Decision-making in severe traumatic brain injury: patient outcome, hospital costs, and research practice

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PART I

Patient outcome, in-hospital healthcare consumption, in-hospital costs, and treatment decision-making in severe traumatic brain injury

CHAPTER 2

Decision-making in very severe traumatic brain injury (Glasgow Coma Scale 3-5): a literature review of acute neurosurgical management

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ABSTRACT

Introduction: Patients presenting with an early Glasgow Coma Scale (GCS) Score of 3-5 after blunt or penetrating skull-brain assaults are categorized as having sustained a very severe traumatic brain injury (vs-TBI). This category is often overlooked in literature. Impact on patients and families lives however is huge and the question "whether to surgically treat or not" frequently poses a dilemma to treating physicians. Little is known about mortality and outcome, compared to what is known for the group of severe TBI patients (s-TBI) (GCS 3-8). The main goal of this review was creating more awareness for the neurosurgical treatment of this patient group.

Evidence acquisition: A literature search (2000-2017) was conducted discussing "severe TBI (GCS 3-8)", "(neuro)surgical management" and "outcome". Ultimately 45 out of 2568 articles were included for further analysis.

Evidence synthesis: Mortality rates and unfavorable outcome are high for s-TBI patients and as expected higher for vs-TBI patients. Mortality rates reach up to 100% for specific subgroups with GCS=3 and bilaterally fixed dilated pupils. Functional outcome was generally poor, but sometimes, although seldom, favorable in specific groups of vs-TBI patients after neurosurgical intervention. Factors like initial GCS, pupillary abnormalities and age seem to be associated with worse outcome.

Conclusions: Overall this literature review showed high rates of unfavorable outcome and mortality for vs-TBI patients. However, some studies, reporting relatively low mortality rates, reported "good" outcome for specific groups of vs-TBI patients. It is concluded that clinical decision-making, in particular those on treatment limitations, should never be taken based on the GCS alone.

INTRODUCTION

Patients with severe traumatic brain injury (s-TBI) are generally defined as those with a Glasgow Coma Scale Score (GCS) between 3 and 8. These patients are, in most instances in Western World, directly intubated and transported to the nearest level I trauma center. Obviously, s-TBI has high emotional, humanitarian and financial impact on patients, their proxy's as well as on society. Of hospitalized TBI patients about 1 out of 25 are classified as having s-TBI.[1] The nature and extent of brain injury in this group may vary from closed to penetrating trauma,[2, 3] including intracranial hematomas (epidural, subdural or hemorrhagic contusion injury) observed in up to 35% of the s-TBI patients and varying degrees of diffuse axonal injury.[2, 4] Mortality rates are high (40%) and chance for clinically favorable outcome, as assessed by the Glasgow Outcome Scale (GOS), relatively low (40%).[5-8]

Within the population of s-TBI, very severe TBI (vs-TBI) is being proposed by the authors to sub-classify the group of patients with an extremely low initial coma score, categorized as having a very low GCS, ranging between 3 and 5. Obviously, for the latter patients, mortality and severe disability rates are higher, and clinical outcome is worse than for the entire group of severe TBI. Still, this sub-classification is useful to analyze detailed outcome for this group specifically, because vs-TBI is the most challenging group of patients in treatment decision-making for neurosurgeons, traumatologists, intensivists and neurologists. As time is limited in the acute phase, communication with family and friends of the patient is short, if ever performed at all. It creates difficulties for those, who have to determine whether or not to treat these patients surgically in the acute setting. Surgical options, range from inserting an intracranial pressure (ICP) monitoring device up to a large decompressive craniectomy, in order to try to control "severe brain swelling", which may develop secondarily. The latter treatment may increase the chance for survival, but also increases the chance for survival of a patient with severe disability,[9-13] which might not be acceptable for all people and to society.

The goal of this literature review was to investigate reported outcome for patients with vs-TBI, in particular the effect of different neurosurgical interventions. Besides important essential factual information, the authors try to identify gaps in the diagnostic and treatment evidence, for which more research will be needed to eventually improve surgical treatment for this important group of TBI patients.

EVIDENCE ACQUISITION

The literature review was conducted according to a predefined search protocol. A systematic review attempt was abandoned as randomized studies and methodological sound prospective studies were lacking. Keywords were “brain injury”, “traumatic”, “surgery”, “neurosurgical procedures”, “operative” and “severe” (Appendix I). The sections discussing penetrating brain injury (PBI) are separately informed by the literature search used for the *Guidelines for the Management of Penetrating Brain Injury*,[14] which was expanded by an additional literature search in Medline. Search terms included “penetrating head or brain injuries”, “brain”, “head”, “wounds” and “gunshot” (Appendix I).

Two reviewers independently selected relevant studies, extracted data and discussed disagreements until consensus was reached. If consensus was not reached one of the senior authors was capable to take the final decision.
Two stages of study selection were needed (Figure 1). First, studies were selected on title and abstract at least containing: (1) s-TBI patients, (2) (neuro) surgical treatment and (3) clinical outcome. Secondly, during full-text screening, only original data studies with patient cohorts (N>10) consisting of vs-TBI patients (early GCS Score 3-5) were included if data on (neuro) surgical treatment and outcome were presented. Studies were excluded when published before 2000 and non-English. Authors excluded series without a detailed initial GCS and only mentioning mean or median scores for obvious clinimetric reasons.

Manuscripts containing information on outcome in vs-TBI in adult populations were subsequently divided based on surgical treatment; ICP monitoring, decompressive craniectomy and other surgical interventions. Studies discussing elderly and pediatric patients were discussed separately. Authors used various synonyms for good or favorable outcome (GOS 4 or 5), representing “moderate disability” and “good outcome” respectively. The same classification and denomination was used in the specific references.

EVIDENCE SYNTHESIS

The search resulted in 2568 manuscripts. After screening of abstracts, 751 studies were selected for full-text assessment. Manuscripts were excluded for three main reasons: 1) no original data (N.=173); 2) no vs-TBI patient cohort (N.=504); 3) no surgical treatment or outcome specified for vs-TBI (N.=29) and other reasons (N.=6). Finally, 39 scientific manuscripts met inclusion criteria. After checking reference lists on possible relevant publications another 6 emerged, resulting in a final selection of 45 studies[15-20] (Figure 1). In addition, a total of 126 manuscripts formed the evidence base for the sections on penetrating brain injury.

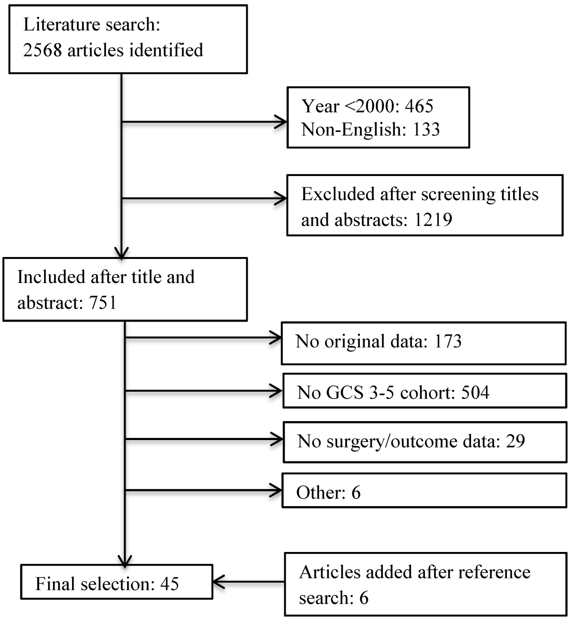

Figure 1: Article selection

Intracranial pressure monitoring

Eight studies from all global continents reported results of ICP guided treatment in vs-TBI patients (Table I).[21-28] Only three studies reported prospective data collection.[21-23] Cohort sizes varied between 78 and 4880 patients,[24, 25] presenting male dominance (mean 77%) and young age (mean 42 years).

Tabel I: ICP Monitoring

Study information	Purpose	Population	♂	Age
Farahvar (2012)[21] USA, 2000-2009 Prospective	Examine 2-week mortality of s-TBI patients with or without ICP monitor.	N=1446 ICP:1202 (83.1%) GCS3-5: 761	75	36.6
Mauritz (2008)[22] Austria, 1998-2004 Prospective	Reasons for receiving ICP monitoring and factors influencing mortality.	N=1856 1:ICP:1031 (56%) 2:No-ICP:825 GCS3+4: 959	73	1: 46 2: 53
Dawes (2015)[23] USA, 2009-2010 Prospective	Determine the impact of ICP monitor placement on inpatient mortality.	N=822 ICP: 378 (46%) GCS3: 449	75	42
Kim (2014)[24] Korea, 2010-2012 Retrospective	Effect of ICP monitoring on the two-week mortality after early DC in s-TBI	N=78 ICP: 25 (32.1%) GCS3-5: 38 ICP: 10 (26.3%)	82	44
Alice (2017)[25] USA, 2013-2014 Retrospective	Assess both compliance and outcomes of ICP monitoring.	N=4880 GCS3-5 sub: 3352 ICP: 381 (11.4%)	72	50
Griesdale (2010)[26] Canada, 2000-2006 Retrospective	Evaluate guideline adherence and relationship between EVD use and mortality.	N=171 1:EVD: 98 (57%) 2:No EVD: 73 GCS<6: 52	77	1: 35 2: 42
Haddad (2011)[27] Saudi Arabia, 2001-2008 Retrospective	Examine outcome of ICP monitoring in s-TBI patients.	N=477 ICP: 52 (10.9%) GCS3-4: 231	96	±28 .5
Zeng (2010)[28] China, 2004-2006 Retrospective	Evaluate treatment guided by ICP monitoring in s-TBI patients.	N=136 ICP: 136 (100%) GCS3-5: 58	66	44.8

Table I legend:
* Multivariable logistic regression models predicting 2-week mortality for all-age sample ((OR; 95%CI;P))
** Risk-adjusted mortality rate reduction for ICP monitoring.
*** Logistic regression analyses predicting 2-week mortalities for all 78 patients.

