Critical Care

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Diagnosis of in-hospital mortality using admission CT perfusion in severe traumatic brain injury patients (ACT-TBI study)

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Abstract

Background Severe traumatic brain injury (TBI) stands as the leading cause of post-injury hospitalization, disability, and mortality globally. Imaging serves as a cornerstone in the assessment of patients with severe TBI and CT Perfusion (CTP) has emerged as an early prognostic tool. Our study aims to validate CTP features of non-survivable brain injury, upon hospital admission to characterize in-hospital mortality, through a well-powered prospective cohort study.

Methods In a prospective cohort study, adult patients with severe TBI were recruited to undergo whole head CTP at the time of their first imaging. Interpretation of the CTP images were conducted by two independent neuroradiologists (JS and ME), blinded to clinical results and each other's assessment. Non-survivable brain injury was defined as a matched decrease of cerebral blood flow (CBF) and cerebral blood volume (CBV) in the brainstem. The results of CTP were not disclosed to the clinical team providing patient care, and the patients received standard institutional management.

The primary outcome was a binary outcome of in-hospital mortality. The primary validity analysis involved calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for features of non-survivable brain injury on admission CTP compared to in-hospital mortality, along with 95% confidence intervals.

Results Out of the 201 patients initially enrolled in the study, 195 patients (mean age 42.9 years; Male- 160, 82%) were included in the final analysis. Among the participants, a total of 55 patients (28.2%) died during their hospital stay.

The odds ratio (OR) was highest for the presence of intracranial hemorrhage (ICH) (OR-20.25; 95% CI- 7.08–71.80, $p < 0.001$) and gun shot wound (GSW) (OR-22.67; 95% CI- 3.66–257.5, $p = 0.003$), which were independently associated with in-hospital mortality. With every decade of age, there was 1.77 times of (95% CI- 1.37–2.36, $p < 0.001$) higher odds of in-hospital mortality.

Of the 55 patients with in-hospital mortality, 17 (31%) met the criteria of non-survival brain injury on the CTP at the time of hospital admission. Both CTP and CT-angiogram (CTA)A had 100% specificity and PPV. The highest sensitivity of 33% and NPV of 80% was seen with non-survivable criteria of CTP. As a result, this variable exhibited the highest accuracy of 82% with an area under the curve (AUC) of 0.67.

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The inter-rater reliability for CTP ranged from poor (kappa = 0.07) to fair (kappa = 0.44), indicating variability in agreement between raters. In contrast, the inter-rater reliability for CTA scales ranged from fair (kappa = 0.39) to substantial (kappa = 0.79), suggesting more consistent agreement among raters.

CTP was found to be safe as no patients experience any complications associated with CTP.

Conclusion CTP features of non-survivable brain injury showed very high specificity and positive predictive value for diagnosing in-hospital mortality in patients with severe TBI.

Introduction

Traumatic brain injury (TBI) presents a significant and dire public health challenge, primarily affecting individuals who previously enjoyed a high quality of life [1]. The severity of TBI is typically categorized as mild, moderate, and severe, with a Glasgow Coma Scale (GCS) ≤ 8 on presentation defining severe TBI [2]. Severe TBI is the leading cause of post-injury hospitalization, disability, and mortality globally [8, 9]. In Canada, TBI is anticipated as the most prevalent and financially burdensome neurological condition by 2031, with its total indirect costs projected to exceed $8 billion [2]. On a global scale, TBI affects over 50 million individuals annually, with an estimated economic toll of $ 400 billion per year [5].

Severe TBI constitues a clinical emergency, demanding swift intervention from trauma teams to deliver appropriate care. Despite the intensive resources allocated, including complex surgeries and neurocritical care, as many as 50% of these patients die within 48 h of hospital admission [1, 2]. Early in-hospital mortality appears to be influenced by pre-injury conditions and the injury itself [11, 12]. It's plausible that a significant portion of these patients present with irreversible brain damage upon admission, possibly including death by neurological criteria (DNC), though detecting this acutely poses a challenge. The gold standard for diagnosing DNC relies on an unconfounded clinical examination [8], which is not generally possible in the hyperacute period. Consequently, patients often undergo elaborate, resource-intensive treatment despite uncertain prognoses.

Imaging serves as a cornerstone in the assessment of patients with severe TBI, typically employed as the first diagnostic tool in the emergency room. However, recent systematic reviews suggest limited utility of routine diagnostic imaging in predicting in-hospital mortality among patients with TBI [9, 10]. This underscores the necessity to leverage advanced imaging techniques in identifying risk factors for early mortality. CT Perfusion (CTP), an advanced CT scan providing both functional and anatomic insights into the brain, has emerged as a practical solution [11–16]. By quantifying brain perfusion through temporal change in contrast density, CTP offers promise in declaring of brain death in intensive care unit (ICU) patients [17, 18]. Moreover, small pilot studies suggest its efficacy in predicting in-hospital mortality among comatose cardiac arrest patients and patients with severe TBI [19, 20]. Our study aims to validate CTP features of non-survivable brain injury, upon hospital admission to characterize in-hospital mortality, through a well-powered prospective cohort study. The hypothesis for our study was that features of non-survivable brain injury on CTP done at hospital admission could accurately identify in-hospital mortality in patients with severe TBI.

