

Risk factor profiles, drug usage, and prevalence of aspirin-associated gastroduodenal injuries among high-risk cardiovascular Japanese patients: the results from the MAGIC study	Uemura N, Sugano K, Hiraishi H, Shimada K, Goto S, Uchiyama S, Okada Y, Origasa H, Ikeda Y; MAGIC Study Group.	J Gastroenterol	2014/5月	国外
Recombinant Tissue-type Plasminogen Activator (rt-PA) Therapy in an Acute Stroke Patient Taking Dabigatran Etexilate: A Case Report and Literature Review	Tabata E, Yasaka M, Wakugawa Y, Okada Y	Internal Medicine	2014/6月	国外
Which should Be the Essential Components of Stroke Centers in Japan? A Survey by Questionnaires Sent to the Directors of Facilities Certified by the Japan Stroke Society	Uehara T, Yasui N, Okada Y, Hasegawa Y, Nagatsuka K, Minematsu K	Cerebrovascular Diseases	2014/8月	国外
Randomized clinical trial : prevention of recurrence of peptic ulcers by rabeprazole in patients taking low-dose aspirin	Iwakiri R, Higuchi K, Kato M, Fujishiro M, Kinishita Y, Watanabe T, Takeuchi T, Yamauchi M, Sanomura M, Nakagawa H, Sugisaki N, Okada Y, Ogawa H, Arakawa T, Fujimoto K	Aliment Pharmacol Ther	2014/10月	国外

抗凝固療法と頭蓋内出血	外山祐一郎、 矢坂正弘、齋藤正樹、下濱俊、岡田靖	脳と循環	2014/5月	国内
心原性脳塞栓症のチーム医療	岡田靖	Cardio-Coagulation	2014/6月	国内
日本人における脳梗塞再発抑制戦略を考える	田中耕太郎、 岡田靖、高木誠、橋本洋一郎、長谷川泰弘、松本昌泰	Cardio Vascular Contemporary	2014/6月	国内
心房細動に対するワルファリンと新規抗凝固薬：脳梗塞・脳出血の発症リスクは異なるのか？	外山祐一郎、 矢坂正弘、齋藤正樹、下濱俊、岡田靖	血栓と循環	2014/9月	国内

TOAST (The trial of Org 10172 in Acute Stroke Treatment) 分類と脳卒中病型診断の現状	芝原友也、桑城貴弘、岡田靖	日本臨牀	2014/7月	国内
Cautionプレゼンテーションの禁句「もともと」「フォローアップ」	岡田靖	日本医事新報	2014/8月	国内
IST、CAST	外山祐一郎、岡田靖、齋藤正樹、下濱俊、矢坂正弘	Clinical Neuroscience	2014/10月	国内
血栓塞栓症のリスク評価と抗凝固療法に伴う出血のリスク評価	森高千尋、矢坂正弘、岡田靖	Medical Practice	2014/10月	国内
プラタナス 医療者としての4段階目標	岡田靖	日本医事新報	2014/11月	国内
脳卒中 顔・腕・言葉ですぐ受診	岡田靖	Branch	2014/11月	国内

日本脳卒中協会 福岡県支部の活動について	岡田靖	脳梗塞と心房細動	2014/11月	国内
----------------------	-----	----------	----------	----

書籍

著者氏名	タイトル	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
Okada Y	Transient ischemic attack as a medical emergency	Uchiyama S, Amarenco P, Minematsu K, Wong K.S.L.	TIA as Acute Cerebrovascular Syndrome	KARGER	Basel	2014	19～29
岡田靖	脳卒中の前触れ「崖っぷち警報」を見逃さずすぐ治療すれば脳卒中の発作を予防できる	『健康』編集部	高血圧が自分で治せる101のワザ	株式会社主婦の友社	東京	2014	62～63
岡田靖	脳卒中は顔、腕、言葉で判断。周囲に疑わしい人がいたらすぐ救急車を呼ぶ！	『健康』編集部	高血圧が自分で治せる101のワザ	株式会社主婦の友社	東京	2014	64～65

#### IV. 研究成果の刊行物・別刷

# The Impact of Comprehensive Stroke Care Capacity on the Hospital Volume of Stroke Interventions: A Nationwide Study in Japan: J-ASPECT Study

Koji Iihara, MD, PhD,\* Kunihiro Nishimura, MD, PhD,† Akiko Kada, MPH,‡ Jyoji Nakagawara, MD,§ Kazunori Toyoda, MD, PhD,|| Kuniaki Ogasawara, MD, PhD,¶ Junichi Ono, MD, PhD,# Yoshiaki Shiokawa, MD, PhD,\*\* Toru Aruga, MD, PhD,†† Shigeru Miyachi, MD, PhD,‡‡ Izumi Nagata, MD, PhD,§§ Shinya Matsuda, MD, PhD,|||| Koichi B. Ishikawa, PhD,¶¶ Akifumi Suzuki, MD, PhD,### Hisae Mori, MD,\* and Fumiaki Nakamura, MD,\*\*\* and the J-ASPECT Study Collaborators

---

*Background:* The association between comprehensive stroke care capacity and hospital volume of stroke interventions remains uncertain. We performed a nationwide survey in Japan to examine the impact of comprehensive stroke care capacity on the hospital volume of stroke interventions. *Methods:* A questionnaire on hospital characteristics, having tissue plasminogen activator (t-PA) protocols, and 25 items regarding personnel, diagnostic, specific expertise, infrastructure, and educational components recommended for comprehensive stroke centers (CSCs) was sent to 1369 professional training institutions. We examined the effect of hospital characteristics, having a t-PA protocol, and the number of fulfilled CSC items (total CSC score) on the hospital volume of t-PA infusion, removal of intracerebral hemorrhage, and coiling and clipping of intracranial aneurysms performed in 2009. *Results:* Approximately 55% of hospitals responded to the survey. Facilities with t-PA protocols (85%) had a significantly higher likelihood of having 23 CSC items, for example, personnel (eg, neurosurgeons: 97.3% versus 66.1% and neurologists: 51.3% versus 27.7%), diagnostic (eg, digital cerebral angiography: 87.4% versus 43.2%), specific expertise (eg, clipping and coiling: 97.2% and 54% versus 58.9% and 14.3%, respectively), infrastructure (eg, intensive care unit: 63.9% versus 33.9%), and education (eg, professional education: 65.2% versus 20.7%). On multivariate analysis adjusted for hospital characteristics, total CSC score, but not having a t-PA protocol, was associated with the volume of all types of interventions with a clear increasing trend ( $P$  for trend < .001). *Conclusion:* We demonstrated a significant association between

---

From the \*Department of Neurosurgery, National Cerebral and Cardiovascular Center, Osaka; †Department of Preventive Medicine, National Cerebral and Cardiovascular Center, Osaka; ‡Advanced Medical Technology Development, National Cerebral and Cardiovascular Center, Osaka; §Integrative Stroke Imaging Center, National Cerebral and Cardiovascular Center, Osaka; ||Department of Cerebrovascular Medicine, National Cerebral and Cardiovascular Center, Osaka; ¶Department of Neurosurgery, Iwate Medical University, Iwate; #Chiba Cardiovascular Center, Chiba; \*\*Department of Neurosurgery, Kyorin University, Tokyo; ††Showa University Hospital, Tokyo; ‡‡Department of Neurosurgery, Nagoya University, Nagoya; §§Department of Neurosurgery, Nagasaki University, Nagasaki; ||||Department of Preventive Medicine and Community Health, School of Medicine, University of Occupational and Environmental Health, Fukuoka; ¶¶Center for Cancer Control and Informa-

tion Services, National Cancer Center, Tokyo; ###Research Institute for Brain and Blood Vessels, Akita; and \*\*\*Department of Healthcare Epidemiology, Faculty of Medicine, Kyoto University, Kyoto, Japan.

Received May 16, 2013; revision received August 8, 2013; accepted August 21, 2013.

Conflict of interest: None declared.

This study was supported by Grants-in-Aid from the Ministry of Health, Labor, and Welfare of Japan (principal investigator: KI).

Address correspondence to Koji Iihara, MD, PhD, Department of Neurosurgery, National Cerebral and Cardiovascular Center, 5-7-1 Fujishiro-dai, Suita, Osaka 565-8565, Japan. E-mail: kiihara@hsp.ncvc.go.jp.

1052-3057/\$ - see front matter

© 2014 by National Stroke Association

<http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2013.08.016>

comprehensive stroke care capacity and the hospital volume of stroke interventions in Japan. **Key Words:** Stroke facilities—stroke units—ischemic stroke—intracerebral hemorrhage—subarachnoid hemorrhage—acute stroke therapy.

© 2014 by National Stroke Association

## Introduction

Stroke is the third leading cause of death worldwide and a leading cause of long-term disability. In 2000, the Brain Attack Coalition discussed the concept of stroke centers and proposed 2 types of centers: primary<sup>1</sup> and comprehensive.<sup>2</sup> Most stroke patients can be treated appropriately at primary stroke centers (PSCs), and the Joint Commission has established programs for the certification of, and measurement of performance in, PSCs. The concept of a comprehensive stroke center (CSC) enables intensive care and the use of specialized techniques, which are not available at most PSCs.<sup>2</sup> A set of metrics and associated data elements that cover the major types of care that distinguish CSCs from PSCs have been published recently.<sup>3</sup> At present, when the certification of CSCs has been initiated worldwide, there are no nationwide reports on the associations between primary and comprehensive stroke care capacity and impact of comprehensive stroke care capacity on hospital volume of stroke interventions.

