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Original Article

Rapid Response System for In-Hospital Large Vessel Occlusion: A Case-Control Study

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Objective: Acute ischemic stroke due to large vessel occlusion (LVO) in hospitalized patients is relatively rare but important condition. However, unlike community-onset cases, there are only few time-saving protocols for in-hospital LVO. This study aimed to evaluate the time-saving effects of rapid response system (RRS) for the management of in-hospital LVO.

Methods: We retrospectively evaluated consecutive in-hospital LVO patients who underwent mechanical thrombectomy (MT) between April 2015 and January 2020. In November 2017, we added "acute hemiparesis, eye deviation, and convulsive seizures" to the activation criteria for RRS. In this protocol, the patient is immediately transported from the ward to the emergency room (ER) by Medical Emergency Team (MET). The stroke team can then start assessment in the same manner as for community-onset cases. The time metrics between those with and without RRS intervention were compared. The primary outcome was time from detection to the first assessment by stroke team and to initial CT. To investigate the validity of the revised criteria, we also analyzed all RRS-activated cases.

Results: In total, 26 patients (RRS group, 11 patients; non-RRS group, 15 patients) were included. The median time from detection to stroke team assessment (10.0 [interquartile range: IQR, 8–15] minutes vs 65.5 [18–89] minutes) and to CT (22.0 [16–31] minutes vs. 46.5 [35–93] minutes) were significantly shorter in the RRS group. RRS was activated in 34 patients (mean, 1.3/month) according to the added criteria, of whom 20 (58.8%) had cerebral infarction and 9 underwent MT. About two-thirds of the other patients developed neurological emergencies (e.g., epileptic seizure, syncope, or hypoglycemia) that required acute care.

Conclusion: RRS has the potential to shorten response time efficiently in the management of in-hospital LVO. Prompt transportation of the patient to the ER by MET enables faster intervention by the stroke team.

Keywords ▶ rapid response system, in-hospital stroke, large vessel occlusion, endovascular treatment, emergency medical services

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Introduction

In-hospital stroke is not an uncommon yet a serious problem; while it accounts for 2.2–17.0% of all cases of stroke,[1,2] the frequency and clinical outcomes of large vessel occlusion (LVO) in hospitalized patients remain to be clarified. In-hospital stroke is known to be more severe and has a less favorable outcome than community-onset stroke,[1] and this is partly because of delays in recognition and assessment.[3] Among the major treatment modalities for LVO, intravenous tissue plasminogen activator (IV-tPA) is less commonly used in in-hospital stroke cases than in community-onset cases due to medical contraindications.[4] Therefore, mechanical thrombectomy (MT) is considered to be extremely important for in-hospital LVO patients; however, unlike community-onset LVO, few time-saving protocols for MT in in-hospital LVO have been reported.

Rapid response system (RRS) is a hospital-wide system used to avoid unexpected cardiac arrest or death in inpatients through intervention provided by a medical team as soon as a patient meets certain criteria.[5] In more than 50% of cases of unexpected cardiac arrest, the patient's vital signs or clinical condition has reported to deteriorate 6–8 hours before the event occurs.[6,7] Thus, each medical institution has developed an original activation criteria based on these early warning signs. RRS is already widely practiced in the United States and Europe, and implementing this system is a Class IIa recommendation in the 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care.[8] Component teams of RRS include physician-led medical emergency teams (METs) and non-physician-led rapid response teams (RRTs),[9] all of who go straight to the patient's bedside upon activation for initial assessment and treatment.

In the present study, we will describe our brand-new protocol for time-saving in responding to in-hospital LVO cooperating with RRS. This study aimed to evaluate the time-saving effects of our new protocol using RRS in the treatment of in-hospital stroke.

Materials and Methods

Kobe City Medical Center General Hospital is the flagship hospital in Kobe City. It has a 768-bed capacity and an emergency medical care center that maintains a near 100% acceptance rate. In April 2015, we developed a protocol to shorten the time between patients' arrival and initiation of IV-tPA or MT. In this protocol, for the patients who arrived within 4.5 hours after onset or last time seen normal, we skip taking MRI and determine treatment indication only by the findings of non-contrast CT and CT angiography. Then in these cases, we included a median door-to-needle time of 31.5 min (interquartile range [IQR], 24–43 min) and a median door-to-puncture time of 33.0 min (IQR: 26–42 min). Although MT was performed for 15 cases of in-hospital LVO from April 2015 to October 2017, no standardized code for initial response had been established.

