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Other Hospital-onset Acute Ischemic Stroke Due to Large Vessel Occlusion Treated by Mechanical Thrombectomy after Inter-hospital Transfer

Noriaki MATSUBARA,[1] Ryo HIRAMATSU,[1] Ryokichi YAGI,[1] Hiroyuki OHNISHI,[1,2] Shigeru MIYACHI,[1,3] Yuichiro TSUJI,[1] Yangtae PARK,[1] Koji TAKEUCHI,[1] and Toshihiko KUROIWA[1]

[1]Department of Neurosurgery and Neuroendovascular Therapy, Osaka Medical College, Takatsuki, Osaka, Japan;
[2]Department of Neurosurgery, Ohnishi Neurological Center, Akashi, Hyogo, Japan;
[3]Department of Neurosurgery, Aichi Medical University, Nagakute, Aichi, Japan

Abstract

The purpose of this study was to investigate the in-hospital acute ischemic stroke due to large vessel occlusion (LVO) that developed in another thrombectomy-incapable hospital, treated by mechanical thrombectomy after inter-hospital transfer. In eight other hospital-onset LVO patients, clinical characteristics, treatment results, and the timeline of thrombectomy were retrospectively investigated and compared to the results of 17 patients developed LVO at our own hospital and 18 developed in the community. In the analysis of timeline, the mean recognition-to-arrival time in other hospital-onset patients was 169 ± 78 min, significantly longer than for the community-onset patients (79 ± 78 min). Arrival-to-puncture time was 42 ± 19 min, significantly shorter than for the own hospital-onset patients (166 ± 80 min) and the community-onset patients (155 ± 76 min). Recognition-to-puncture times for the other hospital-onset patients, the own hospital-onset patients, and the community-onset patients were 212 ± 74, 166 ± 80, and 216 ± 83 min, respectively, and recognition-to-recanalization times were 285 ± 73, 200 ± 81, and 275 ± 125 min. Both these times were shorter for the own hospital-onset patients. The rates of modified Rankin Scale (mRS) of 0–2 in the three groups were 12%, 30%, and 23%, respectively. The rate of mRS 0–2 was lowest in the other hospital-onset patients. In conclusion, the other hospital-onset patients required additional time for their initial management and inter-hospital transfer although arrival-to-puncture time was shorter. Favorable outcomes were observed less frequently in them. Improving inter-hospital cooperation systems and to educate the medical staff in a thrombectomy-incapable hospital concerning stroke management is important measures for other hospital-onset stroke with LVO.

Key words: in-hospital stroke, large vessel occlusion, mechanical thrombectomy, inter-hospital transfer, thrombectomy-incapable hospital

Introduction

Mechanical thrombectomy has been shown to provide effective treatment for acute ischemic stroke due to intracranial large vessel occlusion (LVO),[1)] and it has become widespread and the standard treatment. Acute stroke due to LVO commonly arises in patients in the community, but LVO can also develop at medical facilities during hospitalization.[2–6)] Mechanical thrombectomy is provided only at comprehensive and thrombectomy-capable stroke centers.[7)] However, in-hospital acute ischemic stroke due to LVO can occur in hospitals without this provision, requiring the patient to be transferred to a thrombectomy-capable facility for endovascular intervention.

With thrombectomy for LVO, early management is required and it is important to minimize the time to recanalization.[8)] Medical management starts early at the time of recognition of the condition; however, in-hospital LVO can occur in a ward where the staffs are unfamiliar with stroke, potentially resulting in a long time for the examination, diagnosis, and intervention.[9–12)] When in-hospital LVO develops in a

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hospital that does not provide thrombectomy, additional time is required for the inter-hospital transfer.

The purpose of this retrospective study was to investigate the characteristics of in-hospital stroke due to LVO that developed in another thrombectomy-incapable hospital, treated by mechanical thrombectomy after inter-hospital transfer, and to compare the timeline and treatment results of mechanical thrombectomy between, patients who developed LVO at our own hospital, and patients who developed LVO in the community.