Abbreviations: ♂: Male; s-TBI: severe Traumatic Brain Injury; ICP: Intracranial Pressure; GCS: Glasgow Coma Scale (score); ICU: Intensive Care Unit; ED: Emergency Department; ISS: Injury Severity Score; FIM: Functional Independence Measure; EVD: External Ventricular Drain; GOS: Glasgow Outcome Scale.

Average reported proportion of ICP monitoring in s-TBI was 42% (range: 10.8-83.1%). Two studies specifically assessed guideline adherence and found only 10.8% and 46% of eligible patients receiving ICP monitoring.[23, 25] A third study found that 86% of patients without an extra ventricular drain would have qualified for having one.[26] One study investigated inter-center differences and found that ICP monitoring occurred more often in medium-sized trauma centers compared to large centers (OR 3.09, 95% CI 2.42-3.94).[22]

Type of GCS score.	Outcome measure	Results
Initial day 1 post-resuscitation	14-day mortality	**Mortality** (OR; 95% CI; P) GCS6-8 vs. GCS3-5 = (0.44; 0.36 - 0.53; <0.0001) ICP monitoring is a statistically significant predictor of 2-week mortality: (0.63; 0.41-0.94; 0.02)*
Admission	ICU/Hospital mortality	**Mortality:** GCS3 (N=796): ICU: 48.5%, Hospital: 51.1% GCS>3: ICU: 24.8%, Hospital: 29.3% Age 65 and GCS=3: ICU 67%; Hospital 71.1% Numbers irrespective the presence of ICP monitoring
ED	Inpatient mortality	**Mortality:** GCS(3): -13.3% (95% CI: -6.0 to -20.5). P:<0.001 GCS(3)+ High ISS (>25): -32.9% (95% CI: -20.3 to -45.4) P:<0.001**
Initial	2-week mortality	**Overall mortality**: ICP: 24%, no-ICP: 50.9% (p=0.025) **Mortality**: GCS3-5: 57.8% GCS3-5: Crude OR 3.625 (1.406-9.343)*** Adjusted OR: 2.506 (0.712-8.822)***
Presentation	Mortality (in hospital)/ FIM (good)	**Mortality** Overall ICP/no-ICP: 27.2% / 22.4% **FIM (good)** Overall ICP/no-ICP: 17.8% / 28.7% **Mortality**: GCS3-5: 26.3%. Overall: 22.9% GCS3-5: Independent predictor of mortality: OR1.84
Best in first 12 hours.	Hospital and 28-day mortality	**Hospital mortality** (OR; 95% CI; P): GCS<6: 0.76; 0.18–3.2; 0.71, GCS≥6: 5.6; 1.7-18.4; <0.01 **28-day mortality** (OR; 95% CI; P): GCS<6: 0.47; 0.11–2.1; 0.32, GCS≥6: 5.0; 1.5-16.7; <0.01
Admission	Hospital mortality	**Mortality ICP/No-ICP**, (OR; 95%CI; P) GCS3-4: 12.9%/ 24.5%, (0.51; 0.17-1.59; 0.25) GCS5-6: 18.2%/ 7%, (3.74; 0.61-22.82; 0.15) GCS7-8: 50%/ 7.2%, (12.89; 3.14-52.95; 0.0004)
Admission	GOS (>6M)	GCS3-5: GOS1= 16%, GOS2=12%, GOS3= 24%, GOS4= 10%, GOS5=38% GCS6-8: GOS1= 4%, GOS2=4%, GOS3= 13%, GOS4= 10%, GOS5=69%

Multiple factors seemed likely to be associated with more frequent placement of an ICP monitoring device, including age (<65 years), female gender, the presence of at least one reactive pupil and more isolated TBI with a higher Abbreviated Injury Scale (AIS) head score and higher Injury Severity Score (ISS).[22, 23] Increased likelihood ratios for ICP monitoring were also found when the CT-scan showed subdural hematoma, cerebral contusion or diffuse mass effect.[23] Reasons for not providing ICP monitoring included higher age,[21-23] pupillary abnormalities,[21] history of cancer,[22] cardiac insufficiencies,[22] alcoholism, coagulopathy or injury from a fall [23] and a higher estimated mortality as assessed by the treating physician.[22] A cohort of 1856 patients, showed ICP rates rise with TBI severity, but interestingly again decreased for vs-TBI.[22]

Monitoring ICP, with therapeutic consequences, was reported to be associated with an 8.3% reduction in risk-adjusted mortality rate.[23] Reduction in risk-adjusted mortality rate increased to 13.3% for low GCS Score (3) and to 32.9% in high (>25) and low GCS Score (3) combined.[23] But there was no consensus. Some found a lower GCS Score to be a predictor for mortality [21, 25] and others showed no significant difference for GCS 5-6 and GCS 3-4 subgroups.[27] Even the opposite was found. A higher hospital and 28-day mortality in patients with GCS>5, but not in patients with GCS<6.[26]

Despite ICP guided treatment, up to 12% was diagnosed as sustaining a persistent vegetative state at 6 months, besides which 24% having severe cognitive and somatic disabilities.[28] Favorable outcome (GOS 4-5) was reached in 48% (GCS 3-5) and 79% (GCS 6-8) of patients.[28]

Although possibly due to selection bias, ICP monitored patients showed longer duration of mechanical ventilation,[25-27] a higher need for tracheostomy [27] and significantly longer intensive care unit (ICU) stay [22, 25-27] compared to non-ICP monitored patients. Also more complications and poorer functional outcome at discharge are reported.[25]

Decompressive craniectomy

Seventeen of 45 selected studies concerned decompressive craniectomy (DC) procedures. Results (Table II)[15-17, 29-42] showed a predominance of young males (age range: 25-56 years) and most cohorts involved less than 50 patients, with one prospective study and other studies being retrospective.[29] Most studies used the Glasgow Outcome Scale (GOS) and one study used the modified Rankin Scale (mRS).[30]

Wide ranges in outcome were identified for overall s-TBI mortality rates (11% to 68.5%).[30, 31] Rates for vs-TBI patients were higher near 80%,[32, 33] up to 100% in two GCS=3 subgroups.[30, 34] Favorable outcome in vs-TBI patients ranged from 0% (mRS 0-2) to 63% (GOS3-5).[30, 35] Up to 80% of patients with initial GCS≥6 achieved favorable outcome.[36]

Nine studies investigated outcome of standard DC, without comparing different ICU and surgical treatment methods.[15-17, 31, 32, 34, 36-38] A bilateral decompression for bilateral injury or diffuse edema/swelling was used in 3.3-34% of total procedures. The identified two typical reasons for performing DC are: 1) directly to prevent secondary injury; 2) posttraumatic ICP elevation, after failed ICU treatment; and 3) posttraumatic surgical lesions like epidural hematoma (EDH), acute subdural hematoma (ASDH) or cerebral contusions, depending on their location, extent and presence of brain edema and CT recorded midline shift.[31, 34, 36-38] With 34% of all patients receiving bilateral decompressive surgery for posttraumatic intractable intracranial hypertension, overall 84% achieved unfavorable outcome increasing to 96.6% for vs-TBI.[17]

Timing of surgery varied between cohorts from 86% of patients within first hour after admission, to 33% within 6 hours from trauma.[31, 36] One study with only ASDH patients, showed a 30-day mortality rate of nearly 40 percent. The vs-TBI subgroup showed higher mortality rates (64% *vs*. 26%) and more 6-month unfavorable outcome (GOS1-3) (91% *vs*. 55%) compared to patients with GCS>5.[34] A second study (79% ASDH) found similar unfavorable outcome rates for vs-TBI patients after 6 months approaching 90%, but found higher mortality rates (79.3%).[32] With 86% of cohort being patients with ASDH, Huang *et al*. found 59.7% 30-day mortality for vs-TBI subgroup and 12.4% mortality for GCS 6-8 [16]. In other studies ASDH was the most prevalent focal intracranial space-occupying lesion (32-86%).[16, 17, 30, 31, 38] A study investigating "malignant" brain swelling reported no difference in mortality rates, but worse outcome for vs-TBI patients (70% *vs*. 16.7%) than GCS>5 patients.[37] Within a cohort of 66 vs-TBI patients, neurosurgeons performed 86% of all DC within approximately one hour after admission and this study reported an overall 1-year mortality rate of 11%, with good outcome in 68%.[31] Worse outcome was reported in patients with higher initial ICPs and GCS<5.[31] A relatively favorable overall mortality rate (12.5%) was found in Italy, where 37% of GCS 3-5 patients achieved favorable outcome.[15]

Five studies compared different surgical techniques and varying timing of surgery.[30, 35, 39-41] All studies were retrospective and contained a subgroup of GCS 3-5 patients. Early bilateral decompressive craniectomy as a first treatment option in s-TBI was compared to secondary DC for refractory ICP.[39] It was shown to be an effective treatment option for ICP control, resulting in overall significant better one-year favorable outcome of 50% and 27.8%, respectively.[39] Compared to the GCS 6-8 subgroup, the vs-TBI subgroup showed a 2 times higher rate of mortality (50% *vs*. 25%) and splits favorable outcome (45% *vs*. 25%) [39]. Ultra-early DC (<4 h of trauma onset) compared with DC after 4 hours did not seem to improve patient outcome.[30] Worse mortality rates were found for vs-TBI patients (GCS 3:100%, GCS 4-5:82.2%, GCS>5:41%) and showed 0% favorable outcome, compared to 4.7% in GCS>5 patients.[30] Another study reported significantly better outcome for patients with GCS 6-8 who were operated within 24 h compared to patients with GCS 3-5, operated within the same time window.[41]

