Lung-protective Ventilation in Patients with Brain Injury: A Multicenter Cross-sectional Study and Questionnaire Survey in China

Xu-Ying Luo[1], Ying-Hong Hu[2], Xiang-Yuan Cao[3], Yan Kang[4], Li-Ping Liu[5], Shou-Hong Wang[6], Rong-Guo Yu[7], Xiang-You Yu[8], Xia Zhang[9], Bao-Shan Li[10], Zeng-Xiang Ma[11], Yi-Bing Weng[12], Heng Zhang[13], De-Chang Chen[14], Wei Chen[15], Wen-Jin Chen[16], Xiu-Mei Chen[17], Bin Du[18], Mei-Li Duan[19], Jin Hu[20], Yun-Feng Huang[21], Gui-Jun Jia[22], Li-Hong Li[23], Yu-Min Liang[24], Bing-Yu Qin[25], Xian-Dong Wang[26], Jian Xiong[27], Li-Mei Yan[28], Zheng-Ping Yang[29], Chen-Ming Dong[30], Dong-Xin Wang[31], Qing-Yuan Zhan[32], Shuang-Lin Fu[33], Lin Zhao[34], Qi-Bing Huang[35], Ying-Guang Xie[36], Xiao-Bo Huang[37], Guo-Bin Zhang[38], Wang-Bin Xu[39], Yuan Xu[40], Ya-Ling Liu[41], He-Ling Zhao[42], Rong-Qing Sun[43], Ming Sun[44], Qing-Hong Cheng[45], Xin Qu[46], Xiao-Feng Yang[47], Ming Xu[1], Zhong-Hua Shi[1], Han Chen[1], Xuan He[1], Yan-Lin Yang[1], Guang-Qiang Chen[1], Xiu-Mei Sun[1], Jian-Xin Zhou[1];
on behalf of the Acute Brain Injury and Critical Care Research Collaboration (ABC Research Collaboration)

[1]Department of Critical Care Medicine, Beijing Tiantan Hospital, Capital Medical University, Beijing 100050, China
[2]Department of Critical Care Medicine, Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, Zhejiang 310009, China
[3]Department of Critical Care Medicine, General Hospital of Ningxia Medical University, Yinchuan, Ningxia 750004, China
[4]Department of Critical Care Medicine, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China
[5]Neurological Intensive Care Unit, Beijing Tiantan Hospital, Capital Medical University, Beijing 100050, China
[6]Department of Critical Care Medicine, Guangdong General Hospital, Guangzhou, Guangdong 510000, China
[7]Surgical Intensive Care Unit, Fujian Province Hospital, Fuzhou, Fujian 350000, China
[8]Department of Critical Care Medicine, First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang 830054, China
[9]Department of Critical Care Medicine, Bethune International Peace Hospital, Shijiazhuang, Hebei 050000, China
[10]Department of Critical Care Medicine, Yuncheng Central Hospital, Yuncheng, Shanxi 044000, China
[11]Department of Emergency and Critical Care Medicine, Cangzhou People's Hospital, Cangzhou, Hebei 061000, China
[12]Department of Critical Care Medicine, Beijing Luhe Hospital, Capital Medical University, Beijing 101100, China
[13]Department of Critical Care Medicine, First Hospital of China Medical University, Shenyang, Liaoning 110000, China
[14]Department of Critical Care Medicine, Shanghai Changzheng Hospital, Shanghai 200000, China
[15]Department of Critical Care Medicine, Beijing Shijitan Hospital, Capital Medical University, Beijing 100038, China
[16]Department of Critical Care Medicine, Xuanwu Hospital, Capital Medical University, Beijing 100053, China
[17]Department of Critical Care Medicine, Miyun County Hospital, Beijing 100038, China
[18]Medical Intensive Care Unit, Peking Union Medical College Hospital, Beijing 101500, China
[19]Department of Critical Care Medicine, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China
[20]Department of Critical Care Medicine, Huashan Hospital of Shanghai Fudan University Medical College, Shanghai 200040, China
[21]Intensive Care Unit, Changsha Central Hospital, Changsha, Hunan 410018, China
[22]Department of Critical Care Medicine, Shanxi Provincial People's Hospital, Taiyuan, Shanxi 030012, China
[23]Department of Critical Care Medicine, Tangdu Hospital, Fourth Military Medical University, Xi'an, Shaanxi 710000, China
[24]Neurosurgery Intensive Care Unit, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200240, China
[25]Department of Critical Care Medicine, Henan Provincial People's Hospital, Zhengzhou, Henan 450000, China
[26]Department of Critical Care Medicine, Gansu Provincial Hospital, Lanzhou, Gansu 730000, China
[27]Department of Critical Care Medicine, General Hospital of Shenyang Military, Shenyang, Liaoning 110000, China
[28]Department of Critical Care Medicine, Inner Mongolia People's Hospital, Hohhot, Inner Mongolia 010017, China
[29]Department of Critical Care Medicine, Qinghai Provincial People's Hospital, Xining, Qinghai 810000, China
[30]Department of Critical Care Medicine, Lanzhou University Second Hospital, Lanzhou, Gansu 730030, China
[31]Department of Critical Care Medicine, Peking University First Hospital, Beijing 100034, China
[32]Department of Critical Care Medicine, China-Japan Friendship Hospital, Beijing 100029, China

Address for correspondence: Prof. Jian-Xin Zhou, Department of Critical Care Medicine, Beijing Tiantan Hospital, Capital Medical University, Beijing 100050, China
E-Mail: zhoujx.cn@icloud.com

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.185869

Received: 01-03-2016 **Edited by:** Li-Min Chen
How to cite this article: Luo XY, Hu YH, Cao XY, Kang Y, Liu LP, Wang SH, Yu RG, Yu XY, Zhang X, Li BS, Ma ZX, Weng YB, Zhang H, Chen DC, Chen W, Chen WJ, Chen XM, Du B, Duan ML, Hu J, Huang YF, Jia GJ, Li LH, Liang YM, Qin BY, Wang XD, Xiong J, Yan LM, Yang ZP, Dong CM, Wang DX, Zhan QY, Fu SL, Zhao L, Huang QB, Xie YG, Huang XB, Zhang GB, Xu WB, Xu Y, Liu YL, Zhao HL, Sun RQ, Sun M, Cheng QH, Qu X, Yang XF, Xu M, Shi ZH, Chen H, He X, Yang YL, Chen GQ, Sun XM, Zhou JX, on behalf of the Acute Brain Injury and Critical Care Research Collaboration (ABC Research Collaboration). Lung-protective Ventilation in Patients with Brain Injury: A Multicenter Cross-sectional Study and Questionnaire Survey in China. Chin Med J 2016;129:1643-51.