## Aims

We performed a nationwide survey in Japan to determine the association between primary and comprehensive stroke care capacity and the impact of comprehensive stroke care capacity on the annual hospital volume of tissue plasminogen activator (t-PA) infusion, removal of intracerebral hemorrhage (ICH), and coiling and clipping of intracranial aneurysms (IAs).

## Methods

### Eligible Hospitals

The J-ASPECT study (Nationwide survey of Acute Stroke care capacity for Proper designation of Comprehensive stroke cenTer in Japan) group developed a 49-question survey regarding hospital characteristics (eg, bed number, academic status, geographic location, and participation in the diagnosis procedure combination [DPC] payment system), primary and comprehensive stroke care capacity, and hospital volume of stroke interventions. The questionnaire was mailed on February 2011 to the 1369 certified training institutions of the Japan Neurosurgical Society, the Japanese Society of Neurology, and the Japan Stroke Society. In the case of nonresponders, a second mail was sent to the medical directors to ensure that the questionnaire was completed and returned.

### Assessment of Comprehensive and Primary Stroke Care Capacities and Hospital Volume of Stroke Interventions

This survey included 25 items related to the 5 major components of CSCs (personnel, diagnostic programs, specific expertise, infrastructure, and educational components) and 5 items related to PSC certification (Tables 1 and 2).<sup>2</sup> Personnel were assessed according to 7 categories (eg, board-certified neurologists, board-certified neurosurgeons, and board-certified endovascular physicians). Because the original questions were highly specific, they were modified if necessary. Six advanced neuroimaging capabilities (eg, magnetic resonance imaging [MRI] with diffusion-weighted imaging [DWI] and digital cerebral angiography [DSA]) were investigated based on their availability 24 h/d, 7 d/wk (24/7). The availability of specific expertise for the stroke interventions was examined according to 5 categories (eg, carotid endarterectomy [CEA] and clipping and coiling of IAs). Regarding infrastructure, the availability of 5 items (eg, stroke unit and intensive care unit [ICU]) was surveyed.

**Table 1.** Characteristics of the responding hospitals and items of primary stroke care capacity

Variables	Category	n	%
Number of beds	<50	20	2.7
	50-99	30	4
	100-299	232	31
	300-499	260	34.7
	≥500	207	27.6
Academic hospital		90	12
DPC hospital		553	73.8
Geographic locations	MEA-central	381	50.9
	MEA-outlying	239	31.9
	McEA-central	90	12
	McEA-outlying	12	1.6
	Unclassified	27	3.6
PSC component	t-PA protocol	637	85
	t-PA physician*	688	92
	NIHSS*	529	70.7
	Acute stroke team*	198	26.5
	Direct phone with EMS*	435	58.5

Abbreviations: DPC, diagnosis procedure combination; EMS, emergency medical services; MEA, metropolitan employment area; McEA, micropolitan employment area; NIHSS, National Institutes of Health Stroke Scale; PSC, primary stroke center; t-PA, tissue plasminogen activator.

\*Data missing: t-PA physician, 1; NIHSS, 1; acute stroke team, 1; direct phone with EMS, 5.

**Table 2.** Number (percentage) of responding hospitals (n = 749) with the recommended items of comprehensive stroke care capacity

Components	Items	n	%
Personnel	Neurologists	358	47.8
	Neurosurgeons	694	92.7
	Endovascular physicians	272	36.3
	Critical care medicine	162	21.6
	Physical medicine and rehabilitation	113	15.1
	Rehabilitation therapy	742	99.1
	Stroke rehabilitation nurses*	102	13.8
	Diagnostic (24/7)	CT*	742
MRI with diffusion		647	86.4
Digital cerebral angiography*		602	80.8
CT angiography*		627	84
Carotid duplex ultrasound*		257	34.5
TCD*		121	16.2
Specific expertise	Carotid endarterectomy*	603	80.6
	Clipping of IA	685	91.5
	Hematoma removal/drainage	689	91.9
	Coiling of IA	360	48.1
	Intra-arterial reperfusion therapy	498	66.5
Infrastructure	Stroke unit*	132	17.6
	Intensive care unit	445	59.4
	Operating room staffed 24/7*	451	60.4
	Interventional services coverage 24/7	279	37.3
	Stroke registry*	235	31.7
Education	Community education*	369	49.4
	Professional education*	436	58.6

Abbreviations: CT, computed tomography; IA, intracranial aneurysm; MRI, magnetic resonance imaging; TCD, transcranial Doppler.

\*Data missing: stroke rehabilitation nurse, 9; CT, 1; digital cerebral angiography, 4; CT angiography, 3; carotid endarterectomy, 1; carotid duplex, 3; TCD, 3; stroke unit, 1; operating room staffed, 2; stroke registry, 7; community education, 2; professional education, 5.

Educational/research programs were assessed according to 2 items (community and professional education). Overall organizational and staffing levels of the hospitals in terms of CSC capacity were scored on the basis of the results of a questionnaire referring to 25 items originally recommended by the Brain Attack Coalition (total CSC score). A score of 1 was assigned for meeting each recommended item, and the maximum total CSC score was 25. Hospital volume of stroke interventions (eg, t-PA infusion, removal of ICH, and clipping and coiling of IAs) performed in 2009 was assessed.

*Other Hospital Characteristics*

Hospital characteristics pertaining to the number of beds, academic status (university/nonuniversity hospital), participation in the DPC-based payment system, and geographic location were described. The DPC database is a nationwide database in Japan comprising discharge abstract and administrative claim data.<sup>4,5</sup> In 2010, approximately 1388 acute care hospitals in Japan, representing approximately 18% and 50% of the number of hospitals and hospital beds, respectively, adopted the DPC-based payment system.<sup>6</sup> The geographic location of the hospitals was classified according to urban employment areas,<sup>7</sup> which are divided into Metropolitan Employment Areas (MEAs) and Micropolitan Employment Areas (McEAs). The MEAs and McEAs are further classified into central and outlying areas based on the commuting pattern of their inhabitants. These classifications are based on the 2005 population census.<sup>8</sup>

*Selection Bias of the Responding Hospitals*

To overcome selection bias, we compared the proportion of hospitals that adopted the Japanese DPC-based payment system (DPC hospital) between the responding and nonresponding hospitals. Among the eligible DPC hospitals, we compared the proportion of hospitals that treated more than 10 cases of ischemic stroke (IS), ICH, and subarachnoid hemorrhage between July and December 2008, by using the DPC data from the responding and nonresponding hospitals.

*Statistical Analyses*

We used Fisher's exact test to detect significant differences in the proportions of hospitals. Kruskal-Wallis and Wilcoxon tests were used to determine differences in categorical and total CSC scores. Multiple linear regression analysis was used to examine the impact of total CSC score and availability of t-PA protocol adjusted for other hospital characteristics on hospital volume of stroke interventions. We also calculated *P* values (2 tailed) for trend across total CSC score categorized into quartiles, and *P* less than .05 was considered significant. Percentages were calculated excluding missing data. SAS version 9.2 (SAS Institute, Inc., Cary, NC) and STATA version 12 (STATA Corp., College Station, TX) were used for all statistical analyses.

*Ethics*

This research was approved by the Institutional Review Board of the National Cerebral and Cardiovascular Center, which waived the requirement for individual informed consent.



## Results

### *Response Rate and Responding-Hospital Characteristics*

In total, 55% (749 hospitals) of the eligible institutions completed the questionnaire. The characteristics of the responding hospitals are shown in Table 1. DPC hospitals represented 65.3% of the eligible hospitals and 73.8% and 55% of the responding and nonresponding hospitals, respectively ( $P < .0001$ ). The response rate of the DPC hospitals was significantly higher than that of the remaining hospitals (61.9% versus 41.3%,  $P < .0001$ ). Among the DPC hospitals, a greater proportion of responding hospitals, rather than nonresponding hospitals, treated more than 10 cases of ICH (65.6% versus 49.9%,  $P < .0001$ ) and subarachnoid hemorrhage (30.7% versus 17%,  $P < .0001$ ) per 6 months but not of IS (79% versus 76.8%,  $P = .454$ ).

### *Primary Stroke Care Capacity Recommended for PSCs*

Written t-PA protocols were available in 85% of hospitals, and the National Institutes of Health Stroke Scale score was routinely documented in 70.7% of hospitals; however, an acute stroke team was available only in 26.5% of hospitals (Table 1).

### *Comprehensive Stroke Care Capacity Recommended for CSCs*

Regarding the recommended personnel components of CSCs, 92.7% of hospitals had a neurosurgeon, 47.8% had a neurologist, and 36.3% had an endovascular physician (Table 2). The proportion of hospitals with critical care medicine physicians and physical medicine and stroke rehabilitation nurses was 21.6% and 15.1% and 13.8%, respectively. The availability of the personnel component ranged from 0 to 7 (median, 3; interquartile range [IQR], 2-4).