Apart from the timing of decompressive surgery, another factor was the surgical technique, which varied, caused by the extent of diffuse swelling and presence of intracranial hematoma. The difference between DC with and without mass evacuation was investigated comparing 93 patients with mass lesions and 71 patients with diffuse injury and swelling.[40] The first group showed lower mortality (14 *vs*. 32.4%) and appeared to be a significant predictor to 60-day mortality (OR=0.31). Only good outcome was significantly worse for vs-TBI patients.[40] Performing large DC (10 cm x (13-15)cm) on patients resulted in overall satisfactory outcome (GOS 3-5) in 71.1% compared to 58.6% in the routine DC group (6-8 cm diameter) (P<0.05).[35] Superiority was especially seen in vs-TBI patients (63.0% *vs*. 36.7%, P<0.01).[35]

A higher initial GCS Score, typically compared to GCS 3-5 (vs-TBI) subgroups, was correlated with more favorable outcome in almost all studies.[15-17, 30-32, 34, 36-41] Patients with GCS 6-8 were more likely to have a good outcome than the GCS 3-5 group (OR 10.0, 95% CI 1.6-60.9).[37] A GCS motor-score of 5-6 resulted more in good outcome than a motor-score of 1-4 (OR 4.2, 95% CI 1.1-16.3).[37] Pupillary abnormalities were associated with mortality,[36, 40] even up to 100% when bilaterally fixed and dilated [32] (except in one study).[37] A younger age was associated with a favorable outcome,[15-17, 30, 31, 34, 38-42] only two studies mentioned no statistical significance between age and prognosis.[32, 37] Other factors like small size of bone flap,[31, 35] association of intracranial lesions, midline shift> 15 mm, ICP>20 at time of DC,[31] Revised Trauma Score <5, Charlson Comorbidity Index Scores >5, glucose >180 (mg.dL-1), PaO_2 <160 (mmHg), SO_2 <96 (%) were all linked to poor prognosis and unfavorable outcome.[34]

Outcome, hypothetically can be improved by two suggested changes in technique.[29, 33, 42] A prospective study showed that DC combined with a new multi-dural stabs technique (SKIMS) in patients with ASDH and severe brain edema seems very effective in patients with low GCS.[29] Patients with vs-TBI receiving DC with SKIMS showed a mortality of 36.7% and favorable outcome (GOS 4+5) in 30%, while 59% of the conventional group died and 19% achieved favorable outcome.[29] Two small retrospective patient series described that creating vascular tunnels during decompressive surgery dropped mortality for GCS<5 patients with severe brain edema (ICP>30 mmHg for >3 hours) from 80% to ±40% and good outcome (GOS 4+5) improved from 10% to ±40%.[33, 42] Series were compared with a historic control group receiving a large bilateral frontotemporoparietal craniectomy.

Neurosurgical interventions

Eleven studies discussed surgical interventions, mainly craniotomy for hematoma evacuation (Table III).[19, 43-51] One study used prospectively collected data and six discussed cohorts with exclusively GCS 3-5 patients, with four only including GCS=3 patients.

The choice between surgical intervention or not and which technique showed substantial variation between centers (9-77%). Fewer patients with a cerebral contusion received surgical intervention (34%) compared to patients having an EDH or ASDH (88%, 68%).[43] Factors positively associated with quantities of surgical intervention appeared to be fall injury, more severe injuries (according to ISS and head AIS), bradycardia and injuries like skull fractures, EDH and ASDH. Negative associating factors seem to be a diagnosis of intracerebral hemorrhage and hypotension or tachycardia at ED presentation.[44] Although suffering from more extra-axial bleedings, significantly lower rates of surgical intervention were found in patients with bilaterally fixed dilated pupils, compared to patients with reactive pupils (16.4% *vs.* 34.8%).[45] The execution of bilateral surgery instead of unilateral surgery seems to be associated with absence of pupillary response, lower GCS (6.7% *vs.* 9.2%), more large-volume lesions, complete cistern compression and CT-visible deep lesions.[46] Timing of surgical intervention was not always mentioned, but 50 and 73% was performed <24 hours [43, 47] up to 83% within 4 hours in one cohort.[44] Several studies show lower GCS scores to be linked to worse outcome and higher mortality rates.[46, 48] Unfavorable outcome (GOS 1-3) in up to 94.11% was found for GCS 3-5 subcategories.[49]

Surgical intervention resulted in improved mortality.[43, 44, 46, 49] One study found better prognosis for both GCS 6-8 and GCS 3-5 surgical treatment subgroups and poorer outcome for conservative treatment especially in patients with GCS≥6.[46] A significant 4-fold survival benefit was found for surgically treating mass lesions in patients with GCS=3, but this study also found surgery to be significantly related to more complications, especially pneumonia (P<0.001).[44] Significant higher mortality (48% *vs.* 23%) and poorer outcome was found in the conservative group.[43] Two studies reported no significant difference in surgical interventions between survivors and non-survivors and another found no effect from immediate neurosurgery on outcome in patients without a mass lesion.[44, 50]

Multiple studies report poor outcome and increased mortality rates to be associated with pupillary abnormalities.[45, 46, 48, 50] In normally bilateral reactive pupils a mortality rate of 23.5% and a good outcome in 1 out of 4 patients is reported [50] and in another study absence of pupillary response correlated with unfavorable outcome (OR3.16, 95% CI 1.38-7.25).[46] In patients with gunshot wound to the head 96% and 100% died when having a unilateral dilated pupil or a medium fixed pupil.[48] Another study found mortality rates in patients with bilaterally fixed dilated pupils of nearly 80% and good outcome in only 1.5% of patients.[50] Other possibilities, like unilateral fixed dilated pupils showed good outcome in 27.5% and bilateral fixed, non-dilated pupils achieve good outcome in only 7.5%.[50] Patients with both a GCS=3 and bilaterally fixed dilated pupils presented good outcome (GOS 4-5) after neurosurgery in 9.3%. In the overall group, difference in good outcome was found between field and post resuscitation GCS of 3 (8.7% *vs*. 4%).[19] Patients with bilaterally fixed dilated pupils showed increased numbers of extra-axial bleedings (81.4% *vs*. 56.5%, P=0.002), midline shifts (70.0% *vs*. 24.2%, P<0.0001) and herniation (64.3% *vs*. 11.3%, P<0.0001) and ultimately higher mortality compared to patients with RP (100% *vs*. 42%, P<0.0001).[45] Sometimes, patients with bilaterally fixed dilated pupils were not stable enough to undergo a CT scan.[45]

Aggressive presurgery medical treatment with single high mannitol dosage (90-106g) resulted in significant lower risks of death and persistent vegetative state (OR=0.016) with lower unfavorable outcome (57.1% *vs*. 95.5%). However at 1 year follow up, more patients survived with severe disabilities.[51]

One study showed survival was most positively linked to acute epidural hematomas, followed by cerebral contusions, and worst with acute subdural hematomas.[47] Another study however, found no correlation between dominant lesions, presence of midline shift and outcome.[46] Compression of basal cisterns was linked to death (OR3.24, 1.04-10.12) and unfavorable outcome (OR: 2.74, 1.17-6.42).[19, 46] For patients with gunshot wounds to the head, especially transventricular or bihemispheric central type trajectory, and bilobar or multilobar wounds are suggested as predictive factors of high morbidity and mortality.[48]

Other factors mentioned to be associated with lower survival or unfavorable prognosis are: higher age [19, 47, 50, 51] and ICP.[50] Alcohol, gender, mechanism of injury, hypotension on admission, and extracranial injuries are mentioned not to be related with outcome.[50]

Elderly patients

Five studies focusing on elderly patients matched our criteria (Table IV) [18, 20, 52-54] and three articles from other categories contained information concerning elderly patients.[22, 31, 38]
Mortality rates ranged between 53.6% (6 month) and 77% (1 year) for all GCS scores.[52, 53] For this severity group, surgical management resulted in lower mortality compared to conservative treatment (32.9% *vs*. 88.1% and 62% *vs*. 81%).[18, 52] For vs-TBI patients, results are worse, with rates around 80% even up to 100% after DC.[18, 20, 53, 54] An earlier discussed study found better outcome in patients younger than 66 years old, which seemed to be a cut-off point, since groups aged <40 and 40-65 showed no differences.[38]

Almost 6% of GCS 3-4 patients achieved functional recovery (GOS 4-5) 6-months after evacuation of an ASDH.[54] In another study, GCS 3-4 patients achieved 11% favorable outcome (GOS 4-5) one year after >80% received non-specified neurosurgical intervention.[20] Our biggest included cohort showed only 3% of vs-TBI patients with favorable outcome, compared to 13% with less severe injury (GCS 6-15).[18] Both positive and negative association of surgical intervention with outcome was reported.[18, 20, 52, 53] GCS Score was an important outcome predictor [18, 52-54] and other factors associated with unfavorable outcome are treatment method, pupillary abnormality, higher trauma severity, closed basal cisterns (100% mortality) and midline shift (≥10 or ≥15 mm) on first CT-scan.[20, 52] Age was said to be both a significant [18, 54] and insignificant predictor [53] and also gender associations remained non-conclusive.[20, 53]

