Endovascular recanalisation therapy for prolonged basilar artery occlusion based on clinical-diffusion MRI mismatch

Xuegan Lian\textsuperscript{a,b,1}, Debing Xu\textsuperscript{b,1}, Jian Wu\textsuperscript{a,1}, Min Lin\textsuperscript{b}, Qin Yin\textsuperscript{b}, Gelin Xu\textsuperscript{b}, Xinfeng Liu\textsuperscript{b,\*}, Renliang Zhang\textsuperscript{b,\*}

\textsuperscript{a}Department of Neurology, Third Affiliated Hospital, Soochow University, Changzhou 213003, China
\textsuperscript{b}Department of Neurology, Jinling Hospital, Nanjing University School of Medicine, Nanjing 210002, China

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Objectives: Clinical-diffusion magnetic resonance imaging (MRI) mismatch (CDM) in patients with anterior circulation occlusions is an optional method used to select patients for recanalisation outside the 3-h time window. A similar concept has not been reported with posterior circulation occlusions.

Methods: CDM was defined as a Glasgow Coma Scale (GCS) score $<8$ with DWI lesions not located in the dorsal pons, midbrain or thalamus at the time of admission. Eligible patients were treated with endovascular recanalisation therapy (ERT). The treatment included intra-arterial rt-PA thrombolysis and angioplasty and stenting performed separately or combined. The recanalisation result was assessed by angiography immediately after the treatment according to the trial reports in the Thrombolysis in Myocardial Infarction Criteria (TIMI). The complications and outcome 3 months later were recorded.

Results: Nine patients with a mean age of 66.6 years were included in the study (7 men and 2 women). The median durations of clinical presentation and coma were 31 h (range 25–53 h) and 6 h (range 2–13 h). The median GCS score at admission was 6 (range 4–7). Occlusions were located in the proximal basilar artery (BA) ($n=2$) and the middle BA ($n=7$). ERT was successful in 8 patients (TIMI 2, $n=2$ and TIMI 3, $n=6$) but failed in 1 patient because recanalisation was not possible (TIMI 0). No intracranial haemorrhage or dissections occurred during treatment. The recanalised patients recovered consciousness within 9–27 h after treatment. The median GCS score upon discharge was 14 (range 3–15). Three months later, 6 patients had a good outcome (modified Rankin Score (mRS) 0–2), and 2 patients had a moderate outcome (mRS 3). The patient who did not undergo recanalisation died in the rehabilitation hospital 21 days later.

Conclusions: CDM may be a valid method for selecting patients with prolonged basilar artery occlusion (BAO) who are eligible for recanalisation treatment. ERT was feasible for patients with BAO. A good clinical outcome was achieved with successful recanalisation.

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Basilar arterial disease accounts for 5–10\% of all strokes [1–3]. Fatality rates without treatment are near 90\% and the likelihood of a good outcome is nearly zero (2\%) without artery recanalisation [4–6]. To expand the time window for recanalisation treatment, the mismatch in magnetic resonance imaging (MRI) between the perfusion-weighted imaging (PWI) lesion and the smaller diffusion-weighted imaging (DWI) lesion was used as a criterion to select patients for the emergency therapies beyond 3 h in clinical trials [7–10]. Based on the perfusion–diffusion-weighted MRI (PDM) mismatch, the Echoplanar Imaging Thrombolytic Evaluation Trial (EPITHTET) [7, 11] reported that patients with middle cerebral artery (MCA) occlusion could achieve good prognosis when treated by intravenous thrombolysis (IVT) within a 3- to 6-h window. Another study evaluated the safety and efficacy of intravenous desmoteplase in patients 3–9 h after the onset of acute ischaemic stroke and was also based on PDM [10, 12]. The Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) Study [13] was also based on PDM. Recently a new convenient diagnostic approach, clinical-diffusion mismatch (CDM), has been proposed to indicate the potentially salvageable ischaemic brain tissue was proposed as a simpler tool than perfusion-diffusion mismatch [14–17]. CDM was used for anterior circulation because it was based on the mismatch between National Institutes of Health Stroke Scale (NIHSS) score and the DWI lesion volumes. However in posterior circulation stroke patients, the DWI lesion volume did not significantly correlate with the NIHSS score, suggesting that the NIHSS score is more weighted towards anterior circulation stroke symptoms [16]. Therefore CDM
based on the NIHSS score and the DWI lesion volume has not been reported in posterior circulation stroke. A previous study reported that the Glasgow Coma Scale (GCS) score is a more important predictor of outcome than the initial NIHSS score [18]. A GCS score <8 indicated that the dorsum pons, midbrain or thalamus was in an ischaemic or infarcted state. Therefore in this study, we used the CDM concept to select patients with a posterior circulation stroke outside the time window for recanalisation treatment, which has been reported as <24 h after stroke onset [19]. In this study, CDM was defined as a GCS score <8 and the DWI lesions were not localised in the dorsal pons, midbrain or thalamus at admission.