Subjects and Methods

Our University Hospital provides secondary emergency medical care, with around 880 beds and a comprehensive stroke center. Between January 2016 and May 2019, 51 patients with acute ischemic stroke due to LVO were treated by mechanical thrombectomy at our institution. Of these, eight were excluded from the analysis: six because they developed LVO in the community and were subsequently transferred to our hospital from another hospital, one who developed postoperative reocclusion after thrombectomy, and one who experienced artery occlusion during coil embolization of the intracranial aneurysm. Thus, 43 patients were included in the analysis. Written informed consent was obtained from all the patients and/or their guardian(s).

The patients were considered in three groups: eight who developed LVO at another hospital and were transferred (other hospital-onset) (mean ± SD age, 71.8 ± 11.8 years; range 51–83 years; four men and four women), 17 who developed LVO at our own institution (own hospital-onset) (mean age, 76.4 ± 10.2 years; range, 54–92 years; 12 men and five women), and 18 who developed LVO in the community (community-onset) (mean age, 76.3 ± 11.7 years; range, 45–87 years; eight men and seven women). Data were collected from the patients' medical records. Background data collected for the other hospital-onset patients included the admitting department, the disease leading to admission, comorbid diseases, invasive procedures, and management with anticoagulants or

Table 1 Characteristics, timelines and results of the mechanical thrombectomy for the patients with other hospital-onset acute ischemic stroke due to large vessel occlusion (*n* = 8)

Case	Age	Sex	Inpatient treatment department	Admitting diagnosis	Comorbid disease	Invasive procedure	Etiology	Occlusion site	IV t-PA	NIHSS	ASPECTS	LKW-to-recognition time (min)
1	80	M	Gastroenterology	Cholangitis	Atrial fibrillation, old MI	Cholangial drainage (withdrawal of DOAC)	Cardioembolism	L MCA (M2)	(–)	6	8	40
2	73	M	Cardiology	Heart failure, atrial fibrillation	NA	NA	Cardioembolism	BA	(+)	24	NA	150
3	83	F	Gastroenterological surgery	Esophageal hiatal hernia	Atrial fibrillation	Laparoscopic surgery (withdrawal of warfarin)	Cardioembolism	R MCA (M2)	(–)	6	8	120
4	51	F	Orthopedic	Anterior cruciate ligament injury	Pulmonary arteriovenous fistula	Ligament repair surgery	Cardioembolism	L ICA	(–)	17	8	0
5	56	M	Cardiology	Heart failure, atrial fibrillation	Malignant lymphoma	NA	Cardioembolism	R MCA (M2)	(–)	17	6	0
6	80	F	Orthopedic	Humerus fracture	Atrial fibrillation	Osteosynthesis (withdrawal of DOAC)	Atherothrombosis	R ICA	(–)	13	11	30
7	74	F	Cardiology	Heart failure	Asthma, old MI	NA	Atherothrombosis	L ICA	(+)	18	10	0
8	77	M	Respiratory surgery	Lung cancer	NA	NA	Trousseau's syndrome	BA	(–)	NA	NA	0

R: right, L: left, MCA: middle cerebral artery, ICA: internal carotid artery, BA: basilar artery, IV: intravenous, t-PA: tissue plasminogen activator, NIHSS: National Institutes of Health Stroke Scale, NA: not available, ASPECTS: Alberta Stroke Programme Early CT Score, LKW: last known well, TICI: thrombolysis in cerebral infarction, ICH: intracerebral hemorrhage, SAH: subarachnoid hemorrhage, mRS: modified Rankin Scale.

antiplatelet agents. The thrombectomy timeline data for all three groups included the time last known well or onset time, recognition time, arrival time after transfer, arterial puncture time, recanalization time and analyzed each required time. In addition, data on the mechanical thrombectomy and treatment outcomes were collected, including the site of the vessel occlusion, etiology of the stroke, National Institutes of Health Stroke Scale (NIHSS), and Alberta Stroke Program Early Computed Tomography Score (ASPECTS), thrombectomy device used, thrombolysis in cerebral infarction (TICI) 2b–3 achievement rate, procedural complications, and modified Rankin Scale (mRS) score at discharge. Because some items of data for some patients were not clearly reliable, the analysis was performed within the range of available data.