Methods

The study received approval from our institutional ethics board (HS23683; B2020:018) and has been registered on clinicaltrials.gov with the trial registration number of NCT04318665. Deferred consent was approved by the ethics board and was obtained from all patients included in the study. The study protocol has been published for dissemination of methods [21].

Participants

In this prospective cohort study, adult patients aged 18 years or older with severe TBI were recruited. Severe TBI was defined as a Glasgow Coma Scale (GCS) score of 8 or lower after initial resuscitation, necessitating mechanical respiratory ventilation at the time of imaging. Patients were excluded if GCS score after intial resuscitation was unknown, or if they were pregnant, or had a contraindication to CT contrast agent administration (e.g., allergy, anaphylactic reaction or end-stage renal disease). Eligible patients were identified by the trauma team in a tertiary emergency department in a trauma centre that serves a population of > 1.4 million people.

Imaging

All participants underwent a whole head CTP using the same protocol as employed for stroke patients. CTP was performed prior to CT scans of other body parts. A total of 40 mL of CT contrast media was injected at a rate of 5 mL/sec. The acquired CTP images were not analyzed immediately to maintain the blinding of the clinical team. Post-processing and interpretation of the CTP images were conducted later using a semi-automatic deconvolution algorithm on a vendor-neutral software package (Oleasphere). For qualitative assessment, two

independent neuroradiologists (JS and ME), blinded to clinical results and each other's assessment, analyzed the CTP images. Non-survivable brain injury was defined as a matched decrease of cerebral blood flow (CBF) and cerebral blood volume (CBV) in the brainstem (Fig. 1). Perfusion maps were assessed for a binary outcome of presence or absence of non-survivable brain injury, with any discrepancies resolved through consensus agreement between the neuroradiologists. For quantitative assessment, non-survivable brain injury was diagnosed if CBF was less than 10 mL/100 g/min and CBV was less than 2 mL/100 g in the brainstem. The results of CTP were not disclosed to the clinical team providing patient care, and the patients received standard institutional management. Intracranial hemorrhage (ICH) was defined as traumatic intra-paranchymal hemorrhage or hemorrhagic contusion.

Circulatory stability was not a part of the inclusion criteria in our study. Use of inotropic or vasoactive agents during imaging was variable. But all patients were managed as per the brain trauma foundation guidelines.

Outcome

The primary outcome was a binary outcome of in-hospital mortality. The proportion of participants exhibiting CTP features of non-survivable brain injury upon presentation and inter-rater reliability were also recorded. Demographic details of participants; duration of stay in ICU and overall hospital stay, and functional outcomes at hospital discharge based on extended Glasgow Outcome

