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Case study

Cerebral perfusion pressure threshold to prevent delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage

Jiawei Cai [a,1], Wenhua Fang [a,1], Fuxiang Chen [a,b], Zhangya Lin [a], Yuanxiang Lin [a], Lianghong Yu [a], Peisen Yao [a], Dezhi Kang [a,b,*]

[a] Department of Neurosurgery, The First Affiliated Hospital of Fujian Medical University, Fuzhou, Fujian 350005, China
[b] The First Clinical Medical College of Fujian Medical University, Fuzhou, Fujian 350005, China

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ABSTRACT

Objective: To seek a cerebral perfusion pressure (CPP) threshold that can reduce the occurrence of delayed cerebral ischemia (DCI) after aneurysmal subarachnoid hemorrhage (aSAH).
Methods: We analyzed the clinical data of patients with the diagnosis of aSAH and underwent CPP monitoring in our department from February 2014 to December 2015. CPP was divided into four specified thresholds by every 10 mmHg increments, which were from 50 mmHg to 80 mmHg. The totally time ratio of CPP below each threshold was calculated. The correlation between the time ratio and DCI were analyzed using binary logistic regression. And receiver operating characteristic curve was performed to identify the cutoff time ratios at higher risk of DCI.
Results: Finally, 17 patients developed DCI from 60 patients who were recruited. The time ratios of CPP which was below 50 mmHg, 60 mmHg and 70 mmHg were found predictors of DCI by the binary logistic regression. The cutoff time ratios were 0.4% (AUC = 0.777), 7.0% (AUC = 0.702), 28.7% (AUC = 0.696) respectively. While at the level of 80 mmHg, the cutoff time ratio was 65% (AUC = 0.595). It was not related to DCI (P = 0.167). Patients suffered from DCI had a worse outcome than who did not at 3 month after aSAH (P = 0.018).
Conclusion: Time ratios at higher risk of DCI had a positive relationship with the CPP thresholds. Keeping CPP above 70 mmHg may be helpful to prevent DCI after aSAH, but it still needs further investigation.

1. Introduction

Delayed cerebral ischemia (DCI) is a complication that results high mortality and morbidity after aneurysmal subarachnoid hemorrhage (aSAH) [1]. It remains lots of difficulties to detect DCI earlier, even though methods such as clinical examination, neuroimaging [2], transcranial Doppler ultrasonography [3] and multimodality monitoring [4] have been utilized. Moreover, therapies to reverse the neurological deficit from DCI are still controversial and unsatisfactory [5–7]. Therefore, preventing DCI plays a vital role to improve the outcome.

Cerebral autoregulation disturbed is an important pathogenesis of DCI after aSAH [8]. When vascular autoregulation was impaired, cerebral blood flow is more relied on the cerebral perfusion pressure (CPP) and blood viscosity [9]. Inadequate perfusion may contributes to ischemia, hypoxia, even progress to irreversible infarction. But little literature is available on the subject about the level of CPP should be contained [10]. We carried out this study to seek a threshold that can reduce the occurrence of DCI.

2. Methods

2.1. Patients

We retrospectively examined a prospective observational database which data were collected from February 2014 to December 2015 in our department. Enrollment criteria were admission within 72 h after SAH, aneurysms detected by computerized tomography angiography (CTA) or digital subtraction arteriography (DSA), aneurysms repaired with surgical clipping, underwent continuous CPP monitoring and age older than 18 years. Besides, patients with coagulation disorder, under pregnancy or incomplete information were ruled out. The study protocol was approved by

* Corresponding author at: Department of Neurosurgery, the First Affiliated Hospital of Fujian Medical University, 88 Jiaotong Road, Fuzhou, Fujian 350005, China.
E-mail address: kdz99988@sina.com (D. Kang).
[1] These authors (Jiawei Cai and Wenhua Fang) contributed equally to this study.

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the ethics committee of the First Affiliated Hospital of Fujian Medical University.

2.2. Clinical management

Patients were treated according to the guideline for the management of aSAH [11]. All patients received nimodipine and valproate sodium. Surgical clipping was performed early after onset unless patients were in an extremely poor clinical condition. Medical management of CPP was targeted at both intracranial pressure (ICP) and arterial blood pressure (ABP). Therapeutic targets were adjusted to avoid ICP > 20 mmHg and mean arterial pressure (MAP) <70 mmHg. Systolic blood pressure was elevated 20–30% higher than baseline to reverse the neurological deficit (with norepinephrine or dopamine) when clinical deterioration was considered caused by delayed cerebral ischemia. All patients had CT scan within 24–48 h postoperative. CTA/DSA was performed to evaluate vasospasm and status of aneurysm occlusion after surgery. Head CT was performed in time if decline of GCS score, local neural deficit or refractory high ICP were found.

