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Concomitant spine trauma in patients with traumatic brain injury: Patient characteristics and outcomes

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Objective: Spine injury is highly prevalent in patients with poly-trauma, but data on the co-occurrence of spine trauma in patients with traumatic brain injury (TBI) are scarce. In this study, we used the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) database to assess the prevalence, characteristics, and outcomes of patients with TBI and a concurrent traumatic spinal injury (TSI).

Methods: Data from the European multi-center CENTER-TBI study were analyzed. Adult patients with TBI (≥18 years) presenting with a concomitant, isolated TSI of at least serious severity (Abbreviated Injury Scale; AIS ≥3) were included. For outcome analysis, comparison groups of TBI patients with TSI and systemic injuries (non-isolated TSI) and without TSI were created using propensity score matching. Rates of mortality, unfavorable outcomes (Glasgow Outcome Scale Extended; GOSe < 5), and full recovery (GOSe 7–8) of all patients and separately for patients with only mild TBI (mTBI) were compared between groups at 6-month follow-up.

Results: A total of 164 (4%) of the 4,254 CENTER-TBI core study patients suffered from a concomitant isolated TSI. The median age was 53 [interquartile range (IQR): 37–66] years and 71% of patients were men. mTBI was documented in 62% of cases, followed by severe TBI (26%), and spine injuries were mostly cervical (63%) or thoracic (31%). Surgical spine stabilization was performed in 19% of cases and 57% of patients were admitted to the ICU. Mortality at 6 months was 11% and only 36% of patients regained full recovery. There were no significant differences in the 6-month rates of mortality, unfavorable outcomes, or full recovery between TBI patients with and without concomitant isolated TSI. However, concomitant non-isolated TSI was associated with an unfavorable outcome and a higher mortality. In patients with mTBI, a negative association with full recovery could be observed for both concomitant isolated and non-isolated TSI.

Conclusion: Rates of mortality, unfavorable outcomes, and full recovery in TBI patients with and without concomitant, isolated TSIs were comparable after 6 months. However, in patients with mTBI, concomitant TSI was a negative predictor for a full recovery. These findings might indicate that patients with moderate to severe TBI do not necessarily exhibit worse outcomes when having a concomitant TSI, whereas patients with mTBI might be more affected.

KEYWORDS

traumatic brain injury, traumatic spine injury, outcome, CENTER-TBI, spine trauma

Introduction

Traumatic brain injury (TBI) contributes to the global burden of disease in a sizeable manner (1). The incidence of TBI has risen in the past years (2) and is estimated to become even more relevant with increasing events of traffic accidents and falls of the elderly (3, 4).

Traumatic brain injury can be complicated by additional injuries, such as traumatic spinal injuries (TSIs). When studying patients with spinal cord injury, the rate of concomitant TBI was estimated between 40 and 74% (5, 6). TBI in most of these patients was classified as mild (7). It is postulated that in the context of spine trauma, simultaneous TBI events are underdiagnosed (8). Unsurprisingly, TBI pertaining to spinal cord injury was found to be most frequent when the cervical and thoracic spine are affected (9).

Although various reports on TBI from a spinal injury perspective exist, little is known about the converse case of concomitant isolated spine trauma in patients suffering primarily from TBI. A recent meta-analysis found the rate of concomitant TSI in patients with TBI to be at around 13%, with cervical spinal injury amounting to almost half of the injuries diagnosed (10). This consolidates previous reports on cervical spine injury in larger patient cohorts with TBI (11). Indeed, patients with severe TBI were found to be at a particularly higher risk for sustaining injuries to the cervical spine (12).

Previous literature, while epidemiologically describing the prevalence of and risk factors for concomitant TBI and TSI, rarely elucidates the neurological outcomes of affected patients. In a retrospective analysis, patients with simultaneous TBI and TSI were reported to show increased motor deficits and limited functional gains in rehabilitation (13). Nevertheless, the question whether patients with concomitant TBI and TSI bear an inherent risk for a worse neurological outcome or a higher rate of mortality has yet to be tackled by prospectively collected observational data.