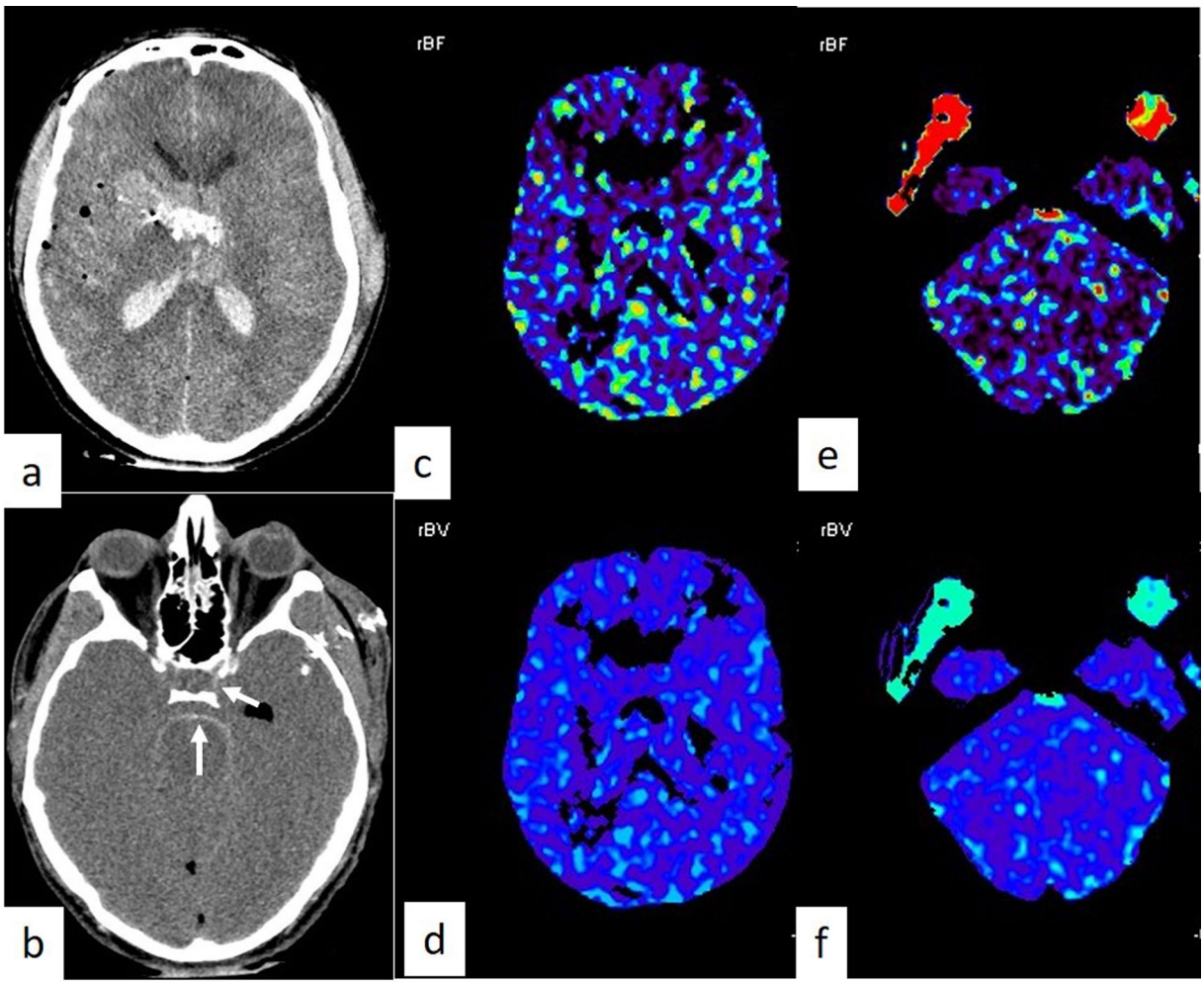

Fig. 1 Young male patient in 20 s with gun-shot injury. CT head **a**, at the time of their hospital presentation, shows traumatic intra-parenchymal, intraventricular and subarachnoid hemorrhages. CT angiogram of head **b** shows subtle filling of the basilar artery and proximal bilateral posterior cerebral arteries (arrows) as well as filling of the left internal carotid artery. CT perfusion showed marked decrease in cerebral blood flow **c** and **e** and volume **d** and **f** for both supra- **c** and **d** as well as infra-tentorial **e** and **f** compartment in keeping with CTP features of non-survivable brain injury

Scale (GOSe) were recorded [22]. The safety of CTP was assessed based on the frequency of adverse reactions, including allergic reaction and renal failure secondary to contrast injection.

Sample size calculation and statistical analyses

Based on preliminary results showing 100% specificity and positive predictive value (PPV), as well as 75% sensitivity and 94% negative predictive value (NPV) for correctly classifying in-hospital mortality [20], using Buderer's formula [23], a sample size of 200 patients with severe TBI was deemed appropriate [21]. This would allow to achieve a sensitivity of at least 75% and specificity of 95% with a confidence interval (CI) ± 5% around the point estimate.

The primary validity analysis involved calculating sensitivity, specificity, PPV, and NPV for features of non-survivable brain injury on admission CTP compared to in-hospital mortality, along with 95% confidence intervals. Sensitivity was defined as the ability of CTP to correctly classify an individual with non-survivable brain injury, while specificity was defined as the ability of CTP to correctly classify an individual with absent non-survivable brain injury. PPV was the percentage of patients showing features of non-survivable brain injury on CTP, who were deceased. NPV is the percentage of patients with no features of non-survivable brain injury on CTP, who were clinically not deceased. Area under the receiver operating characteristics (ROC) curves were generated to characterize the diagnostic ability of features non-survivable brain injury on CTP for in-hospital mortality. Inter-observer agreement between two neuroradiologists was calculated to assess the reliability of CTP. Logistic regression models were employed to construct predictive models for clinical outcomes at discharge. Complications associated with CTP were reported as numbers and proportions.

Results

Out of the 201 patients initially enrolled in the study, 195 patients (mean age 42.9 years; Male- 160, 82%) were included in the final analysis (Table 1 and Table 1S). The remaining 5 patients declined to provide consent and one additional patient was still hospitalized at the time of analysis. Among the participants, a total of 55 patients (28.2%) died during their hospital stay (Fig. 2). The death

Table 1 Demographic details and baseline characteristics of the patients in our study

