AJNR

Thrombolytic Therapy of Acute Ischemic Stroke: Correlation of Angiographic Recanalization with Clinical Outcome

Osama O. Zaidat, Jose I. Suarez, Jeffrey L. Sunshine, Robert W. Tarr, Michael J. Alexander, Tony P. Smith, David S. Enterline, Warren R. Selman and Dennis M. D. Landis

AJNR Am J Neuroradiol 2005, 26 (4) 880-884
http://www.ajnr.org/content/26/4/880

AJNR Am J Neuroradiol 26:880–884, April 2005

Thrombolytic Therapy of Acute Ischemic Stroke: Correlation of Angiographic Recanalization with Clinical Outcome

Osama O. Zaidat, Jose I. Suarez, Jeffrey L. Sunshine, Robert W. Tarr, Michael J. Alexander, Tony P. Smith, David S. Enterline, Warren R. Selman, and Dennis M. D. Landis

BACKGROUND AND PURPOSE: **The effect of vessel patency, following recombinant tissue plasminogen activator (rtPA) administration, on clinical outcome in acute ischemic stroke (AIS) has been controversial. We studied the effect of recanalization following intraarterial (IA) and intravenous/IA (IV/IA) rtPA on clinical outcome in AIS.**

METHODS: **Recanalization was classified angiographically as complete (as compared with unoccluded vessel, thrombolysis in myocardial infarction classification [TIMI] 3), none (with no change from prethrombolysis, TIMI 0), and partial (when a change in the flow from baseline was noted, TIMI 1–2). Outcomes were symptomatic intracranial hemorrhage (sICH), 90-day modified Rankin scale (≤ 2 as a good outcome), and 3-month mortality.**

RESULTS: **Ninety-six patients had either combined IV/IA (41) or IA (55) rtPA for AIS during a 7-year period. Any recanalization occurred in 69%; 55% of those had a good outcome versus 23% in the rest (Odds ratio = 3.9; 95% confidence interval [CI] = 1.4–11.2; *P* = .007). Only 24% had complete recanalization; 74% had a good outcome versus 36% in the nonrecanalization group (OR = 5.1; 95% CI = 1.6–16.8; *P* = .002). When adjusted to time to therapy and vessel occluded, these results lessened but remained significant. The sICH rate with any recanalization was 7.6% versus 13.3% in patients with persistent clot (relative risk (RR) = 0.6; 95% CI = 0.2–2.0; *P* = .45). Death occurred in 19.7% of those whose vessels recanalized versus 33.3% in the rest (RR = 0.56; 95% = 0.26–1.19; *P* = .2).**

CONCLUSION: **A total of 24% and 69% of patients had complete and any recanalization, respectively, following endovascular rtPA therapy of AIS. The degree of recanalization was directly related to time to therapy and associated with good clinical outcome without an increase in the rate of adverse effect.**

The effect of arterial recanalization following thrombolytic therapy of acute ischemic stroke (AIS) is a complicated and controversial issue. Several studies have shown that restoration of cerebral perfusion per se may not be adequate to have a favorable clinical outcome (1–5). Time to achieving vessel patency has been shown to be crucial in achieving a better clinical outcome (2–4). The traditional therapeutic window in AIS, <6 hours from the onset of symptoms, is influenced by additional variables that may shift the balance toward good or bad clinical outcomes. Certain factors may lead to an unfavorable outcome even when treatment is administered rapidly, such as reperfusion injury and hemorrhagic transformation, poor collateral circulation, dehydration, poor cardiac output, hypotension, hyperglycemia, and fever (1–5).

Recanalization, however, remains the main goal of endovascular stroke therapy. Achieving this goal may be related to the original source of the blood clot. An animal model study showed a higher rate of successful lysis in red clots than white clots (6). The additional factor that may be added to this complexity is the type of vessel occluded (7, 8). Top-of-carotid occlusion is associated with poor clinical outcome and low rate of recanalization when compared with middle cerebral artery (MCA) occlusion (7, 8). The response of thrombolysis at different vascular occlusion sites may well be related to the thrombus burden.