[33]Neurosurgery Intensive Care Unit, First Clinical Hospital, Norman Bethune College of Medicine, Jilin University, Changchun, Jilin 130000, China
[34]Department of Critical Care Medicine, Jiangsu Province Hospital, Nanjing, Jiangsu 210029, China
[35]Department of Critical Care Medicine, Qilu Hospital of Shandong University, Ji'nan, Shandong 250012, China
[36]Department of Critical Care Medicine, Jining No. 1 People's Hospital, Jining, Shandong 272011, China
[37]Department of Critical Care Medicine, Sichuan Provincial People's Hospital, Chengdu, Sichuan 610072, China
[38]Department of Critical Care Medicine, Tianjin Huanhu Hospital, Tianjin 300060, China
[39]Department of Emergency and Critical Care Medicine, First Affiliated Hospital of Kunming Medical University, Kunming, Yunnan 650032, China
[40]Department of Critical Care Medicine, Beijing Tongren Hospital, Capital Medical University, Beijing 100041, China
[41]Department of Critical Care Medicine, Beijing Pinggu Hospital, Beijing 101200, China
[42]Department of Critical Care Medicine, Hebei General Hospital, Shijiazhuang, Hebei 050051, China
[43]Department of Critical Care Medicine, First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan 450052, China
[44]Department of Critical Care Medicine, Liaocheng People's Hospital, Liaocheng, Shandong 252004, China
[45]Department of Critical Care Medicine, First Affiliated Hospital of The Medical College, Shihezi University, Shihezi, Xinjiang 832008, China
[46]Department of Critical Care Medicine, Shandong Provincial Hospital, Jinan, Shandong 250021, China
[47]Neurosurgery Intensive Care Unit, First Affiliated Hospital, Zhejiang University, Hangzhou, Zhejiang 310003, China

Abstract

Background: Over the years, the mechanical ventilation (MV) strategy has changed worldwide. The aim of the present study was to describe the ventilation practices, particularly lung-protective ventilation (LPV), among brain-injured patients in China.
Methods: This study was a multicenter, 1-day, cross-sectional study in 47 Intensive Care Units (ICUs) across China. Mechanically ventilated patients (18 years and older) with brain injury in a participating ICU during the time of the study, including traumatic brain injury, stroke, postoperation with intracranial tumor, hypoxic-ischemic encephalopathy, intracranial infection, and idiopathic epilepsy, were enrolled. Demographic data, primary diagnoses, indications for MV, MV modes and settings, and prognoses on the 60th day were collected. Multivariable logistic analysis was used to assess factors that might affect the use of LPV.
Results: A total of 104 patients were enrolled in the present study, 87 (83.7%) of whom were identified with severe brain injury based on a Glasgow Coma Scale ≤8 points. Synchronized intermittent mandatory ventilation (SIMV) was the most frequent ventilator mode, accounting for 46.2% of the entire cohort. The median tidal volume was set to 8.0 ml/kg (interquartile range [IQR], 7.0–8.9 ml/kg) of the predicted body weight; 50 (48.1%) patients received LPV. The median positive end-expiratory pressure (PEEP) was set to 5 cmH_2O (IQR, 5–6 cmH_2O). No PEEP values were higher than 10 cmH_2O. Compared with partially mandatory ventilation, supportive and spontaneous ventilation practices were associated with LPV. There were no significant differences in mortality and MV duration between patients subjected to LPV and those were not.
Conclusions: Among brain-injured patients in China, SIMV was the most frequent ventilation mode. Nearly one-half of the brain-injured patients received LPV. Patients under supportive and spontaneous ventilation were more likely to receive LPV.
Trial Registration: ClinicalTrials.org NCT02517073 https://clinicaltrials.gov/ct2/show/NCT02517073.

Key words: Brain Injury; Epidemiology; Lung-protective Ventilation; Mechanical Ventilation

Introduction

Over the past two decades, lung-protective ventilation (LPV), including limiting the tidal volume (V_T) and plateau pressure while providing adequate positive end-expiratory pressure (PEEP) levels, has gradually been adopted in the mechanical ventilation (MV) of patients with acute respiratory distress syndrome (ARDS).[1-3] Recently, several studies have also shown that LPV decreased the risk for the development of pulmonary complications in patients without ARDS.[4-7] However, in patients with brain injury, particularly those with increased intracranial pressure, low V_T and high PEEP might have potential deleterious effects on the cerebral perfusion.[8,9] Consequently, physicians are reluctant to apply the LPV in brain-injured patients.[10,11] However, several studies have reported that high V_T was associated with the development of ARDS in severe brain-injured patients[12-14] or other patients without ARDS at the onset of MV.[15,16] Sporadic reports suggested that LPV, as employed in brain-injured patients, might not significantly impair the intracranial hypertension[17] and might improve the clinical outcome and reduce the duration of MV.[18,19] Roquilly *et al*. concluded that LPV was associated with a reduction in the duration of MV in patients with brain injury.[18] Protective ventilation could also improve clinical outcomes in patients after cardiac arrest.[19] To date, there is no consensus regarding the application of LPV among patients with brain injury. Until recently, only few studies have described the characteristics and practice of MV in patients with brain injury.[10,11,13,14,19] We conducted a multicenter, 1-day point cross-sectional study to describe the ventilation practices, particularly LPV, among brain-injured patients in China.

Methods

Study design

We conducted a multicenter, 1-day point, cross-sectional study on the practice of MV among patients with brain injury in China. The study was performed at 11:00 a.m. on August 10, 2015.

Ethics and dissemination

The study was approved by the Institutional Review Board of Beijing Tiantan Hospital, Affiliated with Capital Medical

University. The Institutional Review Board specifically approved the informed consent waiver, reflecting the anonymous and purely observational nature of this study. During the study period, no attempt was made to change the routine clinical practice in each participating Intensive Care Unit (ICU).

Study population

Adult patients with brain injury, including traumatic brain injury, stroke (ischemic stroke, spontaneous intracerebral hemorrhage, and subarachnoid hemorrhage), postoperation with intracranial tumor, hypoxic-ischemic encephalopathy, intracranial infection and idiopathic epilepsy, and receiving MV for at least 24 h, were enrolled in the present study. Severe brain injury was identified using a Glasgow Coma Scale (GCS) ≤8 points.[20] The exclusion criteria included age <18 years, undergoing a spontaneous breathing trial with a T-piece, or participating in another MV trial during the study period.

