**Brain tissue oxygenation guided therapy and outcome in non-traumatic subarachnoid hemorrhage**

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**Supplemental Figure 1:** Flow-chart of the protocolized brain oxygen (PbtO2) guided therapy in patients suffering from subarachnoid hemorrhage (SAH). ICHT = intracranial hypertension.

**![Diagrama

Descrição gerada automaticamente]()**

\*Cerebral CT-scan with angiography and perfusion evaluation

\*\*The order of which intervention to be started first is dependent on patients’ condition and treating physician

#These includes: a) induced hypertension; b) intra-arterial vasodilators; c) cerebral angioplasty; d) rescue therapies (i.e. intra-carotid catheter for continuous infusion of vasodilators; therapeutic hypothermia; steroids; high-dose magnesium)

**Supplemental Table S1:** Characteristics of the study population, according to mortality and neurological outcome. Data are presented as count (%), mean ±SD or median (IQRs).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Survivors**  **N=95** | **Non-survivors**  **N=68** | **p value** | **FO**  **(N=65)** | **UO**  **(N=98)** | **p value** |
| Age, years | 54 (±11) | 56 (±15) | 0.34 | 53 (45-60) | 56 (47-67) | 0.08 |
| Male gender, n (%) | 43 (45) | 23 (34) | 0.15 | 32 (49) | 34 (35) | 0.07 |
| APACHE on admission | 17 (12-21) | 20 (15-23) | 0.008 | 16 (11-19) | 20 (15-23) | 0.001 |
| SOFA on admission | 6 (4-9) | 9 (5-10) | 0.02 | 6 (3-8) | 9 (5-10) | 0.001 |
| GCS on admission | 6 (3-13) | 3 (3-10) | 0.09 | 7 (3-13) | 5 (3-8) | 0.01 |
| Poor grade (WFNS 4-5), n (%) | 71 (75) | 55 (81) | 0.45 | 44 (68) | 82 (84) | 0.02 |
| High risk modified Fisher scale, n (%) | 91 (96) | 63 (93) | 0.49 | 63 (97) | 91 (93) | 0.32 |
| Intraparenchymal hematoma, n (%) | 30 (32) | 30 (44) | 0.14 | 15 (23) | 45 (46) | 0.005 |
| Hypertension, n (%) | 51 (54) | 29 (43) | 0.20 | 31 (48) | 49 (50) | 0.87 |
| Diabetes mellitus, n (%) | 12 (13) | 6 (9) | 0.61 | 9 (14) | 9 (9) | 0.45 |
| Heart disease, n (%) | 10 (11) | 8 (12) | 0.81 | 5 (8) | 13 (13) | 0.32 |
| Previous neurological disease, n (%) | 9 (10) | 8 (12) | 0.80 | 8 (12) | 19 (9) | 0.60 |
| Chronic Kidney Disease, n (%) | 3 (3) | 1 (2) | 0.64 | 2 (3) | 2 (2) | 0.99 |
| COPD, n (%) | 4 (4) | 13 (19) | 0.003 | 4 (6) | 13 (13) | 0.19 |
| Immunosuppression, n (%) | 5 (5) | 4 (6) | 0.99 | 2 (3) | 7 (7) | 0.32 |
| Cancer, n (%) | 3 (3) | 8 (12) | 0.05 | 3 (5) | 8 (8) | 0.53 |
| Cirrhosis, n (%) | 3 (3) | 4 (6) | 0.45 | 1 (2) | 6 (6) | 0.25 |
| Vasopressors, n (%) | 63 (66) | 61 (90) | 0.001 | 40 (62) | 82 (84) | 0.001 |
| Inotropic agents, n (%) | 21 (22) | 24 (36) | 0.08 | 14 (22) | 31 (32) | 0.21 |
| Mechanical ventilation, n (%) | 78 (82) | 68 (100) | 0.001 | 52 (80) | 94 (96) | 0.002 |
| RRT, n (%) | 0 | 1 (2) | 0.42 | 0 | 1 (1) | 0.99 |
| ECMO, n (%) | 0 | 3 (4) | 0.07 | 0 | 3 (3) | 0.28 |
| Endovascular treatment (coiling), n (%) | 62 (65) | 40 (59) | 0.42 | 45 (69) | 57 (58) | 0.19 |
| Surgical treatment (clipping), n (%) | 14 (15) | 19 (28) | 0.05 | 5 (8) | 28 (29) | 0.001 |
| Nimodipine (prophylaxis), n (%) | 86 (91) | 55 (81) | 0.10 | 63 (97) | 78 (80) | 0.001 |
| ICP only guided therapy | 18 (19) | 30 (44) | 0.001 | 7 (11) | 41 (42) | 0.001 |
| ICP/PbtO2 guided therapy | 28 (30) | 26 (38) | 0.31 | 20 (31) | 34 (35) | 0.62 |
| Seizures, n (%) | 35 (37) | 24 (35) | 0.87 | 20 (31) | 39 (40) | 0.25 |
| Re-bleeding, n (%) | 3 (3) | 12 (18) | 0.002 | 1 (2) | 14 (14) | 0.005 |
| Hydrocephalus, n (%) | 71 (75) | 40 (59) | 0.04 | 49 (75) | 62 (63) | 0.12 |
| DCI, n (%) | 27 (28) | 32 (47) | 0.02 | 14 (22) | 45 (46) | 0.002 |
| Intracranial hypertension, n (%) | 38 (40) | 57 (84) | 0.001 | 19 (29) | 76 (78) | 0.001 |
| Induced Hypertension, n (%) | 59 (62) | 38 (56) | 0.52 | 40 (62) | 57 (58) | 0.75 |
| Osmotic therapy, n (%) | 26 (27) | 48 (71) | 0.001 | 11 (17) | 63 (64) | 0.001 |
| Barbituric coma, n (%) | 9 (10) | 25 (37) | 0.001 | 4 (6) | 30 (31) | 0.001 |
| Hypothermia, n (%) | 8 (8) | 22 (32) | 0.001 | 4 (6) | 26 (27) | 0.001 |
| Decompressive craniectomy, n (%) | 9 (10) | 6 (9) | 0.99 | 4 (6) | 11 (11) | 0.41 |
| Intra-arterial nimodipine, n (%) | 31 (33) | 22 (32) | 0.99 | 21 (32) | 32 (33) | 0.99 |
| Cerebral angioplasty, n (%) | 15 (16) | 8 (12) | 0.50 | 10 (15) | 13 (13) | 0.84 |
| ICU LOS, days | 19 (15-27) | 10 (5-15) | 0.001 | 18 (14-23) | 14 (6-21) | 0.001 |
| Hospital LOS, days | 45 (29-85) | 11 (5-16) | 0.001 | 40 (27-70) | 15 (7-38) | 0.001 |

