Title	Retrospective Survey of Endovascular Treatment for Ruptured Intracranial Aneurysm in Japan : Retrospective Endovascular Subarachnoid Aneurysm Treatment (RESAT) Study(本文 (Fulltext))
Author(s)	SAKAI, Nobuyuki; TAKI, Waro; YOSHIMURA, Shinichi; HYOGO, Toshio; EZURA, Masayuki; MATSUMOTO, Yasushi; ITO, Yasushi; ABE, Hiroshi; SONOBE, Makoto; KOBAYASHI, Shigeki; NEMOTO, Shigeru; MURAYAMA, Yuichi; MATSUMARU, Yuji; OISHI, Hidenori; KUWAYAMA, Naoya
Citation	[Neurologia medico-chirurgica = 神経外科] vol.[50] no.[11] p.[961]-[965]
Issue Date	2010-11-15
Rights	The Japan Neurosurgical Society (一般社団法人日本脳神経外科学会)
Version	出版社版 (publisher version) postprint
URL	http://hdl.handle.net/20.500.12099/43640

Neurol Med Chir (Tokyo) 50, 961～965, 2010

Retrospective Survey of Endovascular Treatment for Ruptured Intracranial Aneurysm in Japan: Retrospective Endovascular Subarachnoid Aneurysm Treatment (RESAT) Study

Nobuyuki SAKAI,[1] Waro TAKI,[2] Shinichi YOSHIMURA,[3] Toshio HYOGO,[4] Masayuki EZURA,[5] Yasushi MATSUMOTO,[6] Yasushi ITO,[7] Hiroshi ABE,[8] Makoto SONOBE,[9] Shigeki KOBAYASHI,[10] Shigeru NEMOTO,[11] Yuichi MURAYAMA,[12] Yuji MATSUMARU,[13] Hidenori OISHI,[14] Naoya KUWAYAMA,[15] Shigeru MIYACHI,[16] Tomoaki TERADA,[17] Masaki KOMIYAMA,[18] Toshiyuki FUJINAKA,[19] Kenji SUGIU,[20] Koichi SATO,[21] Ichiro NAKAHARA,[22] Kiyoshi KAZEKAWA,[23] Masaru HIROHATA,[24] Akio HYODO,[25] and Chiaki SAKAI[26]; RESAT Study Group

[1]*Department of Neurosurgery, Kobe City Medical Center General Hospital, Kobe, Hyogo;*
[2]*Mie University, Tsu, Mie;* [3]*Gifu University, Gifu;*
[4]*Nakamura Memorial Hospital, Sapporo, Hokkaido;* [5]*Sendai Medical Center, Sendai, Miyagi;*
[6]*Konan Hospital, Sendai, Miyagi;* [7]*Niigata University, Niigata;*
[8]*Tachikawa Hospital, Nagaoka, Niigata;* [9]*Mito Medical Center, Ibaraki;*
[10]*Chiba Emergency Medical Center, Chiba;* [11]*Jichi Medical University, Shimotsuke, Tochigi;*
[12]*Jikei University, Tokyo;* [13]*Toranomon Hospital, Tokyo;* [14]*Juntendo University, Tokyo;*
[15]*Toyama University, Toyama;* [16]*Nagoya University, Nagoya, Aichi;*
[17]*Wakayama Medical University, Wakayama;* [18]*Osaka City General Hospital, Osaka;*
[19]*Osaka University, Suita, Osaka;* [20]*Okayama University, Okayama;*
[21]*Tokushima University, Tokushima;* [22]*Kokura Memorial Hospital, Kitakyushu, Fukuoka;*
[23]*Fukuoka University Chikushi Hospital, Chikushino, Fukuoka;*
[24]*Kurume University, Kurume, Fukuoka;*
[25]*Dokkyo University Koshigaya Hospital, Koshigaya, Saitama;*
[26]*Institue of Biomedical Research and Innovation, Kobe, Hyogo*

