The Incidence and Outcome of Intraoperative Hypotension in Traumatic Brain Injured Patients Reported by an Alternative Definition of Hypotension: A Prospective Cohort Study A Preliminary Report

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Background: *Hypotension is a major risk factor of morbidity and mortality in traumatic brain injured patients. According to the Brain Trauma Foundation Guideline (2007), hypotension is defined as systolic blood pressure (SBP) lower than 90 mmHg. However, some authors suggested that one absolute number could not be suitable to apply for all patients. In the present study, we had set the MAP lower than 20% from the baseline (preoperative) blood pressure as an alternative definition for hypotension. We reported the incidence of perioperative hypotension in regard to the traditional definition of hypotension (SBP lower than 90 mmHg) and an alternative definition of hypotension.*

Objective: *To identify the blood pressure value that can be used as a surrogate to predict the 48-hour postoperative mortality of adult traumatic brain injured patients.*

Material and Method: *We conducted a prospective cohort study. One hundred adult, traumatic brain-injured patients had been recruited. All patients were scheduled for emergency intracranial surgery. The first, in-operating room, recorded blood pressure and heart rate had been listed as their baseline vital signs. The occurrence of hypotension and the duration of hypotension in according to the traditional and an alternative definition had been recorded. The mortality rate was assessed at 48 hours postoperatively.*

Results: *For the traditional definition of hypotension (SBP lower than 90 mmHg), the incidence of hypotension during the induction period was 22%. The mean duration of hypotension was 11±6 minutes. The incidence of hypotension during the intraoperative period was 33%. The mean duration of hypotension was 24±19 minutes. For the alternative definition of hypotension (MAP lower than 20% from baseline), the incidence of hypotension during the induction period was 58%. The mean duration of hypotension was 19±15 minutes. The incidence of hypotension during the intraoperative period was 67%. The mean duration of hypotension was 77±69 minutes. The overall mortality rate was 10%.*

Conclusion: *The duration of intraoperative SBP lower than 90 mmHg was a significant predictor of postoperative mortality in TBI patients. The MAP reduction greater than 20% from baseline did not accurately predict the cerebral well-being so long as the baseline blood pressure was not validated.*

Keywords: *Intraoperative hypotension, Traumatic brain injury, Incidence, Outcome, Morbidity, Mortality*

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Traumatic brain injury (TBI) is a major cause of permanent morbidity and mortality in all age-groups people. The overall annual rates of TBI were significantly higher in men compared to women[1]. Long-term outcome of the injured-brain patients depend on the severity of the primary impact and secondary damage, which includes hypoxia, hypercarbia, hypertension, hypotension, hyperglycemia, hypoglycemia, and hyperthermia[2,3]. Prevention of the secondary brain injury, especially in the pre-hospital period, may improve the survival rate and outcomes[3]. One of the recommendation of the Brain Trauma Foundation guidelines is the prevention of hypotension [defined as systolic blood pressure (SBP) lower than 90 mmHg] after TBI (Class II evidence)[3]. While the general recommendation of mean

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arterial pressure (MAP) maintenance is within the 20% range of the preoperative baseline pressure[4]. Increasing evidence suggests SBP lower than 90 mmHg indicates a late sign of circulatory insufficiency and impending hypovolemic shock[5,6]. Recently, hypotension had been redefined to a higher absolute number of 110 mmHg[5,7]. However, the arbitrary solitary number is not suitable to apply for all patients, specifically chronic hypertension, poor-control hypertension, and post-trauma conditions. The purpose of the present study was to report the incidence of perioperative hypotension defined by SBP lower than 90 mmHg, and the MAP lower than 20% of the baseline blood pressure, and the postoperative mortality. Accordingly, the correlation between each hypotensive definition and mortality rate was analyzed and reported. We hypothesized that the MAP lower than 20% from baseline pressure will predict the postoperative mortality better and earlier than the SBP of lower than 90 mmHg.

Material and Method

We conducted a prospective cohort, single-center study of the moderate to severe TBI patients. The primary objective was to determine the incidence of perioperative hypotension defined by SBP lower than 90 mmHg, and the MAP lower than 20% of the baseline blood pressure. The secondary objective was to assess the association of each hypotensive definition and mortality rates at 48-hour after intracranial surgery.

