

**TABLE 3. Demographics of the Patient Study Cohort at the Time of Diagnosis and Hospital Characteristics According to Stroke Type Between April 1, 2010, and March 31, 2011 in Japan<sup>a</sup>**

	Total (n = 53 170)	Ischemic Stroke (n = 32 671)	Intracerebral Hemorrhage (n = 15 699)	Subarachnoid Hemorrhage (n = 4934)
Male	29 353 (55.2)	18 816 (57.6)	9030 (57.5)	1584 (32.1)
Age, mean $\pm$ SD, y	72.5 $\pm$ 13.1	74.4 $\pm$ 12.2	70.7 $\pm$ 13.5	64.7 $\pm$ 14.8
Hypertension	39 918 (75.1)	22 531 (69.0)	13 281 (84.6)	4229 (85.7)
Diabetes mellitus	13 725 (25.8)	9318 (28.5)	3278 (20.9)	1174 (23.8)
Hyperlipidemia	15 015 (28.2)	11 104 (34.0)	2529 (16.1)	1412 (28.6)
Smoking (n = 44842)	12 761 (24.0)	8188 (25.1)	3540 (22.5)	1074 (21.8)
Medications during hospitalization				
Antihypertensive agent	34 136 (64.2)	17 694 (54.2)	12 537 (79.9)	4019 (81.5)
<i>Anti-renin-angiotensin system agent</i>	19 881 (37.4)	10 262 (31.4)	8280 (52.7)	1410 (28.6)
<i>Calcium channel antagonist</i>	25 984 (48.9)	10 469 (32.0)	11 719 (74.6)	3903 (79.1)
Sympathetic antagonist	6334 (11.9)	3821 (11.7)	2172 (13.8)	364 (7.4)
<i><math>\beta</math>-blocker<sup>b</sup></i>	4357 (8.2)	3048 (9.3)	1133 (7.2)	188 (3.8)
<i><math>\alpha</math>-blocker</i>	2374 (4.5)	953 (2.9)	1232 (7.8)	200 (4.1)
Diuretic agent	9950 (18.7)	5860 (17.9)	3074 (19.6)	1049 (21.3)
<i>Loop diuretic</i>	7434 (14.0)	4609 (14.1)	1912 (12.2)	940 (19.1)
<i>Other diuretic</i>	4425 (8.3)	2527 (7.7)	1653 (10.5)	255 (5.2)
Antidiabetic agent	10 295 (19.4)	6784 (20.8)	2473 (15.8)	1075 (21.8)
<i>Insulin</i>	7654 (14.4)	4597 (14.1)	2044 (13.0)	1046 (21.2)
<i>Oral antidiabetic agent</i>	5749 (10.8)	4459 (13.6)	1110 (7.1)	197 (4.0)
Antihyperlipidemic agent	12 387 (23.3)	9264 (28.4)	1839 (11.7)	1310 (26.6)
<i>Statin</i>	10 099 (19.0)	7840 (24.0)	1366 (8.7)	912 (18.5)
Antiplatelet agent	23 635 (44.5)	21 746 (66.6)	625 (4.0)	1298 (26.3)
<i>Aspirin</i>	11 929 (22.4)	11 119 (34.0)	378 (2.4)	447 (9.1)
Japan Coma Scale score				
0	19 635 (36.9)	15 027 (46.0)	3620 (23.1)	1024 (20.8)
1-digit code	19 371 (36.4)	12 375 (37.9)	5934 (37.8)	1117 (22.6)
2-digit code	6937 (13.0)	3396 (10.4)	2705 (17.2)	852 (17.3)
3-digit code	7227 (13.6)	1873 (5.7)	3440 (21.9)	1941 (39.3)
Emergency admission by ambulance	31 995 (60.2)	17 336 (53.1)	10 909 (69.5)	3830 (77.6)
Average time in hospital (range), d	21 (11-40)	20 (12-38)	22 (10-43)	30 (12-54)
Hospital characteristics (mean $\pm$ SD CSC scores)				
Total score (25 items)		16.7 $\pm$ 3.8	16.8 $\pm$ 3.4	17.1 $\pm$ 3.4
Personnel (7 items)		3.7 $\pm$ 1.2	3.7 $\pm$ 1.2	3.8 $\pm$ 1.2
Diagnostic techniques (6 items)		4.4 $\pm$ 1.1	4.5 $\pm$ 1.0	4.5 $\pm$ 1.0
Specific expertise (5 items)		4.4 $\pm$ 1.0	4.4 $\pm$ 0.9	4.5 $\pm$ 0.8
Infrastructure (5 items)		2.8 $\pm$ 1.3	2.9 $\pm$ 1.3	2.9 $\pm$ 1.3
Education (2 items)		1.4 $\pm$ 0.8	1.4 $\pm$ 0.8	1.4 $\pm$ 0.8