The effect of cerebral recanalization per se on

Received June 24, 2004; accepted August 24.

From the Departments of Neurology (O.O.Z., J.I.S., D.M.D.L.), Interventional Neuroradiology (J.L.S., R.W.T.), and Neurological Surgery (J.I.S., W.R.S.), Case Western University Medical Center, Cleveland, OH; and the Divisions of Neurological Surgery (M.J.A.), Interventional Neuroradiology (O.O.Z., T.P.S., D.S.E.), and Interventional Vascular Radiology (T.P.S.), Duke University Health System, Durham, NC.

Address correspondence to Osama O. Zaidat, MD, MSc, Duke University Medical Center, Box 3808, Durham, NC 27710.

clinical outcome after adjusting for all potential clinical factors that may affect outcome is less well defined, and controversy still exists. The restoration of cerebral blood flow is thought to potentially increase the risk of hyperperfusion injury, hemorrhagic transformation, and symptomatic intracerebral hemorrhage. We investigated the effect of vessel recanalization on clinical outcome following local thrombolytic therapy of AIS patients.

Methods

We reviewed our collected brain-attack data base of patients presenting within 6 hours of AIS symptoms during a 7-year period. Inclusion criteria for thrombolytic therapy were 18 years of age or older, presenting within 6 hours of stroke symptoms onset with initial National Institute of Health Stroke Scale (NIHSS) of 8 or more, except for aphasia and visual field deficit, and normal initial head CT scan. Exclusion criteria were recent major surgery in the past 2 weeks; terminal illness with life expectancy of 6 months or less; international normalized ratio of 1.5 or greater; platelet count of <100,0000 and creatinine of at least 2.0; and systolic blood pressure <180 mm Hg with diastolic <110 mmHg, before initiating thrombolytic therapy.

We evaluated patients who received either intrarterial (IA) recombinant tissue plasminogen activator (rt-PA) or combined intravenous and intraarterial (IV/IA) rtPA. This allowed us to assess the immediate postthrombolysis recanalization by digital subtraction angiography (DSA). We collected DSA imaging data before and after thrombolytic therapy. Patients with complete vessel occlusion on DSA at baseline were included. Admission NIHSS, time of stroke onset, time of thrombolytic therapy, patient demographics, and medical comorbidities were collected.

Endovascular Therapy

The institutional review board approved our protocol as standard of care and allowed the data base collection and the current paper objectives, design, and analysis. Patients or their legal representatives give written informed consent before therapy. Patients presenting within 3 hours of the onset of stroke symptoms received IV (0.6 mg/kg) followed by IA (up to 0.3 mg/kg) rtPA if their symptoms persisted or if the diffusion- and perfusion-weighted images showed a mismatch. Patients presenting 3–6 hours after the onset underwent immediate cerebral angiography and IA rtPA was administered. All patients had an initial head CT with section thickness of 10 mm within the first 4 years of the study and 7.5 mm in the last 3 years of the study. Repeat CT scan immediately following thrombolytic therapy and in 24 hours was obtained. The head CT abnormality was classified as early infarction, hemorrhagic infarction, or cerebral hematoma (7, 8).

Recanalization Classification

The baseline cerebral angiography results were defined according to the type of vessel occluded. Recanalization following thrombolytic therapy was classified as none, partial, or complete. Complete recanalization was defined as passage of contrast with normal rate of contrast filling and clearance (thrombolysis in myocardial infarction classification [TIMI] 3). If the rate of contrast clearance was slower compared with normal arteries, however, recanalization was classified as partial (TIMI 1 and 2). If no change was found from baseline then the flow rate, it was classified as none, or TIMI 0 (7). The leptomeningeal arteries, ophthalmic artery, and the anterior and posterior communicating arteries collaterals were determined by the neurointerventionalist as present or absent, on a case-by-case basis.