This study hence aimed at assessing the prevalence and characteristics of patients with TBI and concurrent, isolated TSI and comparing outcomes of such patients with TBI only in the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) cohort.

Methods

Study design

In the present study, data collected as part of the CENTER-TBI core study were analyzed. CENTER-TBI is a European multi-center, observational, longitudinal cohort study of patients presenting with TBI of all severities. Patients were eligible for enrollment when presenting with a clinical diagnosis of TBI to a participating study center within 24 h and when a computed tomography (CT) scan was performed at admission. Informed consent was required from all patients and had to be obtained prior to enrollment. The study protocol adhered to all national and local ethical committee requirements of participating study centers. Patients were enrolled from December 2014 to December 2017 in 59 centers across Europe and Israel. More details on the CENTER-TBI study and main descriptive findings have been published elsewhere (14, 15).

Study cohort and outcome parameters

For this study, we included adult CENTER-TBI core study patients (i.e., 18 years or older) with TBI that presented with a concomitant, isolated TSI. TSI was defined by an Abbreviated Injury Scale (AIS) score of $\geq$3 (indicating an injury of at least serious severity) in the cervical, thoracic, or lumbar spine. To study the impact of the TSI separately from poly-traumatic injuries, patients were excluded when also suffering from serious injuries (also defined as an AIS score of $\geq$3) in other body regions, namely, injuries to the thorax and chest, abdomen, pelvis, upper and lower extremities, or skin. As a complementary investigation, the same analyses were repeated for patients with non-isolated TSI, i.e., those with spine injuries (AIS scores $\geq$3) and concomitant injuries (AIS scores $\geq$3) in any of the other body regions. Primary outcome parameters were mortality [i.e., Glasgow Outcome Scale Extended (GOSe) = 1], unfavorable outcomes (i.e., GOSe < 5), and full recovery (i.e., GOSe = 7–8). All data were retrieved from the CENTER-TBI core study database in version 3.0 *via* the accessing tool Neurobot (RRID: SCR_ 017004).

Statistical analysis

Patient characteristics were analyzed using descriptive statistics. Continuous variables are reported as medians and interquartile ranges (INRs), while ordinal and categorical variables are presented as numbers and frequencies unless stated otherwise. The completeness of data is reported in Supplementary Table S1. Prior to outcome analysis, multiple imputation with 100 imputed datasets was used to address missing data in the control variables (age, sex, baseline Glasgow Coma Scale [GCS], performed cranial surgery, intracranial CT abnormality (mass lesion, extra-axial hematoma, epidural hematoma, acute subdural hematoma, chronic and subacute subdural hematoma, a subdural collection of mixed density, contusion, traumatic axonal injury, traumatic subarachnoid hemorrhage, intraventricular hemorrhage, midline shift, or cisternal compression), and American Society of Anesthesiologists [ASA] class) and the primary outcome variables (GOSe). Missing data were assumed to be missing at random. GCS and GOSe were defined as ordinal variables. The mortality, unfavorable outcomes, and full recovery of the variables were subsequently derived from imputed GOSe scores. After multiple imputation, propensity score matching with the above-named control variables and GOSe at 6-month follow-up as outcome variable was performed to create a matched comparison group of patients with TBI without concomitant TSI. The control variables were chosen *a priori* based on clinical expertise. Matching was performed within each imputed dataset. Effect estimates of concomitant TSI to outcomes were analyzed using weighted logistic regression models in each dataset. Additionally, logistic multivariable regression with (isolated or non-isolated) TSI as predictor and adjustment for the same control variables used in the propensity score analysis were performed for the three outcomes as a complementary analysis. Finally, effect estimates from each model were pooled according to Rubin's rules (16). The statistical software R was used for all analyses (https://www.r-project.org/ - version 4.1.1) (17).