All adult patients (age older than18 years) with moderate to severe TBI (defined as the GCS score of less than 13) admitted between January and December 2014 were included. They all scheduled for emergency craniotomy. Because of a decreased level of consciousness, written informed consent to participate in the study were from the patients' first-degree relative. Patients who were (1) multiple injuries, (2) pregnant women, (3) graded as American Society of Anesthesiologists (ASA) classification V, (4) penetrating head injury, (5) dead on arrival, and (6) admitted in the neuro-intensive care unit (N-ICU) for supportive treatment or inoperable cases were excluded. We excluded the patients with multiple injuries and penetrating head injury because they might have severe cardiovascular depression[8,9].

The study protocol was approved by the Ethical Committee (EC), Faculty of Medicine, Chiang Mai University. When arrival to the OR, all patients were monitored by a non-invasive blood pressure, electrocardiogram, and oxygen saturation. The first OR recorded BP was used as the baseline BP. The arterial catheter was inserted at the radial artery of the appropriate hand under local anesthesia before the anesthetic induction. Types and dosage of induction agent, muscle relaxant, opioid, and technique of anesthetic maintenance were regulated per the attending anesthesiologists. The central venous catheter insertion was considered case-by-case. Blood pressure (from the arterial catheter), heart rate, and oxygen saturation were recorded in every 5-minute period throughout the operation.

Sample size calculation

Manley et al reported the mortality rate of 65% among the severe TBI patients who experienced hypotension (SBP lower than 90 mmHg) while they were in the emergency department (ED)[10]. We expected that the MAP lower than 20% of the baseline BP, recognized as an alternative cut-off point of early treatment for hypotension in moderate to severe TBI, should decrease the mortality rate to less than 50%. For a two-sided test to compare the two proportions at 95% confidence interval, overall, we needed n = 182 to achieve 80% power.

Results

During the one year period, 100 patients were enrolled. The demographic data were shown in Table 1.

Table 1. Demographic data

Demographic parameters	Results (n)
Age (mean $\pm$ SD)	42$\pm$16
Age range	19 to 84
Male	84
ASA physical status	
2E	5
3E	77
4E	16
5E	2
Diagnosis	
Epidural hematoma	44
Subdural hematoma	33
Intracerebral hemorrhage	4
Others	19
Preoperative GCS	
8 to 12	31
<8	69

ASA = American Society of Anesthesiologists; GCS = Glasgow Coma Scale Score

During the induction period, twenty-two patients experienced at least one episode of SBP lower than 90 mmHg. The mean duration was 11±6 minutes. Fifty-eight patients experienced at least one episode of MAP lower than 20% from baseline, the mean duration was 19±14 minutes.

During the intraoperative period, sixty-seven patients experienced MAP lower than 20% from baseline compared to 33 patients who had SBP lower than 90 mmHg. The mean duration was 77±69 minutes (MAP lower than 20% from baseline) compared to 23±19 minutes.

Possible associated factors of intraoperative hypotension included blood loss, fluid replacement, and blood transfusion. They are summarized in Table 2.

The patients who had the intraoperative SBP lower than 90 mmHg, received greater blood transfusion than those who had the MAP lower than 20% from baseline (odd ratio 4.39, 95% CI 1.5 to 12.5, $p = 0.006$). Overall, fifty-eight patients required intraoperative blood transfusion. The average volume of blood transfusion was 604±371 ml. Preoperative GCS lower than 8 increased the occurrence of intraoperative hypotension (OR = 4.2, 95% CI 1.1 to 15.9, $p = 0.03$). The mortality rate within 48 hours postoperatively was 10%. The odd ratio of hypotension and mortality rate are presented in Table 3.

