Table SI. GCS.

Group	Severity	GCS
1	Mild	13-15
2	Moderate	9-12
3	Severe	< 9

The GCS receives values between 3 and 15, with the literature associating higher scores with a better prognosis (1). According to the admission GCS, three categories were used to classify injury severity (2,3). During statistical analysis, GCS scores were binarized as follows: Mild and moderate (GCS 9-15) and severe (GCS <9). GCS, Glasgow Coma Scale.

Table SII. Summary of studies on IL-6 in animals with TBI.

Significance	Increased levels after TBI or higher than controls	Increased after weight drop	Increased after controlled cortical impact	Increased after fluid percussion injury	Increase after blast injury	Histological findings	Outcome
Significant effect	Yang *et al*, 2013 (4) Chatzipanteli *et al*, 2012 (5) Holmin *et al*, 1997 (6) Rhodes *et al*, 2002 (7) Stover *et al*, 2003 (8) Stover *et al*, 2000 (9) Gao *et al*, 2017 (10) Li *et al*, 2019 (11) Bai *et al*, 2017 (12) Jia *et al*, 2012 (13) Yang *et al*, 2013 (14)	Yang *et al*, 2013 (4) Holmin *et al*, 1997 (6) Rhodes *et al*, 2002 (7) Bai *et al*, 2017 (12) Jia *et al*, 2012 (13)	Stover *et al*, 2003 (8) Stover *et al*, 2000 (9) Gao *et al*, 2017 (10) Yang *et al*, 2013 (14)	Chatzipanteli *et al*, 2012 (5)	Li *et al*, 2019 (11)	Li *et al*, 2019 (11) Swartz *et al*, 2001 (15)	Yang *et al*, 2013 (4) Ley *et al*, 2011 (16) Ley *et al*, 2012 (17)

No statistical significance						Stahel *et al*, 2000 (18)	Stahel *et al*, 2000 (18) Marklund *et al*, 2005 (19)
Notes	IL-6 levels in plasma and cerebrospinal fluid or expression of IL-6 in cell cultures.					BBB disturbances (Stahel *et al*, 2000) (18), PMN accumulation (Stahel *et al*, 2000) (18), tissue repair (Swartz *et al*, 2001) (15), neurodegeneration (Li *et al*, 2019) (11)	Outcome was assessed by mortality and performance on cognitive tests

Table SIII. Summary of studies on IL-6 in human TBI populations.

Significance	Increased in TBI vs control	GCS on admission	ICP	BBB disturbances	Radiology findings	Complications	Other biomarkers	Outcome
Significant effect	Rodney *et al*, 2020 (20) Bell *et al*, 1997 (21) Kossmann *et al*, 1996 (22) Ondruschka *et al*, 2018 (23) Thompson *et al*, 2020 (24) Bell *et al*, 1997 (25) Liao *et al*, 2013 (26) Hergenroeder *et al*, 2010 (27) Terrell *et al*, 2018 (28) Me *et al*, 2022 (29) Gill *et al*, 2017 (30) Hayakata *et al*, 2004 (31) Ravi *et al*, 2022 (32) Meier *et al*, 2022 (33) Edwards *et al*, 2020 (34) Berger *et al*, 2009 (35) Yang *et al*, 2017 (36)	Yang *et al*, 2017 (36) He *et al*, 2009 (40) Chiaretti *et al*, 2005 (41)	Hergenroeder *et al*, 2010 (27) Shore *et al*, 2004 (42)	Vajtr *et al*, 2009 (43)	Vajtr *et al*, 2009 (43) Mellergård *et al*, 2011 (44) Pleines *et al*, 2001 (45) Singhal *et al*, 2002 (46)	Lustenberger *et al*, 2016 (37) Aisiku *et al*, 2016 (47) Lenski *et al*, 2019 (48) Choudhary *et al*, 2021 (49) Woiciechowsky *et al*, 2002(50)	Kossmann *et al*, 1996 (22) Pleines *et al*, 2001 (45)	Chiaretti *et al*, 2005 (41) Chiaretti *et al*, 2008 (51) Aisiku *et al*, 2016 (47) Woiciechowsky *et al*, 2002 (50) Davidson *et al*, 2015 (52) Peltz *et al*, 2020 (53) Winter *et al*, 2004 (54) Nwachuku *et al*, 2016 (55) Feng *et al*, 2018 (56) Ferreira *et al*, 2014 (57) Lewis *et al*, 2019 (58) Kumar *et al*, 2015 (59) Raheja *et al*, 2016 (60) Zwirner *et al*, 2021 (61)

