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Predictors of good functional outcomes and mortality in patients with severe rebleeding after aneurysmal subarachnoid hemorrhage

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ABSTRACT

Objective: Aneurysmal rebleeding is a major cause of morbidity and mortality after aneurysmal subarachnoid hemorrhage (aSAH); however, limited data on severity of rebleeding and outcomes after severe rebleeding are available. We aimed to determine predictors of good outcome and mortality after severe rebleeding.
Materials and methods: In a multicenter poor-grade aneurysm study, 60 patients with severe rebleeding, defined as new hemorrhage with poor clinical condition caused by rebleeding, were identified. Good functional outcome was defined as a modified Rankin scale (mRS) of ≤2, and mortality was defined as a mRS of 6. Multivariate logistic analyses were used to determine predictors of good outcome and mortality.
Results: Of the 58 patients included in this report, 24 (41.3%) patients experienced rebleeding within 24 h after ictus. 42 (72.4%) patients had died at 12 months. The rate of good outcome increased from 5.2% at discharge to 13.8% at 6 months and 19.0% at 12 months. In multivariate analysis, World Federation of Neurosurgical Societies (WFNS) grade IV after rebleeding ($P = 0.007$) and aggressive treatment ($P = 0.039$) were independently associated with good outcome. A higher modified Fisher grade before rebledding ($P = 0.040$), larger aneurysms ($P = 0.005$), and lower Glasgow coma score after rebleeding ($P = 0.003$) were independently associated with increased mortality.
Conclusions: A better clinical condition after rebleeding were independently associated with good outcome and inversely associated with morality after severe rebleeding. Despite high mortality of rebleeding, patients with WFNS grade IV treated with aggressive treatment were more likely to have good outcomes regardless of their condition before rebleeding,

1. Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a devastating stroke subtype. Aneurysm rebleeding occurs in about 5.8–19.3% of patients after initial aSAH [1–4], however, rebleeding is a major cause of morbidity and mortality. Numerous studies have demonstrated the risk factors for rebleeding, including poor-grade aSAH, higher modified Fisher grade, posterior circulation aneurysms, larger aneurysms, and the presence of intraventricular hemorrhage [4–8]. However, no study has focused on the severity of rebleeding. Limited data are available on clinical outcomes and predictors of outcomes after rebleeding [9–11]. Detailed knowledge about predictors of the outcomes after severe rebleeding is essential for treatment decision-making process.

In this report, we defined severe rebleeding after initial aSAH and performed a retrospective analysis of data from a multicenter poor-grade aneurysm study (AMPAS). We aimed to determine predictors of good functional outcomes and mortality after severe rebleeding.

2. Material and methods

2.1. Patient cohorts

The AMPAS was a prospective, multicenter, observational registry of patients who presented with poor-grade aSAH. The study

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protocol was approved by the Chinese Ethics Committee of Registering Clinical Trials. From October 2010 to March 20 2012, 366 patients were enrolled from 11 tertiary referral centers. Details of characteristics of patient population have been described previously [12,13]. Severe rebreeding was defined as rebleeding (an increase of subarachnoid, intracerebral, or intraventricular hemorrhage on repeat CT scan) with poor clinical condition caused by rebleeding. A poor clinical condition was defined as a World Federation of Neurosurgical Societies (WFNS) grade of IV or V. 60 patients with severe rebleeding were identified, and 2 patients were lost to follow-up at 12 months and were excluded.

2.2. Treatment protocol

For poor-grade aSAH, the clinical treatment protocol, including aggressive resuscitation, early angiography, aggressive treatment, and intensive critical care, was reported elsewhere [12–16]. For sever rebleeding after aSAH, the treatment protocol was similar to the protocol for poor-grade aSAH. The treatment decision was made by the treating physicians based on the family wish and the patients' clinical conditions.

2.3. Data collection

We collected the following data: demographic characteristics, medical history, Glasgow coma score (GCS) and WFNS grade before rebleeding and after rebleeding, radiologic findings (intraventricular hemorrhage, Fisher grade and modified Fisher grade) before rebleeding and after rebleeding, ruptured aneurysm characteristics, timing of rebleeding, external ventricular drainage, type of treatment, and clinical outcomes.

