Cerebral venous thrombosis in traumatic brain injury: a cause of secondary insults and added mortality

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OBJECTIVE Cerebral venous thrombosis (CVT) is increasingly recognized in traumatic brain injury (TBI), but its complications and effect on outcome remain undetermined. In this study, the authors characterize the complications and outcome effect of CVT in TBI patients.

METHODS In a retrospective, case-control study of patients included in the Oslo University Hospital trauma registry and radiology registry from 2008 to 2014, the authors identified TBI patients with CVT (cases) and without CVT (controls). The groups were matched regarding Abbreviated Injury Scale 1990, update 1998 (AIS'98) head region severity score 3–6. Cases were identified by AIS'98 or ICD-10 code for CVT and CT or MR venography findings confirmed to be positive for CVT, whereas controls had no AIS'98 or ICD-10 code for CVT and CT venography or MR venography findings confirmed to be negative for CVT. All images were reviewed by a neuroradiologist. Rates of complications due to CVT were recorded, and mortality was assessed both unadjusted and in a multivariable logistic regression analysis adjusting for initial Glasgow Coma Scale score, Rotterdam CT score, and Injury Severity Score. Complications and mortality were also assessed in prespecified subgroup analysis according to CVT location and degree of occlusion from CVT. Lastly, mortality was assessed in an exploratory subgroup analysis according to the presence of complications from CVT.

RESULTS The CVT group (73 patients) and control group (120 patients) were well matched regarding baseline characteristics. In the CVT group, 18% developed venous infarction, 11% developed intracerebral hemorrhage, and 19% developed edema, all representing complications secondary to CVT. Unadjusted 30-day mortality was 16% in the CVT group and 4% in the no-CVT group ($p = 0.004$); however, the difference was no longer significant in the adjusted analysis (OR 2.24, 95% CI 0.63–8.03; $p = 0.215$). Subgroup analysis by CVT location showed an association between CVT location and rate of complications and an unadjusted 30-day mortality of 50% for midline or bilateral CVT and 8% for unilateral CVT compared with 4% for no CVT ($p < 0.001$). The adjusted analysis showed a significantly higher mortality in the midline/bilateral CVT group than in the no-CVT group (OR 8.41, 95% CI 1.56–45.25; $p = 0.032$).

CONCLUSIONS There is a significant rate of complications from CVT in TBI patients, leading to secondary brain insults. The rate of complications is dependent on the anatomical location of the CVT, and midline and bilateral CVT is associated with an increased 30-day mortality in TBI patients.

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KEYWORDS cerebral venous thrombosis; traumatic brain injury; complications; mortality; outcome

EMERGING literature suggests that traumatic brain injury (TBI) may be an important etiology of cerebral venous thrombosis (CVT).¹ However, apart from multiple case reports and small case series, the literature on CVT in the setting of TBI is scarce.

Pathophysiologically, thrombosis of cerebral dural ve-

nous sinuses leads to obstructed venous drainage, resulting in increased hydrostatic pressure in upstream veins and capillaries.² This in turn can lead to complications of CVT in the form of parenchymal edema, decreased arterial perfusion causing venous infarctions, and rupture of vessels causing parenchymal hemorrhage. These compli-

ABBREVIATIONS AIS'98 = Abbreviated Injury Scale 1990, update 1998; ASA-PS = American Society of Anesthesiologists Physical Status; CVT = cerebral venous thrombosis; GCS = Glasgow Coma Scale; ICH = intracerebral hemorrhage; ISS = Injury Severity Score; OUH = Oslo University Hospital; OUH-TR = OUH trauma registry; RIS = radiological information system; TBI = traumatic brain injury.

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cations will typically involve the specific drainage area of the affected dural venous sinus. In addition, venous stasis may cause reduced reabsorption of CSF via the arachnoid granulations protruding into the dural venous sinuses, which may lead to a global increase in intracranial pressure.