Computed tomography (CT), MRI with DWI, DSA, and CT angiography (CTA) were available 24/7 in 99.2%, 86.4%, 80.8%, and 84% of institutions, respectively, whereas carotid duplex ultrasonography and transcranial Doppler (TCD) were available only in 34.5% and 16.2% of hospitals, respectively. The availability of diagnostic components ranged from 0 to 6 (median, 4; IQR, 4-5).

CEA, clipping of IAs, and removal of ICH were available in 80.6%, 91.5%, and 91.9% of hospitals, respectively, whereas coiling of IAs and intra-arterial thrombolysis were available in 48.1% and 66.5% of hospitals, respectively. The availability of surgical and interventional components ranged from 0 to 5 (median, 4; IQR, 3-5).

A stroke unit and an ICU were available in 17.6% and 59.4% of hospitals, respectively. The availability of interventional service coverage on a 24-hour basis was observed in 37.3% of hospitals, whereas an operating room staffed 24/7 was available in 60.4% of hospitals. The availability of infrastructure components ranged from 0 to 5 (median, 2; IQR, 1-3).

Professional and community education were available in 58.6% and 49.4% of institutions, respectively (Table 2). The availability of the educational component ranged from 0 to 2 (median, 1; IQR, 0-2).

### *Geographical Disparity of Primary and Comprehensive Stroke Care Capacity*

Among certified personnels, the proportion of neurologists, interventional physicians, and stroke nurses available at MEA-central institutes was significantly higher ( $P < .001$ ,  $P < .001$ , and  $P = .045$ , respectively), whereas neurosurgeons, critical care medicine, and physical medicine were in place, irrespective of the location. Imaging techniques, such as MRI, diffusion-weighted MRI, CTA, digital subtraction angiography, and carotid duplex ultrasonography, were available on a 24-hour basis in similar proportions irrespective of the location, whereas TCD was available in a significantly higher proportion at MEA-central institutes except for TCD ( $P = .003$ ). Specific surgical and interventional services for CEA ( $P = .002$ ), coiling of IAs ( $P < .001$ ), and intra-arterial reperfusion therapy ( $P = .04$ ) were available in a significantly higher proportion at MEA-central institutes. The availability of stroke unit ( $P < .001$ ), operating room staffed, and interventional services on a 24/7 basis ( $P < .001$ ) was significantly more established at MEA-central institutes, whereas no significant differences were found with regard to the ICU. Community ( $P = .011$ ) and professional education ( $P = .003$ ) were more established at MEA-central institutes (Appendix Tables 2 and 3).

### *Associations between the Implementation of a t-PA Protocol and Comprehensive Stroke Care Capacity*

Facilities with t-PA protocols had a higher likelihood of having a neurosurgeon (97.3% versus 66.1%,  $P < .0001$ ), neurologist (51.3% versus 27.7%,  $P < .0001$ ), endovascular physician (41.1% versus 8.9%,  $P < .0001$ ), and physicians in critical care medicine (23.7% versus 9.8%,  $P = .0007$ ) and physical medicine and rehabilitation (16.5% versus 7.1%,  $P = .006$ ) (Table 3). There were no differences in the availability of personnel in rehabilitation therapy ( $P = .355$ ) or of stroke rehabilitation nurses ( $P = .695$ ). Facilities with t-PA protocols had a higher percentage of 24/7 availability of CT (99.5% versus 97.3%,  $P = .042$ ), MRI with DWI (89.6% versus 67.9%,  $P < .0001$ ), DSA (87.4% versus 43.2%,  $P < .0001$ ), carotid duplex ultrasonography (37% versus 19.8%,  $P = .0003$ ), and TCD (18.1% versus 5.4%,  $P = .0002$ ). Moreover, hospitals with a t-PA protocol had greater availability of CEA (87.1% versus 43.8%,  $P < .0001$ ), clipping of IAs (97.2% versus 58.9%,  $P < .0001$ ), removal of ICH (97.5% versus 60.7%,  $P < .0001$ ), coiling of IAs (54% versus 14.3%,  $P < .0001$ ), and intra-arterial thrombolysis (73% versus 29.5%,  $P < .0001$ ) and greater availability of a stroke unit (20.1% versus 3.6%,  $P < .0001$ ), an ICU (63.9% versus

**Table 3.** Characteristics of comprehensive stroke care capacity according to the presence or absence of a t-PA protocol

Variables	t-PA protocol (+) n, %		t-PA protocol (-) n, %		OR	95% CI	P value
<b>Personnel</b>							
Neurologists	327	51.3	31	27.7	2.8	1.8-4.3	<.0001
Neurosurgeons	620	97.3	74	66.1	18.7	10.1-34.8	<.0001
Endovascular physicians	262	41.1	10	8.9	7.1	3.7-13.9	<.0001
Critical care medicine	151	23.7	11	9.8	2.9	1.5-5.5	.0007
Physical medicine and rehabilitation	105	16.5	8	7.1	2.3	1.2-5.4	.006
Rehabilitation therapy	632	99.2	110	98.2	1.14	0.4-12	.355
Stroke rehabilitation nurses	88	14	14	12.6	1.1	0.6-2.1	.695
<b>Diagnostic</b>							
CT*	634	99.5	108	97.3	5.9	1.2-29.5	.042
MRI with diffusion	571	89.6	76	67.9	4.1	2.6-6.6	<.0001
Digital cerebral angiography*	554	87.4	48	43.2	9.1	5.8-14.2	<.0001
CT angiography*	566	89.1	61	55	6.7	4.3-10.5	<.0001
Carotid duplex ultrasound*	235	37	22	19.8	2.4	1.5-3.9	.0003
TCD*	115	18.1	6	5.4	3.9	1.7-9.1	.0002
<b>Specific expertise</b>							
Carotid endarterectomy*	554	87.1	49	43.8	8.7	5.6-13.5	<.0001
Clipping of IA	619	97.2	66	58.9	24	13.1-43.7	<.0001
Hematoma removal/drainage	621	97.5	68	60.7	25.1	13.4-46.9	<.0001
Coiling of IA	344	54	16	14.3	7	4.1-12.2	<.0001
Intra-arterial reperfusion therapy	465	73	33	29.5	6.5	4.2-10.1	<.0001
<b>Infrastructure</b>							
Stroke unit*	128	20.1	4	3.6	6.8	2.5-18.8	<.0001
Intensive care unit	407	63.9	38	33.9	3.4	2.3-5.3	<.0001
Operating room staffed 24/7	426	67.1	25	22.3	7.1	4.4-11.4	<.0001
Interventional services coverage 24/7	268	42.1	11	9.8	6.7	3.5-12.7	<.0001
Stroke registry*	229	36.3	6	5.4	10	4.3-23.1	<.0001
<b>Education</b>							
Community education*	348	54.8	21	18.8	5.3	3.2-8.7	<.0001
Professional education*	413	65.2	23	20.7	7.2	4.4-11.7	<.0001

Abbreviations: CI, confidence interval; CT, computed tomography; IA, intracranial aneurysm; MRI, magnetic resonance imaging; OR, odds ratio; TCD, transcranial Doppler.

\*Data missing: CT, 1; digital cerebral angiography, 4; carotid U/S, 3; TCD, 3; carotid endarterectomy, 1; stroke unit, 1; stroke registry, 7; community education, 2; professional education, 5.

33.9%,  $P < .0001$ ), an operating room staffed 24/7 (67.1% versus 22.3%,  $P < .0001$ ), interventional service coverage 24/7 (42.1% versus 9.8%,  $P < .0001$ ), and a stroke registry (36.3% versus 5.4%,  $P < .0001$ ). Finally, hospitals with a t-PA protocol had greater availability of professional (65.2% versus 20.7%,  $P < .0001$ ) and community (54.8% versus 18.8%,  $P < .0001$ ) education (Table 3).

*Impact of Total CSC Score on Hospital Volume of Stroke Interventions*

The total CSC score, which ranged from 0 to 24 (median, 14; IQR, 11-18), was significantly higher in facilities with a t-PA protocol than in other facilities (median, IQR: 15, 12.5-18 versus 9, 5-11;  $P < .0001$ ). On univariate analysis, the implementation of a t-PA protocol and total CSC score categorized into quartiles (Q1, 0-10; Q2, 11-13; Q3, 14-17; and Q4, 18-24) were each significantly associated with hospital volume of stroke interventions, as shown in Table 4. The impact of total CSC score (Q1-Q4) and the implemen-

tation of a tPA protocol on the annual case volume of stroke interventions in the participating hospitals was shown in Figure 1. On multiple linear regression analysis, the availability of a t-PA protocol and total CSC score each had a significant impact on the hospital volume of the stroke interventions after adjustment for other hospital characteristics (Appendix Tables 4-6). The inclusion of total CSC score, availability of a t-PA protocol, and other hospital characteristics in the model revealed that total CSC score, but not availability of a t-PA protocol, was significantly associated with the hospital volume of stroke interventions (Table 5).

**Discussion**

This study demonstrated a significant impact of comprehensive stroke care capacity represented by the total CSC score on the hospital volume of stroke interventions and unique aspects of comprehensive stroke care capacity in Japan.