Development and revision of the RRS criteria

For the revision, we retrospectively reviewed the medical records and determined the typical time course and the causes of delays in responding to in-hospital LVO (**Fig. 1A**). Causes of delay included waiting for the attending physician and conducting tests unnecessary for determining treatment indications. In November 2017, to create a system by which the MET could be immediately deployed to attend to a patient developing signs of LVO, we added "acute hemiparesis, eye deviation, and convulsive seizures" to the previous RRS activation criteria. Of these, convulsive seizure was added to deal with posterior circulation LVO or other neurological emergencies such as epileptic seizure or hypoglycemia. With this protocol, if a medical staff identified a patient who exhibited any of these symptoms and called the RRS, the immediately deployed MET physician transports the patient to the emergency room (ER) while contacting the stroke team without conducting any tests. The stroke physician waiting at the ER can then initiate the neurological examination or imaging studies in the same way as for community-onset cases. Then, the patient is transported to the catheterization laboratory (Cath lab) via the shortest route (**Fig. 1B**). To reduce the workload, we decided that the MET's duty should end upon transfer of the patient to the ER. We then prepared a manual for determining which ward should the patient be transferred to from the ER depending on the treatment. We revised the RRS activation criteria with the permission of the Hospital Safety Committee and disseminated this information by putting up posters (**Fig. 1C**) and distributing nametag-sized cards describing the new criteria to all the nurses. The MET involved around 10 physicians (internal medicine specialists and intensive care unit [ICU] physicians), and they were trained on acute stroke diagnosis and typical symptoms indicative of LVO before the new criteria were introduced. After the criteria were introduced, the feedback was collected regarding all subsequent cases in which RRS was activated for suspected stroke, and the time metrics and clinical outcomes of the patients were recorded.

Study design and patients

This case–control study was approved by the institutional research ethics committees of Kobe City Medical Center General Hospital (k200304). The committee decided that the acquisition of informed consent was not required because this was a retrospective study. The subjects were consecutive in-hospital LVO patients who underwent arterial puncture for MT between April 2015 and January 2020. We conducted a comparative study of the cases in which the RRS was activated (RRS group) and the cases wherein it was not (non-RRS group).

Outcome measures

The primary endpoints included the time from detection of patients by medical staff to contact with our stroke team and the time from detection to the initial CT imaging. The sec-