Abstract

Annual retrospective surveys of 20 to 31 medical centers performing endovascular treatment of cerebral aneurysms in Japan from 1997 to 2008 were performed to analyze technical and clinical outcomes of endovascular treatment for ruptured cerebral aneurysm. Patients treated with dome embolization using bare platinum coils within 14 days after onset were retrospectively selected, and clinical features, and technical and clinical outcomes at discharge were studied. Retrospective Endovascular Subarachnoid Aneurysm Treatment (RESAT) 1 covers patients treated from 1997, when the Guglielmi detachable coil was introduced, to 2002, just after International Subarachnoid Aneurysm Trial was reported. RESAT 2 to RESAT 7 were conducted annually between 2003 and 2008. Among 5,624 patients with ruptured aneurysms treated within 14 days after onset, 4,782 patients were treated by dome embolization using platinum detachable coils. The patients in this large retrospective survey included 35.8% aged over 70 years, 36.6% with posterior circulation aneurysms, and 29.3% with poor grades (Hunt and Kosnik grades IV and V). The proportion of patients aged over 70 years tended to increase each year from 33.4% in RESAT 1 to 39.8% in RESAT 7, and the proportion of those with posterior circulation aneurysms decreased from 44.2% in RESAT 1 to 23.8% in RESAT 7 ($p<0.001$). Overall technical success was obtained in 4,666 patients (97.6%), and favorable clinical outcome (good recovery and moderate disability) at discharge was obtained in 88.0% of grade I–III cases and 73.6% of grade I–V cases. Procedure-related morbidity was 2.9% and mortality was 0.8%. Despite this survey involving high proportions of aged, posterior circulation, and poor-grade patients, the technical success rate and immediate clinical results were relatively favorable. The patient prognosis and aneurysm changes must be investigated over a longer period, together with the effects of the introduction of new endovascular devices for cerebral aneurysms.

Key words: subarachnoid hemorrhage, ruptured aneurysm, endovascular treatment, clinical survey, International Subarachnoid Aneurysm Trial

Received February 17, 2010; Accepted May 31, 2010

Introduction

Subarachnoid hemorrhage is associated with mortality rates of 32% to 67% and long-term dependence in 10% to 20% of survivors because of the resultant brain damage.[5] Early treatment within 24 to 72 hours has been recommended for ruptured aneurysms, because the risk of subsequent rupture is high, with approximately 20% of patients experiencing another rupture in the first 2 weeks after subarachnoid hemorrhage.[8]

Following the introduction of Guglielmi detachable coils (GDCs) in Japan in 1997, surgical and endovascular treatment modalities have been available for ruptured cerebral aneurysms. Initially, surgically difficult aneurysms such as basilar bifurcation aneurysms were treated using detachable platinum coils.[4] However, a prospective randomized trial, the International Subarachnoid Aneurysm Trial (ISAT), reported that endovascular treatment of ruptured cerebral aneurysms with detachable coils was superior to surgical clipping as defined by the proportion of patients dead or disabled at 1 year among 2,143 of 9,559 patients deemed suitable for either therapy.[10] Since then, coil embolization has been increasingly used as an alternative to surgical clipping. More recently, the risk of death at 5 years was significantly lower in the coiled group than in the clipped group in the long-term follow up of the patients registered in the ISAT.[9]

The Retrospective Endovascular Subarachnoid Aneurysm Treatment (RESAT) studies 1 to 7 tried to determine the status of endovascular treatment for ruptured aneurysms in Japan from the GDC launch until just before the ISAT report was published for comparison with the ISAT data, and to elucidate how ISAT influenced the top Japanese medical centers annually from 2003 to 2008.

Clinical Material and Methods

A total of 13,711 patients with ruptured or unruptured cerebral aneurysms underwent endovascular treatment conducted by members of the study group (from 31 different institutions; both surgical and endovascular treatments were possible, and endovascular treatments were conducted by board-certified senior trainers) between January 1997 and December 2008. Among them, 5,624 patients underwent endovascular treatment, of whom 4,782 patients were treated by dome embolization using platinum detachable coils within 14 days after onset. These 4,782 patients were analyzed in this study.

The following clinical factors were studied: age, sex, location and size of the aneurysm, duration after onset, neurological grade (Hunt & Kosnik grade), technical complications and type (ischemic, hemorrhagic, or others), and repeated bleeding and retreatment within the annual study period. The Glasgow Outcome Scale (GOS) of disability at discharge was used for evaluation of patient outcome. A death was included in the mortality rate if it occurred within the annual study period. Morbidity was evaluated when the patient was discharged from the institute.

Timing, indication, and method of endovascular treatment and perioperative therapy such as antithrombotic therapy, cerebrospinal fluid drainage, and management for cerebral vasospasm after subarachnoid hemorrhage were all determined by each institute. Technical success was defined as successful dome embolization with parent artery preservation regardless of degree of aneurysm obliteration.

