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Angiographic outcome of endovascular stroke therapy correlated with MR findings, infarct growth, and clinical outcome in the DEFUSE 2 trial

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Abstract

Background—DEFUSE 2 demonstrated that patients with magnetic resonance imaging mismatch had a favorable clinical response to tissue reperfusion assessed by magnetic resonance imaging. This study reports the endovascular results and correlates angiographic reperfusion with clinical and imaging outcomes.

Methods—Prospectively enrolled ischemic stroke patients underwent baseline magnetic resonance imaging and started endovascular therapy within 12 h of onset. Patients were classified as either target mismatch or no target mismatch using magnetic resonance imaging. The pre- and postprocedure angiogram was evaluated to determine thrombolysis in cerebral infarction scores. Favorable clinical response was determined at day 30, and good functional outcome was defined as a modified Rankin Scale 0–2 at day 90.

Results—One-hundred patients had attempted endovascular treatment. At procedure end, 23% were thrombolysis in cerebral infarction 0–1, 31% thrombolysis in cerebral infarction 2A, 28% thrombolysis in cerebral infarction 2B, and 18% thrombolysis in cerebral infarction 3. More favorable thrombolysis in cerebral infarction-reperfusion scores were associated with greater magnetic resonance imaging reperfusion ($P < 0.001$). thrombolysis in cerebral infarction scores correlated with 30-day favorable clinical response ($P = 0.041$) and 90-day modified Rankin Scale 0–2 ($P = 0.008$). These correlations were significant for target mismatch patients at 30 days ($P = 0.034$) and 90 days ($P = 0.003$). Infarct growth was strongly associated with poorer thrombolysis in cerebral infarction scores in target mismatch patients ($P < 0.001$). Patients with thrombolysis in cerebral infarction 2A reperfusion had less magnetic resonance imaging reperfusion ($P = 0.004$) and poorer clinical outcome at 90 days ($P = 0.01$) compared with thrombolysis in cerebral infarction 2B–3 patients.

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Conclusion—Thrombolysis in cerebral infarction reperfusion following endovascular therapy for ischemic stroke is highly correlated with magnetic resonance imaging reperfusion, infarct growth, and clinical outcome.

Keywords

acute stroke therapy; cerebral infarction; intervention; ischemic stroke; magnetic resonance imaging; therapy

Introduction

Endovascular treatment is increasingly utilized in the management of acute stroke. A randomized trial has shown benefit for a thrombolytic agent administered arterially in this setting (1). Single-armed prospective studies have shown that thrombectomy devices improve outcome when angiographic reperfusion is successfully attained as compared with patients where the thrombectomy device does not successfully recanalize or reperfuse ischemic territory (2–4). A meta-analysis has also shown that recanalization or reperfusion by any means (intravenous or intra-arterial) is associated with a lower rate of mortality and improved clinical outcome (5). Nevertheless, controversy exists because recent randomized studies have not shown a benefit to endovascular therapy (6–8). There are clearly questions as to which candidates are best suited for revascularization and whether imaging can help to identify those patients. The DEFUSE 2 study was a prospective study of acute stroke patients who underwent endovascular therapy following magnetic resonance imaging (MRI). It was hypothesized that a target mismatch (TMM) profile could be identified where patients had a relatively small area of injured tissue [as seen on diffusion-weighted imaging (DWI)] relative to a larger volume of ischemic tissue which was still salvageable [identified by perfusion-weighted imaging (PWI)], and that these patients would respond favorably to reperfusion. Primary clinical outcomes of this study as they correlated to the MRI findings before and after treatment have recently been reported (9), but the primary angiographic results were not included in this report. This paper describes the endovascular results of the study and correlates the angiographic outcomes with MR data obtained before and after endovascular therapy, infarct growth, and clinical outcomes.

Methods

DEFUSE 2 was a multicenter, prospective, single-arm study conducted at nine centers between July 2008 and September 2011. The study was approved by the institutional review boards of the individual institutions. Patients with anterior circulation strokes were able to be enrolled if they had a large vessel anterior circulation with occlusion at the time of MRI and endovascular therapy could be initiated within 12 h of symptom onset. Patients who met local criteria for acute endovascular therapy were eligible for enrollment. Patients underwent MRI prior to the endovascular procedure and could be enrolled in the study if they had a large vessel occlusion. If they had received earlier treatment with intravenous tissue plasminogen activator (tPA), the large vessel occlusion had to be persistent on the baseline MRI. Patients had to be adults (≥ 18 years old) and have a National Institutes of Health Stroke Scale (NIHSS) score ≥ 5.

