthermore, some patients may consider death to be a preferable outcome to living in a permanent vegetative state or coma. In such situations, withdrawal of life-sustaining therapies may be the most acceptable option of care for families, relatives and medical teams according to patients' wishes and the philosophy

Table 4: Deaths and percentage of deaths following withdrawal of life-sustaining therapy within the first three days of care

Centre	No. of admissions	Deaths within first 3 d of care, no.	Among all deaths within the first 3 d of care, deaths following withdrawal of life-sustaining therapy		Among deaths following withdrawal of life-sustaining therapy, deaths occurring within the first 3 d of care	
			No.	% (95% CI)	No.	% (95% CI)
A	120	15	11/15	73.3 (48.1–89.1)	11/26	42.3 (25.5–61.1)
B	120	28	26/28	92.9 (77.4–98.0)	26/46	56.5 (42.3–69.8)
C	120	4	2/4	50.0 (15.0–85.0)	2/9	22.2 (6.3–54.7)
D	120	22	14/22	63.6 (43.0–80.3)	14/39	35.9 (22.7–51.6)
E	120	23	7/23	30.4 (15.6–50.9)	7/18	38.9 (20.3–61.4)
F	120	22	13/22	59.1 (38.7–76.7)	13/22	59.1 (38.7–76.7)
Total	720	114	73/114	64.0 (54.9–72.3)	73/160	45.6 (38.1–53.4)

Note: CI = confidence interval.

of care. However, caution is warranted regarding prognostication and early withdrawal of life-sustaining therapy following severe traumatic brain injury before accurate and clinically useful prognostic tests and models are available.

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