Data collection

During the study period, the total number of patients in each ICU, the number of patients with brain injury, and the number of ventilated patients with brain injury were recorded. A uniform case report form was used to collect the data and was completed by the doctors in charge of the patient, who were provided with detailed instructions and the related definitions. For each patient enrolled, we collected baseline data, including demographics, the date of admission to the hospital and ICU, and the primary diagnosis. The severity of illness, as estimated using Sequential Organ Failure Assessment (SOFA) scores,[21] and the related clinical data were recorded upon admission to the ICU and at study entry. The GCS was recorded upon admission to the ICU and at study entry. The cases of organ failure (cardiovascular, respiratory, renal, hepatic, and hematologic), defined as more than 2 points according to SOFA scores,[21] were collected at admission to ICU. The date and reasons for the initiation of MV and mode of artificial airway were recorded. For each patient, the ventilator mode and settings and arterial blood gas analysis, including arterial pH, partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ratio (P/F ratio), and partial pressure of carbon dioxide partial pressure ($PaCO_2$), were recorded under the settings described above. For patients receiving assist/control ventilation (A/C), volume-controlled ventilation (VCV), pressure-controlled ventilation (PCV), and pressure-regulated volume control ventilation (PRVC), the V_T under mandatory ventilation was adapted; for patients receiving biphasic positive airway pressure (BIPAP), the V_T under the high-level pressure was recorded; for patients receiving pressure support ventilation (PSV) and continuous positive airway pressure (CPAP), the V_T of monitoring was adapted; and for patients receiving synchronized intermittent mandatory ventilation (SIMV) combined with PSV, the V_T under mandatory ventilation and pressure support were both recorded and the larger of the two values was adapted. Based on the proportion of mandatory ventilation, we defined three MV mode groups: supported and spontaneous ventilator mode, including PSV and CPAP, was identified as Group 1; partially ventilator mode, including SIMV, A/C, BIPAP, and PRVC, was identified as Group 2; and totally mandatory ventilator mode, including PCV and VCV, was identified as Group 3.

LPV was defined as V_T ≤6 ml/kg of the predicted body weight (PBW) or V_T ≤8 ml/kg of the PBW and peak airway pressure <30 cmH_2O.[1] Sepsis and septic shock were defined according to the American College of Chest Physicians/Society of Critical Care Medicine consensus conference definitions.[22] ARDS was identified according to the berlin definition.[23] The patients were followed up until hospital discharge, death, or 60 days after the day of investigation whichever occurred first. The date of discharge from ICU, prognosis of artificial airway, the Glasgow Outcome Scale (GOS) on the 60th day, duration of MV, and the weaning outcome were documented. On the afternoon of August 10, 2015, a questionnaire concerning the preferred MV mode and settings was sent to the physicians involved in the study, which was anonymous and collected by the investigator at each center. The details are presented in Supplement File 1.

Statistical analysis

Continuous variables were presented as median and interquartile range (IQR) values and compared using the Mann–Whitney *U*-test or Kruskal–Wallis test with Bonferroni's correction. Bonferroni's correction provides a straightforward approach to control the Type I error rate when multiple testing is performed. The adjusted alpha (α) level after Bonferroni's correction was shown as α'. The categorical variables were reported as numbers and percentages and subsequently compared using either Chi-square test or Fisher's exact test when appropriate. Multivariable logistic analysis was used to assess factors that might affect the use of LPV. All variables with a $P < 0.2$ and those which we thought might be associated with the use of LPV were included in the multivariate model. Backward selection based on the likelihood ratio test was used to select the final multivariate model for factors associated with the use of LPV. All analyses were performed using the statistical software package SPSS 21 (SPSS Inc., Chicago, IL, USA). A $P < 0.05$ was considered statistically significant.

Results

We identified 47 ICUs in China, 20 of which were Neurologic ICUs (NICUs). The median number of beds in each ICU was 20 (IQR, 15–26). There were 839 patients in the ICUs of participating hospitals at the time of the present study and the bed occupancy rate was 79.8%; 365 patients were identified with brain injury, and the patient flowchart is shown in Figure 1. A total of 104 patients were enrolled in the study, including 32 patients with traumatic brain injury, 45 with stroke, 11 with hypoxic-ischemic encephalopathy, and 16 with other brain injuries. Moreover, 87 (83.7%) patients were identified with severe brain injury with GCS ≤8 points. The characteristics of the entire cohort were shown in Table 1 and the outcome of patients alive at ICU discharge was shown in Table 2.

Indication for mechanical ventilation and artificial airway

In the present study, the most frequent indication for MV was acute respiratory failure, accounting for 76% of the entire cohort; pneumonia was the most common indication (29.8%), followed by postoperative respiratory failure (21.2%), aspiration (14.4%), trauma (10.6%), sepsis (5.8%), and heart failure (3.8%). Among the patients, 10 (9.6%) were identified with ARDS. There were overlaps among pneumonia, aspiration, trauma, heart failure, and sepsis. An abnormal respiratory rhythm was the second common indication for MV, accounting for 24% of the entire cohort. A total of 66 (63.5%) patients were ventilated using an endotracheal tube and 38 (36.5%) patients were ventilated using a tracheostomy tube. Among the patients who were ventilated with endotracheal tubes, 93.9% tubes were passed through the mouth and 6.1% of the tubes were passed through the nose. Among the 38 patients who were ventilated with tracheostomy tubes, the tracheostomy was performed at a median of 2 days (IQR, 0–9 days) after intubation.

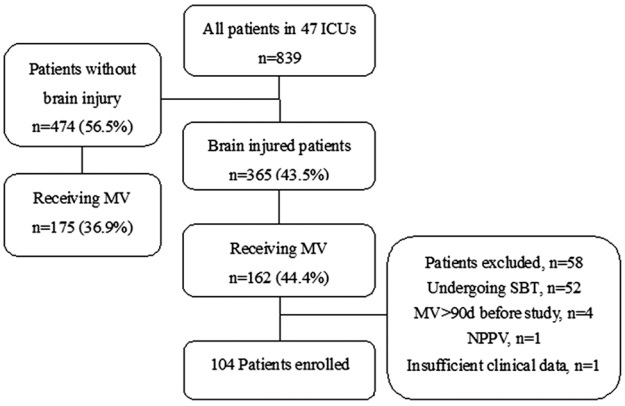

Figure 1: Flowchart of patients into the study. ICU: Intensive Care Unit; MV: Mechanical ventilation; SBT: Spontaneous breathing trial; NPPV: Noninvasive positive pressure ventilation.