Tabel II Decompressive Craniectomy

Study information	Purpose	Population	♂	Age	Type of GCS score	Pupils
Chibbaro (2007)[15] Italy, 2003-2005 Retrospective	Effects of DC in the treatment of severe head injury	N=48 GCS3-5: 19	63	47	Preoperative	BFDP: 6 UFDP: 18
Huang (2013)[16] Taiwan, 2006-2008 Retrospective	Investigate factors related to 30-day mortality after DC	N=201 GCS3-5: 67 ASDH: 86% TSAH: 84% CC: 56% EDH: 12%	72	46	Pre-decompression	Unilateral FP: 12 Bilateral FP: 91
Ucar (2005)[17] Turkey 2001-2003 Retrospective	Evaluate benefits of DC in intractable ICH	N=100 GCS4-5: 60 ASDH: 32%	68	30	Initial	NP
Bhat (2013)[29] India, 2006-2011 Prospective	Effects of combining DC and multi-dural stabs	N=225 s-TBI ASDH+BE GCS3-4: 30	> 80	65%= 21-40	Following trauma	NP
Park (2014)[30] Korea, 2007-2013 Retrospective	Outcomes of Ultra-Early DC after s-TBI	N=127 GCS3: 27 GCS4-5: 45 ASDH: 62.2% EDH: 2.4% CC: 32.3%	76	50	Admission	Many GCS=3 patients with bilateral DP
Fotakopoulos (2016)[31] Greece, 2009-2013 Retrospective	Clinical outcome after DC in s-TBI patients	N=101 s-TBI. GCS3-5: 60 ASDH :37% BE:30% IP:21% CC:8%, EDH:7%	80	42.8	Time of intubation	NP
Saade (2014)[32] Brazil, 2004-2012 Retrospective	Prognostic factors of DC in treating s-TBI patients	N=56 GCS4-5: 29 ASDH:79% CC:28.6% EDH:18% TSAH:18%	83	Most 40-50	Admission/ Prehospital	ANI: 48% BFDP: 18% Normal: 34%
Csokay (2002)[33] Hungary, 1997-1999 Retrospective	Outcome of a new surgical technique: vascular tunnelling (VT)	N=28 All GCS<5, BE 1: VT: 28 2: Previous cohort: 20	NP	NP	NP	NP
Kalayci (2013)[34] Turkey, 2001-2009 Retrospective	Prognostics and value assessment in DC for ASDH	N=34 GCS3-4: 11 ASDH 100%	76	37	Preoperative	BFDP:12 Unilateral DP: 9 Isocoria: 13

Surgical intervention.	Outcome measure	Results
DC(≥35cm²): 48 Unilateral: 42 Bilateral: 6 <16h trauma: 28 <48h trauma: 48	GOS	**GOS1:** Overall:12.5%, GCS3-5: 16%, GCS6-8:11% **GOS2:** GCS3-5: 37%, GCS6-8: 7% **Favourable (GOS4+5)**: Overall: 55%, GCS3-5: 37%, GCS6-8: 67% LTFU: 2 (Mean FU 14 months)
Primary: 187 Secondary: 14 Unilateral: 183 Bilateral: 8 Bifrontal: 10 <24h trauma: 166	30- day Mortality	**Mortality:** Overall: 26.4%, GCS9-15: 4.4%. GCS6-8: 12.4%, GCS3-5: 59.7% >90% died within 14 days.
Unilateral: 66% Bilateral: 34% 94 < mean17.1h 6 after secondary ICP increase.	GOS (6M)	**Unfavourable (GOS1-3):** Overall: 84%, GCS4-5: 96.6%, GCS6-8: 65% **Favourable (GOS4-5):** Overall: 16%, GCS4-5: 3.4%, GCS6-8: 25%
Conventional DC: 106 Multi-dural stabs technique: 119	Discharge GOS	**Conventional** GCS3-4: GOS1: 59%, GOS (2+3): 22%, GOS (4+5): 19% **SKIMS** GCS3-4: GOS1: 36.7%, GOS(2+3): 33.3%, GOS (4+5): 30%
1: Ultra-early DC<4h: 60 2: DC>4h: 67	Mortality / mRS	**Mortality:** Overall: 68.5%, DC<4h: 65.0%, DC>4h: 71.6%, (p: 0.430) **Mortality:** GCS3: 100%, GCS4-5: 82.2%, GCS>5: 41% **Favourable (mRS0-2)**: GCS3-5: 0%, GCS>6: 4.7%
Early DC (±1h after admission): 85.9% Secondary: 14.1% (4-6 days). 8.2% bilateral.	GOS (6M/12M)	**At surgery:** Mortality 1.9%, morbidity 31.9%. **6M** (overall): GOS1: 11%, GOS2: 26%, GOS3: 9%, GOS4: 26%, GOS5: 28% **12M** (overall): GOS1: 11%, GOS2: 6%, GOS3: 15%, GOS4: 25%, GOS5: 43% **Other:** >60Y + GCS ≤5 (N=11) = 100% GOS<4. Poorer outcome in higher ICP and GCS <5
Unilateral DC: 96.4% Bilateral DC: 3.6% <6h admission: 71.4%	Mortality/ GOSE (6M)	**Mortality**: All: 58.9%, GCS4-5: 79.3%, GCS>5: 37% **Unfavourable(GOSE1-4)**: All: 78.5%, GCS4-5: 89.7%
Uni/bilateral FTPC (with/without vascular tunnel construction). <4h admission: 20	GOS	**Group 1:** GOS1: 39.3%, GOS4-5: 42.9%, GOS2-3: 17.8% **Group 2**: GOS1: 80%, GOS4-5: 10%, GOS2-3: 10%
Uni/bilateral FTPC ±5 hours from trauma	Mortality (30d)/ GOS (6M)	**30d: Mortality**: Overall: 38.2%, GCS≤5: 64%, GCS>5: 26% (P=0.042), GCS3 (N=3): 100%, GCS4 (N=5): 80% **6M: Mortality:** 47%, **GOS2**: 20%. **Favourable (GOS4-5):** Overall: 35%, GCS≤5: 9%, GCS>5: 45% **Unfavourable (GOS1-3):** GCS≤5: 91%, GCS>5: 55%

Tabel II continued

Study information	Purpose	Population	♂	Age	Type of GCS score	Pupils
Li (2008)[35] China, 2001-2006 Retrospective	Compare large DC (LDC) with routine DC (RDC) in s-TBI patients	N=263 LDC: 135 -GCS3-5: 54 RDC: 138 -GCS3-5: 49	69	±47	Administration	Bilateral DP:38 Unilateral DP: 97
Gouello (2014)[36] France, 2005-2011 Retrospective	Outcome of DC in s-TBI patients	N=60 GCS3-5: 26 Primary: 20 Secondary: 40	77	33	Initial management	CSP:43% UnilateralDP:57% Bilateral DP:22% ACR:8%
Aarabi (2006)[37] USA, 2000-2004 Retrospective	DC in TBI (malignant brain swelling)	N=50 GCS3-5: 15 BS: 88%	66	25	Post-resuscitation	ALR:22%
Pompucci (2007)[38] Italy, 1994-2004 Retrospective	Effect of DC.	N=55 GCS3-5: 31 No focal lesion: 38% ASDH+ BE: 62%	63	53	Post-resuscitation	NP
Akyuz (2010)[39] Turkey, 2003-2008 Retrospective	Effectiveness of early bilateral DC in s-TBI patients	N=76 GCS4+5: 20 1: Second-tier DC: 36 2: First-tier: 40	59	1:37.6 2:41.3	Initial	NP
Yuan (2013)[40] China, 2005-2009 Comparative	Difference between DC with and without mass evacuation in TBI	N=164 GCS3-5: 51 2 groups.	75	48	Admission	ALR: 1: 56% 2: 48%
Limpastan (2013)[41] Thailand 2006-2008 Retrospective	Evaluate risk factors influencing outcome after DC in s-TBI	N=159 GCS3-5: 63	82	36	Preoperative	80.3% of deceased group had no pupillary light reflex
Csokay (2001)[42] Hungary, 1998-2000 Retrospective comparative	Evaluation of new operative technique: vascular tunnelling (VT).	N=20 (19TBI) All GCS<6, BE. 1: VT: 20 2: Previous cohort: 20	NP	NP	NP	Bilateral DP: 20% Unilateral DP: 35%

Table II: Abbreviations: ♂: Male; ACR; Absent Corneal Reflex; ALR; Abnormal Light Response; ANI: Anisocoria; ASDH: Acute Subdural Hematoma; BE: Brain Edema; BFDP: Bilateral Fixed Dilated Pupils; BS: Brain Swelling; CC: Cerebral Contusion; CSP: Constricted Symmetrical Pupils; DC: Decompressive Craniectomy; DP: Dilated Pupil(s); EDH: Epidural Hematoma, FP: Fixed Pupil; FTPC: Frontotemporoparietal Craniectomy; GCS: Glasgow Coma Scale; GOS(E): Glasgow Outcome Scale (Extended); ICH: Intracranial Hypertension; ICP: Intracranial Pressure; IP: Intraparanchymal; LTFU: Loss to Follow Up; mRS: modified Rankin Scale; NP: Not Provided; s-TBI: severe Traumatic Brain Injury; TBI: Traumatic Brain Injury; TSAH: Traumatic Subarachnoid Hemorrhage; UFDP: Unilateral Fixed Dilated Pupil.

