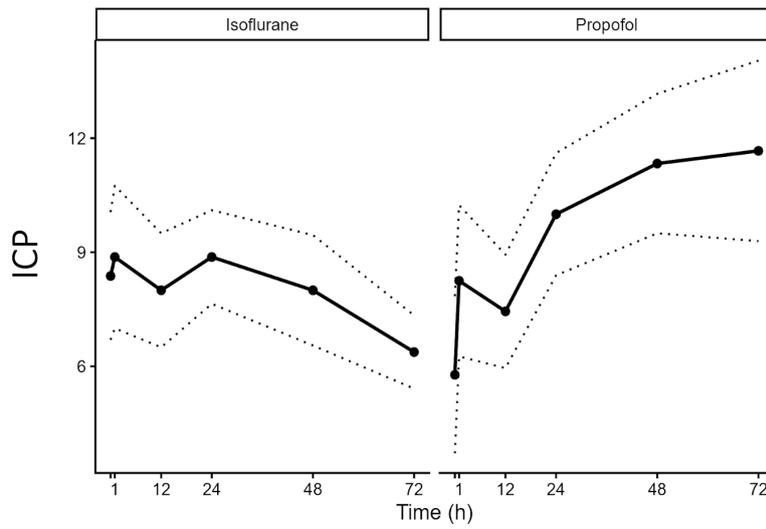
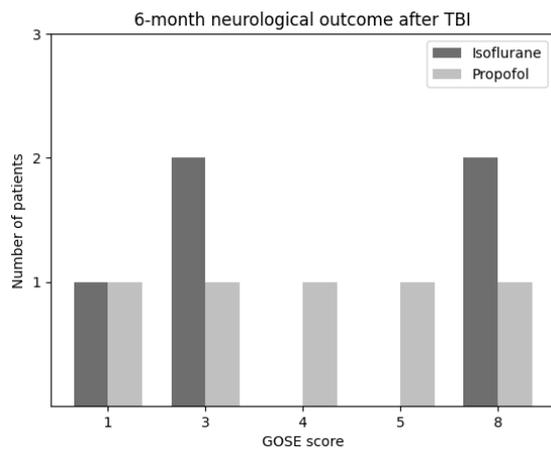


**SUPPLEMENTARY MATERIAL:**



**Supplementary Figure 1.** Evolution of intracranial pressure during the study period in the TBI subgroup. Abbreviations: Intracranial Pressure (ICP).



**Supplementary Figure 2.** GOSE score at 6 months in patients with TBI. Abbreviations: Traumatic Brain Injury (TBI), Glasgow Outcome Scale-Extended (GOSE).

	N=30	Isoflurane N=15	Propofol N=15	p.value
<b>NOL 0h</b>				1.000
<10	17 (73.91%)	9 (75.00%)	8 (72.73%)	
10-25	6 (26.09%)	3 (25.00%)	3 (27.27%)	
<b>NOL 1h</b>				1.000
<10	18 (78.26%)	9 (75.00%)	9 (81.82%)	
10-25	5 (21.74%)	3 (25.00%)	2 (18.18%)	
<b>NOL 12h</b>				0.378
<10	19 (76.00%)	11 (84.62%)	8 (66.67%)	
10-25	6 (24.00%)	2 (15.38%)	4 (33.33%)	
<b>NOL 24h</b>				0.386
<10	17 (70.83%)	9 (81.82%)	8 (61.54%)	
10-25	7 (29.17%)	2 (18.18%)	5 (38.46%)	
<b>NOL 48h</b>				0.820
<10	12 (54.55%)	7 (58.33%)	5 (50.00%)	
>25	1 (4.55%)	1 (8.33%)	0 (0.00%)	
10-25	9 (40.91%)	4 (33.33%)	5 (50.00%)	
<b>NOL 72h</b>				0.311
<10	17 (77.27%)	7 (63.64%)	10 (90.91%)	
10-25	5 (22.73%)	4 (36.36%)	1 (9.09%)	