<sup>a</sup>CSC, comprehensive stroke center.<sup>b</sup>A composite variable with a pure  $\beta$  antagonist and a mixed  $\alpha/\beta$ -adrenergic antagonist (eg, labetalol). Reproduced from Iihara et al<sup>11</sup> with permission.

scores ranged from 1 to 23 (mean, 15.4; standard deviation, 4.2; median, 14; IQR, 11-18). Mortality rates were 7.8% for patients with ischemic stroke, 16.8% for patients with ICH, and 28.1% for patients with subarachnoid hemorrhage. Mortality of patients with ischemic stroke was significantly correlated with the patient characteristics of male sex (odds ratio [OR] = 1.23), age (10 incremental years, OR = 1.4), and level of consciousness (1-digit code, OR = 2.4; 2-digit code, OR = 7.46; 3-digit code, OR = 21.62 vs zero as the control) and the hospital characteristics of total CSC score (OR = 0.97) adjusted for age, sex, and level of consciousness (Table 4). Mortality of patients with ICH was also

significantly correlated with the patient characteristics of male sex (OR = 1.72), age (10 incremental years, OR = 1.36), and level of consciousness (1-digit code, OR = 1.45; 2-digit code, OR = 4.22; 3-digit code, OR = 49.59 vs zero as the control) and the hospital characteristic of total CSC score (OR = 0.97) adjusted for age, sex, and level of consciousness (Table 5). Mortality of patients with subarachnoid hemorrhage was also significantly correlated with the patient characteristics of male sex (OR = 1.39), age (10 incremental years, OR = 1.37), and level of consciousness (2-digit code, OR = 2.01; 3-digit code, OR = 17.12 vs zero as the control) and the hospital characteristic of total CSC score (OR = 0.95)

**TABLE 4. The Impact of Total Comprehensive Stroke Care Score on In-Hospital Mortality After Ischemic Stroke Adjusted by Age, Sex, and Level of Consciousness at Admission According to the Japan Coma Scale<sup>a</sup>**

Factor	OR	95% CI	P Value
Male sex	1.23	1.12-1.35	<.001
Age	1.40	1.34-1.47	<.001
CSC total score	0.97	0.96-0.99	.001
JCS			
Normal	1		
1-digit code	2.40	2.11-2.74	<.001
2-digit code	7.46	6.47-8.60	<.001
3-digit code	21.62	18.69-25.02	<.001

<sup>a</sup>CI, confidence interval; CSC, comprehensive stroke care; JCS, Japan Coma Scale; OR, odds ratio. Reproduced from Iihara et al<sup>11</sup> with permission.

**TABLE 6. The Impact of Total Comprehensive Stroke Care Score on In-Hospital Mortality After Subarachnoid Hemorrhage Adjusted by Age, Sex, and Level of Consciousness at Admission According to the Japan Coma Scale<sup>a</sup>**

Factor	OR	95% CI	P Value
Male sex	1.39	1.17-1.65	<.001
Age	1.37	1.29-1.45	<.001
CSC total score	0.95	0.93-0.98	<.001
JCS			
Normal	1		
1-digit code	1.05	0.75-1.46	.79
2-digit code	2.01	1.46-2.77	<.001
3-digit code	17.13	13.14-22.35	<.001