Imaging

A head MRI was performed on 1.5 or 3.0 T MR system. A gradient recalled echo sequence, DWI sequence, and PWI sequence were performed, along with an magnetic resonance angiography (MRA) study in the Circle of Willis. Image reconstruction was done offline using a computer system generating quantitative DWI and PWI lesion maps (RAPID, Stanford University, Stanford, CA. USA) (10). Results of the MRI scan (before RAPID processing) could be used to influence the decision to proceed with endovascular therapy.

RAPID maps were provided within four to seven-minutes. The RAPID output included a DWI map with an outline and volume estimate of ischemic core (irreversibly injured tissue) based upon an apparent diffusion coefficient (ADC) threshold of $<600 \times 10^{-6} \text{ mm}^2/\text{s}$. It also included a PWI map with an outline and volume estimate of hypoperfused salvageable tissue (tissue which is likely to go on to infarction if not reperfused). The volume estimate of hypoperfused salvageable tissue was based on the time to maximum of the tissue residue function (T_{max}) threshold of $>\text{six-seconds}$. Values for ischemic core and hypoperfused salvageable tissue were validated using the results of the DEFUSE 1 study and pooled analysis of the DEFUSE and EPITHET studies (10–13). TMM was defined by a ratio between the hypoperfused tissue and ischemic core of 1.8 , with an absolute difference of 15 ml . Lesions with a TMM profile also had to have an ischemic core volumes $\geq 70 \text{ ml}$ and volume of tissue with severe hypoperfusion ($T_{\text{max}} > 10 \text{ s}$) of $\geq 100 \text{ ml}$.

An early follow-up scan with the same sequences was obtained within 12 h of endovascular therapy. An additional MRI study was obtained at discharge or on day 5, and included a fluid-attenuated inversion recovery (FLAIR) sequence.

Endovascular treatment

Intra-arterial intervention had to be started within 12 h of ictus onset and 90 min of completion of the baseline MRI. Start of intervention was defined as the time of the introduction of the femoral artery sheath. The study did not mandate a set technique or device choice for intervention, but the intervention conformed to the practices used at the local institution. Local sites were encouraged to use Food and Drug Administration (FDA)-approved devices for thrombectomy which included the Concentric Merci Retriever and the Penumbra Suction Thrombectomy catheter. In addition, sites were encouraged to minimize intra-arterial (IA)-tPA use. If no prior tPA had been used, centers were encouraged to use $<25 \text{ mg}$ of tPA maximum intra-arterially. If patients received prior IV-tPA, centers were encouraged to use $\leq 5 \text{ mg}$ intra-arterially.

Core lab evaluation

The core lab evaluated the MRI and cerebral angiography studies blinded to clinical information, with each modality evaluated independently and blinded to the results of the other modality. The core lab calculated infarct growth as the difference between the baseline DWI lesion and the five-day FLAIR infarct volume. MR reperfusion was defined as $>50\%$ reduction in the PWI lesion which had a T_{max} of $>\text{six-seconds}$, comparing the baseline study with the immediate follow-up MRI.

Angiograms sent to the core lab included the baseline or pre-treatment angiogram, and the final angiogram after endovascular therapy had been performed. The baseline angiogram prior to treatment was evaluated to identify the primary arterial occlusive lesion (AOL), and a baseline thrombolysis in cerebral infarction (TICI) score which indicated how well the territory was perfused from the AOL. The final angiogram available from the territory in question was evaluated for a final TICI score using previously described definitions for TICI flow (14). These were modified to define TICI 2A as partial perfusion of <50% of the vascular distribution of the occluded artery, and 2B as partial perfusion of 50% of the vascular distribution. This value was chosen to correlate with the MRI definition of reperfusion. The full arterial tree in the arterial phase of the angiogram was used for the TICI score. TICI 2B-3 reperfusion was prespecified as constituting angiographic reperfusion.

Clinical assessment

Favorable clinical response (FCR) was predefined as an improvement in the NIHSS of 8 points or an NIHSS score of 1 at day 30. A modified Rankin scale (mRS) score was assigned at day 90, and good functional outcome was defined as mRS 2.

