

〈特集:脳血管攣縮の病態と治療〉

Factors influencing the Effectiveness of Hemodilution Therapy for Patients with Ruptured Cerebral Aneurysm

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Summary : We operated on 621 patients with subarachnoid hemorrhage (SAH) due to ruptured intracranial aneurysm from 1979 to 1987. All the patients were operated on within 72 hours after the rupture of aneurysm. From 1979 to 1983, 312 patients with ruptured intracranial aneurysm were treated without postoperative hemodilution therapy (No-Hemodilution). From 1984 to 1987, 309 patients were treated with hemodilution therapy (Hemodilution). We have performed the hemodilution therapy for the prevention of cerebral ischemia due to vasospasm following SAH since January, 1984. Indication for the hemodilution therapy was the hematocrit value of above 30.0-33.0 % at Day 7 after onset. In the No-Hemodilution period (1979-1983), the mean value of hematocrit of 253 patients was 36.7 % and in the Hemodilution period (1984-1987), the value of 150 patients was 31.9 %. The difference in these values is statistically significant.

From the viewpoint of over-all outcome, the rate of Good Recovery was higher and that of Death was lower in the Hemodilution period ($p < 0.001$).

1. The correlation of the age and outcome:

The mortality was higher with increasing age especially in patients over 60 years ($p < 0.001$).

This result seemed to be due to the vulnerability of the brain by cerebral ischemia in the old age.

2. The correlation of the sites of ruptured aneurysm and outcome:

In the ruptured aneurysm of the anterior cerebral artery, the mortality was higher than that of other sites ($p < 0.001$). Generally, the symptoms of ischemia in the anterior cerebral artery territory are more severe than those of other sites. By the hemodilution therapy the symptoms of ischemia in the anterior cerebral artery territory seemed to be prevented.

3. The correlation of the preoperative grade and outcome:

The mortality and morbidity were higher especially in the preoperative grade III ($p < 0.001$). In the preoperative grade III the outcome has a tendency to be determined by the severity of cerebral vasospasm. By the hemodilution therapy the occurrence of ischemia is decreased.

We conclude that the hemodilution therapy is effective for the prevention and treatment of cerebral ischemia due to vasospasm.

Key words :

- cerebral vasospasm
- cerebral ischemia
- ruptured cerebral aneurysm
- early surgery
- hemodilution therapy

Introduction

The primary therapy for subarachnoid hemorrhage (SAH) due to ruptured aneurysm is to prevent rebleeding and ischemia secondary to cerebral vasospasm. In our hospital the therapy for the ruptured aneurysm is an earliest possible surgery and a postoperative hemodilution therapy for the prevention of cerebral ischemia due to vasospasm following SAH. The hemodilution therapy was first introduced in January, 1984. Indication for the hemodilution therapy is the hematocrit value of above 30.0-33.0% at Day 7 and it was maintained below that value¹⁾.

We discuss the factors which may influence the effective hemodilution therapy from the viewpoint of the clinical outcome.

Materials and Methods

From 1979 to 1987, we operated on 621 patients within 72 hours after the rupture of aneurysm. From 1979 to 1983, 312 patients were treated without the postoperative hemodilution therapy. From 1984 to 1987,

309 patients were treated with the postoperative hemodilution therapy. We name one group of patients in the period before December, 1983, "No-Hemodilution" and the other in the period after January, 1984, "Hemodilution". We statistically analyzed the clinical outcome of the two groups. The preoperative grading was classified by the Hunt & Kosnik's grade and the outcome was classified by the Glasgow Outcome Scale (GOS) : Good Recovery (GR), Moderate Disability (MD), Severe Disability (SD), Persisted Vegetative State (VS), Death (D). We used the chi-square test and student-t test as the statistical methods.

Results

The results were analyzed statistically concerning the No-Hemodilution period (1979-1983) group and the Hemodilution period (1984-1987) group.

1. Sex difference (Table 1)

Table 1 shows the sex difference. Between the two groups of "Hemodilution" and "No-Hemodilution", there are no statistically significant differences.