Ventilation mode and settings

Among all 104 patients, 48 (46.2%) received SIMV combined with PSV (volume-controlled SIMV 28.8%, pressure-controlled SIMV 17.3%), which was the most frequent mode of ventilation, followed by PSV (18.3%), CPAP (10.6%), A/C (9.6%), PCV (4.8%), VCV (4.8%), BIPAP (2.9%), and PRVC (2.9%). Although mandatory ventilation was the most common method used, the distribution of the ventilator mode was different among patients with different brain injuries ($P = 0.035$).

The median V_T of all patients was set to 8.0 ml/kg (IQR, 7.0–8.9) of the PBW. There was no significant difference among different brain injuries ($P = 0.729$). The details of the ventilator modes and settings among patients with different brain injuries are presented in Table 3. The V_T of patients under partial mandatory ventilation was slightly higher than that of patients receiving supported and spontaneous ventilation (8.3 ml/kg [IQR, 7.5–9.0] vs. 7.4 ml/kg [IQR, 6.4–8.4], $P = 0.025$), accompanied by a higher peak pressure (20 cmH_2O [IQR, 17–24] vs. 15 cmH_2O [IQR, 13–18], $P = 0.001$). Compared with patients receiving supported and spontaneous ventilation, the peak pressure under total mandatory ventilation was higher (15 cmH_2O [IQR, 13–18] vs. 21 cmH_2O [IQR, 18.0–24.5], $P = 0.005$). The details of the ventilator data among different ventilator modes are shown in Table 4. Compared with patients without ARDS, the V_T was slightly lower among patients with ARDS although this value was not statistically significant (8.0 ml/kg [IQR, 7.2–8.9] vs. 7.3 ml/kg [IQR, 6.2–8.0], $P = 0.073$).

Table 1: Baseline characteristics of the patients in this study

Characteristics of all subjects	Traumatic brain injury ($n = 32$)	Stroke ($n = 45$)	Hypoxic-ischemic encephalopathy ($n = 11$)	Others* ($n = 16$)	Total ($n = 104$)
Age, median (IQR), years	51 (40, 68)	58 (48, 69)	47 (37, 84)	55 (37, 63)	55 (46, 67)
Male, *n* (%)	28 (87.5)	37 (82.2)	7 (63.6)	5 (31.3)	77 (74.0)
Height, median (IQR), cm	173.0 (170.0, 175.0)	172.0 (168.0, 175.0)	171.0 (157.0, 175.0)	161.5 (156.3, 171.0)	172.0 (165.0, 175.0)
SOFA score, median (IQR)	8 (6, 9)	7 (5, 9)	12 (10, 12)	7 (4, 10)	8 (6, 10)
GCS, median (IQR)	5 (3, 8)	5 (3, 6)	5 (3, 8)	7 (4, 9)	5 (3, 7)
GCS ≤8, *n* (%)	27 (84.4)	39 (86.7)	9 (81.8)	12 (75.0)	87 (83.7)
Organ failure, *n* (%)	17 (53.1)	28 (62.2)	9 (81.8)	9 (56.3)	63 (60.6)
Arterial blood gas analysis					
pH, median (IQR)	7.45 (7.40, 7.48)	7.46 (7.43, 7.50)	7.41 (7.36, 7.47)	7.47 (7.43, 7.50)	7.46 (7.42, 7.49)
$PaCO_2$, median (IQR), mmHg	35.5 (31.1, 41.8)	33.1 (29.2, 40.3)	36 (29.0, 40.0)	35.5 (30.3, 37.9)	35.0 (30.0, 40.4)
PaO_2/FiO_2 ratio, median (IQR)	312.5 (214.6, 392.4)	262.5 (178.5, 355)	280.0 (128.3, 548.6)	312.8 (231.9, 373.2)	286.3 (201.0, 372.2)
ICU mortality, *n* (%)	6 (18.8)	8 (17.8)	3 (27.3)	1 (6.3)	18 (17.3)
GOS on the 60th day, median (IQR)	3 (2, 3)	2 (2, 3)	2 (1, 4)	2 (2, 3)	3 (2, 3)
Tracheostomy, *n* (%)	19 (59.4)	27 (60.0)	7 (63.6)	10 (62.5)	63 (60.6)

*Other patients included 16 patients, 9 with brain tumor, 3 with central nervous system involved were identified as Sjogren syndrome, drug abuse, and leukoencephalopathy, respectively, two diagnosed as idiopathic epilepsy[1], and two identified as intracranial infection. IQR: Interquartile range; SOFA: Sequential Organ Failure Assessment; GCS, Glasgow Coma Scale; ICU: Intensive Care Unit; GOS: Glasgow Outcome Scale; $PaCO_2$: Partial pressure of carbon dioxide partial pressure; PaO_2: Partial pressure of oxygen; FiO_2: Fraction of inspired oxygen.

The median PEEP level was 5 cmH_2O (IQR, 5–6). All PEEP values were no more than 10 cmH_2O. Patients with hypoxic-ischemic encephalopathy received a higher level of PEEP than did those with traumatic brain injury (6 cmH_2O [IQR, 5–7] vs. 5 cmH_2O [IQR, 4–5], $P = 0.001$). For patients with severe hypoxemia (PaO_2/FiO_2 <100 mmHg), moderate hypoxemia (100≤ PaO_2/FiO_2 <200 mmHg), mild hypoxemia (200≤ PaO_2/FiO_2 <300 mmHg), and P/F ratios higher than 300 mmHg, the PEEP levels were set to 8 cmH_2O (IQR, 7–9), 5 cmH_2O (IQR, 5–7), 5 cmH_2O (IQR, 4–6), and 5 cmH_2O (IQR, 4–5), respectively and there was a significant difference among different levels of hypoxemia ($P = 0.005$). Patients with severe hypoxemia had higher PEEP levels than the others did. In contrast, there was no significant difference among the other groups. A higher level of PEEP was applied for patients with ARDS than for non-ARDS patients (6.6 cmH_2O [IQR, 5–8] vs. 5.0 cmH_2O [IQR, 4–5], $P < 0.05$).

Table 2: Outcome of patients alive at ICU discharge

Outcome	Traumatic brain injury ($n = 26$)	Stroke ($n = 37$)	Hypoxic-ischemic encephalopathy ($n = 8$)	Others* ($n = 15$)	Total ($n = 86$)
MV duration, median (IQR), days	11 (8, 23)	12 (6, 21)	15 (10, 71)	21 (7, 30)	13 (7, 25)
LOS in ICU, median (IQR), days	23 (11, 30)	20 (15, 35)	18 (14, 69)	23 (11, 47)	21 (14, 34)
Patients with weaning, *n* (%)	24 (92.3)	29 (78.4)	4 (50.0)	8 (53.3)	65 (75.6)

*Other patients included 15 patients, 8 with brain tumor, 3 with central nervous system involved were identified as Sjogren syndrome, drug abuse, and leukoencephalopathy, respectively, two diagnosed as idiopathic epilepsy, and two identified as intracranial infection. IQR: Interquartile range; ICU: Intensive Care Unit; MV: Mechanical ventilation; LOS: Length of stay.