Statistics

Trends in proportions of FCR and good functional outcome across ordered TICI scores were tested using Cochran–Armitage test for trend. Differences in proportions of outcomes between any two groups were compared with Fisher’s exact test. Agreement on reperfusion status by TICI scores and PWI was tested using McNemar’s test. We used Jonckheere–Terpstra test for ordered alternatives to test the hypotheses that lesion growth diminishes and reperfusion degree seen on postprocedure MRI increases with increase of TICI scores. All tests were two sided, with statistical significance defined at $\alpha < 0.05$. Statistical tests were performed using SAS 9.3 (SAS Institute Inc., Cary, NC, USA) and IBM SPSS Statistics 20 (IBM Corporation, Armonk, NY, USA) statistical software packages.

Results

One hundred thirty-eight patients were prospectively enrolled, and 110 were sent for endovascular treatment. The reasons for the 28 patients not sent to angiography from the local sites were previously reported (9). In 10 patients, the endovascular therapist decided that treatment was not warranted after performing a diagnostic angiogram because no angiographic lesion was seen (four patients) or more distal lesions (M2, M3, or M4 branches) were encountered, and the interventionalist felt they should not be treated (six patients). This left 100 patients who had treatment attempted. One of these patients had difficulty with femoral artery access and bleeding, and the interventionalist decided they could not safely proceed. A second patient was found to have a carotid occlusion just distal to the aortic arch which the interventionalist felt could not be opened safely. Table 1 shows the baseline characteristics, lesion locations, and endovascular therapies employed in the 100 patients. Mismatch profiles were available in 94 patients (in six patients the baseline PWI was technically inadequate), with 75 showing a TMM profile and 19 not having TMM.

The pretreatment angiogram demonstrated TICI 0, 1 flow in 87 patients (87%), and TICI 2A or 2B flow in 13 (13%). Following treatment or attempted treatment, 23% remained TICI 0–1, 31% were TICI 2A, 28% TICI 2B, and 18% were TICI 3. The patient with difficulty with femoral artery access and the patient with a carotid occlusion just distal to the aortic arch were scored as TICI 0,1 pre-and postattempted treatment. In these two cases pre- and postattempted treatment MRA studies confirmed the TICI 0, 1 scores.

Table 2 shows clinical outcome at 30 and 90 days based on final TICI scores for the 100 patients with attempted treatment. TICI scores correlated with 30-day FCR ($P = 0.041$) and 90 mRS 0–2 ($P = 0.008$), with higher proportions of good outcome seen with higher TICI scores. These relationships were more favorable in the TMM group: 30 days ($P = 0.034$) and 90 days ($P = 0.003$). In the no TMM patients, there was no correlation between TICI scores and clinical outcome at 30 or 90 days. Sixty-three percent (22/35) of the TMM patients with angiographic reperfusion (TICI 2B–3) had good functional outcome, whereas 29% (2/7) of the no-TMM patients with angiographic reperfusion had good functional outcome ($P = 0.118$).

In the entire study group, there was no significant difference in the rate of good functional outcome comparing TICI 2A patients with the TICI 0–1 patients ($P = 1.0$), and there was also no difference in good functional outcome rates at 90 days between TICI 0–1 and 2A in TMM patients ($P = 0.286$). TICI 2A patients had significantly less good functional outcome at 90 days than the TICI 2B–3 patients ($P = 0.010$), and in the TMM patients there was a trend to lower rates of good functional outcome for the TICI 2A patients ($P = 0.062$). Figure 1 shows the stratified outcomes comparing the TICI 0–2A vs. the TICI 2B–3 patients achieving mRS 0–2 at 90 days (24% (95%CI 15–37) vs. 57% (95%CI 42–70), $P = 0.001$ among all patients, and 28 (95%CI 16–43) % vs. 63% (95%CI 46–77), $P = 0.003$ in the TMM patients. This relationship was maintained when we excluded three patients with pretreatment TICI 2B: 25% (95%CI 15–38) vs. 59% (95%CI 44–72), $P = 0.001$ among all patients, and 28% (95%CI 17–44) vs. 67% (95%CI 50–80), $P = 0.002$ in the TMM patients.

