Seung-Hoon Lee *Editor*

Stroke Revisited: Diagnosis and Treatment of Ischemic Stroke

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Stroke Revisited
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Preface

The most frequently used starting sentence in books or articles on stroke is: "stroke is a disease ranked 4th in worldwide mortality, and 1st in worldwide adult disabilities." Although I am personally sick of using this sentence and no longer use it when writing an article or a paper, there are still tons of papers and books that start with this sentence. Why is that? Do the readers not know the significance? Or is it to provide the readers with self-esteem, in that the disease you are reading about and treating is extremely important? Maybe both. Unfortunately, the importance of the disease is not emphasized enough or recognized by the public, probably due to the modesty of the clinicians and researchers treating and studying stroke. In most countries, both the patients and the medical staff have very low awareness of stroke compared to heart diseases, and the sizes of both the clinical and research workforce for stroke are incomparably small. The stroke unit is sometimes a part of the department of neurology and sometimes a part of internal medicine and rarely an independent department in many countries. Considering the severity and importance of the disease, this system is too inconsistent and insufficient. In addition to developing an integrated and systematic treatment protocol for stroke, the presence of a textbook that provides up-to-date knowledge and standard of treatment is essential.

I once had a meeting with the director of cardiovascular medicine in one of the biggest multinational pharmaceutical companies in the world. The director of the Europe-based company was an impressive, old, Caucasian madam. She said that the stroke department in her company was being managed entirely by the cardiovascular department. The meeting was held so that I could provide advice on research and development (R&D) in medications on stroke. Then, I was really puzzled about her lack of background knowledge on stroke. She graduated from a recognized medical school in Europe and practiced as a medical doctor in the cardiovascular division of the department of internal medicine. How could she know so little about stroke? She thought that stroke was simply another coronary artery disease that occurred in the brain, and I was the first person to tell her about stroke due to small vessel occlusion—which is an important subtype of stroke. Considering the fact that the head of R&D from a leading pharmaceutical company barely knew anything about stroke, it is not a surprise to see no medication or unsuccessful medication being developed for stroke treatment. Even now, I believe that the situation has not changed. If there was a textbook that provides a

simple explanation of stroke and discusses the key differences between stroke and heart diseases, would the situation be any different?

Actually, there are not many textbooks that explain stroke in detail. During my residency and fellowship, there were only two or three books that I could read to study stroke. Even these books were not enough to fully appreciate the advancement in stroke treatment during 1990–2000. Brain imaging dramatically improved the quality of treatment by allowing immediate recognition of the continuously changing pathophysiology of the stroke patient. Nevertheless, majority of textbooks contain a big portion explaining outdated neurological examinations, providing no support for development in the practical field. Furthermore, most textbooks simply outlined the results from various studies and did not focus on helping readers to understand the key concepts or providing appropriate schemes for treatment protocols. Although the situation was probably similar for other fields, studying stroke during this period required extensive patience.

Recent development of smartphones and tablets allowed international communications through social media, and people now have access to extensive amount of information. Textbooks to deliver medical knowledge should also change to reflect the rapidly advancing modern technology and must focus on providing simple and clear explanations of key concepts. The content of each chapter should be minimized, and visual diagrams should be utilized to help the readers better understand key concepts. Listing unnecessary results from studies should be avoided, while standard treatment guidelines from various academic societies would be better to be collated and described. I decided to write such a textbook reflecting these changes and contacted Springer Nature. Springer Nature was very helpful and planned a new series of textbooks entitled *Stroke Revisited*. There are many difficulties, such as language barriers, for a Korean to contact a European publisher to plan and publish a series of textbooks. I would like to sincerely thank Springer Nature and its employees for their assistance in the publication of this textbook.

The target readers of this textbook are trainees such as residents and fellows, specialists in their early careers specializing in stroke treatment, and doctors and researchers from various fields who wish to understand stroke in more depth. Most individual chapters have a single focus and have minimal text so that it is convenient to read the entire chapter in a short period of time. Unnecessary text was not included, and the use of visual aids was maximized. Only the essential reference literature has been included. The key characteristic of this textbook is the presentation of treatment procedures in sequence, starting at the initial admission of stroke patient in the emergency room, diagnosis, treatment, up to discharge and/or preventive measures. Most textbooks are organized in the traditional literature form. Therefore, in practice, sorting and selecting the section to obtain the knowledge from is difficult and time--consuming. This textbook attempts to simulate the actual practice, providing simultaneous explanation of diagnosis and treatment. At the same time, I tried to provide the highest quality of academic depth and up-to-date information on stroke. I hope the readers can fully benefit from these efforts.

In order to ensure that this textbook provides cutting-edge, yet authoritative and reliable, knowledge on stroke, experts from different parts of the world were invited to write each chapter. I would like to thank all the authors who participated in writing this textbook. This textbook is the first part of the *Stroke Revisited* series, and I hope it provides a flavor for the parts to follow.

