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Interhospital variation in reperfusion rates following endovascular treatment for acute ischemic stroke

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Abstract

Background—Patients who have successful reperfusion following endovascular therapy for acute ischemic stroke have improved clinical outcomes. We sought to determine if the chance of successful reperfusion differs among hospitals, and if hospital site is an independent predictor of reperfusion.

Methods—Nine hospitals recruited patients in the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution Study 2 (DEFUSE 2), a prospective cohort study of endovascular stroke treatment conducted between 2008 and 2011. Patients were included for analysis if they had a baseline Thrombolysis in Cerebral Infarction (TICI) score of 0 or 1. Successful reperfusion was defined as a TICI reperfusion score of 2b or 3 at completion of the procedure. Collaterals were assessed using the Collateral Flow Grading System and were dichotomized as poor (0–2) or good (3–4). The association between hospital site and successful reperfusion was first assessed in an unadjusted analysis and subsequently in a multivariate analysis that adjusted for predictors of successful reperfusion.

Results—36 of 89 patients (40%) achieved successful reperfusion. The rate of reperfusion varied from 0% to 77% among hospitals in the univariate analysis (χ^2 $p < 0.001$) but hospital site did not

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Competing interests GWA reports personal fees from Covidien, Codman, and Concentric, and equity interest in iSchemaView. He also has a patent pending for the RAPID software. RB reports equity interest in iSchemaView.

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remain as an independent predictor of reperfusion in multivariate analysis ($p=0.81$) after adjustment for the presence of good collaterals ($p<0.01$) and use of the Merci retriever ($p<0.05$).

Conclusions—Reperfusion rates vary among hospitals, which may be related to differences in treatment protocols and patient characteristics. Additional studies are needed to identify all of the factors that underlie this variability as this could lead to strategies that reduce interhospital variability in reperfusion rates and improve clinical outcomes.

INTRODUCTION

Successful reperfusion following endovascular therapy for acute ischemic stroke is associated with good clinical outcomes.¹ As endovascular treatment protocols are not standardized, it is likely that protocols differ between hospitals.² The goals of the present study were (1) to determine if the rate of successful reperfusion differs among hospitals and, if so, (2) to explore the possible causes of this variation.

METHODS

Nine hospitals recruited acute ischemic stroke patients in the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution Study 2 (DEFUSE 2), a prospective cohort study of endovascular treatment conducted between 2008 and 2011.³ The degree of vessel occlusion was assessed with the Thrombolysis in Cerebral Infarction (TICI) criteria.⁴ Patients were included for analysis if they had a baseline TICI score of 0 or 1. Successful reperfusion was defined as a post-treatment TICI reperfusion score of 2b or 3. Collaterals were assessed using the Collateral Flow Grading System rated on the baseline digital subtraction angiography images⁵: 0—no collaterals visible to the ischemic site; 1—slow collaterals to the periphery of the ischemic site with persistence of some of the defect; 2—rapid collaterals to the periphery of the ischemic site with persistence of some of the defect and to only a portion of the ischemic territory; 3—collaterals with slow but complete angiographic blood flow of the ischemic bed by the late venous phase; 4—complete and rapid collateral blood flow to the vascular bed in the entire ischemic territory by retrograde perfusion. For the present study, collateral flow was dichotomized as poor (0–2) or good (3–4), examples of which are shown in figure 1.

The association between hospital site and successful reperfusion was first assessed in an unadjusted analysis and subsequently in a multivariate analysis that adjusted for predictors of successful reperfusion. Univariate analyses were conducted with χ^2 or Fisher exact tests for categorical variables and Mann–Whitney U tests for continuous variables. Variables with a p value ≥ 0.1 were included in a stepwise multivariate logistic regression analysis and those variables with a p value <0.05 were retained in the model.

RESULTS

Of 98 patients who were enrolled in DEFUSE 2 and underwent endovascular therapy, 89 patients had a baseline TICI score of 0 or 1 and were included in this analysis. The overall rate of reperfusion was 40.4% (36 of 89 patients). Variables associated with successful reperfusion in univariate analysis were hospital site, good collaterals, and use of the Merci

retriever (table 1). Hospital site did not remain as a significant predictor of reperfusion ($p=0.81$) after adjustment for good collaterals ($p<0.01$) and use of the Merci retriever ($p<0.05$) in the multivariate analysis.

Two additional sets of analyses were conducted to test the robustness of these results. First, because several hospitals enrolled few patients, the analyses were restricted to patients treated at the top three enrolling hospitals. Second, the good collaterals variable was removed from the multivariate analysis as it was only rated in a subset ($n=70$) of patients. This did not change the main results. In both analyses, hospital site was associated with reperfusion in the univariate but not in the multivariate analysis.

DISCUSSION

This study demonstrates that endovascular reperfusion rates differ among hospitals and that these differences might have been related to variation in an operator dependent variable (use of the Merci retriever). Although the Merci retriever is no longer commonly used, this finding raises the possibility that interhospital differences in endovascular treatment protocols could influence angiographic outcomes. This is an important observation as variation in the rate of endovascular reperfusion among hospitals may have a profound impact on the clinical outcomes of individual patients as well as on the results of multicenter clinical studies of endovascular stroke therapy.

In our study, use of the Merci retriever and good collaterals at baseline were both independent predictors of successful reperfusion. The relationship between good collaterals and successful recanalization following endovascular treatment has been reported previously.⁶ The nature of this association is not fully understood. It has been speculated that collaterals could facilitate clot removal by delivering thrombolytic substances to the clot through retrograde flow.⁶ It is also plausible that collaterals could create backpressure that helps to dislodge the clot during mechanical clot retrieval.