Odd ratio of patients who had intraoperative SBP lower than 90 mmHg is 12, compared to those who had the intraoperative MAP lower than 20% from baseline (95% CI 1.96 to 73, $p = 0.007$). Univariate analysis showed that preoperative GCS lower than 8 ($p = 0.001$), intraoperative blood loss ($p = 0.014$), intraoperative SBP lower than 90 mmHg ($p = 0.005$), and duration of intraoperative SBP lower than 90 mmHg ($p = 0.005$) were significantly predictive factors of 48-hour postoperative mortality. Hypotension during the induction period did not increase the mortality rate ($p = 0.157$). However, multivariate analysis showed that only a preoperative GCS lower than 8 was a significant risk of postoperative mortality ($p = 0.004$).

Among the survivals (n = 90), 70 patients (87.5%) experienced at least one episode of hypotension defined either by SBP lower than 90 mmHg or MAP lower than 20% from baseline. Nevertheless, all patients who died within 48-hour postoperatively had at least one hypotensive episode during the operation.

Discussion

The present study is a preliminary report of an ongoing research. The data of 100 recruited TBI patients were summarized. The 48-hour mortality rate was 10%. Intraoperative SBP lower than 90 mmHg was a major risk factor of postoperative death. Other factors

Table 2. Associated factors of intraoperative hypotension

Associated factors	SBP <90 mmHg			MAP <20% from baseline		
	Yes (n = 33)	No (n = 67)	*p*-value	Yes (n = 67)	No (n = 33)	*p*-value
Blood loss (ml)	1,406±249	643±66	<0.001	1,003±136	675±111	0.120
Fluid replacement (ml)	3,525±255	2,230±141	<0.001	2,842±161	2,283±260	0.060
Blood transfusion (n, %)	27 (82)	31 (46)	0.001	44 (66)	14 (42)	0.027
Blood transfusion (ml)	746±65	480±64	0.005	638±50	496±126	0.220

SBP = systolic blood pressure; MAP = mean arterial pressure

Table 3. The odd ratio of mortality rate at 48-hour postoperatively of each definition of hypotension

Definition of hypotension	Odd ratio	95% confidence interval	*p*-value
SBP <90 mmHg, induction	2.66	0.68 to 10.4	0.160
MAP <20%, induction	1.09	0.29 to 4.15	0.890
SBP <90 mmHg, intraop	10.40	2.06 to 52.4	0.005
MAP <20%, intraop	2.10	0.42 to 10.5	0.360

included preoperative GCS lower than 8, intraoperative blood loss, and duration of intraoperative SBP lower than 90 mmHg.

Intraoperative blood pressure maintenance to achieve the cerebral well-being, especially in traumatic brain injured patients, is inconclusive. According the Brain Trauma Foundation (BTF) recommendation, SBP lower than 90 mmHg should be avoided to prevent cerebral hypo-perfusion. Frequently, the optimal intraoperative blood pressure maintenance is referred to a percentage reduction from baseline BP[11,12]. However, a preoperative BP of traumatic brain injured patients, taken at the operating room or at the emergency room, is not a good approximation of baseline BP prior to the injury. Existing evidence suggested that the average BPs recorded during ambulatory clinic visits are reasonable representation of the typical waking BPs in the patients' population[13]. Nevertheless, we could not obtain the recorded BP preceding the injury because of the emergency situation. Some patients presented to the hospital for the first time, with no previously recorded BPs. Likewise, the presenting BP after the injury might overestimate the actual baseline BPs because of the sympathetic stimulation. The preoperative BPs of some decompensated patients might be lower than the real baseline BPs. We decided to use the MAP because it is of greater relevance to cerebral perfusion pressure than SBP[14].

For the solitary number idea, Berry et al reported the age-adjusted optimal SBP to define hypotension[7]. The results showed that for TBI patients, aged 15 to 49 years and 70 years and older, hypotension was optimally defined as SBP less than 110 mm Hg. For TBI patients, aged 50 to 69 years, hypotension was defined as SBP less than 100 mmHg. However, Edwards et al found that the optimal definition of hypotension was SBP of 140 mmHg for patients 70 years and older[6]. Fuller et al studied the association between the admission SBP and mortality rate in TBI patients, reported case-mix adjusted odds of death were 1.5 times greater at lower than 120 mmHg, doubled at lower than 100 mmHg, tripled at lower than 90 mmHg, and six times greater at SBP lower than 70 mmHg, $p<0.01$[15]. We agree with Fuller that, for TBI studies, we should consider SBP as a continuous variable rather than a dichotomous variable.