All analyses were performed with SAS software (SAS Institute Inc., Cary, N.C., U.S.A.). Ordered categorical data were examined by Mantel-Haenszel X2 statistics. Mann-Whitney U tests were used to compare the non-parametric data, and unpaired t-tests were used to compare normally distributed data.

Results

The numbers of registered patients and institutes participating in RESAT 1–7 are summarized in Table 1. The mean number of patients treated with dome embolization within 14 days at each institute increased annually from 12.4 in RESAT 1 to 26.8 in RESAT 7.

The proportion of female patients showed no significant serial change during the period of this study (Fig. 1). The distribution of ages of the patients is shown in Fig. 2. The proportion of patients aged

Table 1 Numbers of registered patients and institutes participating in RESAT 1–7

	Survey period	No. of patients	No. of institutes	Calculated no. of patients in an institute in a year
RESAT 1	1997–2002	1488	20	12.4
RESAT 2	2003	439	23	19.1
RESAT 3	2004	418	23	18.2
RESAT 4	2005	617	31	19.9
RESAT 5	2006	696	28	24.9
RESAT 6	2007	566	24	23.6
RESAT 7	2008	562	21	26.8

Patients treated by dome embolization within 14 days after onset were included in this study. The calculated annual number of patients treated with dome embolization at each institute increased from 12.4 to 26.8.

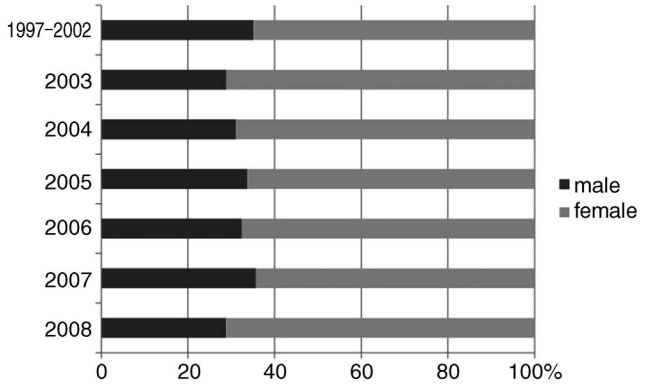

Fig. 1 Sex distribution of the patients in RESAT 1–7. Each bar shows the proportion of patients registered in each study. There were no significant changes in the sex ratio between the studies.

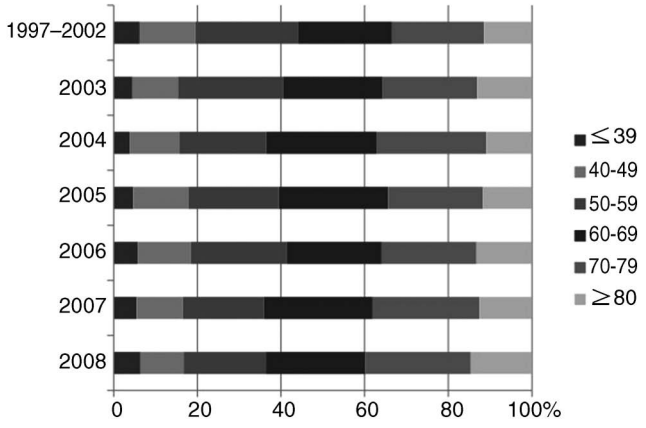

Fig. 2 Age distribution of the patients in RESAT 1–7. The distribution of patient ages is shown. The proportion of patients aged over 70 years tended to increase each year from 33.4% in RESAT 1 to 39.8% in RESAT 7.

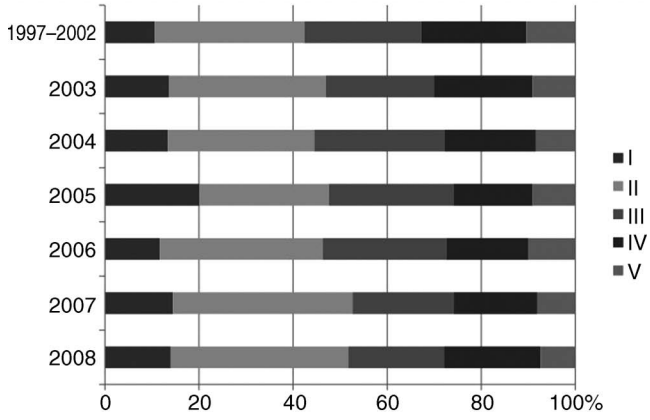

Fig. 3 Hunt and Kosnik grade before treatment in RESAT 1–7. The neurological grade of the patients before treatment is shown. The proportion of patients with Hunt and Kosnik grades I–III was around 70% and almost constant in this study.