**Table 4.** Impact of the availability of a t-PA protocol and of total CSC score on hospital volume of stroke interventions performed in 2009: hospital volume of stroke interventions based on the availability of a t-PA protocol and on total CSC score (univariate analysis)

	t-PA protocol			Total CSC score				
	(+)	(-)	P value	Q1	Q2	Q3	Q4	P value
t-PA infusion	5 (2-11)	0 (0-1)	<.0001	1 (0-3)	4 (1-7)	6 (4-10.5)	10 (5-16)	<.0001
Removal of ICH	7 (3-13)	0 (0-3)	<.0001	2 (0-4)	5 (3-9)	7.5 (3-15)	11.5 (6-18)	<.0001
Clipping of IA	17 (8-29)	0 (0-10)	<.0001	3 (0-11.5)	12 (6-21.25)	18 (10-30)	27 (18-43.75)	<.0001
Coiling of IA	4 (0-13)	0 (0-1)	<.0001	0 (0-1)	1 (0-4)	5.5 (1.25-13)	13 (5-22)	<.0001

Abbreviations: CSC, comprehensive stroke center; IA, intracranial aneurysm; ICH, intracerebral hemorrhage; t-PA, tissue plasminogen activator.

#### Unique Aspects of Comprehensive Stroke Care Capacity in Japan

This study illustrated several unique aspects of comprehensive stroke care capacity in Japan, for example, higher availability of neurosurgeons (92.7% versus 24%-54% in the United States)<sup>9,10</sup> and endovascular surgeons (36.3% versus 15%-22% in the United States),<sup>9-11</sup> which was in sharp contrast with the relative shortage of neurologists (47.8% versus 31%-73% in the United States) and other personnel.<sup>9-11</sup> In the United States, only 7% of neurosurgeons play an active role in nontraumatic cranial emergencies,<sup>12</sup> whereas in Japan, 59% of the board-certified neurosurgeons are engaged in stroke care. The proportion of Japanese hospitals offer-

ing MRI with DWI and CTA corresponded with the gradual increase in the availability of certain special diagnostic tests in the United States, whereas the availability of DSA (80.8%) was in contrast with the temporal decrease in the availability of catheter angiography observed in North Carolina (from 38% in 1998 to 30% in 2008) because of declines in the proportion of hospitals with neurointerventionalists.<sup>11</sup>

A stroke unit/stroke care unit as the critical infrastructure for acute stroke, which has been proven to reduce the number of deaths and long-term dependency,<sup>13</sup> was available in only 17.6% of hospitals in Japan; this was comparable with the proportion observed in hospitals in the United States (6.6%-28%).<sup>9-11,14</sup>

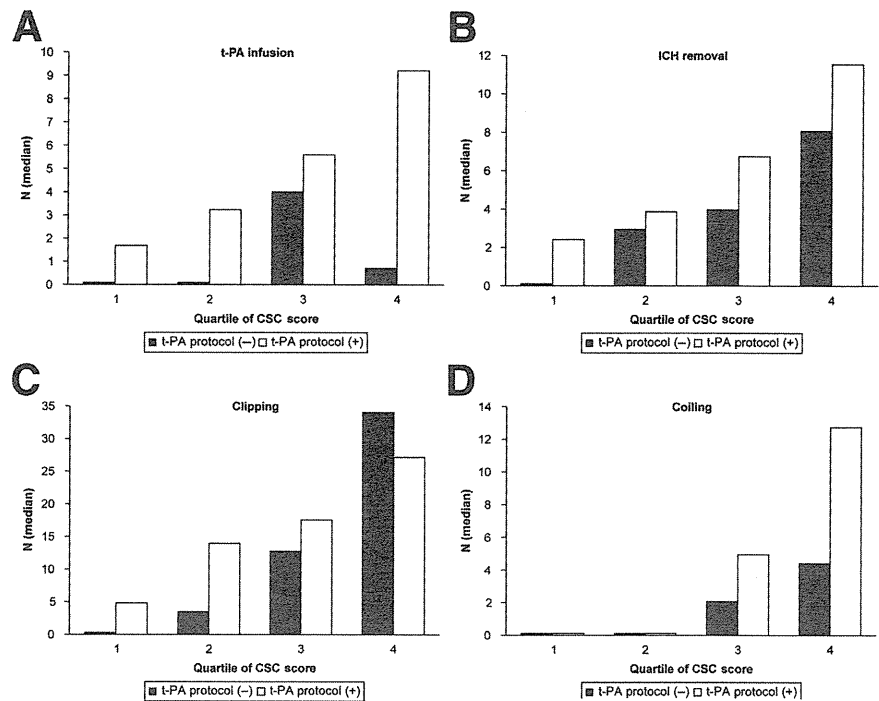
To determine the relationship between primary and comprehensive stroke care capacity, we used the implementation of a written t-PA protocol as a key item of primary stroke care capacity<sup>1</sup> as it is a key step in reducing t-PA-related complications.<sup>15</sup> The availability of a t-PA protocol (85%) recorded in the present study was comparable with that reported in 2 US statewide studies performed in Illinois in 2000 (72.8%)<sup>9</sup> and in North Carolina between 1998 (43%) and 2008 (69%).<sup>11</sup> Notably, facilities with a t-PA protocol in Japan had a higher availability of nearly all (92%) recommended items of comprehensive stroke care capacity, with the exception of personnel in rehabilitation therapy and stroke rehabilitation nurses. In a previous study performed in the United States,<sup>9</sup> however, no significant differences were noted in the availability of a larger number of critical items corresponding to the CSC items in this study (eg, endovascular physicians, CTA, conventional cerebral angiography, carotid duplex ultrasound, intra-arterial thrombolysis, stroke unit, and community stroke awareness program) according to the presence or absence of a t-PA protocol. Therefore, comprehensive stroke care capacity tended to coexist in hospitals with primary stroke care capacity in Japan than in the United States. A relatively larger commitment of neurosurgeons in acute stroke care (eg, t-PA infusion) in Japan may explain such a coexistence.

**Table 5.** Impact of the availability of a t-PA protocol and of total CSC score on hospital volume of stroke interventions performed in 2009: multivariate linear regression analysis of the impact of total CSC score and availability of a t-PA protocol on hospital volume of stroke interventions

	$\beta$	P value	95% CI	
tPA				
Total CSC score	.83	<.001	.67	.98
tPA protocol (+)	-1.31	.117	-2.95	.33
ICH				
Total CSC score	.97	<.001	.76	1.18
tPA protocol (+)	-1.17	.297	-3.36	1.03
Clipping				
Total CSC score	2.23	<.001	1.68	2.79
tPA protocol (+)	-4.33	.146	-10.17	1.51
Coiling				
Total CSC score	1.20	<.001	.92	1.48
tPA protocol (+)	-1.01	.496	-3.92	1.90

Abbreviations: CI, confidence interval; CSC, comprehensive stroke center; IA, intracranial aneurysm; ICH, intracerebral hemorrhage; t-PA, tissue plasminogen activator; Total CSC score, availability of a t-PA protocol, and other hospital characteristics were included in the model as independent variables.

**Figure 1.** A bar graph showing the impact of total CSC score (Q1-Q4) and the implementation of a tPA protocol on the annual case volume of stroke interventions (A, t-PA infusion; B, ICH removal; C, clipping; and D, coiling of intracranial aneurysms) in the participating hospitals. Abbreviations: CSC, comprehensive stroke center; t-PA, tissue plasminogen activator.



*Geographical Disparity of Primary and Comprehensive Stroke Care in Japan*

These findings could assist in identifying underserved, high-population density areas that may benefit from professional and hospital education by national organizations, such as the Japan Stroke Society and Japan Neurosurgical Society. In light of insufficient advanced acute stroke capacities, these findings represent fundamental information for the establishment of a spoke-and-hub stroke care system.<sup>2</sup> Such a system could maximize use of acute reperfusion therapies for IS and surgical/endovascular management of hemorrhagic stroke, depending on the personnel and specific expertise of the hospital and the geographical access of the potential population in Japan.

*The Impact of Comprehensive Stroke Care Capacity on the Hospital Volume of Stroke Interventions*

The present study demonstrated a significant impact of comprehensive stroke care capacity, as represented by the total CSC score, but not the availability of a t-PA protocol, on the hospital volume of stroke interventions performed in Japan in 2009, after adjustment for other hospital characteristics. High volume is associated with better outcomes across a wide range of procedures and conditions; however, the magnitude of the association varies greatly.<sup>16</sup> High annual hospital volume was reported to be consistently associated with lower IS mortality.<sup>17</sup> In the field of comprehensive stroke care, in-hospital mortality increases when the annual number of craniotomies for aneurysms is lower than 30<sup>18</sup> and when CEA is performed by less experienced surgeons (<5 procedures/y).<sup>19</sup> Conversely, a previous Japanese nationwide study

found no correlation between case volume and outcome after cerebral aneurysm clipping.<sup>20</sup> The mechanism via which volume influences outcomes remains uncertain. Specific processes of care, which are correlated with volume, are the most likely explanatory factors.<sup>16</sup> The strong associations between comprehensive stroke care capacity and hospital volume of the stroke interventions observed in this study may support this notion. Further studies are necessary to establish the association between comprehensive stroke care capacity and in-hospital mortality after all types of stroke. If such association is established, as recently reported for PSC,<sup>21</sup> the total CSC score may be used as a quality indicator of comprehensive stroke care capacity for benchmarking purposes.