There were no differences in the rates of good functional outcome for patients with Internal Carotid Artery (ICA) vs. M1 lesions for the entire study group. There also were no differences in the rates of good functional outcome when patients with ICA vs. M1 lesions with TICI 0–2A reperfusion were compared or when patients with ICA vs. M1 lesions with TICI 2B–3 reperfusion were compared. Similarly, when we compared patients treated at six-hours with those treated at >six-hours, there were also no differences in the rates of good functional outcome for the entire study group or when the times to treatment were compared based on reperfusion status.

Overall mortality rate was 19 (19%, 95%CI 13–28) in the 100 patients. Causes of death as reported by the local centers included: the initial stroke (12 patients), cardiopulmonary complications or arrest (5 patients), bowel perforation (1 patient) and pelvic abscess (1 patient). Seventeen deaths occurred in patients TICI 0–2A (32%, 95% CI 21–45) vs. 2 with TICI 2B–3 (4%, 95% CI 1–15), $P < 0.001$. Six patients had parenchymal hematomas type 2 (2 patients) and type 2 (4 patients) using the European Cooperative Acute Stroke Study

criteria (15), as seen on either computed tomography or MRI performed within 5 days of the procedure. Four of these patients died (PH1 – 1 patient and PH2 – 3 patients).

In the 10 patients where the interventionalists decided that treatment was not warranted, 8 (80%) had 30-day FCR and 8 (80%) had 90-day mRS 0–2.

Figure 2 shows the relationship between TICI reperfusion and MR reperfusion. Overall, 34/40 [85% (95% CI 71–93)] of TICI 2B-3 patients achieved the prespecified end-point of >50% reperfusion between the baseline PWI and the immediate posttreatment MRI vs. 22/43 [51% (95% CI 37–65)] of the TICI 0-2A patients ($P = 0.004$). These relationships were similar among patients that received intravenous (IV) or IA tPA [26/30 (87%) vs. 17/33 (52%)] and those who did not receive tPA [8/10 (80%) vs. 5/10 (50%)].

Figure 3 shows the relationship between TICI scores and the amount of infarct growth seen at five-days. The median infarct growth was significantly lower for greater TICI scores ($P < 0.001$). These differences were seen in the TMM group ($P < 0.001$), but not in the no TMM patients ($P = 0.839$). Those patients with TMM and angiographic reperfusion (TICI 2B-3) had 32 ml median infarct growth (IQR 3–63) vs. the no TMM patients with angiographic reperfusion with 85 ml (52–109), $P = 0.062$.

In 100 patients, there were 15 complications reported by the operators. Six (6%) had an arterial perforation or contrast extravasation seen at the time of angiography. Three (3%) had carotid artery dissection, with two described as nonflow limiting (no additional therapy) and one which underwent stenting. Three (3%) had distal embolization, one into the same territory and two into unaffected territories. Three patients had femoral artery injury or bleeding, with one requiring surgical repair. One of six patients with perforation or contrast extravasation had a good functional outcome (mRS 2) at 90 days. One of the three patients with carotid dissection and none of the three patients with distal embolization had a good functional outcome at 90 days.

Discussion

The primary analysis of the DEFUSE 2 study showed that patients with TMM who achieved MR reperfusion (>50% reduction in PWI volume) had more favorable clinical outcomes (9). This current analysis of angiographic data shows that TICI reperfusion correlates well with MR reperfusion and those patients with TICI 2B-3 reperfusion and a TMM did better than patients with TICI 0-2A reperfusion. In this analysis of TICI scores, the patients with TICI 2A reperfusion had less favorable 90-day outcomes compared with those who had TICI 2B-3 flow.

A recent pooled analysis from two thrombectomy trials showed that increasing angiographic reperfusion was highly associated with improved outcomes (16). A number of reperfusion scales have been applied to acute stroke studies, including the Thrombolysis In Myocardial Infarction (TIMI) scale (1,3,4,17), the Mori scale (18), and the TICI scale (19). Most trials have not distinguished between degrees of partial angiographic reperfusion in measuring outcome. A pooled analysis of the IMS I and II patients did show a trend to better outcome for TICI 2B vs. TICI 2A patients (20). In addition, a recently published retrospective

analysis from a single center showed significantly lower rates of in-hospital mortality for TICI 2B-3 vs. TICI 2A reperfusion, and that the final infarct was more likely to be <70 ml for the TICI 2B-3 patients compared with the TICI 2A patients (21). Another recently reported retrospective analysis also found that TICI 2B-3 reperfusion had better sensitivity for predicting good outcome at 90 days (22). If the degree of angiographic reperfusion has prognostic significance, definitions of partial reperfusion are important. Different degrees of partial reperfusion have been assigned to TICI 2A flow (14,19). In this trial, we prospectively defined TICI 2A flow as partial perfusion of <50% of the vascular distribution of the occluded artery and 2B as partial perfusion of 50% of the vascular distribution. This definition was used because it correlated with the predefined MR reperfusion definition of >50% reduction in the PWI lesion.

