Original Article

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Acute Ischemic Stroke Therapy in a Hybrid Emergency Room: An Institutional Observational Cohort Study

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Background: Endovascular therapy within an appropriate time has been shown to improve neurological outcomes in patients with ischemic stroke. A hybrid emergency room is an emergency unit that can be used for resuscitation, computed tomography (CT), surgery, and angiography. Therefore, immediate CT and endovascular therapy can be performed without transfer to other rooms. We aimed to evaluate the possibility of using a hybrid emergency room to shorten the time to endovascular therapy in patients with ischemic stroke.
Methods: This was a single-institutional, retrospective, and observational study. Patients with acute ischemic stroke who underwent endovascular therapy in the hybrid emergency room between May 2018 and May 2020 were included in the study. The main outcome was door-to-puncture time. The secondary outcomes were door-to-reperfusion and onset-to-puncture time. Descriptive statistics were also calculated. Outcome times were compared with those recommended by recent guidelines.
Results: Twenty-seven patients were included in this analysis. The median age was 77 (69–83) years. The median National Institutes of Health Stroke Scale score on admission was 15 (10–21.25), while the median door-to-puncture, door-to-reperfusion, and onset-to-puncture times were 45 (29–63), 140 (100–170), and 120 (71–224) minutes, respectively. The door-to-puncture time was within the recommended time of 60 minutes for approximately 75% of the patients.
Conclusions: The door-to-puncture time in our study was shorter than that recommended by the guidelines. Acute ischemic stroke management in a hybrid emergency room could shorten door-to-puncture time, which may contribute to improving patients' neurological outcomes.

Keywords: *Acute Ischemic Stroke; Endovascular Therapy; Hybrid Emergency Room System*

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INTRODUCTION

Reperfusion therapy for acute ischemic stroke is evolving remarkably. Recently, the effectiveness of endovascular therapy has been proven in patients with large vascular occlusions in both the anterior and posterior circulation [1–7]. Although the eligible time window for endovascular therapy can be up to 24 h from the time last known to be well [8], a large observational study that enrolled 6,756 patients with anterior circulation large vessel occlusion acute ischemic stroke treated with endovascular therapy showed that a shorter time to reperfusion was significantly associated with better neurological and survival outcomes [9].

A hybrid emergency room is an emergency unit that can be used to perform resuscitation, computed tomography (CT), surgery, and angiography, and is designed for treating patients with severe trauma. Using this has been suggested to improve clinical outcomes in patients with trauma [10,11], however, only one report has suggested its efficacy in treating patients with acute ischemic

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stroke [12]. Immediate endovascular therapy following CT evaluation can be performed without transfer to other rooms, which may contribute to improving the outcome in patients with ischemic stroke.

In this study, we aimed to evaluate the possibility of using a hybrid emergency room to shorten the time to endovascular therapy in patients with ischemic stroke.

METHODS

Study Design, Setting, and Participants

This observational cohort study retrospectively collected the data of all patients admitted to the hybrid emergency room system at Tohoku University Hospital between May 2018 and May 2020. Patients were eligible if they were ≥18 years of age and suspected to have had a stroke. Patients were excluded if they were: (a) not diagnosed with ischemic stroke; (b) diagnosed with intracranial hemorrhage, subarachnoid hemorrhage, or transient ischemic attack; (c) diagnosed with ischemic stroke but were not candidates for revascularization; or (d) if data were not available. We analyzed patients who received reperfusion therapy in the hybrid emergency room, after excluding patients who had undergone magnetic resonance imaging (MRI) before endovascular therapy, were transferred to other hospitals after administration of recombinant tissue-type plasminogen activator (rt-PA), received endovascular therapy not at the hybrid emergency room, or were treated with rt-PA but without endovascular therapy.

The study protocol was reviewed and approved by the institutional review board of Tohoku University (2020-1-805). The requirement for informed consent was waived because of the retrospective nature of the study, and the analysis used anonymous clinical data.

Data Collection and Measurements

We collected the following data: age, sex, Glasgow Coma Scale (GCS) score on admission, National Institutes of Health Stroke Scale (NIHSS) score [13], Alberta Stroke Program Early CT Score (ASPECTS) [14], past medical history, and medications before admission. We also collected data on the time course of door-to-image, puncture, needle, revascularization, last-known well to arrival, culprit vessel, thrombolysis in cerebral infarction (TICI) grade [15], Modified Rankin Scale (mRS) at discharge [16], time spent in the ICU, and the hospital discharge date. All information was collected from the medical records.