2. Age distribution (Table 2)

Table 1

Sex	No-Hemodilution (%)	Hemodilution (%)	Total
Male	138 (44.2)	126 (40.8)	264
Female	174 (55.8)	183 (59.2)	357
	312	309	621

Table 2

Age	No-Hemodilution (%)	Hemodilution (%)	Total
<10	0 (0)	2 (0.6)	2
<20	0 (0)	2 (0.6)	2
<30	14 (4.5)	4 (1.3)	18
<40	37 (11.9)	40 (12.9)	77
<50	78 (25.0)	79 (25.6)	157
<60	105 (33.7)	98 (31.7)	203
<70	71 (22.8)	58 (18.8)	129
≥70	7 (2.2)	26 (8.4)	33
	312	309	621

Table 3

Site	No-Hemodilution (%)	Hemodilution (%)	Total
ACA	131 (42.0)	123 (39.8)	254
R-MCA	48 (15.4)	55 (17.8)	103
L-MCA	47 (15.1)	38 (12.3)	85
R-ICA	43 (13.8)	32 (10.4)	75
L-ICA	42 (13.5)	50 (16.2)	92
VBA	1 (0.3)	11 (3.6)	12
	312	309	621

Table 4

Grade	No-Hemodilution (%)	Hemodilution (%)	Total
I	46 (14.7)	23 (7.4)	69
II	91 (29.2)	101 (32.7)	192
III	94 (30.1)	101 (32.7)	195
IV	61 (19.6)	77 (24.9)	138
V	20 (6.4)	7 (2.3)	27
	312	309	621

Table 5

Outcome	No-Hemodilution (%)	Hemodilution (%)	Total
GR	120 (38.5)	167 (54.0)	287
MD	49 (15.7)	33 (10.7)	82
SD	31 (9.9)	34 (11.0)	65
VS	12 (3.8)	23 (7.4)	35
D	100 (32.1)	52 (16.8)	152
	312	309	621

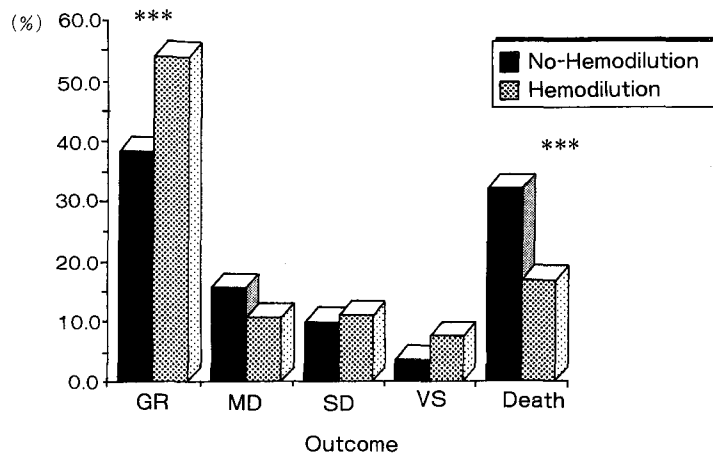


Fig.1 Outcome distribution

Table 2 shows the age distribution. Between the two groups, there are no statistically significant differences.

3. The aneurysmal sites (Table 3)

Table 3 shows the sites of ruptured aneurysm. Between the two groups, there are no statistically significant differences.

4. The preoperative grade distribution (Table 4)

Table 4 shows the distribution of preoperative grade by Hunt and Kosnik's Grade. There are no statistically significant differences.

There are no significant differences in the basic data and the factors such as age, aneurysmal site and

preoperative grade between the two groups.

5. The outcome (Table 5, Fig. 1)

Table 5 and Figure 1 show the outcome by the Glasgow Outcome Scale. In the Hemodilution period the percentage of Good Recovery is higher and that of Death is lower statistically.