1. Subjects and methods

Patients were selected from the Nanjing Stroke Registry Program between December 2009 and November 2010. All patients were diagnosed and treated before admission in other hospitals. The GCS score evaluation and multimodal MRI were performed at admission. A computed tomography (CT) scan was performed if necessary. The inclusion criteria for endovascular recanalisation therapy (ERT) were as follows: (1) clinical diagnosis of prolonged basilar artery occlusion (BAO) (duration from onset >24 h); (2) GCS score <8 and DWI lesions not localised in the dorsal pons, midbrain or thalamus at admission; (3) exclusion of intracranial haemorrhage using MRI and/or CT; (4) BAO confirmed by digital subtraction angiography (DSA); (5) no clinical or laboratory contraindications for intra-arterial rt-PA thrombolysis; (6) informed consent from a legal representative. Nine patients with prolonged BAO underwent ERT according to these criteria in our department. The recanalisation result was assessed by angiography immediately after treatment according to the Thrombolysis in Myocardial Infarction Criteria (TIMI) Criteria. The GCS score was reassessed at discharge. The modified Rankin Score (mRS) was assessed 90 days after treatment. This study protocol was approved by the Medical Ethics Committee of Jiangling Hospital.

1.1. Endovascular recanalisation therapy

ERTs were performed in the interventional centre of our department on a dynaCT angiography machine (Siemens Axiom Artis dTA, Siemens Healthcare, Germany). The patients were all treated under local anaesthesia. The right femoral artery was punctured routinely and a 6 Fr catheter sheath was placed. Baseline angiography was performed to assess the site of vessel occlusion and collateral circulation. A 6 Fr guiding catheter (MPA, Cordis, USA) was advanced through the sheath into the parent artery or a convenient vertebral artery. The tip of the guide catheter was located at the distal end of the V2 segment. A 0.014-in. diameter microwire (PTGraphix, Boston Scientific, USA) with a microcatheter (Prowler 14, Cordis, USA) was navigated through the occluded vessel. After placing the microcatheter distal to the thrombus site, the microwire was retrieved and the contrast medium was injected through the microcatheter to verify the distal vessel of the occluded segment. A long microwire (Transend 300, Boston Scientific, USA) was then navigated through the microcatheter, and the tip was located at the P2 segment of a convenient posterior cerebral artery (PCA). The microcatheter was then retrieved. A balloon catheter (Maverick, Cordis, USA) was advanced over the microwire to the occlusion site, and percutaneous balloon angioplasty (PTA) was performed. Angiography was performed to confirm the result of recanalisation. If severe stenosis (stenotic ratio >70%) was found, a stent was placed to remodel the vessel. The occlusion length and vessel diameter were measured before treatment to allow entry of the moderate size of the balloon and the stent to avoid vessel rupture. If the distal BA was not visible before treatment, PTA was performed using the shortest available balloon (usually 2 mm) from the distal to the proximal BA. The balloons used in this study were Maverick and Gateway balloons (Boston Scientific, USA). The stents used in this study were Apollo (Microport, Shanghai, China) and Wingspan (Boston Scientific, USA) stents. If the post-treatment angiography confirmed an embolus in the distal vessel, additional intra-arterial thrombolysis (IAT) was performed through the microcatheter, which was navigated proximal to or into the embolus. The agent for thrombolysis in this study was rt-PA or urokinase (UK). UK was administered up to a dose of 500,000 IU, and rt-PA was administered up to a dose of 20 mg. After ERT, angiography was performed to confirm the recanalisation result and exclude local and distal vessel complications (such as dissection or vessel rupture).

