Original Article

Clinical Outcomes of Endovascular Thrombectomy in Tissue Plasminogen Activator versus Non-Tissue Plasminogen Activator Patients at Primary Stroke Care Centers

Gregory Imbarrato, Joshua Bentley[1], Ajeet Gordhan[2,3]

Department of Graduate Medical Education, Advocate Bromenn Neurological Surgery Residency Program, [2]Department of Neurosciences, Advocate Bromenn Hospital, Normal, [3]St. Joseph Medical Center, Bloomington, IL, [1]Swedish Medical Center, Swedish Neuroscience Institute, Cherry Hill, Seattle, WA, USA

Abstract

Background: The effect of intravenous tissue plasminogen activator (IV tPA) administration before endovascular intervention as compared to without at thrombectomy-capable low-volume centers on procedural aspects and patient outcomes has not been investigated. **Methods:** Retrospective chart review was performed in all consecutive large vessel cerebrovascular accident patients treated with endovascular therapy at two select rural primary stroke centers between 2011 and 2015. Patients' data regarding age, sex, and medical history, as well as thrombus location by catheter-based cerebral angiography, postprocedural reperfusion status, and clinical outcomes were reviewed. The primary outcome measure of the study was a comparison of modified Rankin scale (MRS) at 90 days in patients' postendovascular thrombectomy with prior IV tPA administration versus those who underwent thrombectomy and did not qualify for preprocedural IV tPA. **Results:** After application of the set inclusion and exclusion criteria, data of 46 out of 65 patients were analyzed. Twenty-three patients (50%) received IV tPA before thrombectomy and 23 patients did not qualify for IV tPA (50%). Successful recanalization (thrombolysis in cerebral infarction 2b/3) was achieved in 86% (20/23 patients) of thrombectomy patients without preprocedural IV tPA and 82% (19/23) of patients who received it (odds ratio [OR]: 0.03, confidence interval [CI]: 95% 0.062–0.16, $P < 0.0001$). MRS of 2 or less at 90 days was 43.4% (10/23) in patients with no preprocedural IV tPA and 39.1% (9/23) in the combined therapy group (OR: 0.84, CI: 0.26–2.70, $P = 0.8$). **Conclusion:** Patients undergoing endovascular thrombectomy for large vessel occlusion at select low-volume rural centers showed benefit from this treatment regardless of IV tPA administration. Clinical outcomes and complications at select low-volume thrombectomy-proficient centers are comparable to large volume comprehensive stroke centers as well as the landmark studies proving the efficacy of endovascular treatment.

Keywords: *Cerebrovascular accident, intravenous tissue plasminogen activator, large vessel occlusion, thrombectomy*

Introduction

Improved clinical outcomes for patients with acute emergent large vessel thromboembolic cerebrovascular accidents (CVA) at high-volume centers have been demonstrated. Prolonged transfer times to such institution are associated with less favorable outcomes. Direct access to smaller thrombectomy-capable low-volume centers is in most cases the only immediate viable revascularization option. The development

Access this article online

Quick Response Code:

Website: www.ruralneuropractice.com

DOI: 10.4103/jnrp.jnrp_497_17

Address for correspondence: Dr. Ajeet Gordhan, Endovascularneuro LLC, St Joseph Medical Center, Advocate Bromenn Hospital, 11 Lexis Court, Bloomington, Illinois 61704, USA. E-mail: gordhana@gmail.com

How to cite this article: Imbarrato G, Bentley J, Gordhan A. Clinical outcomes of endovascular thrombectomy in tissue plasminogen activator versus non-tissue plasminogen activator patients at primary stroke care centers. J Neurosci Rural Pract 2018;9:240-4.

of primary stroke centers and intravenous tissue plasminogen activator (IV tPA) administration protocols have established clear metrics for treatment with improved clinical outcomes' event at these smaller centers.[1] The efficacy of endovascular reperfusion in emergent large vessel occlusion has been verified by five landmark studies. Rapid complete revascularization with minimizing risk is a prerequisite for favorable clinical outcomes.[2,3] IV tPA administration before endovascular intervention at thrombectomy-capable low-volume centers and how this affects procedural aspects and patient outcomes have not been investigated. This study was performed to determine if patients who qualify for endovascular intervention benefit from prior IV tPA administration at low-volume thrombectomy-proficient centers.