**Supplementary Table 1.** Objective nociception monitoring. Abbreviations: Nociception Level Index (NOL®).

	N=30	Isoflurane N=15	Propofol N=15	p.value
<b>0h</b>				
rSO2 R (%)	66.28 (12.61)	68.79 (12.19)	63.93 (12.96)	0.308
rSO2 L (%)	63.87 (13.02)	64.93 (10.17)	62.80 (15.67)	0.662
ICP (mmHg)	7.68 (5.23)	7.57 (4.57)	7.79 (5.99)	0.916
CPP (mmHg)	68.57 (10.55)	67.60 (8.58)	69.53 (12.45)	0.625
SV R (cm/s)	112.03 (43.68)	103.27 (26.59)	120.80 (55.50)	0.283
DV R (cm/s)	37.87 (22.43)	33.27 (15.02)	42.47 (27.78)	0.272
CVR R (mmHg/mL/min)	0.661 ± 0.124	0.681 ± 0.122	0.642 ± 0.127	0.393
CBF R (ml/100g/min)	107.48 ± 27.51	102.53 ± 23.22	112.43 ± 31.23	0.334
SV L (cm/s)	112.67 (36.71)	103.80 (33.71)	121.53 (38.56)	0.191
DV L (cm/s)	40.90 (22.64)	36.00 (17.23)	45.80 (26.70)	0.244
CVR L (mmHg/mL/min)	0.661 ± 0.124	0.681 ± 0.122	0.642 ± 0.127	0.393
CBF L (ml/100g/min)	107.5 ± 27.5	102.5 ± 23.2	112.4 ± 31.2	0.334
<b>1h</b>				
rSO2 R (%)	66.96 (13.34)	70.57 (12.97)	63.36 (13.17)	0.156
rSO2 L (%)	63.76 (12.57)	65.67 (9.26)	61.71 (15.46)	0.417
ICP (mmHg)	8.93 (5.13)	8.27 (4.98)	9.69 (5.39)	0.476
CPP (mmHg)	70.30 (8.61)	70.07 (9.21)	70.53 (8.29)	0.885
SV R (cm/s)	119.57 (42.26)	110.40 (29.31)	128.73 (51.58)	0.244
DV R (cm/s)	41.63 (17.44)	38.13 (12.81)	45.13 (20.97)	0.281
CVR R (mmHg/mL/min)	0.646 ± 0.091	0.650 ± 0.087	0.642 ± 0.099	0.816
CBF R (ml/100g/min)	111.51 ± 23.63	110.51 ± 25.74	112.50 ± 22.17	0.822
SV L (cm/s)	121.37 (30.18)	118.20 (22.53)	124.53 (36.84)	0.576
DV L (cm/s)	42.71 (21.01)	40.13 (14.54)	45.29 (26.23)	0.512
CVR L (mmHg/mL/min)	0.646 ± 0.091	0.650 ± 0.087	0.642 ± 0.099	0.816
CBF L (ml/100g/min)	111.5 ± 23.6	110.5 ± 25.7	112.5 ± 22.2	0.822
<b>12h</b>				
rSO2 R (%)	65.79 (12.47)	68.50 (12.40)	63.27 (12.42)	0.266
rSO2 L (%)	66.77 (12.82)	68.00 (9.58)	65.53 (15.66)	0.608
ICP (mmHg)	8.10 (4.25)	7.53 (3.58)	8.67 (4.88)	0.475
CPP (mmHg)	70.57 (8.52)	68.20 (8.68)	72.93 (7.94)	0.130
SV R (cm/s)	129.60 (41.67)	121.13 (39.09)	138.07 (43.76)	0.273
DV R (cm/s)	46.63 (21.64)	41.20 (19.90)	52.07 (22.59)	0.173
CVR R (mmHg/mL/min)	0.643 ± 0.101	0.660 ± 0.111	0.626 ± 0.089	0.376
CBF R (ml/100g/min)	112.60 ± 23.63	105.84 ± 19.34	119.36 ± 26.17	0.120
SV L (cm/s)	128.67 (68.80)	122.87 (45.14)	134.47 (87.72)	0.654
DV L (cm/s)	48.97 (30.66)	49.64 (19.11)	48.33 (39.24)	0.909
CVR L (mmHg/mL/min)	0.643 ± 0.101	0.660 ± 0.111	0.626 ± 0.089	0.376
CBF L (ml/100g/min)	112.6 ± 23.6	105.8 ± 19.3	119.4 ± 26.2	0.120
<b>24h</b>				
rSO2 R (%)	67.83 (12.55)	71.53 (11.20)	63.86 (13.10)	0.103
rSO2 L (%)	65.14 (12.01)	69.60 (8.20)	60.36 (13.82)	<b>0.042</b>
ICP (mmHg)	9.80 (4.76)	9.47 (4.91)	10.13 (4.75)	0.708
CPP (mmHg)	71.03 (8.60)	71.07 (9.51)	71.00 (7.86)	0.984
SV R (cm/s)	140.93 (57.81)	147.33 (55.72)	134.07 (61.28)	0.548
DV R (cm/s)	48.10 (25.35)	50.53 (23.51)	45.50 (27.83)	0.605
CVR R (mmHg/mL/min)	0.665 ± 0.090	0.660 ± 0.091	0.671 ± 0.091	0.738
CBF R (ml/100g/min)	109.08 ± 23.59	110.93 ± 29.75	107.10 ± 15.41	0.711
SV L (cm/s)	133.69 (47.47)	126.67 (36.35)	141.21 (57.55)	0.428
DV L (cm/s)	50.17 (27.26)	49.13 (24.70)	51.29 (30.67)	0.837
CVR L (mmHg/mL/min)	0.665 ± 0.090	0.660 ± 0.091	0.671 ± 0.091	0.738
CBF L (ml/100g/min)	109.1 ± 23.6	110.9 ± 29.7	107.1 ± 15.4	0.711
<b>48h</b>				
rSO2 R (%)	65.36 (10.87)	68.20 (13.14)	62.08 (6.54)	0.126
rSO2 L (%)	66.62 (9.83)	69.07 (10.92)	64.00 (8.08)	0.166
ICP (mmHg)	9.52 (4.52)	7.93 (4.15)	11.21 (4.41)	<b>0.049</b>
CPP (mmHg)	74.28 (12.08)	77.00 (11.42)	71.36 (12.49)	0.216
SV R (cm/s)	140.47 (38.47)	138.40 (38.21)	142.53 (39.95)	0.774
DV R (cm/s)	50.07 (21.89)	51.53 (25.16)	48.60 (18.83)	0.721
CVR R (mmHg/mL/min)	0.648 ± 0.084	0.638 ± 0.099	0.659 ± 0.066	0.498
CBF R (ml/100g/min)	118.24 ± 30.50	125.46 ± 35.53	110.50 ± 22.80	0.187
SV L (cm/s)	139.17 (51.79)	129.40 (31.24)	148.93 (66.15)	0.313
DV L (cm/s)	48.50 (19.87)	47.67 (13.66)	49.33 (25.10)	0.823
CVR L (mmHg/mL/min)	0.648 ± 0.084	0.638 ± 0.099	0.659 ± 0.066	0.498
CBF L (ml/100g/min)	118.2 ± 30.5	125.5 ± 35.5	110.5 ± 22.8	0.187
<b>72h</b>				
rSO2 R (%)	64.68 (11.70)	68.20 (11.35)	60.62 (11.15)	0.087
rSO2 L (%)	62.97 (11.13)	64.33 (12.40)	61.50 (9.85)	0.500
ICP (mmHg)	8.72 (5.42)	6.60 (4.15)	11.00 (5.82)	<b>0.029</b>
CPP (mmHg)	75.28 (15.06)	80.53 (15.29)	69.64 (13.06)	<b>0.049</b>
SV R (cm/s)	155.87 (40.09)	145.87 (32.65)	165.87 (45.26)	0.177
DV R (cm/s)	55.20 (18.48)	52.20 (18.78)	58.20 (18.32)	0.383
CVR R (mmHg/mL/min)	0.643 ± 0.092	0.641 ± 0.110	0.645 ± 0.073	0.772
CBF R (ml/100g/min)	119.59 ± 31.31	129.14 ± 32.29	109.36 ± 27.76	0.088
SV L (cm/s)	137.93 (46.84)	131.00 (35.91)	144.87 (56.15)	0.428
DV L (cm/s)	49.07 (18.67)	47.67 (16.33)	50.47 (21.25)	0.689
CVR L (mmHg/mL/min)	0.643 ± 0.092	0.641 ± 0.110	0.645 ± 0.073	0.772
CBF L (ml/100g/min)	119.6 ± 31.3	129.1 ± 32.3	109.4 ± 27.8	0.088