The results are presented as the mean ± standard deviation. The data were evaluated statistically with the Kruskal–Wallis and Chi-square tests using Statcel Ver 2.0 statistical analysis software (OMS Ltd., Tokyo, Japan). *P*-values <0.05 were regarded as statistically significant.

Results

Admitting department, disease on admission, and contributing factors for the other hospital-onset patients

The background characteristics for the eight other hospital-onset patients are shown in Table 1. They were transported by inter-hospital transfer from five regional hospitals. Four of these hospitals did not have stroke specialists and one had stroke physicians but no neurointerventionist. The admitting departments of the transferred patients were cardiology for three (38%), orthopedic for two (25%), and respiratory surgery, gastroenterological surgery, and gastroenterology (one each, 12%). The disease on admission for the three patients admitted to the cardiology department was heart failure; two had atrial fibrillation and overlapped one suffered from malignant lymphoma. The patients treated at the orthopedic department had both undergone surgery; direct oral anticoagulants had been withdrawn from one of them perioperatively, and the other had

Recognition-to-arrival time (min)	Arrival-to-puncture time (min)	Puncture-to-recanalization time (min)	LKW-to-recanalization time (min)	Recognition-to-puncture time (min)	Recognition-to-recanalization time (min)	Arrival-to-recanalization time (min)	Thrombectomy device	TICI grade	Procedural complication	mRS at discharge
150	60	125	375	210	335	185	Penumbra → Solitaire	2b	Asympt SAH	4
120	15	25	310	135	160	40	Penumbra	2b	(–)	2
110	50	115	400	165	280	170	Trevo → Penumbra → Trevo	3	(–)	4
130	30	170	325	155	325	200	Trevo + Penumbra	2b	(–)	4
180	45	25	250	225	250	70	Solitaire	3	(–)	4
90	70	NA	NA	160	NA	NA	Trevo + Penumbra	0	(–)	4
280	50	NA	NA	330	NA	NA	Trevo + Penumbra → PTA/stent	1	(–)	5
295	20	45	360	315	360	65	Solitaire	2b	Sympt ICH	6

undiagnosed pulmonary arteriovenous fistula as the causative disease of the embolism. For the patient admitted for respiratory surgery, the thrombosis was caused by Trousseau's syndrome associated with lung cancer. The patient admitted for gastroenterological surgery had a past history of atrial fibrillation, and warfarin had been withdrawn prior to laparoscopic surgery. The patient admitted to the gastroenterology department was suffering from acute cholangitis; this patient had a past history of atrial fibrillation, and direct oral anticoagulants had been withdrawn before percutaneous transhepatic cholangial drainage.

The etiologies of the ischemic stroke were cardioembolism in five (62%), atherothrombosis in two (25%), and cancer-related embolism in one (12%). Six had heart disease and two had malignant tumors. Factors contributing to the LVO included invasive procedures for four patients (two open surgeries, one laparoscopic surgery, and one percutaneous drainage), with the perioperative withdrawal of anticoagulant agents in three of these patients.

All eight other hospital-onset patients received an initial assessment by the physicians in their initial hospitals and contact with stroke center was made after MRI imaging examination and obtaining the diagnosis of LVO. Tissue plasminogen activator (t-PA) was administered at the initial hospital for two of the transferred patients (25%). The other six patients did not receive t-PA, four because they had undergone an invasive procedure and two because no stroke physician was present.