Results

Patient characteristics, injury details, and prehospital course

A total of 164 adult patients with TBI and concomitant TSI were included in this study, representing about 4% of the entire CENTER-TBI study population (Figure 1). The median age in this subgroup of patients with simultaneous head and isolated spine injury was 53 years (IQR: 37–66 years) and 116 (71%) were men. The majority of injuries were caused by either incidental falls (47%, $n = 77$) or by road-traffic incidents (42%, $n = 68$). Alcohol intoxication confirmed by increased alcohol blood levels was found in 16% of patients ($n = 26$) and suspected in another 8% ($n = 13$). Most patients were brought to the hospital by ambulance (76%, $n = 123$) or by helicopter (12%, $n = 19$). Some patients even presented as walk-ins or drop-offs (6%, $n = 9$). Endotracheal intubation at the scene of an accident was performed in 22% of patients ($n = 33$). In total, 86% of patients ($n = 141$) were directly transported to the study center, while the remainder were referred to the study center from another hospital (see also Figure 2).

Clinical presentation and clinical course of TBI patients with concomitant TSI

Upon admission at the study center, severe TBI (GCS 3–8) was present in 26% of patients ($n = 42$), while moderate or mild TBI (mTBI) was documented in 10% ($n = 16$) and 62% ($n = 101$) of cases, respectively. A traumatic spine injury of at least serious severity was located in the lumbar spine in 32 patients (20%), in the thoracic spine in 51 patients (31%), and in the cervical spine in 104 patients (63%). In 21 patients (13%), more than one region of the spine was affected (e.g., both cervical and thoracic spine injuries). The majority of patients (57%, $n = 93$) were admitted to the ICU, while 63 patients (38%) were admitted to the regular ward. Among patients admitted to the ICU, the requirement for mechanical ventilation was named as the primary reason in 40 patients (43%), followed by the need for frequent neurological observations in 22 patients (24%) and neurosurgical intervention in 13 patients (14%). Spine stabilization surgery was performed in 32 patients (20%). During the hospital stay, respiratory complications were documented in 14 patients (12%), making it the most common type of complication. Further complications included seizures in 5 patients (4%), cardiac complications in 4 patients (3%), and urinary tract infections in 6 patients (5%). Patients with TBI and concomitant TSI stayed in the hospital for a median of 9 (3–20) days. Most patients could be discharged home (56%, $n = 70$), while 26 patients (21%) were discharged to a rehabilitation facility, and 24 patients (19%) were transferred to another hospital (see also Figure 2).

Outcomes of TBI patients with concomitant TSI

In this cohort of patients with TBI and concomitant TSI, 18 of 164 patients were dead after 6 months, yielding a mortality rate of 11%. Of those, 13 died in the ICU. In 9 patients, the initial head injury was documented as the cause of death whereas secondary intracranial damage was documented in 2 patients. For the remaining deceased patients, no cause of death was documented. A total of 48 patients (29%) were considered to have an unfavorable outcome (GOSe < 5). Approximately,