The TICI reperfusion scores correlated with the amount of MR reperfusion seen, comparing PWI volumes from the baseline MRI with the posttreatment MRI. However, there were disparities, with 85% of the TICI 2B-3 reperfusion patients having >50% MRI reperfusion and 51% of the TICI 0-2A showing >50% MRI reperfusion. Stated another way, 15% of the time when TICI 2B-3 reperfusion was seen, it did not agree with the amount of MR reperfusion (it overestimated the amount of reperfusion) seen on follow-up MRI. Whereas, 51% of the time when TICI 0-2A was seen, it underestimated the amount of reperfusion seen on follow-up MRI. These results suggest it was more likely to have continued improvement in perfusion after completion of the endovascular procedure rather than a subsequent decline. A number of patients received IV or IA tPA, and this (along with any inherent thrombolysis) may have resulted in continued reperfusion. However, we did not see a difference in the numbers of patients showing MR reperfusion in the tPA group vs. the non-tPA group.

A number of different endovascular techniques were utilized in this study, with the majority of patients undergoing treatment with the FDA-approved MERCI and/or Penumbra thrombectomy systems. The overall rate of 77% TICI 2–3 reperfusion seen is in keeping with previously published reperfusion rates for these thrombectomy devices (3,4). There was a 12% rate of cerebrovascular complications (dissection, contrast extravasation, and distal embolization) reported by the endovascular therapists. Eleven patients in this group of 12 patients had a TMM, and only one patient had TICI 2B-3 reperfusion. Only two of these patients (both with TICI 2A flow) had a favorable clinical outcome at 90 days.

A major limitation of this study is the small sample size, particularly in the no TMM group. These patients may be less likely to respond favorably to endovascular therapy. However, due to the small sample size of the group, no definitive conclusions can be drawn from the no TMM patients.

While the study did show an association between higher levels of TICI reperfusion and favorable clinical outcomes in patients with TMM, it was not designed to assess the benefits of endovascular therapy because there was no untreated control group. A recent randomized trial using penumbral imaging did not show a benefit of endovascular reperfusion in either the penumbral or nonpenumbral group (8). This study treated patients with considerably larger baseline infarct cores, had longer delays between imaging and endovascular

treatment, and had poorer reperfusion rates; only 24% of the penumbral patients had TICI 2B-3 reperfusion. In addition, identification of penumbral patients was based on different methodology than our study (8).

While it seems that higher levels of angiographic reperfusion are likely of benefit in TMM patients, it is not possible to determine whether endovascular therapy was beneficial for these patients without a control group that did not receive endovascular therapy. A randomized trial is needed to establish whether endovascular therapy is beneficial. Our results suggest that MRI is a promising modality to select patients likely to benefit in a randomized trial, and the goal of endovascular therapy should be to achieve TICI 2B-3 flow in these patients.

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Fig. 1.
Percent of patients mRS 0–2 at 90 days. TICl, thrombolysis in cerebral infarction.

Fig. 2. Box plots showing relationship of TICI scores to MR reperfusion seen on immediate follow-up MRI. Box represents interquartile range, line within box represents median value, and bars show ranges of values. TICI, thrombolysis in cerebral infarction; MRI, magnetic resonance imaging.

Fig. 3.

Box plots showing relationship of TICI scores to infarct growth seen between baseline DWI and 5 day FLAIR images. Box represents inter-quartile range, line within box represents median value, and bars show ranges of values. TICI, thrombolysis in cerebral infarction; FLAIR, fluid-attenuated inversion recovery; DWI, diffusion-weighted imaging; TMM, target mismatch.