2.3. ICP/CPP monitoring

Ventricular drain monitors (Codman, Johnson & Johnson, USA) were placed in opposite side ventricular before the operation in patients with hematoma broken into ventricular or symptomatic hydrocephalus. And parenchymal transducers were placed in lateral frontal, 1.5–2.0 cm beneath the cortical surface. If ICP was <20 mmHg without any treatment for more than 24 h, the probes were removed. Arterial pressure catheter was placed in radial artery, and the transducer was zero with the external acoustic meatus as reference point. CPP was calculated by MAP and ICP (CPP = MAP − ICP).

2.4. Data collection

A data acquisition system (Patient Data Management and Review System, Mindray 1.0.0.1) was used to access digital data every minute from monitors (Mindray BeneView T6). ICP values were filtered when external ventricular drainage was open. CPP was divided into four specified thresholds by 10 mmHg increments, which were 50 mmHg, 60 mmHg, 70 mmHg and 80 mmHg. Time ratios of CPP below each threshold was calculated every 12 h (8:00 am–8:00 pm, 8:00 pm–8:00 am). Then totally time ratios of CPP below each threshold were calculated for every patient. Only the data before ischemia developed was in count in patients suffered from DCI. Other collected clinical characteristics including gender, age, admission Hunt-Hess grade, modified Fisher scale, location of aneurysms and image information.

2.5. Follow-up

Patients were followed up by telephone investigation with Glasgow Outcome Scale (GOS) 3 months after the onset. GOS Scores were classified by favorable (4–5) or unfavorable (1–3).

2.6. Definition of DCI

At current study, DCI was defined as radiologically confirmed new hypodensities on CT or MR scan, not present on the CT or MR scan between 24 and 48 h after early aneurysm occlusion, and not attributable to other causes, such as surgical clipping, ventricular catheter or intraparenchymal hematoma.

2.7. Statistical analysis

Univariate analysis was used to explore factors which were related to DCI. The *t*-test was used to analyze continuous variables and Chi-square test for proportions. Then, binary logistic regression models were built. Variables with p value <0.10 in univariate analysis were entered into the models as independent variables. Finally, a dichotomous variable was created by using receiver operating characteristic (ROC) analysis to identify cutoff time ratios below the thresholds at higher risk for DCI. SPSS17 software (SPSS) was used for data analysis. P < 0.05 was considered as a statistically significant.

3. Results

3.1. General data

During the period, a total of 67 patients were fulfilled the enrollment criteria. Two patients with coagulation disorder, one with pregnancy and four without completed information were ruled out. From the analysis of the 60 patients left, 17 (28%) patients developed DCI. DCI was diagnosed at an average of 9.2 days after aSAH (range, 4–14 days). Median length of CPP monitoring was 114 h (range, 10–201 h). Other clinical characteristics are displayed in Table 1.

3.2. Factors associated with DCI

In univariate analysis, DCI was significantly associated with cerebral vasospasm (moderate-to-severe arterial narrowing on digital subtraction angiography), temporary clipping time during operation and lowest heamoglobin <10 g/dL (Table 2). In binary logistic regression, time ratios that CPP below 50 mmHg, 60 mmHg and 70 mmHg were related to DCI, controlling CVS, temporary clipping time, heamoglobin <10 g/dL and modified Fisher score. While, at the level of 80 mmHg, no significance was found (P = 0.167, Table 3).

3.3. Cutoff time ratio of CPP below each threshold at higher risk of DCI

According to the ROC curves, the cutoff time ratios of CPP which were below 50 mmHg and 60 mmHg at higher risk of DCI were 0.4% (AUC = 0.777), 7.0% (AUC = 0.702). The areas under the curve (AUC) were between 0.7 and 0.9. While at the levels of 70 mmHg and 80 mmHg, the cutoff time ratios were 28.7% (AUC = 0.696), 65% (AUC = 0.595) respectively. AUC were between 0.5 and 0.7 (Fig. 1). In addition, with the decrease of CPP thresholds, the cutoff time ratios at higher risk of DCI were also decreased (Table 4).

3.4. Relationship between DCI and outcome

All patients were followed up successful. Among them, 7 (11%) patients dead and 34 (57%) had favorable outcome at 3 months after SAH. The GOS score of patients with DCI were 2.88 ± 0.99, while the score of patients without DCI were 3.72 ± 1.28. Patients suffered from DCI had a worse outcome than who did not (P = 0.018).

4. Discussion

In physiological condition, when cerebral autoregulation mechanisms were intact, cerebral blood flow autoregulation typically operated when mean blood pressure was between the order of 60 mmHg and 150 mmHg [12]. Small arterioles <100 mm in diameter dilate as response to a reduction in CPP and can expand to