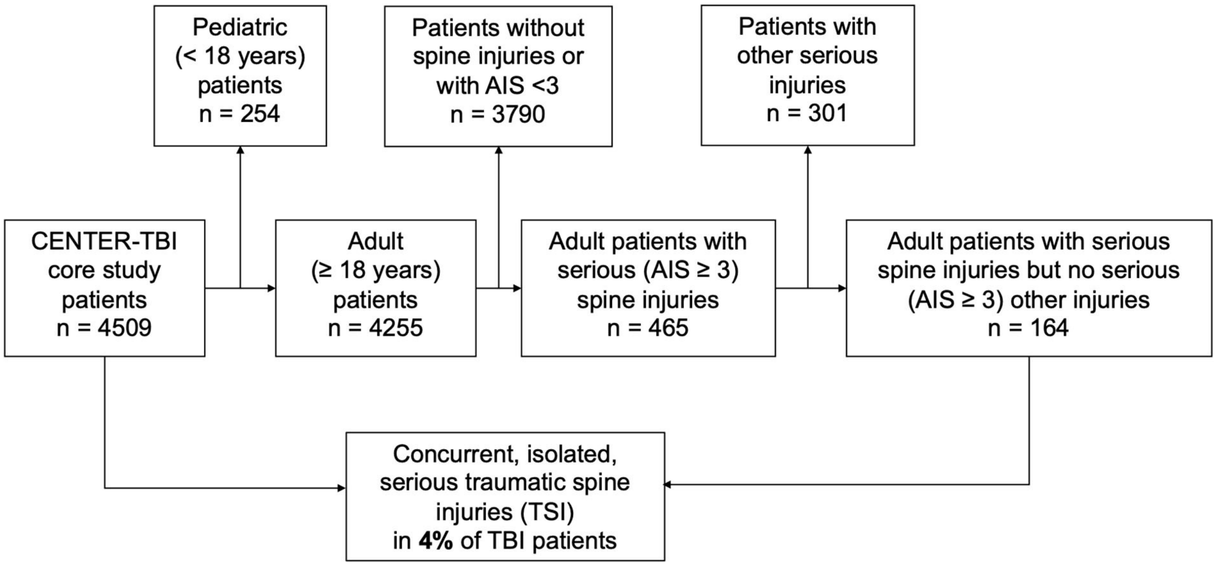

FIGURE 1
Study design. Adult patients in the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) database were screened. Patients with poly-trauma were excluded. Only patients sustaining TBI along with isolated traumatic spine injury (TSI) without the presence of further trauma were included in the analyses.

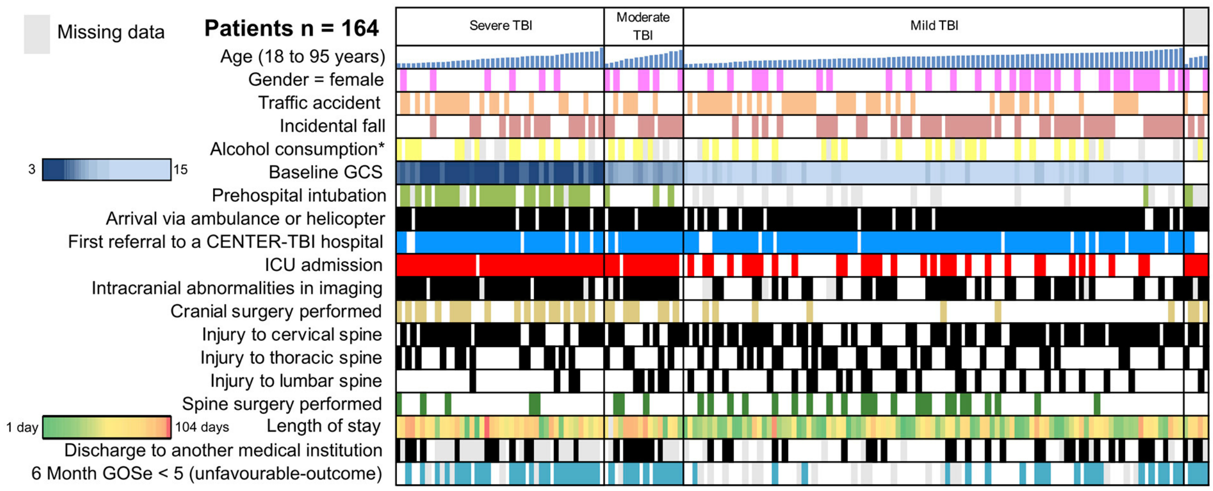

FIGURE 2
Traumatic brain injury (TBI)-traumatic spine injury (TSI) study cohort. Selected variables of the 164 patients included in the analysis are depicted. Rows represent representative variables, and each column represents one patient. Sub-cohorts are separated based on TBI severity (severe TBI: GCS < 8; moderate TBI: GCS 9–12; and mild TBI: GCS 13–15). In the sub-cohorts, patients are sorted by age from youngest (19 years) to oldest (95 years). A heat-map was utilized to visualize the length of stay (green: short, red: long) and GCS (dark blue: 15, light blue: 3). ICU, intensive care unit; GOSe, Glasgow Outcome Scale Extended. *Confirmed or suspected alcohol consumption. Gray represents missing data.