	Lustenberger *et al*, 2016 (37) Meier *et al*, 2020 (38) McKeating *et al*, 1997 (39)							
No statistical significance	Edwards *et al*, 2020(34) Di Battista *et al*, 2020(62)	Hayakata *et al*, 2004(31) Park and Hwang, 2018(63) Chiaretti *et al*, 2008(51)	Hergenroeder *et al*, 2010(27) Hayakata *et al*, 2004(31)	Maier *et al*, 2001(64)				Hayakata *et al*, 2004(31) Park and Hwang, 2018(63) Crichton *et al*, 2021(65)
Notes			Association between IL-6 and ICP in patients with isolated TBI but not in polytrauma patients with TBI (Hergenroeder *et al*, 2010)(27)		Expansion of lesions (Vajtr *et al*, 2009)(43) (Pleines *et al*, 2001)(45) (Singhal *et al*, 2002)(46) , subarachnoid haemorrhage (Mellergård *et al*, 2011)(44)	ARDS (Aisiku *et al*, 2016)(47), Infection (Woiciechowsky *et al*, 2002)(50), Ventriculitis(Lenski *et al*, 2019)(48), Epilepsy (Choudhary *et al*, 2021)(49), Sepsis (Lustenberger *et al*, 2016)(37), Multiorgan Failure (Lustenberger *et al*, 2016)(37)	NGF (Kossmann *et al*, 1996)(22), S100B, NSE (Pleines *et al*, 2001)(45)	Outcome assessed by mortality, GOS, GOS – E

Table SIV. Studies on IL-8 in human populations suffering from TBI.

Significance	Concentration differences in TBI vs control	GCS on admission	ICP	BBB disturbances	Radiology findings	Complications	Other biomarkers	Outcome
Significant effect	Rowland *et al*, 2020(66) Chaban *et al*, 2020(67) Whalen *et al*, 2000(68)	He *et al*, 2009(40)	Stein *et al*, 2012(69)	Kossmann *et al*, 1997(70)	Chaban *et al*, 2020(67)	Aisiku *et al*, 2016(47)	Kossmann *et al*, 1997(70)	Mussack *et al*, 2002(71) Gopcevic *et al*, 2007(72) Crichton *et al*, 2021(65) Ferreira *et al*, 2014(57) Yang *et al*, 2022(73) Nwachuku *et al*, 2016(55) Kushi *et al*, 2003(74)
No statistical significance	Mussack *et al*, 2002(71)	Polat *et al*, 2019(75) Hayakata *et al*, 2004(31)	Perez-Barcena *et al*, 2011(76)	Maier *et al*, 2001(64)	Hayakata *et al*, 2004(31) Rhodes *et al*, 2009(77)		Hayakata *et al*, 2004(31)	Hayakata *et al*, 2004(31) Gopcevic *et al*, 2007(72)

Notes	Size of lesions	ARDS	S100B (Hayakata *et al*, 2004)(31), NGF (Kossmann *et al*, 1997)(70), (Hayakata *et al*, 2004)(31)	Outcome assessed by mortality, GOS, GOS -E One study found association between plasma IL-8 levels with the outcome but no association between CSF IL-8 levels with the outcome (Gopcevic *et al*, 2007)(72)

Table SV. Studies on IL-10 in animals with provoked TBI.