6. The correlation between the age and the outcome (Table 6, Fig. 2)

Table 6 and Figure 2 show the correlation between the age and the outcome. The mortality of the patients over 50 years in the Hemodilution period is low as compared with that in the No-Hemodilution period. It

Table 6
Age and Outcome (No-Hemodilution)

Age	Outcome					Total
	GR (%)	MD (%)	SD (%)	VS (%)	Death (%)	
<10	0(0)	0(0)	0(0)	0(0)	0(0)	0
<20	0(0)	0(0)	0(0)	0(0)	0(0)	0
<30	13(92.9)	0(0)	1(7.1)	0(0)	0(0)	14
<40	19(51.4)	6(16.2)	2(5.4)	0(0)	10(27.0)	37
<50	41(52.6)	11(14.1)	5(6.4)	2(2.6)	19(24.4)	78
<60	37(35.2)	20(19.0)	13(12.4)	3(2.9)	32(30.5)	105
<70	10(14.1)	11(15.5)	8(11.3)	7(9.9)	35(49.3)	71
≥70	0(0)	1(14.3)	2(28.6)	0(0)	4(57.1)	7
	120	49	31	12	100	312

Age and Outcome (Hemodilution)

Age	Outcome					Total
	GR (%)	MD (%)	SD (%)	VS (%)	Death (%)	
<10	1(50.0)	1(50.0)	0(0)	0(0)	0(0)	2
<20	2(100)	0(0)	0(0)	0(0)	0(0)	2
<30	3(75.0)	0(0)	0(0)	1(25.0)	0(0)	4
<40	28(70.0)	5(12.5)	2(5.0)	1(2.5)	4(10.0)	40
<50	44(55.7)	9(11.4)	5(6.3)	6(7.6)	15(19.0)	79
<60	54(55.1)	10(10.2)	13(13.3)	7(7.1)	14(14.3)	98
<70	26(44.8)	6(10.3)	10(17.2)	4(6.9)	12(20.7)	58
≥70	9(34.6)	2(7.7)	4(15.4)	4(15.4)	7(26.9)	26
	167	33	34	23	52	309

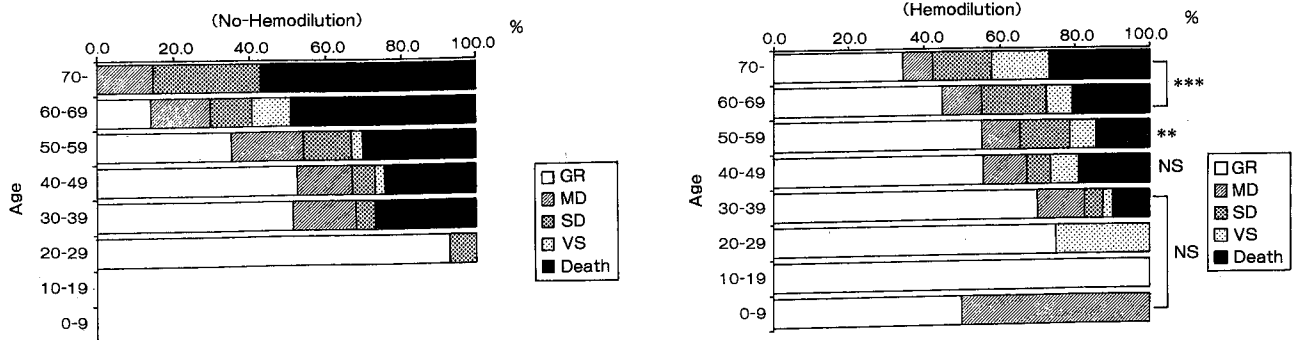


Fig.2 Correlation of age and outcome

Table 7
Site and Outcome (No-Hemodilution)