Timelines for the mechanical thrombectomy

The mechanical thrombectomy timelines are shown in Table 1 and summarized in Table 2. The mean time to recognition from the time last known well or onset time was 42 ± 60 min for the other hospital-onset patients; this was shorter than that for the own hospital-onset patients (105 ± 147 min) and for the community-onset cases (110 ± 171 min). The mean time from recognition-to-arrival for the other hospital-onset patients was 169 ± 78 min, which was longer than for the community-onset cases (79 ± 78 min). The recognition-to-arrival time for own hospital-onset patients was defined as 0 min. These times were significantly different (*P* <0.001). The mean time from arrival-to-puncture for the other hospital-onset patients was 42 ± 19 min; this was significantly shorter than the times for the own hospital-onset patients (166 ± 80 min) and for the community-onset cases (155 ± 76 min) (*P* <0.001). The mean times from recognition-to-puncture for the other hospital-onset patients, the own hospital-onset patients, and the community-onset cases were 212 ± 74, 166 ± 80, and 216 ± 83 min, respectively. The mean recognition-to-recanalization times for the three groups were 285 ± 73, 200 ± 81, and 275 ± 125 min, respectively. The recognition-to-puncture and recognition-to-recanalization times were shortest for the own hospital-onset patients; however, there was no statistically significant difference.

Treatment results of the mechanical thrombectomy

The results of the mechanical thrombectomy for the eight other hospital-onset patients are shown in Table 1 and summarized in Table 3. The site of vessel occlusion was the internal carotid artery in three patients, the middle cerebral artery in three, and the basilar artery in two. The first thrombectomy device used was a stent retriever in three patients, the Penumbra System in two, and a combination of stent retriever and the Penumbra System in three. TICI 2b–3 recanalization was achieved for six patients (75%). The mean puncture-to-recanalization time was 84 ± 61 min. Two procedure-related

Table 2 Timelines of mechanical thrombectomy for the three patient groups: the other hospital-onset LVO patients (*n* = 8), the own hospital-onset LVO patients (*n* = 17), and the community-onset LVO patients (*n* = 18)

Acute ischemic stroke due to LVO treated by mechanical thrombectomy	Other hospital-onset LVO patients (*n* = 8)	Own hospital-onset LVO patients (*n* = 17)	Community-onset LVO patients (*n* = 18)	*P*-value
LKW-to-recognition time (min)	42 ± 60	105 ± 147	110 ± 171	NS
Recognition-to-arrival time (min)	169 ± 78	0	79 ± 78	<0.001
Arrival-to-puncture time (min)	42 ± 19	166 ± 80	155 ± 76	<0.001
Recognition-to-puncture time (min)	212 ± 74	166 ± 80	216 ± 83	NS
Puncture-to-recanalization time (min)	84 ± 61	43 ± 22	73 ± 48	NS
Recognition-to-recanalization time (min)	285 ± 73	200 ± 81	275 ± 125	NS
Arrival-to-recanalization time (min)	122 ± 71	200 ± 81	230 ± 94	NS
LKW-to-recanalization time (min)	337 ± 54	296 ± 155	412 ± 226	NS

Time-line data are presented as mean ± SD. LVO: large vessel occlusion, LKW: last known well, NS: not significant.

Table 3 Procedural and clinical results of mechanical thrombectomy for large vessel occlusion (LVO) for the three patient groups: the other hospital-onset patients (*n* = 8), the own hospital-onset LVO patients (*n* = 17), and the community-onset LVO patients (*n* = 18)

Acute ischemic stroke due to LVO treated by mechanical thrombectomy	Other hospital-onset LVO patients (*n* = 8)	Own hospital-onset LVO patients (*n* = 17)	Community-onset LVO patients (*n* = 18)	*P*-value
Age (mean)	71.8 ± 11.8	76.4 ± 10.2	76.3 ± 11.7	NS
Male/Female (number)	4/4	12/5	11/7	NS
Occlusion site	ICA3, MCA3, BA2	ICA5, MCA10, BA1, PCA1	ICA6, MCA10, BA1, ICA + MCA1	NS
Etiology	Cardiac 5, atheromatous 2, tumor-related 1	Cardiac 11, atheromatous 2, tumor-related 3, Iatrogenic 1	Cardiac 10, atheromatous 6, tumor-related 2	NS
t-PA administration	25%	12%	22%	NS
NIHSS	14.4 ± 6.6	12.8 ± 4.3	14.9 ± 5.3	NS
ASPECTS	8.5 ± 1.8	6.9 ± 2.7	7.9 ± 1.3	NS
TICI grade 2b–3	75%	82%	78%	NS
Symptomatic procedural complication	12%	12%	17%	NS
mRS 0–2 at follow-up	12%	30%	23%	NS
mRS 5–6 at follow-up	25%	29%	22%	NS