2017.1.17 Seung-Hoon Lee, M.D., Ph.D., F.A.H.A.

How to Read

To give readers practical information on stroke management, I tried to organize this book with a different style from conventional academic books. First, assuming that the readers are duty doctors in emergency units, the parts and chapters in this book were organized as time sequence after visit of stroke patients. Part I covers the establishment and organization of stroke units and centers, and Part II comprehensively describes the diagnosis and treatment of ischemic stroke in acute stage. Part III gives cutting-edge knowledge on certain but relatively frequent causes, and secondary prevention after stroke was fully illustrated in Part IV. Part V covering clinical practice guidelines, which play a critical role in current medical practice, delineates their history, usefulness, and disadvantages and suggests my improvement direction of the guidelines. In particular, Chap. 4 in Part II entitled "Overview of Patient Management Flow" summarizes contents of diagnosis and management in stroke unit, general ward, and rehabilitation center and indicates corresponding chapters with more detailed information. Accordingly, if you choose to read a chapter among them, you will easily find to learn its position from the whole stroke management flow. Second, if you read abstract in the beginning of each chapter, you can easily obtain essential summary of the whole content of the chapter. Third, I tried to provide a simple but conceptual diagram covering all aspects of contents as a figure in each chapter. You just look into the diagram, and you will find the essential points of the chapter. Finally, there are "suggestions from current clinical practice guidelines" in the final part of each chapter. This part briefly summarizes essential recommendations of clinical practice guidelines in the world, especially from the American Heart Association/American Stroke Association. Thus, you can easily get up-to-date recommendations and notice information gaps between cutting--edge knowledge and current guidelines.

As stated in the preface, I tried to convey real, practical, but cutting-edge knowledge of stroke management with the unique organization style. However, this book is not a manual nor a protocol on stroke management. This is because top-class authors in the world gathered together to organize the most up-to-date knowledge. I hope that this book will be a guide to better understanding of stroke, which is a better way to deal with stroke patients.

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Acknowledgments

Although I had an ideal model for a textbook in my brain, I rarely had an active conversation with publishers about my idea. This textbook was conceived in an e-mail proposal of the textbook after an unplanned meeting with Ms. Lauren Kim, the editor of Springer Nature. The editorial team and I have obtained manuscripts from renowned medical experts in the world and have edited the manuscripts according to the principles we have set for this textbook. Therefore, the contents of this book were completed only after tremendous efforts from the editorial team. I would like to thank Dr. Jung Min Kim, Dr. Tae-Jung Kim, and Ms. Eun-Sun Park for their effort in the editorial team. In addition, I would like to thank the executive members of edition who agreed with the philosophy behind this textbook and provided the title for this textbook series—*Stroke Revisited*—in addition to providing active support in publishing this book. Finally, I would like to thank the Cerebrovascular Research Society in Korea and its members for their financial and technical support.

Throughout my research career, I focused on publishing papers as an author and becoming a famous, prosperous scientist. I rarely thought of writing a textbook. I would like to express my love towards my wife, my children, and my family, for changing my selfish thoughts and helping me understand my responsibilities, that is, to help others and provide education to nurture future doctors.

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Part I

Initial Assessment of Patients with Stroke-Like Symptoms

Stroke Center

1

Toshiyuki Uehara and Kazuo Minematsu

Abstract

Although intravenous recombinant tissue-type plasminogen activator therapy was approved for treating acute ischemic stroke within 3 h of symptom onset in 1996, less than 5% of patients with acute stroke were receiving this treatment. To facilitate adequate care for acute stroke patients, the Brain Attack Coalition (BAC) discussed the need to establish primary stroke centers (PSCs) where patients can receive emergency stroke care from qualified teams and developed recommendations with criteria for PSCs in 2000. A consensus statement from the BAC with extensive recommendations for comprehensive stroke centers (CSCs), a facility for stroke patients who require high-intensity medical and surgical care, was published in 2005. The Joint Commission began to certify PSCs in 2003 and CSCs in 2012. The "Get With The Guidelines®-Stroke" program, a popular database tool to record and track performance measures, was developed by the American Heart Association as a national quality improvement program. A third type of facility, the acute stroke-ready hospital (ASRH), is currently under development. An ASRH would have fewer capabilities than a PSC, but would be able to provide initial diagnostic services, stabilization, emergent care, and therapies to patients with acute stroke. This chapter introduces literature about stroke centers from the United States, Europe, and Japan and discusses the effectiveness and future challenges of stroke centers.

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In 1996, the Food and Drug Administration in the United States approved intravenous recombinant tissue-type plasminogen activator (rt-PA) administered within 3 h of symptom onset as a treatment for acute ischemic stroke. However, less than 5% of patients with acute stroke were receiving this treatment. To assist in ensuring adequate

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care for acute stroke patients, in 2000, the Brain Attack Coalition (BAC) discussed the concept of stroke centers and proposed two levels: primary stroke centers (PSCs) to stabilize and provide emergency care for patients with acute stroke and comprehensive stroke centers (CSCs) to diagnose and treat stroke patients who require high-intensity medical and surgical care, specialized tests, or interventional therapies. The BAC developed recommendations with criteria for PSC in 2000 [1] and for CSC in 2005 [2] and updated recommendations for the establishment of PSCs in 2011 [3]. The concept is that stroke centers, by providing vital infrastructure, expertise, protocols, and monitoring care in accordance with nationally recognized guidelines and performance expectations, would provide improved care leading to better outcomes [4]. In an effort to improve the care of stroke patients nationally, a strong push has been made to develop care systems based on an organized hierarchy of stroke hospitals, similar to systems of trauma centers [1, 2]. In this chapter, we discuss components of PSCs and CSCs proposed by the BAC and evidence supporting the effectiveness of stroke centers.

1.1 Components of Stroke Centers Proposed by the BAC

1.1.1 PSCs

The recommendations for PSCs proposed by the BAC were organized around 11 major elements of stroke care. These elements were grouped into direct patient care areas and support services. Patient care areas included acute stroke teams, written care protocols, emergency medical services, emergency departments, stroke units, and neurosurgical services. Support services included commitment and support of a medical organization, a stroke center director, neuroimaging services, laboratory services, outcome and quality improvement activities, and continuing medical education [1]. A key message from the BAC recommendations was timely provision of acute stroke services and the resulting need for general laboratory services, electrocardiography, and chest X-rays to be available 24 h a day, 7 days a week (24/7); brain computed tomography (CT) on a 24/7 basis; and the availability of neurosurgical services within 2 h [5].