one-third of the patients achieved a full recovery (GOSe 7 or 8). To compare the outcomes of TBI patients with and without isolated, concomitant TSI, we performed propensity score matching with subsequent weighted logistic regression to estimate the effect of the simultaneous spine injury on patient outcomes. Patients were matched with age, sex, baseline GCS, performed cranial surgery, intracranial CT abnormalities, and ASA class as covariables (see Supplementary Tables S2, S3 for balance statistics and exemplary descriptions of the matched cohorts). In the outcome analysis, the presence of an isolated, concomitant TSI was neither significantly associated with mortality [$\beta = -0.12$ (-0.84 to 0.59), $p = 0.732$] nor with unfavorable outcomes [$\beta = 0.28$ (-0.21 to 0.77), $p = 0.270$], or full recovery [$\beta = -0.29$ (-0.76 to 0.18), $p = 0.228$].

Similar results were obtained in the logistic regression analysis (Supplementary Table S4), which showed that an isolated TSI, when controlling for age, sex, baseline GCS, performed cranial surgery, intracranial CT abnormalities, and ASA class, was neither a significant predictor of full recovery ($p = 0.084$) nor of unfavorable outcomes ($p = 0.184$) or death ($p = 0.355$) in our cohort. To put these results into a broader context, we performed a similar analysis but examined patients with TBI and concomitant TSI in conjunction with systemic injuries (i.e., non-isolated TSI) instead of an isolated TSI. In comparison with a matched cohort, TSI with concomitant systemic injuries in patients with TBI was negatively associated with full recovery ($p \leq 0.001$), but not with unfavorable outcomes ($p = 0.130$) or mortality ($p = 0.282$). In logistic regression analysis, a TSI with systemic injuries was a significant negative predictor of full recovery ($p < 0.001$) and unfavorable outcomes ($p = 0.003$), but not mortality ($p = 0.355$; Supplementary Table S4).

When only patients with mTBI were included in a subgroup analysis, no significant associations between isolated TSI and full recovery [$\beta = -0.468$ (-1.127 to 0.190), p-value = 0.160] and unfavorable outcomes [$\beta = 0.899$ (-0.175 to 1.973), p-value = 0.099] were seen when using propensity score matching. In the logistic regression analysis, isolated TSI was a significant negative predictor of full recovery [$\beta = -0.507$ (-0.994 to 0.012), $p = 0.042$] and a predictor of unfavorable outcomes [$\beta = 0.770$ (0.145–1.394), $p = 0.016$]. In mTBI patients with TSI and systemic injuries, TSI was significantly associated with unfavorable outcomes [$\beta = 0.853$ (0.006–1.699), p-value = 0.048] and inversely with full recovery [$\beta = -1.311$ (-1.925 to -0.698), p-value < 0.001] in the propensity score-matching analysis. Similarly, in the logistic regression analysis, a TSI in mTBI patients with systemic injuries was significantly associated with unfavorable outcomes [$\beta = 1.150$ (0.610–1.691), $p < 0.001$] and, in a negative direction, with full recovery [$\beta = -1.345$ (-1.772 to -0.918), $p < 0.001$]. The outcome analysis was not performed for mortality in the subgroup analysis of patients with mTBI due to the very low mortality rate (i.e., zero, and three patients among mTBI patients with isolated and non-isolated TSI were dead at the follow-up timepoint after 6 months, respectively) in this subgroup.

Discussion

While there is a wealth of epidemiological data on TBI studied from an SCI perspective, the potential role of a simultaneous TSI in exacerbating neurological deficits in patients with TBI remains largely unexplored. This study reported on concomitant TSI using data from a large prospectively followed up cohort of patients presenting with TBI as their main diagnosis and provided propensity-matching analyses to determine the influence of such injury on their global functional outcomes.