Surgical intervention.	Outcome measure	Results
LDC: 10cm x (13-15) cm RDC: 6-8 cm diameter	GOS (6M)	**Satisfactory** (GOS3-5)**:** GCS3-8: LDC 71.1%, RDC: 58.6% (P<0.05), GCS3-5: LDC 63%, RDC 36.7% (P<0.01) **LDC** (GCS3-5): GOS1: 30%, GOS2: 7%, GOS 3-5: 63% **RDC** (GCS3-5): GOS1: 57%, GOS2: 6%, GOS 3-5: 37%
Unilateral DC: 58. Bilateral DC: 2. Mean size 100cm^2 <6h: 33%. 6-24h: 12%	Mortality/ GOS (3/24M)	**Mortality**: GCS3-5: 50%, GCS6-8: 12%, GCS>8: 12% **Unfavourable (GOS2+3)**: GCS3-5: 54%, GCS6-8: 20%, GCS>8: 20%. **Favourable (GOS4+5)**: GCS3-5: 46%, GCS6-8: 80%, GCS>8: 80%. All significant
FTPC: 49 Bifrontal:1 <48h: 34%	Mortality/ GOS (3M)	**Mortality** (30d): Overall: 28%, GCS 3-5: 20%, GCS 6-8: 21.7%, GCS 9-15: 25%. **Good outcome (GOS4+5)**: Overall: 51.3%, GCS 3-5: 16.7%, GCS6-8: 66.7%, GCS 9-15: 66.7%.
Unilateral FTPC:50 Bilateral FTPC: 5 <5h: 29% >10h: 35%	GOS (12-102M)	**GOS1**: Overall: 39%. **Favourable (GOS4-5)** Overall: 47% GCS3-5: 26.7%, GCS6-8: 76.9%, GCS9-15: 66.7% **Unfavourable (GOS1-3)** GCS3-5: 76.3%, GCS6-8: 23.1%, GCS9-15: 33.3% Age>65 + GCS3–5 (N=11): 100%
Group 1: Unilateral: 22. Bilateral: 14. Group 2: Bilateral:40	GOS (12M)	**Favourable (GOS4+5):** Group 1: 27.8%, Group 2: 50% GCS4-5: GOS1: 50%, GOS2+3: 25%, GOS4+5: 25% GCS6-8: GOS1: 20%, GOS2+3: 35%, GOS4+5: 45%
1: DC for mass lesion: 93 2: DC for diffuse injury and swelling: 71	Mortality (60d)/ GOS	**Overall:** GOS1: 22%, GOS4-5: 42% **Mortality**: Group 1/Group 2: 14% / 32.4% **Mortality**: GCS3-5: 27.5%, GCS6-8: 26.9%, GCS9-12=13.1%. P=0.197 **Good outcome (GOS4-5) (%):** GCS3-5: 29.7%, GCS6-8: 52.6%, GCS9-12: 71.7% P=0.002
≤24h after admission: 76% (N=122) Unilateral: 88% Bilateral: 12%	GOS (discharge / 6M)	**Mortality:** Overall: 44.7%, GCS3-5: 59%, GCS>5: 35% (p=0.004). **Surgery ≤24h: (discharge): GOS1**: GCS3-5: 68%, GCS6-8: 42%, **GOS4-5**: GCS3-5: 26%, GCS6-8: 41.7% (p=0.013) **(6M): GOS1**: GCS3-5: 26.7% GCS6-8: 61.7% **GOS4-5**: GCS3-5: 6.7%, GCS6-8: 14.7% (p=0.013)
Bilateral FTPC (with/ without vascular tunnel construction).	GOS	**Group 1**: GOS1: 40%, GOS4-5: 40%, GOS2-3: 20% **Group 2:** GOS1: 80%, GOS4-5: 10%, GOS2-3: 10%

Tabel III Neurosurgical Interventions

Study Information	Purpose	Population	♂	Age	Type of GCS score	Pupils
Mauritz (2009)[19] Europe, 2001-2005 Prospective data	Investigate outcome of s-TBI with GCS 3 and BFDP.	N=92 F-GCS3: 100% PR-GCS3: 74 ASDH: 46% EDH: 13% TSAH: 64%	79	32	Field (F) and Post-resuscitation (PR)	BFDP: 100% ≥1 reactive pupil PR (N= 18)
Kawamata (2006)[43] Japan, 1998-2001 Retrospective	Effects of surgical excision of necrotic brain tissue in severe cerebral contusion.	N=182 GCS3-5: 58 CC: 182	NP	1: 47.8 2: 54.4	Admission	NP
Salottolo (2016)[44] USA, 2009-2013 Retrospective	Outcome in TBI treated with cranial surgery (CRANI).	N=541 Surgery: 103 GCS3: 100% ASDH: 58% TSAH: 53% CC/laceration: 40%	74	49	Presentation	NP
Tien (2006)[45] Canada, 2001-2003 Retrospective	Mortality of s-TBI+GCS3 comparing BFDP with RP.	N=173 GCS3: 100%	68	±41	Admission	BFDP:104 Reactive pupils (RP):69
Hu (2015)[46] China, 2010-2012 Retrospective	Outcome of traumatic acute bilateral mass lesions.	N=80 GCS3-8:47 GCS3-5:15 ASDH: 42.5% EDH: 21.3% HC: 36.3%	82	46	Admission	Absent pupillary response: One: 7.5%, Two: 26.3 %
Bindal (2015)[47] India, 2009-2011 Retrospective	Outcome of surgery for supratentorial mass lesions after blunt s-TBI.	N=72, All GCS4 (M2) EDH: 38% CC: 26% ASDH/CC:26% ASDH: 10%	79	19% >60 year	Time operation	NP
Martins (2003)[48] Brazil, 1994-2000 Retrospective	Evaluate morbidity and mortality in civilians with head gunshot wounds.	N=319. GCS3-5: 125 Damaged dura=265	93	26	Admission	Unilateral Dilated Pupils (UDP): 27 Medium Fixed (MF): 38
de Souza (2013)[49] Brazil, 1991-2005 Retrospective	Prognostic factors associated with TBI by a firearm projectile.	N=181 GCS3-5: 68 Penetrating 84% Tangential 16%	85	31	Admission	NP

Surgical intervention.	Outcome measure	Results
Neurosurgery: 43 Not further specified.	GOS (12M)	**Total group: Poor outcome (GOS1-3):** Field GCS: 91.3%, PR-GCS: 96% **Good outcome (GOS4-5):** Field GCS: 8.7%, PR-GCS: 4% ≥1 reactive pupil (N=18): Good outcome: 28% After neurosurgery (N=43): Good outcome: 9.3%, non-significant
1: Conservative 66% 2: Surgery 34% Internal decompression with/without external decompression: 90% Only external decompression: 10% <24h in 73%	GOS (6M)	**Surgical GCS3-5 (N=11):** GOS1: 55%, GOS2: 0%, GOS3: 27%, GOS4: 9%, GOS5: 9%. **Conservative GCS3-5 (N=47)**: GOS1: 70%, GOS2: 11%, GOS3: 11%, GOS4: 2%, GOS5: 7%. **Surgical GCS6-8 (N=21):** GOS1: 14%, GOS2: 10%, GOS3: 24%, GOS4: 29%, GOS5: 24% **Conservative GCS6-8 (N=58)**: GOS1: 29%, GOS2: 10%, GOS3: 10%, GOS4: 21%, GOS5: 29%
Craniotomy: 87% Craniectomy: 13% <4h arrival: 83% Mean time: 1.9h	Mortality (discharge) / favorable (home, rehabilitation) / FIM	**Overall mortality GCS=3:** 48% (9% Emergency room) **Overall survivors (favorable):** 74%.**Overall FIM:** (feeding/ expression/locomotion): 61%, 63%, 38%. **Survival:** CRANI/no CRANI: 61%/50% (P=0.04) **Favorable (home/rehab):** CRANI/no CRANI: 39%/39% **Matched mass lesion population:** **Survival:** CRANI/no CRANI: 65%/34% **Favorable outcome:** CRANI/no CRANI: 43%/26%
Neurosurgical procedures: BFDP 16.4% and RP 34.8% (P=0.005)	Mortality	**Mortality**: GCS3 + BFDP: 100% GCS3+RP: 42% (P<0.0001)
Conservative 22.5%. Unilateral 48.8%. Bilateral 28.8% (78.3% simultaneously).	Mortality/ GOS (6M)	**Overall mortality:** 31.3%, **Unfavorable (GOS1-3):** 56.3% **Surgical group:** GCS3–5: GOS1: 53.3%, GOS2: 26.7%, GOS3: 20.0% GCS≥6: GOS1: 14.9%, GOS2: 6.4%, GOS3: 17% LTFU: 3.8%
EDH:37%, ASDH: 10% Removal contusion/ lobectomy: 33% Persistent brain swelling (DC): 21%. 50% <24h.	Mortality/ GOS.	**In-hospital mortality**: 79%. **Overall**: 83%. **Mortality** isolated ASDH: 100%. **>60 years:** 100% 70% of survivors, operated <24h **GOS4-5**: Overall: 14%, EDH: 26%, CC: 11%, ASDH/CC: 5% LTFU: 3%
Large craniotomy. Surgery in 156 patients. GCS3-5 + Surgery: 26	Mortality/ GOS (hospital discharge)	**Overall mortality**: 65% **Mortality**: GCS3-5: 98.5% (PVS:1.5%), UDP: 96%, MF:100% **After surgery:** GCS3-5: Death: 92.5%, PVS: 7.5% GCS6-8: Death: 62.5%, GOS4-5: 22.5% GCS9-12: Death 22%, GOS4-5: 67.5% GCS13-15: Death: 9%, GOS4-5: 91%
Surgery: Overall: 91 GCS3-5: 13	GOS	**Satisfactory (GOS3-5):** Overall: 50.3%, surgery: 71.4% **Poor (GOS1-2):** Overall: 49.7%, surgery: 29.9% **Poor outcome (GOS 1-2)**: GCS3-5: 94%, GCS6-8: 40%, GCS-9-12: 25%

Tabel III continued

Study Information	Purpose	Population	♂	Age	Type of GCS score	Pupils
Chamoun (2009)[50] USA, 1997-2007 Retrospective	Outcome of blunt s-TBI patients with GCS=3.	N=189 GCS3: 100% Surgery: 110 Died: 93	83	36.5	Presentation	BRP: 1: 41% 2: 12.9% BFDP: 1: 14.6% 2: 59.1%
Chieregato(2017)[51] Italy, 1997-2012 Retrospective	Outcome of medical management in ASDH after craniotomy.	N=115 All ASDH GCS3-4: 100%	67	34	Presentation	BFDP 100%
Weisbrod (2012)[59] USA, 2003-2011 Prospective data	Outcomes of combat casualties sustaining penetrating TBI.	N=137 GCS3-5: 31 Gunshot: 31% Blast: 69%	98	25	Admission	NP

Table III: Abbreviations: ♂: Male; ASDH: Acute Subdural Hematoma; BFDP: Bilateral Fixed Dilated Pupils; BRP: Bilateral Reactive Pupils; CC: Cerebral Contusion; DC: Decompressive Craniectomy; FIM: Functional Independence Measure; GCS: Glasgow Coma Scale; GOS: Glasgow Outcome Scale; HC: Haemorrhagic Contusion; ICP: Intracranial Pressure; LTFU: Loss to Follow Up; NP: Not Provided; PVS: Persistent Vegetative State; s-TBI: severe Traumatic Brain Injury; TBI: Traumatic Brain Injury; TSAH: Traumatic Subarachnoid Haemorrhage.

