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Original Article

The Comparative Study of Microsurgical Cerebral Aneurysm Clip Implants; Titanium Clip vs. Stainless Steel Clip

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Objective : To perform a comparative study between two groups of populations, titanium (T) group versus stainless steel (S) group, who were clipped with titanium and stainless steel materials, respectively, the incidence of regrowth from the original aneurysms, the clip slippage, and post-clipping seizure attack were analyzed. The patients were followed more than 5 years after microsurgical cerebral aneurysms clipping.

Methods : Data from 1986 through 2008 were extensively reviewed on a consecutive series of 3,770 patients who referred for ruptured/unruptured cerebral aneurysms. Forty-seven patients in the S group and 48 in the T group who met inclusion criteria, were selected for this study.

Results : The incidence of regrowth were noted that two out of total 47 patients (4.3%) in the S group, and none in the T group. The clip slippage was not observed in both groups. And there was no statistical difference (p = 0.242) in terms of regrowth between two groups. Seven out of 47 cases (14.9%) developed post-clipping seizure in the S group. On the other hand, two (4.2%) of 48 patients presented the symptom in the T group. Also, there was no significant difference (p = 0.091) between two groups.

Conclusions : The metallic types of clip employed for the microsurgical cerebral aneurysm clipping does not have any significant clinical outcome differences in this study.

Keywords Microsurgical clipping, Aneurysm, Stainless steel aneurysmal clip, Titanium aneurysmal clip

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INTRODUCTION

Microsurgical clipping marks one of the ultimate standard treatments to occlude intracranial aneurysm over the past several decades. Recently, the clinical application of newly developed and commercially available titanium cerebral aneurysmal clips (T) in the treatment of patients with aneurysmal SAH has demonstrated their safety on the closing force, biocompatibility and effectiveness to reduce clip artifacts on MRI 3-fold compared with conventional stainless steel and cobalt alloy clips (S).[1)2)] Because of these important advantages over the conventional clips, T have been extensively exploited into routine use in aneurysm surgery.

Yet, a number of publications have pointed out and raised a controversial issue on a relatively weak closing force of T compared to that of conventional S.[3)4)] Also, because the reliability of T has not been demonstrated in a large number of cases, some physicians

have not advocated its use in spite of such benefits for neuro-imaging.[5]

In our institution, since the introduction of T at December 2000, microsurgical cerebral aneurysm clipping has been done through T implant. Before then, S had been extensively exploited over several decades. Currently available literature review informed us that more than 5-year -interval follow-up outcomes and efficacy of clipping with different types of clip material remain elusive. Subsequently, it is intriguing to perform a comparative study between 2 groups of populations of more than 5 year mean follow-up; T group versus S group.

Considering virtues and drawbacks of two different metal clips, in this retrospective study, we evaluated the incidence of post-clipping seizure which may be attributed to foreign body reaction during the follow-up.[6] Not only that, another more important concern lies in the occurrence of aneurysmal regrowth from the original loci and/or slippage from the original aneurysmal neck owing to weak closing force of T during the follow-up period.[7]

MATERIALS AND METHODS

Under the permission of institutional review board at our institution, the data from 1986 through 2008 were extensively reviewed on a consecutive series of 3,770 patients who referred for ruptured/unruptured cerebral aneurysms and successfully treated with microsurgical clipping. Of those, patients who met the following inclusion criteria were studied: (1) complete obliteration of aneurysm confirmed by postoperative angiography, (2) more than 60 months of follow-up periods after the surgery, (3) availability of complete medical records including pre-, early post-, and late post- (over 60 months) operative angiograms, (4) the clipping done by the same neurosurgeon, and (5) small cerebral aneurysms which have a diameter of less than 10 mm. In addition to the above conditions, clipped patients who were previously treated with other modalities of occluding aneurysm such as bypass, wrapping, and coiling, and patients with multiple aneurysms were excluded.

Medical records of the selected patients were reviewed, focusing the data on aneurysm location, size, regrowth and slippage of clip on follow-up angiography, severity of initial presentation, type of clip used, presence of seizure attack, and follow-up interval. Patients' pre- and post-operative cerebral angiograms were examined by the 3rd and 4th neurosurgeons who were blinded to the current study to identify aneurysmal regrowth or clip slippage by any chance. Only the examined results that reached a consensus by those neurosurgeons were chosen. If there were no consensus on a case, a senior neurosurgeon arbitrated the dispute between the neurosurgeons. Out of 3,770 patients, only 47 cases met the criteria in the S group, while 48 patients were selected in the T group.

