Treatment Result in the Initial Stage of Kanazawa Mobile Embolectomy Team for Acute Ischemic Stroke

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Abstract

Five recent multicenter randomized controlled trials (RCTs) have clearly shown the superiority of mechanical thrombectomy in large vessel occlusion acute ischemic stroke compared to systemic thrombolysis. Although 14 hospitals in Ishikawa prefecture have uninterrupted availability of systemic thrombolysis, mechanical thrombectomy is not available at all of these hospitals. Therefore, we established a Kanazawa mobile embolectomy team (KMET), which could travel to these hospitals and perform the acute reperfusion therapy. In this article, we report early treatment outcomes and validate the effectiveness of a network between affiliated hospitals and KMET. Between January 2014 and December 2015, 48 patients, aged 45–92 years (mean: 73.0 years), underwent acute reperfusion therapy provided by KMET in 10 affiliated hospitals of Kanazawa University Hospital. The pre-treatment NIHSS scores ranged from 5 to 39 (mean: 19.1). ASPECTS+W ranged from 1 to 11 (mean: 7.3). Successful revascularization, defined as thrombolysis in cerebral infarction (TICI) 2b or 3, was achieved in 38/48 cases (80%), and a good outcome, defined as modified Rankin Scale (mRS) score from 0 to 2 at 90 days after the treatment, was achieved in 24/48 cases (50%). There were two cases of intracranial bleeding (4%). Mean time from onset to recanalization was 297 min. These results, which are similar to those of five previous RCTs, suggest that a collaborative network between affiliated hospitals and KMET is effective for acute reperfusion therapy in local areas wherein experienced neuroendovascular specialists are insufficient.

Key words: ischemic stroke, embolectomy, recanalization

Introduction

Recently, five randomized clinical trials of endovascular acute reperfusion therapy against medical treatment have established the benefit of the endovascular treatment in patients with proximal artery occlusions.1–5 All trials have shown a substantial reduction in disability at 90 days after treatment. Based on these results, the American Heart Association/American Stroke Association (AHA/ASA) provided a focused update of the current recommendations for the endovascular treatment of acute ischemic stroke.6 It recommends that the patients who meet the criteria should receive endovascular therapy with a stent retriever.

In Japan, the Japan Stroke Society, the Japan Neurosurgical Society, and the Japanese Society for Neuroendovascular Therapy (JSNET) jointly published
a guideline concerning the proper use of embolectomy devices for acute ischemic stroke (version 2) in April, 2015.\textsuperscript{7} It recommends that a specialist certified by the Specialist Qualification System of the JSNET\textsuperscript{5} or a physician who has managed at least 100 cases with neuroendovascular treatment should perform the recanalization therapy. Although there are 14 hospitals regarded as primary stroke centers (PSCs), in which there is uninterrupted availability of intravenous r-tPA therapy in Ishikawa prefecture, neuroendovascular therapy specialists work full-time in only four hospitals. Therefore, we established a Kanazawa mobile embolectomy team (KMET), which could travel to these hospitals and perform reperfusion therapy. In this article, we report treatment outcomes in the initial stage and validate the effectiveness of a network between affiliated hospitals and KMET.

### Materials and Methods

#### Organization of KMET

KMET was organized by two consulting specialists (NU, MM), one specialist (KM), and one fellow (TK) acknowledged by the JSNET in January 2014. All members are board certified Japanese Neurosurgeons who work full-time in the department of Neurosurgery at Kanazawa University Hospital (KUh).

#### Treatment

When a stroke patient arrived at an affiliated hospital of KUh, which was thought to be equivalent to a PSC, the physician of first contact in the PSC started intravenous r-tPA therapy if patients were eligible, and call the KMET if the patient met the following criteria, 1) causative occlusion of the internal carotid artery (ICA), middle cerebral artery (MCA), vertebral artery (VA), or basilar artery (BA), 2) Age \( \geq 18 \) years, 3) NIHSS \( \geq 5 \), 4) Alberta Stroke Programme Early Computed Tomography Score (ASPECTS)+W (which is proposed by the ASIST-JAPAN; \url{http://assist.umin.jp} \( \geq 5 \), and 6) treatment can be initiated (groin puncture) within 6 hours of symptom onset. Two members of the KMET went to the PSC immediately following the call from the PSC. The physician in the PSC obtained informed written consent from the patient or a legal representative before treatment. The physician and KMET then performed acute reperfusion therapy together.