In this cohort, the rate of patients with TBI sustaining further isolated injury of at least serious intensity to the spine was found to be 4%. The rift between our current findings and previous analyses indicating higher rates of TSI in patients with TBI of up to 13% (10) could well be attributed to differences in the applied methodology, especially as to what is defined as an "injury." One key difference could be the AIS used in this study. The AIS is a standardized tool to reliably classify injuries and assess their severity (18, 19). Patients with TBI were regarded to have suffered a concomitant TSI when the AIS score of the cervical, thoracic, or lumbar spine satisfied at least serious severity. In this functional outcome-oriented analysis, thresholds for defining TSI were set as a trade-off between including patients with very minor and clinically negligible injuries that would otherwise skew the analysis and over-estimate TSI in patients with TBI vs. solely including patients undergoing surgical spinal stabilization and hence overlooking patients sustaining TSI with a "relevant" burden of disease that was managed non-surgically.

In a similar vein, an analysis excluding patients showing further injuries beyond TSI was envisaged to help eliminate possible confounders through further injuries (for example, to the skeletal system), and, therefore, yield a less-biased analysis that could compare characteristics and outcomes of isolated TSI+TBI vs. TBI-only patients. Indeed, further propensity-matching and logistic regression analyses compared patients with TBI, and systemic injuries (that included TSI) did show systemic injuries to be associated with unfavorable outcomes and to prevent full recovery.

Confirming data in previous studies, more than 60% of the spinal injuries diagnosed in our cohort were cervical (10). This was previously linked to the physiological bio-mechanical proximity of the cervical spine to the head (20), rendering concomitant injury to the cervical spine in TBI cases more likely than to other regions of the spine (10). Regarding injury causes, incidental falls and road traffic accidents accounted for the majority of TBIs (47 and 40%, respectively). On the one hand, the rate of road traffic accidents seems to be higher in this cohort than what has been previously reported in (isolated) TBI in high-income countries (21), which lends grounds for speculation that road accidents (which are usually poly-traumas in nature), might contribute to an increased risk of concomitant injury, especially with previous studies showing a high proportion of SCI patients with TBI to be victims of road traffic accidents (9). In addition, motor traffic accidents and herein old age, in particular, have been associated with higher odds of cervical spine injury (22). On the other hand, the larger proportion of incidental falls confirms a worldwide trend of increasing TBI rates secondary to falls of the elderly (4). In this cohort, patients with suspected or confirmed alcohol use amounted to 26%. Indeed, alcohol has been previously shown to be the strongest risk factor for clinical TBI in patients with SCI (7), hinting at the possibility that this could be another factor that fosters concomitant injury.

Missed diagnosis of simultaneous spinal injury in patients with TBI was deemed detrimental in the past and accounted for further neurological deterioration (11), especially because patients suffering severe TBI are difficult to assess clinically and possess a higher risk of sustaining injuries to the cervical spine (12). In terms of prognosis, this observation is, however, not reflected by the data we present, in which outcomes were comparable between TBI+TSI and TBI-only patients. Rather, it is conceivable that the probability of missing relevant spine trauma in the wake of comprehensive CT and MRI imaging [that was less available 20 years earlier (11)] in the participating study centers should be low. This is further supported by the fact that in this cohort, 86% of the patients were primarily transported to a more specialized trauma center (part of the CENTER-TBI study group) where the availability of the necessary infrastructure for diagnosis and treatment of spine trauma (especially spine stabilization surgery) is expected to be higher. It is therefore advisable that given the relevant rate of TSI in patients with TBI and the complex spine surgery these patients might potentially require, patients with TBI are primarily presented to specialized trauma centers of maximum care, especially when concomitant TSI is suspected. This effect could indeed be of even more relevance in the context of patients with mTBI since our analysis demonstrated how in the case of the subgroup of patients with mTBI, isolated TSI (or TSI in conjunction with systemic injuries) does indeed hinder full recovery and negatively influence outcomes.