Site	Outcome					Total
	GR (%)	MD (%)	SD (%)	VS (%)	Death (%)	
ACA	44 (33.6)	20 (15.3)	9 (6.9)	6 (4.6)	52 (39.7)	131
R-MCA	22 (45.8)	6 (12.5)	5 (10.4)	3 (6.3)	12 (25.0)	48
L-MCA	15 (31.9)	8 (17.0)	7 (14.9)	1 (2.1)	16 (34.0)	47
R-ICA	21 (48.8)	8 (18.6)	3 (7.0)	2 (4.7)	9 (20.9)	43
L-ICA	18 (42.9)	7 (16.7)	7 (16.7)	0 (0)	10 (23.8)	42
VBA	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	1
	120 (38.5)	49 (15.7)	31 (9.9)	12 (3.8)	100 (32.1)	312

Site and Outcome (Hemodilution)

Site	Outcome					Total
	GR (%)	MD (%)	SD (%)	VS (%)	Death (%)	
ACA	73 (59.3)	7 (5.7)	12 (9.8)	6 (4.9)	25 (20.3)	123
R-MCA	30 (54.5)	7 (12.7)	6 (10.9)	3 (5.5)	9 (16.4)	55
L-MCA	17 (44.7)	3 (7.9)	6 (15.8)	5 (13.2)	7 (18.4)	38
R-ICA	17 (53.1)	4 (12.5)	3 (9.4)	4 (12.5)	4 (12.5)	32
L-ICA	25 (50.0)	11 (22.0)	6 (12.0)	2 (4.0)	6 (12.0)	50
VBA	5 (45.5)	1 (9.1)	1 (9.1)	3 (27.3)	1 (9.1)	11
	167 (54.0)	33 (10.7)	34 (11.0)	23 (7.4)	52 (16.8)	309

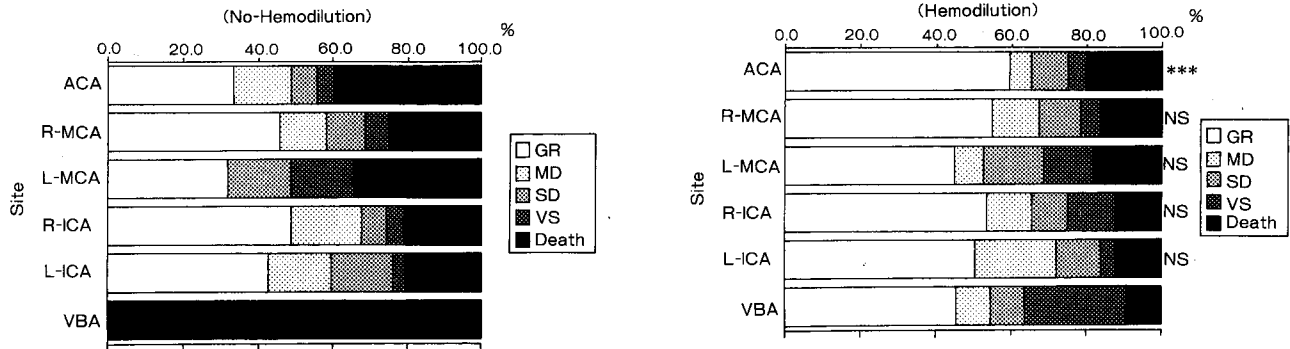


Fig.3 Correlation of aneurysmal site and outcome

is statistically significant. Especially in the patients over 60 years, it is with $p < 0.001$.

7. The correlation between the aneurysmal site and the outcome (**Table 7**, **Fig. 3**)

Table 7 and **Figure 3** show the correlation between the site of ruptured aneurysm and the outcome. In the anterior cerebral artery aneurysm (including the anterior communicating artery aneurysm) the

Hemodilution period has the lower mortality. It is statistically significant ($p < 0.001$).

8. The correlation between the preoperative grade and the outcome (Table 8, Fig. 4)

Table 8 and Figure 4 show the correlation between the preoperative grade and the outcome. Except for the Grade I, the percentage of Good Recovery is

statistically higher and that of Death is lower in the Hemodilution period especially in the Grade III ($p < 0.001$).