Outcome Measures

The rate of recanalization was correlated with the main outcome variables. A good outcome was defined as 90-day modified Rankin scale score (mRS) ≤ 2. Bad outcomes were sICH, which was defined as a neurologic worsening ≥ 4 points in NIHSS attributable to the well-defined hematoma on head CT, and 90-day mortality.

Statistical Analysis

Bivariate comparisons of demographic and clinical data were completed by using Student's t test, Fisher's exact test, and the median log rank test, as appropriate. Recanalization was correlated with clinical outcome by using the bivariate and logistic regression analyses to adjust for confounders in the multivariate model.

Results

A total of 1057 patients were screened for potential thrombolytic therapy between September 7, 1996, and April 10, 2003. Of them, 383 patients (36%) received some type of thrombolytics. The IV rtPA was administered to 183 patients (48%), IA urokinase before its withdrawal from the market to 104 patients (37%), and IA or IV/IA rtPA to the remaining 96 patients (25%). We present the relation of the outcome measures to any recanalization (partial or complete), followed by the relation of the clinical outcome to complete recanalization.

Any Recanalization

A total of 69% of patients had any recanalization (partial or complete). The relation of recanalization to baseline variables is shown in Table 1.

There was no significant statistical difference between the group that had any recanalization and the group that did not, except for a higher proportion of patients with acute carotid occlusion in the group that did not show any recanalization, as expected. The hyperattenuated MCA sign on the CT was not statistically different between the two groups (10 vs. 9; $P = .1$). The diffusion and perfusion MR imaging (DWI/PWI) before therapy was performed in 30 patients, 19 of whom had mismatch, which was divided between the two groups (10 vs. 9; $P = .1$). The difference between the two groups in NIHSS and time to therapy did not reach statistical significance. The median initial NIHSS was slightly lower in the group with any recanalization compared with those who had a persistent clot (14 vs. 18; $P = .08$). The time to therapy was not different between the two groups, although the patients who had some vessel patency following thrombolysis were treated earlier than the group who did not (209 minutes for any vs. 223 minutes for no recanalization; $P = .47$). The difference in treatment type, whether IV/IA or IA, was not statistically significant between the two groups.

The relation of any recanalization to clinical outcome is shown in Table 2. Good outcome at 90 days was more likely to occur with any recanalization than with no recanalization (55% vs. 23%; OR 3.9 [1.4–11.2]; $P = .007$). Symptomatic ICH occurred more

TABLE 1: Baseline clinical characteristics

Characteristics	Any Recanalization			Complete Recanalization		
	Yes (66)	No (30)	*P*	Yes (25)	No (30)	*P*
Age, y	66.7 ± 12.8	69.9 ± 9.5	.22	67.1 ± 13	69.9 ± 9.5	.37
Sex, male	33 (50%)	14 (46%)	.76	13 (57%)	14 (46%)	.48
Race, white	50 (76%)	24 (80%)	.46	17 (74%)	24 (80%)	.60
Hypertension	40 (63%)	20 (64%)	.63	14 (60.9%)	20 (64)	.66
Diabetes	20 (29.8%)	9 (30%)	.94	9 (39.1%)	9 (30%)	.49
Prior aspirin	13 (20.3%)	4 (13.3%)	.57	5 (22.7%)	4 (13.3%)	.38
Baseline NIHSS (median, IQR)	14 (8, 20)	18 (9, 22)	.08	16 (9, 20)	18 (9, 22)	.66
SBP, mm Hg	153 ± 28.2	160 ± 32.9	.31	157 ± 31.7	160 ± 32.9	.74
Glucose, mg/dL	146.9 ± 67.6	145.4 ± 65.1	.90	151.1 ± 15.3	145.4 ± 65.1	.77
Occluded vessel:						
MCA	49 (75.2%)	17 (56.7%)	.09	20 (87%)	17 (56.7%)	.02
ICA	10 (15.2%)	11 (36.7%)	.02	2 (8.7%)	11 (36.7%)	.02
BA	5 (7.6%)	2 (6.7%)	.80	1 (4.4%)	2 (6.7%)	.72
IV/IA	26 (39.4%)	15 (50%)	.33	9 (36%)	15 (50%)	.43
Onset to therapy (min)	208.9 ± 31	222.9 ± 92.2	.47	172.6 ± 79.2	222.9 ± 92.2	.04