Table 3: Ventilator modes and settings among patients with different brain injury

Variables	Traumatic brain injury ($n = 32$)	Stroke ($n = 45$)	Hypoxic-ischemic encephalopathy ($n = 11$)	Others* ($n = 16$)	*P*
Mode, *n* (%)					
Group 1	5 (15.6)	17 (37.8)	1 (9.1)	7 (43.8)	0.035†
Group 2	25 (78.1)	25 (55.6)	8 (72.7)	6 (37.5)	
Group 3	2 (6.3)	3 (6.7)	2 (18.2)	3 (18.8)	
Ventilator data					
V_T, median (IQR), ml/kg	8.0 (6.9, 8.9)	8.0 (7.2, 8.7)	8.3 (6.3, 8.7)	8.0 (7.3, 9.3)	0.729
PEEP, median (IQR), cmH_2O	5 (4, 5)	5 (5, 6)	6 (5, 7)	5 (4, 7)	0.009‡

*Other patients included nine patients with brain tumor, three with central nervous system involved were identified as Sjogren syndrome, drug abuse, and leukoencephalopathy, respectively, two were diagnosed as idiopathic epilepsy and two were identified as intracranial infection; Group 1 of mode included PSV and CPAP; Group 2 of mode included SIMV, A/C ventilation, PRVC and BIPAP; Group 3 of mode included PCV and VCV. V_T: Tidal volume; IQR: Interquartile range; PEEP: Positive end-expiratory pressure. The adjusted alpha level (α′) was 0.008 after Bonferroni's correction. †There was no significant difference in ventilation mode between patients with any two kinds of brain injuries, after Bonferroni's correction ($P_{min} = 0.019 > \alpha'$). ‡There were significant differences in PEEP level between patients with traumatic brain injury and those with hypoxic-ischemic encephalopathy, even after Bonferroni's correction ($P = 0.001 < \alpha'$). PCV: Pressure-controlled ventilation; VCV: Volume-controlled ventilation; SIMV: Synchronized intermittent mandatory ventilation; A/C: Assist/control; PRVC: Pressure-regulated volume control; BIPAP: Biphasic positive airway pressure.

Table 4: Comparisons of ventilator data among different ventilation modes

Variables	Group 1 ($n = 30$)	Group 2 ($n = 64$)	Group 3 ($n = 10$)	*P*
V_T (ml/kg)	7.4 (6.4, 8.4)	8.3 (7.5, 9.0)	7.6 (6.7, 8.3)	0.038*
PEEP (cmH_2O)	5 (4, 5)	5 (5, 6)	5 (5, 6)	0.195
RR of setting (breaths/min)	NA	15 (12, 16)	15 (10, 15)	0.352
RR of monitoring (breaths/min)	20 (15, 22)	16 (13, 20)	15 (12, 15)	0.035†
pH	7.47 (7.44, 7.50)	7.45 (7.41, 7.49)	7.45 (7.26, 7.47)	0.053
$PaCO_2$ (mmHg)	34.0 (29.8, 39.3)	34.5 (29.0, 39.8)	40.8 (33.8, 47.8)	0.095
Ratio PaO_2/FiO_2	265.6 (199.9, 357)	295 (202.6, 392.4)	326.1 (205.4, 373.8)	0.522
Peak pressure (cmH_2O)	15 (13, 18)	20 (17, 24)	21 (18, 25)	0.001‡
Plateau pressure (cmH_2O)	NA	12 (9, 15)	14 (8, 17)	0.660

Data are shown as median (IQR). Group 1 of mode included PSV and CPAP; Group 2 of mode included SIMV, A/C ventilation, PRVC and BIPAP; Group 3 of mode included PCV and VCV. V_T: Tidal volume; PEEP: Positive end-expiratory pressure; RR: Respiratory rate. The adjusted alpha level (α′) was 0.017 after Bonferroni's correction. *There was no significant difference in tidal volume between any two groups, after Bonferroni's correction ($P_{min} = 0.025 > \alpha'$); †There was no significant difference in respiratory rate between any two groups, after Bonferroni's correction ($P_{min} = 0.021 > \alpha'$); ‡There were significant differences in Peak pressure between Groups 1 and 2, as well as Groups 1 and 3, even after Bonferroni's correction ($P = 0.001 < \alpha'$, $P = 0.005 < \alpha'$, respectively). IQR: Interquartile range; CPAP: Continuous positive airway pressure; PCV: Pressure-controlled ventilation; VCV: Volume-controlled ventilation; SIMV: Synchronized intermittent mandatory ventilation; A/C: Assist/control; PRVC: Pressure-regulated volume control; BIPAP: Biphasic positive airway pressure; $PaCO_2$: Partial pressure of carbon dioxide partial pressure; PaO_2: Partial pressure of oxygen; FiO_2: Fraction of inspired oxygen. NA: Not available.

Lung-protective ventilation practice

A total of 50 (48.1%) patients received LPV. The comparison between patients who received LPV and those who did not revealed that there was no significant difference in baseline characteristics, ventilator mode, PEEP setting, arterial pH, P/F ratio, or $PaCO_2$. It seemed that patients who received LPV had a slightly higher respiratory rate (RR) than those who did not (18 breaths/min [IQR, 15–22] vs. 16 breaths/min [IQR, 12–19], P = 0.02]. The distribution of the ventilator mode between LPV and non-LPV was different (P = 0.01). The details are shown in Table 5. According to the multivariable logistic regression analysis (covariates entered: age, gender, height, SOFA and GCS at admission to ICU, arterial pH, P/F ratio, $PaCO_2$, ventilator mode, PEEP setting, RR of monitoring, and ICU category), age and gender were associated with the practice of LPV; compared with partially mandatory ventilation (Group 2), supported and spontaneous ventilation (Group 1) was associated with the use of LPV (odds ratio 5.401, 95% confidence interval 1.878–15.536, P = 0.002). The details are shown in Table 6. Among older patients (≥60 years), 26 (59.1%) individuals received LPV, but among younger patients (<60 years), 24 (40%) individuals received LPV, suggesting that older patients were more likely to receive LPV although there was no significant difference (P = 0.054).