Outcomes

The main outcome measure was door-to-puncture time. The secondary outcome measures were door-to-reperfusion and onset-to-puncture times.

Comparison with Recommendations and Evidence

We compared door-to-puncture and door-to-reperfusion times demonstrated or recommended to be appropriate in large studies or guidelines. We performed a literature review to identify the recommended door-to-puncture, door-to-reperfusion, and onset-to-puncture times associated with better neurological outcomes. First, we performed a PubMed database search using the keywords (stroke AND endovascular AND [reperfusion OR "endovascular therapy" OR "mechanical thrombectomy"] AND guideline) for guidelines and ([door-to-puncture OR door-to-reperfusion OR onset-to-puncture] AND stroke) for clinical studies. Subsequently, eligible articles were reviewed. We selected guidelines regarding recommended or better neurological outcomes-associated door-to-puncture, door-to-reperfusion, or onset-to-puncture times. For clinical studies, we selected articles that evaluated the association between door-to-puncture, door-to-reperfusion, or onset-to-puncture time and neurological outcomes as primary or secondary outcomes.

Definitions

We defined the time from the event to the procedure as follows: door-to-image time was the time from the arrival of patients at the hospital to the start of head CT; door-to-puncture time was the time from arrival of patients at the hospital to groin puncture; door-to-reperfusion time was the time from arrival of patients at the hospital to reperfusion of the culprit-vessel proven by angiography; and onset-to-puncture time was the time from presentation of patients with stroke symptoms to puncture.

Statistical Analyses

This study used descriptive statistics. The median and interquartile range (IQR) were used for all continuous variables. Categorical variables are presented as numbers and proportions. All statistical analyses were performed using the JMP Pro Version 15 software (SAS Institute Japan Ltd., Tokyo, Japan).

Ethical Approval and Informed Consent

Ethical approval was not required. Informed consent was not required.

RESULTS

During the study period, 270 patients with suspected stroke were eligible. Of these, 58 patients with stroke mimics, 70 patients with intracranial hemorrhage, 65 patients with transient ischemic attack or ischemic stroke but not applicable for revascularization, and one patient whose data were unavailable, were excluded. Of the remaining 41 patients who received reperfusion

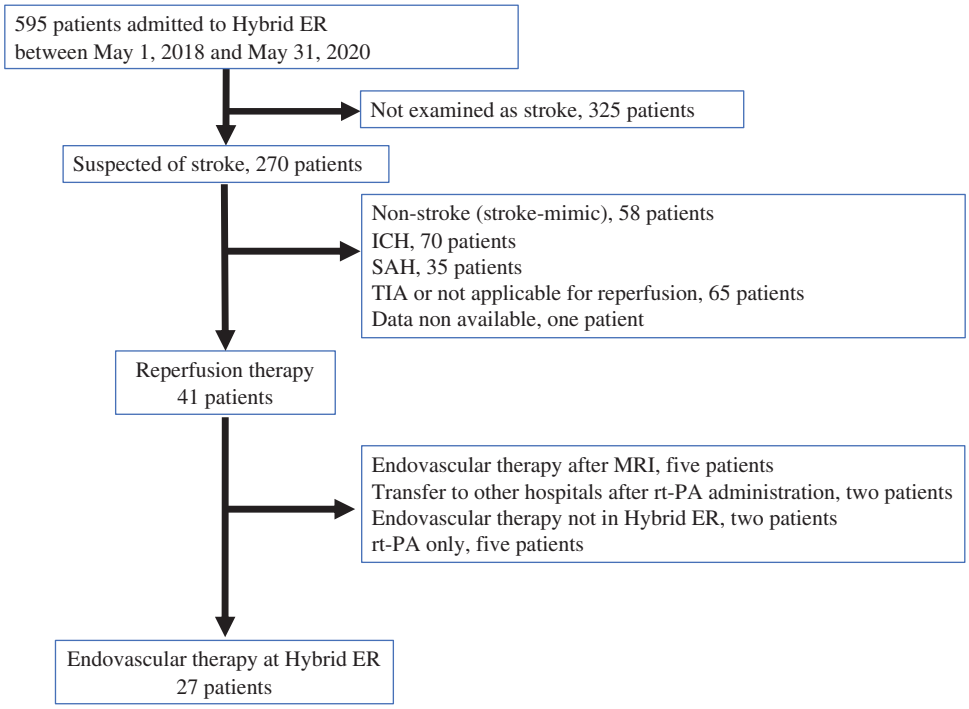

Figure 1 Flow chart of patient selection and exclusion details. ER, emergency room; ICH, intracranial hemorrhage; MRI, magnetic resonance imaging; rt-PA, recombinant tissue-type plasminogen activator; SAH, subarachnoid hemorrhage; TIA, transient ischemic attack.

therapy, five patients who received endovascular therapy after MRI, five patients who were treated with rt-PA only, two patients who were treated with rt-PA and then transferred to other hospitals, and two patients who received endovascular therapy not in a hybrid emergency room were excluded. Finally, 27 patients were included in the final analysis (Figure 1).