*Limitations*

This study was likely to have included a potential information bias (self-report, recall, and nonresponse). Hospitals actively working to improve stroke care are more likely to respond to the questionnaire. The fact that a greater proportion of the responding DPC hospitals treated more than 10 cases of hemorrhagic stroke in the latter half of the previous year than did the nonresponding DPC hospitals may support such selection bias. We did not attempt to assess the self-report bias as no official information was available that could have been used to verify the data.

**Conclusion**

The present study demonstrated a significant impact of comprehensive stroke care capacity, as represented by the total CSC score on the hospital volume of stroke

interventions and unique aspects of comprehensive stroke care capacity in Japan.

## References

1. Alberts MJ, Hademenos G, Latchaw RE, et al. Recommendations for the establishment of primary stroke centers. Brain Attack Coalition. *JAMA* 2000;283:3102-3109.
2. Alberts MJ, Latchaw RE, Selman WR, et al. Recommendations for comprehensive stroke centers: a consensus statement from the Brain Attack Coalition. *Stroke* 2005; 36:1597-1616.
3. Leifer D, Bravata DM, Connors JJ III, et al. Metrics for measuring quality of care in comprehensive stroke centers: detailed follow-up to Brain Attack Coalition comprehensive stroke center recommendations: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2011;42:849-877.
4. Kadono Y, Yasunaga H, Horiguchi H, et al. Statistics for orthopedic surgery 2006-2007: data from the Japanese Diagnosis Procedure Combination database. *J Orthop Sci* 2010;15:162-170.
5. Shoda N, Yasunaga H, Horiguchi H, et al. Risk factors affecting in-hospital mortality after hip fracture: retrospective analysis using the Japanese Diagnosis Procedure Combination Database. *BMJ Open* 2012;2. <http://dx.doi.org/10.1136/bmjopen-2011-000416>.
6. Current status of DPC hospitals [online]. Available at: <http://www.mhlw.go.jp/stf/shingi/2r9852000000bart-att/2r9852000000bc5v.pdf>. Accessed January 19, 2013.
7. Kanemoto Y, Kurima R. Urban employment areas: defining Japanese metropolitan areas and constructing the statistical database for them. In: Okabe A, ed. *GIS-based studies in the humanities and social sciences*. Boca Raton, FL: CRC Taylor & Francis 2006:85-97.
8. Population census [online]. Available at: <http://www.stat.go.jp/english/data/kokusei/2005/outline.htm>. Accessed September 15, 2013.
9. Ruland S, Gorelick PB, Schneck M, et al. Acute stroke care in Illinois: a statewide assessment of diagnostic and treatment capabilities. *Stroke* 2002;33:1334-1339.
10. Shultis W, Graff R, Chamie C, et al. Striking rural-urban disparities observed in acute stroke care capacity and services in the Pacific Northwest: implications and recommendations. *Stroke* 2010;41:2278-2282.
11. Goldstein LB. Statewide hospital-based stroke services in North Carolina: changes over 10 years. *Stroke* 2010; 41:778-783.
12. Seaver MJ. Baseline ER survey explores system's cracks: 2004 AANS/CNS neurosurgical emergency and trauma services survey [online]. Available at: <http://www.aans.org/Media/Article.aspx?ArticleId=26367>. Accessed January 23, 2013.
13. Organised inpatient (stroke unit) care for stroke. *Cochrane Database Syst Rev* 2007. CD000197.
14. Kidwell CS, Shephard T, Tonn S, et al. Establishment of primary stroke centers: a survey of physician attitudes and hospital resources. *Neurology* 2003;60:1452-1456.
15. Albers GW, Bates VE, Clark WM, et al. Intravenous tissue-type plasminogen activator for treatment of acute stroke: the Standard Treatment with Alteplase to Reverse Stroke (STARS) study. *JAMA* 2000;283:1145-1150.
16. Halm EA, Lee C, Chassin MR. Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. *Ann Intern Med* 2002;137:511-520.
17. Saposnik G, Baibergenova A, O'Donnell M, et al. Hospital volume and stroke outcome: does it matter? *Neurology* 2007;69:1142-1151.
18. Solomon RA, Mayer SA, Tarmey JJ. Relationship between the volume of craniotomies for cerebral aneurysm performed at New York state hospitals and in-hospital mortality. *Stroke* 1996;27:13-17.
19. Hannan EL, Popp AJ, Tranmer B, et al. Relationship between provider volume and mortality for carotid endarterectomies in New York state. *Stroke* 1998;29: 2292-2297.
20. Hattori N, Katayama Y, Abe T. Case volume does not correlate with outcome after cerebral aneurysm clipping: a nationwide study in Japan. *Neurol Med Chir (Tokyo)* 2007;47:95-100. discussion 1.
21. Lichtman JH, Jones SB, Wang Y, et al. Outcomes after ischemic stroke for hospitals with and without Joint Commission-certified primary stroke centers. *Neurology* 2011;76:1976-1982.

**Appendix Table 1.** *List of the responding hospitals*

Abashiri Neurosurgical Rehabilitation Hospital  
 Ageo Central General Hospital  
 Aichi Medical University Hospital  
 Aidu Chuo Hospital  
 Aizawa Hospital  
 Akiba Hospital  
 Akiru Municipal Medical Center  
 Akita General Hospital  
 Akita Kumiai General Hospital  
 Akita Rosai Hospital  
 Akita University Hospital  
 Ako Central Hospital  
 Ako City Hospital  
 Almeida Memorial Hospital  
 Amakusa Medical Center  
 Anji Kosei Hospital  
 Aomori Kyoritsu Hospital  
 Aomori Municipal Hospital  
 Aomori Rosai Hospital  
 Aoyama Hospital  
 Araki Neurosurgical Hospital  
 Arao City Hospital  
 Arita Kyouritsu Hospital  
 Asahikawa Medical University Hospital  
 Asahikawa Red Cross Hospital  
 Asao General Hospital  
 Ashikaga Red Cross Hospital  
 Atsumi Hospital  
 Ayabe City Hospital  
 Azuma Neurosurgical Hospital  
 Azumi General Hospital  
 Azumino Red Cross Hospital  
 Baba Memorial Hospital  
 Bellland General Hospital  
 Beppu Medical Center, National Hospital Organization  
 Bizen Municipal Hospital  
 Central Gunma Neurosurgical Hospital  
 Chiba Cardiovascular Center  
 Chiba Central Medical Center  
 Chiba Emergency Medical Center  
 Chiba Neurosurgical Clinic  
 Chiba University Hospital  
 Chichibu City Hospital  
 Chigasaki City Hospital  
 Chikamori Hospital  
 Chubu-Tokusyukai Hospital  
 Chugoku Rousai Hospital  
 Chuno Kosei Hospital  
 Daiichi Hospital  
 Daini Okamoto General Hospital  
 Daiwa Hospital  
 Dohtoh Neurosurgical Hospital  
 Dokkyo Medical University Hospital  
 Ehime Prefectural Central Hospital  
 Ehime Prefectural Imabari Hospital  
 Ehime University Hospital  
 Enshu Hospital  
 Fuchu Hospital

*(Continued)*

**Appendix Table 1.** *(Continued)*

Fuji Brain Institute and Hospital  
 Fuji City General Hospital  
 Fujii Neurosurgical Hospital  
 Fujimoto Hayasuzu Hospital  
 Fujisawa City Hospital  
 Fujisawa Neurosurgical Hospital  
 Fujita General Hospital  
 Fujita Health University Hospital  
 Fujiyoshida Municipal Medical Center  
 Fukaya Red Cross Hospital  
 Fukui Red Cross Hospital  
 Fukui General Hospital  
 Fukui Kosei Hospital  
 Fukui Social Insurance Hospital  
 Fukui University Hospital  
 Fukuoka City Hospital  
 Fukuoka Kieikai Hospital  
 Fukuoka Seishukai Hospital  
 Fukuoka Shin Mizumaki Hospital  
 Fukuoka Tokushukai Medical Center  
 Fukuoka University Hospital  
 Fukuroi Municipal Hospital  
 Fukushima Medical University Hospital  
 Fukushima Prefectural Aizu General Hospital  
 Fukushima Red Cross Hospital  
 Fukushima Takanori Memorial Hospital  
 Furukawa Seiryō Hospital  
 Fussa Hospital  
 Gamagohri City Hospital  
 Geriatrics Research Institute and Hospital  
 Gifu Central Hospital  
 Gifu Municipal Hospital  
 Gifu Prefectural General Medical Center  
 Gifu Prefectural Tajimi Hospital  
 Gifu University Hospital  
 Goshi Hospital  
 Gunma University Hospital  
 Hachinohe Heiwa Hospital  
 Hachisuga Hospital  
 Hakodate Neurosurgical Hospital  
 Hakodate Shintoshō Hospital  
 Hakuai Hospital  
 Hakuo-kai Sumi Hospital  
 Hamamatsu Medical Center  
 Hamamatsu University School of Medicine, University  
 Hospital  
 Hamamatu Rosai Hospital  
 Hamanomachi Hospital  
 Hanwa Memorial Hospital  
 Harada Hospital  
 Hashima City Hospital  
 Hata Kenmin Hospital  
 Hayashi Hospital  
 Health Insurance Amakusa Chuo General Hospital  
 Health Insurance Nankai Hospital  
 Health Insurance Naruto Hospital  
 Heart Life Hospital  
 Heisei Memorial Hospital