Outcomes

There was no significant difference in ICU mortality among patients with different brain injuries (P = 0.548). The median GOS of the entire cohort was 3 points (IQR, 2–3), suggesting that most ventilated patients with brain injury could not live alone. A total of 63 (60.6%) patients received tracheostomy during their stay in the ICU. For patients who were alive upon discharge from the ICU, the median MV duration was 13 days (IQR, 7–25 days), the median length of stay in the ICU was 21 days (IQR, 14–34 days), and there was no difference among patients with different brain injuries in either MV duration or length of ICU stay (P = 0.530, P = 0.701, respectively). The details are shown in Table 2.

Questionnaire for physicians

On the afternoon of August 10, 2015, a questionnaire of preferred ventilator mode and settings for patients with brain injury was sent to the doctors in charge of the patients enrolled in the present study. Three questionnaires were delivered to each center; 25 questionnaires were not completed and 116 (82.3%) questionnaires were analyzed. Consistent with the results of the present study,

Table 5: Comparison between patients received lung-protective ventilation and those did not

Variables	LPV (n = 50)	Non-LPV (n = 54)	P
Age, median (IQR), years	60 (47, 69)	52 (44, 65)	0.164
Male, n (%)	40 (80.0)	37 (68.5)	0.182
Height, mean (range), cm	172.5 (165, 175)	170 (160, 175)	0.073
SOFA score, median (IQR)	7 (6, 9)	8 (6, 10)	0.441
GCS, median (IQR)	5 (4, 7)	5 (3, 7)	0.175
pH, median (IQR)	7.46 (7.43, 7.48)	7.45 (7.41, 7.49)	0.523
$PaCO_2$, median (IQR), mmHg	35.4 (31.0, 40.0)	34.5 (29.0, 41.0)	0.410
Ratio PaO_2/FiO_2, median (IQR)	273.1 (197.3, 360.3)	296.3 (221.9, 405.0)	0.081
Patients in NICU, n (%)	27 (54.0)	31 (57.4)	0.727
Brain injury category			0.573
Traumatic brain injury, n (%)	14 (28.0)	18 (33.3)	
Stroke, n (%)	25 (50)	20 (37)	
Hypoxic-ischemic encephalopathy, n (%)	5 (10.0)	6 (11.1)	
Others*, n (%)	6 (12.0)	10 (18.5)	
Ventilator mode, n (%)			0.010
Group 1	20 (40.0)	10 (18.5)	
Group 2	24 (48.0)	40 (74.1)	
Group 3	6 (12.0)	4 (7.4)	
RR of monitoring, median (IQR), breaths/min	18 (15, 22)	16 (12, 19)	0.020
PEEP, median (IQR), mmHg	5.0 (4.8, 6.0)	5.0 (4.8, 6.0)	0.585
LOS in ICU, median (IQR), days	21.0 (12.8, 34.0)	18.0 (10.8, 28.5)	0.309
Mortality, n (%)	9 (14.5)	9 (21.4)	0.432
MV duration, median (IQR), days	14.0 (7.5, 25.5)	12.0 (7.0, 24.0)	0.537

*Other patients included 16 patients, 9 with brain tumor, 3 with central nervous system involved were identified as Sjogren syndrome, drug abuse and leukoencephalopathy, respectively, 2 diagnosed as idiopathic epilepsy, and two identified as intracranial infection. LPV: Lung-protective ventilation; IQR: Interquartile range; SOFA: Sequential Organ Failure Assessment; GCS: Glasgow Coma Scale; NICU: Neurologic Intensive Care Unit; Group 1 of mode included PSV and CPAP; Group 2 of mode included SIMV, A/C ventilation, PRVC ventilation and BIPAP; Group 3 of mode included PCV and VCV; RR: Respiratory rate; PEEP: Positive end-expiratory pressure; LOS: Length of stay; MV: Mechanical ventilation. PCV: Pressure-controlled ventilation; VCV: Volume-controlled ventilation; SIMV: Synchronized intermittent mandatory ventilation; A/C: Assist/control; PRVC: Pressure-regulated volume control; BIPAP: Biphasic positive airway pressure; CPAP: Continuous positive airway pressure; $PaCO_2$: Partial pressure of carbon dioxide partial pressure; PaO_2: Partial pressure of oxygen; FiO_2: Fraction of inspired oxygen.

Table 6: Association of factors with the use of lung-protective ventilation by multivariable logistic regression analysis

Variables	*OR* (95% *CI*)	*P*
Age	1.030 (1.001–1.059)	0.039
Gender	2.847 (1.014–7.995)	0.047
Ventilator mode		
Group 1	5.401 (1.878–15.536)	0.002
Group 3	4.284 (0.934–19.654)	0.095

The model is adjusted for height, SOFA and GCS at admission to ICU, arterial pH, PaO_2/FiO_2, $PaCO_2$, ventilator mode, PEEP, RR of monitoring and ICU category. *CI*: Confidence interval; Group 1 of mode included PSV and CPAP; Group 3 of mode included PCV and VCV. SOFA: Sequential Organ Failure Assessment; GCS: Glasgow Coma Scale; ICU: Intensive Care Unit; PEEP: Positive end-expiratory pressure; RR: Respiratory rate; PSV: Pressure support ventilation; CPAP: Continuous positive airway pressure; PCV: Pressure-controlled ventilation; VCV: Volume-controlled ventilation; *OR*: Odds ratio; $PaCO_2$: Partial pressure of carbon dioxide partial pressure; PaO_2: Partial pressure of oxygen; FiO_2: Fraction of inspired oxygen.

SIMV (60.3%) was the most frequent ventilator mode, followed by PCV (13.8%), VCV (10.3%), PSV (8.6%), and others (7%). For neurologic patients, regardless of the presence of ARDS, the V_T of 6–8 ml/kg was preferred to 8–10 ml/kg (58.6% vs. 41.4%, $P = 0.012$). There were more physicians in the general ICU preferring to practice LPV, compared with those in NICU (64.5% vs. 47.5%, $P = 0.078$), although the difference was not significant. A total of 51 (44%) doctors preferred a relatively lower PEEP level of <5 cmH_2O whereas other physicians preferred to set the PEEP level between 5 and 10 cmH_2O. None of the physicians set the PEEP level above 10 cmH_2O. For patients with severe refractory hypoxemia, the recruitment maneuver was the most frequently used, followed by the prone position. Extracorporeal membrane oxygenation was rarely used.

