Characteristics and Treatment Results of In-hospital Acute Ischemic Stroke due to Large Vessel Occlusion Treated by Mechanical Thrombectomy

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Objective: The purpose of this study was to investigate the characteristics, time-line, and treatment results of in-hospital acute ischemic stroke due to large vessel occlusion (LVO) treated by mechanical thrombectomy.

Methods: The authors investigated 10 patients (six males and four females; mean age 78.6 years, range 65–92) with in-hospital LVO treated by thrombectomy between January 2016 and July 2018 in our institute. Patient characteristics, procedural results, clinical outcome, and time-line data of thrombectomy (last well known [LWK]/onset, recognition, arterial puncture, and recanalization) were retrospectively evaluated. Results obtained from in-hospital LVO were compared with those from 13 patients with community-onset LVO (eight males and five females; mean age 78.3 years, range 45–87).

Results: The initial admitting departments of in-hospital LVO were cardiology in six (60%) and hematology, otolaryngology, urology, and gastroenterology in one each (10%). The etiologies of ischemic stroke were cardioembolism in eight (80%), thrombosis in one (10%), and iatrogenic consequence in one (10%). The comorbid disease of in-hospital LVO included cardiac disease in eight (80%) and malignant tumor in four (40%) with overlapping. The factor contributing to in-hospital LVO was invasive procedure with withdrawal of antithrombotic agents in three (30%). The interval between LWK and recognition was a median of 60 minutes in in-hospital LVO, which was shorter than LWK-to-arrival time in community-onset LVO (median 225 minutes). The interval between recognition and consultation to the neuroendovascular team was a median of 50 minutes. The recognition-to-puncture time was compared with arrival-to-puncture time in community-onset LVO. That presented no difference between them (median 130 vs 150 minutes). The LWK-to-recanalization time in in-hospital LVO was shorter than that in community-onset LVO (median 240 vs 495 minutes). The procedural results of thrombectomy demonstrated no differences between them. The rate of thrombolysis in cerebral infarction (TICI) 2b-3 was 70% in in-hospital vs 85% in community-onset LVO. The rate of favorable outcome (modified Rankin Scale [mRS] 0-2) at discharge was not different (30% vs 23%); however, higher rates of mortality and severe disability (mRS 5-6) were observed in patients with in-hospital LVO compared to those with community-onset LVO (40% vs 15%).

Conclusion: In this series, the procedural results of thrombectomy were not different between in-hospital and community-onset LVO. The recognition-to-puncture time in in-hospital LVO was similar to the arrival-to-puncture time in community-onset LVO, although the LWK-to-recognition/recanalization time in in-hospital LVO was shorter compared with the LWK-to-arrival/recanalization-time in community-onset LVO. The rate of clinical favorable outcome was similar, although a higher rate of poor outcome was observed in in-hospital LVO. Comorbid diseases may be associated with poor outcome in in-hospital ischemic stroke due to LVO.

Keywords ▶ in-hospital stroke, ischemic stroke, large vessel occlusion, mechanical thrombectomy

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Introduction

The efficacy of mechanical thrombectomy for acute ischemic stroke due to intracranial large vessel occlusion (LVO) has been demonstrated and it has become actively performed. Many cases of acute LVO are community-onset and transported by ambulance, but there are some in-hospital cases which develop at a medical department during hospitalization. In thrombectomy for LVO, shortening of the time to recanalization is needed and prompt management is necessary. Most of cases with in-hospital LVO are handled by staff unfamiliar with it in comparison with the staff in emergency department handing transport cases. Thus, examinations, diagnoses, and interventions may not smoothly progress despite early medical assessment. The purpose of this study was to investigate the characteristics, time-line, and treatment results of in-hospital acute ischemic stroke due to LVO treated by mechanical thrombectomy in comparison with those of community-onset LVO.