In 1 patient, the microwire and microcatheter could not be navigated into the occlusion site. Therefore, an IAT was performed from the microcatheter, in which the tip of the microcatheter was proximal to the occlusion site. No thrombus regression was observed using angiography after rt-PA was administered up to a dose of 20 mg in 20 min. The microcatheter could not be navigated into the thrombus after IAT. So the procedure was abandoned.

1.2. Postoperative management and follow up

After ERT, the patients were transferred to the neurointensive care unit of our department. A neurological examination was performed every 30 min for the first 3 h and every 1 h for the next 21 h. Brain CT was performed in cases of neurological deterioration or 24 h after IAT to exclude intracranial haemorrhage. The GCS score was reassessed at discharge. The clinical outcome was assessed according to the mRS 3 months after the intervention. A good outcome was defined as an mRS of 0–2, a moderate outcome as an mRS of 3 and a poor outcome as an mRS of 4–6.

2. Results

Nine patients (7 men and 2 women, mean age 66.6 ± 9.1 years) with prolonged BAO underwent ERT. The median durations of clinical presentation and coma were 31 h (range 25–53 h) and 6 h (range 2–13 h), respectively. The median GCS score at admission was 6 (range 4–7), and it was 14 (range 3–15) at discharge. BAO was observed in the middle BA in 7 patients and the proximal BA in 2 patients. One of the 2 patients with proximal BAO showed a concurrent occlusion of the bilateral VA, of which the right posterior anterior cerebellar artery (PICA) was not affected (Fig. 1). The distal BA beyond the occlusion site was visualized through the leptomeningeal anastomosis from the proximal vessel (such as the PICA or anterior inferior cerebellar artery (AICA)) to the distal vessel (such as the AICA or superior cerebellar artery (SCA)) in 5 (5 out of 9) patients and through the posterior communicating artery (PCoA) from the left inferior carotid artery (ICA) to the left posterior cerebral artery (PCA) in 1 (1 out of 9) patient. The distal BA could not be visualized in 3 (3 out of 9) patients because there was no collateral flow. PTA was successfully performed in 8 (88.9%) patients, of which 3 (33.3%) were treated with PTA and stenting. Additional pharmacological thrombolysis was performed in 5 (5 out of 9) patients; UK was used in 1 (1 out of 9) patient, and the remaining 4 (4 out of 9) patients were treated with rt-PA. Recanalisation was achieved in 8 (8 out of 9) patients (TIMI 2, 2 patients and TIMI 3, 6 patients), but it was not achieved in 1 (1 out of 9) patient (case 3). The median duration of treatment (from femoral artery puncture to vessel recanalisation) was 72 min (range 44–104 min). No haemorrhage complications were observed during or after treatment. Three months later, 6 patients had a good outcome (mRS 0–2), 2 patients had a moderate outcome (mRS 3). The patient who did not undergo recanalisation died in
the rehabilitation hospital 21 days later. The patient demographics and clinical outcomes are shown in Table 1. The manipulation characteristics and angiographic outcomes are shown in Table 2.

3. Discussion

Although a coma duration of more than 3 h is believed to be futile [20], in this study, we successfully recanalised 8 out of 9 patients with CDM. All of the recanalised patients regained consciousness, and 6 had a good outcome at 3 months after treatment. Additionally, 2 patients had a moderate outcome, while only 1 patient, in whom recanalisation was not performed, died in the rehabilitation hospital.