Discussion

In this multicenter, 1-day, cross-sectional study, MV mode, ventilator data, and the practice of LPV among brain-injured patients in the ICUs of China were described. To the best of our knowledge, studies describing the practice of LPV among neurologic patients were rare.[17-19]

In the present study, the most frequent indication for MV was acute respiratory failure, similar to nonneurologic patients, but abnormal respiratory rhythm and aspiration were more common.[24,25] Perhaps further attention should be devoted to the consciousness and airway protection of patients with brain injury. During the study period, 36.5% of the patients were ventilated using a tracheostomy tube, which was slightly higher than the number of patients treated in the international study by Esteban *et al*., and the tracheostomy was performed at a median of 2 days (IQR, 0–9) after MV, in contrast to the treatment for 11 days (IQR, 5–19) described by Esteban *et al*.[25] For patients with brain injury, physician preferred early tracheostomy (performed within 10 days after initiation of laryngeal intubation). However, whether early tracheostomy could reduce the duration of MV, the incidence of ventilation-associated pneumonia and hospital mortality in critically ill patients remains controversial.[26,27]

In the present study, SIMV was the most frequent ventilator mode for patients with brain injury. In contrast to the recent studies, A/C was the most common and SIMV dramatically declined.[3,11] More patients received LPV than in the study of Kahn *et al*. among patients with subarachnoid hemorrhage and identified as having acute lung injury (48.1% vs. 30.0%).[28] According to the results of the multivariable logistic analysis, older and male patients were associated with the use of LPV. There was a significant difference in height between males and females (175 cm [IQR, 170–175] vs. 160 cm [IQR, 155–160], $P < 0.001$). That is, taller patients with higher PBW, as calculated based on the height, were more likely to receive LPV, which likely indicates that the LPV was not deliberately set but varied in accordance with the height of the patient. Compared with partially mandatory ventilation, supported and spontaneous ventilation was associated with the use of LPV. Patients receiving supportive and spontaneous ventilation were at the later stages of MV compared with those receiving mandatory ventilation during the present study (7.5 days [IQR, 3.0–18.5] vs. 4.5 days [IQR, 2.0–11.5], $P = 0.066$). Among the thirty patients receiving supportive and spontaneous ventilation, 19 were ventilated with PSV with a median supportive pressure of 5 cmH_2O [IQR, 4–6] and 11 were ventilated with CPAP. We speculated that supportive and spontaneous MV might be performed during the late stages of MV and that the supportive level was lowered to initiate weaning. Therefore, the V_T was lower in patients receiving supportive MV. The results of the present study indicated that the use of LPV in the enrolled patients might represent the characteristics of the patient without a deliberate setting by physicians.

Between patients receiving LPV and those who did not, there was no significant difference in the P/F ratio or $PaCO_2$ or in the outcomes, including ICU mortality, length of stay in ICU, and MV duration, in the present study. Thus, we concluded that LPV might be safe for patients with brain injury. Although a relatively higher PEEP was applied for patients with severe hypoxemia, the PEEP level applied in neurologic patients was lower than that in nonneurologic patients in a previous study.[11] First, the median P/F ratio of patients in the present study was 250 mmHg higher, indicating a relatively improved lung condition, which did not require a high level of PEEP. Second, considering that the reduction of cerebral blood flow might be caused by high PEEP levels, physicians prefer relatively lower PEEP levels,[8,9] consistent with the results of the questionnaire. The median V_T was similar to the results of the study in Poland[24] but was lower than that reported in the previous study.[25]

There are several limitations in this study. First, this study was a 1-day point study, which could not represent the entire cohort of ventilated patients with brain injury. Second, only 104 patients were enrolled in the present study and the small sample might affect the results. Third, we did not collect the data for nonbrain-injured patients in participating ICUs during the study period. Moreover, we did not record the comorbidity of the enrolled patients, which might affect the evolution of the disease severity; thus, the relationship between hospital mortality and ventilator settings, including V_T and PEEP, was not analyzed. Furthermore, we did not record the lung complication, such as ventilator-associated pneumonia and pneumothorax, or the use of sedative and analgesic drugs, which might also affect the MV mode.

In conclusion, among brain-injured patients in China, SIMV was the most frequent ventilation mode. Nearly one-half of brain-injured patients received LPV. Patients under supportive and spontaneous ventilation were more likely to receive LPV. In the present study, the use of LPV in the enrolled patients might represent the characteristics of the patients not the deliberately settings of physicians.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