APACHE : acute physiology and chronic health evaluation; SOFA : sequential organ failure assessment; GCS: Glasgow coma scale WFNS: world federation of neurological surgeons; COPD: chronic obstructive pulmonary disease; RRT: renal replacement therapy; ECMO: extra-corporeal membrane oxygenation. PbtO2: brain tissue oxygenation; DCI: delayed cerebral ischemia; ICHT: Intracranial hypertension; ICU: intensive care unit; LOS: length of stay.

**Supplemental Table 2:** Cox regression to identify variables independently associated with hospital mortality. Data are reported as hazard ratio (HR) and 95 % confidence intervals (CIs).

|  |  |  |
| --- | --- | --- |
|  | **Univariable analysis**  **HR (95% CI)** | **Multivariable analysis**  **HR (95% CI)** |
| **Age** | 1.009 (0.99-1.03) | 1.06 (1.01-1.11) |
| **Nimodipine** | 0.51 (0.28-0.94) | 0.63 (0.34-1.18) |
| **Endovascular (coiling) treatment** | 0.74 (0.46-1.20) | 0.76 (0.45-1.27) |
| **Intracranial hypertension** | 5.37 (2.81-10.26) | 5.04 (2.60-9.77) |
| **DCI** | 1.51 (0.94-2.44) | 1.20 (0.73-1.97) |
| **Intraparenchymal hematoma** | 1.49 (0.93-2.41) | 1.10 (0.67-1.82) |
| **Combined ICP/PbtO2 guided therapy** | 1.23 (0.75-2.00) | 1.11 (0.67-1.84) |