While CVT is increasingly recognized with the increasing availability of more advanced imaging, the incidence of CVT in TBI patients remains undetermined. In one study of 240 consecutive patients with moderate and severe TBI, 17% were diagnosed with either external compression or thrombosis of a dural venous sinus.⁶ Other studies have found a CVT incidence of 22%–35% among patients with skull fractures in relation to dural venous sinuses.^{3–5} With regard to risk factors of CVT in TBI, both skull fractures and epidural hematomas in relation to dural venous sinuses have been reasonably well established.^{3–6}

However, CVT and its effect on outcome of TBI patients remains undetermined, and available data are diverging. In their prospective study from 2008, Fujii et al. reported significantly higher mortality in their cohort of 22 patients with CVT and skull fracture compared with a control group with skull fractures alone.⁴ They found a mortality rate of 50% in the CVT group compared with 9% in the control group. Of note, the authors found no significant difference between the 2 groups in regard to the initial Glasgow Coma Scale (GCS)⁷ score or in the incidence of other TBIs. In a more recent publication, Rivkin and colleagues reported a retrospective study conducted in an otherwise similar design.⁵ As in the study by Fujii et al., 22 patients with CVT and skull fractures were compared with a control group with skull fractures alone; outcome was measured by looking at in-hospital mortality and discharge destination. In contrast to the previous study, no statistically significant difference with regard to measured outcome parameters were found between the two groups. In comparison, a large multicenter study (n = 624) looking at all-cause CVT (mainly nontraumatic) reported a 7.7% 30-day mortality, the majority due to cerebral edema and herniation.⁸ Hence, in TBI patients, the question remains whether CVT has an effect on outcome.

If CVT has an adverse effect on the outcome of TBI patients, this would have implications on our clinical practice. First, its diagnosis should be prioritized. Second, and more importantly, it would imply a more aggressive approach to treatment once discovered, although the dilemma of anticoagulant treatment, to balance the risk between thrombus propagation and expansion of any traumatic hematomas present, would remain.

In this study, we characterize the complications of CVT and its effect on mortality in TBI patients.

Methods

Study Design and Data Sources

We performed a retrospective, case-control study based on prospectively collected registry data of patients admitted to Oslo University Hospital (OUH) between 2008 and 2014.

OUH is the major trauma hospital for more than 660,000 inhabitants in Oslo and the regional trauma referral center for approximately 3 million inhabitants in

southeastern Norway, serving as a tertiary care center for all cases of TBI in the region. Currently, approximately 1850 patients are prospectively enrolled in the Oslo University Hospital trauma registry (OUH-TR) per year. Eligible for inclusion in the OUH-TR are all head-injured patients with Abbreviated Injury Scale 1990, update 1998 (AIS'98)¹⁰ score for the head region ≥ 3 , as well as all patients admitted with trauma team activation; all patients with penetrating injuries in the head, neck, torso and/or extremities proximal to the elbow or knee; and all patients with Injury Severity Score (ISS) ≥ 10 .⁹ In accordance with the data validation protocol of the OUH-TR, all information is thoroughly screened for inconsistencies and non-logical values before extraction.

The in-hospital radiological information system (RIS) registry is a registry that prospectively records and stores all radiological examinations performed at OUH. In our standard clinical management protocol for TBI, initial CT scans are performed on admission as part of the trauma team evaluation. CT or MR venography is performed if there is a fracture crossing a dural venous sinus, if there is an epidural hematoma overlying a dural venous sinus, and/or if there is clinical or radiological suspicion of CVT for any other reason. The first follow-up CT scan is typically obtained 6 hours after initial scanning; further follow-up CT and MR imaging is thereafter performed as per the clinician's judgment of need.

The OUH-TR and the RIS registry were utilized to include patients with CVT (cases) and without CVT (controls) according to the aforementioned criteria (Fig. 1). All head and neck images of included patients were reevaluated by a single neuroradiologist (M.M.-E.), and electronic patient records were reviewed by a single clinician (D.F.N.).

The study was approved by the OUH data protection officer, the board of the OUH-TR, and the research committee of the OUH Radiology Department.

Patient Inclusion

Both the CVT group and the control group included TBI patients of any age with an AIS'98 head region severity score 3–6 who were admitted to OUH between 2008 and 2014 from the OUH-TR.

Patients in the CVT group were identified by an AIS'98 and/or ICD-10¹¹ code for CVT. CVT was confirmed by diagnostically adequate CT or MR venography deemed to be positive on radiological reevaluation. CVT was radiologically defined by criteria as detailed below.

Controls were identified from the trauma registry by the absence of an AIS'98 or ICD-10 code for CVT. To confirm absence of CVT, these patients were then cross-matched with patients having undergone either CT or MR angiography in the same time period from our in-house RIS registry. Absence of CVT was confirmed by a diagnostically adequate CT or MR venogram deemed to be negative on radiological reevaluation.

Where venography was of inadequate diagnostic quality to rule in or out CVT, patients were excluded from either group. If CVT was identified in a control patient, or if CVT was ruled out in a case, the patient crossed over to the opposite group.