	Total ***N*** **= 195**	**Death** ***N*** **= 55**	**Survival** ***N*** **= 140**	***P*-value**
Age mean (SD)	43.0 (18.9)	52.8 (22.4)	39.2 (15.9)	< 0.001
Female n (%)	35 (100)	11 (0.31)	24 (0.69)	0.640
Length of hospital stay, median (days)	4	2	9	0.024
Length of ICU stay, median (days)	4	2	6	0.073
Injury to CT time in hours (SD)	5.1 (16.6)	10.3 (27.4)	3.1 (8.9)	0.008
Admission to CT time in hours (SD)	0.6 (3.5)	1.0 (3.7)	0.4 (3.4)	0.327
Glasgow Coma Scale mean (SD) Admission GCS total	(193) 6.1 (3.3)	(54) 5.0 (2.7)	(139) 6.5 (3.4)	0.003
Admission GCS motor sub-score	(170) 2.8 (1.9)	(50) 2.2 (1.5)	(120) 3.0 (2.0)	0.010
On-scene GCS total	(179) 5.8 (3.2)	(52) 5.4 (3.7)	(127) 6.0 (3.0)	0.294
On-scene GCS motor sub-score	(128) 2.3 (1.7)	(43) 2.1 (1.8)	(85) 2.4 (1.7)	0.330
Pupillary response (%) Bilateral reactive	106/161 (100)	14/44 (13.2)	92/117 (86.8)	< 0.001
Unilateral reactive	10/161 (100)	2/44 (20.0)	8/117 (80.0)	
Bilateral unreactive	45/161 (100)	28/44 (62.2)	17/117 (37.8)	
ISS score (SD)	33.7 (25.2)	56.2 (25.9)	24.9 (18.6)	< 0.001
Rotterdam Score (SD)	2.3 (0.8)	2.8 (1.0)	2.2 (0.5)	< 0.001
ICH n (%)	88 (100)	46 (0.52)	42 (0.48)	< 0.001
TBI mechanism n (%) MVI	45 (100)	9 (0.20)	36 (0.80)	0.163
Physical assault	39 (100)	6 (0.15)	33 (0.85)	0.271
GSW	9 (100)	7 (0.78)	2 (0.22)	< 0.001
Stabbing	3 (100)	0	3 (100)	0.274
Other	129 (100)	34 (0.26)	95 (0.74)	0.423

SD standard deviation; *ICU* intensive care unit; *GCS* Glasgow Coma Scale; *ISS* Injury Severity Score; *TBI* traumatic brain injury; *ICH* intra-cranial hemorrhage; *MVI* motor vehicle injury; *GSW* gunshot wound

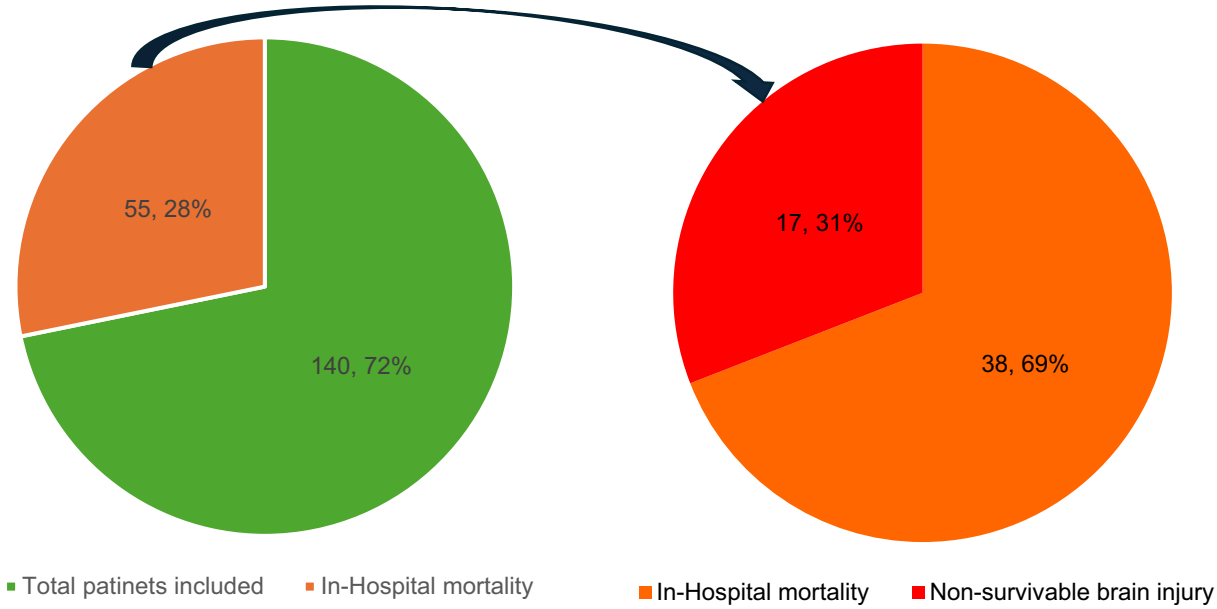

Fig. 2 Summary of the results of our study- 55 of the 195 (28.2%) patients, with severe traumatic brain injury, died during their hospital stay and 17 of these 55 (31%) patients demonstrated the CT perfusion features of non-survivable brain injury at their hospital admission