<sup>a</sup>CI, confidence interval; CSC, comprehensive stroke care; JCS, Japan Coma Scale; OR, odds ratio. Reproduced from Iihara et al<sup>11</sup> with permission.

adjusted for age, sex, and level of consciousness (Table 6). Therefore, total CSC score was independently associated with in-hospital mortality for all stroke types after adjustment for age, sex, and stroke severity. The impact of total CSC score on in-hospital mortality for ischemic stroke and ICH remained significant after adjustment for age, sex, severity of stroke, and existence of comorbid conditions (hypertension, diabetes mellitus, and hyperlipidemia; data not shown). Figure 2 shows the impact of total CSC score classified into quintiles (quintile 1, 4-12; quintile 2, 13-14; quintile 3, 15-17; quintile 4, 18; quintile 5, 19-23) on the in-hospital mortality of patients with all types of stroke, ischemic stroke, ICH, and subarachnoid hemorrhage after adjustment for age, sex, and level of consciousness. In summary, we found that the total CSC score was significantly associated with in-hospital mortality rates regardless of stroke type after adjustment for age, sex, and initial level of consciousness according to the Japan Coma Scale.

**TABLE 5. The Impact of Total Comprehensive Stroke Care Score on In-Hospital Mortality After Intracerebral Hemorrhage Adjusted by Age, Sex, and Level of Consciousness at Admission According to the Japan Coma Scale<sup>a</sup>**

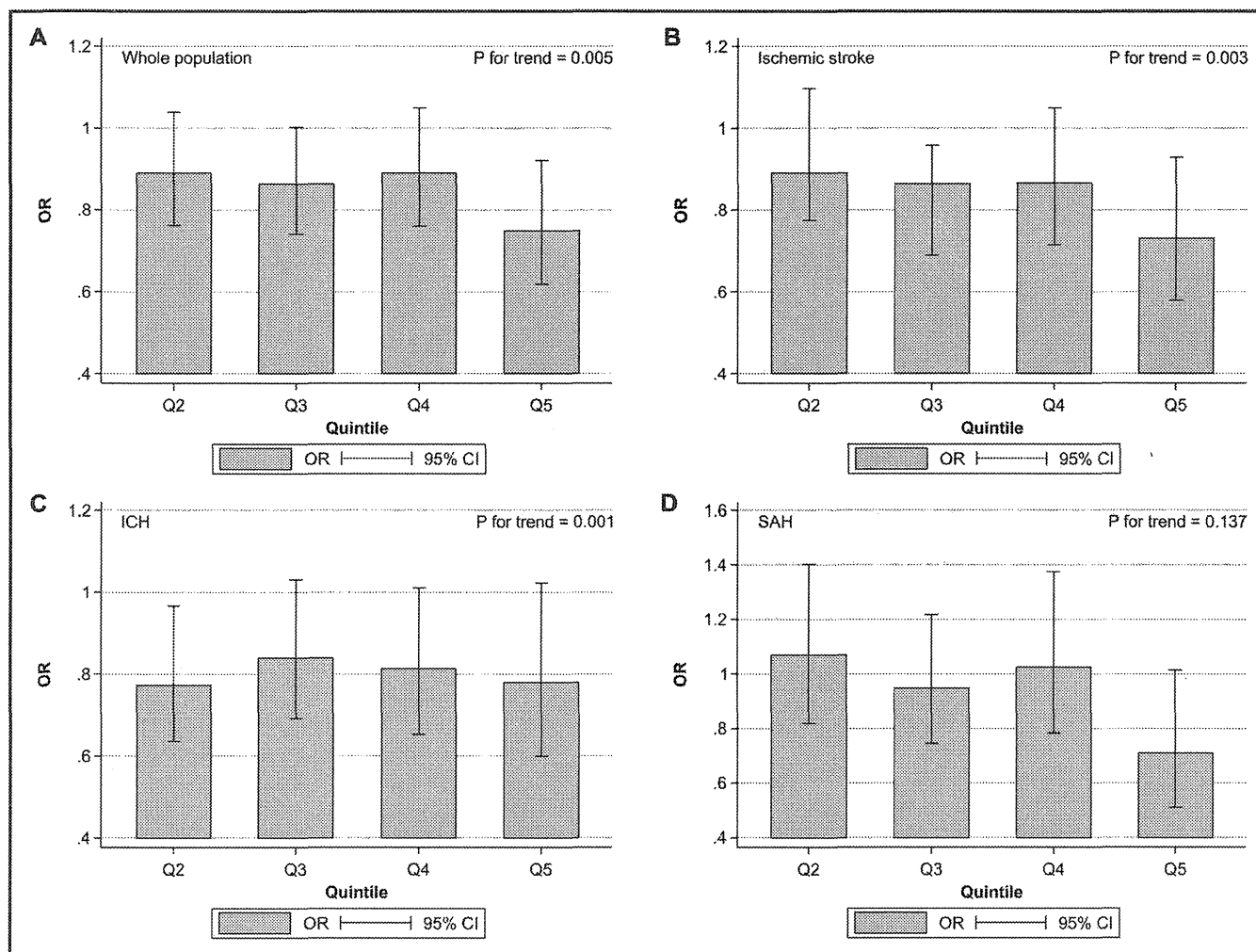
Factor	OR	95% CI	P Value
Male sex	1.72	1.54-1.92	<.001
Age	1.36	1.30-1.42	<.001
CSC total score	0.97	0.95-0.99	.003
JCS			
Normal	1		
1-digit code	1.45	1.14-1.83	.002
2-digit code	4.22	3.34-5.33	<.001
3-digit code	49.59	40.12-61.27	<.001