The natural history of BAO is poor. The associated mortality ranges from 40% to 86% and is increased with coma [21]. Recanalisation is significantly associated with increased survival (an absolute decrease in mortality of nearly 50%), and the clinical outcomes are favourable in 57–71% of survivors [5,22]. Therefore recanalisation of the occluded vessel should be attempted considering the benefit after recanalisation. Intravenous pharmacological thrombolysis treatment could improve the outcome of patients with acute ischaemic stroke in the 3–4.5 h time window [23–25]. IAT and mechanical thrombolysis could expand the time window to
6 h or longer in the anterior circulation [19]. However, few patients have received IVT or IAT because of the limited time window. To select patients eligible for recanalisation, multimodal imaging plays an increasingly important role in the initial evaluation of patients with acute stroke [19]. CDM was a good concept for simplifying the procedure of evaluating ischaemic brain tissue, although the validity of CDM in predicting the beneficial effects of reperfusion has been contradictory in some studies [17,26–28,16]. In the posterior circulation, there was no rigid time window for recanalisation, although it was reported to be less than 24 h from onset in the Guidelines of the American Heart Association (AHA) in 2007 [19]. Outside the time window, it is important to select patients eligible for recanalisation treatment because recanalisation raises the risk of haemorrhage. In this study, we used the concept of CDM to select patients for recanalisation based on the mismatch between the consciousness level and DWI lesions. We found that the occlusion sites were all located in the middle and proximal BA, which led to the infarct in the cerebellum and brainstem. The dorsal pons, midbrain and thalamus were not affected, as shown using DWI MRI. However, the clinical presentation indicated that the brain tissue in these areas was ischaemic. Angiography also demonstrated that the distal BA beyond the occlusion sites was opacified, which was visible in the collateral circulation from the leptomeningeal anastomosis or the PCoA in 6 patients. Additionally, 3 patients without visible collateral circulation had a lower GCS score at admission. This mismatch demonstrated that these tissues could be salvaged after vessel recanalisation.

Successful recanalisation was performed in 8 patients, who recovered consciousness. The ratio of good and moderate outcomes was higher than that for IVT and IAT in the Basilar Artery International Cooperation Study (BASICS) [29], demonstrating that ERT is a valid method for the treatment of patients with prolonged BAO. Bergui et al. [30] called for mechanical thrombolysis as the first-line treatment for patients with acute BAO based on their study of 12 patients treated with ERT.

Although the duration of clinical presentation was long in our study, the prognosis was good after successful recanalisation, demonstrating that the brainstem may be more resistant to ischaemia than the cerebral hemispheres because of the higher proportion of white matter. In this study, the visual collateral circulation to the distal BA beyond the occlusion site might be attributed to the good prognosis of 6 of the patients. von Campe

### Table 1

<table>
<thead>
<tr>
<th>No/age (years)/gender</th>
<th>Risk factors</th>
<th>Hours from onset</th>
<th>Hours from coma</th>
<th>GCS score on admission</th>
<th>Haemorrhage complications</th>
<th>Hours of consciousness recovered after ERT</th>
<th>GCS score on discharge</th>
<th>mRS score at 3 months</th>
</tr>
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<tbody>
<tr>
<td>1/74/M</td>
<td>Smoking, hypertension, DM, CHD</td>
<td>28</td>
<td>10</td>
<td>6</td>
<td>No</td>
<td>23</td>
<td>14</td>
<td>2</td>
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<tr>
<td>2/50/M</td>
<td>Smoking, hypertension AF</td>
<td>53</td>
<td>5</td>
<td>7</td>
<td>No</td>
<td>14</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>3/74/M</td>
<td>Hypertension</td>
<td>37</td>
<td>13</td>
<td>5</td>
<td>No</td>
<td>No</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>4/67/P</td>
<td>Hypertension</td>
<td>25</td>
<td>3</td>
<td>7</td>
<td>No</td>
<td>11</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>5/77/M</td>
<td>Hypertension</td>
<td>29</td>
<td>6</td>
<td>4</td>
<td>No</td>
<td>27</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>6/72/M</td>
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<td>27</td>
<td>2</td>
<td>7</td>
<td>No</td>
<td>9</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>7/55/M</td>
<td>Hypertension, smoking, AF</td>
<td>47</td>
<td>11</td>
<td>5</td>
<td>No</td>
<td>21</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>8/65/F</td>
<td>Hypertension, smoking, AF</td>
<td>31</td>
<td>6</td>
<td>6</td>
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<td>19</td>
<td>14</td>
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</tr>
<tr>
<td>9/65/M</td>
<td>Hypertension, CHD, AF</td>
<td>50</td>
<td>7</td>
<td>5</td>
<td>No</td>
<td>16</td>
<td>12</td>
<td>3</td>
</tr>
</tbody>
</table>

*Note: F, female; M, male; DM, diabetes mellitus; CHD, coronary heart disease; AF, atrial fibrillation; GCS, Glasgow Coma Scale; ERT, endovascular recanalisation therapy; mRS, modified Rankin Score.