Significance	Concentration increases after TBI or concentration difference with controls	Concentration increases after weight drop	Concentration increases after controlled cortical impact	Concentration increases after fluid percussion injury	Concentration increases after blast injury	Histological findings	Outcome
Statistical Significance	Kamm *et al*, 2006(78)	Kamm *et al*, 2006(78)				Peruzzaro *et al*, 2019(79)	Maiti *et al*, 2019(80) Zhou *et al*, 2014(81) Knoblach and Faden, 1998(82)
No Statistical Significance	Kamm *et al*, 2006(78) Maegele *et al*, 2007(83)	Kamm *et al*, 2006(78)		Maegele *et al*, 2007(83)			
Notes	One study found statistically significant increase of IL-10 in the brain parenchyma but not in the plasma (Kamm *et al*, 2006)(78)					Undamaged tissue	Outcome was assessed by mortality and performance on cognitive tests

Table SVI. Research on IL-10 studied in humans suffering from TBI.

Significance	Concentration differences in TBI vs control	GCS on admission	ICP	BBB disturbances	Radiology findings	Complications	Other biomarkers	Outcome
Statistical Significance	Lagerstedt *et al*, 2018(84) Csuka *et al*, 1999(85) Lagerstedt *et al*., 2018(86) Bell *et a*l, 1997(21)		Shiozaki *et al*, 2005(87)		Lagerstedt *et al*, 2018(86) Shiozaki *et al*, 2005(87)			Bell *et al*, 1997)(21) Lagerstedt *et al*, 2020(88) Posti *et al*, 2020(89) Ferreira *et al*, 2014(57) Vedantam *et al*, 2021(90) Lewis *et al*, 2019(58) Schneider Soares *et al*, 2012(91) Kirchhoff *et al*, 2008(92)
No statistical significance	Koivikko *et al*, 2022(93)		Perez-Barcena *et al*, 2011(76) Müller *et al*, 2001(94)	Csuka *et al*, 1999(85)	Perez-Barcena *et al*, 2011(76)			
Notes					Increased in patients with visible lesions in CT (Lagerstedt *et al*, 2018)(86) and in patients with additional extracranial lesions(Shiozaki *et al*, 2005)(87)			Outcome assessed by mortality, GOS, GOS - E

Table SVII. mGCS.

Group	Severity	mGCS
1	Mild and Moderate	4-6
2	Severe	<4

The mGCS receives values between 1-6, with the literature associating higher scores with an improved prognosis (1). During statistical analysis, mGCS scores were binarized as follows: Mild and moderate (GCS 4-6) and severe (GCS <4). mGCS, motor Component of Glasgow Coma Scale.

Table SVIII. Karnofsky Performance Scale.

Severity	Component
Mild/Moderate	Capable of performing daily tasks and working without the need for special care (80-100) or Unable to work but capable of taking care of the majority of their personal needs while living independently (50-70).
Severe	Unable to look for themselves requiring constant care (0-40).

The Karnofsky Performance Scale was developed in the 1940s to rate quality of life in patients undergoing chemotherapy (95). Currently, it is used as a broad scale to evaluate the patient's functional status on a scale of 0 (poor) to 100 (good) (95). In the present study the KPS was used as a grading scale for the patient's functional status, irrespective of the criteria for hospital admission. Accordingly, it was assessed in all hospitalized patients on the first and seventh post-traumatic days. During statistical analysis, KPS scores were binarised as follows: Mild and Moderate (KPS 50-100) and severe (KPS 0-40).

Table SIX. MRS.

Group	Severity	MRS
1	Favorable	0-3
2	Unfavorable	4-6

The MRS was established to assess the functional status of stroke victims (96). John Rankin designed its first version in 1957, and scientists from the UK-TIA study and Charles Warlow improved it in 1980 (96). It rates patients on a scale of 0 to 6 (dead) depending on their functional status. During statistical analysis, MRS scores were binarized as follows: Favorable (0-3), and unfavorable (4-6). MRS, Modified Rankin Scale.

Table SX. ECOG/WHO score.