The present study has some limitations, most notably the moderate number of total patients and the small number of patients enrolled at several of the hospitals. Consequently, our study could have been underpowered to detect hospital site as an independent predictor of successful reperfusion. In addition, there were no data available for baseline variables related to operator and hospital experience, such as annual hospital volume of endovascular stroke treatments. This could be important as these variables have been shown to relate to outcome in other surgical procedures, such as carotid stenting.⁷⁸ Future studies with a larger sample of patients would be ideal to further clarify which hospital, operator, and protocol specific variables cause variability in the rates of successful reperfusion among hospitals.

In conclusion, the rate of reperfusion following endovascular therapy varies among hospitals, which may be related to differences in treatment protocols and patient characteristics. This variability may have an impact on patient outcomes and should therefore be taken into consideration when selecting sites for multicenter clinical trials of endovascular stroke therapy. Additional studies are needed to identify all of the factors that underlie the variability in reperfusion rates among hospitals. The results of such studies may

lead to strategies that reduce interhospital variability in reperfusion rates and improve clinical outcomes.

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Figure 1.

Examples of poor and good collateral flow. Lateral projection images of the digital subtraction angiograms in a patient with poor collaterals (top row) and a patient with good collaterals (bottom row). (A1) The early arterial phase in the patient with poor collaterals demonstrates a middle cerebral artery (MCA) occlusion and, in addition, an occlusion of the anterior cerebral artery (ACA) (arrow). (A2) In the late arterial phase, there is a lack of collateral flow to the MCA branches that supply the posterior frontal lobe and parietal lobe (region between the arrows) and limited collateral flow to the anterior frontal lobe through the remaining ACA branches. (A3) In the venous phase, there remains a lack of collateral flow to the MCA branches of the posterior frontal and parietal lobes. (B1) The arterial phase in the patient with good collaterals demonstrates an MCA occlusion but intact antegrade flow to the ACA and posterior cerebral artery. (B2) The late arterial/early capillary phase shows early retrograde filling of distal branches of the MCA through leptomeningeal collaterals (arrows) and a good capillary blush in the frontal and parietal lobes. (B3) During the venous phase, the more proximal MCA branches (M2 and M3) are filling through collateral flow (arrows).

Table 1

Comparison of groups with and without successful Thrombolysis in Cerebral Infarction reperfusion

	TICI reperfusion (n=36)	No TICI reperfusion (n=53)	p Value
Age (years) (median (IQR))	60.5 (50.0–73.3)	68.0 (53.5–79.5)	0.4
Male (n (%))	18/36 (50.0)	28/53 (52.8)	0.8
Baseline NIHSS (median (IQR))	15.0 (8.3–20.5)	17.0 (12.5–19.5)	0.3
Onset to catheterization time (h) (median (IQR))	6.0 (4.5–8.7)	5.4 (3.9–7.0)	0.2
General anesthesia used (n (%))	9/36 (25.0)	22/53 (41.5)	0.1
IV tPA used (n (%))	20/36 (55.6)	33/53 (62.3)	0.5
Patient history (n (%))			
Atrial fibrillation	14/36 (38.9)	16/53 (30.2)	0.5
Hypercholesterolemia	15/36 (41.2)	26/53 (49.1)	0.5
Diabetes	8/36 (22.2)	10/53 (18.9)	0.7
Antiplatelet use	9/36 (25.0)	19/52 (36.5)	0.3
Anticoagulant use	5/36 (13.9)	5/52 (9.6)	0.5
Radiographic			
Good collaterals (n (%))	20/29 (69.0)	11/41 (26.8)	<0.001
DWI volume (mL) (median (IQR))	17.3 (8.3–42.3)	19.6 (8.0–43.0)	0.9
PWI volume (mL) (median (IQR))	88.9 (58.9–115.9)	89.2 (44.5–135.6)	0.9
ICA occlusion (n (%))	8/35 (22.9)	17/47 (36.2)	0.2
M1 or M2 occlusion (n (%))	27/35 (77.1)	30/47 (63.8)	0.2
Endovascular treatment modalities used* (n (%))			
Merci	24/36 (66.7)	18/53 (34.0)	<0.01
Penumbra	14/36 (38.9)	22/53 (41.5)	0.8
Other device	14/36 (38.9)	13/53 (24.5)	0.2
Intra-arterial tPA	14/36 (38.9)	20/53 (37.7)	0.9
Hospital site† (n (%))			<0.001
A	20/26 (76.9)	6/26 (23.1)	
B	9/24 (37.5)	15/24 (62.5)	
C	3/9 (33.3)	6/9 (66.7)	
D	2/11 (18.2)	9/11 (81.8)	
E	1/6 (16.7)	5/6 (83.3)	
F	0/5 (0.0)	5/5 (100.0)	
G	0/4 (0.0)	4/4 (100.0)	
H	0/3 (0.0)	3/3 (100.0)	

DWI, diffusion weighted imaging; ICA, internal carotid artery; NIHSS, National Institutes of Health Stroke Scale; PWI, perfusion weighted imaging; TICI, Thrombolysis in Cerebral Infarction; tPA, tissue plasminogen activator.

* For endovascular treatment used, percentages do not add up to 100% because multiple devices or techniques could be used per patient.

† Data from the ninth site are omitted as only one patient was treated at that site.