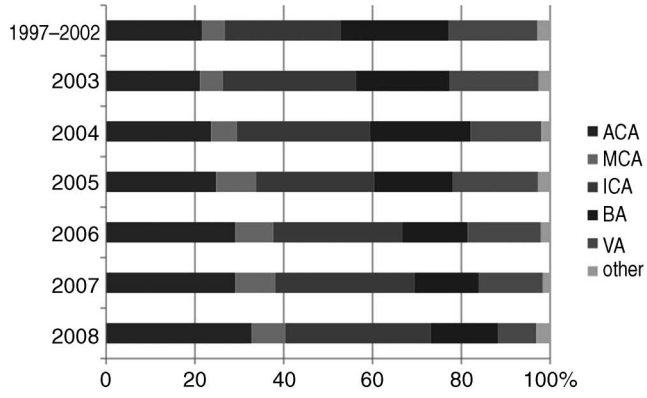

Fig. 4 Location of the aneurysms in RESAT 1–7. The proportion of posterior circulation aneurysms, such as vertebral artery (VA) or basilar artery (BA), significantly decreased from 44.2% in RESAT 1 to 23.8% in RESAT 7 ($p < 0.001$). ACA: anterior cerebral artery, ICA: internal carotid artery, MCA: middle cerebral artery.

over 70 years tended to increase each year from 33.4% in RESAT 1 to 39.8% in RESAT 7. The neurological grade of the patients evaluated before treatment is shown in Fig. 3. The proportion of patients with Hunt and Kosnik grades I–III was 70.7% in this study, and gradually increased from 67.2% in RESAT 1 to 72.1% in RESAT 7, although the difference was not statistically significant.

The distribution of aneurysm size was as follows: less than 5 mm in 38.6%, 5–10 mm in 48.8%, 11–24 mm in 11.6%, and 25 mm or more in 1.0%. There was no significant change in the size of the aneurysm by year (data not shown). In contrast, the proportion of posterior circulation aneurysms significantly decreased from 44.2% in RESAT 1 to 23.8% in RESAT 7 ($p < 0.001$) (Fig. 4).

The proportion of cases with early treatment within 72 hours after onset was consistently above 80% in this study (data not shown). Overall technical success was obtained in 4,666 patients (97.6%), and this value remained between 96.5% and 99.3% throughout the study.

In this study, clinical outcome was evaluated by GOS at discharge separately for patients with Hunt and Kosnik grades I–V and I–III. Overall favorable clinical outcome, good recovery and moderate disability by GOS, was obtained in 73.6% of the patients with grades I–V (Fig. 5 *upper*) and in 88.0% of the patients with grades I–III (Fig. 5 *lower*). Favorable clinical outcome was obtained in more