FIG. 1. Flowchart detailing inclusion. CTV = CT venography; MRV = MR venography.

Data Collection and Radiological Reevaluation

Demographics, preinjury patient data, and trauma-related variables were collected from the OUH-TR and review of electronic patient records. Information on preinjury comorbidity was extracted from the OUH-TR in form of the American Society of Anesthesiologists Physical Status (ASA-PS) classification level.¹² Physiological derangement from the present injury is not reflected in our preinjury ASA-PS class;¹³ only the comorbidities present before trauma are taken into account. Trauma severity indicators such as GCS score and ISS were collected from the trauma registry. Mortality data were gathered via the electronic patient record, which is linked, and continuously synced, to the national population registry. In the few instances when patients were of foreign nationality (approximately 6%), the end of the observation time was set as the last recorded contact with our hospital service.

Radiological variables, including presence, characteristics, and complications of CVT and the presence and extent of other head injuries, were gathered by reevaluation of all head CT and MRI scans, both initial scans and follow-up scans, of all cases and controls by a single neuroradiologist. CVT was defined as radiological signs of intraluminal thrombus in a dural venous sinus on CT or MR venography. External compression alone (e.g., by an epidural hematoma) was not regarded as CVT. Similarly, total external compression that recanalized on repeat venography without signs of intraluminal thrombus was not regarded as CVT. Characteristics of CVT, including degree of occlusion and anatomical location, were evaluated. All images were further evaluated systematically for complications of CVT, namely, venous infarctions, intracerebral hemorrhage (ICH) secondary to CVT, and edema secondary to CVT. Venous infarction was defined as signs of infarction on CT or MRI in the drainage area of the thrombosed dural venous sinus deemed by the neuroradiologist to be most likely caused by the CVT. Intracerebral hemorrhage secondary to CVT was defined as hemorrhage on CT or MRI in the drainage area of the dural venous sinus deemed by the neuroradiologist to be most likely caused by the CVT and not representing a primary traumatic hemorrhage. Focal edema secondary to CVT was defined as signs of edema in the drainage area of the thrombosed dural venous sinus deemed by the neuroradiologist to be most likely caused by the CVT and not by other causes. Generalized edema was defined secondary to CVT if it was deemed that the CVT was of a type and location that was explanatory and no other more likely cause was present. Both initial and follow-up scans were evaluated so that temporal changes could aid in distinguishing primary traumatic lesions from CVT complications. The Rotterdam CT score¹⁴ was calculated for all cases and controls based on systematic evaluation of the images for other TBIs.

Data Analysis

Endpoints and performed subgroup analyses were specified by study protocol prior to commencement of data collection. The primary endpoint was 30-day mortality in the CVT group vs no-CVT group. Two prespecified subgroup analyses were performed: by degree of occlusion due to

the CVT and by anatomical location of the CVT. Subgrouping by degree of CVT occlusion was based on the hypothesis that CVT leading to total occlusion of a dural venous sinus is associated with a greater complication rate and effect on outcome than CVT leading to subtotal luminal occlusion. Subgrouping by anatomical CVT location was based on the hypothesis that disturbance of flow in locations where there is no opportunity for alternative contralateral flow diversion has a greater complication rate and hence effect on outcome than for locations where flow can be diverted to contralateral drainage. We therefore categorized locations into midline/bilateral (midline = in the superior sagittal sinus and/or deep cerebral veins; bilateral = bilateral in the transverse sinus, sigmoid sinus, and/or internal jugular vein); and unilateral (unilateral = unilateral in the transverse sinus, sigmoid sinus, and/or internal jugular vein) (Fig. 2). Lastly, an exploratory subgroup analysis by presence of CVT complications was performed. This was based on indications from our data that CVT with complications present (complicated CVT) was associated with greater mortality than CVT without secondary complications (noncomplicated CVT).

Univariable analyses were carried out using the chi-square or Fisher's exact test for categorical variables and the Mann-Whitney U-test for continuous variables, as appropriate. Survival analysis based on mortality data 2 years posttrauma was performed using the Kaplan-Meier method, and between-group differences were analyzed using the log-rank test. The risk of mortality was further assessed using multivariable logistic regression adjusting for the initial GCS score, Rotterdam CT score, and ISS. Adjustment for these variables was chosen to account for differences in TBI severity between groups, GCS score representing a clinical indicator of TBI severity, Rotterdam score representing an anatomical indicator of TBI severity, and ISS representing an indicator of whole-body trauma burden. The same adjusted analysis was applied in both the primary and subgroup analyses. All statistical analyses were performed using IBM SPSS for Windows (version 25.0, 2017, IBM Corp.); $p < 0.05$ was considered significant.