ICP: intracranial pressure; PbtO2: brain tissue oxygenation

**Supplemental Table S3 :** Characteristics of the patients undergoing ICP- or ICP/PbtO2 guided-therapy, according to hospital mortality and neurological outcome. Data are presented as count (%), mean ±SD or median (IQRs).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Survivors**  **N=46** | **Non-survivors**  **N=56** | **p value** | **FO**  **N=27** | **UO**  **N=75** | **p value** |
| Age, years | 54 (±11) | 55 (±15) | 0.81 | 52 (±11) | 55 (±14) | 0.20 |
| Male gender, n(%) | 18 (39) | 20 (36) | 0.84 | 12 (44) | 36 (35) | 0.49 |
| APACHE on admission | 18 (13-21) | 20 (15-22) | 0.09 | 18 (12-20) | 20 (15-22) | 0.03 |
| SOFA on admission | 8 (5-10) | 9 (5-10) | 0.67 | 6 (5-10) | 9 (5-10) | 0.24 |
| GCS on admission | 6 (3-13) | 3 (3-10) | 0.25 | 7 (3-13) | 5 (3-8) | 0.23 |
| Poor grade (WFNS 4-5), n (%) | 35 (76) | 46 (82) | 0.47 | 18 (67) | 63 (84) | 0.09 |
| High risk modified Fisher scale, n (%) | 43 (94) | 51 (91) | 0.73 | 26 (96) | 68 (91) | 0.68 |
| Intraparenchymal hematoma, n (%) | 20 (44) | 28 (50) | 0.55 | 9 (33) | 39 (52) | 0.12 |
| Hypertension, n (%) | 24 (52) | 21 (38) | 0.16 | 12 (44) | 33 (44) | 0.99 |
| Diabetes mellitus, n (%) | 6 (13) | 4 (7) | 0.34 | 4 (15) | 6 (8) | 0.45 |
| Heart disease, n (%) | 5 (11) | 7 (13) | 0.99 | 2 (7) | 10 (13) | 0.51 |
| Previous neurological disease, n (%) | 4 (9) | 6 (11) | 0.99 | 4 (15) | 6 (8) | 0.45 |
| Chronic Kidney Disease, n (%) | 0 | 1 (2) | 0.99 | 0 | 1 (1) | 0.99 |
| COPD, n (%) | 2 (4) | 9 (16) | 0.11 | 2 (7) | 9 (12) | 0.73 |
| Immunosuppression, n (%) | 2 (4) | 4 (7) | 0.68 | 0 | 1 (1) | 0.34 |
| Cancer, n (%) | 1 (2) | 5 (9) | 0.22 | 1 (4) | 5 (7) | 0.99 |
| Cirrhosis, n (%) | 2 (4) | 3 (5) | 0.99 | 0 | 5 (7) | 0.32 |
| Vasopressors, n (%) | 39 (85) | 52 (93) | 0.22 | 24 (89) | 67 (89) | 0.99 |
| Inotropic agents, n (%) | 19 (41) | 21 (38) | 0.84 | 13 (48) | 27 (36) | 0.36 |
| Mechanical ventilation, n (%) | 42 (91) | 56 (100) | 0.04 | 25 (93) | 73 (97) | 0.29 |
| RRT, n (%) | 0 | 1 (2) | 0.99 | 0 | 1 (1) | 0.99 |
| ECMO, n (%) | 0 | 2 (4) | 0.50 | 0 | 2 (3) | 0.99 |
| Endovascular treatment (coiling), n (%) | 32 (70) | 33 (59) | 0.31 | 22 (82) | 43 (57) | 0.04 |
| Surgical treatment (clipping), n (%) | 8 (17) | 18 (32) | 0.11 | 1 (4) | 25 (33) | 0.002 |
| Nimodipine (prophylaxis), n (%) | 40 (87) | 45 (80) | 0.43 | 26 (96) | 59 (79) | 0.04 |
| PbtO2 guided therapy, n (%) | 28 (61) | 26 (46) | 0.17 | 20 (74) | 34 (45) | 0.02 |
| Seizures, n (%) | 17 (37) | 17 (30) | 0.53 | 8 (30) | 26 (35) | 0.82 |
| Re-bleeding, n (%) | 3 (7) | 10 (18) | 0.14 | 1 (4) | 12 (16) | 0.18 |
| Hydrocephalus, n (%) | 28 (61) | 32 (57) | 0.84 | 15 (56) | 45 (60) | 0.82 |
| DCI, n (%) | 20 (44) | 26 (46) | 0.84 | 10 (37) | 36 (48) | 0.38 |
| Intracranial hypertension, n (%) | 29 (63) | 52 (93) | 0.001 | 14 (52) | 67 (89) | 0.001 |
| Induced Hypertension, n (%) | 35 (76) | 31 (55) | 0.04 | 21 (78) | 45 (60) | 0.11 |
| Osmotic therapy, n (%) | 26 (57) | 48 (86) | 0.002 | 11 (41) | 63 (84) | 0.001 |
| Barbituric coma, n (%) | 9 (20) | 25 (45) | 0.01 | 4 (15) | 30 (40) | 0.02 |
| Hypothermia, n (%) | 8 (17) | 21 (38) | 0.03 | 4 (15) | 25 (33) | 0.08 |
| Decompressive craniectomy, n (%) | 9 (20) | 6 (11) | 0.27 | 4 (15) | 11 (15) | 0.99 |
| Intra-arterial nimodipine, n (%) | 25 (54) | 18 (32) | 0.03 | 17 (63) | 26 (35) | 0.01 |
| Cerebral angioplasty, n (%) | 13 (28) | 5 (9) | 0.02 | 8 (30) | 10 (13) | 0.08 |
| ICU LOS, days | 26 (19-34) | 10 (5-15) | 0.001 | 26 (18-30) | 13 (6-21) | 0.001 |
| Hospital LOS, days | 53 (34-92) | 10 (5-16) | 0.001 | 50 (33-84) | 14 (6-29) | 0.001 |