TABLE 2: Recanalization status at the completion of thrombolysis and clinical outcome

	Any Recanalization			Complete Recanalization		
	Yes (66)	No (30)	*P*	Yes (25)	No (30)	*P*
Good outcome (mRS, 2, 90 d)	55%	23%	.007	74%	23%	.0002
Symptomatic ICH	7.6%	13.3%	.45	4.4%	13.3%	.27
Mortality, 90 d	19.7%	33.3%	.20	17.4%	33.3%	.20

frequently when no recanalization occurred versus when any vessel patency was achieved (7.6% vs. 13.3%; RR 0.57 [0.16–1.92]; $P = .45$), but did not reach statistical difference. Mortality during the first 90 days was more frequent in the persistent clot group (33%) than when any recanalization occurred (20%), but the difference was not statistically significant (RR 0.56 [0.26–1.19]; $P = .2$). No significant change occurred when adjusting for the baseline variables of sex, age, ethnicity, coronary artery disease, initial NIHSS, time to therapy, type of therapy, collateral presence, and vessel occluded (good outcome, $P = .02$).

Complete Recanalization

The success rate of complete recanalization was relatively low, with only 24% of patients achieving complete recanalization. For the variables measured, there was no significant statistical difference between this group and the group with complete lack of recanalization, except in time to treatment and type of vessel occluded. Time to treatment was significantly shorter in the complete recanalization group (173 minutes vs. 223 minutes; $P = .04$). The complete recanalization group had more patients with MCA occlusion than did the persistent clot group (87% vs. 57%; $P = .02$), and fewer patients with acute carotid occlusion (9% vs. 37%; $P = .02$). The complete recanalization group had a higher proportion of patients with history of diabetes and prior aspirin use and lower NIHSS, but this was not statistically different from the recanalization failure group.

The percentage of patients who had a good outcome, when complete clot lysis was achieved, was significantly higher than when the clot burden did not change (74% vs. 23%; OR 9.31 [2.27–40.98]; $P = .0002$). The rate of sICH was not statistically different between the two groups, with approximately 4.4% in the complete versus 13.3% in the nonrecanalization patients (RR 0.33 [0.04–2.72]; $P = .27$), but a trend in favor of complete recanalization group was noted. The mortality rate within the first 90 days was 17.4% when vessel patency was achieved versus 33.3% when no change in the vessel patency occurred (RR 0.52 [0.19–1.45]; $P = .20$). The results did not significantly change when adjusting for the baseline variables of sex, age, ethnicity, initial NIHSS, time to therapy, type of therapy, collateral presence, and vessel occluded. The results lessened when comparing the complete recanalization to any recanalization or no recanalization but remained significant (good outcome $P = .004$). Figure 1 summarizes the above findings, depicting the relation between clinical outcome and the degree of recanalization following interventional stroke therapy.

Discussion

Our study provides significant confirmation of the intuitive fact that vessel recanalization following acute endovascular stroke therapy is one of the main determinants of clinical recovery and may not be associated with significant adverse effect. The second important issue that this report highlights is the poor rate of recanalization attained by the current thrombolytic treatment modalities. We treated our patient