**Supplementary Table 2.** Neuromonitoring parameters. Abbreviations: Right and left regional cerebral oxygen saturation (rSO2 R and rSO2 L), intracranial pressure (ICP), cerebral perfusion pressure (CPP), right and left transcranial Doppler systolic velocity (SV R and SV L), right and left cerebrovascular resistance (CVR = (SV-DV)/SV), Doppler diastolic velocity (DV), right and left cerebral blood flow (CBF = CPP / CVR)

	N=30	Isoflurane N=15	Propofol N=15	p.value
<b>0h</b>				
Lactate (mmol/L)	1,42 (0,665)	1,35 (0,369)	1,49 (0,64)	0.590
ScvO <sub>2</sub> (%)	79.22 (7.78)	77.58 (7.27)	80.62 (8.20)	0.325
Pv-aCO <sub>2</sub> gap (mmHg)	5.76 (3.10)	5.45 (3.33)	6.00 (3.01)	0.676
Hemoglobin (g/dl)	11.98 (1.92)	12.49 (1.55)	11.47 (2.15)	0.146
Glucose (mg/dl)	148.03 (42.43)	135.07 (21.81)	161.00 (53.79)	0.100
Temperature (°C)	36.04 (0.88)	36.00 (0.65)	36.09 (1.09)	0.794
<b>1h</b>				
Lactate (mmol/L)	1,5 (0,82)	1,4 (0,81)	1,61 (0,85)	0.499
ScvO <sub>2</sub> (%)	79.59 (7.53)	79.88 (7.24)	79.34 (8.01)	0.852
Pv-aCO <sub>2</sub> gap (mmHg)	5.68 (2.26)	5.15 (1.34)	6.13 (2.80)	0.242
Hemoglobin (g/dl)	12.13 (1.77)	12.57 (1.18)	11.69 (2.17)	0.182
Glucose (mg/dl)	154.50 (40.61)	138.53 (25.26)	170.47 (47.25)	<b>0.031</b>
Temperature (°C)	36.11 (0.92)	35.97 (0.79)	36.25 (1.04)	0.414
<b>12h</b>				
Lactate (mmol/L)	1,49 (0,87)	1,68 (1,02)	1,3 (0,67)	0.241
ScvO <sub>2</sub> (%)	81.38 (5.54)	81.64 (6.07)	81.08 (5.11)	0.803
Pv-aCO <sub>2</sub> gap (mmHg)	3.88 (2.03)	4.15 (1.86)	3.62 (2.22)	0.509
Hemoglobin (g/dl)	11.52 (1.83)	11.80 (1.46)	11.25 (2.15)	0.417
Glucose (mg/dl)	140.67 (37.20)	139.67 (37.80)	141.67 (37.89)	0.886
Temperature (°C)	36.25 (0.69)	36.26 (0.67)	36.23 (0.73)	0.917
<b>24h</b>				
Lactate (mmol/L)	1,27 (0,73)	1,38 (0,86)	1,17 (0,58)	0.448
ScvO <sub>2</sub> (%)	79.05 (7.67)	81.39 (8.62)	76.71 (6.00)	0.110
Pv-aCO <sub>2</sub> gap (mmHg)	4.69 (2.78)	4.47 (2.97)	4.93 (2.64)	0.662
Hemoglobin (g/dl)	11.15 (2.01)	11.62 (1.76)	10.68 (2.18)	0.205
Glucose (mg/dl)	136.48 (24.54)	131.40 (27.45)	141.93 (20.59)	0.251
Temperature (°C)	36.24 (0.53)	36.33 (0.38)	36.14 (0.64)	0.328
Fluid balance (ml)	970.62 (966.85)	942.17 (1044.36)	999.07 (918.67)	0.875
<b>48h</b>				
Lactate (mmol/L)	1,01 (0,48)	0,98 (0,44)	1,05 (0,52)	0.679
ScvO <sub>2</sub> (%)	78.33 (8.10)	81.15 (6.15)	74.75 (9.11)	0.062
Pv-aCO <sub>2</sub> gap (mmHg)	4.40 (1.63)	4.00 (1.71)	4.91 (1.45)	0.164
Hemoglobin (g/dl)	10.65 (1.83)	10.98 (1.72)	10.32 (1.94)	0.333
Glucose (mg/dl)	129.53 (26.71)	130.00 (19.67)	129.07 (33.02)	0.926
Temperature (°C)	36.32 (0.69)	36.48 (0.70)	36.16 (0.67)	0.212
<b>72h</b>				
Lactate (mmol/L)	0,88 (0,29)	0,92 (0,33)	0,84 (0,25)	0.455
ScvO <sub>2</sub> (%)	77.64 (7.48)	77.97 (7.83)	77.36 (7.45)	0.843
Pv-aCO <sub>2</sub> gap (mmHg)	4.84 (2.01)	5.36 (2.34)	4.43 (1.70)	0.279
Hemoglobin (g/dl)	10.34 (1.72)	10.57 (1.89)	10.10 (1.56)	0.460
Glucose (mg/dl)	137.90 (27.89)	133.47 (26.05)	142.33 (29.84)	0.394
Temperature (°C)	36.44 (0.79)	36.61 (0.62)	36.28 (0.92)	0.266