Statistical method

All retrieved data were converted into categorical or binominal variables. To assess the relationship between variables and presence of postoperative seizure or regrowth of aneurysm as well as clip slippage, statistical method was utilized by adopting SPSS, version 13.0 (SPSS Inc., Chicago, IL, USA). The chi-square or Fisher's exact test were used for nominal factors, and Mann-Whitney test was used for continuous variables. Statistical significance was accepted for P value of < 0.05.

RESULTS

Demographic data (Table 1)

Overall, the baseline characteristics in both groups demonstrated that there are no significant difference in demographic data, clinical severity, aneurysm size, dome to neck ratio and location of the aneurysms.

The mean durations of follow-up were 65.9 months (range, 60 to 96 months, SD 9.91 months) in the T group and 87.1 (range, 60 to 144 months, SD 23.1 months) in the S groups, respectively. There was a

Table 1. The baseline data of the S group and the T group

Characteristics	S group	T group	*p* value
Age (years)	52.77 ± 21.92 (12-90)	53.38 ± 19.79 (18-88)	0.879
No. of patients			0.683
Female	24 (51.1%)	27 (56.2%)	
Male	23 (48.9%)	21 (43.8%)	
Aneurysm locations			0.666
Anterior cerebral artery	19 (40.4%)	20 (41.7%)	
Middle cerebral artery.	14 (29.8%)	10 (20.8%)	
Posterior Communicating artery	10 (21.3%)	10 (20.8%)	
Internal Carotid artery	1 (2.1%)	4 (8.3%)	
Others	3 (6.4%)	4 (8.3%)	
Aneurysm size (mm)	7.23 ± 1.93 (4-10)	7.63 ± 1.83 (5-10)	0.353
Dome to neck ratio	2.19 ± 0.16 (1.83-2.45)	2.25 ± 0.11 (1.93-2.45)	0.134
Fisher Grade			1.000
I	0 (0.0%)	0 (0.0%)	
II	2 (4.3%)	3 (6.3%)	
III	44 (93.6%)	43 (89.6%)	
IV	1 (2.1%)	2 (4.2%)	
Hunt - Hess scale			0.499
I			
II	0 (0.0%)	0 (0.0%)	
III	30 (63.8%)	25 (52.1%)	
IV	16 (34.0%)	21 (43.8%)	
V	1 (2.1%)	2 (4.2%)	
	0 (0.0%)	0 (0.0%)	
Follow-up period (month)	87.1 (60-144)	65.9 (60-96)	0.000

S = stainless-steel aneurysm clip; T = Titanium aneurysm clip; No = Number

significant statistical difference in the follow-up period between 2 groups ($p < 0.001$).

Regrowth of aneurysm or slippage of clip (Table 2)

Incidence of regrowth of the original aneurysm revealed that 2 out of total 47 patients (4.3%) in the S group were noted. None of the cases were found in the T group, and clip slippage was not observed in both groups. In terms of incidence of aneurysmal regrowth during the follow-up period, there was no statistical difference between 2 groups ($p = 0.242$).

Post-clipping seizure (Table 2)

Seven out of 47 cases (14.9%) developed post-clipping seizure in the S group. On the other hand, 2 (4.2%) of 48 patients presented seizure in the T group. The statistics told us that with respect to incidence of post-clipping seizure development during the follow-up period, no significant difference was made between 2 groups ($p = 0.091$). There was neither generalized foreign body reaction among the patients who developed post-clipping seizure nor space-occupying lesion around the clipped aneurysm via follow-up computed tomography (CT) or MRI.

DISCUSSION

The result concerning regrowth of aneurysm seems contradicting to what was anticipated in that T group will have a higher recurrence rate. On the other hand, it is speculated that the possibility of misinter-

Table 2. The incidence of regrowth of original aneurysms and post-clipping seizure

	S group (n = 47)	T group (n = 48)	*p* value
Regrowth	2 (4.3%)	0 (0%)	0.242
Post clipping seizure	7 (14.9%)	2 (4.2%)	0.091

pretation of the angiographic data, especially in the S group owing to the poor resolution in the angiogram from the old-fashioned angiographic machine cannot be overlooked.