In 2011, the BAC revised and updated recommendations for the establishment of PSCs based on the past 10 years of experience and advances in medical care and technology [3]. The major elements of a PSC are shown in Table 1.1. Important revisions and additions are summarized in Table 1.2. Based on a literature review and local experience, the following areas were stressed in the revised, updated statement: (1) the importance of acute stroke teams to improve rapid diagnosis and treatment; (2) importance of stroke units with telemetry monitoring; (3) utilization of magnetic resonance imaging (MRI) with diffusion-weighted sequences; (4) MR angiography or CT angiography to assess the cerebral vasculature; (5) cardiac imaging studies, including transthoracic echocardiography, transesophageal echocardiography, and cardiac MRI assessment; (6)

Table 1.1 Major elements of a primary stroke center

Patient care elements
Acute stroke team
Written care protocols
Emergency medical services
Emergency department
Stroke unit
Neurosurgical services
Imaging services: brain, cerebral vasculature, cardiac
Laboratory services
Rehabilitation services
Administrative/support elements
Institutional commitment and support
Primary stroke center director, reimbursement for call
Stroke registry with outcomes and quality improvement components
Educational programs: public and professional
Support certification process
Participation in stroke system of care

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Table 1.2 Key revisions to primary stroke center recommendations

Service/element	Recommendation/revision	Comment
Acute stroke team	At least two members	At bedside within 15 min
Emergency medical services	Transport patient to nearest PSC	Class 1, Level B recommendation
Emergency department	Monitoring protocol for patients	Vital signs and neurologic status
Stroke unit	Multichannel telemetry; clinical monitoring protocol	Includes who to call and when to call for deterioration
Imaging	MRI, MRA, or CTA and cardiac imaging available	May not apply to all patients; not required in acute setting; performed within 6 h; read within 2 h of completion (for MRI/MRA/CTA)
Laboratory	HIV testing for admitted patients; toxicology screen	Centers for Disease Control and Prevention recommendation (HIV)
Rehabilitation	Early assessment and initiation	If patient clinically stable
Administrative support	Call pay consideration	May improve acute response
Center certification	Independent organization; performance measures	Self-certification not recommended

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importance of early initiation of rehabilitation therapy; and (7) independent local site certification, including site visits and disease performance measures [5].

1.1.2 CSCs

In 2005, the BAC developed recommendations for the establishment of CSCs [2]. These recommendations emphasized that service needs to deliver specialized care and included the following key components: (1) personnel with expertise, (2) diagnostic techniques, (3) surgical and interventional therapies, (4) infrastructure, and (5) educational/research programs (Table 1.3) [2]. The CSCs are the highest-level and well-equipped hospitals which can treat all types of stokes. The CSCs require infrastructures, highly qualified specialists, and specialized process for diagnosis and treatment of complex stroke patients who needed a high level of medical and surgical care, specialized intensive care unit (ICU) facilities such as neuroscience ICU, specialized tests, or intervention treatments. Moreover, the trained and expertise stroke team must be available 24/7 for surgical treatment or intervention therapies. Some stroke patients could benefit from CSCs treatment, those with stroke caused by unusual etiologies and demanding specialized testing, or multispecialty management. In addition, CSC would be to act as a resource center for other facilities in their region, such as PSCs. The CSCs could receive patients initially treated at a PSC and provide expertise about the diagnosis and management of particular patients, guidance for patient triage, and educational resource for other hospitals and healthcare professionals at a given geographical area [2]. In 2011, the American Heart Association (AHA)/American Stroke Association (ASA) proposed a set of metrics and related data elements covering the major aspects of specialized care for patients with ischemic stroke and nontraumatic subarachnoid and intracerebral hemorrhages at CSCs [6].

The BAC outlined the organization of stroke centers in a hospital network or geographical area in a consensus statement for CSCs [2]. In the current healthcare environment, hospital networks and systems are continuing to grow. Within such a network or system, one approach to acute stroke care might be to designate some hospitals as PSCs and others as CSCs (Fig. 1.1).

Table 1.3 Components of a comprehensive stroke center

Recommendation
Personnel with expertise in the following areas
Vascular neurology
Vascular neurosurgery
Advanced practice nurses
Vascular surgery
Diagnostic radiology/neuroradiology
Interventional/endovascular physician(s)
Critical care medicine
Physical medicine and rehabilitation
Rehabilitation therapy (physical, occupational, speech therapy)
Staff stroke nurse(s)
RT
Swallowing assessment
Diagnostic techniques
MRI with diffusion-weighted image
MRA/MRV
CTA
Digital cerebral angiography
TCD
Carotid duplex ultrasound
Transesophageal echo
Surgical and interventional therapies
Carotid endarterectomy
Clipping of intracranial aneurysm
Placement of ventriculostomy
Hematoma removal/draining
Placement of intracranial pressure transducer
Endovascular ablation of IAs/AVMs
IA reperfusion therapy
Endovascular therapy of vasospasm
Infrastructure
Stroke unit
ICU
Operating room staffed 24/7
Interventional services coverage 24/7
Stroke registry
Educational/research programs
Community education
Community prevention
Professional education
Patient education

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1.2 Certification of Stroke Centers