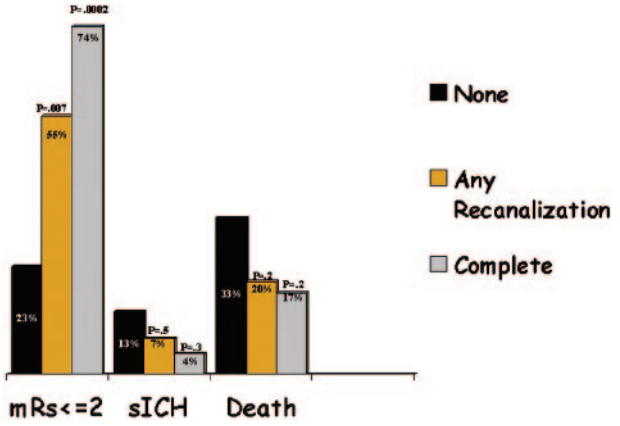

FIG 1. Relation of degree and completeness of recanalization to the clinical outcome (good clinical outcome with mRs ≤2, sICH, and death), following endovascular acute ischemic stroke therapy.

with IA rtPA within 3–6 hours of the onset of symptoms and used the combined approach of IV followed by IA rtPA within 3 hours of the onset of symptoms.

Recanalization and Clinical Outcome

Previous smaller-scale case series studies have shown that rate and completeness of recanalization affect clinical outcome (7–10). Recanalization has been studied in different acute intervention approaches. In one study, where IV rtPA was used, 35% of the patient had stenotic or normal flow pattern of recanalization on transcranial Doppler sonography and were associated with better clinical outcome (11). In the PROACT study (8), the rate of any recanalization was 66% in the IA group versus placebo. A total of 40% of patients had a good clinical outcome, compared with 25% in the placebo. In the Interventional Management of Stroke (IMS) study (12), the patients were treated with IV followed by IA rtPA within 3 hours of the onset of symptoms. The good clinical outcome was significantly better than the historical control of the National Institute of Neurological Disorders and Stroke (NINDS) placebo study group (43% vs. 28%; OR 2.18 [1.20–3.99]) (13).

In our series, we found that the rate of clinical improvement was directly related to the degree of recanalization achieved at the end of the endovascular therapy. This is consistent with previously published clinical series and trials. One interesting finding in our study was that the rate of sICH might be inversely related to completeness of recanalization, although it was not statistically significant. This worst clinical outcome with no recanalization may be related to several factors that are known to be associated with poor outcome. Our patients with no or incomplete recanalization presented with more severe stroke, later time to treatment, and worse type of vessel occluded than did the recanalization group. Moreover, with incomplete or no recanalization, rtPA may still be bound to the clot and delayed vessel patency may occur with restoration of blood flow to an area of the brain tissue with prolonged period of ischemia leading to sICH. In addition, stroke severity, time to therapy, comorbidities, hyperglycemia, fever, age, and reperfusion injury may confound the effect of recanalization on clinical outcome (15).

The Poor Recanalization Rate

Most of the studies correlate the success rate of recanalization following interventional stroke therapy with the underlying stroke etiology, type of vessel occluded, and modalities of interventional stroke therapy. The composition of the clot may play a pivotal role in the efficacy of rtPA in achieving recanalization, and the red clot has been shown to be more amenable to fibrinolytic therapy than the white clot in animal model studies (5). Subtypes of stroke did not seem to play a role in the effect of the intravenous rtPA (16), but it may be of paramount significance in local endovascular therapy. Cardiac emboli in the context of atrial fibrillation are less responsive to thrombolytic therapy than the paradoxical and nonatrial fibrillation emboli (17). Similarly, superimposed clot over an atherosclerotic artery may be more responsive to fibrinolytic agents than plaque rupture with distal embolization (17). These are preliminary data, and more detailed and comprehensive studies are needed to better correlate the stroke etiology with the success of vessel recanalization.