Methods

This was an Institutional Review Board-approved study with waived individual consent. Retrospective chart review of all consecutive CVA patients treated with endovascular therapy at two select rural primary stroke centers between 2011 and 2015 was performed. Inclusion criteria were all anterior circulation large vessel occlusions within an 8 h time window from symptom onset with subsequent endovascular intervention.[4] Patients' data regarding age, sex, and medical history, as well as thrombus location by catheter-based cerebral angiography and postprocedural reperfusion status were reviewed. Computed tomography (CT) head to procedure commencement time was determined from the time of CT acquisition recorded to the time documented in the chart as the time of procedure commencement. Total procedural times were obtained from the chart as noted by the time the procedure commenced to the time the procedure was considered complete, inclusive of anesthesia time and groin arteriotomy closure device placement. Revascularization was performed with a mechanical stent retriever, aspiration or a combination of local aspiration, and mechanical thrombectomy. Successful recanalization was defined as modified thrombolysis in cerebral infarction (TICI) score of 2b or 3. The initial NIHSS and the 90-day functional outcome were assessed using the modified Rankin scale (MRS) at a follow-up neurology visit. The primary outcome measure of the study was a comparison of MRS at 90 days in patients with IV tPA administration before thrombectomy versus those who did not qualify for IV tPA administration. A Modified Rankin Score of ≤2 at 90 days was considered a good functional outcome. All data points above were stratified into IV tPA versus no-IV tPA for comparison.

Statistical analysis

The data were analyzed using the social science statistics web-based calculator. The Chi-square test and the Fisher's exact test were used to compare categorical variables between the non-IV tPA and the IV tPA groups, and the one-way ANOVA was used to compare distributions of continuous variables. $P < 0.05$ was considered statistically significant.

Results

Demographics

A total of 65 patients were initially assessed for inclusion in this study through retrospective chart review. After application of the set inclusion and exclusion criteria, 46 remained. Twenty-three patients (49%) received IV tPA before thrombectomy and 23 patients did not qualify for IV tPA (51%). There was no statistical difference in medical comorbidities (atrial fibrillation, carotid stenosis, hypertension, diabetes, or hyperlipidemia) between the two groups. Average age was 69.2 (±14.7) years in the preprocedural IV tPA group and 71.1 (±16.2) years in the no-IV tPA group.

Intervention

Thromboembolic occlusion at the carotid terminus was identified in 26% (6/23) of patients in both groups. Middle cerebral artery (MCA) M1 occlusion was noted in 47.8% (11/23) of patients in no-IV tPA group and 43.4% (10/23) patients in the IV tPA group. MCA M2 and other small branch occlusions in the no-IV tPA group constituted 21% (5/23) and 30% (7/23) in the group that received IV tPA. TICI 2b/3 recanalization was achieved 86% (20/23 patients) in the no-IV tPA arm and 82% (19/23 patients) in the IV tPA arm (odds ratio [OR]: 0.03, confidence interval [CI] 95%: 0.062–0.16, $P < 0.0001$). Average CT to procedure commencement time was 126.6 min (±43.01) in the no-IV tPA group and 142.2 (±42.87) min in the IV tPA group ($P = 0.2$). Procedural duration for the no-IV tPA group was 126.6 min (±43.01) and in the IV tPA group was 121.8 (±42.87) ($P = 0.8$). Mechanical thrombectomy alone was performed in 43% (10/23) of patients in the non-IV tPA group and in 56% (13/23) of patients in the IV tPA group. Aspiration with combined mechanical thrombus extraction was performed in 39% (9/23) of patients in the non-IV tPA group and in 22% (5/23) of patients in the IV tPA group. The remainder in each category was aspiration alone.