<sup>a</sup>CI, confidence interval; CSC, comprehensive stroke care; JCS, Japan Coma Scale; OR, odds ratio. Reproduced from Iihara et al<sup>11</sup> with permission.

At present, no official certification of stroke centers in Japan has been launched, and the present study indicates that patients with acute ischemic stroke or hemorrhagic stroke are being admitted on an emergent basis to hospitals with similar CSC total and subcategory scores, as measured with the use of 25 items originally recommended by the Brain Attack Coalition. Although there is increasingly good evidence from initiatives like Get With The Guidelines–Stroke<sup>15</sup> that a process based on the systematic collection and evaluation of stroke performance measures can rapidly improve the quality of stroke care delivered by hospitals, current metrics are limited mostly to process measures that address the care of patients with ischemic stroke in acute hospital-based settings.<sup>16</sup> In addition, there is a pressing need to demonstrate a direct link between better adherence to stroke performance measures and improved patient-oriented outcomes.<sup>3,17</sup> Finally, one could argue that there really is no concept of “3 of 4” CSCs but rather only CSCs or PSCs. In light of the existing evidence regarding the impact of the recommended CSC items on stroke outcomes, we advocate a CSC scoring system that examines the impact of the availability of the recommended items on in-hospital mortality for all types of stroke. Considering the marked impact of the CSC score on mortality after all types of stroke, the differential impacts of CSC subcategory scores for different stroke types may make a single, simple, and effective CSC criterion unrealistic to produce a nationwide reduction in stroke mortality. In our opinion, it may be a more viable option to use CSC scores in a more limited fashion, that is, to benchmark the state of care currently provided by medical centers treating stroke patients.

## ADVANCED NEUROIMAGING CAPABILITIES AT THE CSC

Advanced neuroimaging capabilities such as MRI and various types of cerebral angiography are a key area for a CSC that is