In 2003, the AHA/ASA and The Joint Commission (TJC) convened and agreed on a certification process for stroke through a Disease-Specific Certification program, including a voluntary evaluation process driven by demonstration of a consistent approach to the measurement of clinical outcomes and minimum standards for stroke care [7]. The three major requirements were necessary for Primary Stroke Center Certification. These three requirements were in compliance with the use of evidence-based guidelines, implementation of TJC standards, and measurement of clinical outcomes [7]. The stroke performance measures were developed to improve the quality of stroke. The stroke performance measures in ischemic stroke included deep venous thrombosis prophylaxis, acute treatment such as antithrombotic therapy and anticoagulation therapy at discharge in patients with atrial fibrillation, dysphagia screening, stroke education, smoking cessation advice/counseling, risk factor modification, and rehabilitation [8]. Furthermore, a subset of these stroke performance measures was included for hemorrhagic stroke patients [5]. In 2009, the stroke 8-measure set was approved as a core measure set (Table 1.4) [8].

The "Get With The Guidelines®-Stroke" (GWTG-Stroke) became a popular database tool to record and track performance measures. The GWTG-Stroke program was developed by the AHA as a national quality improvement program for hospitals to improve stroke care infrastructure utilizing a multidisciplinary team approach and incorporating elements such as patient management toolkits, multidisciplinary workshops, and stakeholder organizational meetings and offering data collection and decision support. The patient management tool measures seven achievement elements, including deep venous thrombosis prophylaxis, early antithrombotic administration, and time

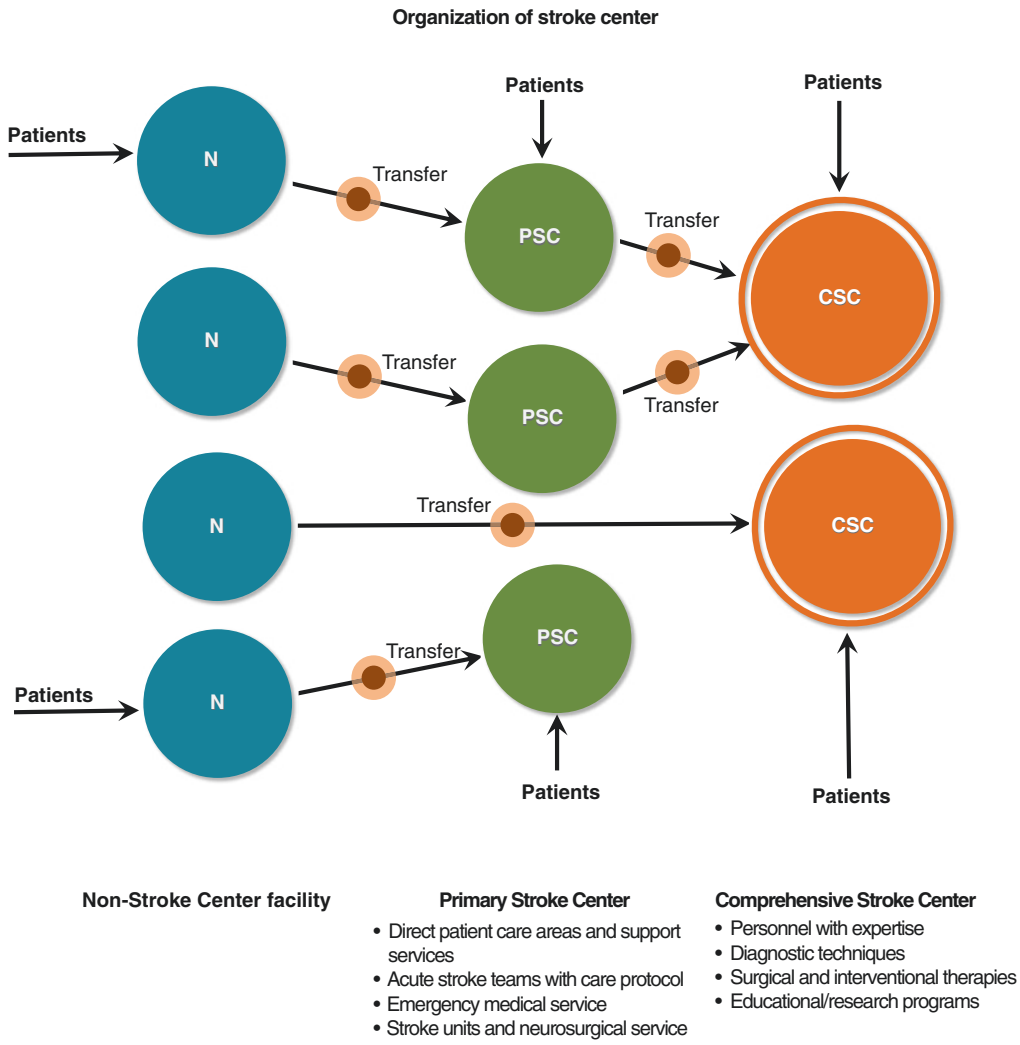

Fig. 1.1 Organization of stroke centers in a hospital network or geographical area. Representation of how various facilities caring for stroke patients could be organized based on a hospital network or defined geographical area. Patients can arrive at the various facilities via direct admission or transfer between facilities. *N* non-stroke center facility

Table 1.4 Stroke performance measures set

Prophylaxis against venous thromboembolism
Discharged on antithrombotic therapy
Anticoagulation therapy for atrial fibrillation/flutter
Thrombolytic therapy
Antithrombotic therapy by end of hospital day 2
Discharged on statin medication
Stroke education
Assessed for rehabilitation

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to intravenous thrombolysis for eligible acute ischemic stroke patients [9]. After a pilot phase, hospitals began enrolling in GWTG-Stroke in April 2003.