*(Continued)*

Appendix Table 1. (Continued)

Heisei Neurosurgical Hospital  
 Hibino Hospital  
 Hidaka General Hospital  
 Higashimatsuyama Medical Association Hospital  
 Higashiyamato Hospital  
 Hikone Municipal Hospital  
 Himeji Central Hospital  
 Himi Municipal Hospital  
 Hiratsuka City Hospital  
 Hirosaki University Hospital  
 Hiroshima City Asa Hospital  
 Hiroshima General Hospital  
 Hiroshima Prefectural Hospital  
 Hiroshima Red Cross Hospital and Atomic-bomb  
 Survivors Hospital  
 Hiroshima University Hospital  
 Hokkaido Neurosurgical Memorial Hospital  
 Hokkaido University Hospital  
 Hokushin General Hospital Nagano Prefectural Fideration  
 of Agricultural Cooperatives for Health and Welfare  
 Hokushinkai Megumono Hospital  
 Hokuto Hospital  
 Hoshigaoka Koseinenkin Hospital  
 Houetsu Hospital  
 Hskinan Municipal Hospital  
 Hyogo Brain and Heart Center  
 Hyogo Prefectural Amagasaki Hospital  
 Hyogo Prefectural Awaji Hospital  
 Hyogo Prefectural Nishinomiya Hospital  
 Ibaraki Prefectural Central Hospital  
 Ibaraki Seinan Medical Center Hospital  
 Ibi Kousei Hospital  
 Ichinomiya Neurosurgery Hospital  
 Ichinomiya West Hospital  
 Ichinose Hospital  
 Iida Municipal Hospital  
 Iizuka Hospital  
 Ikeda Neurosurgical Center Hospital  
 Ikuwakai Memorial Hospital  
 Imakiire General Hospital  
 Imamura Bun-in Hospital  
 Inagi Municipal Hospital  
 International University of Health and Welfare ATAMI  
 HOSPITAL  
 Inuyama Chuo Hospital  
 Iseikai Hospital  
 Iseikai Yahata Central Hospital  
 Isesaki Municipal Hospital  
 Ishikawa Prefectural Central Hospital  
 Ishinkai Yao General Hospital  
 Ishinomaki City Hospital  
 Ishioka Dai-Ichi Hospital  
 Isogo Central Hospital  
 Itami Kousei Neurosurgical Hospital  
 Itoigawa General Hospital  
 Itsukaichi Memorial Hospital  
 Iwaki Kyoritsu Hospital  
 Iwamizawa Municipal General Hospital

(Continued)

Appendix Table 1. (Continued)

Iwata City Hospital  
 Iwate Medical University Hospital  
 Iwate Prefectural Iwai Hospital  
 Iwate Prefectural Ninohe Hospital  
 Iwate Prefecture Isawa Hospital  
 Izumi General Medical Center  
 Izumino Hospital  
 Izumu Municipal Hospital  
 JA Kochi Hospital  
 JA Toride Medical Center  
 Japan Medical Alliance Higashi Saitama General Hospital  
 Japanese Red Cross Hadano Hospital  
 Japanese Red Cross Kitami Hospital  
 Japanese Red Cross Kobe Hospital  
 Japanese Red Cross Kochi Hospital  
 Japanese Red Cross Koga Hospital  
 Japanese Red Cross Kyoto Daini Hospital  
 Japanese Red Cross Medical Center  
 Japanese Red Cross Nagasaki Genbaku Hospital  
 Japanese Red Cross Ogawa Hospital  
 Japanese Red Cross Society Hachinohe Medical Center  
 Japanese Red Cross Society Himeji Hospital  
 Jiaikai Kajiura Hospital  
 Jichi Medical University Hospital  
 JR Tokyo General Hospital  
 Junshin Hospital  
 Juntendo University Hospital  
 Juntendo University Nerima Hospital  
 Juntendo University Urayasu Hospital  
 Junwakai Kinen Hospital  
 Juzenkai Hospital  
 Jyuzen General Hospital  
 Kaga City Hospital  
 Kagawa Prefectural Central Hospital  
 Kagawa Rosai Hospital  
 Kagawa University Hospital  
 Kagoshima City Hospital  
 Kagoshima prefectural Oshima Hospital  
 Kagoshima Tokushukai Hospital  
 Kagoshima University Medical and Dental Hospital  
 Kainan Hospital  
 Kaiseikai Onishi Hospital  
 Kakegawa Municipal General Hospital  
 Kakizoe Hospital  
 Kakogawa City Hospital  
 Kameda Medical Center  
 Kameoka Shimizu Hospital  
 Kamiichi General Hospital  
 Kamitsuga General Hospital  
 Kanazawa Medical University Hospital  
 Kanazawa Municipal Hospital  
 Kanazawa Neurosurgical Hospital  
 Kanazawa University Hospital  
 Kanetsu Hospital  
 Kanoya Medical Center  
 Kansai Medical University Takii Hospital  
 Kanto Central Hospital for Public School Teachers  
 Kantoh Neurosurgical Hospital

(Continued)

**Appendix Table 1. (Continued)**

Karatsu Red Cross Hospital  
 Kariya Toyota General Hospital  
 Kasai Cardiology Neurosurgery Hospital  
 Kasaoka Daiichi Hospital  
 Kashima Rosai Hospital  
 Kashiwaba Neurosurgical Hospital  
 Kashiwazaki General Hospital and Medical Center  
 Kasugai Municipal Hospital  
 Kasukabe Chuo General Hospital  
 Katagi Neurosurgical Hospital  
 Katano Hospital  
 Katsuta Hospital  
 Kawachi General Hospital  
 Kawakita General Hospital  
 Kawano Neurosurgical Hospital  
 Kawasaki Hospital  
 Kawasaki Medical School Hospital  
 Kawasaki municipal Hospital  
 Kawasaki Municipal Tama Hospital  
 Kawasakisaiwai Hospital  
 Kazuno Kosei Hospital  
 Keijin Kai Kawasaki Hospital  
 Keiwakai Ebetsu Hospital  
 Kenwakai Otemachi Hospital  
 Kimitsu Chuo Hospital  
 Kinan Hospital  
 Kinki University Hospital  
 Kiryuu Kohsei General Hospital  
 Kishiwada Tokushukai Hospital  
 Kitakyushu Municipal Medical Center  
 Kitamurayama Hospital  
 Kitano Hospital  
 Kizawa Memorial Hospital  
 KKR Sapporo Medical Center  
 Kobari General Hospital  
 Kobe University Hospital  
 Kochi Health Sciences Center  
 Kochi Medical School Hospital  
 Kofu Jonan Hospital  
 Kofu Municipal Hospital  
 Kofu Neurosurgical Hospital  
 Kohka Public Hospital  
 Kohnan Hospital  
 Kokubu Neurosurgical Clinic  
 Kokura Memorial Hospital  
 Komaki City Hospital  
 Komatsu Municipal Hospital  
 Komono Kosei Hospital  
 Konan Kosei Hospital  
 Konan Tobu General Hospital  
 Kosei Hospital  
 Koshigaya Municipal Hospital  
 Koto Memorial Hospital  
 Kousei General Hospital  
 Kouseikai Takai Hospital  
 Kouseiren Murakami Hospital  
 Kugayama Hospital  
 Kumamoto City Hospital

(Continued)

**Appendix Table 1. (Continued)**

Kumamoto Red Cross Hospital  
 Kumamoto Rousai Hospital  
 Kumamoto Takumadai Hospital  
 Kumamoto University Hospital  
 Kurashiki Central Hospital  
 Kurashiki Heisei Hospital  
 Kure Kyosai Hospital  
 Kurobe City Hospital  
 Kuroishi City Hospital  
 Kurosawa Hospital  
 Kurosu Hospital  
 Kurume University Hospital  
 Kusatsu General Hospital  
 Kushiro Kojinkai Memorial Hospital  
 Kushiro Rosai Hospital  
 Kuwana Hospital  
 Kuwana West Medical Center  
 Kyorin University Hospital  
 Kyoritsu General Hospital  
 Kyosai Tachikawa Hospital  
 Kyoto City Hospital  
 Kyoto Kujo Hospital  
 Kyoto Min-iren Chuo Hospital  
 Kyushu University Hospital  
 Machida Municipal Hospital  
 Maebashi Red Cross Hospital  
 Makita General Hospital  
 Masu Memorial Hospital  
 Matsudo City Hospital  
 Matsunami General Hospital  
 Matsushita Memorial Hospital  
 Matsuyama Red Cross Hospital  
 Matsuyama Shimin Hospital  
 Mattoh-Ishikawa Central Hospital  
 Mazda Hospital  
 Medical Corporation Kawamura Society Kubokawa  
 Hospital  
 Meisei Hospital  
 Meitetsu Hospital  
 Midorigaoka Hospital  
 Mie Prefectural General Medical Center  
 Mie University Hospital  
 Mihara Memorial Hospital  
 Minamata City General Hospital and Medical Center  
 Minamisoma City General Hospital  
 Minase Hospital  
 Mine City Hospital  
 Minei Daiichi Hospital  
 Mino Municipal Hospital  
 Minoh City Hospital  
 Mishuku Hospital  
 Mishuku Hospital  
 Mito Medical Center  
 Mito Saiseikai General Hospital  
 Mitoyo General Hospital  
 Mitsugi General Hospital  
 Miyakononojo Regional Medical Center  
 Miyoshi Central Hospital