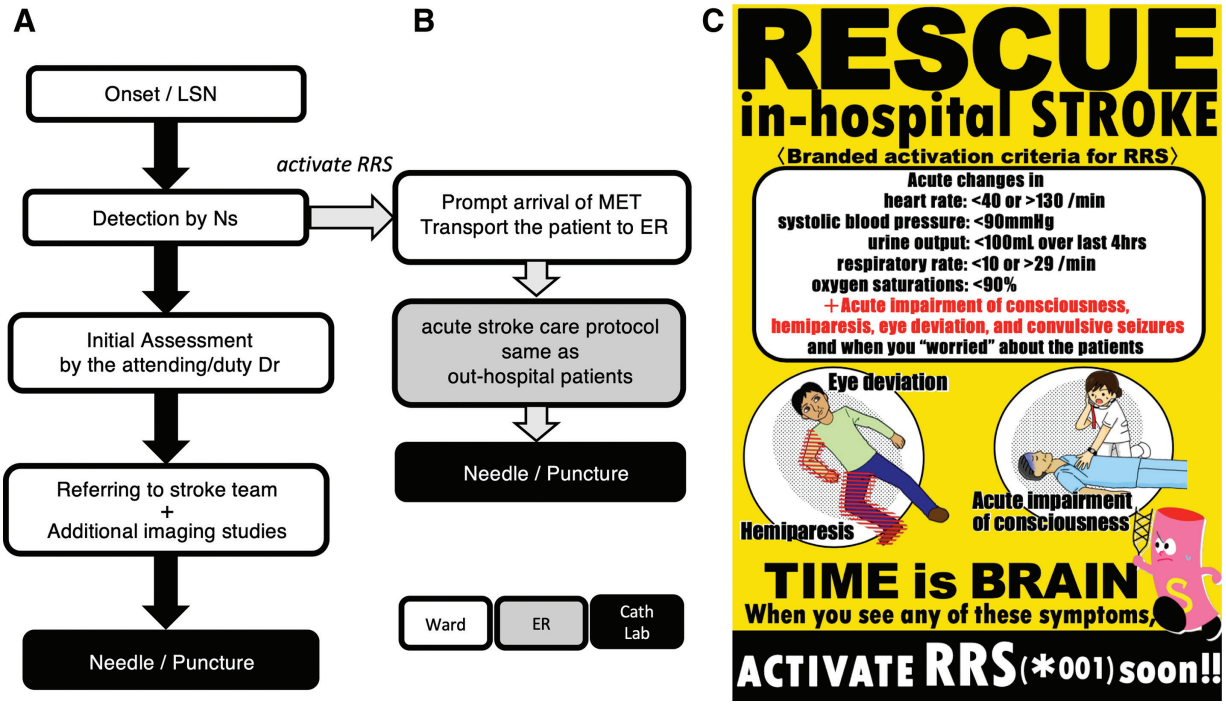

Fig. 1 Differences in typical time course in the management of in-hospital LVOs with and without RRS intervention and the revised criteria. (**A**) Without RRS, when a medical staff (mainly a nurse) discovered an abnormality in the patient, the attending physician or the physician on duty was called first, and it typically took a long time for them to arrive, or unnecessary tests were included for determining treatment indications. Even after the stroke team was consulted, additional imaging was required to examine the occluded vessel, and the transfer from the general ward to the Cath lab was challenging. (**B**) With RRS, if the caregiver recognized any of the four neurological symptoms and activated the system, the MET physician immediately arrives on scene, then transports the patient to the ER. The stroke team can then begin to assess the patient in the ER in the same manner as that for community-onset stroke cases, and the patient can be smoothly transferred to the Cath lab in the usual way. (**C**) RRS activation criteria. We placed posters in common areas for the medical staff (Adapted with permission from Yuriko Murakami). Cath lab: catheterization laboratory; ER: emergency room; LSN: last seen normal; LVO: large vessel occlusion; MET: medical emergency Team; RRS: rapid response system

ondary endpoints were effective revascularization (modified treatment in cerebral ischemia [mTICI] 2b-3), symptomatic intracerebral hemorrhage and mortality during hospitalization. Given that not all patients underwent MRI, the detection-to-puncture time was compared only in the patients in which MRI was skipped. Time metrics were obtained from nursing records, the call register from the mobile phone of MET or stroke team, and the surgical records. Patients for which time information could not be confirmed in the chart were excluded from the analysis. In addition, to evaluate the appropriateness of the revised RRS criteria, we investigated all the cases for which RRS was activated for suspected stroke.

Statistics

Quantitative variables are described as mean (standard deviation) or median (IQR), whereas categorical variables are presented as number (percentage). The patients were divided into subgroups according to whether RRS interventions were provided, and bivariate comparisons were performed using the χ^2 test for categorical variables and the Student's t test (or Mann–Whitney U test in case of non-Gaussian distribution) for quantitative variables. All statistical analyses were performed using JMP 14 (SAS Institute, Cary, NC, USA). P value of <0.05 was considered statistically significant.