Acknowledgments

We would like to thank Prof. Yi-Long Wang (Clinical Trial and Research Center, Beijing Tiantan Hospital, Capital Medical University) and Prof. Hong-Qiu Gu (Department of Neurology, Beijing Tiantan Hospital, Capital Medical University) for their valuable suggestions on statistical analysis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342:1301-8. doi: 10.1056/NEJM200005043421801.
2. Villar J, Kacmarek RM, Pérez-Méndez L, Aguirre-Jaime A. A high positive end-expiration pressure, low tidal volume ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: A randomized, controlled trial. Crit Care Med 2006;34:1311-8. doi: 10.1097/01.CCM.0000215598.84885.01.
3. Esteban A, Frutos-Vivar F, Muriel A, Ferguson ND, Peñuelas O, Abraira V, *et al.* Evolution of mortality over time in patients receiving mechanical ventilation. Am J Respir Crit Care Med 2013;188:220-30. doi: 10.1164/rccm.201212-2169OC.
4. Serpa Neto A, Cardoso SO, Manetta JA, Pereira VG, Espósito DC, Pasqualucci Mde O, *et al.* Association between use of lung-protective ventilation with lower tidal volumes and clinical outcomes among patients without acute respiratory distress syndrome: A meta-analysis. JAMA 2012;308:1651-9. doi: 10.1001/jama.2012.13730.
5. Sutherasan Y, Vargas M, Pelosi P. Protective mechanical ventilation in the non-injured lung: Review and meta-analysis. Crit Care 2014;18:211. doi: 10.1186/cc13778.
6. Neto AS, Simonis FD, Barbas CS, Biehl M, Determann RM, Elmer J, *et al.* Lung-protective ventilation with low tidal volumes and the occurrence of pulmonary complications in patients without acute respiratory distress syndrome: A systematic review and individual patient data analysis. Crit Care Med 2015;43:2155-63. doi: 10.1097/CCM.0000000000001189.
7. Ladha K, Vidal Melo MF, McLean DJ, Wanderer JP, Grabitz SD, Kurth T, *et al.* Intraoperative protective mechanical ventilation and risk of postoperative respiratory complications: Hospital based registry study. BMJ 2015;351:h3646. doi: 10.1136/bmj.h3646.
8. Muench E, Bauhuf C, Roth H, Horn P, Phillips M, Marquetant N, *et al.* Effects of positive end-expiratory pressure on regional cerebral blood flow, intracranial pressure, and brain tissue oxygenation. Crit Care Med 2005;33:2367-72. doi: 10.1097/01.CCM.0000181732.37319.DF.
9. Doblar DD, Santiago TV, Kahn AU, Edelman NH. The effect of positive end-expiratory pressure ventilation (PEEP) on cerebral blood flow and cerebrospinal fluid pressure in goats. Anesthesiology 1981;55:244-50.
10. Elmer J, Kahn J. Implementing evidence-based practice in the neuroscience intensive care unit. Crit Care 2014;18:303. doi: 10.1186/cc13740.
11. Pelosi P, Ferguson ND, Frutos-Vivar F, Anzueto A, Putensen C, Raymondos K, *et al.* Management and outcome of mechanically ventilated neurologic patients. Crit Care Med 2011;39:1482-92. doi: 10.1097/CCM.0b013e31821209a8.
12. Elmer J, Hou P, Wilcox SR, Chang Y, Schreiber H, Okechukwu I, *et al.* Acute respiratory distress syndrome after spontaneous intracerebral hemorrhage. Crit Care Med 2013;41:1992-2001. doi: 10.1097/CCM.0b013e31828a3f4d.
13. Marhong JD, Ferguson ND, Singh JM. Ventilation practices in subarachnoid hemorrhage: A cohort study exploring the use of lung protective ventilation. Neurocrit Care 2014;21:178-85. doi: 10.1007/s12028-014-0014-8.
14. Mascia L, Zavala E, Bosma K, Pasero D, Decaroli D, Andrews P, *et al.* High tidal volume is associated with the development of acute lung injury after severe brain injury: An international observational study. Crit Care Med 2007;35:1815-20. doi: 10.1097/01.CCM.0000275269.77467.DF.
15. Fuller BM, Mohr NM, Drewry AM, Carpenter CR. Lower tidal volume at initiation of mechanical ventilation may reduce progression to acute respiratory distress syndrome: A systematic review. Crit Care 2013;17:R11. doi: 10.1186/cc11936.
16. Gajic O, Frutos-Vivar F, Esteban A, Hubmayr RD, Anzueto A. Ventilator settings as a risk factor for acute respiratory distress syndrome in mechanically ventilated patients. Intensive Care Med 2005;31:922-6. doi: 10.1007/s00134-005-2625-1.
17. Petridis AK, Doukas A, Kienke S, Maslehaty H, Mahvash M, Barth H, *et al.* The effect of lung-protective permissive hypercapnia in intracerebral pressure in patients with subarachnoid haemorrhage and ARDS. A retrospective study. Acta Neurochir (Wien) 2010;152:2143-5. doi: 10.1007/s00701-010-0761-z.
18. Roquilly A, Cinotti R, Jaber S, Vourc'h M, Pengam F, Mahe PJ, *et al.* Implementation of an evidence-based extubation readiness bundle in 499 brain-injured patients. A before-after evaluation of a quality improvement project. Am J Respir Crit Care Med 2013;188:958-66. doi: 10.1164/rccm.201301-0116OC.
19. Sutherasan Y, Peñuelas O, Muriel A, Vargas M, Frutos-Vivar F, Brunetti I, *et al.* Management and outcome of mechanically ventilated patients after cardiac arrest. Crit Care 2015;19:215. doi: 10.1186/s13054-015-0922-9.
20. Maas AI, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. Lancet Neurol 2008;7:728-41. doi: 10.1016/S1474-4422(08)70164-9.
21. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, *et al*. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 1996;22:707-10.
22. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, *et al*. Definitions for sepsis and organ failure and guidelines for the

use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/ Society of Critical Care Medicine. Chest 1992;101:1644-55.
23. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, *et al.* Acute respiratory distress syndrome: The Berlin Definition. JAMA 2012;307:2526-33. doi: 10.1001/jama.2012.5669.
24. Kübler A, Maciejewski D, Adamik B, Kaczorowska M. Mechanical ventilation in ICUs in Poland: A multi-center point-prevalence study. Med Sci Monit 2013;19:424-9. doi: 10.12659/MSM.883930.
25. Esteban A, Anzueto A, Alía I, Gordo F, Apezteguía C, Pálizas F, *et al.* How is mechanical ventilation employed in the intensive care unit? An international utilization review. Am J Respir Crit Care Med 2000;161:1450-8. doi: 10.1164/ajrccm.161.5.9902018.
26. Griffiths J, Barber VS, Morgan L, Young JD. Systematic review and meta-analysis of studies of the timing of tracheostomy in adult patients undergoing artificial ventilation. BMJ 2005;330:1243. doi: 10.1136/bmj.38467.485671.E0.
27. Andriolo BN, Andriolo RB, Saconato H, Atallah ÁN, Valente O. Early versus late tracheostomy for critically ill patients. Cochrane Database Syst Rev 2015;1:CD007271. doi: 10.1002/14651858.CD007271.pub3.
28. Kahn JM, Caldwell EC, Deem S, Newell DW, Heckbert SR, Rubenfeld GD. Acute lung injury in patients with subarachnoid hemorrhage: Incidence, risk factors, and outcome. Crit Care Med 2006;34:196-202. doi: 10.1097/01.CCM.0000134835.05161.B6.

Supplement File 1

Questionnaire of mechanical ventilation practice among patients with brain injury

1. Gender: □ Male □ Female

2. Category of the ICU: □ NICU □ General ICU

3. For patients with brain injury, which is your preferred mechanical ventilation mode?
   - □ Volume-controlled ventilation
   - □ Pressure-controlled ventilation
   - □ Synchronized intermittent mandatory ventilation
   - □ Biphasic positive airway pressure
   - □ Pressure support ventilation
   - □ Continuous positive airway pressure

4. For patients with brain injury, which are your preferred mechanical ventilation settings?
   4.1 Tidal volume
   - □ 6–8 ml/kg of the predicted body weight
   - □ 8–10 ml/kg of the predicted body weight
   - □ >10 ml/kg of the predicted body weight

   4.2 Positive end-expiratory pressure
   - □ <5 cmH_2O
   - □ 5–10 cmH_2O
   - □ 10–15 cmH_2O
   - □ >15 cmH_2O

5. For patients with severe refractory hypoxemia, which procedures would you do?
   - □ Recruitment maneuver
   - □ Prone position
   - □ Extracorporeal membrane oxygenation
   - □ High-frequency oscillatory ventilation.