

結果

未調整の odds 比では、脳卒中全体では退院時の outcome は深夜に向かって悪くなった。JCS 以外を調整したものでは、全体、脳虚血、くも膜下出血、非外傷性の出血いずれも深夜で outcome が悪い傾向にあったが、JCS も含めて調整すると、有意差はなかった。

年齢・性・併存疾患を調整すると受療時間帯により退院時の outcome に差を認めたと、時間帯によって患者の重症度に差があり、モデルに JCS を投入して調整すると、受療時間帯が違うことの outcome への影響は大きく減弱した。

Limitation について

強みとしては、単年で集めた大規模データでの評価であること、深夜のリスクに焦点を当てたこと、重症度を調整したこと、脳卒中全体と各病型での評価をしたことであるが、limitation としては、JCS を用いていること（国際的な先行研究では JCS を用いているものは少ない）、時間外加算の有無に関して欠損値が多いこと、DPC の outcome の妥当性についての検討が必要であることである。

今後の検討課題

今回 CSC score との関連の検討は行っておらず、今後行う必要がある。感度分析では出血性脳卒中では結果は robust ではなかったが、重症度で説明できないところは CSC score に関連している可能性がある。

Q & A

豊田：神谷先生の今の発表で outcome が深夜帯で悪かったのは、初期重症度で調整をかけた後もということの良いか。

神谷：初めは年齢と性と併存疾患などを調整しても依然 outcome には差があったが、それに JCS を加えると差がなくなった。

豊田：資料では明らかに off hour, midnight になるにつれて昏睡の患者が日勤帯の倍くらいいるが、夜発症する脳卒中が重症であるという感覚はないので、J-ASPECT の登録施設の 262 の病院に夜間帯の重症な患者が選択的に集まっている実態を表していると思われる。決して夜になると、この 262 の病院の診療体制が落ちてしまうということではない。

神谷：そうではない。ただ初期重症度で調整すると有意差は消えるので、やはり予後が悪いことの説明原因の一つとして、より夜間に重症の人が集まっていることを見ているのだと思われる。逆にそこを消してしまうと昼間と変わらないということになる。

豊田：ただ重症例が集まっているから、ある程度夜になると医療資源を投入しないといけないという話にはつながるかもしれない。

飯原：救急車の搬入は、症例を選んではないはず。救急車搬入での緊急入院患者からある程度の患者を省いているということなのか。

神谷：緊急入院した 53000 件のうち、今回は mRS のデータが確認できた症例の中から時間外加算が欠損しているものを省いた約 35000 件である。

長谷川：「現況報告」

この研究班の成果で、2点政策に結びつきそうなことがある。

雇用の質について

次の通常国会で医療法改正を予定しているが、その中で都道府県に医療従事者の雇用状況について改善する相談窓口を設置することとなった。また、日本医師会で労働基準法をきちんと経営者等々含め守って行くという宣言がなされた。さらに診療報酬、雇用の質の改善についてはメインの一つに取り上げられており、この研究会の成果だと考えている。

レジストリについて

夏の国民会議の中で症例レジストリを作るべきだという結論になっていたが、その具体的な内容はまだ決まっていなかった。例えば外科の症例や循環器疾患についてレジストリを作るなどの提案はあるが、実際としてなかなか現実に至っていなかった。指導課の方では救急をキーワードにしたレジストリを今提案している。具体的には救急搬送と walk-in で来られた患者について、日本全国で全てデータベース化することである。基本のコア部分については厚労省の事業で作る、さらに他の関連学会がそのコアをベースにサブ調査を行えないか検討している。現在予算要求の時期であり、医政局全体でできれば億単位の最初のモデル事業を開始し、地域を限って population base で、全救急搬送、救急車を利用した患者のデータと、あとはいくつかの病院で、日中夜間を含めて救急外来を受診された患者についてまずは全てを把握し、さらに関連するデータとリンケージしていくことができないかを検討中である。

問題点

調査の重要性はみなさんにご理解いただけるが、現実どういう形になるのか、何が分かるのか、という疑問があること、また関係学会が多数あり、それぞれ自分たち中心でやりたいと思っている。