declaration by neurological criteria (65.5%) was higher ($p=0.024$) among these compared to cardio-circulatory arrest (45.5%). Patients who experienced in-hospital mortality were notably older, with a mean age of 52.8 years compared to 39.2 years for survivors ($p<0.001$). Those with in-hopstial mortality were brought to the hospital later compared to the survivors. The mean length of survival for those with in-hospital mortality was shorter (2 days vs 9 days, $p=0.024$). Those with in-hospital mortality admitted to the hospital with lower mean GCS (5 vs 6.5, $p=0.003$), in particular lower motor sub-score (2.2 vs 3, $p=0.01$) had a higher percentage of bilateral unreactive pupils (62.2 vs 37.8%, $p<0.001$). Additionally, they were more likely to have intracranial hemorrhage (52 vs 48%, $p<0.001$) and gun-shot injury (78 vs 22%, $p<0.001$). Those with in-hospital mortality scored higher on the injury severity score (ISS) (56.2 vs 24.9, $p<0.001$) and Rotterdam score (2.8 vs 2.2, $p<0.001$) compared to the survivors. The detail of the ISS is given in the Table 2S of supplementary material. Only 7.7% of patients had isolated TBI. These findings underscore the association between age, specific injury types, injury severity, presenting features and mortality risk among patients with severe TBI.

Patients who experienced in-hospital mortality also presented to the hospital with significantly higher blood glucose levels (10.2 vs 8.3 mmol/L, $p=0.007$), serum creatinine levels (89 vs 78.5 µmol/L, $p=0.051$) blood urea nitrogen levels (5.6 vs 4.2 mmol/L, $p=0.003$), blood CO2 levels (55.4 vs 49.9 mmHg, $p=0.041$); and fraction of inspired oxygen (FiO2) (62 vs 49.1%, $p=0.003$) compared to survivors (Table 2). Additionally, they exhibited significantly lower hemoglobin (126.9 vs 136.1 g/L, $p=0.008$); eGFR (87 vs 104.2, $p=0.001$) and blood pH (7.2 vs 7.3, $p=0.001$). These differences highlight the association between certain biochemical variables and the risk of mortality among patients with severe TBI, underscoring the importance of comprehensive physiological assessment in clinical management. On conversion to binary variable using clinically relevant cut offs hemoglobin < 100 g/L ($p=0.201$), FiO2 > 21% ($p=0.124$) and blood glucose < 3.9 mmol/L ($p=0.986$) were found to be not significantly different between the two groups.

In the multivariate logistic regression model, variables including age scaled by 10 years; sex, blood CO2 level ≤ 50 mmHg, eGFR < 60 ml/min/1.73 m^2, admission GCS, admission GCS motor sub-score and the presence of ICH and GSW were included (Table 3). Among these variables, the odds ratio (OR) was highest for the presence of ICH (OR-20.25; 95% CI- 7.08–71.80, $p<0.001$) and GSW (OR-22.67; 95% CI- 3.66–257.5, $p=0.003$), which were independently associated with in-hospital mortality. With every decade of age, there was 1.77 times of (95% CI- 1.37–2.36, $p<0.001$) higher odds of in-hospital mortality.

Of the 55 patients with in-hospital mortality, 17 (31%) showed CTP features of non-survivable brain injury at the time of hospital admission (Fig. 2). Sensitivity, specificity, PPV and NPV for CTP and CTA variables are summarised in Table 4 and the details for the two readers are

Table 2 Biologic variables at admission between those with and without in-hospital mortality

Biologic variable	Total *N* = 195 Mean (SD)	Death *N* = 55 Mean (SD)	Survival *N* = 140 Mean (SD)	*P*-value
Blood glucose (mmol/L)	8.8 (4.4)	10.3 (5.1)	8.2 (4.0)	0.003
Hemoglobin (g/L)	133.6 (21.4)	127.4 (22.6)	136.0 (20.4)	0.011
Na + (mmol/L)	140.7 (6.0)	141.0 (8.6)	140.6 (4.6)	0.743
K + (mmol/L)	3.8 (0.6)	3.8 (0.7)	3.8 (0.6)	0.988
Creatinine (µmol/L)	81.2 (32.4)	88.2 (35.2)	78.4 (31.0)	0.057
BUN (mmol/L)	4.6 (3.0)	5.6 (3.8)	4.2 (2.5)	0.003
eGFR	99.4 (34.4)	87.0 (33.2)	104.2 (33.7)	0.001
Baseline pH	(194) 7.3 (0.1)	7.2 (0.2)	(139) 7.3 (0.1)	0.001
HCO3 (mmol/L)	(192) 22.4 (4.2)	(54) 22.8 (4.1)	(138) 22.3 (4.2)	0.465
PCO2 (mmHg)	(194) 51.1 (16.5)	55.1 (19.2)	(139) 49.5 (15.1)	0.031
PaO2 (mmHg)	(192) 51.6 (34.9)	49.6 (34.1)	(137) 52.4 (35.3)	0.612
FiO2 (%)	(187) 52.7 (27.1)	(52) 62.0 (29.6)	(135) 49.1 (25.3)	0.003
Vital signs				
Systolic BP (mmHg)	131.9 (28.3)	135.0 (32.8)	130.7 (26.3)	0.343
Diastolic BP (mmHg)	82.5 (21.0)	85.9 (23.3)	81.1 (20.0)	0.154
MAP (mmHg)	99.0 (22.3)	102.3 (25.1)	97.7 (21.1)	0.195
Heart rate (bpm)	(194) 94.4 (29.4)	(54) 93.7 (35.6)	94.7 (26.8)	0.846
Body temperature (°C)	(184) 36.5 (1.2)	(50) 36.4 (1.8)	(134) 36.5 (0.8)	0.596