Materials and Methods

Of 34 patients with acute ischemic stroke due to LVO treated by mechanical thrombectomy between January 2016 and July 2018 (2 years and 7 months) at Osaka Medical College Hospital (secondary emergency medical institution with about 880 beds), 10 in-hospital LVO patients (mean age: 78.6 years old [65–92 years old], male: 6, female: 4) were retrospectively investigated and compared with 13 community-onset LVO patients transported by ambulance in the same period (mean age: 78.3 years old [45–87 years old], male: 8, female: 5). In all, 11 patients with LVO were excluded for analysis: eight patients were transferred from other hospitals (transfer of community-onset cases: 4), 24 hours or more had passed after the onset in 1, postoperative re-occlusion after thrombectomy in 1, and LVO occurred during coil embolization of cerebral aneurysm in 1.

Following factors were evaluated, initial admitting departments, causative diseases leading to admission, comorbid diseases, proceeding surgeries and invasive procedures, and course to contacts the neuroendovascular team in in-hospital LVO cases. Regarding time-lines related to thrombectomy, last well known (LWN) time/ onset time, recognition time in hospital cases, arrival time in community-onset cases, arterial puncture, and recanalization times were evaluated. Since the accurate time was unclear in some patients, analysis was performed within the range of available data. In addition, information on mechanical thrombectomy and treatment outcomes were also evaluated. Location of LVO, etiology of stroke, National Institutes of Health Stroke Scale (NIHSS), Alberta Stroke Programme Early CT Score (ASPECTS), thrombectomy device, thrombolysis in cerebral infarction (TICI) 2b-3 achievement rate, procedural complications, and modified Rankin Scale (mRS) at discharge were investigated. The results are presented as the median (interquartile range). For statistical analysis, the Mann–Whitney U test and chi-square test were used. For statistical analysis software, Statcel Ver2.0 (OMS Ltd., Tokyo, Japan) was used and p <0.05 was regarded as significant.

Results

The results of 10 patients with in-hospital acute ischemic stroke due to LVO treated by mechanical thrombectomy are shown in Table 1.

The initial admitting departments, comorbid diseases, and contributing factors of in-hospital LVO

Six patients (60%) initially admitted in cardiology. The comorbid disease was heart failure in three patients, acute myocardial infarction in one patient, takotsubo cardiomyopathy in one patient, and after pacemaker placement for bradycardiac atrial fibrillation (edoxaban was withdrawn for pacemaker implantation surgery) in one patient. Other initial admitting departments were urology, gastroenterology, otorhinolaryngology, and hematology in one patient (10%) each. The patient initially admitted at the urology department with urinary bladder cancer. This patient had a past medical history of atrial fibrillation and edoxaban had been withdrawn prior to transurethral resection of urinary bladder tumor. The other patient with a past medical history of ischemic heart disease admitted at the gastroenterology department for treatment of cholangitis. Aspirin had been withdrawn before endoscopic retrograde cholangiopancreatography. The third patient admitted at the otorhinolaryngology department. An iatrogenic embolism occurred during arterial injection chemotherapy for maxillary cancer. The fourth patient admitted at the hematology department, thrombosis occurred due to leukemia-associated disseminated intravascular coagulation.

The etiology of in-hospital LVO was cardiac embolism in eight patients (80%), iatrogenic embolism in one (10%),...
and other thrombosis in one patient (10%). Regarding underlying disease with overlapping, eight (80%) and four (40%) patients were accompanied with heart disease and malignant tumor, respectively. Anticoagulants and anti-platelet agents had been withdrawn for invasive procedure in three patients.

Tissue plasminogen activator (t-PA) was used in two in-hospital patients (20%) and the time to initiation of t-PA administration from recognition was 110 and 255 minutes, respectively. In the community-onset cases, t-PA was administered to 3 (23%) of the 13 patients. The reason for the avoidance of t-PA in the eight in-hospital patients was being after surgery or invasive procedure in four, unclear onset time in one, a low platelet count in one, immediate application of thrombectomy for acute onset of cerebral embolism in an angiography room in one, and first-line thrombectomy without t-PA for prompt recanalization in one patient.