The other significant factor associated with clot lysis and restoring vessel patency is the type of treatment technique implemented. In the preliminary phase of the NINDs study using IV rtPA in AIS patients, the rate of any recanalization was limited to 34.4%, and that was associated with significantly smaller infarct size than placebo on head CT scan (18). Of 121 patients with MCA occlusion treated with IA pro-urokinase followed by IV heparin in the PROACT study, a total of 66% had any recanalization. Recanalization was complete (TIMI 3) in 20% and partial (TIMI 1 and 2) in 46% of the cases. Of the 62 patients who had IV followed by IA rtPA in the IMS study, a total of 56% achieved some recanalization. Recanalization was complete (TIMI 3) in 11% and partial (TIMI 1 and 2) in 45% of the cases. The mechanical clot disruption was allowed in the IMS study. Application of newer and innovative techniques to improve the success rate of recanalization has been attempted. The recently published Mechanical Embolus Removal in Cerebral Ischemia (MERCI; 19) and the Endovascular PhotoAcoustic Recanalization (EPAR; 20) studies used a corkscrew-like clot retrieval device and a photolaser energy microcatheter, respectively. The rates of any recanalization was 54% in the MERCI trial and 61% in the EPAR study. Aggressive mechanical clot disruption with angioplasty or a snare device with a low-dose third-generation thrombolytic agent was reported in a series of 19 patients, and 12 patients had complete recanalization (modified TIMI 4). An additional four patients had near-complete recanalization with modified TIMI 3 (21).

The rate of any recanalization (TIMI 1, 2, and 3) in

our study is similar to those previously published, whereas the complete recanalization rate or TIMI 3 (24%) may be slightly higher than the IMS and PROACT studies. We believe that the rate of complete recanalization may be higher due to the nature of our study, in which we allowed more leverage for the neurointerventionalist for the time allowed for clot lysis, the dose of rtPA, and use of mechanical clot disruption by using soft microwires. Moreover, we treated all stroke patients presenting within the time window and did not exclude any patient with less or more probability to respond to thrombolysis such as basilar and carotid occlusion or MCA and its branches.

Because there is no control group in our study to compare the incidence of spontaneous lysis of occlusive clot as well as spontaneous recovery from stroke, firm conclusion about the real result of any treatment may not be reached. This study demonstrates the correlation between thrombolytic vessel recanalization, which may also occur spontaneously, and clinical outcome. Advances in acute imaging technology with prescreening by using DWI/PWI, thin-sliced head CT, CT perfusion, and CT angiography would further improves the chances of successful therapeutic recanalization (22).

Conclusion

This study highlights the role of successful vessel recanalization following endovascular AIS therapy with local thrombolytic therapy. The degree of recanalization plays a pivotal role in improving clinical outcome following thrombolytic treatment for acute ischemic stroke patients and does not appear to increase the rate of sICH or death. Applying the currently available technique, the rate of vessel patency is very modest. Studies using a single or combination of pharmacological agents and newer mechanical devices are needed to enhance our ability for clot lysis.

Acknowledgments

We wish to thank neurology, radiology, and neurosurgery residents, emergency room physicians and nurses, and neuroscience intensive care unit nurses, for their support in taking care of the stroke patients.