**Supplementary Table 3.** Laboratory parameters and temperature. Abbreviations: Central venous oxygen saturation (ScvO<sub>2</sub>), veno-arterial carbon dioxide partial pressure difference (Pv-aCO<sub>2</sub> gap).

	N=30	Isoflurane N=15	Propofol N=15	p.value
<b>0h</b>				
FIO <sub>2</sub>	0.43 (0.10)	0.41 (0.05)	0.45 (0.12)	0.278
PEEP (cmH <sub>2</sub> O)	8.23 (1.52)	8.27 (1.28)	8.20 (1.78)	0.907
pO <sub>2</sub> /FIO <sub>2</sub>	350.67 (140.23)	371.47 (166.72)	329.87 (109.59)	0.427
Vt (ml)	427.50 (51.14)	436.00 (52.21)	419.00 (50.36)	0.372
RR (breaths/min)	18.57 (2.85)	19.33 (2.35)	17.80 (3.17)	0.144
pH	7.40 (0.06)	7.40 (0.08)	7.39 (0.05)	0.517
pCO <sub>2</sub> (mmHg)	37.20 (5.81)	37.73 (7.39)	36.67 (3.83)	0.625
pO <sub>2</sub> (mmHg)	322.20 (939.93)	499.33 (1326.54)	145.07 (55.71)	0.319
HCO <sub>3</sub> (mmol/l)	22.63 (1.78)	23.53 (1.70)	21.72 (1.39)	<b>0.004</b>
BE (mmol/l)	-2.33 (2.26)	-1.43 (2.55)	-3.23 (1.52)	<b>0.028</b>
SatO <sub>2</sub> (%)	98.29 (1.32)	98.36 (1.58)	98.22 (1.06)	0.778
EtCO <sub>2</sub> (mmHg)	31.79 (5.09)	33.40 (5.26)	30.07 (4.45)	0.076
<b>1h</b>				
FIO <sub>2</sub>	0.40 (0.08)	0.39 (0.04)	0.42 (0.10)	0.219
PEEP (cmH <sub>2</sub> O)	8.30 (1.47)	8.40 (1.12)	8.20 (1.78)	0.716
pO <sub>2</sub> /FIO <sub>2</sub>	375.17 (103.10)	387.87 (114.69)	362.47 (92.31)	0.510
Vt (ml)	426.83 (51.44)	430.67 (47.88)	423.00 (56.18)	0.691
RR (breaths/min)	18.27 (2.83)	18.87 (2.80)	17.67 (2.82)	0.252
pH	7.39 (0.05)	7.37 (0.05)	7.40 (0.04)	0.095
pCO <sub>2</sub> (mmHg)	36.77 (4.89)	39.33 (4.59)	34.20 (3.78)	<b>0.002</b>
pO <sub>2</sub> (mmHg)	144.93 (45.28)	140.53 (47.03)	149.33 (44.65)	0.603
HCO <sub>3</sub> (mmol/l)	22.09 (2.05)	22.77 (2.40)	21.40 (1.39)	0.068
BE (mmol/l)	-3.06 (2.31)	-2.55 (2.67)	-3.57 (1.83)	0.231
SatO <sub>2</sub> (%)	98.29 (1.21)	97.97 (1.38)	98.61 (0.96)	0.154
EtCO <sub>2</sub> (mmHg)	32.93 (5.80)	34.73 (6.28)	30.67 (4.38)	0.059
<b>12h</b>				
FIO <sub>2</sub>	0.37 (0.08)	0.38 (0.10)	0.36 (0.06)	0.503
PEEP (cmH <sub>2</sub> O)	8.50 (1.87)	8.67 (1.95)	8.33 (1.84)	0.634
pO <sub>2</sub> /FIO <sub>2</sub>	381.35 (64.06)	385.37 (81.76)	377.33 (42.21)	0.738
Vt (ml)	422.83 (54.04)	432.67 (48.91)	413.00 (58.73)	0.328
RR (breaths/min)	18.37 (2.93)	19.33 (2.55)	17.40 (3.04)	0.070
pH	7.40 (0.05)	7.40 (0.06)	7.40 (0.04)	1.000
pCO <sub>2</sub> (mmHg)	38.07 (4.86)	39.60 (5.54)	36.53 (3.62)	0.085
pO <sub>2</sub> (mmHg)	136.37 (26.45)	141.60 (25.75)	131.13 (26.97)	0.286
HCO <sub>3</sub> (mmol/l)	23.77 (2.37)	24.67 (2.77)	22.86 (1.47)	<b>0.036</b>
BE (mmol/l)	-1.19 (2.55)	-0.31 (2.86)	-2.07 (1.89)	0.057
SatO <sub>2</sub> (%)	98.55 (0.92)	98.69 (1.03)	98.41 (0.81)	0.415
EtCO <sub>2</sub> (mmHg)	34.72 (4.00)	36.01 (4.38)	33.23 (3.03)	0.059
<b>24h</b>				
FIO <sub>2</sub>	0.35 (0.06)	0.35 (0.08)	0.35 (0.05)	0.934
PEEP (cmH <sub>2</sub> O)	8.50 (1.87)	8.67 (1.95)	8.33 (1.84)	0.634