通常はまず何を明らかにしたいのかという仮説を複数作った上で、それを明らかにする為にどういうデータが必要か、どういう調査が必要か、という形で調査設計を行って行くものであろうが、先行している調査が色々ある中で、その議論が抜けてスタートしてしまっている点が残念なところである。

今後の方針

仮説をいくつかきちんと作った上で何を明らかにするのか、最終目標は何なのか、私は救命の質の向上であると思っているが、その部分の蓄積が必要だろうと考えている。

《平成 25 年度研究計画》

西村：「アウトカム指標の validation について」

本研究はレセプトデータを使用しているのでこれが本当に正しいのかということが問われる。最近投稿した論文が、データの validation がなされていないことが根源的な問題と言われ reject された。死亡や mRS などの予後データが正しいかどうかの確認が必要である。

既存の疾患や重症度(JCS)についてのリスク調整や Quality of care(医療の質)に関しての検討が必要である。例として AHA の registry では施設をランダムに選んで調査することで validation をかけている。がん登録に関しては診療情報管理士と連携を行いデータ管理をしている。

今後はプリズムに依頼して限られた項目に関して validation をかけていく予定である。

《第 34 回日本脳神経外科コンgres・日本脳神経外科学会との合同調査》

中溝：「脳神経外科医療の可視化に関する研究」の概要

来年開催される第 34 回脳神経外科コンgres総会では「脳神経外科医療の可視化」をテーマとして掲げており、J-ASPECT と同様の手法を用いて脳神経外科領域の各疾患について研究を行っていく方針としている。

Q & A

飯原：松田先生の研究では DPC 病名の validation はどうしているか？

松田：脳卒中データベースにデータを流し込む作業でほぼ問題ないことを確認した。脳卒中に関しては行った医療行為で病名が推定できるので問題ないと思われる。副傷病のデータが正確に入っているかどうかは問題である。他の脳卒中レジストリと合わせることや、DPC データからいくつかのサンプルをとって項目が合っているか確かめたほうがいいと思う。

《分担研究者 自己紹介と個別研究課題》

松田：「National data base を用いた脳卒中急性期医療の現状分析」

DPC や national data base(NDB)を用いて脳卒中の急性期医療の現状分析を行っている。電子レセプトを様式 1 と E/F ファイルに分解する技術を開発した。外来・急性期・慢性期全て DPC より加工することができ、傷病構造の分析を行っている。今回は年齢階級別に当該診療行為がどれくらい発生しているかを都道府県、各医療圏別に実際の期待数に実数をかける手法を用いて、各地域で当該医療行為がどれくらい行われているかのマクロな指標を作成している。

実際に SCU と ICU に関して見てみると、SCU のほうがより地域差が大きい。さらに脳梗塞の年齢調整死亡率との相関を見てみると、ICU では死亡率との相関が見られるが、SCU に関しては全く関係ない。これは SCU では軽症の患者が診られているからと考えられる。また救急車の搬送距離と死亡率との相関を見てみると移送距離が長い方が死亡率が高いことがわかる。

DPC のデータを解析することで日本の脳卒中急性期医療に関する分析を行うことが可能であった。我が国の脳卒中急性期の医療のアクセスの地域差が生命予後に関係している可能性があるためその配置を考慮する必要があることが言える。

Q & A

豊田：NDB はレセプトの全ての病名が入っているのか？脳卒中の発生率や急性期、慢性期などもわかるか？

松田：わかる。急性期か慢性期かは直接はわからず、使用した薬剤で推定して判断している。NDB のいいところは個人の ID が個別についているので同じ人のデータが double count されないところである。できれば ICD10 を細かく、例えば脳梗塞の病型などがきちんと入れてもらえるようになると思う。DPC は詳細不明のコードがなるべくないようになっているが、電子レセプトはそうではないところが欠点である。