Table 1

Baseline characteristics and endovascular therapies employed in patients included in the angiographic profile cohort

Characteristic	All patients with attempted treatment (n = 100)	Post-TICI 0-2a (n = 54)	Post-TICI 2b-3 (n = 46)	P value
Mean (SD) age – year	65 (16)	66 (17)	63 (16)	0.318
Female gender – no. (%)	51 (51)	26 (48)	25 (54)	0.554
Hypertension – no. (%) [*]	66 (67)	39 (74)	27 (59)	0.138
Diabetes mellitus – no. (%) [*]	18 (18)	10 (19)	8 (17)	1.0
Hyperlipidemia – no. (%) [*]	50 (51)	28 (53)	22 (48)	0.689
Atrial fibrillation – no. (%) [*]	35 (35)	17 (32)	18 (39)	0.530
Prior stroke/TIA – no. (%) [*]	21 (21)	14 (26)	7 (15)	0.221
Median NIHSS score (IQR)	16 (11–20)	17 (12–19)	15 (9–21)	0.332
Intravenous tPA pretreatment – no. (%)	53 (53)	32 (59)	21 (46)	0.228
Median (IQR) time from symptom onset to start of MRI – hours [*]	4.5 (2.8–6.1)	4.4 (2.7–5.8)	4.7 (3.4–7.3)	0.164
Median (IQR) time from symptom onset to femoral puncture – hours	5.8 (4.5–7.8)	5.4 (3.9–7.3)	6.0 (4.7–8.3)	0.133
Median (IQR) time from arrival at study site to femoral puncture – hours	2.3 (1.6–3.1)	2.3 (1.6–3.1)	2.3 (1.8–3.2)	0.370
Median (IQR) volume of infarct core – ml	16 (8–34)	19 (8–42)	14 (7–32)	0.498
Median (IQR) volume of perfusion lesion – ml [†]	87 (50–116)	90 (48–134)	79 (50–112)	0.391
Vessel occlusion on angiogram [‡] – no. (%)				0.003
Internal carotid artery, proximal	17 (17)	14 (26)	3 (7)	
Internal carotid artery, distal	12 (12)	5 (9)	7 (15)	
Middle cerebral artery, proximal	58 (58)	24 (44)	34 (74)	
Middle cerebral artery, distal	12 (12)	10 (19)	2 (4)	
M2	8 (8)	7 (13)	1 (2)	
M3	4 (4)	3 (6)	1 (2)	
None	1 (1)	1 (2)	0 (0)	
Endovascular therapy employed [§] – no. (%)				0.363
Merci device	48 (48)	18 (33)	30 (65)	
Penumbra system	42 (42)	23 (43)	19 (41)	
Intra-arterial tPA	42 (42)	22 (41)	20 (44)	
Other	31 (31)	14 (26)	17 (37)	

^{*} Data unknown for 1 patient, therefore only 99 patients are used to determine percentages.

[†] Data unknown for seven patients.

[‡] Significant difference at $\alpha < 0.05$.

[§] Combinations of more than one endovascular therapy were used in 49% (43% among patients with TICI 0-2a vs. 57% with TICI 2b-3, $P = 0.229$).

NIHSS, National Institutes of Health Stroke Scale; IQR, interquartile range; tPA, tissue plasminogen activator; MRI, magnetic resonance imaging; TIA, transient ischemic attack; TICI, thrombolysis in cerebral infarction; SD, standard deviation.

Table 2

Clinical outcome based on TICI score

Final TICI score	30-day FCR			90-day mRS < 2		
	All patients	TMM*	No TMM	All patients	TMM	No TMM
0-1	9/23 (39%, 22-59)	6/18 (33%, 16-56)	3/5 (60%, 23-88)	5/23 (22%, 10-42)	3/18 (17%, 6-39)	2/5 (40%, 12-77)
2a	13/31 (42%, 26-59)	10/22 (45%, 27-65)	3/7 (43%, 16-75)	8/31 (26%, 14-43)	8/22 (36%, 20-57)	0/7 (0%, 0-35)
2b-3	31/46 (67%, 53-79)	24/35 (69%, 52-81)	4/7 (57%, 25-84)	26/46 (57%, 42-70)	22/35 (63%, 46-77)	2/7 (29%, 8-64)

*The number of TMM plus no TMM is 94 due to the fact that PWI failed in six patients and therefore the mismatch status is not known. Proportions, 95% CI. TICI, thrombolysis in cerebral infarction; TMM, target mismatch; FCR, favorable clinical response; mRS, modified Rankin Scale; PWI, perfusion-weighted imaging.