APACHE : acute physiology and chronic health evaluation; SOFA : sequential organ failure assessment; GCS: Glasgow coma scale WFNS: world federation of neurological surgeons; COPD: chronic obstructive pulmonary disease; RRT: renal replacement therapy; ECMO: extra-corporeal membrane oxygenation. PbtO2: brain tissue oxygenation; DCI: delayed cerebral ischemia; ICHT: Intracranial hypertension; ICU: intensive care unit; LOS: length of stay.

**Supplemental Table S4:** Cox regression to identify variables independently associated with hospital mortality in patients undergoing ICP- or PbtO2 guided-therapy (n=102). Data are presented as hazard ratio (HR) and 95% confidence intervals (CI).

|  |  |  |
| --- | --- | --- |
|  | **Univariable analysis**  **HR ( 95% CI)** | **Multivariable analysis**  **HR (95% CI)** |
| **Nimodipine** |  |  |
| **Endovascular treatment** |  |  |
| **Combined ICP/PbtO2 guided therapy** | 0.62 (0.37-1.06) |  |

ICP: intracranial hypertension; PbtO2: brain tissue oxygenation.

**Supplemental Table S5:** Characteristics of the patients undergoing PbtO2 monitoring, according to mortality and neurological outcome. Data are presented as count (%), mean ±SD or median (IQRs). Brain hypoxia = PbtO2 < 20 mmHg; severe brain hypoxia = PbtO2 < 10 mmHg.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Survivors**  **N=32** | **Non-survivors**  **N=30** | **p value** | **FO**  **N=25** | **UO**  **N=37** | **p value** |
| Age, years | 53 (46-63) | 53 (46-64) | 0.89 | 52 (±10) | 55 (±14) | 0.44 |
| Male gender, n(%) | 13 (41) | 12 (40) | 0.99 | 12 (42) | 13 (35) | 0.43 |
| APACHE on admission | 19 (13-21) | 21 (13-23) | 0.43 | 19 (13-20) | 19 (14-22) | 0.24 |
| SOFA on admission | 8 (5-10) | 9 (2-10) | 0.83 | 7 (5-10) | 9 (3-10) | 0.45 |
| GCS on admission | 6 (3-13) | 3 (3-12) | 0.76 | 6 (3-13) | 3 (3-11) | 0.49 |
| Poor grade (WFNS 4-5), n (%) | 22 (69) | 24 (80) | 0.39 | 16 (64) | 30 (81) | 0.15 |
| High risk modified Fisher scale, n (%) | 29 (91) | 26 (87) | 0.70 | 23 (92) | 32 (87) | 0.69 |
| Intraparenchymal hematoma, n (%) | 15 (47) | 15 (50) | 0.99 | 11 (44) | 19 (51) | 0.61 |
| Hypertension, n (%) | 14 (44) | 24 (40) | 0.61 | 12 (48) | 13 (35) | 0.43 |
| Diabetes mellitus, n (%) | 5 (16) | 0 | 0.06 | 5 (20) | 0 | 0.008 |
| Heart disease, n (%) | 3 (9) | 2 (7) | 0.99 | 2 (8) | 3 (8) | 0.99 |
| Previous neurological disease, n (%) | 1 (3) | 2 (7) | 0.61 | 1 (4) | 2 (5) | 0.99 |
| Chronic Kidney Disease, n (%) | 1 (3) | 0 | 0.99 | 1 (4) | 0 | 0.40 |