豊田：個人 ID は転院しても一緒か？

松田：一緒である。ただ後期高齢者になると追いかけるのは難しい。

青木：「ドクターヘリ・ドクターカーによる超急性期からの医療提供体制ニーズの把握に係る研究」

テキサス大学と NPO 法人に属しており、日本では奈良県で救急医療の仕組み作りを奥地教授と一緒にやっている。

ドクターカーやドクターヘリが導入されたことによってどのような臨床効果や医療経済効果が得られたかの評価を行った。

GIS のデータに国勢調査の人口データおよび論文から得た疾患発生率を使用することにより、各 3 次メッシュの中でどれくらい脳卒中の患者がいるかが推定できる。それを全国のメッシュに対して、そのメッシュで傷病が発生した場合に医師接触まで要する時間を GIS を利用して算出し、その結果に基づいて、救急車、ドクターカー、ドクターヘリでカバーされる患者数を地図上に視覚化した。

ドクターヘリが使える状況では、ドクターヘリがない状況と比較すると、どの程度の患者をカバーできるかを試算した結果、全国で 12782 人の脳梗塞患者をカバーできると算出され、それに対し、tPA の NNT を利用し、患者一人に対して生じる経済的利得をかけて計算したものが全体の医療経済的利得を算出した。

これらの手法でドクターヘリによりどのような医療経済効果・臨床的効果が得られるか算出して表を用いて可視化した。

Q & A

松田：病院とドクターヘリが別々にあるところでは医師と看護師がずっとそこに待機することになるため機会コストが大きなものになるので、それを入れて考えるかどうかが問題である。またドクターヘリの飛べる昼間と夜間では発生率に差があるので、その補正が必要になるのではないか。

青木：基地と病院が違うという点では基地から病院までに数分で行けてトータルで 30 分で行けるという仮説をとった。機会コストに関しては、新たな人員を増加しない、すなわち、人員のコストは発生しないという仮定で分析した。昼夜の発生率の差は、実際の奈良の発生データを用いてその割合を分析に取り込んでいる。

奥地：「奈良県における救急搬送体制」

5 年前より青木先生と奈良県内でやってきたことを紹介する。5 年前より救急搬送基準を作成し 3 年前より搬送基準を紙ベースで作り、2 年前よりまず消防に導入して 1 年前より病院にも取り入れるようになった。その中から脳卒中のデータを用いてこの研究に協力したい。

塩川：「首都圏における脳卒中救急診療の現状」

東京は脳卒中医療に関しては遅れている。急性期脳卒中の患者が comprehensive stroke center に適切に搬送されるようなシステムの構築ができるよう協力していきたい。

豊田：「脳卒中内科の立場から」

内科の立場から tPA のことなどで協力していきたい。今回の研究は DPC を利用して registry を作っていることが興味深いと思っている。脳卒中の全例登録の registry を作ることで良いと思っている。

永田，林：「脳卒中診療における専門医の地域差」

永田：長崎は島があることが特徴であるのでその点で協力できている。Comprehensive stroke center が血管内や内科と三位一体で治療できるような施設は全国的にもまだ多くはないので、そういった形が広まるようになれば良いと思っている。

林：これまで SCU の観点から脳卒中の診療体制について検討し、昨年の脳卒中学会ではシンポジウムで脳卒中に関わる専門医の都道府県分布について報告した。専門医数の地域差という観点では脳神経外科については一般的な範囲内であって、脳卒中に関わる専門医は 2-5 倍と高く、血管内治療専門医に至っては 20 倍と専門性が高くなるほど大きな地域差がある。

吉村：「急性期脳梗塞に対する血管内治療」

急性期脳梗塞に対する血管内治療を積極的に行っている。近年 tPA 静注療法が認可されてから徐々に施行される頻度は多くなってきたが、軽症例では予後良好群が 3 割を超えるが重症例では減ってしまう。また主幹動脈に関しても tPA の有効率が低いことから、これらの症例に血管内治療の適応があるのではないかと考えている。tPA の非適応・無効例に対し 8 時間以内の症例に対しメルシーレトリーバー、ペナンプラなどのデバイスが保険適応になっている。まずは tPA 静注療法を施行して、救急車で血管内治療ができる施設に転送するという Drip-Ship-Retrieve という方針で効果を得ている。

神戸(市立医療センター中央市民病院)の坂井(信幸)先生と行った登録調査において太い血管において tPA の無効例・非適応例どちらも血管内治療の有効性に優位差があり日本ではその効果が期待できることが示されたが、欧米から 3 つのランダム化試験で血管内治療の有効性が示せなかったため逆風状態である。ただアメリカでもヨーロッパでも次のデバイスに対してランダム化試験が行われており、日本でも計画している。