Clinical

Average NIHSS was 17.6 in the IV tPA group and 16.6 in the no-IV tPA group ($P = 0.7$). MRS of 2 or less at 90 days was 10/23 patients (43.4%) in the non-IV tPA arm and 9/23 (39.1%) in the IV tPA group

(OR: 0.84, CI: 0.26–2.70, P = 0.8). The mean MRS score for thrombectomy without tPA was 3.6 and with IV tPA was 3.3. Intracranial hemorrhage on CT was identified in 1/23 (4.3%) of patients in the no-IV tPA group and in 5/23 (21%) of patients in the IV tPA group (OR: 0.16, CI: 0.017–1.5, P = 0.07). Symptomatic intracranial hemorrhage with a fatal outcome was present in 1/23 (4.3%) of patients in the IV tPA group and none in the non-IV tPA group.

Discussion

Patients undergoing endovascular thrombectomy for large vessel occlusion at select low-volume rural centers in our study showed benefit from this treatment regardless of IV tPA administration. The benefit of prethrombectomy IV tPA in improving clinical outcomes has been controversial.[5,6] A prospective study identified a dramatic improved functional outcome of 51.5% with prethrombectomy IV tPA administration versus 18.2% for endovascular intervention alone.[7] A meta-analysis of five studies comparable to our study period identified 37.2% good functional outcomes with thrombectomy alone and 49.2% with combined therapy.[8] Functional outcome in the thrombectomy alone group in our study was 43.4% and 39.1% with combined therapy, which was not statistically significant. In comparison to studies at a similar time period,[2,3,9] reperfusion rates and clinical outcomes of our data are comparable to most comprehensive stroke centers with large volumes as well as the landmark studies proving the efficacy of endovascular treatment.

IV tPA theoretically facilitates thrombus dissolution and may address more distal or procedural new territory small vessel thromboembolism. This may translate to increased recanalization rates and decreased procedural times. In our study, the overall time from CT scan to procedure start in each group was not statistically significant. Administration of IV tPA requires clinical decision-making and drug preparation that delays noncontrast head CT to procedure commencement time. In our study, an average delay of 15.6 min was identified with IV tPA administration that was not statistically significant. At low-volume centers, prolonged symptom onset time to endovascular reperfusion has been identified, without published data identifying the root causes.[10] Potential reasons for workflow inefficiency include delays in considering endovascular therapy, staffing with nondedicated endovascular neurointerventional call teams, the use and availability of general anesthesia, operator experience, and lack of dedicated neurocritical care. Given that the workflow times may be longer at low-volume centers, the addition of IV tPA bridging to mitigate this potential delay did not appear to be advantageous in our study. Our data identified increased symptomatic and nonsymptomatic intracranial hemorrhages in the combined therapy group, which was not statistically significant. The only intracranial hemorrhage-related mortality postthrombectomy was in the thrombectomy with IV tPA group. This is comparable to data from a published study of 1275 patients.[8]

Comprehensive high-volume center data have shown a superiority in measured efficiency for times to recanalization and outcomes when compared to low-volume centers.[10] Access to comprehensive centers may not always be a feasible option. Seventy percent of high-volume centers are more likely to be urban teaching hospitals.[11] For multiple centers' concentrated large urban environments, it is a plausible premise to direct patient care to the highest volume center. In nonurban rural areas, often further than an hour travel time from a comprehensive center, a thrombectomy-capable primary care center is a more viable alternative. Theoretically, only 56% of the US population have access to endovascular-capable hospital by road in 1 h.[12] For every 1 h delay in reperfusion, the odds of good clinical outcome decreases by 38%.[13] A prolonged symptom onset to reperfusion time has been shown to be an independent limiting factor for favorable outcomes.[14] Transfer delay is a major factor limiting the use of intra-arterial treatment in acute ischemic stroke and significantly limits favorable outcomes.[9,15] One in four patients becomes ineligible for endovascular thrombectomy during transfer with a trend toward poorer outcomes once transferred.[16] The mortality rate is significantly lower in directly admitted patients as compared to transferred patients.[17] Primary care centers capable of thrombectomy, with established and sustained treatment time proficiency protocols, will reduce the number of patients requiring transfer and reduce symptom onset to reperfusion times with resultant improved functional outcomes.