Course of recognition to contact the neuroendovascular team

All patients received initial assessment from the physicians in charge of each department and they were then consulted to the neuroendovascular team after taking a CT or MRI. The median time to consultation to the neuroendovascular team from recognition was 50 minutes (interquartile range: 85). A consultation was delayed in a patient with serious consciousness disturbance due to basilar artery occlusion. This patient was hospitalized for myocardial infarction in the cardiology department and MRI could not be performed because of implantation of cardiac pacemaker. It was difficult to diagnose based on CT alone and 120 minutes were taken to consult to the neuroendovascular team. The time to femoral artery puncture from recognition (recognition-to-puncture time) was 230 minutes, and the time to recanalization after puncture (puncture-to-recanalization time) was 25 minutes, but the patient eventually died (Case 4).

Time-line from recognition to treatment and recanalization

The results of the time-lines are presented as the median (interquartile range). The median time to recognition from LWK or onset (LWK-to-recognition time) was 60 minutes (40) in the in-hospital cases, being significantly shorter than the time between LWK/onset and arrival at hospital (LWK-to-arrival time) 225 minutes (327.5) in the community-onset cases (p = 0.040). When the time-line was compared between the in-hospital and community-onset cases, recognition-to-puncture time and arrival-to-puncture time was 130 minutes (65) vs 150 minutes (82.5) (p = 0.838), puncture-to-recanalization time was 35 minutes (25) vs 80 minutes (46.25) (p = 0.037), and LWK-to-recanalization time was 240 minutes (75) vs 495 minutes (350) (p = 0.059). Recognition-to-recanalization time and arrival-to-recanalization time was 180 minutes (95) vs 255 minutes (115) (p = 0.289) in in-hospital and community-onset LVO cases, respectively.

Treatment results of mechanical thrombectomy

Table 1 describes data of in-hospital cases. In in-hospital cases, the location of LVO was the internal carotid artery in three patients, middle cerebral artery in five, and basilar artery and posterior cerebral artery in one patient each. The thrombectomy device used was a stent-retriever in five patients, Penumra system in four, and other in one patient. TICI 2b-3 recanalization was achieved in seven patients (70%). The median time of puncture-to-recanalization was 35 minutes. A patient with low ASPECTS score of 4 was treated for socially reason (Case 7). Regarding complications, symptomatic subarachnoid hemorrhage occurred in one patient (10%), asymptomatic cerebral hemorrhage and subarachnoid hemorrhage occurred in one patient each. No procedure-related major complication was noted. mRS at discharge was 0-2 in three patients (30%), 3-4 in three (30%), and 5-6 in four (40%) patients. The main reason for mRS 5-6 was delayed management in two patients, and aggravation of primary disease in two patients (aggravation of heart failure in one patient and progression of leukemia in one patient).

The treatment outcomes of the in-hospital LVO cases were compared with those of the community-onset cases (in-hospital vs community-onset) (Table 2). The median NIHSS score was 16 (7) vs 15 (4.5) (p = 0.733), the median ASPACTS was 8 (1.5) vs 7.0 (2.0) (p = 0.337), the TICI 2b-3 achievement rate was 70.0% vs 84.6% (p = 0.37), the complication rate was 10.0% vs 7.7% (p = 0.69), the rate of mRS 0-2 at discharge was 30.0% vs 23.1% (p = 0.54), and the rate of mRS 5-6 was 40.0% vs 15.4% (p = 0.20) (Fig. 1).