pO <sub>2</sub> /FIO <sub>2</sub>	374.79 (98.60)	393.70 (104.68)	355.88 (91.73)	0.302
Vt (ml)	431.30 (53.07)	442.00 (51.16)	420.60 (54.52)	0.277
RR (breaths/min)	18.73 (2.63)	19.87 (2.64)	17.60 (2.13)	<b>0.015</b>
pH	7.42 (0.04)	7.43 (0.04)	7.41 (0.05)	0.136
pCO <sub>2</sub> (mmHg)	37.83 (4.37)	38.60 (4.88)	37.07 (3.81)	0.346
pO <sub>2</sub> (mmHg)	129.43 (25.40)	133.67 (21.62)	125.20 (28.82)	0.371
HCO <sub>3</sub> (mmol/l)	24.72 (1.84)	25.72 (1.53)	23.72 (1.60)	<b>0.002</b>
BE (mmol/l)	0.32 (2.44)	1.53 (1.92)	-0.89 (2.34)	<b>0.005</b>
SatO <sub>2</sub> (%)	98.14 (0.86)	98.27 (0.98)	98.01 (0.74)	0.420
EtCO <sub>2</sub> (mmHg)	33.46 (6.15)	34.43 (6.39)	32.50 (5.97)	0.417
<b>48h</b>				
FIO <sub>2</sub>	0.35 (0.06)	0.35 (0.07)	0.35 (0.05)	0.735
PEEP (cmH <sub>2</sub> O)	8.38 (1.78)	8.40 (2.03)	8.36 (1.55)	0.949
pO <sub>2</sub> /FIO <sub>2</sub>	346.79 (76.75)	360.60 (87.33)	332.00 (63.39)	0.320
Vt (ml)	424.31 (53.85)	438.00 (48.58)	409.64 (57.06)	0.163
RR (breaths/min)	19.13 (3.04)	20.13 (2.77)	18.13 (3.04)	0.071
pH	7.44 (0.05)	7.45 (0.04)	7.43 (0.05)	0.201
pCO <sub>2</sub> (mmHg)	39.27 (4.59)	39.60 (4.67)	38.93 (4.65)	0.698
pO <sub>2</sub> (mmHg)	121.70 (34.87)	123.40 (31.69)	120.00 (38.83)	0.795
HCO <sub>3</sub> (mmol/l)	26.40 (2.68)	27.15 (3.27)	25.64 (1.72)	0.128
BE (mmol/l)	2.12 (3.17)	3.25 (3.51)	0.98 (2.39)	<b>0.049</b>
SatO <sub>2</sub> (%)	98.18 (1.04)	98.19 (1.02)	98.17 (1.10)	0.959
EtCO <sub>2</sub> (mmHg)	33.41 (5.30)	34.40 (5.28)	32.17 (5.29)	0.286
<b>72h</b>				
FIO <sub>2</sub>	0.34 (0.04)	0.33 (0.05)	0.34 (0.03)	0.470
PEEP (cmH <sub>2</sub> O)	8.28 (1.49)	8.13 (1.60)	8.43 (1.40)	0.600
pO <sub>2</sub> /FIO <sub>2</sub>	340.25 (64.27)	362.59 (57.11)	317.92 (65.00)	0.056
Vt (ml)	426.86 (58.19)	438.27 (56.97)	414.64 (59.05)	0.283
RR (breaths/min)	18.87 (3.50)	19.93 (3.39)	17.80 (3.38)	0.096
pH	7.45 (0.05)	7.47 (0.06)	7.43 (0.04)	<b>0.038</b>
pCO <sub>2</sub> (mmHg)	39.87 (4.48)	39.40 (4.17)	40.33 (4.86)	0.577
pO <sub>2</sub> (mmHg)	114.43 (21.01)	119.67 (16.00)	109.20 (24.48)	0.178
HCO <sub>3</sub> (mmol/l)	27.48 (2.88)	28.35 (2.87)	26.61 (2.70)	0.097
BE (mmol/l)	3.58 (3.31)	4.72 (3.38)	2.36 (2.86)	0.052
SatO <sub>2</sub> (%)	98.17 (1.50)	98.54 (1.05)	97.79 (1.82)	0.181
EtCO <sub>2</sub> (mmHg)	35.23 (5.83)	36.00 (5.41)	34.33 (6.41)	0.486

**Supplementary Table 4.** Respiratory parameters. Abbreviations: Inspired oxygen fraction (FIO<sub>2</sub>), positive end-expiratory pressure (cmH<sub>2</sub>O), arterial oxygen pressure / inspired oxygen fraction ratio (PO<sub>2</sub>/FIO<sub>2</sub>), tidal volume (VT) (mL), respiratory rate (RR), pH, partial pressure of carbon dioxide (PCO<sub>2</sub>), partial pressure of oxygen (PO<sub>2</sub>), bicarbonate (HCO<sub>3</sub><sup>-</sup>), base excess (BE), arterial oxygen saturation (SatO<sub>2</sub>), end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>).