The TJC established an advanced disease-specific care certification requirements for CSCs in 2012 [8]. This new requirements were designed to improve the substantial resources needed to establish and manage complex stroke and

cerebrovascular cases. The certification requires centers to meet the following criteria: the program is in the United States and certified by TJC, uses standard methods to deliver clinical care and uses performance measures over time, and cares for a minimum number of patients [5].

The goal of stroke center certification was to improve stroke care and draw patients with stroke into capable centers. Since TJC and other entities/organizations started formally certifying and recognizing certain hospitals as PSCs, the number of such hospitals has increased dramatically [3].

1.3 Evidence to Support the Effectiveness of Stroke Centers

1.3.1 rt-PA Utilization and Quality of Stroke Care

Admission of certified stroke centers is associated with increased rates of rt-PA utilization and improvements in the quality of stroke care according to core measure adherence. Data from quality improvement programs such as GWTG-Stroke also showed that a PSC status improved compliance with and achievement of many disease performance measures. In recent studies, hospital participation in the GWTG-Stroke program was associated with increased achievement of process quality metrics, including increased frequency of acute pharmacological treatment (thrombolysis and early antithrombotic therapy), interventions to prevent early complications (deep venous thrombosis prophylaxis and swallowing assessments), and start of secondary stroke prevention before discharge (anticoagulation for atrial fibrillation and cholesterol reducing medication).

1.3.2 Functional Outcome

A nationwide observational register study of all patients with first-ever ischemic stroke treated in Finland showed an association between the level of acute stroke care and patient outcome. Admission to a PSC or CSC resulted in 1.5% and 2.4% reductions in mortality compared with admission to a general hospital (GH), respectively. The number needed to treat to allow one more patient to live at home 1 year after stroke was 40 for PSCs and 29 for CSCs when compared with GHs. For survival probability adjusted with Cox modeling for age, sex, comorbidities, previous medication and hospital use, and year of stroke, hazard ratios were 0.87 for CSCs and 0.90 for PSCs when compared with GHs (Fig. 1.2) [10]. A similar study in New York State also found significantly reduced mortality for patients cared for in a PSC compared with a non-PSC facility [11]. Lichtman et al. reported that TJC-certified status was associated in Medicare patients with decreased early mortality due to subarachnoid or intracerebral hemorrhage and with decreased early mortality, shorter hospitalization, and favorable disposition in ischemic stroke [12].

Song et al. found that patients hospitalized with acute ischemic stroke at GWTG-Stroke hospitals had greater improvement of clinical outcomes over time than at similar hospitals not participating in the GWTG-Stroke program. Compared with secular changes at control hospitals, GWTG-Stroke hospitals exhibited accelerated increases in the proportion of patients discharged to home and accelerated reductions in 30-day and 1-year mortality rates [9]. These findings indicate that hospital adoption of the GWTG-Stroke program is associated not only with improvements in the processes of care but also in improved functional outcome at discharge and reduced post-discharge mortality. One study indicated that care at a PSC for patients with acute ischemic stroke was cost-effective and improved outcomes [13].

1.4 Questionnaire Survey for Main Components of Stroke Centers in Europe and Japan

1.4.1 Europe

In 2007, the European Stroke Initiative Executive Committee reported the results of the European

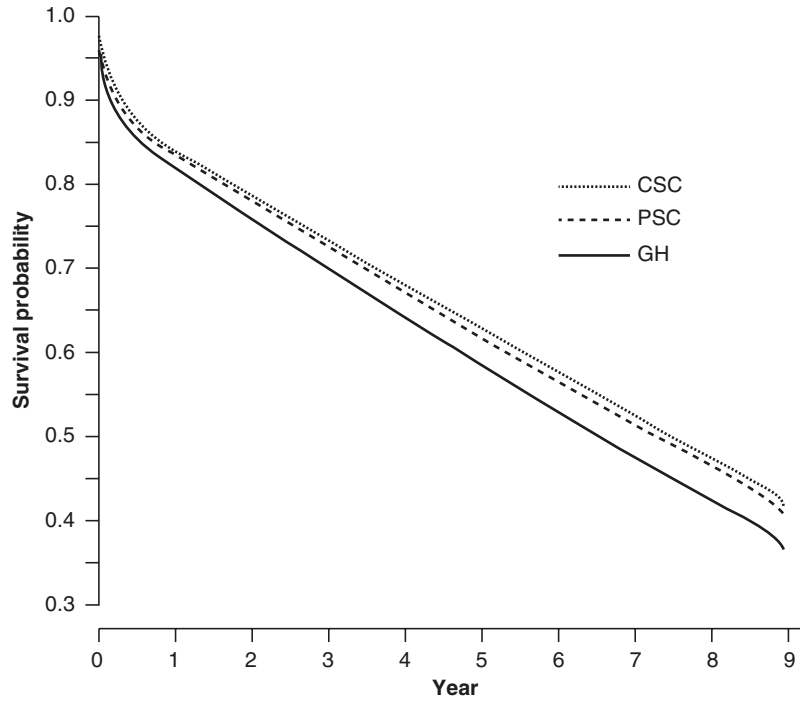

Fig. 1.2 Survival probability based on acute treating hospital facilities adjusted with a Cox model for age, sex, comorbidities, previous medication and hospital use, and year of stroke. Reproduced by permission of Stroke [10]

Expert Survey conducted to identify from expert opinions what the major components of stroke units should be [14]. This study showed the components considered "absolutely necessary" for CSCs and PSCs by 75% or more of directors of certified stroke teaching facilities. As a result, eight components were considered "absolutely necessary" by more than 75% of experts for both CSCs and PSCs: a multidisciplinary team, stroke-trained nurses, brain CT available 24/7, CT priority for stroke patients, extracranial Doppler sonography, automated electrocardiogram monitoring, intravenous rt-PA protocols available 24/7, and in-house emergency department. Eleven other components were considered necessary in CSCs by more than 75% of the experts: physiotherapy starting within 2 days, extracranial duplex sonography, transthoracic echocardiography, automated monitoring of pulse oximetry, automated monitoring of blood pressure, carotid surgery, angioplasty and stenting, collaboration with outside rehabilitation centers, stroke faculty, stroke pathways, and clinical research.