Discussion

Cause of in-hospital LVO

The etiology of in-hospital LVO was cardiac embolism in the most cases and the most frequent admitting department was cardiology. Patients with atrial fibrillation, heart failure, and myocardial infarction were hospitalized in the cardiology department.
department. Generally, cardiogenic cerebral embolism is the major cause of acute LVO and thrombectomy could be applied for such patients. In the previous registries and reviews, heart disease was the most frequent background factors of in-hospital stroke including cases other than LVO. Other underlying diseases include malignant tumor and blood disease. In addition, withdrawing of anticoagulants and antiplatelet agents before/after surgeries and invasive procedures, cerebral hypoperfusion due to low blood pressure, and iatrogenic thromboembolism were included as factors related to LVO.3–6 The results of the present series were mostly the same and these were not caused by a single factor but caused by various combinations of these factors.

**Time-line of treatment for in-hospital LVO**
In the present study, excluding cases which onset during sleep, LWK-to-recognition time in the in-hospital cases was shorter than LWK-to-arrival time in the community-onset cases. In-hospital cases were recognized earlier than community-onset cases. Therefore, the time to initial assessment and LWK-to-recanalization time were shorter in the in-hospital LVO cases than those of community-onset cases.

In the present study, the recognition-to-puncture time in the in-hospital cases was 130 minutes, whereas the arrival-to-puncture time in the community-onset cases was 150 minutes. There was no significant difference between two groups. In previous reports, in-hospital stroke took a long time for examination and treatment compared with the time taken for community-onset stroke and this was also the same for ischemic stroke due to LVO.5,8 In the third version of the guidelines for proper use of thrombectomy devices in Japan dated March 2018, the rational target and ideal arrival-to-puncture times are within 75 and 60 minutes, respectively.7,9 Compared to the recommendation in the guideline, recognition/arrival-to-puncture times in the present study were quite unsatisfactory. It has been reported that the time to detection or evaluation of in-hospital ischemic

### Table 1
Summary of in-hospital acute ischemic stroke patients with large vessel occlusion and results of mechanical thrombectomy

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Initial admitting department</th>
<th>Admitting diagnosis</th>
<th>Comorbid disease</th>
<th>Invasive procedure</th>
<th>Etiology</th>
<th>Occlusion site</th>
<th>IV t-PA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65</td>
<td>F</td>
<td>Cardiology</td>
<td>Heart failure</td>
<td></td>
<td></td>
<td>Cardioembolism</td>
<td>R MCA (M1)</td>
<td>(−)</td>
</tr>
<tr>
<td>2</td>
<td>85</td>
<td>M</td>
<td>Cardiology</td>
<td>Atrial fibrillation</td>
<td></td>
<td>Pacemaker implantation*</td>
<td>Cardioembolism</td>
<td>R ICA top</td>
<td>(−)</td>
</tr>
<tr>
<td>3</td>
<td>67</td>
<td>F</td>
<td>Otolaryngology</td>
<td>Maxillary cancer</td>
<td></td>
<td>Arterial infusion chemotherapy</td>
<td>Iatrogenic embolism</td>
<td>R MCA (M2)</td>
<td>(−)</td>
</tr>
<tr>
<td>4</td>
<td>78</td>
<td>F</td>
<td>Cardiology</td>
<td>Acute MI</td>
<td>Pacemaker</td>
<td></td>
<td>Cardioembolism</td>
<td>BA</td>
<td>(+)</td>
</tr>
<tr>
<td>5</td>
<td>69</td>
<td>M</td>
<td>Cardiology</td>
<td>Heart failure</td>
<td>Atrial fibrillation</td>
<td></td>
<td>Cardioembolism</td>
<td>R ICA</td>
<td>(−)</td>
</tr>
<tr>
<td>6</td>
<td>91</td>
<td>F</td>
<td>Gastroenterology</td>
<td>Cholangitis</td>
<td></td>
<td>ERCP*</td>
<td>Cardioembolism</td>
<td>Bil ICA</td>
<td>(+)</td>
</tr>
<tr>
<td>7</td>
<td>81</td>
<td>M</td>
<td>Cardiology</td>
<td>Heart failure</td>
<td></td>
<td></td>
<td>Cardioembolism</td>
<td>R MCA (M1)</td>
<td>(−)</td>
</tr>
<tr>
<td>8</td>
<td>78</td>
<td>M</td>
<td>Urology</td>
<td>Bladder cancer</td>
<td></td>
<td>TuR-Bt*</td>
<td>Cardioembolism</td>
<td>L MCA (M2)</td>
<td>(−)</td>
</tr>
<tr>
<td>9</td>
<td>80</td>
<td>M</td>
<td>Cardiology</td>
<td>Takotsubo cardiomyopathy</td>
<td></td>
<td></td>
<td>Cardioembolism</td>
<td>L PCA (P1)</td>
<td>(−)</td>
</tr>
<tr>
<td>10</td>
<td>92</td>
<td>M</td>
<td>Hematology</td>
<td>DIC due to leukemia</td>
<td></td>
<td></td>
<td>Other thrombosis</td>
<td>R MCA (M1)</td>
<td>(−)</td>
</tr>
</tbody>
</table>