Results

After excluding one patient with incomplete time course data, a total of 26 patients were included in the final analysis; of them, 11 and 15 patients were categorized to the RRS group and the non-RRS group, respectively. Two patients in the RRS group did not undergo MT because the spontaneous recanalization was identified after puncture. Two in-hospital LVOs occurred after the implementation of this protocol, but RRS was not activated. The reasons why the RRS was not utilized was that in one case, the attending physician was the first contact and called the stroke physician directly, and in the other case, a nurse who

Table 1 Patient characteristics

	RRS group (n = 11)	Non-RRS group (n = 15)	*P* value
Background			
Mean age, y (SD)	80.7 (9.5)	77.7 (11.7)	0.49
Sex, female, n (%)	8 (72.7)	10 (66.7)	1.00
post operation, n (%)	3 (27.3)	7 (46.7)	0.43
Atrial fibrillation, n (%)	4 (36.3)	7 (46.7)	0.70
Pre-OAC use, n (%)	5 (45.5)	8 (33.3)	1.00
Time metrics			
Median admission to onset, day (IQR)	9.0 (8–12)	8.5 (5–13)	0.76
Median LSN to detection, min (IQR)	85.0 (50–110)	47.0 (34–60)	0.20
Symptoms and imaging findings			
Mean baseline NIHSS (SD)	21.0 (3.5)	20.3 (7.6)	0.79
Median CT ASPECTS (IQR)	10.0 (10–10)	9.5 (8–10)	0.12
MRI before treatment, n (%)	2 (4.2)	6 (40)	0.40
Occlusion site			
ICA, n (%)	2 (18.2)	7 (46.7)	0.21
M1, n (%)	1 (9.1)	2 (13.3)	1.00
M2-3, n (%)	8 (72.7)	5 (33.3)	0.11
VA-BA, n (%)	0 (0)	1 (6.7)	1.00
Etiology			
Cardiac embolism, n (%)	8 (72.7)	8 (53.3)	0.43
Large artery atherosclerosis, n (%)	0 (0)	3 (20)	0.24
ESUS, n (%)	3 (27.3)	4 (26.7)	1.00
Treatment			
IV-tPA, n (%)	3 (27.3)	2 (13.3)	0.62

ASPECTS: Alberta Stroke Program Early CT Score; BA: basilar artery; ESUS: embolic stroke of undetermined source; ICA: internal carotid artery; IQR: interquartile range; IV: intravenous; LSN: last seen normal: NIHSS: National Institute of Health Stroke Scale; OAC: oral anticoagulant; RRS: rapid response system; SD: standard deviation; tPA: tissue plasminogen activator; VA: vertebral artery

was not familiar with the system was the first discoverer and called the attending physician first as in the previous system. All patients in the RRS group were transported to the ER and then moved to the Cath lab. The patients' clinicodemographic characteristics are shown in **Table 1**. In total, 10 patients (38.4%) underwent surgery with general anesthesia before onset, and interventional thrombolysis was administered in only 5 out of 24 patients (20.8%).

The time from detection to contact with a stroke physician (10.0 [IQR, 8–15] minutes vs. 65.5 [IQR, 18–89] minutes) and detection to initial CT scan (22.0 [IQR, 16–31] minutes vs. 46.5 [IQR, 35–93] minutes) were significantly shorter in the RRS group. Meanwhile, there were no significant differences in the effective recanalization rate, the fatality rate during hospitalization, and the prevalence of symptomatic intracranial hemorrhage between the two groups. However, among the patients who did not undergo pretreatment MRI (n=18, 9 patients per group), the detection-to-puncture time was significantly shorter in the RRS group (57.0 [55–72] minutes vs. 112.5 [59–148] minutes) (**Table 2**).

After the revision, the added activation criteria were applied to 34 patients (monthly average, 1.3 cases); of them, 20 patients (58.8 %) received a final diagnosis of cerebral infarction. Among these 20 patients, four patients were administered IV tPA, and nine patients underwent MT. Of the remaining 14 patients, epileptic seizure and transient loss of consciousness occurred in six and four patients, respectively, and hypoglycemia, metabolic encephalopathy, reversible posterior leukoencephalopathy, and hysteria occurred in one patient each. Most of these conditions required acute treatment and there was no delay in treatment for them.