Discussion

The two major factors influencing the outcome after ruptured aneurysm, i.e., rebleeding and vasospasm, have

Table 8
Grade and Outcome (No-Hemodilution)

Grade	Outcome					Total
	GR (%)	MD (%)	SD (%)	VS (%)	Death (%)	
I	33(71.7)	8(17.4)	2(4.3)	0(0)	3(6.5)	46
II	48(52.7)	11(12.1)	11(12.1)	3(3.3)	18(19.8)	91
III	27(28.7)	19(20.2)	8(8.5)	6(6.4)	34(36.2)	94
IV	11(18.0)	11(18.0)	7(11.5)	2(3.3)	30(49.2)	61
V	1(5.0)	0(0)	3(15.0)	1(5.0)	15(75.0)	20
	120(38.5)	49(15.7)	31(9.9)	12(3.8)	100(32.1)	312

Grade and Outcome (Hemodilution)

Grade	Outcome					Total
	GR (%)	MD (%)	SD (%)	VS (%)	Death (%)	
I	18(78.3)	2(8.7)	1(4.3)	0(0)	2(8.7)	23
II	77(76.2)	8(7.9)	2(2.0)	4(4.0)	10(9.9)	101
III	55(54.5)	12(11.9)	14(13.9)	4(4.0)	16(15.8)	101
IV	16(20.8)	10(13.0)	16(20.8)	13(16.9)	22(28.6)	77
V	1(14.3)	1(14.3)	1(14.3)	2(28.6)	2(28.6)	7
	167(54.0)	33(10.7)	34(11.0)	23(7.4)	52(16.8)	309