《今後の予定》

中溝：

本日の会議の議事録は後日送付する。次回の会議は年度末に予定しており、メールで連絡する。

《閉会の挨拶》

飯原：

順調にデータは集まっており、解析も進んでいる。一番問題なのは validation についてであり今後も先生方にご協力頂きたい。そこが済めば DPC を使用することの限界がわかり、またそれを踏まえて利用することで様々な論文にできるのではないと思う。かなり大きなデータベースになっているので脳卒中のみならず脳神経外科全体の医療の質を上げることに役立てられればと思っている。

脳卒中急性期医療の地域格差の可視化と縮小に関する研究

平成 25 年度 第 1 回班会議

日 時：平成 25 年 11 月 15 日（金） 11：00～14：00

場 所：京都大学東京オフィス 「会議室 3」

11：00

1. 挨拶

研究代表者	飯原 弘二
厚生労働省医政局指導課	長谷川 学

11：10～11：50

2. J-ASPECT Study 研究結果報告

全体研究（論文化進捗状況）

「脳卒中診療施設調査」 飯原 弘二

「脳卒中診療医の勤務状況と疲労度調査」 西村 邦宏

「脳卒中患者の退院調査」（平成 22 年度版）

院内死亡率と CSC スコア 飯原 弘二

患者受療圏とアウトカム 嘉田 晃子、西村 邦宏

患者受療日とアウトカム 神谷 諭

12：00～12：30 昼食

12：40～13：20

3. 平成 25 年度研究計画

「脳卒中患者の退院調査」（平成 25 年度版）

新規登録疾患について 飯原 弘二

アウトカム指標の validation について 西村 邦宏

4. 第 34 回日本脳神経外科コンGRESS・日本脳神経外科学会との合同調査

「脳神経外科医療の可視化に関する研究」の概要 中溝 玲

13：20～14：00

5. 分担研究者 自己紹介と個別研究課題

産業医科大学 松田 晋哉

NPO 法人 Chord-J

奈良県立医科大学

杏林大学

国立循環器病研究センター

国立循環器病研究センター

長崎大学

兵庫医科大学

名古屋医療センター

青木 則明

奥地 一夫

塩川 芳昭

西村 邦宏

豊田 一則

永田 泉

吉村 紳一

嘉田 晃子

6. 今後の予定

事務局

7. 閉会の挨拶

飯原 弘二

厚生労働科研費（飯原班）

「脳卒中急性期医療の地域格差の可視化と縮小に関する研究」 研究組織

氏名	所属	
飯原 弘二	九州大学大学院医学研究院 脳神経外科 教授	研究代表者
小笠原 邦昭	岩手医科大学脳神経外科 教授	研究分担者
有賀 徹	昭和大学大学院救急医学講座 教授	研究分担者
塩川 芳昭	杏林大学脳神経外科 教授	研究分担者
宮地 茂	名古屋大学大学院脳神経外科 准教授	研究分担者
吉村 紳一	兵庫医科大学脳神経外科 教授	研究分担者
豊田 一則	国立循環器病研究センター脳血管内科 部長	研究分担者
西村 邦宏	国立循環器病研究センター予防医学疫学情報部 EBM・リスク情報解析室 室長	研究分担者
嘉田 晃子	名古屋医療センター臨床研究センター臨床研究企画部生物統計研究室 室長	研究分担者
青木 則明	NPO 法人ヘルスサービス R&D センター（CHORD-J）理事長、テキサス大学健康情報科学大学院 准教授	研究分担者
中川原 譲二	国立循環器病研究センター脳卒中統合イメージングセンター 部長	研究分担者
松田 晋哉	産業医科大学公衆衛生学 教授	研究分担者
永田 泉	長崎大学脳神経外科 教授	研究分担者
奥地 一夫	奈良県立医科大学救急医学講座 教授	研究分担者
矢島 務	東京消防庁救急部救急指導課	研究分担者
小野 純一	千葉県循環器病センター センター長	研究協力者
長谷川 学	厚生労働省医政局指導課 課長補佐	研究協力者
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The Impact of Comprehensive Stroke Care Capacity on the Hospital Volume of Stroke Interventions: A Nationwide Study in Japan: J-ASPECT Study