	<b>N=17</b>	<b>Isoflurane N=8</b>	<b>Propofol N=9</b>	<b>p.value</b>
<b>Age (years)</b>	54.35 (20.14)	44.88 (22.05)	62.78 (14.71)	0.076
<b>Sex</b>				1.000
<b>Male</b>	14 (82.35%)	7 (87.50%)	7 (77.78%)	
<b>Female</b>	3 (17.65%)	1 (12.50%)	2 (22.22%)	
<b>Weight (kg)</b>	79.29 (13.67)	74.62 (13.14)	83.44 (13.48)	0.193
<b>Height (m)</b>	1.73 (0.12)	1.74 (0.11)	1.72 (0.12)	0.735
<b>BMI</b>	26.92 (5.20)	25.07 (5.73)	28.58 (4.34)	0.182
<b>CCI</b>	1.82 (2.32)	1.00 (2.45)	2.56 (2.07)	0.182
<b>SAPS II</b>	41.35 (10.25)	38.00 (10.98)	44.33 (9.12)	0.220
<b>Pre-intubation GCS</b>	8.82 (3.54)	10.25 (3.33)	7.56 (3.40)	0.120
<b>Mechanical ventilation days</b>	16.12 (10.25)	14.14 (7.78)	17.50 (11.89)	0.732
<b>ICU LOS</b>	19.06 (11.43)	17.62 (9.44)	20.33 (13.40)	0.634
<b>Hospital LOS</b>	26.06 (17.73)	23.25 (13.24)	28.56 (21.45)	0.545

**Supplementary Table 5.** Demographic, clinical, and severity characteristics in the traumatic brain injury subpopulation. Abbreviations: Body mass index (BMI), Charlson Comorbidity Index (CCI), Glasgow Coma Scale (GCS), Intensive care unit (ICU).

	N=17	Isoflurane N=8	Propofol N=9	p.value
<b>0h</b>				
RASS	-5.00 (0.00)	-5.00 (0.00)	-5.00 (0.00)	1.000
BIS	51.94 (12.94)	53.88 (12.06)	50.22 (14.16)	0.574
ICP (mmHg)	7.00 (5.56)	8.38 (4.75)	5.78 (6.20)	0.345
CPP (mmHg)	67.35 (12.59)	64.50 (9.30)	69.89 (15.03)	0.384
Norepinephrine (mcg/kg/min)	0.10 (0.08)	0.08 (0.07)	0.12 (0.10)	0.510
MAP (mmHg)	76.94 (11.08)	75.88 (8.66)	77.89 (13.34)	0.715
HR (bpm)	74.29 (21.05)	72.38 (22.65)	76.00 (20.74)	0.737
<b>1h</b>				
RASS	-5.00 (0.00)	-5.00 (0.00)	-5.00 (0.00)	1.000
BIS	50.06 (7.55)	52.12 (6.49)	48.22 (8.32)	0.296
ICP (mmHg)	8.56 (5.46)	8.88 (5.30)	8.25 (5.97)	0.828
CPP (mmHg)	71.24 (8.24)	70.62 (8.23)	71.78 (8.71)	0.783
Norepinephrine (mcg/kg/min)	0.11 (0.08)	0.12 (0.08)	0.10 (0.08)	0.689
MAP (mmHg)	76.12 (10.58)	73.88 (9.79)	78.11 (11.43)	0.423
HR (bpm)	71.06 (24.57)	71.88 (28.37)	70.33 (22.39)	0.904
<b>12h</b>				
RASS	-4.88 (0.33)	-5.00 (0.00)	-4.78 (0.44)	0.169
BIS	44.18 (11.31)	44.00 (13.04)	44.33 (10.34)	0.955
ICP (mmHg)	7.71 (4.24)	8.00 (4.24)	7.44 (4.48)	0.796
CPP (mmHg)	71.18 (8.18)	69.50 (7.84)	72.67 (8.65)	0.441
Norepinephrine (mcg/kg/min)	0.15 (0.10)	0.17 (0.12)	0.13 (0.08)	0.441
MAP (mmHg)	78.76 (9.16)	76.25 (9.30)	81.00 (8.96)	0.302
HR (bpm)	65.29 (22.42)	67.88 (27.01)	63.00 (18.81)	0.677
<b>24h</b>				
RASS	-4.65 (1.00)	-4.38 (1.41)	-4.89 (0.33)	0.344
BIS	48.76 (10.88)	49.25 (11.96)	48.33 (10.54)	0.870
ICP (mmHg)	9.47 (4.16)	8.88 (3.48)	10.00 (4.82)	0.587
CPP (mmHg)	70.88 (9.29)	72.62 (10.97)	69.33 (7.84)	0.494
Norepinephrine (mcg/kg/min)	0.11 (0.09)	0.14 (0.11)	0.09 (0.08)	0.380
MAP (mmHg)	79.29 (7.66)	79.25 (7.55)	79.33 (8.22)	0.983
HR (bpm)	63.35 (18.89)	68.25 (21.33)	59.00 (16.45)	0.339
<b>48h</b>				
RASS	-4.65 (0.61)	-4.88 (0.35)	-4.44 (0.73)	0.140
BIS	47.35 (9.44)	44.00 (10.07)	50.33 (8.26)	0.182
ICP (mmHg)	9.76 (5.04)	8.00 (4.11)	11.33 (5.50)	0.175
CPP (mmHg)	73.12 (11.19)	76.12 (10.95)	70.44 (11.33)	0.310
Norepinephrine (mcg/kg/min)	0.07 (0.04)	0.09 (0.05)	0.06 (0.03)	0.170
MAP (mmHg)	84.00 (8.80)	82.62 (10.24)	85.22 (7.73)	0.569
HR (bpm)	61.24 (17.79)	63.12 (20.88)	59.56 (15.65)	0.699
<b>72h</b>				
RASS	-4.47 (0.72)	-4.62 (0.74)	-4.33 (0.71)	0.422
BIS	45.29 (11.03)	44.12 (11.00)	46.33 (11.62)	0.693
ICP (mmHg)	9.18 (6.00)	6.38 (2.72)	11.67 (7.12)	0.064
CPP (mmHg)	71.65 (15.35)	78.12 (17.56)	65.89 (11.04)	0.117
Norepinephrine (mcg/kg/min)	0.13 (0.26)	0.10 (0.08)	0.15 (0.33)	0.695
MAP (mmHg)	82.06 (13.22)	82.75 (17.59)	81.44 (8.83)	0.853
HR (bpm)	65.76 (15.90)	72.62 (17.94)	59.67 (11.63)	0.107
<b>ICU mortality</b>				
ICU mortality	4 (23.53%)	2 (25.00%)	2 (22.22%)	1.000
<b>WOLST mortality</b>				
WOLST mortality	4 (100.00%)	2 (100.00%)	2 (100.00%)	1.000
<b>Hospital mortality</b>				
Hospital mortality	4 (23.53%)	2 (25.00%)	2 (22.22%)	1.000