References

1. von Kummer R, Holle R, Rosin L, et al. **Does arterial recanalization improve outcome in carotid territory stroke?** *Stroke* 1995;26:581–587
2. Alvarez-Sabin J, Molina CA, Montaner J, et al. **Effects of admission hyperglycemia on stroke outcome in reperfused tissue plasminogen activator–treated patients.** *Stroke* 2003;34:1235–1241
3. Labiche LA, Al-Senani F, Wojner AW, et al. **Is the benefit of early recanalization sustained at 3 months? A prospective cohort study.** *Stroke* 2003;34:695–698
4. Molina CA, Alexandrov AV, Demchuk AM, et al. **CLOTBUST Investigators: improving the predictive accuracy of recanalization on stroke outcome in patients treated with tissue plasminogen activator.** *Stroke* 2004;35:151–156
5. Hallenbeck JM, Dutka AJ. **Background review and current concepts of reperfusion injury.** *Arch Neurol* 1990;47:1245–1254
6. Kirchhof K, Sikinger M, Welzel T, et al. [**Does the result of thrombolysis with recombinant tissue-type plasminogen activator (rt-PA) in rabbits depend on the erythrocyte- and fibrin-content of a thrombus?**] *Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr* 2004;176:98–105
7. Zaidat OO, Suarez JI, Santillan C. **Intrarterial and combined intravenouns and intra-arterial thrombolytic therapy for distal carotid artery occlusion.** *Stroke* 2002;33:1828–1833
8. Furlan A, Higashida R, Weschler L, et al., for the PROACT II Investigators. **Intra-arterial prourokinase for acute ischemic stroke: the PROACT II Study: a randomized controlled trial.** *JAMA* 1999;282:2003–2011
9. Zaidat OO, Welter E, Love TE, et al. **Combined intra-venous and intra-arterial versus intra-arterial recombinant tissue plasminogen activator in acute ischemic stroke patients: propensity score analysis.** *J Neurosurg* 2004;100: A181 [abstract]
10. Neumann-Haefelin T, du Mesnil de Rochemont R, Fiebach JB, et al. **Effect of incomplete (spontaneous and postthrombolytic) recanalization after middle cerebral artery occlusion: a magnetic resonance imaging study.** *Stroke* 2004;35:109–114
11. Demchuk AM, Burgin WS, Christou I, et al. **Thrombolysis in brain ischemia (TIBI) transcranial Doppler flow grades predict clinical severity, early recovery, and mortality in patients treated with intravenous tissue plasminogen activator.** *Stroke* 2001;32:89–93
12. IMS Study Investigators. **Combined intravenous and intra-arterial recanalization for acute ischemic stroke: the Interventional Management of Stroke Study.** *Stroke* 2004;35:904–911
13. National Institute of Neurological Disorders and the Stroke rt-PA Stroke Study Group. **Tissue plasminogen activator for acute ischemic stroke.** *N Engl J Med* 1995;333:1581–1587
14. Kim JJ, Fischbein NJ, Lu Y, et al. **Regional angiographic grading system for collateral flow: correlation with cerebral infarction in patients with middle cerebral artery occlusion.** *Stroke* 2004;35:1340–1344
15. Kent TA, Soukup VM, Fabian RH. **Heterogeneity affecting outcome from acute stroke therapy: making reperfusion worse.** *Stroke* 2001;32:2318–2327
16. NINDS t-PA Stroke Study Group. **Generalized efficacy of t-PA for acute stroke: subgroup analysis of the NINDS t-PA Stroke Trial.** *Stroke*1997;28: 2119–2125
17. Kirmani JF, Safdar A, Siddiqui AM, et al. **Correlation of rates of re-canalization to the thromboembolic source in acute stroke thrombolytic therapy.** *J Neurosurg* 2004;100:A189 [abstract]
18. Wolpert SM, Bruckmann H, Greenlee R, et al. **Neuroradiologic evaluation of patients with acute stroke treated with recombinant tissue plasminogen activetor: the rt-PA Acute Stroke Study Group.** *AJNR Am J Neuroradiol* 1993;14:3–13
19. MERCI Investigators. **Results of the combined MERCI I–II (Mechanical Embolus Removal in Cerebral Ischemia) trials.** *Stroke* 2004; 35:240 [abstract]
20. Berlis A, Lutsep H, Barnwell S, et al. **Mechanical thrombolysis in acute ischemic stroke with endovascular photoacoustic recanalization.** *Stroke* 2004;35:1112–1116
21. Qureshi AI, Siddiqui AM, Suri MF, et al. **Aggressive mechanical clot disruption and low-dose intra-arterial third-generation thrombolytic agent for ischemic stroke: a prospective study.** *Neurosurgery* 2002;51:1319–1327; discussion 1327–1329
22. Provenzale JM, Jahan R, Naidich TP, Fox AJ. **Assessment of the patient with hyperacute stroke: imaging and therapy.** *Radiology* 2003;229:347–359