SD standard deviation; NA + – sodium; K + –potassium; *BUN* blood urea nitrogen; *eGFR*-estimated glomerular filtration rate; FiO_2 fraction of inspired oxygen; BP blood pressure; *MAP* mean arterial pressure; *bpm* beats per minute

Table 3 Results of multivariate analysis using logistic regression for significant variables from the univariate analysis showing risk factors associated with in-hospital mortality in the patients with severe TBI

	Univariate			Multivariate		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Age, scaled by 10 years	1.46	1.23–1.75	< 0.001	1.77	1.37–2.36	< 0.001
Female	1.20	0.53–2.62	0.640	1.54	0.47–4.93	0.464
Admission GCS total	0.84	0.74–0.94	0.004	0.96	0.71–1.27	0.771
Admission GCS motor sub-score	0.78	0.64–0.94	0.012	0.79	0.47–1.31	0.372
eGFR < 60 ml/min/1.73 m^2	3.25	1.29–8.31	0.012	3.30	0.88–13.25	0.079
ISS < 25	0.20	0.09–0.40	< 0.001	0.41	0.13–1.22	0.117
Rotterdam > 2	4.54	2.27–9.25	< 0.001	1.31	0.41–4.03	0.644
ICH	11.93	5.58–28.07	< 0.001	20.25	7.08–71.80	< 0.001
GSW	10.06	2.34–69.12	0.005	22.67	3.66–257.5	0.003

OR odds ratio; *CI* confidence interval; *CTP* computed tomography perfusion; *TBI* traumatic brain injury; *eGFR* estimated glomerular filtration rate; *ISS* injury severity score; *GCS ISS* injury severity score; *ICH* intra-cranial hemorrhage; *GSW* gunshot wound

summarized in the supplementary material (Table 3S and 4S). Notably, both CTP and CTA had 100% specificity and PPV. However, the maximum sensitivity of 33% and NPV of 80% was seen with non-survivable criteria of CTP. As a result, this variable exhibited the highest accuracy of 82% with an area under the curve (AUC) of 0.67. Quantitative assessment of non-survivable criteria of CTP was not accurate for in-hospital mortality (Table 5S and 6S).

Inter-rater agreement was seen ranging from 90 to 99% with higher agreement with CTA findings and lower agreement with the CTP findings. The inter-rater reliability for CTP ranged from poor (kappa = 0.07) to fair (kappa = 0.44), indicating variability in agreement between raters. In contrast, the inter-rater reliability for CTA scales ranged from fair (kappa = 0.39) to substantial (kappa = 0.79), suggesting more consistent agreement among raters.

Table 4 Diagnostic assessment of the non-survivable features on CTP, CTA and plain CT head in discriminating those with and without in-hospital mortality

Criteria	SE	95% CI	SP	95% CI	Accuracy	95% CI	PPV	95% CI	NPV	95% CI	AUC
CTP											
Brainstem	0.33	0.21–0.48	1.0	0.97–1.0	0.82	0.76–0.87	1.0	0.97–1.0	0.80	0.74–1.0	0.67
Isolated brainstem	0.25	0.14–0.40	1.0	0.97–1.0	0.80	0.74–0.85	1.0	0.97–1.0	0.79	0.72–0.84	0.63
Whole Brain	0.10	0.03–0.20	1.0	0.97–1.0	0.74	0.68–0.80	1.0	0.48–1.0	0.74	0.67–0.80	0.55
CTA											
4 points, peak phase	0.10	0.03–0.20	1.0	0.97–1.0	0.74	0.68–0.80	1.0	0.48–1.0	0.74	0.67–0.80	0.55
7 points, peak phase	0.10	0.03–0.20	1.0	0.97–1.0	0.74	0.68–0.80	1.0	0.48–1.0	0.74	0.67–0.80	0.55
10 points, peak phase	0.10	0.01–0.15	1.0	0.97–1.0	0.73	0.67–0.79	1.0	0.29–1.0	0.73	0.66–0.79	0.55
4 points, late phase	0.10	0.03–0.20	1.0	0.97–1.0	0.74	0.68–0.80	1.0	0.48–1.0	0.74	0.67–0.80	0.55
7 points, late phase	0.10	0.02–0.18	1.0	0.97–1.0	0.74	0.67–0.80	1.0	0.40–1.0	0.73	0.66–0.79	0.55
10 points, late phase	0.04	0.00–0.13	1.0	0.97–1.0	0.73	0.66–0.79	1.0	0.16–1.0	0.72	0.65–0.78	0.52
Plain CT head	0.11	0.04–0.23	1.0	0.96–1.0	0.74	0.68–0.81	0.86	0.42–1.0	0.74	0.67–0.80	0.56