#### Statistics

We recorded baseline characteristics, time intervals, and interventional procedural data as well as outcome. In detail this comprised age, sex, pretreatment NIHSS score, ASPECTS+W, site of large vessel occlusion, onset time (or last known normal time), patient arrival time, time of MRI, time of the call to KMET, when iv-rtPA was started, time of groin puncture and recanalization, type of reperfusion treatment and devices, result of recanalization (thrombolysis in cerebral infarction: TICI), and disability (modified Rankin Scale: mRS) at 90 days following treatment. The data are expressed as means unless indicated otherwise.

The patients were divided by the mRS score into the good outcome group (mRS score from 0 to 2) or the poor outcome one (mRS score from 3 to 6). Various time intervals were compared between the two groups using Student's \( t \) test. The cause of stroke, site of vessel occlusion, TICI grade, and distance from KUh to the PSC were compared between the two groups using chi-square test. Additionally, the patients were divided by onset to recanalization (O2R) time into three groups—less than 4 h, from 4 to 5 h, and above 5 h. The proportion of the patients with good outcome were compared between the three groups using Kruskal-Wallis test. Odds ratios (ORs) of good outcome with corresponding 95\% confidence intervals (CIs) were calculated by using univariate and multivariate logistic regression for the following four clinical characteristics: NIHSS \( < 20 \), ASPECTS+W \( \geq 8 \), onset to recanalization \( < 240 \) min, and TICI 2b or 3.

Standard statistical tests (Student's \( t \) test, chi-square test, and the Kruskal-Wallis test for non-parametric data) were applied when applicable. Logistic regression was used for univariate and multivariate analyses. P values less than or equal to the \( \alpha \) level of 0.05 were considered significant. All statistical analyses were performed using SPSS 20 software (IBM, Armonk, NY, USA).

#### Results

Between January 2014 and December 2015, 48 patients underwent acute reperfusion therapy provided by KMET for acute ischemic stroke in 10 affiliated hospitals of KUh. Ishikawa Prefectural Central Hospital, Kanazawa Municipal Hospital, Kanazawa Medical Center, Asanogawa General Hospital, and Kanazawa Neurosurgical Hospital in Ishikawa central medical district are located within 20 km of KUh. Komatsu Municipal Hospital in South Kaga medical district, Keiju Medical Center and Noto General Hospital in Middle Noto medical district are located between 20 and 80 km from KUh. Suzu General Hospital in North Noto medical district and Toyama Rosai Hospital in Toyama prefecture are further than 80 km from KUh (Fig. 1). These hospitals function as PSCs in Ishikawa and Toyama prefecture.

Patient characteristics are summarized in Table 1. The patients were 36 males and 12 females, aged...
Fig. 1 Kanazawa University Hospital and the affiliated hospitals in Ishikawa and Toyama prefectures. Circles of solid and dotted lines indicate 20 and 80 km from Kanazawa University Hospitals, respectively. A: Ishikawa Prefectural Central Hospital, B: Kanazawa Municipal Hospital, C: Kanazawa Medical Center, D: Asanogawa General Hospital, E: Kanazawa Neurosurgical Hospital, F: Komatsu Municipal Hospital, G: Keiju Medical Center, H: Noto General Hospital, I: Suzu General Hospital, and J: Toyama Rosai Hospital.

Fig. 2 Grading of Thrombolysis in Cerebral Infarction (TICI) and score on Modified Rankin Scale (mRS) at 90 days after treatment.