The AHA/ASA published a scientific statement of metrics for measuring quality of care in CSCs in 2011 [6]. However, the survey questionnaire conducted by the Executive Committee of the European Stroke Initiative demonstrated that less than 10% of European hospitals admitting acute stroke patients have optimal facilities and that even the minimum level was unavailable in 40% [15]. Recently, the European Stroke Organization (ESO) Stroke Unit Certification Committee published a special report of "ESO recommendations to establish a stroke unit and stroke center" [16]. The ESO Stroke Center is the coordinating body of the entire chain of care and covers prehospital care, emergency room assessment and diagnosis, emergency medical treatment, stroke unit care, ongoing rehabilitation and secondary prevention, and access to related neurosurgical and vascular intervention. A stroke unit is the most important component of the ESO Stroke Center [16].

1.4.2 Japan

In 2007, we conducted a questionnaire survey to identify the essential components of stroke

centers in Japan and compared our results with the European Expert Survey [17]. Compared with the European Expert Survey, our results of surveys in Japan showed the following characteristics: (1) neurosurgical treatments were more likely to be emphasized; (2) MRI and MR angiography were better recognized than carotid and transcranial ultrasonography; and (3) a multidisciplinary stroke team and stroke-trained nurses in the category of personnel and stroke pathway, community stroke awareness programs, and prevention programs in the category of protocols and procedures were less likely to be emphasized. Approximately three-quarters of respondents were neurosurgeons in our survey, whereas most European stroke experts were neurologists. Given the results of separately analyzed responses from neurosurgeons and neurologists in our study, the differences in results between the surveys in Europe and Japan may be partly explained by the different proportions of neurologists and neurosurgeons.

1.5 Future Challenges for Establishing Stroke Center Systems

Significant geographic disparities exist in access to PSCs. Access is limited in suburban and rural areas. Demographic factors are strongly associated with access to care in smaller cities, but were found to have little impact elsewhere, including in major cities [18]. Currently, a 3-tier system has been proposed, consisting of acute stroke-ready hospitals (ASRHs), PSCs, and CSCs, in order of increasing resources/capabilities [19]. The AHA/ASA has published policy recommendations for stroke systems of care, some of which are applicable to the operations of the ASRH [4]. ASRHs would have fewer capabilities than PSCs, but would be able to provide initial diagnostic services, emergent care and therapies, and inducing stabilization in patients with stroke in their emergency department. They then transferred appropriate patients to another hospital, such as PSCs or CSCs for advanced medical services and definitive care. After the acute event has resolved, most patients are expected to return to their local facilities and healthcare professionals for outpatient care and perhaps rehabilitation [4].

Mullen et al. found that 36.9% of the US population, approximately 114 million people, would be unable to access a CSC within 60 min by ground transportation, even if CSCs are optimally located throughout the United States [19]. A British study showed that stroke interventional endovascular services were available in only a small number of hospitals and only about 50% of those with no endovascular service available for stroke had transfer plans with a center that did provide those services [20]. Systems planning and policy initiatives that incentivize certification of selected hospitals should be considered to ensure maximum population benefit. A systems planner will need to carefully assess the local need in rural areas to determine whether a CSC is justified. If not, alternative strategies such as PSCs and ASRHs may be used to provide basic stroke care, with telemedicine and a rapid transfer protocol linking these hospitals to more distant CSCs [19].

With the advent of new diagnostic and therapeutic options, as well as the evaluation of evidence-based guidelines, stroke care systems will continue to be further improved and refined.

Suggestions from Clinical Practice Guidelines Establishment of primary stroke centers (PSCs) or regional acute stroke-ready hospital (ASRH) is needed to provide emergency care to acute stroke patients, which is based upon local resources. These systems should be closely associated with comprehensive stroke centers (CSCs). The centers or hospitals for acute stroke care should have a multidisciplinary committee to monitor stroke care quality and outcomes and are needed to be certified by an independent external institution.

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Stroke Unit

2

Joung-Ho Rha

Abstract

A stroke unit is an organized in-hospital care for acute stroke. It was first conceptualized in the 1960s but has become the mainstream of acute stroke treatment in the twenty-first century. It consists of stroke team, stroke ward with monitoring function, and operating protocol. Other medical supports such as emergency room, laboratory, and neuroradiology service are also required. Its effect is comparable to other proven treatments of acute stroke, and as the evidence accumulates, it has become key element of acute stroke care organization, and now most guidelines state that an acute stroke patient should be cared in a stroke unit with a high grade of recommendation. Nationwide effort to disseminate stroke unit to afford most stroke patients is required to lessen the death and disability, which also leads to decreased total medical cost, as a stroke unit is cost-effective. Recently, a mobile stroke unit, which is an ambulance with CT and telemedicine support, is being established so that hyperacute stroke treatment can be started even faster at prehospital stage.