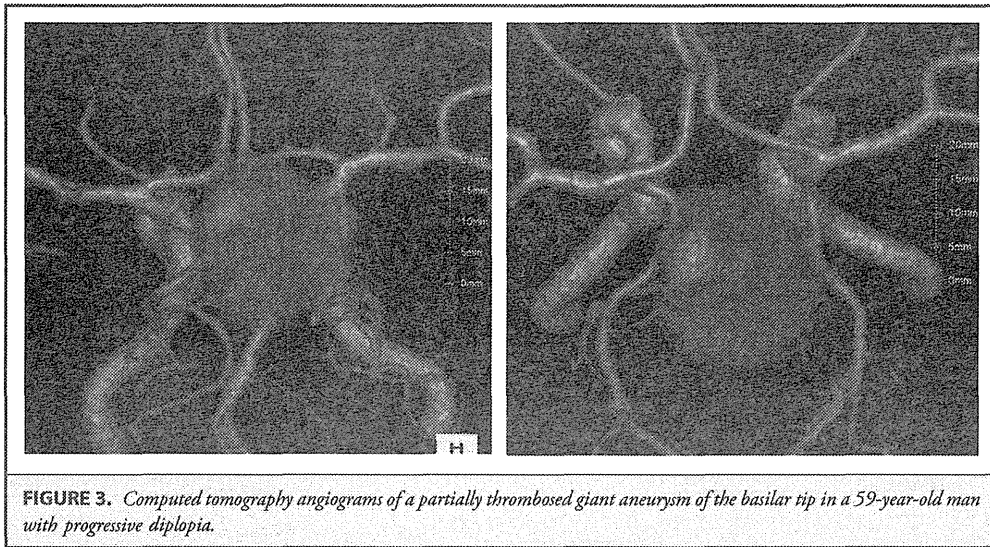
**FIGURE 2.** Associations between total comprehensive stroke care scores separated into quintiles (Q) and in-hospital mortality of patients after all types of stroke (A), ischemic stroke (B), intracerebral hemorrhage (ICH; C), and subarachnoid hemorrhage (SAH; D) after adjustment for age and sex. Odds ratios (ORs) and 95% confidence intervals (CIs) of in-hospital mortality for each quintile are depicted compared with that of Q1 as the control (Q1, 4-12 points; Q2, 13-14 points; Q3, 15-17 points; Q4, 18 points; Q5, 19-23 points). Reproduced from Iihara et al<sup>11</sup> with permission.

supported by evidence-based medicine. Here, I describe the role of tests for cerebral blood flow and metabolism using positron emission tomography in hyperperfusion after revascularization in patients with moyamoya disease. These parameters have not been quantitatively analyzed in these patients in any previous study. Despite favorable long-term outcomes after successful surgery for moyamoya disease, increasing evidence suggests that this may be complicated by temporary neurological deterioration during the postoperative acute stage owing to focal cerebral hyperperfusion around the site of the anastomosis. We found that an increased oxygen extraction fraction preoperatively was the only significant risk factor for postoperative hyperperfusion, and 2 patients with markedly increased cerebral metabolic rates of oxygen at hyperperfusion were complicated with postoperative seizures.<sup>18</sup> This

study revealed that symptomatic hyperperfusion in moyamoya disease is characterized by temporary increases in cerebral blood flow >100% of preoperative values caused by prolonged recovery of increased cerebral blood volume and illustrated a critical role of advanced neuroimaging capabilities in CSCs to clarify the pathophysiology of a rare but clinically important phenomenon using positron emission tomography, considering its difficult logistics.<sup>18,19</sup>

## MULTIMODALITY TREATMENT FOR COMPLEX NEUROVASCULAR LESIONS

Multimodality treatment for complex neurovascular lesions is one of the most important roles and responsibilities for CSCs.



**FIGURE 3.** *Computed tomography angiograms of a partially thrombosed giant aneurysm of the basilar tip in a 59-year-old man with progressive diplopia.*

Next, I illustrate our cutting-edge microsurgical management of partially thrombosed large or giant aneurysms in the posterior circulation.<sup>20</sup>