Table 1 Patient characteristics

| Patient no. | 48 |
|-------------|----|
| Age (mean ± SD) | 73.0 ± 8.9 |
| Male sex no. (%) | 36 (75) |
| NIHSS (mean ± SD) | 19.1 ± 7.8 |
| ASPECTS+W (mean ± SD) | 7.3 ± 2.4 |
| Cause of stroke – no. (%) | |
| Cardioembolic occlusion | 38 (79) |
| Atherothrombotic occlusion | 8 (17) |
| Dissection | 2 (4) |
| Site of vessel occlusion – no. (%) | |
| Internal carotid artery | 22 (46) |
| Proximal middle cerebral artery | 11 (23) |
| Distal middle cerebral artery | 8 (17) |
| Vertebral artery | 1 (2) |
| Basilar artery | 6 (12) |

ASPECTS: Alberta Stroke Program Early Computed Tomography Score, NIHSS: National Institutes of Health Stroke Scale.

Neurol Med Chir (Tokyo) 56, December, 2016
Fig. 3 Mean time course of all patients in the acute recanalization therapy. call: the time to call KMET (Kanazawa mobile embolectomy team).

Table 2. Pre-treatment NIHSS score, ASPECT+W, TICI grade were significantly different between the two groups. Mean time from onset to recanalization of the good outcome and poor outcome groups were 291 min and 304 min, respectively, which were not significantly different. Various time intervals other than puncture to recanalization were not significantly different.

The relationship between rates of good outcome and O2R time is shown in Table 3. When O2R was less than 4 h, there was a good outcome 62% in all patients. It decreased to 42%, when O2R was from 4 to 5 h. However, it increased again to 50%, when O2R was more than 5 h. As analyzed by cause of stroke, the rate of good outcome in the 38 patients with cardioembolic occlusion (CEO) gradually decreased as O2R time increased (58% → 47% → 36%), although it was not statistically significant. On the other hand, there was no relationship between the rate of eight patients with atherothrombotic occlusion (ATO) and the time course (100% → 33% → 100%).

The relative contribution of different variables to good outcome at 90 days is shown in Table 4. On univariate analysis, baseline NIHSS score <20, ASPECTS+W ≥ 8, and TICI 2b or 3 were significantly associated with a good outcome at 90 days. The multivariate logistic regression analysis identified ASPECTS+W ≥ 8 (OR, 4.46; 95% CI, 1.116–17.82, p = 0.0344), and TICI 2b or 3 (OR, 8.204; 95% CI, 1.146–58.71, p = 0.0361) as independent factors for a good outcome at 90 days.

Discussion

The rate of revascularization in our study was 80%, similar to five previously published randomized controlled trials (RCTs), ranging from 59% in MR CLEAN to 86% in EXTEND-IA and 88% in SWIFT PRIME.1–5 The good outcome rate, defined as mRS 0–2 at 90 days after treatment, was 50%, again similar to the RCTs, ranging from 33% in MR CLEAN to 71% in EXTEND-IA (Table 5).1–5 These results indicate that acute recanalization therapy of the KMET can be safely applied under real-world conditions in our local area.

Although improved clinical outcomes are observed with decreased time to reperfusion in general, there was no significant difference in the total time course between the good outcome group and the poor outcome one in our study. Only time from puncture to recanalization in the poor outcome group was significantly longer than that in the good outcome one, because it took more time for refractory cases in which occluded vessels could not be opened in the poor outcome group. In patients with CEO, the greater the time to reperfusion extended, the lower the better outcome rate decreased. On the other hand, all patients with ATO achieved a good outcome, even if the time to reperfusion was more than 5 h. Most cases of ATO have better collateral flow compare to CEO, in particular in cases of vertebrobasilar occlusion.20 In fact, three cases of atherothrombotic basilar occlusion in this study, whose time from onset to recanalization was 280–666 min, had a good outcome. The relatively high proportion of such patients with ATO (22%) in our study might make the relationship between the time course and the outcome obscure.

Time from onset to groin puncture is one of the most important time-interval metrics. The mean and median time from onset to groin puncture in our study were 224 and 205 min, respectively. Though it took about 60–70 min for the KMET to reach the affiliated hospitals, the median time of 205 min is similar to those in the five published RCTs, ranging from 200 min in ESCAPE to 269 min in REVASCAT (Table 5). This result suggests that the treatment system of a mobile embolectomy team does not extend the total time of the recanalization therapy. Furthermore, we may reduce time to revascularization. Mean time from patient arrival to MRI and to groin puncture in our study were 67 and 157 min, 42 and 37 min longer than the recommended time,10 respectively. We will be able to reduce the door-to-imaging (MRI) time after carefully investigating workflow in the PSC. In addition, physicians in the PSC should call the KMET immediately after learning of large vessel occlusion on MRI. The sooner the KMET depart to the affiliated hospital, the earlier the endovascular treatment can start. Reduction of the total time from onset to recanalization can increase the rate of patients with favorable outcome.11