**Supplementary Table 6.** Sedation efficacy and safety outcomes in TBI subgroup. Abbreviations: Richmond Agitation-Sedation Scale (RASS), Intracranial pressure (ICP), cerebral perfusion pressure (CPP), mean arterial pressure (MAP), heart rate (HR), Intensive Care Unit (ICU), Withdrawal of life-sustaining therapies (WOLST).

	N=30	Isoflurane N=15	Propofol N=15	p.value
<b>0h</b>				
rSO2 R (%)	67.12 (12.73)	69.38 (13.85)	65.11 (12.11)	0.512
rSO2 L (%)	68.00 (11.53)	67.62 (11.25)	68.33 (12.44)	0.904
ICP (mmHg)	7.00 (5.56)	8.38 (4.75)	5.78 (6.20)	0.345
CPP (mmHg)	67.35 (12.59)	64.50 (9.30)	69.89 (15.03)	0.384
SV R (cm/s)	112.59 (25.66)	111.38 (24.05)	113.67 (28.43)	0.860
DV R (cm/s)	36.82 (11.65)	40.25 (10.58)	33.78 (12.30)	0.262
CVR R (mmHg/mL/min)	0.656 ± 0.120	0.630 ± 0.103	0.680 ± 0.135	0.409
CBF R (ml/100g/min)	106.1 ± 29.2	105.6 ± 26.2	106.6 ± 33.2	0.95
SV L (cm/s)	110.47 (36.05)	101.50 (34.45)	118.44 (37.52)	0.347
DV L (cm/s)	40.29 (18.03)	40.12 (22.32)	40.44 (14.63)	0.973
CVR L (mmHg/mL/min)	0.638 ± 0.118	0.621 ± 0.138	0.653 ± 0.102	0.598
CBF L (ml/100g/min)	109.6 ± 29.9	109.4 ± 30.7	109.7 ± 31.1	0.98
<b>1h</b>				
rSO2 R (%)	65.88 (13.04)	68.88 (13.78)	62.88 (12.41)	0.376
rSO2 L (%)	68.06 (10.34)	68.00 (10.80)	68.12 (10.60)	0.982
ICP (mmHg)	8.56 (5.46)	8.88 (5.30)	8.25 (5.97)	0.828
CPP (mmHg)	71.24 (8.24)	70.62 (8.23)	71.78 (8.71)	0.783
SV R (cm/s)	121.35 (28.76)	116.88 (28.95)	125.33 (29.72)	0.562
DV R (cm/s)	41.12 (13.20)	42.62 (12.08)	39.78 (14.70)	0.668
CVR R (mmHg/mL/min)	0.654 ± 0.092	0.627 ± 0.089	0.678 ± 0.093	0.267
CBF R (ml/100g/min)	111.6 ± 23.2	115.2 ± 23.9	108.5 ± 23.6	0.57
SV L (cm/s)	120.88 (23.18)	119.75 (18.75)	121.89 (27.65)	0.853
DV L (cm/s)	42.47 (17.83)	44.12 (16.85)	41.00 (19.54)	0.728
CVR L (mmHg/mL/min)	0.653 ± 0.110	0.635 ± 0.116	0.669 ± 0.109	0.546
CBF L (ml/100g/min)	112.9 ± 27.2	115.3 ± 29.6	110.7 ± 26.5	0.74
<b>12h</b>				
rSO2 R (%)	67.12 (12.60)	69.00 (13.51)	65.44 (12.29)	0.581
rSO2 L (%)	70.41 (11.94)	69.88 (11.51)	70.89 (12.99)	0.867
ICP (mmHg)	7.71 (4.24)	8.00 (4.24)	7.44 (4.48)	0.796
CPP (mmHg)	71.18 (8.18)	69.50 (7.84)	72.67 (8.65)	0.441
SV R (cm/s)	125.88 (37.72)	131.88 (48.71)	120.56 (26.49)	0.571
DV R (cm/s)	45.94 (18.65)	50.75 (22.04)	41.67 (15.05)	0.346
CVR R (mmHg/mL/min)	0.636 ± 0.091	0.615 ± 0.097	0.655 ± 0.086	0.390
CBF R (ml/100g/min)	113.5 ± 16.5	114.5 ± 15.0	112.6 ± 18.6	0.82
SV L (cm/s)	119.65 (38.99)	133.50 (47.46)	107.33 (26.58)	0.196
DV L (cm/s)	47.25 (19.49)	62.86 (14.58)	35.11 (13.18)	<b>0.002</b>
CVR L (mmHg/mL/min)	0.630 ± 0.097	0.570 ± 0.098	0.677 ± 0.069	<b>0.032</b>
CBF L (ml/100g/min)	115.0 ± 23.1	123.0 ± 25.7	108.8 ± 20.1	0.25
<b>24h</b>				