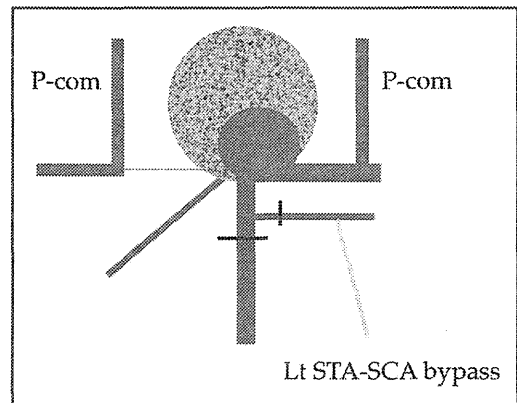
Giant thrombosed aneurysms often present with symptoms related to the mass effect by compressing the surrounding neural structure. Because their natural history is extremely poor, early intervention should be considered; however, the optimum treatment of giant thrombosed aneurysms remains unknown because it is often difficult to surgically manage these anomalies owing to their location, wide neck, calcification, or intra-aneurysmal thrombosis, especially in the posterior circulation. Therefore, flow alteration or isolation strategies are often considered as the first line of treatment for such unclippable aneurysms<sup>21-23</sup>; however, there are several critical issues to be considered in these strategies. The most important issue is the prediction of a reduced mass effect after flow alteration or isolation strategies, especially if the aneurysm is symptomatic.<sup>24-26</sup> Another important issue is the fate of critical perforators around the neck of the aneurysms after such treatment.

**ILLUSTRATIVE CASE**

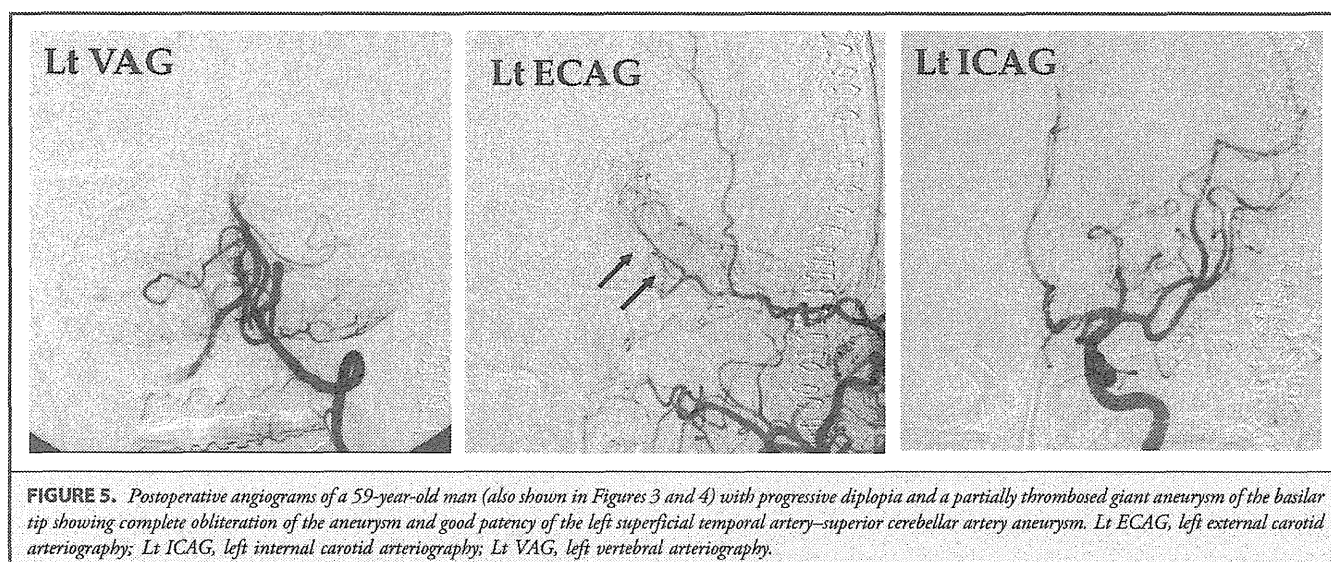
A 59-year-old man presented with progressive diplopia. CTA demonstrated a partially thrombosed giant aneurysm at the basilar tip with a maximum diameter of 37 mm (Figure 3). A maximum flow reduction strategy was used for this case (Figure 4). The right P1 was hypoplastic; bilateral posterior communicating arteries were well developed; and the left superior cerebellar artery originated near the basilar tip. A combination of proximal basilar clip occlusion and left superficial temporal artery–superior cerebellar artery bypass was performed with a subtemporal approach. To prevent inadvertent occlusion of the critical perforators in response to flow alteration, aspirin was administered perioperatively. Patency of the superficial temporal artery–superior cerebellar

artery bypass and patency of the critical perforators from the basilar artery adjacent to the clip were confirmed with indocyanine green videoangiography. Postoperative angiography showed no filling of the aneurysm with good patency of the bypass (Figure 5). No new ischemic lesion was noted on postoperative DWI-MRI. The diplopia gradually improved in response to this operation.