Tsutsumi and his colleagues[7] elucidated the importance of follow-up angiography in patients with clipped aneurysms 9 to 10 years after surgery. They performed a relatively long-term follow-up study with the mean 9.3 years from surgery for all patients and 9.0 years for the clipped aneurysms. In the study, four aneurysm regrowths were detected out of the total 140 (4/140, 2.9%) clipped aneurysms in the angiographically controlled study. Also, the authors reported that de novo aneurysms were detected in nine of 112 (8.0%) patients claiming the annual rate of de novo aneurysm formation was 0.89%. This study showed that the annual rate of de novo aneurysm formation after clipping surgery is relatively high (0.89%) and that the cumulative risk becomes significant after nine years in consideration of the fatality rate of SAH. Although current study revealed no de novo aneurysm formation in the follow-up period, because intracranial aneurysms develop during life time, even successfully occluded aneurysms are at risk for a recurrence or regrowth after clipping surgery. Thus, long-term prospective angiographic follow-up results are crucial to evaluate outcome of surgically treated aneurysms. Subsequently, these findings support the rationale for late angiographic follow-up in patients with clipped cerebral aneurysms.[8]

In the light of screening cerebral aneurysms preventing future aneurysmal SAH or rebleeding from the previously clipped aneurysms, it is crucial to obtain late follow-up angiography and define "meaningful aneurysmal regrowth". Ahn and Kim[9] made a great emphasis on defining what aneurysm remnant is because its definition can affect the rate of aneurysm remnants to be obtained and subsequent planning for treatment. Sindou et al.[10] further expanded their thought, studying the detected aneurysm remnants after clipping surgery, and made Sindou's classification of aneurysm remnants. Such aneurysm remnant classification helped the neurosurgeons' articulate a legitimate treatment plan. In parallel with their effort to establish its definition, it is urged to define significant regrowth of aneurysm in cerebral angiography and make a new guideline based upon the clinical correlation with aneurysm regrowth in a specific imaging modality to come up with screening/preventing and decent therapeutic strategies in cerebral aneurysms.

With respect to the reliability of conventional S in mechanical properties, it has been approved by American Society for Testing and Material,[11] While due to its constant contact with the cerebrospinal fluid (CSF), the metal clips, especially, S, applied to intracranial aneurysms are vulnerable to corrosion given the fact that the chloride ion concentration in CSF is about 119 mEq/L. In addition, amino acids and proteins in CSF can possibly accelerate implant corrosion, leading to metal ion dissolution. As a result, toxicity and allergic reactions as well as deterioration of the mechanical properties of the metal implant can occur.[12-14] These insidious events were documented in the case that conventional S can activate T-lymphocytes and cause a delayed-type hypersensitive immune reaction in the central nervous system, giving rise to diffuse and severe pruritic symptoms.[6] Fisher et al.[15] evaluated and compared T to S where they studied seizure and electroencephalographic changes in the T, S implanted, or non-operated rabbits. They observed that there were no epileptiform activity in the T implanted rabbits as well as in the S implanted and non-operated rabbits. Subsequently, we proposed that the presence of intracranial metal clips which maintain constant contacts with brain can be one of the etiologic factors for post-clipping seizure attacks.[16-18]

Tracing back to search for any foreign body reaction among the patients who developed post-clipping seizure in each group, we could not find any remarkable documentation reported on the generalized allergic reaction in their medical records. Although the authors hypothesized that the retention of intracranial

metal clips can be one of the etiologic factors for post-clipping seizure, the occurrence of post-clipping seizure was more likely happened due to other causes such as increased intracranial pressure, postoperative vasospasm, large intracerebral hemorrhage, shunt-dependent hydrocephalus and sequelae of initial hemorrhage rather than foreign body reaction per se.[18)]

The limitations of this study are those inherent to the retrospective study of small populations where data have been collected in a clinical context so that bias cannot be completely excluded. It was also hard to make a fair evaluation when the long-term follow-up angiograms were compared with pre- and early post-operative angiograms due to substantial resolution differences among different angiographic machines. In addition, difference in mean follow-up period between two groups was quite significant (87.1 months versus 65.9 months, $p = 0.000$) so that it could possibly give rise to another source of bias in aneurysm regrowth. Nevertheless, the strength of this study holds fairly long-term follow-up periods more than 60 months.

CONCLUSION

The metallic types of clip employed for the microsurgical cerebral aneurysm clipping does not make any significant clinical outcome differences in this study. Thus, T holds similar efficacy over the conventional S especially, in terms of regrowth rate of clipped aneurysm and clip slippage.

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