To our knowledge, this is the report that attempts to re-consider hypotension cut-off value in TBI patients. One of the limitations of our study was the unfeasibility to obtain the actual baseline blood pressure. We did not analyze the effect of age-group to hypotension and mortality rate. However, we adjusted age for the multivariate analysis. Regarding the research question, the observational study design is the only reasonable method. While the experimental study investigating the relationship between hypotension and mortality rate seems unethical. The overall 182 subjects are required for the internal validity and the strength of causal inference. However, the number of sample size was derived from the referenced article that the mortality rate obtained at the ED rather than at the 48-hour postoperatively as in the present study protocol[10].

In summary, the results of the present study support the occurrence and duration of intraoperative SBP lower than 90 mmHg significantly associated with the 48-hour postoperative mortality. To use the MAP percentage reduction from baseline, the baseline values must be validated and accurately reflect the blood pressure prior to the injury. For future TBI patients' recruitment, the SBP must be treated as a continuous variable rather than a dichotomous value of greater or lower than 90 mmHg.

What is already known on this topic?

According to the recommendation of the Brain Trauma Foundation (BTF) Guidelines (2007), hypotension [defined as systolic blood pressure (SBP) lower than 90 mmHg] after TBI should be avoided (Class II evidence). Recently, the definition of hypotension in

Table 4. Episodes and duration of intraoperative hypotension of each definition

Intraoperative events	SBP <90 mmHg	MAP <20% of baseline
Number of observation (n)	33	67
Episodes (mean ± SD)	1.60±1.05	4.0±8.06
Episodes (min-max)	1 to 5	1 to 56
Duration, minutes (mean ± SD)	24±19	77±69
Duration, minutes (min-max)	5 to 65	5 to 320

TBI patients has been re-considered to a higher value.

What this study adds?

We reported the incidence of perioperative hypotension, based on the definition of SBP lower than 90 mmHg and MAP lower than 20% from baseline, as well as the 48-hour postoperative mortality. We found the incidence and duration of hypotension, defined by MAP was significantly greater and longer than that reported based on the SBP. However, the result showed that intraoperative SBP lower than 90 mmHg was a significant predictor of postoperative mortality. Even MAP is relevant to cerebral perfusion pressure; the percentage reduction from baseline was not suitable to be a prognosticator of TBI mortality so long as the baseline blood pressure did not represent the real value of individual patient prior to the injury.

What is/are the implication(s) for public health practice?

To improve the outcome and decrease the mortality rate in TBI adult patients, the definition of hypotension and the cut point value to be treated should be re-considered. MAP represents the adequacy of cerebral perfusion pressure. Maintenance MAP within the 20% range from baseline is reasonably applied to the new cut point to be treated in TBI patients. However, the baseline BP should be validated to represent the real pressure of individual patient prior to the injury.

Potential conflicts of interest

None.

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อุบัติการณ์และผลลัพธ์ของการเกิดภาวะความดันโลหิตต่ำในผู้ป่วยที่ได้รับการบาดเจ็บต่อสมองรายงานตามนิยามทางเลือกของภาวะความดันโลหิตต่ำ

ปฐมพร ปิ่นอ่อน, ภูริพงศ์ จันทิมา, เกศกนก ศรีวิทะ

ภูมิหลัง: ภาวะความดันโลหิตต่ำเป็นปัจจัยสำคัญที่เพิ่มความเสี่ยงต่อภาวะทุพพลภาพและอัตราการเสียชีวิตในผู้ป่วยที่ได้รับบาดเจ็บต่อสมองทั้งนี้ในปี พ.ศ. 2550 Brain Trauma Foundation (BTF) ได้นิยามภาวะความดันโลหิตต่ำ คือ การที่ความดันโลหิตขณะหัวใจบีบตัวมีค่าต่ำกว่า 90 มิลลิเมตรปรอท ต่อมามีหลายการศึกษาที่สนับสนุนว่าการใช้ค่าตัวเลขเพียงค่าเดียวในการนิยามภาวะความดันโลหิตต่ำนั้นไม่เหมาะสำหรับผู้ป่วยทุกราย บางการศึกษาแสดงผลว่า นิยามความดันโลหิตต่ำควรมีค่าสูงกว่า 90 มิลลิเมตรปรอท ในการศึกษานี้ได้อ้างอิงค่าความดันโลหิตเฉลี่ยที่ต่ำกว่าร้อยละ 20 จากค่าพื้นฐานมานิยามภาวะความดันโลหิตต่ำ