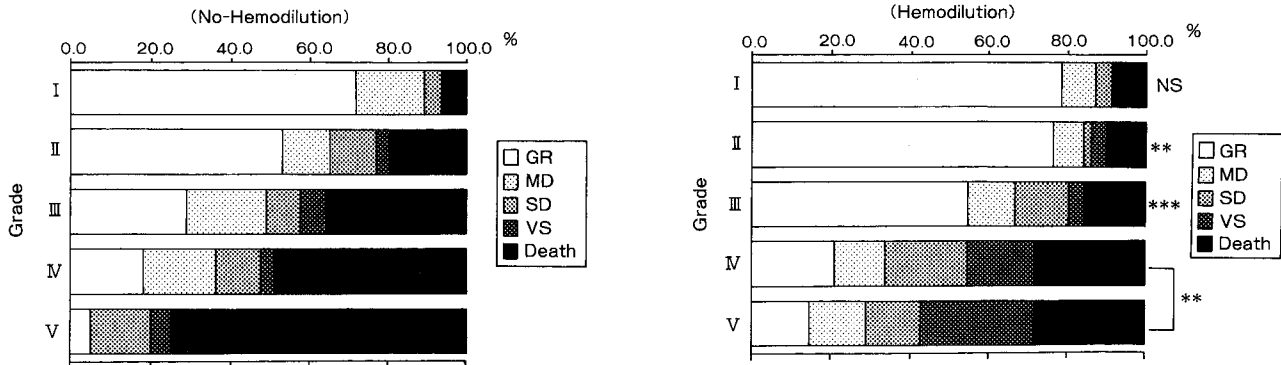


Fig.4 Correlation of preoperative grade and outcome

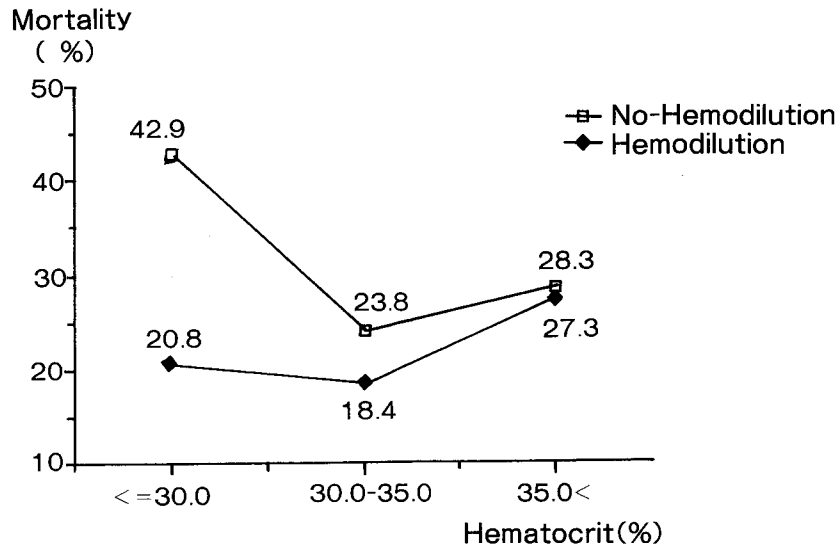


Fig.5 Mortality and hematocrit of day 7 after onset

been described by Kitamura et al. in the "The Japanese Results in the International Cooperative Study on Timing of Aneurysm Surgery"²⁾.

Various therapies for the vasospasm have been tried. Once the vasospasm occurs, it may lead to decreased perfusion and ischemia. Even if there are various kinds of therapies, no reliable therapy against cerebral vasospasm and ischemia is available at present. In our hospital, hypervolemic hemodilution therapy had been performed at first, but this therapy caused side effects by hypervolemia and a decrease of oxygen delivery due to over-hemodilution⁹⁾. Therefore, we selected the hemodilution therapy without hypervolemia, with a hematocrit value of about 30.0%.

Wood et al. reported that an increase of cerebral blood flow occurred by decreasing the blood viscosity in the dog³⁾⁴⁾⁵⁾. Hint reported in 1968 that in an ischemic state with a hematocrit value of about 30.0 to 33.0%, even if the hemoglobin is low, the relative oxygen transport capacity is higher⁶⁾. Contrary to this, Keller et al. reported that in normovolemic hemodilutional condition the regional cerebral blood flow did not increase, especially in the ischemic lesion and the factor of increasing the local cerebral blood flow was the effect of cardiac output⁷⁾. A decrease of mortality in "No-Hemodilution"

with 30.0 to 35.0% hematocrit value may be due to the mechanism of the increase of cerebral blood flow by the decrease of blood viscosity (Fig. 5)¹⁰⁾

With increasing age, the cerebral blood flow is lower by arteriosclerotic changes. In this condition a decrease of cerebral blood flow by the vasospasm give the patient a fatal blow. In over 60 years of age the ratio of Good Recovery significantly increased by the hemodilution therapy.

Most frequent site in the ruptured anterior cerebral artery aneurysm is the anterior communicating artery. If the anterior communicating artery aneurysm ruptures, the subarachnoid hemorrhage is widely spread as compared with other sites. Therefore, the cerebral vasospasm is widely distributed. Cerebral ischemia due to vasospasm is a main factor for outcome. In this study, we did not evaluate the ruptured aneurysm with intracerebral hematoma.

In the grade III, the degree of disturbance of consciousness is not so severe as compared with grade IV and V. However, in the computed tomographic findings of grade III, we recognized extensive subarachnoid hemorrhage following cerebral vasospasm, especially at the basal and Sylvian cisterns. The outcome of grade III seems to be easily influenced by this subarachnoid hemorrhage. The

results of outcome of grade III shows the effectiveness of hemodilution therapy for the cerebral ischemia due to cerebral vasospasm. In the outcome of grade IV and V, the frequency of Good Recovery and Death are also statistically significant¹⁰⁾.

To summarize our results, three factors : age, aneurysmal site, and preoperative grade which is mostly associated with cerebral vasospasm, are important for the evaluation of outcome and the hemodilution therapy is effective for cerebral ischemia due to vasospasm.

Conclusion

The hemodilution therapy was the prevention and treatment of effective for cerebral ischemia due to vasospasm following subarachnoid hemorrhage, especially in the patients of old age, ruptured aneurysm of anterior cerebral arteries, and preoperative grade III.

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