In our study, relatively small ischemic lesions (ASPECTS+W ≥ 8) and good recanalization (TICI
Table 2  Comparison of characteristics between good and poor outcome groups

|                          | Good outcome | Poor outcome | p     |
|--------------------------|--------------|--------------|-------|
| Patient no.              | 24           | 24           |       |
| Age (mean ± SD)          | 73.3 ± 8.1   | 72.8 ± 9.9   | 0.8484|
| Male sex no. (%)         | 21 (88)      | 15 (63)      | 0.0956|
| NIHSS (mean ± SD)        | 16.0 ± 7.4   | 22.2 ± 7.1   | 0.0051|
| ASPECTS+W (mean ± SD)    | 8.4 ± 4.1    | 6.3 ± 2.2    | 0.001 |
| Cause of stroke - no. (%)|              |              | 0.1284|
| Cardioembolic occlusion  | 18 (75)      | 20 (84)      |       |
| Atherothrombotic occlusion| 6 (25)      | 2 (8)        |       |
| Dissection               | 0 (0)        | 2 (8)        |       |
| Site of vessel occlusion - no. (%) |       |              | 0.5334|
| Internal carotid artery  | 9 (37)       | 13 (54)      |       |
| Proximal middle cerebral artery | 6 (25) | 5 (21)      |       |
| Distal middle cerebral artery | 4 (17) | 4 (17)      |       |
| Vertebral artery         | 1 (4)        | 0 (0)        |       |
| Basilar artery           | 4 (17)       | 2 (8)        |       |
| Iv-rtPA                  | 11 (46)      | 13 (54)      | 0.7732|
| TICI - no. (%)           |              |              | 0.0244|
| 0                        | 0 (0)        | 4 (17)       |       |
| 1                        | 0 (0)        | 0 (0)        |       |
| 2A                       | 2 (8)        | 4 (17)       |       |
| 2B                       | 8 (33)       | 11 (46)      |       |
| 3                        | 14 (59)      | 5 (20)       |       |
| Time course - minutes (mean ± SD) |       |              |       |
| LKN to door              | 70.4 ± 69.1  | 64.3 ± 67.6  | 0.7609|
| Door to picture (MRI)    | 67.0 ± 30.7  | 57.7 ± 30.4  | 0.2958|
| Door to call KMET        | 101.0 ± 104.9| 93.3 ± 51.0  | 0.7502|
| Door to puncture         | 159.4 ± 103.4| 152.8 ± 43.5 | 0.775 |
| Puncture to recanalization| 62.3 ± 25.5 | 83.8 ± 34.1  | 0.0175|
| LKN to needle (iv-rtPA)  | 149.6 ± 41.7 | 157.6 ± 45.6 | 0.6612|
| LKN to puncture          | 228.1 ± 110.2| 220.0 ± 75.3 | 0.7691|
| LKN to recanalization    | 290.9 ± 109.9| 303.8 ± 88.5 | 0.6548|
| Distance from KUH - no. (%)|              |              | 0.083 |
| <20 km                   | 16 (67)      | 9 (38)       |       |
| >20 km                   | 8 (33)       | 15 (62)      |       |

ASPECTS: Alberta Stroke Program Early Computed Tomography Score, TICI: thrombolysis in cerebral infarction, LKN: last known normal, KUH: Kanazawa University Hospital, KMET: Kanazawa mobile embolectomy team.

2b or 3) were factors significantly associated with a 90-day good outcome. These results are consistent with the previous reports. We treated the 10 patients with an ASPECTS+W score less than 6. Although all but one patient could not independently perform activities of daily living, conventional conservative therapy alone may worsen their prognosis. As indicated by the AHA/ASA guidelines, the endovascular recanalization therapy may be reasonable for patients with a low ASPECTS score, if the treatment can be initiated within 6 h of symptom onset.