Results

Patients and Baseline Characteristics

A total of 193 patients were included in the study (73 in the CVT group and 120 in the no-CVT group); 145 (75%) of patients were male and 48 (25%) were female. The median age was 37 years (IQR 24–55 years). Baseline characteristics were well matched regarding age, sex, history of venous thromboembolism, antiplatelet or anticoagulation use, preinjury ASA-PS class, and mechanism and type (penetrating vs blunt) of injury (Table 1).

Severity Scores and TBI Characteristics

CVT was associated with a lower median initial GCS score (median 9 [IQR 6–13.5] vs median 14 [IQR 9–15], $p < 0.001$), a higher median ISS (median 26 [IQR 23–35.5] vs median 23 [IQR 17–30], $p < 0.001$), and Rotterdam CT score (median 2 [IQR 2–4] vs 2 [IQR 1–3], $p = 0.002$) compared with no CVT (Table 2).

FIG. 2. Anatomical CVT location categories. Midline: deep cerebral veins (n = 1) and superior sagittal sinus (n = 10). Bilateral: bilateral sigmoid sinus, transverse sinus, and/or internal jugular vein (n = 3). Unilateral: unilateral sigmoid sinus, transverse sinus, and/or internal jugular vein (n = 59). Figure is available in color online only.

CVT Characteristics

The anatomical distribution of CVT is shown in Fig. 2 as well as distribution according to grouping into midline/bilateral and unilateral CVT. Regarding the grade of occlusion, 38% of thrombosed venous sinuses were totally occluded and the remaining 62% were subtotally

TABLE 1. Baseline characteristics

Variable	CVT (n = 73)	No CVT (n = 120)	p Value
Age, yrs	37.0 (25.5–50.0)	37.5 (24.0–56.75)	0.545
Sex			0.772
Male	54 (74%)	91 (76%)	
Female	19 (26%)	29 (24%)	
History of VTE	0 (0%)	2 (1.7%)	0.527
Antiplatelet use	4 (5%)	8 (7%)	>0.99
Anticoagulation use	1 (1%)	2 (2%)	0.872
Preinjury ASA-PS score	1 (1–2)	1 (1–2)	0.989
Mechanism of injury			0.532
Fall	30 (41.1%)	53 (44.2%)	
MVA	17 (23.3%)	29 (24.2%)	
Pedestrian	4 (5.5%)	8 (6.7%)	
Violence	5 (6.8%)	15 (12.5%)	
Sports/recreational	8 (11.0%)	7 (5.8%)	
Self-inflicted	2 (2.7%)	1 (0.8%)	
Other/unknown	7 (9.6%)	7 (5.8%)	
Type of injury			0.429
Penetrating	4 (5.5%)	3 (2.5%)	
Blunt	69 (94.5%)	117 (97.5%)	

MVA = motor vehicle accident; VTE = venous thromboembolism.
Data are median (IQR) or n (%).

TABLE 2. Initial GCS score, severity scores, and radiological TBI characteristics

Variable	CVT (n = 73)	No CVT (n = 120)	p Value
Initial GCS score	9 (6–13.5)	14 (9–15)	<0.001
Initial GCS score by category			0.001
13–15 (mild TBI)	26 (36%)	75 (62%)	
9–12 (moderate TBI)	15 (21%)	17 (14%)	
3–8 (severe TBI)	32 (44%)	28 (23%)	
ISS	26 (23–35.5)	23 (17–30)	<0.001
Rotterdam CT score	2 (2–4)	2 (1–3)	0.002
Radiological TBI characteristics			
Skull fracture	73 (100%)	95 (79.2%)	0.000
EDH	64 (87.7%)	69 (57.5%)	0.000
tSAH	63 (86.3%)	87 (72.5%)	0.025
IVH	20 (27.4%)	25 (20.8%)	0.296
SDH	55 (75.3%)	62 (51.7%)	0.001
tICH	59 (80.8%)	80 (66.7%)	0.034
Midline shift, mm			0.000
None	16 (21.9%)	71 (59.2%)	
≤5	39 (53.4%)	39 (32.5%)	
>5	18 (24.7%)	10 (8.3%)	
Basal cistern compression			0.000
Normal	11 (15.1%)	69 (57.5%)	
Compressed	46 (63.0%)	45 (37.5%)	
Absent	16 (21.9%)	6 (5.0%)	

EDH = epidural hematoma; IVH = intraventricular hemorrhage; SDH = subdural hemorrhage; tICH = traumatic ICH; tSAH = traumatic subarachnoid hemorrhage.
Data are median (IQR) or n (%).