Tabel IV Elderly Patients

Study Information	Purpose	Population	♂	Age	Type of GCS score	Pupils
Shimoda (2014)[18] Japan, 1998-2011 Retrospective	Benefit of surgery in the elderly after TBI.	N=888 GCS3-5: 421	61	±76	Admission	NP
Brazinova(2010)[20] Europe, 2001-2005 Prospective	Outcome in elderly TBI patients with GCS3-4.	N=100 GCS3:71 GCS4:29	71	±74	Initial	NP
Wan (2016)[52] China, 2008-2014 Retrospective	Outcome of surgery in severe intracranial hematoma.	N=112 GCS3-5: 40	±72	±74	Emergency department arrival	Abnormal: Overall:59 Surgery:38
De Bonis (2011)[53] Italy, 2002-2009 Retrospective	Patient outcome and predictors of survival in TBI and DC.	N=44 GCS3-5: 22	59	76.7	Post-resuscitation	NP
Benedetto(2017)[54] Italy, 2011-2014 Retrospective	Outcome after surgery for traumatic ASDH.	N=67 GCS3-5: 17 ASDH: 67	53	80.5	Admission	NP

Table IV: Abbreviations: ♂: Male; ASDH: Acute Subdural Hematoma; DC: Decompressive Craniectomy; GCS: Glasgow Coma Scale; GOS: Glasgow Outcome Scale; ICP: Intracranial Pressure; ICU: Intensive Care Unit; NP: Not provided; TBI: Traumatic Brain Injury

Surgical intervention.	Outcome measure	Results
Evacuation ASDH: 72 Evacuation ASDH+DC:12 Surgery EDH: 5	Mortality/ GOS (6M). LTFU: 7.4%	**Overall mortality**: 49.2% **Good functional outcome (GOS1+2)**: 13.2% **Mortality**: BFDP: 79.9%, BRP: 23.5%, evacuation ASDH: 48.3%, ASDH + DC: 50%, EDH 20% **Outcome survivors (N=96):** GOS1: 22%, GOS2: 8.5%, GOS3: 42.7%, GOS4: 26.8%.
Emergent hematoma evacuation: 53 Pre-operative medical therapy -> Aggressive: 13.2%, Reinforced: 45.3%	GOS (1Y)	**Not operated** (N=62): Mortality: 100% **Surgery**: Mortality: 75.5%, GOS2: 7.5%, GOS3: 13.2%, GOS4: 1.9%, GOS5: 1.9%.
ICP: 80%, Craniotomy: 8%, Craniectomy: 79% -Unilateral 65% -Bilateral: 14%	Mortality/ GOS (6M, 12M, 24M)	**Mortality initial admission:** 5.8% **Including delayed mortality (24M):** 7.3% **Functional independence (GOS≥4) at 24M:** Overall: 68% GCS3-5: 32% GCS6-8: 63% GCS9-11: 74% GCS12-15: 100% **GCS3-5:** Significant improvement at 2 years from discharge

Surgical intervention.	Outcome measure	Results
Surgery: 478 <4h: 92	Mortality(6M)/ GOS(6M)	**Overall mortality:** 71% **Unfavorable** (GOS1-3): 87% **Mortality**: Surgery: 62%. No surgery: 81% (P<0.001) **Unfavorable**: Surgery: 82%. No surgery: 93% (P<0.001) **Surgical group**: GCS3-5: GOS1: 87%. GOS1-3: 96%, GCS6-15: GOS1: 57%, GOS1-3: 79%, both (P<0.001)
Surgery: GCS3: 55 GCS4: 15 ICP monitoring: GCS3: 36 GCS4: 5	Mortality/ GOS(12M)	**ICU-Mortality**:76%. **ICU-Outcome**: 11% favorable (GOS4-5) **Mortality(12M)**: 80%. **Outcome (12M):** 11% favorable.
Surgery: 62.5% -Craniotomy:10 -DC: 60 GCS3-5: 25 surgery	Mortality (6M)/ favorable (6M)	**All Mortality:** 53.6%, **Favorable (GOS4-5):** 68.8%, **Mortality**: GCS≤5: 77.5%, GCS>5: 40%, **Favorable:** GCS≤5: 5%, GCS>5: 46% **Mortality (surgery):** 32.9%, **favorable:** 47.1% **Mortality (conservative):** 88.1%, **favorable:** 4.8%
DC: No focal lesion:11 Focal lesion+ brain oedema: 33	Mortality/ GOS (ICU/hospital discharge, 12-102M)	**Overall mortality:** ICU 48%, Hospital 57%, 1Y and last follow up: 77%. **Bad outcome (GOS1-3):** Hospital discharge and 1Y: 82%. **Mortality:** GCS3-5: 100% **Good outcome (GOS4-5):** GCS6-8=20%, GCS>8 = 50%.
Hematoma evacuation: 67 Second craniotomy: 5	Mortality (6M)/ GOS (1M/6M)	**Overall mortality (1M)**: 55.1%, **(6M):** 67.2% **Mortality (6M)**: GCS3–4: 82.4%, GCS14-15: 14.3% **Functional recovery (6M)**: GCS3–4: 5.9%, GCS14-15: 42.9%

Pediatric patients

Four studies contained pediatric patients, with one using prospectively collected data (Table V).[55-58]

Brain Trauma Foundation (BTF) Guideline adherence for ICP monitoring in the pediatric cohort was low. Close to 8% of patients meeting criteria was actually monitored and monitoring only showed mortality reduction in patients with a GCS of 3 (OR0.64, 95% CI 0.43-1.00).[57] ICP-monitoring was related to significant longer ICU and hospital LOS (12.6 *vs*. 6.3 and 21.0 *vs*. 10.4 days) and higher costs.[57]

Although unfavorable outcome (up to 71.6%) and mortality rates were high (range 36-56.7%), favorable outcome was achieved in 40% to 45% of the patients.[55, 56, 58] In patients with postresuscitation GCS Score 3 and 4; one-year survival was 43.3%, of which almost 12% was normal in every respect and 3% scored GOS=5.[55]

One article mentioned GCS ≤5 to be a significant predictor for poor outcome.[56] Another stated that compared to the GCS 4 patient group, patients with a GCS=3 showed significantly more hypoxia (65.9% *vs*. 39.1%), single seizure (2.3% *vs*. 17.4%) and open cisterns on CT scan (68.2% *vs*. 91.3%) but did not find a statistically significant difference in survival or outcome (P=0.2).[55]

A normal pupillary reaction resulted in 87% chance of survival, which dropped to 23% when at least one eye was abnormal. Pupillary abnormalities resulted in 1-year poor outcome (GOS 1-3) in 92% of cases and 0% good outcome (GOS ≥4) for the combination of absent pupillary reflex and hypothermia. Pupillary response was considered the factor most predictive of both survival and outcome.[55]

Other negatively correlated factors for survival seemed to be a delayed presentation >150 minutes (P=0.010), DC >4 h after hospital arrival (P=0.042), intraoperative blood loss >300 mL (P=0.001) and mechanism of injury (abuse), hypothermia, hypotension, major concurrent symptoms, midline shift on CT scan, and assessment of the fontanelle.[55, 56]

Penetrating brain injury

Three articles in our vs-TBI article selection focussed on PBI.[48, 49, 59] In case of PBI by a firearm projectile, admission GCS of 3-5 resulted in a poor prognosis (GOS 1-3) in up to 94.11%.[49] A second article, investigating gunshot wounds to the head, presents a mortality rate of 65% for all patients and 98.5% for patients with admission GCS 3-5.[48] After surgery, mortality rates dropped to 92.5%, but all survivors were in persistent vegetative state.[48] In contrast to these dramatic results, one study showed 2-year functional outcome (GOS 4-5) in 66% of all patients and in 32% of patients with admission GCS 3-5.[59]

PBI occurs both in military and civilian setting (Table VI). In the context of civilian population, PBI is mainly caused by gunshot wounds, either self-inflicted or caused by (mass) violence. In combat situations, TBI is most commonly caused by improvised explosive devices (IEDs), but also by artillery, rocket and mortar shells, mines or booby traps, aerial bombs and rocket-propelled grenades.[60]

Emergency management in patients with PBI should include aggressive resuscitation like described in the ATLS guidelines, since it appears to be associated with significant improvement of survival.[61, 62] Initial mortality after gunshot wounds is high, with one study reporting a prehospital mortality rate of 76% in a civilian PBI population.[63] If patients reach the hospital and survive initial resuscitation and stabilization, a head CT scan provides information on bullet trajectory, missile fragments, bony destruction and brain damage, including (hemorrhagic) mass lesions. Hemorrhagic contusion and intraventricular bleeding are the most common CT finding.[63, 64]

The surgical management for PBI differs in many aspects from that of closed TBI. PBI represents an open and contaminated type of brain injury, for which prophylactic broad spectrum antibiotics is common practice.[65] Surgical management in PBI consequently should include the prevention of infection [66] and treatment of CSF fistulas.[67-69] Principles of wound debridement have evolved under influence of experience in military settings from extensive debridement with repeated removal of retained fragments to more limited procedures. During the Second World War and Vietnam war, it was disproven that retained bone fragments were linked to the development of brain abcesses.[67, 70-73] Moreover, studies have revealed significant morbidity and mortality associated with repeated and aggressive surgery to remove retained fragments.[74-77] During the Israeli-Lebanese and Croatian conflicts, rapid evacuation and improved medical care, including use of CT-scanning, was broadly available, which led to a less aggressive surgical approach to preserve brain tissue.[78, 79]