SE sensitivity; *CI* confidence interval; *SP* specificity; *PPV* positive predictive value; *NPV* negative predictive value; *AUC* area under the curve; *CTP* computed tomography perfusion; *CTA* computed tomography angiography

CTP was found to be completely safe as no patients experience any complications associated with CTP. The GOSe was calculated at 6 months for those who survived the hospital stay and are summarized in Table 7S. The mean GOSe was 6.2 (SD 1.6) at 6 months.

Of the total patients included in the study, 112 patients underwent surgical interventions during their early hospital stay. These surgical interventions are summarized in the Table 8S of the supplemental material.

Discussion

The study represents the first well powered prospective cohort study aimed at validating the CTP features of non-survivable brain injury in identifying patients with severe TBI suffering in-hospital mortality. Our findings indicate that CTP criteria for non-survivable brain injury demonstrated the highest level of accuracy in diagnosing in-hospital mortality, reaffirming the results of our pilot study [20]. Among the 55 patients with in-hospital mortality, CTP features of non-survivable brain injury were identified in 17 of them, resulting in a sensitivity of 33%. Importantly, none of the survivors exhibited CTP criteria of non-survivable brain injury, leading to a specificity of 100%. Furthermore, there were no false positives meaning that no patients with features of non-survivable brain injury on admission CTP survived, resulting in a PPV of 100%. The patients who succumbed during their hospital stay were alive at the time of admission, suggesting that their demise was likely due either to the initial injury or to the complications arising from both the injury and its management. These results underscore the potential utility of CTP as a diagnostic tool for predicting in-hospital mortality in patients with severe TBI.

CTP has been underutilized in patients with severe TBI due to lack of sufficient reliable evidence regarding its efficacy in this patient population. Wintermark et al. conducted one of the earliest studies utilizing CTP in patients with severe TBI upon hospital adimission [24]. They observed favourable outcome in patients with normal or high brain perfusion on admission CTP, while patients with low perfusion tended to have unfavourable outcomes at three months after patients' admission. Similarly, Bendinelli et al. employed CTP in patients with severe TBI who showed no neurological improvement within the first 48 h post-trauma [25]. They identified low perfusion in one third of their patients and CTP results led to alterations in clinical management for 10% of patients diagnosed with massive and fatal strokes despite minimal changes on plain head CT scans. However, both studies utilized CTP with limited brain coverage due to technological constraints at the time, potentially missing important findings in other brain regions. While these studies addressed neurological outcomes at the end of hospital stays, they did not specifically investigate any association between CTP features with in-hospital mortality.

A triage tool to facilitate early, if not immediate, decision making is crucial in managing patients with severe TBI, as the majority of deaths occur within the first 48 h of hospital admission [1, 3, 6]. During this critical period, the most resource-intensive medical and surgical activities take place. However, some patients with severe TBI may already sustained non-survivable brain injury at the time of hospital admission, with accurate clinical diagnosis obscured by factors such as anesthetic and neuromuscular blockade. Our study validates admission CTP

as a triage tool capable of assisting in diagnosing non-survivable brain injury in these patients. Investing in this triage tool in routine practice for evaluating patients with severe TBI could reduce the use of resource-intensive but futile treatments for patients who sustained non-survivable brain injury in the emergency room. By avoiding unnecessary interventions, we can allocate resources more efficiently and effectively, ensuring that critical care resources are directed toward patients who stand to benefit the most. Furthermore, the adoption of this triage tool has the potential to improve trust and investment in organ transplantation. By accurately identifying patients with irreversible brain injury early on, timely discussions regarding organ donation and transplantation can be facilitated, maximizing the chances of successful transplant outcomes.

The fair inter-rater reliability observed for CTP, in contrast to the excellent reliability for CTA scales, underscores the novelity of the CTP findings of non-survivable brain injury. These results highlight the importance of standardizing interpretation criteria and providing adequate training and education to improve consistency in CTP assessment.

Presence of gun shot wound was found to be independently associated with 22 times higher odds of in-hospital mortality in our study. This is keeping with the described literature where natural history of civilian cranial GSW's is very poor [26–28].