* Died 21 days after ERT.

### Table 2

<table>
<thead>
<tr>
<th>No.</th>
<th>Occlusion sites</th>
<th>Collateral circulation</th>
<th>PTA/balloon</th>
<th>Stenting/stent</th>
<th>rt-PA (mg)</th>
<th>UK (IU)</th>
<th>TIMI grades</th>
<th>Duration of treatment (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Middle BA</td>
<td>AICA to SCA from Lepto</td>
<td>Yes/Maverick</td>
<td>No</td>
<td>No</td>
<td>200,000</td>
<td>3</td>
<td>72</td>
</tr>
<tr>
<td>2</td>
<td>Middle BA</td>
<td>AICA to LPCA from LPCoA</td>
<td>Yes/Maverick</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>2</td>
<td>44</td>
</tr>
<tr>
<td>3</td>
<td>Middle BA</td>
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<td>No</td>
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<td>No</td>
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<td>0</td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td>Middle BA</td>
<td>AICA to SCA from Lepto</td>
<td>Yes/Maverick</td>
<td>Yes/Apollo</td>
<td>No</td>
<td>No</td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>Middle BA</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>3</td>
<td>81</td>
</tr>
<tr>
<td>6</td>
<td>Proximal BA</td>
<td>PICA to AICA and SCA from Lepto</td>
<td>Yes/Gateway</td>
<td>Yes/Winspan</td>
<td>No</td>
<td>No</td>
<td>3</td>
<td>93</td>
</tr>
<tr>
<td>7</td>
<td>Proximal BA and distal V4</td>
<td>Right PICA to SCA from Lepto</td>
<td>Yes/Maverick</td>
<td>Yes/Apollo*</td>
<td>No</td>
<td>No</td>
<td>3</td>
<td>104</td>
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<tr>
<td>8</td>
<td>Middle BA</td>
<td>AICA to SCA from Lepto</td>
<td>Yes/Maverick</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>3</td>
<td>69</td>
</tr>
<tr>
<td>9</td>
<td>Middle BA</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>2</td>
<td>67</td>
</tr>
</tbody>
</table>

* Note: BA, basilar artery; VA, vertebral artery; PICA, posterior inferior cerebellar artery; AICA, anterior inferior cerebellar artery; SCA, superior cerebellar artery; Lepto, leptomeningeal anastomosis; L, left; ICA, internal carotid artery; PCoA, posterior communicating artery; PTA, percutaneous balloon angioplasty; UK, urokinase; TIMI, Trail in Myocardial Infarction Criteria.

* Recanalisation could not be achieved by PTA and rt-PA thrombolysis.

* Two Apollo stents were placed.
et al. [31] reviewed 25 patients with BAO and reported that 29% of the patients with clinical evidence of brainstem ischaemia progressed to coma or death within 6–24 h, 25% within 1–3 days, and only 37% within 0–6 h, indicating that there is a considerable time interval for intervention before a catastrophic event occurs.

In conclusion, our data showed that CDM could be a valid method for selecting patients eligible for recanalisation treatment outside the time window in cases of posterior circulation stroke. ERT was a feasible treatment for BAO, and a good clinical outcome was achieved after successful recanalisation.

4. Limitations

This is an initial experience of 9 patients with prolonged BAO treated with ERT based on CDM. CDM is not a long-tested concept, but it may be a useful method for selecting patients eligible for recanalisation treatment. This is the first time that CDM has been used in the treatment of posterior circulation stroke, the utility of which was not evaluated by other studies or in randomised and controlled trials.

Conflicts of interest

None.

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References