Discussion

The present study showed that RRS enables time saving in responding to in-hospital LVO. Furthermore, the new activation

Table 2 Comparison of outcome measures by RRS intervention

	RRS group (n = 11)	Non-RRS group (n = 15)	*P* value
Primary outcome			
Median time from detection to initial CT, min (IQR)	22.0 (16–31)	46.5 (35–93)	<0.01
Median time from detection to stroke team assessment, min (IQR)	10.0 (8–15)	65.5 (18–89)	<0.01
Secondary outcome			
mTICI scale ≥ 2b-3, n (%)	7 (63.7)	13 (86.7)	0.35
Symptomatic ICH, n (%)*	2 (22.2)	0 (0)	0.13
Median time from detection to puncture, min (IQR)*	57.0 (55–72)	112.5 (59–148)	0.03
In-hospital death, n (%)	1 (9.1)	3 (20)	0.61

*Data of symptomatic ICH and time from detection to puncture are shown for 24 patients (because 2 patients did not undergo MT). ICH: intracranial hemorrhage; IQR: interquartile range; mTICI: modified treatment in cerebral ischemia; RRS: rapid response system

criterion of "acute hemiparesis, eye deviation, and convulsive seizures" accurately predicted ischemic stroke and detected other neurological emergencies efficiently. Although various stroke protocols have demonstrated effectiveness in shortening response times to in-hospital strokes,[3,10] our protocol is unique in that the RRS is activated instead of a stroke team, and the activation criteria are mainly targeted for LVO. Importantly, the results of the current study prove that our protocol effectively shortens response time.

As the MET member directly attended to the patient as soon as the mobile phone rang, the patient could be transported quickly to the ER without conducting tests or waiting for the attending doctor and assessed similarly as that community-onset cases. We considered that the factor in the protocol that contributed most to shortening the response time was transporting the patient promptly to the ER, where we have taken a large number of acute stroke patients and already achieved time saving. The feedback from the nurses clarified that as they are already familiar with RRS as an in-hospital emergency response system, they found it less stressful to contact the RRS team than to directly call the stroke team. Although it is inefficient to continually remind all the medical staff of the importance of shortening response time for in-hospital LVO, the present protocol was a highly sustainable system because it only required the addition of a single line to the existing RRS criteria and the initial training for about 10 MET physicians. Of course, the fact that the RRS was not activated in two LVO cases indicates that continuous awareness is still important. Also, as another point, it was found that this system consumes ER personnel and bed resources and therefore needs to be considered and prepared.

Compared with IV-tPA, MT is rarely contraindicated even in systemic illness or recent surgery. Furthermore, the efficacy of thrombectomy for patients with late-presenting LVO (up to 16–24 hours of onset) who had clinical imaging mismatch or target mismatch has been established by the DAWN and the DEFUSE3 trials.[11,12] Accordingly, MT is an exceedingly important treatment modality for in-hospital LVO, for which the time to treatment must be reduced as much as possible. RRS has the potential to help shorten the time between detection and treatment.

The present study has some limitations. First, this was a study involving a small number of patients at a single institution. Second, we were not able to validate the time-saving effectiveness of RRS for incidentally diagnosed or minor strokes as it was not possible for us to include all of these patients. Third, the generalizability of our results may be limited considering the differences in institutional protocols between hospitals. However, we believe that the concept of preparing a nimble and adaptable team of physicians and transporting the patients suspected of LVO to the same place as the community-onset stroke patients can be applied in various medical institutions. Prospective studies with a larger sample size are needed to further validate the effectiveness of RRS. In addition, we believe that the interval between last time seen normal and detection should be shortened to improve the clinical outcomes of in-hospital LVO. This protocol has raised awareness on in-hospital stroke among the medical staff in our hospital and thus might contribute to reducing the time to detection in the future.

Conclusion

RRS has the potential to shorten response time in the management of in-hospital LVO. Activating RRS according to neurological symptoms and handling the patient in the same

manner as that for community-onset stroke patients may help to shorten time to treatment and improve patient outcomes.

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Disclosure Statement

Hirotoshi Imamura received lecture fees from Stryker Japan K.K. and Medtronic Japan Co., Ltd.; Nobuyuki Sakai received lecture fees from Stryker Japan K.K., Medtronic Japan Co., Ltd., Daiichi Sankyo Company, Limited, Asahi Intecc Co., Ltd., and Biomedical Solutions, Inc.; Nobuyuki Sakai received consigned research fund from DAIICHI Sankyo Company, Limited, TERUMO Corporation, JIMRO Co., Ltd., and Medtronic Japan Co., Ltd. The other authors declare no conflicts of interest.

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