Future directions may involve modelling using CTP in conjunction with other predictors of in-hospital mortality. Further examination of imaging biomarkers is warranted to explore the establishment of functional outcomes beyond in-hospital mortality in patients with severe TBI.

However, it's essential to acknowledge the limitations of our study, notably its small sample size, which may impact the generalizability of the findings. Despite this limitation, our study contributes valuable insights into the potential role of CTP in severe TBI management and highlights areas for future research and development. The other limitation is poor inter-rater agreement between readers of CTP. This highlights the need for further education of radiologists about the CT features of non-survivable brain injury. Tools utilizing artificial intelligence and machine learning will also help automation of the CTP readings obviating or reducing the need of human interpretation in the future.

Quantitative CTP is highly sensitive to artifacts, which may distort the accuracy of perfusion measurements. Artifacts arising from motion, poor contrast enhancement, or inconsistent patient positioning can lead to errors in calculating cerebral blood flow (CBF) and other hemodynamic variables. Since all patients were intubated and sedated, the motion artifacts were minimal to none. The rate, volume and type of contrast injection was also standardized in the study to minimize any possible artifactual variations. Patient positioning is also standard in trauma protocol. But possibility of some variations based on the type of head injury and support needed, can not be ruled out. Patient-specific factors, such as blood pressure, heart rate, and ventilation, can introduce variability in the perfusion data. However, all patients were stabilized as per brain trauma guidelines before getting their CT scan and hence chances of these variations are minimal.

The software used to process CTP data may also introduce limitations, such as the inability to account for complex physiological or pathological variations. This was addressed by using the same post-processing software and same post-processing steps for all the patients. Despite these, quantitative CTP remained in-accurate in our study.

Conclusion

In conclusion, our study demonstrates the potential utility of qualitative CTP features of non-survivable brain injury as a triage tool for diagnosing in-hospital mortality in patients with severe TBI. Although lower sensitivity limits its use for screening of non-survivable brain injury in all patients with severe TBI. The fair inter-rater reliability observed for CTP underscores the novelty of CTP features of non-survivable brain injury, emphasizing the need for standardized interpretation criteria and enhanced training.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13054-025-05410-x.

Supplementary material 1

Acknowledgements

We thank the CT technologists at the Health Science Center, Winnipeg for their help with the study. JS acknowledges research salary support from Radiology Consultants of Winnipeg. FAZ is supported through the Endowed Manitoba Public Insurance (MPI) Chair in Neuroscience/TBI Research Endowment, Natural Science and Engineering Research Council of Canada (NSERC) (DGECR-2022-00260, RGPIN-2022-03621, ALLRP-578524-22, ALLRP-576386-22, I2IPJ 586104–23, ALLRP 586244-23, ALLRP-590680-2023, ALLRP 597442-24, ALLRP-597708-24, and I2IPJ 598125-24), Canadian Institutes of Health Research (CIHR; Grant #: 432061, 505116, 507377, 530549), the Canada Foundation for Innovation (CFI) (Project #: 38583), Research Manitoba (Grant #: 3906, 5429, 5914, 6554), the Health Sciences Centre Foundation Winnipeg, and the Pan Am Clinic Foundation of Winnipeg.

Author contributions

Statement of authorship- JS- conceptualized the study, wrote the grant, monitored the study conduct, analyzed the data and wrote the first draft of the study; SA- monitored the conduct of the study and reviewed the final manuscript; MA- analyzed the data and reviewed the final manuscript; JP, SU, MR, BB, RT, RM- Collected data and reviewed the final manuscript; NS- Helped

with the grant writing and reviewed the final manuscript; AT, DM, RG- monitored the conduct of the study and reviewed the final manuscript; ME- Image interpretation and reviewed the final manuscript; FZ- wrote the grant, monitored the conduct of the study, reviewed the final manuscript.

Funding
This study was directly supported by the Canadian Institutes of Health Research (CIHR) Grant # 432061) and University of Manitoba Bridge funding grant.

Availability of data materials
Research data is available on request.

Declarations

Ethical approval and consent to participate and publication
The study received approval from our institutional ethics board (HS23683; B2020:018) and has been registered on clinicaltrials.gov with the trial registration number of NCT04318665. Deferred consent was approved by the ethics board and was obtained from all patients included in the study.

Competing interests
FAZ currently has NSERC Alliance Advantage grant (ALLRP-597708-24) support in partnership with Medtronic's Patient Monitoring Division (ERP-2024-14025) for work that is unrelated to this manuscript. Funding from the partner organization is provided to match NSERC governmental funding only, in keeping with NSERC policies. Medtronic does not direct the research objectives, data collection, analysis, interpretation, or publication of the findings in any way. JS is PI for EMMA Can study funded by Medtronic Canada, unrelated to this manuscript.

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Received: 25 December 2024 Accepted: 8 April 2025
Published online: 01 May 2025

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