LVO: large vessel occlusion, t-PA: tissue plasminogen activator, NIHSS: National Institutes of Health Stroke Scale, ASPECTS: Alberta Stroke Programme Early CT Score, TICI: thrombolysis in cerebral infarction, mRS: modified Rankin Scale, ICA: internal carotid artery, MCA: middle cerebral artery, BA: basilar artery, PCA: posterior cerebral artery, NS: not significant.

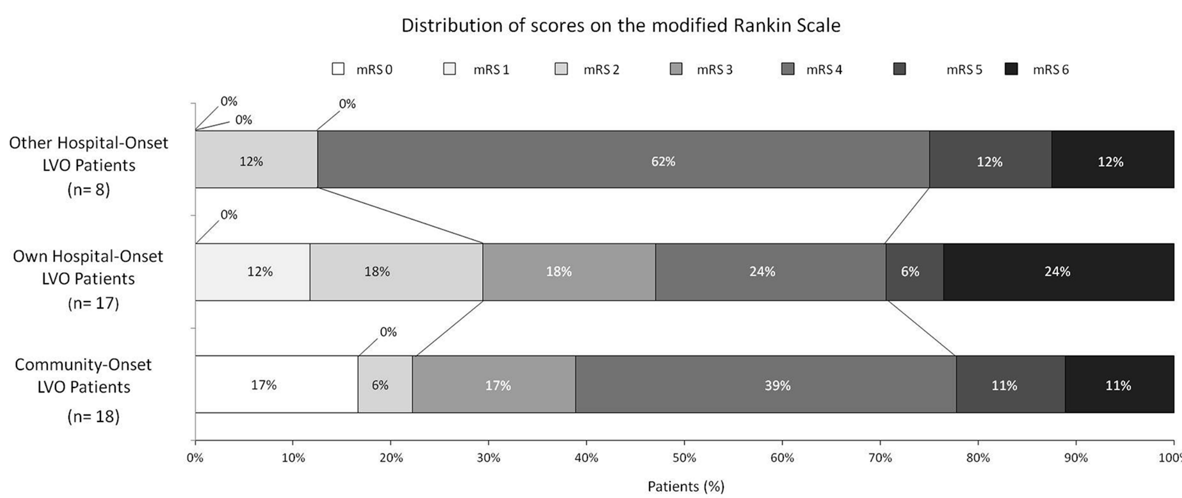

Fig. 1 Distribution of modified Rankin Scale scores at discharge for patients treated with mechanical thrombectomy for ischemic stroke due to large vessel occlusion (LVO). The scores were compared for the other hospital-onset patients (*n* = 8), the own hospital-onset patients (*n* = 17), and the community-onset patients (*n* = 18).

complications were noted: symptomatic intracerebral hemorrhage and asymptomatic subarachnoid hemorrhage, each experienced by one patient (12%). The mRS scores at discharge were 0–2 for only one patient (12%), 3–4 for five patients (62%), and 5–6 for two patients (25%). The reasons for poor outcome (mRS 5–6) included deterioration of the primary disease (aggravation of heart failure and the progression of cancer, each in one patient).