(Continued)



Appendix Table 1. (Continued)

Mizushima Central Hospital  
 Morioka JRC Hospital  
 Moriya-daiichi General Hospital  
 Murakami Memorial Hospital Asahi University  
 Murata Hospital  
 Muroran City General Hospital  
 Musashino General Hospital  
 Nadogaya Hospital  
 Naga District Hospital  
 Nagahama City Hospital  
 Nagahama Red Cross Hospital  
 Nagano Municipal Hospital  
 Nagano Prefectural Kiso Hospital  
 Nagano Prefectural Suzaka Hospital  
 Nagano Red Cross Hospital  
 Nagaoka Chuo General Hospital  
 Nagaoka Red Cross Hospital  
 Nagareyama Central Hospital  
 Nagasaki Kawatana Medical Center  
 Nagasaki Municipal Hospital  
 Nagasaki Prefecture Shimabara Hospital  
 Nagasaki University Hospital  
 Nagatomi Neurosurgical Hospital  
 Nagoya Daini Red Cross Hospital  
 Nagoya Ekisaikai Hospital  
 Nagoya Medical Center  
 Nagoya Memorial Hospital  
 Nagoya University Hospital  
 Naha City Hospital  
 Nakamura Memorial Hospital  
 Nakamura Memorial South Hospital  
 Nakano General Hospital  
 Nakatsu Gastrointestinal Hospital  
 Namegata District General Hospital  
 Nanbu Tokushukai Hospital  
 Nantan General Hospital  
 Nantan General Hospital  
 Nara City Hospital  
 Nara Medical University Hospital  
 Nara Prefectural Hospital  
 Nara Prefectural Mimuro Hospital  
 Narita Red Cross Hospital  
 Nasu Neurosurgical Hospital  
 Nasu Red Cross Hospital  
 National Cancer Center Hospital  
 National Center for Child Health and Development  
 National Center for Global Health and Medicine  
 National Cerebral and Cardiovascular Center  
 National Disaster Medical Center  
 National Fukuoka-Higashi Medical Center  
 National Hospital Organization Chiba Medical Center  
 National Hospital Organization Hamada Medical Center  
 National Hospital Organization Himeji Medical Center  
 National Hospital Organization Kanazawa Medical Center  
 National Hospital Organization Kanmon Medical Center  
 National Hospital Organization Kobe Medical Center

(Continued)

Appendix Table 1. (Continued)

National Hospital Organization Kumamoto Medical Center  
 National Hospital Organization Kure Medical Center  
 National Hospital Organization Maizuru Medical Center  
 National Hospital Organization Minami Wakayama Medical Center  
 National Hospital Organization Nagasaki Medical Center  
 National Hospital Organization Nara Medical Center  
 National Hospital Organization Okayama Medical Center  
 National Hospital Organization Osaka Minami Medical Center  
 National Hospital Organization Saitama National Hospital  
 National Hospital Organization Shizuoka Medical Center  
 National Hospital Organization Takasaki General Medical Center  
 National Hospital Organization Ureshino Medical Center  
 National Hospital Organization Utano Hospital  
 National Hospital Organization Yokohama Medical Center  
 National Kyushu Medical Center  
 Nayoro City General Hospital  
 Nihon University Itabashi Hospital  
 Niigata City General Hospital  
 Niigata Minami Hospital  
 Niigata Neurosurgical Hospital and Brain Research Center  
 Niigata Prefectural Cancer Center Hospital  
 Niigata Prefectural Central Hospital  
 Niigata Prefectural Shibata Hospital  
 Niigata Prefectural Tokamachi Hospital  
 Niigata Rosai Hospital  
 Niigata University Medical and Dental Hospital  
 Nippon Medical School Chiba Hokusoh Hospital  
 Nippon Medical School Hospital  
 Nippon Medical School Musashi Kosugi Hospital  
 Nippon Medical School Tama-Nagayama Hospital  
 Nipponbashi Hospital  
 Nishi-Agatsuma Welfare Hospital  
 Nishi-Kobe Medical Center  
 Nishinara Tyuou Hospital  
 Nishinomiya Kyoritsu Neurosurgical Hospital  
 Nishio Municipal Hospital  
 Nishisaitama-chuo National Hospital  
 Nishiwaki Municipal Hospital  
 North Fukushima Medical Center  
 North Osaka Police Hospital  
 NTT Medical Center Tokyo  
 Obara Hospital  
 Obihiro-Kosei General Hospital  
 Odate Municipal General Hospital  
 Odawara Municipal Hospital  
 Oe Kyodou Hospital  
 Ofunato Hospital  
 Ogachi Central Hospital  
 Ogaki Municipal Hospital  
 Ogori Daiichi General Hospital

(Continued)

**Appendix Table 1. (Continued)**

Ohda Municipal Hospital  
 Ohkawara Neurosurgical Hospital  
 Ohmiya Chuo General Hospital  
 Ohnishi Neurological Center  
 Ohta General Hospital  
 Oita Prefectural Hospital  
 Oita University Hospital  
 Oita-Oka-Hospital  
 Okayama City Hospital  
 Okayama East Neurosurgical Clinic  
 Okayama Kyokuto Hospital  
 Okayama Kyoritsu General Hospital  
 Okayama Rosai Hospital  
 Okayama University Hospital  
 Okazaki City Hospital  
 Okinawa Chubu Hospital  
 Okinawa Hokubu Hospital  
 Okinawa Kyodo Hospital  
 Okinawa Prefectural Miyako Hospital  
 Okinawa Prefectural Nanbu Medical Center and  
     Children's Medical Center  
 Okinawa Prefectural Yaeyama Hospital  
 Okitama Public General Hospital  
 Okyama East Neurosurgical clinic  
 Omihachiman Community Medical Center  
 Omori Red Cross Hospital  
 Omuta City Hospital  
 Ooi-Byouin  
 Ookuma Hospital  
 Ota Memorial Hospital  
 Osaka City General Hospital  
 Osaka City University Hospital  
 Osaka General Medical Center  
 Osaka Kosei-Nenkin Hospital  
 Osaka Medical Center  
 Osaka Medical College Hospital  
 Osaka Mishima Critical Care Medical Center  
 Osaka Neurological Institute  
 Osaka Neurosurgical Hospital  
 Osaka Police Hospital  
 Osaka Prefectural Senshu Critical Care Medical Center  
 Osaka Red Cross Hospital  
 Osaka Rosai Hospital  
 Osaka University Hospital  
 Otemae Hospital  
 Otsu Municipal Hospital  
 Research Institute for Brain and Blood Vessels Akita  
 Rumoi Central Clinic  
 Sadamoto Hospital  
 Saga Prefectural Hospital Koseikan  
 Saga Social Insurance Hospital  
 Sagamihara Kyodo Hospital  
 Sagamihara-chuo Hospital  
 Saisei-kai Yokohama-shi Nanbu Hospital  
 Saiseikai Central Hospital  
 Saiseikai Fukuoka General Hospital  
 Saiseikai Gose Hospital  
 Saiseikai Hita Hospital

(Continued)

**Appendix Table 1. (Continued)**

Saiseikai Hyuga Hospital  
 Saiseikai Imabari Hospital  
 Saiseikai Kumamoto Hospital  
 Saiseikai Kurihashi Hospital  
 Saiseikai Kyoto Hospital  
 Saiseikai Matsusaka General Hospital  
 Saiseikai Matsuyama Hospital  
 Saiseikai Nagasaki Hospital  
 Saiseikai Nakatsu Hospital  
 Saiseikai Nara Hospital  
 Saiseikai Noe Hospital  
 Saiseikai Saijo Hospital  
 Saiseikai Shimonoseki General Hospital  
 Saiseikai Toyama Hospital  
 Saiseikai Utsunomiya Hospital  
 Saiseikai Yahata General Hospital  
 Saiseikai Yamaguchi Hospital  
 Saiseikai Yokohanashi Tobu Hospital  
 Saiseikai-Chuwa Hospital  
 Saitama Cancer Center Hospital  
 Saitama Cardiovascular and Respiratory Center  
 Saitama Medical Center  
 Saitama Medical Center Jichi Medical University  
 Saitama Medical University Hospital  
 Saitama Medical University International Medical Center  
 Saitama Municipal Hospital  
 Saito Memorial Hospital  
 Sakai City Hospital  
 Sakai Hospital Kinki University Faculty of Medicine  
 Sakaide Municipal General Hospital  
 Saku Central Hospital  
 Sakura General Hospital  
 Sakurakai Hospital  
 Sanda City Hospital  
 Sankoukai Miyazaki Hospital  
 Sannocho Hospital  
 Sano Kousei General Hospital  
 Sanyudo Hospital  
 Sapporo City General Hospital  
 Sapporo Higashi-Tokushukai Hospital  
 Sasebo Chuo Hospital  
 Sasebo City General Hospital  
 Sayama Hospital  
 Seguchi Neurosurgery Hospital  
 Seirei Hamamatsu General Hospital  
 Seirei Memorial Hospital  
 Seirei Mikatagahara General Hospital  
 Seirei Yokohama Hospital  
 Seiyu Memorial Hospital  
 Sendai City Hospital  
 Sendai Medical Association Hospital  
 Sendai Open Hospital  
 Senpo Tokyo Takanawa Hospital  
 Senseki Hospital  
 Shakaihoken Kobe Central Hospital  
 Shakaihoken Shimonoseki Kosei Hospital  
 Shiga Medical Center for Adults  
 Shiga University of Medical Science Hospital