In summary, total time course and treatment results of acute reperfusion therapy provided by KMET were almost the same as those reported in five recently published RCTs. Our findings suggest that a collaborative network between affiliated hospitals and KMET is effective for acute
Table 3  Relationship between onset to recanalization (O2R) time and good outcome rate

| O2R       | <4 h | 4–5 h | 5 h< | P value |
|-----------|------|-------|------|---------|
| CEO       |      |       |      |         |
| patient no. | 12   | 15    | 11   |         |
| mRS 0-2   | 7    | 7     | 4    | 0.5773  |
| good outcome rate | 58%  | 47%   | 36%  |         |
| ATO       |      |       |      |         |
| patient no. | 1    | 3     | 4    |         |
| mRS 0-2   | 1    | 1     | 4    | 0.3292  |
| good outcome rate | 100% | 33%   | 100% |         |
| Total     |      |       |      |         |
| patient no. | 13   | 19    | 16   |         |
| mRS 0-2   | 8    | 8     | 8    | 0.6516  |
| good outcome rate | 62%  | 42%   | 50%  |         |

ATO: atherothrombotic occlusion, CEO: cardioembolic occlusion, mRS: modified Rankin Scale.

Table 4  Results of possible factors for a good outcome after acute recanalization therapy using univariate logistic regression analysis

| Variables                                      | n   | Odds ratio | 95% CI (min–max) | p     |
|-----------------------------------------------|-----|------------|------------------|-------|
| NIHSS <20                                     | 26  | 4.0        | 1.210–13.539     | 0.0232|
| ASPECT+W ≥ 8                                  | 26  | 6.0        | 1.711–21.040     | 0.0051|
| Onset to recanalization ≤ 240 min             | 13  | 1.9        | 0.518–6.975      | 0.4175|
| TICI 2B & 3                                   | 38  | 5.5        | 1.027–29.456     | 0.0465|

ASPECTS: Alberta Stroke Program Early Computed Tomography Score, NIHSS: National Institutes of Health Stroke Scale, TICI: thrombolysis in cerebral infarction.

Table 5  Summary of results of the present study and recent randomized control trials in endovascular thrombectomy for ischemic stroke

| Test               | n    | Median onset-to-groin puncture time (min) | TICI 2b or 3 | mRS 0-2 at 90 days | Mortality at 90 days |
|--------------------|------|------------------------------------------|--------------|--------------------|----------------------|
| MR CLEAN           | 233  | 260                                      | 59%          | 33%                | 21%                  |
| EXTEND IA          | 35   | 210                                      | 86%          | 71%                | 9%                   |
| ESCAPE             | 165  | 200                                      | 72%          | 53%                | 10%                  |
| SWIFT PRIME        | 98   | 224                                      | 88%          | 60%                | 9%                   |
| REVASCAT           | 103  | 269                                      | 66%          | 44%                | 18%                  |
| KMET               | 48   | 205                                      | 80%          | 50%                | 8%                   |

mRS: modified Rankin Scale, TICI: thrombolysis in cerebral infarction.

reperfusion therapy in a local area wherein experienced neuroendovascular specialists are insufficient.

**Acknowledgments**

We express our sincere thanks to all of directors of departments of Neurosurgery in affiliated hospitals for their cooperation to our study; Ryuichi Kitani & Yoshio Nakajima (Toyama Rosai Hospital), Hiroaki Onishi (Asanogawa General Hospital), Sotaro Higashi & Yosie Okada (Keiju Medical Center), Masato Ikeda & Hiroyuki Sano (Kanazawa Municipal Hospital), Yutaka Hayashi (Ishikawa Prefectural Central Hospital), Hiroshi Fujisawa & Shuichi Akaike (Kanazawa Medical Center), Hisashi Nitta & Takuya Watanabe (Komatsu Municipal Hospital), Cheho Park (Noto General Hospital), and Shuji Satoh & Jiro Yamamoto (Kanazawa Neurosurgical Hospital).
This study was partially funded by grants from the Japan Agency for Medical Research and Development, AMED.

Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices in the article. All authors who are members of The Japan Neurological Society (JNS) have registered online Self-reported COI Disclosure Forms through the website for JNS members.

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