Table 3 summarizes the treatment outcomes in the three groups. The mean NIHSS scores for the other hospital-onset patients, the own hospital-onset patients, and the community-onset cases were 14.4 ± 6.6, 12.8 ± 4.3, and 14.9 ± 5.3, respectively. The mean ASPECTS scores were 8.5 ± 1.8, 6.9 ± 2.7, and 7.9 ± 1.3. The TICI 2b–3 achievement rates were 75%, 82%, and 78%. The symptomatic complication rates were 12%, 12%, and 17%. Figure 1 summarizes the mRS scores at discharge in the three groups. The rates of mRS 0–2 were 12%, 30%, and 23%, and the rates of mRS 5–6 were 25%, 29%, and 22%. The rate of mRS 0–2 was lowest for the other hospital-onset patients, although there was no statistically significant difference.

Discussion

Causes of LVO in the other hospital-onset patients

Cardioembolism was the most frequent etiology for the LVO among the other hospital-onset patients. Cardioembolism is a major cause of LVO and a large number of patients with the condition are indicated for thrombectomy. The cardioembolic sources for the other hospital-onset patients in the present study included atrial fibrillation, and the patients were hospitalized in the cardiology department. In addition, the development of LVO occurred in some of the patients after surgery or an invasive procedure, with or without the withdrawal of anticoagulant agents. In previous reports, heart disease was the most frequent underlying factor in the in-hospital development of ischemic stroke, with other causative diseases including malignant tumors and blood diseases. In addition, surgery and invasive procedures, and the withdrawal of anticoagulants or antiplatelet agents have been reported as risk factors for in-hospital stroke.[9–11] The results obtained from this study were similar to those previous findings. The LVO was not caused by a single condition but by several combinations of conditions.

Timeline of treatment

The mean interval between the time last known well and recognition time was shorter for the other hospital-onset patients than for the own hospital-onset patients or the community-onset cases, although the difference was not statistically significant. Except when the onset occurs during sleep, in-hospital stroke cases are likely to be recognized early. In this series, the onset for all the other hospital-onset patients occurred during the day; in contrast, the own hospital-onset patients included wake-up stroke cases, which may have contributed to this result.

Because stroke management started at the time of recognition for the patients at our own hospital, the recognition-to-puncture time was shorter than for the other two groups, although the difference was not statistically significant. Because of this, the recognition-to-recanalization time were also shorter for own hospital-onset patients. Conversely, the other hospital-onset patients required additional time for the inter-hospital transfer, resulting in the total time to thrombectomy being similar to that of the community-onset cases. The recognition-to-arrival time was significantly longer for the other hospital-onset patients than for the community-onset cases. This may have been because the initial clinical evaluation and imaging examination were performed in the onset hospital for the other hospital-onset patients. There was no difference in arrival-to-puncture time between the own hospital-onset patients and the community-onset cases; however, the arrival-to-puncture time was significantly shorter for the other hospital-onset patients. The reason for this difference was that our stroke center prepared for the intervention while the patients were being transported between the hospitals, and the thrombectomy was initiated soon after arrival. Hence, there was no difference in recognition-to-puncture time between the other hospital-onset patients and community-onset cases.

The arrival-to-puncture time for the community-onset cases (150 min) was similar to the recognition-to-puncture time for the own hospital-onset patients (165 min). Guidelines for mechanical thrombectomy recommend that the arrival-to-puncture time should be within 75 min and ideally within 60 min.[13,14] This suggests that the acute stroke management at our hospital might be unsatisfactory and that the arrival-to-puncture time should be reduced.

Recently, the increased interest and more widespread understanding of acute stroke management[15] has begun to speed up the processing of in-hospital stroke in major stroke centers.[3] However, some previous studies have reported that the time for examination and treatment was slower for in-hospital stroke than for community-onset stroke.[9–12] In fact, these matters are rather applied to stroke that develops in other hospitals unaccustomed to treat strokes. In-hospital LVO can occur unexpectedly in hospitals incapable for thrombectomy, where the medical staffs are inexperienced in stroke management. One of the causes of the delay seemed to be that the early evaluation was performed by staff unfamiliar with stroke management. Their insufficient knowledge of stroke and lesser awareness of emergency situations may have resulted in the inappropriate timing of imaging, difficulty in diagnosis, or delay before consulting stroke specialists. The time from recognition-to-arrival after inter-hospital transfer was 169 min for the other hospital-onset patients. Reducing this time may shorten the time to intervention. The consultation of the stroke center by the initial hospital occurred after establishing the diagnosis of LVO by imaging. Better outcomes are achieved with early consultation with stroke specialists,[16] so improving inter-hospital cooperation systems is desirable. The effective use of a stroke telephone hotline is one possible way to do this.[17] Another important measure for in-hospital stroke in a stroke-incapable hospital is to educate the medical staff about early stroke management.[18]