วัตถุประสงค์: เพื่อรายงานการเกิดภาวะความดันโลหิตต่ำตามนิยามของ BTF และตามนิยามของค่าความดันโลหิตเฉลี่ยที่ต่ำกว่าร้อยละ 20 จากค่าพื้นฐาน และรายงานอัตราการเสียชีวิตที่เวลา 48 ชั่วโมง ภายหลังผู้ป่วย เข้ารับการผ่าตัดสมองแบบฉุกเฉิน

วัสดุและวิธีการ: รูปแบบการศึกษาแบบเก็บข้อมูลไปข้างหน้าโดยรวบรวมผู้ป่วยที่มีอายุ >18 ปี ที่ได้รับการบาดเจ็บต่อสมองและต้องเข้ารับการผ่าตัดสมองแบบฉุกเฉิน จำนวน 100 ราย สัญญาณชีพที่วัดได้เป็นค่าแรกเมื่อผู้ป่วยมาถึงห้องผ่าตัดถูกใช้เป็นค่าพื้นฐาน ข้อมูลการเกิดภาวะความดันโลหิตต่ำและระยะเวลาของการเกิดความดันโลหิตต่ำตามนิยามความดันโลหิตขณะหัวใจบีบตัวมีค่าต่ำกว่า 90 มิลลิเมตรปรอทและค่าความดันโลหิตเฉลี่ยที่ต่ำกว่าร้อยละ 20 จากค่าพื้นฐานจะถูกบันทึกตลอดการผ่าตัดหลังผ่าตัด 48 ชั่วโมง ผู้ป่วยได้รับการติดตามผลลัพธ์ว่ามีการเสียชีวิตหรือไม่ที่เวลา 48 ชั่วโมงหลังการผ่าตัด

ผลการศึกษา: ตามนิยามความดันโลหิตขณะหัวใจบีบตัวมีค่าต่ำกว่า 90 มิลลิเมตรปรอท เกิดความดันโลหิตต่ำช่วงนำสลบคิดเป็นร้อยละ 22 เป็นเวลานานเฉลี่ย 11±6 นาที เกิดความดันโลหิตช่วงระหว่างการผ่าตัดคิดเป็นร้อยละ 33 นานเฉลี่ย 24±19 นาที ตามนิยามค่าความดันโลหิตเฉลี่ยที่ต่ำกว่าร้อยละ 20 จากค่าพื้นฐาน เกิดความดันโลหิตต่ำช่วงนำสลบ คิดเป็นร้อยละ 58 เป็นเวลานานเฉลี่ย 19±15 นาที เกิดความดันโลหิตช่วงระหว่างการผ่าตัดคิดเป็นร้อยละ 67 นานเฉลี่ย 77±69 นาที อัตราการเสียชีวิตหลังผ่าตัด 48 ชั่วโมงคิดเป็นร้อยละ 10

สรุป: การเกิดความดันโลหิตต่ำระหว่างการผ่าตัดตามนิยามที่ว่าความดันโลหิตขณะหัวใจบีบตัวมีค่าต่ำกว่า 90 มิลลิเมตรปรอท สัมพันธ์กับการเสียชีวิตหลังผ่าตัดที่ประเมินที่เวลา 48 ชั่วโมง ปัจจัยอื่นๆ ที่มีผลต่อการเสียชีวิตหลังการผ่าตัด ได้แก่ ระยะเวลาของการเกิดความดันโลหิตต่ำระหว่างการผ่าตัด ปริมาณการเสียเลือดและระดับความรู้สึกตัวก่อนผ่าตัดน้อยกว่า 8 คะแนน