Tabel V Pediatric Patients

Study Information	Purpose	Population	♂	Age	Type of GCS score	Pupils
Fulkerson (2015)[55] USA, 1988-2004 Prospective	Clinical outcome in children with TBI.	N=67 1: GCS3:44 2: GCS4:23	60	1: 49,8M 2: 66.9M	Post-resuscitation (Modified for pediatric)	Asymmetry: 1: 20.4% 2: 13.0%
Khan (2014)[56] Pakistan, 2000-2010 Retrospective	Risk factors in pediatric patients with DC.	N=25 GCS3-5:11 BE 80% ASDH 24%	84	6	Presentation	Anisocoria: 24%
Alkhoury (2014)[57] USA, 2001-2006 Retrospective	Effect of ICP monitoring on survival in s-TBI.	N=4141 GCS3: 1942 GCS4: 167 GCS5: 169	62	±8.6	Emergency department	NP
Guresir (2012)[58] Germany, 2000-2009 Retrospective	Outcome of DC for sustained high ICP.	N=34 DC for TBI: 23 (67.7%)	60	12	Admission	Normal=6 UDP=7 BDP=10

Table V: Abbreviations: ♂: Male; ASDH: Acute Subdural Hematoma; BDP: Bilateral Dilated Pupils; BE: Brain Edema; DBS: Diffuse Brain Swelling; DC: Decompressive Craniectomy; EVD: Extraventricular Drain; GCS: Glasgow Coma Scale; GOS: Glasgow Outcome Scale; ICP: Intracranial Pressure; mRS: modified Rankin Scale; NP: Not provided; R-ICH: Refractory Intracranial Hypertension; s-TBI: severe Traumatic Brain Injury; TBI: Traumatic Brain Injury; UDP: Unilateral dilated pupil.

Table VI: Differences Civilian & Military patients suffering PBI

	Civilian	Military
Age	All	Young, healthy
Cause	GSW – near contact injury	Explosion; low-velocity shell/shrapnel injury
Mechanism	(self-)assault	Mainly explosive blasts
Time to hospital	30-45 minutes	Up to 2,5 hours
Protection	None	Body armor and helmets
GCS	lower	higher
Mortality	19-88%	5-30%

Table VI: Abbreviations: GSW: gunshot wounds; GCS: Glasgow Coma Scale

Over the past decades multiple studies have been published suggesting a less aggressive approach, with an important adjuvant role for antibiotics.[77, 80-82] However, more recently, Charry *et al.* suggested that early DC as a damage control procedure in civilian patients suffering PBI in a hospital setting with limited resources on ICU neuro-monitoring is a treatment option to improve survival and outcome in these patients.[83] Rapid exploration and exenteration of the injured air sinuses is recommended to prevent infectious complications [84,85]. CSF fistulas pose a very high risk for deep infections [67, 69, 78] with nosocomial organisms and should be closed watertight, and if needed with placement of lumbar drainage.[82]

Surgical intervention	Outcome measure	Results
Surgery: 1: 55% 2: 87% ICP/EVD: 1: 55% 2: 78%	Modified GOS (long term: mean 10.2Y)	**Discharge:** Overall mortality: 55.2%, GCS3: GOS1: 61.4%, GOS2: 6.8%, GOS3: 11.4%, GOS4: 15.9%, GOS5: 4.6% GCS4: GOS1: 43.5%, GOS2: 17.4%, GOS3: 17.4%, GOS4: 13.0%, GOS5: 4.6% **1 year (N=29):** GOS1: 56.7, GOS2: 4.5%, GOS3: 10.4%, GOS4: 6.0%, GOS5: 3.0%, "Normal": 11.9%, Unknown: 7.5%. **Long term (N=22):** 45% GOS5 or "normal".
DC: 9 DBS, 15 mass lesions + DBS, 1 R-ICH. Bilateral: 7	GOS (5M)	**Overall mortality** 36%. GOS5: 40% GCS≤5 significant predictor for poor outcome (GOS1-3), (Univariate analysis p=0.009)
ICP: 318 -GCS3-5: 224	Mortality	**Mortality** ICP (GCS3): OR0.64; 95%CI, 0.43-1.00. No effect on mortality for other GCS groups.
DC	mRS (6M)	Only TBI data used: **Favorable (mRS0-2)**: 40% *We didn't include additional review data.

DISCUSSION

This literature review shows that mortality rate in vs-TBI patients is high and the chance to reach good outcome low. Moreover good outcome is defined quite heterogeneously. Interestingly however, in some studies low mortality and relatively good outcome rates were reported for specific patient groups. It is difficult to point out exactly what contributed to this better outcome in these patients. Good outcome seemed to be associated with factors that are known to have a positive effect such as higher GCS (at least >5), absence of pupillary abnormalities and lower age (<65 year). Factors, which might have contributed were immediate and accurate treatment. However, because comparison of studies showed huge heterogeneity, correlations between the factors mentioned above and outcome could not be determined. Nevertheless, we strongly suggest that, given the chance for successful recovery, surgical intervention should be considered in every very severe TBI patient.

Importantly, treatment-limiting decisions should not be based on the GCS alone. Although a recent review showed adequate reliability of the GCS Score, the use and general applicability has been widely criticized.[86] In our review, outcome results are probably more favorable because of the exclusion of patients with a "true" GCS of 3 and inclusion of patients with a "false" GCS of 3 as a result of intubation and sedation.

Indeed, better survival rates were reported in patients with a "false" compared to a "true" GCS of 3 (61% *vs*. 45%).[44]

Decisions on treatment intensity and in particular withholding and withdrawal of life-sustaining therapies will clearly affect outcome and mortality rates. A random selection of Canadian TBI patients showed that 70% of all deaths were associated with withdrawal of therapy, half within the first three days.[87] In Oslo, 17% of s-TBI patients had treatment limiting decisions, of which the majority (70%) was made within the first 2 days after injury. In 93% of in-hospital deaths, treatment limiting decisions were documented.[88] Worryingly, around 80% of physicians felt at best uncomfortable with withdrawal of care decisions and there were major differences among them regarding neuro prognostication and decision-making.[89] By early withholding/withdrawal, no chance of recovery is offered. The short term of the decision is worrying, given that although the majority (71.4%) of TBI patients with a favorable outcome followed commands (GCS motor score=6) within 1 week, almost 15% regained that ability for the first time from two weeks after injury.

Premature and inappropriate treatment limiting decisions are of particular concern in the elderly. Elderly vs-TBI patients showed higher mortality (80%, 82%, 100%),[20, 53, 54] compared to the whole s-TBI group (53.6-77%).[52, 53] In literature a mortality of 78.5% in elderly s-TBI patients was reported, compared to >80% in vs-TBI patients (GCS 3-5) and 92.6% for patients aged>80 years.[90] Understandably, high mortality rates contribute to the overall belief that aggressive treatment in the elderly population is not effective. A decrease of treatment intensity can have accompanying negative influence on outcome, forming self-fulfilling prophecies.[91, 92] Despite the reported high mortality rates, two studies showed that realizing good outcome in elderly vs-TBI survivors was not impossible (5.9-11%).[20, 54] Although severity according to the GCS was lower, a recent meta-analysis reported a similar percentage of 7.9% for elderly s-TBI patients.[93]

Although surgical intervention can reduce mortality and unfavorable outcome rates, not all studies agree on justifying intervention for vs-TBI patients.[18, 52] Guidance from evidence is lacking, as patients aged ≥65 years are not included in most clinical studies and not in the BTF Guidelines, resulting in absence of guidance, subjective critical care and thus treatment variation. This is of increasing concern because TBI is increasing in the elderly population (>65 years old) [2, 94] and because elderly patients often necessitate a different approach. Specific features include mostly a low energy mechanism of trauma (fall), the frequent occurrence of contusions and (sub)acute subdural hematomas, the use of anticoagulants, but also the presence of some degree of brain atrophy that may allow for more volume compensation. Conversely, however, the lack of cognitive reserve may adversely affect outcome.

Future research is needed to identify specific (subgroups of) patients in whom aggressive surgical intervention will result in good outcome, preferably with a certainty that can be useful in multidisciplinary decision-making. Until that time, physicians should not withhold aggressive treatment options in s-TBI patients, young or old, who have some potential of achieving good outcome even with ominous neurological signs. A more reserved attitude regarding aggressive therapy may be justified in patients in whom a combination of different features indicate very low chances of regaining an acceptable quality of life and no signs of any improvement exist following initial optimal therapy.

ICP monitor

We found no consensus of benefit on mortality rates from ICP monitoring because all three possible outcomes were reported: reduced mortality,[21, 24] no difference and higher mortality.[25] The same inconclusiveness was found in a recent review and meta-analysis[95] and other studies reporting both benefit,[96, 97] and no benefit.[98, 99]

Both the sickest and least sick patients appear to receive less ICP monitor placement [22, 100] and ICP monitoring placement seemed to be influenced by high age,[21-23] which reflects a tendency towards overall lower intensity of care in elderly TBI patients.[92]

The reported lower mortality rates for vs-TBI patients compared to s-TBI patients, can be explained by a decreased advantage of ICP monitoring guided therapy for less severe TBI patients with ongoing, potentially disadvantageous, exposure to intensive therapies.[25] ICP monitoring guided therapy was associated with increased mortality for GCS 7-8 patients (OR12.89) [27] and had a larger protective impact on patients with GCS=3.[23, 57] Included studies showed ICP monitored patients with longer duration of mechanical ventilation,[25-27] higher need for tracheostomy [27] and significantly longer ICU stays.[22, 25-27, 57] These results were confirmed by literature [95, 98] and are likely to influence outcome.