(Continued)

Appendix Table 1. (Continued)

Shimada City Hospital  
 Shimane Prefectural Central Hospital  
 Shimane University Hospital  
 Shimonoseki City Hospital  
 Shimotsuga General Hospital  
 Shin Koga Hospital  
 Shin Yukuhashi Hospital  
 Shin-Tokyo Hospital  
 Shingu Municipal Medical Center  
 Shinko Hospital  
 Shinoda General Hospital  
 Shinonoi General Hospital  
 Shinrakuen Hospital  
 Shinseikai Toyama Hospital  
 Shinshu Ueda Medical Center  
 Shinsuma Hospital  
 Shirahama Hamayu Hospital  
 Shirakawa Kosei General Hospital  
 Shiroishi neurosurgical Hospital  
 Shiroyama Hospital  
 Shiseikai Daini Hospital  
 Shizuoka Children's Hospital  
 Shizuoka City Hospital  
 Shizuoka General Hospital  
 Shobara Red Cross Hospital  
 Shonai Hospital  
 Shonan Kamakura General Hospital  
 Showa General Hospital  
 Showa Inan General Hospital  
 Showa University Fujigaoka Hospital  
 Showa University Hospital  
 Social Insurance Chukyo Hospital  
 Social Insurance Chuo General Hospital  
 Social Insurance Takahama Hospital  
 Soseikai General Hospital  
 South Miyagi Medical Center  
 Southern Tohoku General Hospital  
 St Marianna University School of Medicine Toyoko  
 Hospital  
 St Francisco Hospital  
 St Marianna University School of Medicine Hospital  
 Steel Memorial Hirohata Hospital  
 Steel Memorial Yawata Hospital  
 Suisaikai Kajikawa Hospital  
 Suita Municipal Hospital  
 Suwa Central Hospital  
 Suwakohan Hospital  
 Suzuka Kaisei Hospital  
 Tachikawa Medical Center  
 Takada Chuo Hospital  
 Takamatsu Municipal Hospital  
 Takamatsu Red Cross Hospital  
 Takarazuka City Hospital  
 Takarazuka Daiichi Hospital  
 Takashima Municipal Hospital  
 Takatsuki General Hospital  
 Takeda General Hospital  
 Takikawa Neurosurgery Hospital

(Continued)

Appendix Table 1. (Continued)

Tama-Hokubu Medical Center  
 Tama-Nanbu Chiiki Hospital  
 Tamana Central Hospital  
 Tane General Hospital  
 Tano Hospital  
 Tanushimaru Central Hospital  
 Tatebayashi Kosei Hospital  
 Teiko University Chiba Medical Center  
 Teikyo University School of Medicine Hospital,  
 Mizonokuchi  
 Tekeda Hospital  
 Tenshindo Hetsugi Hospital  
 The Taiju-Kai Foundation Social Medical Corporation  
 Kaisei General Hospital  
 Tochigi National Hospital  
 Toho University Ohashi Medical Center  
 Tohoku KoseiNenkin Hospital  
 Tokai Central Hospital of the Mutual Aid Association of  
 Public School Teachers  
 Tokai University Hachioji Hospital  
 Tokai University Hospital  
 Tokai University Oiso Hospital  
 Toki General Hospital  
 Tokuda Neurosurgical Hospital  
 Tokushima Prefectural Central Hospital  
 Tokushima Prefectural Kaifu Hospital  
 Tokushima University Hospital  
 Tokuyama Central Hospital  
 Tokyo Kyosai Hospital  
 Tokyo Medical And Dental University Hospital Faculty  
 of Medicine  
 Tokyo Medical University Hospital  
 Tokyo Medical University Ibaraki Medical Center  
 Tokyo Metropolitan Hiroo Hospital  
 Tokyo Metropolitan Health and Medical Corporation  
 Toshima Hospital  
 Tokyo Metropolitan Ohtsuka Hospital  
 Tokyo Metropolitan Police Hospital  
 Tokyo Women's Medical University Hospital  
 Tokyo Women's Medical University Yachiyo Medical  
 Center  
 Tokyo Women's University Medical Center East  
 Tokyo-Teishin Hospital  
 Tokyo-West Tokushukai Hospital  
 Tokyu Medical University Hachioji Medical Center  
 Tomakomai Neurosurgical Hospital  
 Tomakomai Nissho Hospital  
 Tomei Atsugi Hospital  
 Tominaga Hospital  
 Tomioka General Hospital  
 Tonami General Hospital  
 Tone Central Hospital  
 Tosei General Hospital  
 Tottori Pref.Kousei Hospital  
 Tottori Red Cross Hospital  
 Tottori Seikyo Hospital  
 Tottori University Hospital  
 Toyama City Hospital

(Continued)

**Appendix Table 1. (Continued)**

---

Toyama Prefectural Central Hospital  
 Toyama Rosai Hospital  
 Toyohashi Medical Center  
 Toyokawa City Hospital  
 Toyooka Chuo Hospital  
 Toyooka Public Hospitals' association Toyooka Hospital  
 Toyota Kosei Hospital  
 Tsuchiura Kyodo General Hospital  
 Tsukazaki Hospital  
 Tsukuba Medical Center Hospital  
 Tsushima City Hospital  
 Tsuyama Central Hospital  
 Ube Industries, Ltd. Central Hospital  
 Ueyama Hospital.  
 Ugadake Hospital  
 University Hospital of the Ryukyus  
 University of Miyazaki Hospital  
 University of Tokyo Hospital  
 University of Tsukuba Hospital  
 University of Yamanashi Hospital  
 Urasoe General Hospital  
 Ushiku Aiwa General Hospital  
 Ushioda General Hospital  
 Uwajima City Hospital  
 Uwajima Tokushukai Hospital  
 Veritas Hospital  
 Wada Hospital  
 Wakakusa Dai-ichi Hospital  
 Wakayama Co-operative Hospital  
 Wakayama Medical University Hospital  
 Wakayama Medical University Kihoku Hospital  
 Wakayama Rosai Hospital  
 Wakayama Saiseikai Hospital  
 Yaentoge Neurosurgery Hospital  
 Yagi Neurosurgical Hospital  
 Yaizu City General Hospital  
 Yamachika Memorial Hospital  
 Yamada Kinen Hospital  
 Yamada Red Cross Hospital  
 Yamagata City Hospital Saiseikan  
 Yamagata Prefectural Kahoku Hospital  
 Yamagata Prefectural Shinjo Hospital  
 Yamagata University Hospital  
 Yamaguchi Grand Medical Center  
 Yamaguchi Red Cross Hospital  
 Yamaguchi Rousai Hospital  
 Yamaguchi University Hospital  
 Yamamoto Memorial Hospital  
 Yamanashi Kosei Hospital  
 Yamanashi Prefectural Central Hospital  
 Yamanashi Red Cross Hospital  
 Yamashiro Public Hospital  
 Yamato Municipal Hospital  
 Yao Tokushukai General Hospital  
 Yasugi municipal Hospital  
 Yatsuo General Hospital  
 Yatsushiro Health Insurance General Hospital  
 Yahata General Hospital

(Continued)

---

**Appendix Table 1. (Continued)**

---

Yayoigaoka Hospital  
 Yodogawa Christian Hospital  
 Yokkaichi Municipal Hospital  
 Yokohama Central Hospital  
 Yokohama City Minato Red Cross Hospital  
 Yokohama City University Hospital  
 Yokohama City University Medical Center  
 Yokohama General Hospital  
 Yokohama Rosai Hospital  
 Yokohama Sakae Kyosai Hospital  
 Yokohama Shin-midori General Hospital  
 Yokohama Stroke and Brain Center  
 Yokohamashintoshi Neurosurgical Hospital  
 Yokosuka General Hospital Uwamachi  
 Yomeikai Obase Hospital  
 Yonabaru Chu-ou Hospital  
 Yonago Medical Center  
 Yonezawa City Hospital  
 Yuaikai Hospital  
 Yukioka Hospital

---