Patient Characteristics

Patient characteristics are shown in Table 1. The median patient age was 75 (69–83) years. The median GCS score on admission was 13 (10–14), the median NIHSS score was 15 (10–21), and the median ASPECTS score was 9 (6–10). In most patients, the culprit vessel was the middle cerebral artery (18/27).

Primary and Secondary Outcomes

The median time for door-to-puncture was 45 (29–63) min (Table 2). The median door-to-reperfusion and onset-to-puncture times were 140 (100–170) min and 120 (71–224) min, respectively (Table 2).

Comparison with Recommendations and Evidence

A literature search yielded 241 guidelines. After a full review, only one guideline provided recommendations for door-to-puncture and door-to-reperfusion times in endovascular reperfusion for patients with acute ischemic stroke. No guidelines have provided recommendations for the onset-to-reperfusion time. The guidelines from the Society of Neurointerventional Surgery state that door-to-puncture and door-to-reperfusion should be performed within 60 min and 90 min, respectively [17]. A literature search for clinical studies on door-to-puncture, door-to-reperfusion, and onset-to-puncture yielded 56, 27, and 61 articles, respectively. After a full review, no studies have evaluated the association between door-to-reperfusion, or onset-to-puncture, and neurological outcome as the primary outcome. In our study, door-to-puncture time was within 60 min for 20 of the 27 patients, and door-to-reperfusion time was within 90 min for three of the 27 patients (Figure 2).

DISCUSSION

We found that the median door-to-puncture, door-to-reperfusion, and onset-to-puncture times were 45, 140, and 120 min, respectively, in patients with ischemic stroke treated in a hybrid emergency room. In 20 of the 27 patients treated with endovascular therapy without preceding MRI, the door-to-puncture time was within the recommended time frame.

According to our systematic review, only one guideline indicated the time goals of door-to-puncture and door-to-reperfusion for endovascular therapy. The guidelines from the Society of Neurointerventional

Table 1 Characteristics of patients with ischemic stroke treated with endovascular therapy in a hybrid emergency room system.

Characteristics	*Total n = 27*
Age, median (IQR)	75 (69–83)
Men (%)	12 (44.4)
GCS on admission, median (IQR)	13 (10–14)
NIHSS, median (IQR)	15 (10–21)
ASPECTS, median (IQR)	9 (6–10)
Culprit vessels	
IC	7
ACA	1
MCA	18
Basilar artery	1
Medical history, ***n*** (%)	
Hypertension	16 (59)
Dyslipidemia	9 (33)
Atrial fibrillation/flutter	9 (33)
Diabetes mellitus	5 (19)
Previous stroke/TIA	5 (19)
Heart failure	3 (11)
Smoker	5 (19)
Renal insufficiency	2 (7)
Vascular disease	3 (11)
Respiratory disease	1 (4)
Malignancy	7 (26)
Medication before admission, n (%)	
Antiplatelets	6 (22)
Anticoagulants	3 (11)
Antihypertensives	13 (48)
Cholesterol reducers	3 (11)
Antidiabetics	2 (7)

ACA, anterior cerebral artery; ASPECTS, Alberta Stroke Program Early CT Score; GCS, Glasgow Coma Scale; IC, internal carotid artery; IQR, interquartile range; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack.

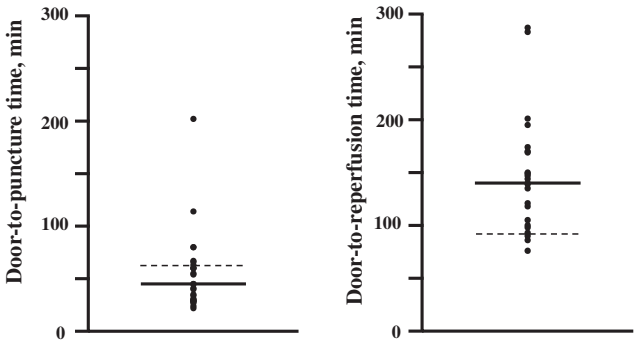

Figure 2 Time distribution of door-to-puncture and door-to-reperfusion times. Each dot indicates the time required by each patient. The horizontal line indicates the median time. A dotted line indicates the time recommended in the NeuroInterventional Surgery guidelines.