*Anticoagulant/antiplatelet agents were discontinued before intervention/examination. ASPECTS: Alberta Stroke Programme Early CT Score; BA: basilar artery; Bil: bilateral; DIC: disseminated intravascular coagulation; ERCP: endoscopic retrograde cholangiopancreatography; ICA: internal carotid artery; ICH: intracerebral hemorrhage; IV: intravenous; L: left; LWK: last known well; MCA: middle cerebral artery; MI: myocardial infarction; mRS: modified Rankin Scale; NA: not available; NIHSS: National Institutes of Health Stroke Scale; PCA: posterior cerebral artery; R: right; SAH: subarachnoid hemorrhage; TICI: thrombolysis in cerebral infarction; t-PA: tissue plasminogen activator; TuR-Bt: transurethral resection of bladder tumor contents
stroke was reduced by preparing an in-hospital stroke alert program\(^{10,11}\) and better outcomes were achieved when it was consulted earlier to stroke specialists.\(^{12}\) In our study, the median time to consultation to the neuroendovascular team was 50 minutes (interquartile range: 85). Shortening this time may facilitate prompt performing the intervention. Therefore, preparing a protocol for in-hospital stroke and making an in-hospital cooperation system are necessary. Cooperation with the cardiology department is especially important for countermeasures for in-hospital LVO.

### Table 2  Treatment results and time-line of mechanical thrombectomy in comparison between in-hospital and community-onset ischemic stroke due to large vessel occlusion