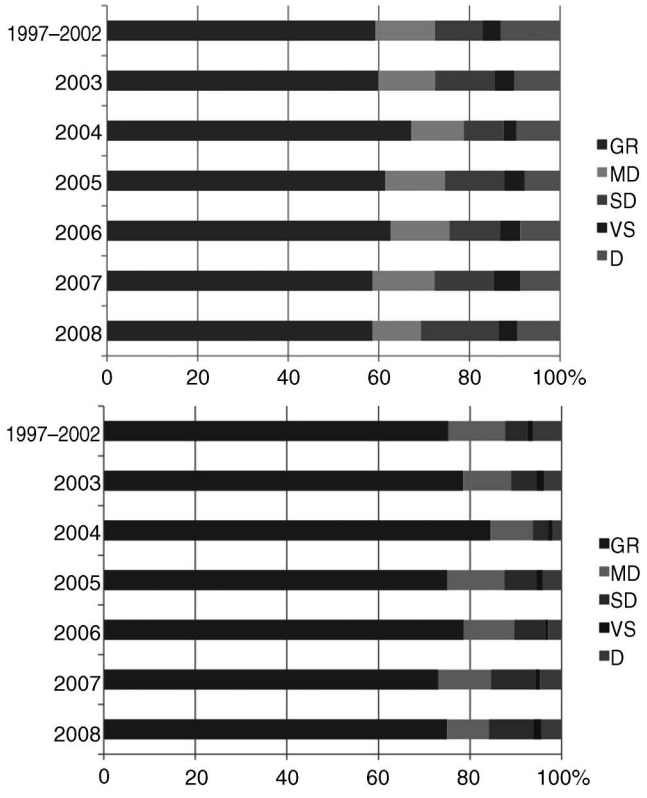

Fig. 5 Overall outcome (Glasgow Outcome Scale: GOS) of the patients at discharge in RESAT 1–7. Clinical outcome was evaluated by GOS at discharge for all the patients including those with Hunt and Kosnik grades I–V (*upper*) and I–III (*lower*). *Upper*: Overall favorable clinical outcome, good recovery (GR) and moderate disability (MD) on GOS, was obtained in more than 70% of cases in each study and the average was 73.6%. *Lower*: The rate of favorable clinical outcome, GR and MD on GOS, was more than 84% in each study and the average was 88.0% in this group. D: dead, SD: severe disability, VS: vegetative state.

than 84% of the patients with grades I–III and 70% of patients with grades I–V throughout the study (Fig. 5).

Procedure-related morbidity was 2.9% and mortality was 0.9%. Morbidity was 0.7% and mortality was 0.6% for hemorrhagic events. Morbidity was 2.0% and mortality was 0.3% for ischemic events. Morbidity was 0.2% for other events.

Discussion

ISAT has encouraged many related commentaries and letters since publication in October 2002.[1,7,12,14] The standard of neurointerventional treatments was asserted to be different at European centers to Japanese centers. However, the Japanese status of endovascular treatment for ruptured intracranial aneurysms has not been described, except for a small series from a single center. The purpose of RESAT 1 was to determine the Japanese status of endovascular treatment for ruptured aneurysms from the GDC launch until just before the ISAT report was published, and to compare these results with the ISAT data obtained 2 months after allocation, although clinical outcome was evaluated at discharge in this study.[10,11] The following surveys were conducted to elucidate how the ISAT influenced the Japanese medical centers annually from 2003 to 2008.

Patient characteristics in this study tended to be different from those in ISAT.[10,11] Regarding age, 5.8% of patients were older than 70 years in ISAT; in contrast, the proportion was 35.8% in RESAT. In terms of neurological grade, 93% of patients were grades I–III in ISAT compared with 70.7% in RESAT. Furthermore, 97.1% of the aneurysms were located at anterior circulation in ISAT compared with 63.4% in RESAT. RESAT included patients who might have been excluded in ISAT, leading to an unfavorable outcome. To compare RESAT with ISAT, only the patients with grades I–III in both studies were analyzed. In ISAT, favorable outcome was obtained in 74.6% of patients at 2 months after allocation compared with 89.1% at discharge in RESAT. Thus, the overall clinical results of RESAT were rather better than those of ISAT.

In RESAT 2, endovascular treatment became the first-line treatment for ruptured cerebral aneurysm at all but 2 centers, indicating that ISAT had an impact on Japanese centers and increased the rate of endovascular treatment. RESAT 2–7 were subsequently performed annually and showed interesting trends. Although there was no significant change in the proportion of elderly or poor-grade patients, the proportion of posterior circulation aneurysms decreased year-on-year. Therefore, the application of endovascular treatment widened to anteriorly located aneurysms, which were previously treated by clipping.

On the other hand, disclosure of the favorable results of RESAT seemed to motivate the participants to conduct endovascular treatment for aneurysms for which either therapy was deemed suitable. In Japan, endovascular treatment was mainly performed by neurosurgeons. This might be an important factor in improving the overall results of treatment for ruptured aneurysms.

We recognize the disadvantages of endovascular treatment such as recanalization, repeated bleeding, and retreatment after procedure.[2,3,6,13] Repeated bleeding from the target aneurysm was observed 2.5

times more frequently in the coiled group.[11] Therefore, follow up of the treated patients is important. We are planning to investigate the clinical events, such as repeated bleeding and retreatment, after treatment in RESAT.

This series of surveys has determined the Japanese status of endovascular treatment for ruptured aneurysms since GDC was launched. Despite this survey involving high proportions of elderly, posterior circulation, and poor-grade patients, the technical success rate and immediate clinical results were relatively favorable. It is necessary to investigate the patient prognosis and aneurysm changes over a longer period, together with the effects of the introduction of new endovascular devices for cerebral aneurysms.