Surgery recommend that door-to-puncture time should be <60 min and door-to-reperfusion time should be <90 min, although there is no clear description of the evidence [17]. The door-to-puncture time in our study was much shorter than that recommended by the guidelines, whereas the door-to-reperfusion time was much longer. It is assumed that since the hybrid emergency room, equipped with CT and angiography, can be used to perform immediate endovascular therapy following a CT scan without patient transfer, we could achieve a shorter door-to-puncture time [10,11].

Recent studies have shown that a reduction in the time to reperfusion leads to favorable neurological outcomes. A recent observational study showed that the probability of a good clinical outcome decreased as the time to angiographic reperfusion increased in patients

Table 2 Clinical course, outcomes, and culprit vessels.

Times to diagnosis and treatment	*Total n = 27*
Last known well to arrival, min, median (IQR)	56 (33–162)
Door-to-image, min, median (IQR)	7 (4–11)
Door-to-puncture, min, median (IQR)	45 (29–63)
Door-to-needle, min, median (IQR)	49 (38–57)
Door-to-reperfusion, min, median (IQR)	140 (100–170)
Onset-to-puncture, min, median (IQR)	120 (71–224)
Clinical outcomes	
TICI grade ≥2a, ***n*** (%)	23 (85)
mRS at discharge, median (IQR)	4 (1–5)
Length of ICU stay, days, median (IQR)	5 (4–9)
Length of hospital stay, days, median (IQR)	19 (13–35)

Door-to-image is the time from arrival of patients at the hospital to the start of head computed tomography. Door-to-needle is the time from the arrival of patients at the hospital to the administration of rt-PA. Door-to-puncture is the time from the arrival of patients at the hospital to the groin puncture. Door-to-reperfusion is the time from the arrival of patients at the hospital to large vessel reperfusion proven by angiography. Onset-to-puncture is the time from the presentation of stroke symptoms to groin puncture. ICU, intensive care unit; IQR, interquartile range; mRS, modified Rankin Scale; rt-PA, recombinant tissue-type plasminogen activator; TICI, thrombolysis in cerebral infarction.

with middle cerebral artery and distal internal carotid occlusions with successful reperfusion [18]. Retrospective analysis of the combined database showed that shorter onset-to-reperfusion time was associated with improved 90-day Modified Rankin Scale (mRS) score in patients with acute ischemic stroke treated with a stent retriever [19]. A meta-analysis of five randomized control trials for patients with acute ischemic stroke due to large-vessel occlusions also showed that a shorter time from onset to reperfusion was associated with an improved 90-day mRS score [6].

The varied door-to-puncture times might have been caused by the situation in our hospital, such as the availability of neurologists or neurosurgeons. The hybrid emergency room may be a novel and favorable space for shortening door-to-puncture time. In-hospital systems are also essential; they are another requirement for the software. Improvements in the in-hospital systems are also required. The door-to-reperfusion times in our cases were longer than those recommended by the guideline [17]. The hybrid ER system is equipped with a single-plane angiography system, whereas the majority of neurosurgeons mostly use a bi-plane system. Inexperience with the single-plane system causes longer door-to-reperfusion times at the early stage of installing the hybrid ER system. This could lead to unfavorable outcomes in patients [6]. However, treating more patients with single-plane system may improve the door-to-reperfusion time. Development of a novel operator-supporting system, such as navigation, is also required.

Acute ischemic stroke management in a hybrid emergency room could shorten door-to-puncture time, which may lead to improved neurological outcomes. The hybrid emergency room has the potential to be an innovative system for acute ischemic stroke management. Further investigation is required to elucidate whether a hybrid emergency room can improve a patient's neurological outcomes.

Ethics Statement

(1) All the authors mentioned in the manuscript have agreed to authorship, read and approved the manuscript, and given consent for submission and subsequent publication of the manuscript.
(2) The authors declare that they have read and abided by the JEVTM statement of ethical standards including rules of informed consent and ethical committee approval as stated in the article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Author Contributions

YI was responsible for the conception, methodology, formal analysis, investigation and drafting the manuscript. DK was responsible for the methodology, formal analysis, investigation, reviewing and editing the manuscript, and funding acquisition. MF was responsible for the methodology and investigation. SO and AN were responsible for the investigation and review of the manuscript. SK was responsible for the conception, reviewing and editing the manuscript, and supervision. All authors commented on the previous versions of the manuscript. All authors read and approved the final manuscript.

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