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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

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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.
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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: primary¹ and comprehensive.² 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.² A set of metrics and associated data elements that cover the major types of care that distinguish CSCs from PSCs have been published recently.³ 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).² 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	99.2
	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.^{4,5} 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.⁶ The geographic location of the hospitals was classified according to urban employment areas,⁷ 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.⁸

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 personnel, 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
Personnel							
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
Diagnostic							
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
Specific expertise							
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/draining	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
Infrastructure							
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
Education							
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
	(+)	(-)	P value	Q1	Q2	Q3	Q4	
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)^{9,10} and endovascular surgeons (36.3% versus 15%-22% in the United States),⁹⁻¹¹ which was in sharp contrast with the relative shortage of neurologists (47.8% versus 31%-73% in the United States) and other personnel.⁹⁻¹¹ In the United States, only 7% of neurosurgeons play an active role in nontraumatic cranial emergencies,¹² 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.¹¹

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,¹³ 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%).^{9-11,14}

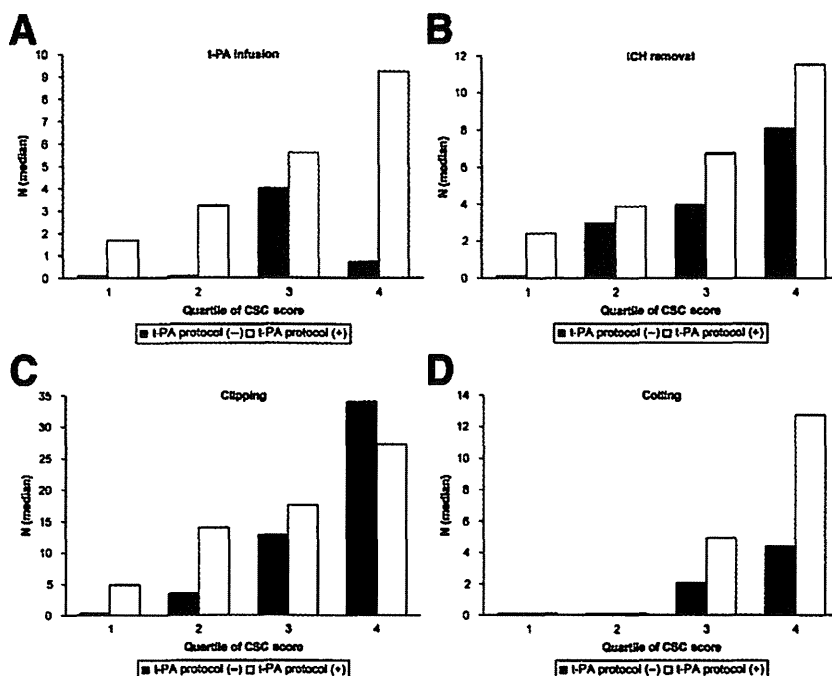
To determine the relationship between primary and comprehensive stroke care capacity, we used the implementation of a written t-PA protocol as a key item of primary stroke care capacity¹ as it is a key step in reducing t-PA-related complications.¹⁵ The availability of a t-PA protocol (85%) recorded in the present study was comparable with that reported in 2 US statewide studies performed in Illinois in 2000 (72.8%)⁹ and in North Carolina between 1998 (43%) and 2008 (69%).¹¹ 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,⁹ 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

	β	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.² 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.¹⁶ High annual hospital volume was reported to be consistently associated with lower IS mortality.¹⁷ In the field of comprehensive stroke care, in-hospital mortality increases when the annual number of craniotomies for aneurysms is lower than 30¹⁸ and when CEA is performed by less experienced surgeons (<5 procedures/y).¹⁹ Conversely, a previous Japanese nationwide study

found no correlation between case volume and outcome after cerebral aneurysm clipping.²⁰ The mechanism via which volume influences outcomes remains uncertain. Specific processes of care, which are correlated with volume, are the most likely explanatory factors.¹⁶ 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,²¹ 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.

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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 Shintoshii 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
 Ikuwaki 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
 Miyakonojo Regional Medical Center
 Miyoshi Central Hospital

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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
 Nambu 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

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