FIG. 3. Complication rates due to CVT. Any complication is venous infarction, ICH secondary to CVT, and/or edema secondary to CVT. Figure is available in color online only.

occluded. Intraluminal air and extravasation in relation to the CVT was seen in 8% and 7% of cases, respectively. The vast majority (99%) had a skull fracture related to the thrombosed venous sinus, and 73% had an epidural hematoma related to the thrombosed venous sinus. Eighty-two percent of patients with CVT were treated with low-molecular-weight heparin with CVT as the indication for treatment. The median time from injury to treatment initiation was 1 day (IQR 1–2 days). Dalteparin was used in all these patients, with a median initial dose of 5000 IU/24 hours (IQR 2500–5000 IU/24 hours).

CVT Complications

Complications were seen in 23% of patients with CVT (Fig. 3); 18% developed a venous infarction, and 11% developed an ICH secondary to the CVT. Edema secondary to CVT was seen in 19% of the patients; in 3% the edema was generalized, and in the remaining 16% it was focal in the drainage area of the thrombosed venous sinus.

In prespecified subgroup analyses, there was no significant association between the rate of complications and degree of occlusion by the CVT. There was, however, a significant association between the rate of complications and the anatomical location of the CVT, with midline/bilateral CVT being associated with significantly higher rates of complications (Table 3).

Mortality

Thirty-day mortality was significantly higher in the CVT group vs the no-CVT group (16%, [12/73] vs 4% [5/120], $p = 0.004$). Kaplan-Meier curves for survival over 2 years illustrate that this difference in mortality occurred early posttrauma, well within the first 30 days (Fig. 4). However, in the multivariable analysis adjusting for GCS score, ISS, and Rotterdam CT score, the difference in 30-day mortality was no longer significant (OR 2.24, 95% CI 0.63–8.03; $p = 0.215$).

Similar to the complications, subgroup analysis by degree of occlusion showed no significant difference in mortality between occlusive CVT vs nonocclusive CVT in either unadjusted or adjusted analysis. However, subgroup analysis by CVT location showed an unadjusted 30-day mortality of 50% (7/14) for the midline/bilateral CVT group and 8% (5/59) for the unilateral CVT group compared with 4% (5/120) for the no-CVT group ($p < 0.001$) (Table 3). In the multivariable analysis adjusting for GCS score, ISS, and Rotterdam CT score, midline/bilateral CVT was associated with a significantly higher risk of mortality when compared with the no-CVT group (OR 8.41, 95% CI 1.56–45.25; $p = 0.032$).

In exploratory subgroup analysis by the presence of complications, results showed an unadjusted mortality of 47% (8/17) for the complicated CVT group, 7% (4/56) for

TABLE 3. Complications and mortality by CVT location

Variable	Midline/Bilat CVT				No CVT (n = 120)	p Value
	DCV (n = 1)	SSS (n = 10)	Bilat (n = 3)†	Unilat (n = 59)†		
Any complication*	1 (100%)	5 (50%)	1 (33%)	10 (17%)		0.032
Venous infarction	1 (100%)	4 (40%)	1 (33%)	7 (12%)		0.019
ICH secondary to CVT	1 (100%)	1 (10%)	1 (33%)	5 (8%)		0.018
Edema secondary to CVT	1 (100%)	4 (40%)	1 (33%)	8 (14%)		0.035
Focal	1 (100%)	3 (30%)	1 (33%)	7 (12%)		
Generalized	0 (0%)	1 (10%)	0 (0%)	1 (2%)		
30-day mortality	1 (100%)	5 (50%)	1 (33%)	5 (8%)	5 (4%)	<0.001

DCV = deep cerebral veins; SSS = superior sagittal sinus.

* Any complication is venous infarction, ICH secondary to CVT, and/or edema secondary CVT.

† Sigmoid sinus, transverse sinus, and/or internal jugular vein.