| COPD, n (%) | 2 (6) | 4 (13) | 0.42 | 2 (8) | 4 (11) | 0.99 |
| Immunosuppression, n (%) | 1 (3) | 1 (3) | 0.99 | 0 | 2 (5) | 0.51 |
| Cancer, n (%) | 0 | 2(7) | 0.23 | 0 | 2 (5) | 0.51 |
| Cirrhosis, n (%) | 1 (3) | 1 (3) | 0.99 | 0 | 2 (5) | 0.51 |
| Vasopressors, n (%) | 28 (88) | 30 (100) | 0.11 | 22 (88) | 36 (97) | 0.29 |
| Inotropic agents, n (%) | 17 (53) | 19 (63) | 0.45 | 13 (52) | 23 (62) | 0.45 |
| Mechanical ventilation, n (%) | 30 (94) | 30 (100) | 0.49 | 23 (92) | 37 (100) | 0.16 |
| RRT, n (%) | 0 | 0 | 0.99 | 0 | 0 | 0.99 |
| ECMO, n (%) | 0 | 1 (3) | 0.48 | 0 | 1 (3) | 0.99 |
| Endovascular treatment (coiling), n (%) | 22 (69) | 18 (60) | 0.60 | 18 (72) | 22 (60) | 0.42 |
| Surgical treatment (clipping), n (%) | 5 (17) | 13 (43) | 0.03 | 3 (12) | 15 (41) | 0.02 |
| Nimodipine (prophylaxis), n (%) | 29 (91) | 23 (77) | 0.18 | 23 (92) | 29 (78) | 0.18 |
| PbtO2 guided therapy, n (%) | 29 (91) | 25 (83) | 0.38 | 22 (88) | 32 (87) | 0.99 |
| Severe brain hypoxia | 16 (50) | 23 (77) | 0.04 | 10 (40) | 29 (78) | 0.003 |
| Burden of severe brain hypoxia | 1.25  (0-22.02) | 26.72  (2.06-147.49) | 0.04 | 0  (0-10.42) | 22.28  (3.0-147.49) | 0.001 |
| Brain hypoxia | 25 (78) | 29 (97) | 0.06 | 18 (72) | 36 (97) | 0.006 |
| Burden of brain hypoxia | 105.66  (6.83-424.49) | 333.16  (128.42-560.89) | 0.01 | 44.45  (0-340) | 350  (136.22-663.54) | 0.001 |
| Seizures, n (%) | 9 (28) | 7 (23) | 0.76 | 6 (24) | 10 (27) | 0.99 |
| Re-bleeding, n (%) | 2 (6) | 8 (27) | 0.04 | 1 (4) | 9 (24) | 0.04 |
| Hydrocephalus, n (%) | 15 (44) | 15 (50) | 0.80 | 11 (44) | 18 (49) | 0.80 |
| DCI, n (%) | 15 (44) | 15 (50) | 0.80 | 9 (36) | 20 (54) | 0.20 |
| Intracranial hypertension, n (%) | 13 (41) | 27 (90) | 0.001 | 9 (36) | 31 (84) | 0.001 |
| Induced Hypertension, n (%) | 24 (75) | 20 (67) | 0.58 | 17 (68) | 27 (73) | 0.78 |
| Osmotic therapy, n (%) | 9 (28) | 22 (73) | 0.001 | 6 (24) | 25 (68) | 0.002 |
| Barbituric coma, n (%) | 5 (16) | 15 (50) | 0.007 | 3 (12) | 17 (46) | 0.006 |
| Hypothermia, n (%) | 5 (16) | 16 (53) | 0.003 | 3 (12) | 18 (49) | 0.003 |
| Decompressive craniectomy, n (%) | 4 (13) | 5 (17) | 0.73 | 2 (8) | 7 (19) | 0.29 |
| Intra-arterial nimodipine, n (%) | 21 (66) | 12 (40) | 0.07 | 16 (64) | 17 (46) | 0.20 |
| Cerebral angioplasty, n (%) | 8 (25) | 3 (10) | 0.19 | 7 (28) | 4 (11) | 0.10 |
| ICU LOS, days | 26 (18-36) | 10 (3-16) | 0.001 | 23 (16-29) | 13 (6-20) | 0.002 |
| Hospital LOS, days | 54 (37-87) | 10 (3-16) | 0.001 | 52 (33-90) | 14 (6-20) | 0.001 |