<table>
<thead>
<tr>
<th>Age (mean)</th>
<th>In-hospital LVO cases (n = 10)</th>
<th>Community-onset LVO cases (n = 13)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female (number)</td>
<td>78.6</td>
<td>78.3</td>
<td>NS</td>
</tr>
<tr>
<td>Occlusion site</td>
<td>6 / 4</td>
<td>8 / 5</td>
<td>NS</td>
</tr>
<tr>
<td>Etiology</td>
<td>Cardioembolism 80%</td>
<td>Cardioembolism 63%</td>
<td>NS</td>
</tr>
<tr>
<td>NIHSS*</td>
<td>16 (7)</td>
<td>15 (4.5)</td>
<td>NS</td>
</tr>
<tr>
<td>ASPECTS*</td>
<td>8.3 (1.6)</td>
<td>7.0 (2.0)</td>
<td>NS</td>
</tr>
<tr>
<td>LWK-to-recognition/arrival time* (min)</td>
<td>60 (40)</td>
<td>225 (327.5)</td>
<td>0.040</td>
</tr>
<tr>
<td>Recognition/arrival-to-puncture time* (min)</td>
<td>130 (85)</td>
<td>150 (82.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Puncture-to-recanalization time* (min)</td>
<td>35 (25)</td>
<td>80 (46.25)</td>
<td>0.037</td>
</tr>
<tr>
<td>Recognition/arrival-to-recanalization time* (min)</td>
<td>180 (95)</td>
<td>255 (115)</td>
<td>NS</td>
</tr>
<tr>
<td>LVO-to-recanalization time* (min)</td>
<td>240 (75)</td>
<td>495 (350)</td>
<td>NS</td>
</tr>
<tr>
<td>TICI grade 2b-3</td>
<td>70.0%</td>
<td>84.6%</td>
<td>NS</td>
</tr>
<tr>
<td>Symptomatic complication</td>
<td>10.0%</td>
<td>7.7%</td>
<td>NS</td>
</tr>
<tr>
<td>mRS 0-2 at discharge</td>
<td>30.0%</td>
<td>23.1%</td>
<td>NS</td>
</tr>
<tr>
<td>mRS 5-6 at discharge</td>
<td>40.0%</td>
<td>15.4%</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Data are presented as median (interquartile range). ASPECTS: Alberta Stroke Programme Early CT Score; BA: basilar artery; ICA: internal carotid artery; LVO: large vessel occlusion; LWK: last well known; MCA: middle cerebral artery; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; NS: not significant; PCA: posterior cerebral artery; TICI: thrombolysis in cerebral infarction
Mechanical thrombectomy for in-hospital LVO
Many in-hospital LVO patients cannot be treated with t-PA due to the comorbid disease, such as surgery or invasive procedure so that thrombectomy plays the major role. As the percentage of favorable outcome in in-hospital LVO in this series was not significantly different from those for community-onset LVO, thrombectomy is an effective treatment method for in-hospital LVO. Puncture-to-recanalization time was significantly shorter in the in-hospital LVO cases and recognition-to-recanalization time (vs arrival-to-recanalization time) was also shorter in the in-hospital LVO cases, although the difference was not significant. The cause of these differences may be due to delay of recanalization after arterial puncture in the community-onset LVO (80 minutes), and also due to the influence of a small number of patients and variation among the patients, such as that the community-onset LVO cases included several cases which took 2 hours or longer to reach recanalization after puncture. The rate of mRS 0-2 at discharge was not different between the in-hospital and community-onset LVO cases, whereas mRS 5-6 at discharge was higher in the in-hospital LVO cases. In the previous studies, the mortality was high and the rate of discharge to home was low in thrombectomy-treated in-hospital LVO patients compared with those in community-onset LVO patients. The comorbid disease was considered to be a major cause of poor prognosis. In our series, LWK-to-recognition time in the in-hospital LVO cases was significantly shorter than LWK-to-arrival time in the community-onset cases and puncture-to-recanalization time was also shorter. However, the rate of achieving a good outcome was similar and the poor outcome was more in patients with in-hospital LVO. This finding may have been due to the fact that many in-hospital patients had comorbid disease associated with the unfavorable outcome, as previously reported.

Limitation of this study
The drawback of the present study was the retrospective study of limited number of LVO patients treated only by thrombectomy. A prospective study including not only thrombectomy cases but all in-hospital ischemic stroke cases should be necessary for future evaluation.

Conclusion
In-hospital ischemic stroke due to LVO treated by mechanical thrombectomy occurred frequently in patients during hospitalization at the cardiology department. The main comorbid diseases of the in-hospital LVO cases were heart disease and malignant tumor. Withdrawal of anticoagulant/antiplatelet agents for invasive procedure was one of the causes. In the present series, the time to initiation of thrombectomy after recognition (recognition-to-puncture time) in the in-hospital LVO cases was not different from arrival-to-puncture time in the community-onset cases. Despite time of LWK-to-recognition/recanalization in the in-hospital LVO cases was shorter than LWK-to-arrival/recanalization time in the community-onset LVO cases, a higher rate of clinical poor outcome was observed in in-hospital LVO cases while the rate of favorable outcome was similar. Comorbid diseases may be associated with poor outcome in in-hospital ischemic stroke due to LVO.
Disclosure Statement

All of the first and co-authors have no conflict of interest.

References