FIG. 4. Kaplan-Meier curves showing overall survival for the CVT group and no-CVT group. Log-rank (Mantel-Cox): $\chi^2 = 8.315$, $p = 0.004$. The number censored at 2 years is as follows: 169 of 193 (88%) overall, 58 of 73 (79%) for the CVT group, and 111 of 120 (93%) for the no-CVT group. Figure is available in color online only.

the noncomplicated CVT group, and 4% (5/120) for the no-CVT group ($p < 0.001$). In the multivariable analysis adjusting for GCS score, ISS, and Rotterdam CT score, complicated CVT was associated with a significantly higher risk of mortality when compared with noncomplicated CVT (OR 7.71, 95% CI 1.62–36.80, $p = 0.017$). Adjusted 30-day mortality for both primary and subgroup analyses is shown in Fig. 5.

Discussion

In the present study, which, to our knowledge, is the largest study to date assessing outcome effects of CVT in the setting of TBI, we show that CVT is associated with a considerable rate of complications leading to secondary brain insults in TBI patients. CVT was associated with a 4-times-higher 30-day mortality rate but also with more severe head injury, and, in our multivariable regression analysis adjusting for GCS score, ISS, and Rotterdam CT score, the difference in mortality was no longer statistically significant.

Our subgrouping by anatomical location was based on a hypothesis that the location of CVT is associated with the severity of its pathophysiological effects, which again is related to potential for contralateral alternate flow diversion from the site of flow disturbance by the thrombus. We hypothesized that severity is associated with anatomical location in the following declining order: deep cerebral veins; superior sagittal sinus; bilateral transverse sinus, sigmoid sinus, or internal jugular vein; unilateral transverse sinus, sigmoid sinus, or internal jugular vein. In our

results, we show a declining rate of complications and mortality that corresponds to our hypothesized declining degree of severity, lending support to the hypothesis. After grouping anatomical location into midline/bilateral and unilateral, we found that midline/bilateral CVT was associated with significantly higher 30-day mortality, also when adjusting for GCS score, ISS and Rotterdam CT score. Further exploratory subgroup analysis by the presence of complications likewise shows significantly higher 30-day mortality for complicated CVT compared with uncomplicated CVT and no CVT, both in unadjusted and adjusted analysis.

Our study has several limitations. First, in our regression analysis, we adjusted for GCS score, Rotterdam CT score and ISS, but these variables are not independent from CVT or its complications. Spontaneous CVT, hence isolated from TBI, is well known to result in reduced consciousness and a corresponding reduced GCS score. Furthermore, the complications of CVT will give points on the Rotterdam CT score, independent of the presence of other head injuries. Also, both CVT and its complications are weighted in the AIS system giving rise to the ISS. Therefore, adjusting for these variables is likely an over-adjustment in that we may well be adjusting for the very thing we are examining for, i.e., the effects of CVT and its complications, and, as a consequence, suppressing the actual outcome effects of CVT. However, we still opt to adjust for just these 3 variables, as they at the same time, in our opinion, offer the most complete adjustment for any differences in TBI severity present between the groups. Second, our study is limited in that we do not present a

FIG. 5. Adjusted 30-day mortality in primary and subgroup analyses. Forest plot of odds ratios for 30-day mortality adjusted for initial GCS score, Rotterdam CT score, and ISS in the CVT group compared with the no-CVT group and in subgroup analyses by grade of occlusion, anatomical location, and presence of complications.

functional outcome measure in addition to the mortality data. Third, our subgroup and exploratory analyses are underpowered for adjusting for multiple confounders and must be interpreted with caution.

Nonetheless, our study does show a clear tendency of both complication rates and mortality rates to follow a similar pattern linked to anatomical CVT location. This is congruent with the expectation that mortality due to CVT is caused by its complications.

Conclusions

CVT is associated with a significant rate of complications leading to secondary brain insults in the setting of TBI. Furthermore, these complications seem dependent on the anatomical location of the CVT and may be associated with an increased risk of mortality, especially in midline and bilateral CVT. Therefore, diagnostic workup of CVT is warranted. Furthermore, treatment of CVT in the setting of TBI should, in our opinion, be considered, balancing the risk of thrombus expansion against the risk of expansion of any traumatic hematomas present. Larger prospective studies are needed to further describe the relationship between CVT and mortality in TBI patients.

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Author Contributions

Conception and design: Netteland. Acquisition of data: Netteland, Skaga. Analysis and interpretation of data: Netteland, Mejlænder-Evjensvold, Sandset, Helseth. Drafting the article: Netteland. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Netteland. Statistical analysis: Netteland, Sandset, Helseth.

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