rSO2 R (%)	72.25 (11.42)	75.00 (12.62)	69.50 (10.16)	0.354
rSO2 L (%)	67.94 (11.35)	71.75 (7.32)	64.12 (13.76)	0.195
ICP (mmHg)	9.47 (4.16)	8.88 (3.48)	10.00 (4.82)	0.587
CPP (mmHg)	70.88 (9.29)	72.62 (10.97)	69.33 (7.84)	0.494
SV R (cm/s)	149.29 (58.89)	172.00 (60.39)	129.11 (52.64)	0.143
DV R (cm/s)	51.47 (24.75)	60.62 (24.07)	43.33 (23.67)	0.157
CVR R (mmHg/mL/min)	0.659 ± 0.078	0.647 ± 0.085	0.670 ± 0.076	0.566
CBF R (ml/100g/min)	109.9 ± 26.7	116.0 ± 36.1	104.4 ± 14.6	0.81
SV L (cm/s)	141.71 (53.89)	135.38 (40.87)	147.33 (65.35)	0.655
DV L (cm/s)	51.06 (27.87)	55.62 (30.45)	47.00 (26.51)	0.546
CVR L (mmHg/mL/min)	0.648 ± 0.098	0.609 ± 0.109	0.683 ± 0.077	0.236
CBF L (ml/100g/min)	113.0 ± 31.5	124.4 ± 40.2	102.9 ± 18.1	0.20
<b>48h</b>				
rSO2 R (%)	66.75 (12.06)	69.12 (16.31)	64.38 (5.73)	0.458
rSO2 L (%)	69.06 (10.53)	70.75 (13.51)	67.56 (7.52)	0.566
ICP (mmHg)	9.76 (5.04)	8.00 (4.11)	11.33 (5.50)	0.175
CPP (mmHg)	73.12 (11.19)	76.12 (10.95)	70.44 (11.33)	0.310
SV R (cm/s)	133.47 (27.90)	140.12 (25.30)	127.56 (30.22)	0.366
DV R (cm/s)	43.76 (13.29)	47.75 (17.59)	40.22 (7.26)	0.288
CVR R (mmHg/mL/min)	0.669 ± 0.080	0.663 ± 0.101	0.675 ± 0.062	0.783
CBF R (ml/100g/min)	111.6 ± 26.0	118.8 ± 32.3	105.1 ± 18.4	0.32
SV L (cm/s)	121.65 (39.92)	128.88 (29.35)	115.22 (48.33)	0.488
DV L (cm/s)	41.06 (20.21)	45.62 (17.19)	37.00 (22.78)	0.389
CVR L (mmHg/mL/min)	0.673 ± 0.087	0.653 ± 0.076	0.690 ± 0.097	0.423
CBF L (ml/100g/min)	110.6 ± 23.7	118.9 ± 27.0	103.2 ± 18.9	0.20
<b>72h</b>				
rSO2 R (%)	67.62 (12.41)	71.50 (13.33)	63.75 (10.87)	0.224
rSO2 L (%)	67.12 (10.11)	69.25 (12.61)	65.22 (7.53)	0.448
ICP (mmHg)	9.18 (6.00)	6.38 (2.72)	11.67 (7.12)	0.064
CPP (mmHg)	71.65 (15.35)	78.12 (17.56)	65.89 (11.04)	0.117
SV R (cm/s)	149.94 (32.63)	151.62 (37.92)	148.44 (29.43)	0.851
DV R (cm/s)	51.71 (15.90)	55.88 (20.82)	48.00 (9.66)	0.351
CVR R (mmHg/mL/min)	0.647 ± 0.098	0.627 ± 0.111	0.666 ± 0.088	0.437
CBF R (ml/100g/min)	114.1 ± 33.7	129.1 ± 38.9	100.8 ± 22.9	0.10
SV L (cm/s)	131.65 (41.21)	141.75 (39.45)	122.67 (42.93)	0.355
DV L (cm/s)	46.53 (17.30)	54.50 (19.46)	39.44 (12.12)	0.085
CVR L (mmHg/mL/min)	0.644 ± 0.090	0.617 ± 0.107	0.667 ± 0.068	0.276
CBF L (ml/100g/min)	115.0 ± 35.8	131.3 ± 41.4	100.6 ± 23.8	0.09

**Supplementary Table 7.** Neuromonitoring parameters Abbreviations: Right and left regional cerebral oxygen saturation (rSO2 R and rSO2 L), intracranial pressure (ICP), cerebral perfusion pressure (CPP), right and left transcranial Doppler systolic velocity (SV R and SV L), right and left cerebrovascular resistance (CVR = (SV-DV)/SV), Doppler diastolic velocity (DV), right and left cerebral blood flow (CBF = CPP - CVR) in TBI subgroup.