Procedural and clinical outcomes of mechanical thrombectomy

Many patients who develop in-hospital stroke cannot be treated with t-PA, even with early medical care, because of being after an invasive procedure.[5] In the present study, it was notable that one of the reasons for not administering t-PA was absence of a stroke physician at the onset hospital. Thus, mechanical thrombectomy plays an important role instead of t-PA.[2,5,6] The procedural and perioperative results of thrombectomy for the other hospital-onset patients in this series were not significantly different from those for the own hospital-onset patients and the community-onset cases, indicating that mechanical thrombectomy is an effective treatment for patients who develop LVO in another hospital. The puncture-to-recanalization time was shorter for the own hospital-onset patients than for the other groups, although the difference was not significant. This may have been due to the influence of a small number of cases and variation among the patients.

When stroke occurs in a hospital with a stroke center, medical management is initiated early, at the time of recognition. However, the underlying disease that led to admission can influence the clinical outcome. Previous studies have reported high mortality and low rates of discharge to home following thrombectomy for patients who develop LVO in-hospital compared to those who develop it in the community.[2,4–6] In this series, the rates of both mRS 5–6 and mRS 0–2 at discharge were a little higher in the own hospital-onset patients than in the other two groups. As mentioned earlier, the increased interest and understanding of emergency stroke management may have helped improve the outcomes of patients who develop in-hospital LVO, especially in comprehensive stroke centers or thrombectomy-capable stroke centers.[3] The rate of mRS 0–2 at discharge was lower for the other hospital-onset patients, suggesting that a favorable outcome is less likely for patients who develop LVO in a hospital without a stroke center. This finding may have been the result of the time required for the initial management and inter-hospital transfer, as well as the presence of comorbid diseases.

Limitations of this study

This study had several limitations. It was retrospective and investigated only patients who developed LVO in another hospital and were transferred to our hospital by inter-hospital transfer; thus, only thrombectomy-treated transferred LVO cases were studied, whereas other patients who developed ischemic stroke at other hospitals and who were not treated with thrombectomy were not investigated. These uninvestigated cases may have been treated by the physicians in the onset hospitals; it is possible that some may have been indicated for thrombectomy without this being recognized. Because the survey was retrospective, the data collected may not all have been reliable. In addition, the number of patients may have been insufficient for the statistical analysis.

Conclusion

This study demonstrated the characteristics, timeline and treatment results of other hospital-onset acute ischemic stroke due to LVO treated by mechanical thrombectomy after inter-hospital transfer. The causes of the LVO included cardioembolic sources and their development was affected by invasive procedures with the withdrawal of anticoagulants agents. The other hospital-onset patients required additional time for the initial management and inter-hospital transfer. The recognition-to-arrival time was longer although the arrival-to-puncture time was shorter. Clinical favorable outcomes were less frequent in them. Improving inter-hospital cooperation systems and to educate the medical staff in a thrombectomy-incapable hospital concerning stroke management is important measures for other hospital-onset stroke with LVO.

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Conflicts of Interest Disclosure

All the authors have no conflicts of interest.

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Address reprint requests to: Noriaki Matsubara, MD, Department of Neurosurgery and Neuroendovascular Therapy, Osaka Medical College, Daigaku-machi 2-7, Takatsuki, Osaka 569-8686, Japan.
e-mail: neu147@osaka-med.ac.jp