Insertion of ICP monitor would appear to be based on physicians' judgement, rather than guidelines, possibly inducing confounding by indication. More severely injured patients are more likely to receive ICP monitoring guided care, but, because being in a worse condition they are prone for worse outcome. Also, patients can be considered to be unsalvageable and because of withholding aggressive therapy (including ICP monitoring), only the patients with an expected chance of survival get a chance, resulting in better outcome in ICP monitored cohorts.

Lack of adherence to guidelines has been previously reported in various studies. A recent study [101] reported major variation in adherence between studies (range 18-100%), with only 31% for the BTF ICP monitoring guidelines, possibly caused by scepticism resulting from the absence of high quality evidence and the invasive character of the intervention.[101] Substantial variation in ICP monitoring indications and subsequent treatment decisions is also reported.[101, 102] We expected high rates of ICP monitoring in included s-TBI cohorts, but found an unweighted mean of 42%. Two studies found poor adherence rates (10.8% and 46% in two studies), corresponding with the literature.[23, 25, 26] Investigating the effect of adherence on survival, literature delivers non-conclusive evidence of benefit,[96] no benefit [99] and even an increase in complications and use of hospital resources.[103]

The relative lack of guideline adherence for ICP monitoring for patients with vs-TBI may also reflect the lack of specific recommendations for this group. International TBI guidelines from BTF and NICE organizations are largely based on best available level III evidence and use GCS 3-8 as s-TBI category.[104, 105] In the BTF-Guidelines the vs-TBI subgroup is separately mentioned only three times and are considered to be part of the GCS 3-8 s-TBI group.[104] There is no mentioning of the GCS 3-5 subgroup in the 2nd edition of the BTF Guidelines for the Acute Medical Management of s-TBI in Infants, Children, and Adolescents.[106] Recent studies conclude both absence of benefit [107] as higher survival and improved outcome, without higher hospital costs following guidelines.[108, 109]

We suggest that therapy guided by ICP monitoring following the guideline recommendations should also be used in vs-TBI patients, since positive effects and good outcome are reported. Because worse results are most likely due to complications, ICP monitoring devices should be removed as soon as possible, hopefully avoiding adverse effects of overtreatment.

Decompressive craniectomy
Although it is clear that DC can decrease ICP effectively and good outcome is reported,[110] its value remains controversial.[9-11, 111]

Mortality rates for s-TBI patients after DC range between 11% and 68.5%,[30, 31] up to 80% for vs-TBI patients [32, 33] and even 100% for patients with a GCS of 3.[30, 34] The overall mortality rate difference is most likely the result of different patient samples, with variation in variables associated with worse prognosis. The cohort with 68.5% mortality rate contained more older patients with GCS=3 and bilaterally dilated pupils (50 *vs*. 42.8 years). The study with 11% mortality (60% vs-TBI), provided no information on pupillary status or potential "false" GCS. The potential beneficial effect of early surgery (<1hour after admission) in 85.9% of patients, remains uncertain. A low mortality rate is not necessarily a good result, since it can be related to a high percentage (37% in GCS 3-5 and 7% in GCS 6-8) of patients remaining in a vegetative state.[15] Since certain traumatic lesions result in worse outcome, by nature of the injury, composition of cohorts regarding traumatic lesions is likely to contribute to confounding by indication and outcome results. One study confirmed this by showing less mortality in s-TBI patients with mass lesion receiving DC compared to DC for diffuse injury and swelling (14 *vs*. 43.4%).[40]

Factors related to timing of surgery and surgical technique may be relevant to outcome. Two studies studied timing of DC and the first found better results for performing early DC within 4 hours,[30] while the second found that early bilateral DC showed better results compared to DC as secondary treatment option.[39] Two others mentioned early DC to be related to better outcome, one only for GCS 6-8 subgroup.[15, 41] Although many physicians will agree with early timing of surgery, a review found that timing of surgery was not significantly related to outcome in 11 out of 16 included studies. Looking at DC studies, 4 out of nine reported a significant effect of time to surgery on patient outcome.[112] As is also recommended in the BTF-Guideline, a large sized bone flap resulted in significantly more satisfactory outcome (GOS 3-5), especially in vs-TBI subgroup (63.0% *vs*. 36.7%, P<0.01).[35] Thus, according to the present evidence, in cases in which decompressive surgery is decided upon, bone flaps should be made large.

We suggest a certain restraint against the early withholding and withdrawal of therapy, especially because prognostication is still inaccurate and decision can result in potentially avoidable deaths. After the (sub) acute setting, additional treatment decisions depending on neurological improvement should be made, preferably after proxy consultation.

Penetrating brain injury

The difference between combat and civilian PBI can explain outcome results. Combat casualties include more blast injury and civilian more gunshot wounds. Also, almost 90% of patients (mean age 25 years) underwent neurosurgical intervention. The combination of young healthy military patients with aggressive neurosurgical intervention might be beneficial. However, in the study reporting favorable results there is 43% loss to follow-up and only 22% of total PBI patients were treated at this institution. In the literature, PBI mortality rates range from 23 to 93% with higher rates (87-100%) in presence of well-known risk factors for poor outcome: GCS <5, pupillary abnormalities, hypotension, high ICP and higher age.[113]

As in all TBI patients, surgical treatment should be meaningful and the indication for surgery balanced against the likelihood of survival, particularly in patients with a low GCS in the civilian setting. Some authors don't recommend surgical intervention in patients with small to zero change of achieving favorable outcome,[48, 49] low admission GCS scores and extensive brain injury [114, 115] or patients with a GCS 3 to 5 without operable hematomas.[61] Nevertheless, it does not preclude possible recovery and some patients may survive. A recent study for example, reported a survival rate of 40% in patients with a GCS of 3-4 on admission, whilst 11% achieved favorable outcome.[116] These investigators attribute their better results to a more aggressive management policy.

We believe that clinical (GCS Score and presence of pupillary abnormalities) and radiological signs should guide physicians decision-making. We advocate minimal surgery in civilian PBI cases with a GCS of 3-5 and optimal medical management for at least 24 hours. In case of improvement, more extensive surgery can be considered. An early decompressive craniectomy with watertight dural closure is a valid surgical option. The removal of retained bone fragments at the cost of healthy brain tissue is not advised and in case of dural defects grafting is possible by using autologous materials like fascia lata or periosteum. Finally, the adequate cranialization of violated air sinuses and the watertight closure of CSF fistulas should be performed as soon as possible.

Limitations of the study

Our strict inclusion criteria resulted in the inclusion of studies reporting on surgical treatment and outcome of vs-TBI patients with a definite GCS 3-5. Most included studies were relatively small observational single center cohort studies and only few used prospectively collected data. As is typical for TBI itself, the huge heterogeneity between patient cohorts regarding injury, treatment and outcome, resulted in inevitable selection bias and makes comparing results and drawing conclusions difficult. For this reason, it was considered impossible to conduct a solid meta-analysis. The independent effect of surgical treatment on outcome is also hard to establish because parameters known to be associated with outcome, were often not mentioned or investigated. Results of this review should be interpreted with care and conclusion only drawn with the recognition of the remarks.

Three promising studies (DECRA, RESCUEicp, STITCH) from the past years did not meet our inclusion criteria but unfortunately also didn't change the controversy of decompressive craniectomy.[117-119] We are looking forward to the results of two ongoing trials, respectively comparing primary DC with craniotomy in adults with an ASDH (RESCUE-ASDH: www.rescueasdh.org) and investigating the effect of therapeutic and prophylactic DC in s-TBI patients with mass lesions (PRECIS).[120]

Future research

Given the current heterogeneity and variability, future research should focus on patient cohorts, (surgical) treatments and outcome measures that are as equal as possible, to improve comparability and generalizability of study results. Alternatively, variability can also contribute to investigating the effectiveness of (surgical) treatment by comparing variation in local practice using a method called "Comparative Effectiveness Research" (CER). International initiatives like CENTER-TBI (www.center-tbi.eu), and a Dutch initiative called Net-QuRe (www.net-qure.nl) are using this method investigating (surgical) treatment effectiveness. Because postdischarge information is considered very important, Net-Qure has a 24 month follow-up period and includes data on the rehabilitation phase. Knowing how much a specific patient will benefit from which specific treatment in terms of functional recovery and quality of life is essential in future decision-making and informed consent conversations. Therefore a long-term follow-up period is necessary and particularly relevant to patients with vs-TBI, as reports show that improvement may not be uncommon between 1 and 3 years after injury.

In addition, a humanistic approach on the quality of life after TBI is needed to explore what can be considered a favorable and desirable outcome for patients, their proxies and for society as a whole. Also, an accurate calculation of hospital and postdischarge healthcare costs following TBI must be undertaken, to improve hospital and public management planning and allocation of appropriate budgets.

Finally, we believe that the currently used s-TBI category remains very heterogeneous. Future research should aim for better characterization and understanding of individual pathophysiology, and identification of subgroups of patients more likely to benefit from specific therapies. Both could hopefully inform more targeted treatment according to specific patient needs.

CONCLUSIONS

The most severely injured TBI patients including patients with penetrating brain injury, frequently confront physicians with great medical and ethical conflicts. This literature review reports that although mortality rates are high and unfavorable outcome is frequent, good outcome is possible for patients with very severe TBI. Multiple different patient and injury specific factors, combined with treatment timing and type of intervention, showed to be related to intervention and outcome. Most important are age, GCS and pupillary abnormalities. Clearly, vs-TBI patients are different from the less severe TBI patients (GCS 6-8) and therefore should be recognized and treated as such. Until the availability of solid evidence, physicians must find an equilibrium between falsely withholding surgical intervention from patients with potential good outcome and aggressive treatment with an inevitable unwanted outcome.

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