APACHE : acute physiology and chronic health evaluation; SOFA : sequential organ failure assessment; GCS: Glasgow coma scale WFNS: world federation of neurological surgeons; COPD: chronic obstructive pulmonary disease; RRT: renal replacement therapy; ECMO: extra-corporeal membrane oxygenation. PbtO2: brain tissue oxygenation; DCI: delayed cerebral ischemia; ICHT: Intracranial hypertension; ICU: intensive care unit; LOS: length of stay.

**Supplemental Table S6:** Logistic regression analysis to identify variables independently associated with unfavorable neurological outcome at 6 months in the PbtO2 group (only brain hypoxia was included).Data are presented as odds ratio (OR) and 95% confidence intervals (CI).

Table S6: Logistic regression models for factors associated with UO in 6 months

|  |  |  |
| --- | --- | --- |
|  | Univariable analysis  OR (95% CI) | Multivariable analysis  OR (95% CI) |
| Intracranial hypertension | 9.07 (2.80-29.32) | 8.56 (2.36-31.12) |
| PbtO2 guided therapy | 0.87(0.19-4.03) | 0.98 (0.11-8.3) |
| Brain tissue hypoxia\* | 5.44 (1.78-16.65) | 12.26 (1.21-124.48) |

Brain hypoxia was defined as PbtO2<20 mmHg. PbtO2: brain tissue oxygenation.

**Supplemental Table S7:** **:** Logistic regression analysis to identify variables independently associated with unfavorable neurological outcome at 6 months in the PbtO2 group(only severe brain hypoxia was included). Data are presented as odds ratio (OR) and 95% confidence intervals (CI).

|  |  |  |
| --- | --- | --- |
|  | Univariable analysis  OR (95% CI) | Multivariable analysis  OR (95% CI) |
| Intracranial hypertension | 9.07 (2.80-29.32) | 8.11 (2.25-29.32) |
| PbtO2 guided therapy | 0.87 (0.19-4.03) | 1.56 (0.21-29.32) |
| Severe brain tissue hypoxia\* | 14 (1.60-122.66) | 4.58 (1.28-16.37) |

Severe brain hypoxia was defined as a PbtO2<10 mmHg. PbtO2: brain tissue oxygenation.

**Supplemental Table S8**: **:** Logistic regression analysis to identify variables independently associated with unfavorable neurological outcome at 6 months in the PbtO2 group (only burden of hypoxia was included). Data are presented as odds ratio (OR) and 95% confidence intervals (CI).

|  |  |  |
| --- | --- | --- |
|  | Univariable analysis  OR (95% CI) | Multivariable analysis  OR (95% CI) |
| Intracranial hypertension | 9.07 (2.80-29.32) | 8.94 (2.45-32.64) |
| PbtO2 guided therapy | 0.87 (0.19-4.03) | 0.90 (0.14-5.79) |
| Burden of hypoxia\* | 14 (1.60-122.66) | 1.003 (1.001-1.005) |

Burden of hypoxia (continuous variable) is defined as the area under the curve (PbtO2 x time, expressed as mmHg\*hour) below 20. PbtO2: brain tissue oxygenation.

**Table S9** : Cox regression models for factors related to hospital mortality in the PbtO2 monitored cohort. Data are presented as hazard ratio (HR) and 95% confidence interval(CI).

|  |  |  |
| --- | --- | --- |
|  | Univariable analysis  HR (95% CI) | Multivariable analysis  HR (95% CI) |
| Intracranial hypertension | 8.00 (2.42-26.52) | 6.78 (2.01-22.79) |
| PbtO2 guided therapy | 0.43 (0.16-1.14) | 0.35 (0.13-0.95) |
| PbtO2<20 mmHg | 5.91 (0.80-43.42) | 4.55 (0.61-34.10) |

PbtO2: brain tissue oxygenation.