Long-Term Outcome in Patients with Subarachnoid Hemorrhage with Negative CT Scan

Ye-Ting Zhou,¹ Dao-Ming Tong,² Guang-Sheng Wang,² Xiao-Dong Chen,² Tong-Hui Yang,² Yuan-Wei Wang² & Han-Pei Gu²

¹ Medical Evaluation Unit, Shuyang People's Hospital, Shuyang, China

² Department of Neurology, Shuyang People's Hospital, Shuyang, China

Correspondence

Dao-Ming Tong, M.D., Department of Neurology, Shuyang People's Hospital, Yingbin Rd. CB9, Shuyang 223600, China.

and

Department of Neurology, the Affiliated Pingxiang Hospital, Southern Medical University, Pingxiang 337000, China.

Tel.: +86-527-8999-0120;

Fax: +86-527-8355-7553;

E-mail: tongdaoming@163.com

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Despite improvements in diagnostic imaging, the initial interpretation of third-generation head CT scans to detect subarachnoid hemorrhage (SAH) has not reached 100% sensitivity [1,2]. The proportion of patients with SAH and a negative CT scan was 3.3% within 0 to 3 days of onset and 3.0% within 4 to 14 days of onset [3]. Another study showed that the proportion of patients with SAH and a negative CT may be close to 7% within 3 days [4]. This indicates that SAH with a negative CT scan is not rare. Recurrent hemorrhage remains a serious consequence of aneurysmal SAH, with a fatality rate of approximately 70%, but it may be the most preventable cause of poor outcomes [5]. However, the recently published guidelines by the American Heart Association do not clearly define the long-term outcome for patients who have SAH with a negative CT scan [5]. This study addresses the long-term outcomes of SAH with a negative CT scan.

A prospective study of outcomes of consecutive patients with SAH with a negative CT scan from January 1995 to September 2009 was commenced at a university teaching hospital in China. Twenty-eight patients included in the study did not have SAH visible on head CT, and the diagnosis of SAH was based on the results of a lumbar puncture (LP) with the xanthochromia of the cerebrospinal fluid. Patients with spontaneous aneurysmal and nonaneurysmal SAH were included. Individuals with SAH caused by trauma, traumatic taps, arteriovenous malformation or other secondary causes were excluded.

A cerebral angiography was performed within 3–5 days after admission in some patients. We divided these patients into two groups based on whether they agreed or rejected angiography: an angiography group and a nonangiography group. Nine of 17

patients of the angiography group showed an aneurysmal pattern of hemorrhage. In addition to eight patients for surgery therapy, the other one patient was not to receive surgery therapy. Those patients who were surviving 30 days after onset of the initial SAH were followed continuously. Rehemorrhage after the initial SAH was defined as a sudden headache with or without coma, and the new bleed was confirmed by head CT or LP.

Follow-up was begun on October 10, 2009. Patients or their surrogates were interviewed either by telephone or in person. Subarachnoid hemorrhage and data regarding any rehemorrhages include the date, postmortem reports, and imaging data. Global outcome and functional status were assessed with the modified Rankin Scale (mRS = 0–6; 0 = no symptoms or disability; 6 = dead). Data for the survival and rehemorrhage analyses were extracted in April 2010. Data for the overall death and rehemorrhage analyses were compiled for the initial hospitalization after the primary SAH and from the date of the first SAH until the end of September of 2009. A *P* value <0.05 was considered to be statistically significant.

Twenty-eight patients who underwent an initial SAH with a negative CT were enrolled during their first hospitalization. One (fatal rehemorrhage) of 11 patients in the nonangiography group died during the first hospitalization. Therefore, the 27 remaining patients were enrolled and contacted for further follow-up. Table 1 shows the baseline characteristics of the patients in this study. As of April 2010, there were 15 survivors in the angiography group (including the eight patients for surgery therapy) and five survivors (except one lost to follow-up and four died) in nonangiography group. The rate of complete loss of follow-up was

Table 1 Long-term outcome and baseline characteristics in patients with SAH with negative CT scan