A stroke unit is a specialized in-hospital treatment unit which is designed for optimized acute stroke care (Fig. 2.1). It is not only confined to hardware facility but also includes stroke team and clinical pathway. Since its evidence of efficacy and usefulness accumulates continuously, establishment of a stroke unit is getting more and more popular in stroke care hospital, and nowadays it has become the essential component of stroke care organization.

Regarding the term "stroke unit," there is a little disparity between the American and European side, probably due to the difference in medical system. American physicians use the term more confined way, as one of the essential components of stroke center. On the other hand, European physicians use the term more broadly, sometimes to mean the stroke center including the rehabilitation unit. In this chapter, stroke unit is used strictly to refer the former to avoid

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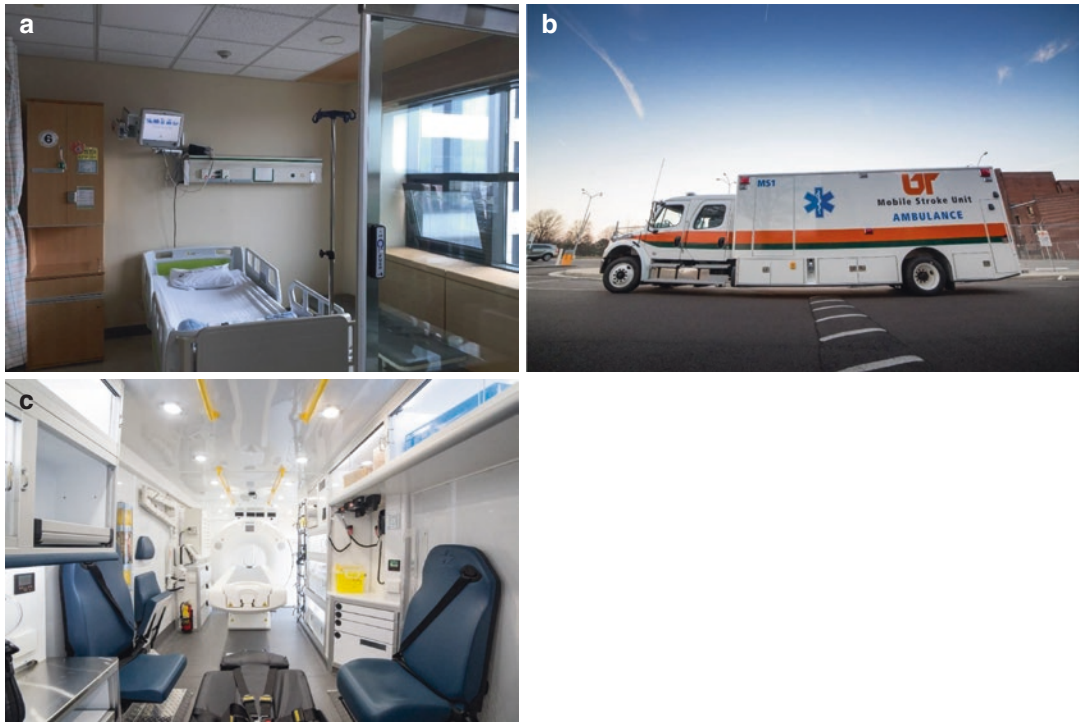

Fig. 2.1 Stroke unit. Interior view of stroke unit (**a**); exterior (**b**) and interior (**c**) view of mobile stroke unit. Reproduced by permission of Business Wire (University of Tennessee Web Site, http://www.businesswire.com/news/home/20160322005420/en/University-Tennessee-College-Medicine-Launches-World%E2%80%99s-Mobile)

confusion, and there is a separate chapter for stroke center in this textbook.

2.1 Historical Perspective

The term "stroke unit" first appeared in 1969 from medical literature [1], but the concept of dedicated in-hospital ward for stroke traces back to 1962 in New York, where the investigator evaluated rehabilitation ward for hemiplegic patient. At that time, most studies compared the dedicated rehabilitation ward for stroke to the other general ward. The first study to investigate modern concept of stroke unit [2], which is an organized inpatient care for acute stroke, would be the Edinburgh study in 1980 [3], which is a randomized controlled study with 311 acute stroke patients to compare stroke unit versus general medical ward. After then, a series of controlled trials followed to investigate the efficacy of a comprehensive stroke unit, mostly performed in the 1990s. Among them, the Trondheim study is most representative, which is a randomized controlled trial comparing stroke unit versus general medical ward in 220 acute stroke patients and showed big success in reducing death and dependency with an odds ratio of 0.36 (95% confidence interval (CI) = 0.21 ~ 0.61) [4]. As the evidences of stroke unit accumulate, stroke unit became one of the essential components of stroke care organization in the twenty-first century [5], and now most clinical practice guidelines in the world state that the acute stroke patient should be treated in the stroke unit with a high grade of recommendation.

2.2 Stroke Unit Efficacy

According to the latest systematic Cochrane review (Stroke Unit Trialists' Collaboration, 2013), a comprehensive stroke unit is estimated

Table 2.1 Efficacy of proven acute stroke treatment by reducing death and dependency

Modality	Background	RRR	ARR	NNT
Stroke unit	Stroke Unit Trialists' Collaboration, 2013	6.9%	4.0%	25
Aspirin	IST, 1997	2.6%	1.2%	83
Intravenous tPA	NINDS, 1995	9.8%	5.5%	18
Endovascular thrombectomy	HERMES Consortium, 2016	32.8%	10.6%	10
Decompression craniectomy	Pooled analysis, 2007	48.8%	23.0%	4

IST International Stroke Trial, *NINDS* National Institute of Neurological Disorder and Stroke, *HERMES* Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials, *RRR* relative risk reduction, *ARR* absolute risk reduction, *NNT* numbers needed to treatment

to reduce death and dependency by an odds ratio of 0.82 (95% CI 0.68 ~ 0.98) [6]. When we compare this result to other proven treatments of acute stroke [7], through indirect comparison by death and dependency, the efficacy of a stroke unit exceeds that of acute aspirin use and is almost comparable to that of intravenous tPA (Table 2.1). This rather unexpectedly big effect made stroke unit a mainstream of acute stroke care as important as thrombolytic treatment. Another study showed that this effect does not fade away as time goes by but lasts more than 10 years of follow-up [8, 9].