Acknowledgments

This study received no sponsorship for data collection, data analysis, data interpretations, or writing.

We express our gratitude to the following participating members of the RESAT study for kindly enrolling their cases and encouraging us to continue this study: A. Takahashi, M.D., Konan Hospital; O. Miyagi, M.D., Tatebayashi Kosei Hospital; S. Ishihara, M.D., Saitama University; T. Hirayama, M.D., Nihon University; T. Shibuya, M.D., Sagamihara Kyodo Hospital; A. Kurata, M.D., Kitazato University; H. Nagashima, M.D., Aizawa Hospital; M. Negoro, M.D., Nagoya University; H. Sakaida, M.D., Mie University; K. Murao, M.D., National Cardiovascular Center; M. Nakamura, M.D., Kobe University; T. Abe, M.D., Kurume University.

References

1) Ausman JI: ISAT study: is coiling better than clipping? *Surg Neurol* 59: 173–175, 2003
2) Byrne JV, Sohn MJ, Molyneux AJ, Chir B: Five-year experience in using coil embolization for ruptured intracranial aneurysms: outcomes and incidence of late rebleeding. *J Neurosurg* 90: 656–663, 1999
3) Campi A, Ramzi N, Molyneux AJ: Retreatment of ruptured cerebral aneurysms in patients randomized by coiling or clipping in the International Subarachnoid Aneurysm Trial (ISAT). *Stroke* 38: 1538–1544, 2007
4) Guglielmi G, Viñuela F, Duckwiler G, Dion J, Lylyk P, Berenstein A, Strother C, Graves V, Halbach V, Nichols D: Endovascular treatment of posterior circulation aneurysms by electrothrombosis using electrically detachable coils. *J Neurosurg* 77: 515–524, 1992
5) Hop JW, Rinkel GJ, Algra A, van Gijn J: Case-fatality rates and functional outcome after subarachnoid hemorrhage: a systematic review. *Stroke* 28: 660–664, 1997
6) Johnston SC, Dowd CF, Higashida R: Predictors of re-hemorrhage after treatment of ruptured intracranial aneurysms: the Cerebral Aneurysm Rerupture After Treatment (CARAT) study. *Stroke* 39: 120–125, 2008
7) Lindsay KW: The impact of the International Subarachnoid Aneurysm Treatment Trial (ISAT) on neurosurgical practice. *Acta Neurochir (Wien)* 145: 97–99, 2003
8) Mayberg MR, Batjer HH, Dacey R, Diringer M, Haley EC, Heros RC, Sternau LL, Torner J, Adams HP Jr, Feinberg W: Guidelines for the management of aneurysmal subarachnoid hemorrhage. A statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. *Stroke* 25: 2315–2328, 1994
9) Molyneux AJ, Kerr RS, Birks J, Ramzi N, Yarnold J, Sneade M, Rischmiller J; ISAT Collaborators: Risk of recurrent subarachnoid haemorrhage, death, or dependence and standardised mortality ratios after clipping or coiling of an intracranial aneurysm in the International Subarachnoid Aneurysm Trial (ISAT): long-term follow-up. *Lancet Neurol* 8: 427–433, 2009
10) Molyneux AJ, Kerr RSC, Stratton I: International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet* 360: 1267–1274, 2002
11) Molyneux AJ, Kerr RSC, Yu LM, Clarke M, Sneade M, Yarnold JA, Sandercock P; International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group: International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. *Lancet* 366: 809–817, 2005
12) Nichols DA, Brown RD, Meyer FB: Coils or clips in subarachnoid haemorrhage? *Lancet* 360: 1262–1263, 2002
13) Raymond J, Guilbert F, Weill A: Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils. *Stroke* 34: 1398–1403, 2003
14) Van den Berg R, Rinkel GJ, Vandertop WP: Treatment of ruptured intracranial aneurysms: implications of the ISAT on clipping versus coiling. *Eur J Radiol* 46: 172–177, 2003

Address reprint requests to: Nobuyuki Sakai, M.D., Department of Neurosurgery, Kobe City Medical Center General Hospital, 4–6 Minatojima–Nakamachi, Chuo–ku, Kobe 650–0046, Japan.
e-mail: n.sakai@siren.ocn.ne.jp