	Angiography group	Nonangiography group	<i>P</i> Value
Baseline characteristics	N = 17	N = 11	
Gender (male, %)	10 (58.8)	6 (54.5)	0.823
Age (years, mean $\pm$ SD)	51.5 $\pm$ 14.3	54.1 $\pm$ 15.3	0.469
Hunt-Hess grade at hospital admission			
I–III	17 (100.0)	11 (100.0)	
IV–V	0 (0)	0 (0)	
Modified Rankin Scale Score in initial hospitalization			
No or mild restriction (mRS 0–3)	15 (88.2)	10 (90.9)	0.823
Severe disability (mRS 4–5)	2 (11.8)	0 (0)	0.238
Death (mRS 6)	0 (0.0)	1 (9.1)	0.206
Follow-up after onset of the initial SAH	N = 17	N = 10	
Rehemorrhage	3 (17.6)	4 (40.0)	0.201
Lost to follow-up	0 (0)	1 (10.0)	0.184
mRS score	N = 17	N = 9	
No or mild restriction (mRS 0–3)	13 (76.5)	5 (55.6)	0.272
Severe disability (mRS 4–5)	2 (11.8)	0 (0)	0.284
Death (mRS 6)	2 (11.8)	4 (44.4)	0.060
Outcome at 5 years (including initial hospitalization)	N = 17	N = 11	
Rehemorrhage	3 (17.6)	6 (54.5)	0.041
Death	2 (11.8)	5 (44.5)	0.044

SAH, subarachnoid hemorrhage; mRS, Modified Rankin Scale.

3.7%. The length of follow-up for those remaining in the study ranged from a minimum of 1 year to a maximum of 14 years.

In the angiography group, 17.6% had a late rehemorrhage. The rebleeds were reported at 2 and 5 years after the initial SAH. Two of the late rehemorrhage patients died and one survived; the survivor died 12 years later from hepatocellular cancer. The patient who died of hepatocellular cancer was eliminated from the analysis of time to death from SAH within 5 years. Two of 17 patients (11.8%) died during the 5-year follow-up.

In the nonangiography group, 40.0% of patients had a late recurrence of SAH during follow-up. The times to late rehemorrhage were over 1, 2, 3, and 5 years. A total of four of the nine patients (excluding one patient lost to follow-up) in this group died (four rehemorrhages) during follow-up. Thereby, the mortality from sequelae of SAH in the nonangiography group was 44.4%; this difference was not statistically significant ($P > 0.05$) in both groups (Table 1).

The rate of rehemorrhage at 5 years in the angiography group was 17.6%, and in the nonangiography group (including the number of rehemorrhage during the first hospitalization) was 54.5%. There was significant difference in the risk of rehemorrhage between 1 month and 5 years in two groups ($P = 0.041$) (Table 1). The mortality rate from SAH during 5 years in the angiography group was 11.8%, and in the nonangiography group (including the number of deaths during the first hospitalization) was 44.5%. There was a significant difference between the groups in mortality rates ($P = 0.044$) (Table 1). Overall, the rate of rehemorrhage at 5 years in both groups was 32.1%, and the death rate from recurrence was 77.8%.

The data here indicate that the Hunt-Hess grade at hospital admission and the Rankin Scale score during the initial 30 days are low in both groups; the risk of the aneurysm rebleeding is high

in patients. This finding indicates that the patients with “minor leaks” or mild SAH remain at high risk of recurrent SAH, particularly with conservative therapy.

The fact that missing a SAH in an otherwise alert patient can lead to catastrophic outcomes [4,6]. Lumbar puncture should be performed in any patient with suspected SAH with negative or equivocal findings on head CT scan [1,2,7]. The present study has confirmed that recurrent SAH in patients who had negative CT scans occurs most often within 5 years of the initial ictus and is associated with highest mortality rate. This suggests that although the early clinical outcome is improved for patients with SAH and negative CT scan, the outcomes are likely to deteriorate over the subsequent 5 years.

Some patients with a SAH with a negative finding on head CT may have a minor perimesencephalic SAH [8]. In addition, patients with three negative angiograms and an aneurysmal pattern of hemorrhage are still at some risk of vascular complications and poor outcome [9]. In present study, the risk of rebleeding within 5 years in the angiography group with surgical treatment is lower than the nonangiography group with conservative therapy. Furthermore, one aim of the current study, which has found that the risk of rehemorrhage for patients with SAH with a negative CT scan is 32.1%, and the death rate from recurrence is 77.8%, is to bring attention to the potentially grievous outcome of SAH with a negative CT scan. This suggests that DSA should be recommend in any patient with SAH with negative CT scan, and early surgery or endovascular therapy should be considered for aneurysmal patients with SAH with negative CT scans.

Conflict of Interest

The authors declare no conflict of interest.

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