2.3 Mechanism of Efficacy

There can be many reasons for the abovementioned efficacy, but the biggest should be attributed to close monitoring and early intervention of patient status, such as vital signs, neurological status, and electrocardiogram, which leads to better management of blood pressure, prompt detection of early neurological deterioration or paroxysmal atrial fibrillation, and effective prevention of possible complications [10]. Optimized clinical pathway by written care protocol according to guideline and early rehabilitation can also accelerate in-hospital process and thus contribute to better outcomes. But all these effects are abolished in the general ward or other types of care, even though applying the same clinical pathway or protocol, probably because the caregiver is not dedicated to stroke care [11].

2.4 Component of Stroke Unit

To be a functionally effective stroke unit, many components are needed, either as human resources, facilities, or operating protocols [12, 13]. These components can be different from hospital to hospital, and many regional variations also exist. In some countries there are criteria to be certified by academic or government authority. However, there are essential components which are almost uniform in most stroke units (Table 2.2).

First of all, there must be an organization of multidisciplinary stroke team to operate a stroke unit. This team is composed of a doctor, nurse, and coordinator. Stroke team doctors are usually neurologist or neurosurgeons with their subspecialty in stroke. The attending duty schedule and emergency hotline are also required. A stroke nurse is a specially trained nurse for a dedicated stroke patient care, receiving continuous education for neurological monitoring and stroke care protocol. In some institution, certification of neurological scale such as the National Institute of Health Stroke Scale (NIHSS) is required. A stroke coordinator is a person who takes an important role to facilitate all the administrative and in-hospital process to be in proper order and time. They notify the stroke team to be ready for the next process, so that most of the in-hospital performance index such as door-to-imaging or door-to-needle/puncture time can be shortened. They also inform the patient or family for better understanding of in-hospital process and later educate them for effective secondary prevention and stroke awareness. Their contribu-

Table 2.2 Essential component of stroke unit

Component		Comment
Stroke team	Neurologist, neurosurgeon with stroke subspecialty regular meeting	By trained program, academic activity, and clinical experience
	Stroke nurse, coordinator	Dedicated for stroke care
	Neuroradiologist, neurointerventionist	Angio-suite team
	Rehabilitation physician social worker	Early rehabilitation
Written care protocol	Operation manual	Admission/discharge criteria
		Neurological flow sheet
	Clinical pathway	
Facility	Stroke ward	Monitoring devices
	Emergency service	
	Neuroradiology Stroke priority fast track laboratory support 24/7	CT, MR with DWI Vessel imaging (CTA, MRA, DSA)
Quality improvement	Regular quality assessment regular education	Set target index to improve stroke team patient and public

DWI Diffusion-weighted image, *CTA* CT angiography, *MRA* MR angiography, *DSA* digital subtraction angiography

tion for good outcome of stroke patient is usually greater than expected and very efficient in the aspect of time and cost. A neuroradiologist or neurointerventionist is also a member of the stroke team, with angio-suite technicians and nurses. A rehabilitation doctor in the stroke team evaluates the patient and conducts early rehabilitation. Regular meeting and education program for a stroke team is recommended for inside communication and quality improvement. Sometimes, a social worker joins the stroke team to provide social service to patients if necessary.

The treatment in the stroke unit can be individualized, but the principle should follow the evidence-based guidelines, and for this purpose written care protocol is required as the operation manual of stroke unit. Also, every stroke unit is recommended to have its own clinical pathway optimized to the hospital. This can contribute to select the right patient for intervention without missing and also to accelerate intrahospital performance such as door-to-needle time. A stroke unit also needs to provide its own flow sheet which can record the patient's neurological status. Most hospitals now adopt electronic medical record and order system, and clinical pathway can be incorporated into it, with an automated notification system which alerts the stroke team by mobile communication and alarming function for fast track investigation and treatment.

The protocol should also describe which patient to admit to the stroke unit and when to discharge. Each stroke unit can set its own criteria, but usually acute stroke patient within 48 or 72 h after onset is the target patient, especially post-thrombolysis or thrombectomy patient. Besides unstable stroke or transient ischemic attack (TIA) patient with fluctuating or progressive neurological status, patient before and after neurovascular intervention such as stent insertion, but not just for diagnostic angiography, can also be a subject of stroke unit admission. Some stroke units also admit acute hemorrhagic stroke patient who needs critical care. But when the stroke patient is comatose and postsurgical status or vital sign is unstable with intubation and ventilator control, admission to intensive care unit is necessary for critical care. Patient moves to general ward when neurological status is stable for 48 to 72 h.

In the aspect of facility, stroke unit ward and monitoring devices are required. The stroke unit ward needs to be spacious enough for each bed, and close monitoring should be possible directly from the nursing station at all times. A stroke unit needs to be equipped with monitoring devices for blood pressure, electrocardiogram, and O_2 saturation and respiration, and all of these should be always available when needed. Because of the emergency characteristic of acute stroke, the emergency department service of the hospital is