Group	Severity	ECOG/WHO
1	Favorable	0-2
2	Unfavorable	3-5

The ECOG/WHO score, which was introduced in the study by Oken *et al* (1982) (97) was utilized to evaluate oncology patients functional status on a scale of 0 to 5 (dead) depending on their functional state. In the present study ECOG/WHO scores were binarized as follows: Favorable (0-2),Unfavorable (3-5). ECOG/WHO, Eastern Cooperative Oncology Group/World Health Organisation.

Table SXI. ISS.

Group	Severity	ISS
1	Mild, Moderate, Severe	1-24
2	Very Severe	>24

The ISS is a complex grading tool for the severity of trauma patient injuries (98). It uses the Abbreviated Injury Scale, which measures the extent of trauma per body location. The three body parts that have sustained the most damage are used to calculate the ISS (99). According to the admission ISS, the following categories were used to classify systematic injury severity: Mild, Moderate and Severe (1-24), or very severe (>24). ISS, Injury Severity Score.

Table SXII. Compression of basal cisterns on the head CT.

Group	Basal Cisterns
1	Normal
2	Partially or fully compressed

Basal cisterns are part of the perimesencephalic cisterns and they typically appear patent. In cases of high intracranial pressure, they may be compressed (100). The following categories were used to classify the compression of basal cisterns: Normal, Partially or fully compressed.

Table SXIII. Midline shift on head CT scan.

Group	Midline Shift (mm)
1	≤5
2	>5

The displacement of midline structures is evaluated on the head CT as an index of subfalcine herniation and a predictor of outcome (100). The following categories were used to classify the presence of midline shift: ≤5 mm, >5mm.

Table SXIV. Volume of hemorrhagic lesions.

Group	Volume
1	≤ 25cc
2	> 25cc

The following categories were used to classify the volume of hemorrhagic lesions: ≤ 25cc, > 25cc.

Table SXV. Imaging CT tools.

Tools	Description
Rotterdam CT Score	The Rotterdam CT Score was published in 2006 and its scoring methodology is based on the findings of TBI patients' admission head CT scans (101). The scoring system takes integer values from 1 to 6 with higher values indicating worse findings (101).
Marshall CT Classification	The Marshall Classification was published in 1992 (102). Throughout the literature, it is regarded as a very significant tool for outcome prediction (103). It classifies patients in 6 categories depending on the findings on the initial head CT (103).
Stockholm CT Score	In order to construct the Stockholm CT Score, researchers collected data from 861 head CT scans of TBI patients (104). First, the tSAH score, then the Tally score, and finally the Probability score are calculated for the computation of the Probability for unfavorable outcome (104). During our statistical analysis Tally score was used.
Helsinki CT Score	The Helsinki CT score was created based on data from 869 head CTs of TBI patients in a single retrospective study using logistic regression (105). The scoring system takes integer values from -3 to 14 with higher values indicating worse findings (105).

Prognostic models	Large datasets with various prognostic markers and external validation have been used to generate the two primary complex predictive models for TBI, the International Mission for Prognosis and Analysis of Clinical Trials (IMPACT) and the Corticosteroid Randomization After Head Injury (CRASH) (106,107). CRASH is a model that estimates 14-day mortality and 6-month mortality risk and severe disability of adult patients with GCS<15 at admission (107).

Table SXVI. GOS.

Group	Severity	GOS
1	Unfavorable outcome	1-3
2	Favorable outcome	4-5

The GOS was introduced in 1975. It is a tool for evaluating TBI outcomes (108,109). It categorizes patients on a scale of 1 to 5 depending on their functional state (108,109). During statistical analysis, GOS scores were divided into 2 categories: Unfavorable outcome (1-3), or favorable outcome (4-5). GOS, Glasgow Outcome Scale.

Table SXVII. GOS-E.

Group	Severity	GOS-E
1	Unfavorable	1-4
2	Favorable	5-8

The GOS-E is a recognized scale for evaluating the disability and level of recovery in TBI patients (108,110) on a scale of 1 to 8. During statistical analysis, GOS-E scores were binarized as follows: Unfavorable outcome [1-4], Favorable outcome [5-8]. GOS-E, Glasgow Outcome Scale-Extended.

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