2.4. Outcome measure

The clinical outcome was measured by an independent neurosurgeon who were not involved in the treatment of patients and was assessed using modified Rankin scale (mRS) at discharge and at 6 months and12 months. Good functional outcome was defined as a mRS of ≤2 at 12 months, and mortality was defined as a mRS of 6.

2.5. Statistical analyses

The analysis were performed with IBM SPSS version 22.0 (IBM SPSS; Armonk, NY, US). Continuous variables were presented as the mean ± standard deviation, and categorical variables as frequencies (percentages). An independent samples *t*-test or the Mantel–Haenszel test was performed for continuous variables, and a x^2 test or the Fisher's exact test was performed for categorical variables. Variables with a *P* value < 0.10 in the univariate analysis were entered into the multivariate logistic regression models to identify independent predictors of good outcomes and mortality with a backward elimination method. Area under receiver operating characteristic curves (AUC) were used to evaluate the model's prediction ability. A *P* value < 0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

Baseline characteristics of the 58 patients are presented in Table 1. 30 (51.7%) patients were female. The mean age was 53.7 ± 12.2 years (range 23–74 years). 24 (41.3%) patients experienced rebleeding within 24 h after ictus, 19 (32.8%) experienced rebleeding between after 24 h and 7 days, and 15 (25.9%) after 7days. The timing of rebleeding after initial aSAH is demonstrated in Fig. 1. Most rebleedings occurred within 24 h and the peak incidence was within the first week. 11 (19.0%) patients had a WFNS grade of IV and 47 (81.4%) had a WFNS grade of V after rebleeding. 27 (46.5%) patients underwent conservative management and 31 (53.4%) underwent aggressive aneurysm treatment, including 20 patients treated with surgical clipping and 11 patients treated with endovascular coiling.

Table 1
Baseline characteristics.

Characteristics	Values
Age (year)	53.7 (12.2)
Women	30 (51.7%)
Current smoking	15 (25.9%)
Hypertension	24 (41.4%)
Clinical condition before rebleeding	
Glasgow coma score	11.2 (4.1)
WFNS grade I–III	29 (50.0%)
WFNS grade IV–V	29 (50.0%)
Fisher grade I–II	31 (53.4%)
Fisher grade III–IV	27 (46.6%)
Modified fisher grade I–II	35 (60.3%)
Modified fisher grade III–IV	23 (39.7%)
Ultra-early rebleeding(≤24 h)	24 (41.4%)
Clinical condition after rebleeding	
Glasgow coma score	4.8 (2.0)
WFNS grade IV	11 (19.0%)
WFNS grade V	47 (81.0%)
Fisher grade I–II	6 (10.5%)
Fisher grade III–IV	52 (89.5%)
Modified fisher grade I–II	13 (22.8%)
Modified fisher grade III–IV	45 (77.2%)
Ruptured aneurysm location	
Anterior circulation artery	50 (86.2%)
Posterior circulation artery	8 (13.8%)
Ruptured aneurysm size(mm)	6.0 (4.2)
Treatment modality	
Conservative treatment	27 (46.5%)
Endovascular coiling	11 (19.0%)
Surgical clipping	20 (34.5%)
External ventricular drainage	6 (10.3%)

WFNS = World Federation Neurosurgical Societies.

Table 2
Functional outcomes after severe rebleeding.

Outcomes	At discharge	At 6 months	At 12 months
mRS 0	0	3 (5.2%)	6 (10.3%)
mRS 1	3 (5.2%)	5 (8.6%)	3 (5.2%)
mRS 2	1 (1.7%)	2 (3.4%)	0
mRS 3	2 (3.4%)	1 (1.7%)	2 (3.4%)
mRS 4	7 (12.1%)	5 (8.6%)	4 (8.6%)
mRS 5	12 (20.7%)	0	0
mRS 6	33 (56.9%)	42 (72.4%)	42 (72.4%)

mRS = modified Rankin score.

3.2. Functional outcomes

The functional outcomes are presented in Table 2. 33 (56.9%) patients died at discharge, and 3 (5.2%) had good outcomes. 8 (13.8%) patients had good outcomes at 6 months and 11 (19.0%) had good outcomes. The rate of good outcome increased over time. No patients treated with conservative management had a good outcome at 12 months. 42 (72.4%) had died, including 26 patients undergoing conservative management and 16 patients treated with aggressive treatment.