Although most of the patients in the TBI+TSI cohort were admitted to the ICU, there was no significant difference in mortality when comparing them to patients with isolated TBI in our study. This hints at the possibility that in TBI patients with concomitant TSI, the intracranial injury still represents the main prognosis-limiting factor, especially in severe and moderate TBI. The disparity between the findings on patients with mTBI and all patients of the cohort emphasizes on how the prognosis of patients with moderate and severe TBI is limited by their cranial injury and how TSI becomes more relevant in patients sustaining mTBI, that are otherwise less limited in terms of their neurological outcomes. The question is to whether the necessity of intubation and mechanical ventilation is a result of loss of consciousness owing to TBI or of respiratory failure secondary to injury of the cervical spine remains and cannot be explored using the data provided, although previous reports have indicated the presence of the latter patient group (12).

Similarly, two-thirds of the patients in the TBI+TSI cohort showed a favorable outcome (divided in half between complete recovery and incomplete recovery with a GOSe > 5), leaving a third with unfavorable outcomes in our current analysis. Interestingly, an older study estimated patients with the recovery of neurological function after severe and moderate TBI and concomitant cervical TSI (no mTBIs included) to be at about a third (11), which is very comparable to the data we present. Apart from that, little data have been provided in previous epidemiological studies on the specific functional outcomes of TBI patients with concomitant TSI. This once again emphasizes the importance of the data presented in this study, in which the rates of mortality and unfavorable outcomes in TBI patients with concomitant TSI were comparable to the respective rates observed in a matched group of TBI patients without TSI.

In summary, this analysis of prospective observational data sheds light on the current prognosis of patients suffering from TBI with a concomitant isolated or non-isolated TSI in the CENTER-TBI participating centers, showing an outcome that is comparable with what is known in the literature (15). The data presented underscore the role of specialized trauma care centers in preventing further neurological deterioration owing to concomitant TSI especially in patients with mTBI through early detection and adequate therapy of spine trauma.

Limitations

Several important limitations must be noted. As an observational study focused on TBI, in general, no additional information on the exact nature of the spine injury or its treatment (that included surgical details) was recorded in the CENTER-TBI database. Thus, injuries to the spinal cord could have been present in some patients but not in others, potentially leading to a considerable heterogeneity for the variable "spine trauma." This should be considered when interpreting our current results. Additional studies are needed to assess how different types of spine and spinal cord injuries relate to outcomes in patients with TBI. To the same end, detailed parameters assessing specifically the spine function, such as motor and sensory function of the extremities, as well as the function of the autonomic nerve system, were not available but would be desirable both for the description of the baseline clinical status and for the evaluation of recovery at follow-up. In terms of outcome analysis, the matching process is dependent on the chosen covariables and unmeasured covariables that might play an important role are not accounted for. Finally, as only TBI patients with concomitant spine trauma were included, the sample sizes of the different subgroups of patients in our analyses were limited. Larger cohorts are needed for a more robust generalizability and to possibly detect more subtle effects of a concomitant spine injury on outcomes in patients with TBI.

Data availability statement

The data analyzed in this study was obtained from the CENTER-TBI database; the following licenses/restrictions apply: Upon a reasonable request, access to the dataset must first be reviewed and approved by the CENTER-TBI Management Committee and should be directed to https://www.center-tbi.eu/data.

Ethics statement

Ethical approval was obtained for each recruiting site. A complete list is given on https://www.center-tbi.eu/project/ethical-approval or available as a Supplementary file. All patients had to give their written informed consent before enrollment in CENTER-TBI.

Author contributions

Study concept and design and data collection and analysis: LR and AY. Data interpretation and reviewing and editing: LR, OA, AU, and AY. Writing the manuscript: LR and OA. Supervision: AY. All authors approved the final version of the submitted manuscript.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2022.861688/full#supplementary-material

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