Over the past 5 years, I have operated on >20 cases of such partially thrombosed large or giant aneurysms in the posterior circulation treated by flow alteration as a main operator. Postoperatively, marked shrinkage of the aneurysm was achieved in 24% of the cases (unpublished data).



**FIGURE 4.** *Concept of maximum flow reduction strategy applied to a 59-year-old man (seen also in Figure 3) with a partially thrombosed giant aneurysm of the basilar tip in progressive diplopia. Aspirin was used perioperatively to preserve the critical perforators. Lt STA-SCT, left superficial temporal artery–superior cerebellar artery; P-com, posterior communicating artery.*



**FIGURE 5.** Postoperative angiograms of a 59-year-old man (also shown in Figures 3 and 4) with progressive diplopia and a partially thrombosed giant aneurysm of the basilar tip showing complete obliteration of the aneurysm and good patency of the left superficial temporal artery–superior cerebellar artery aneurysm. Lt ECAG, left external carotid arteriography; Lt ICAG, left internal carotid arteriography; Lt VAG, left vertebral arteriography.

## CONCLUSION

Here, I briefly summarized the current status of CSC capabilities in Japan from a neurovascular surgeon's perspective, including a nationwide survey of CSC capabilities, the impact of CSC capabilities on stroke mortality outcomes, a role of advanced neuroimaging capabilities in clinical stroke research, and multi-modality treatment for complex neurovascular lesions.

## Disclosures

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## Ⅱ. 研究成果の刊行に関する一覧

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
塩川芳昭	くも膜下出血	福井次矢、 高木誠、 小室一成	今日の治療指針 2014年版	医学書院	東京	2014	836-839
山口竜一、 塩川芳昭	クモ膜下出血の原因と危険因子	内山真一郎	あなたも名医！脳卒中と一過性脳虚血発作を見逃すな！時間が決め手！予防と治療の水際作戦 jmed mook	日本医事新報社	東京	2014	144-8
Toyoda K	Cerebrorenal interaction and stroke.	Toyoda K	Brain, Stroke and Kidney	Karger	Basel	2013	1-6
中川原譲二、 麓健太郎	一過性黒内障(amaurosis fugax, retinal TIA).	峰松一夫、 上原敏志	TIA 急性期医療の実際	診断と治療社	東京	2013	29-35
中川原譲二	循環型地域連携クリニックカパスとその意義	日本リハビリテーション医学会診療ガイドライン委員会・リハビリテーション連携パス策定委員会	リハビリテーションと地域連携・地域包括ケア	診断と治療社	東京	2013	45-49
辻本真範 他	脳血管内治療.	松谷雅生、 田村晃、藤巻高光、森田明夫	脳神経外科 周術期管理のすべて	メジカルビュー社	東京	2014	143-52
友金祐介 他	脳腫瘍の治療-良性と悪性.	兵庫医科大学病院	兵庫医科大学病院 医療最前線	バリュウメディカル	東京	2014	78-80
白川学 他	未破裂脳動脈瘤の治療.	兵庫医科大学病院	兵庫医科大学病院 医療最前線	バリュウメディカル	東京	2014	124-6



江頭裕介 他	急性期脳梗塞に対する血管内治療.	橋本信夫、寺本明、小川彰、嘉山孝正、福島孝徳、寶金清博、富永悌二、吉田一成、平孝臣、若林俊彦、吉峰俊樹、伊達勲、永田泉、寺田弘司	先端医療シリーズ45 臨床医のための最新脳神経外科	株式会社寺田国際事務所／先端医療技術研究所	東京	2014	128-31
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豊田一則	慢性腎臓病および透析患者の脳血管障害	鶴屋和彦、満生浩司、升谷耕介、谷口正智	全人力・科学力・透析力に基づく透析医学	医薬ジャーナル社	大阪	2014	552-56
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