A larger proportion of ischemic stroke patients will be treated at low-volume centers. The incidence of large vessel occlusion has been determined to be 24 per 100,000 person-years and, the most recently estimated annual thrombectomy rate in 2015 of three procedures per 100,000 people indicates that there will be a significant increase in the volume of endovascular procedures.[18] The mean number of thrombectomy cases per institution was 19.3 cases per year in an outcome report database. Nearly 89% of institutions reporting to this database were university hospitals.[17] This falls well short of the 38 thrombectomy cases recommended

for thrombectomy-capable centers and far short of the 50 cases suggested as a designate high-volume center.[10,19] Almost a decade ago, only 0.4%–2.6% of hospitals met the procedural volume recommended by various professional bodies for endovascular thrombectomy.[11] In spite of less favorable outcomes with carotid stenting, a lower proportion of cases are currently treated at high-volume centers.[20] In the state of New Jersey as an example, 60% of stroke admissions were at a primary stroke center as compared to 40% at a comprehensive center.[21] As with carotid stenting, an increase in procedures for large vessel occlusions in thrombectomy-capable low-volume centers is probable with the anticipated increase in procedural volume.

The study is limited by the nonrandomized retrospective nature and the small number of patients in each cohort. The results of select rural centers that have clinical neuroscience services may not reflect outcomes at all rural-based hospitals. The findings of this study may be reflective of other rural institutions that have available resources including appropriate equipment as well as skilled technical and physician staff that will and can promote aspects of care for better functional outcomes. These centers should rather be considered as thrombectomy-proficient centers.

Conclusion

Optimizing care at thrombectomy-proficient low-volume institutions with high-volume center partnership and collaboration is a more tangible goal than promoting transfers out of primary stroke centers as the only viable option for favorable outcomes. Empowering these rural-based thrombectomy-proficient centers with preparedness tools, fostering a vigilant mindset, and frequent staff and physician training to focus on efforts directed at achieving faster recanalization times may allow for continued improvement in patient outcomes that will remain consistent with national data.[22] Further studies are needed to identify the patient population that would benefit from endovascular intervention without tPA administration when compared to the currently favored model of combined therapy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Alberts MJ, Hademenos G, Latchaw RE, Jagoda A, Marler JR, Mayberg MR, *et al.* Recommendations for the establishment of primary stroke centers. Brain attack coalition. JAMA 2000;283:3102-9.
2. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, *et al.* A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015;372:11-20.
3. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, *et al.* Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 2015;372:1019-30.
4. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, *et al.* Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 2015;372:2296-306.
5. Abilleira S, Ribera A, Cardona P, Rubiera M, López-Cancio E, Amaro S, *et al.* Outcomes after direct thrombectomy or combined intravenous and endovascular treatment are not different. Stroke 2017;48:375-8.
6. Chandra RV, Leslie-Mazwi TM, Mehta BP, Derdeyn CP, Demchuk AM, Menon BK, *et al.* Does the use of IV tPA in the current era of rapid and predictable recanalization by mechanical embolectomy represent good value? J Neurointerv Surg 2016;8:443-6.
7. Merlino G, Sponza M, Petralia B, Vit A, Gavrilovic V, Pellegrin A, *et al.* Short and long-term outcomes after combined intravenous thrombolysis and mechanical thrombectomy versus direct mechanical thrombectomy: A prospective single-center study. J Thromb Thrombolysis 2017;44:203-9.
8. Phan K, Dmytriw AA, Maingard J, Asadi H, Griessenauer CJ, Ng W, *et al.* Endovascular thrombectomy alone versus combined with intravenous thrombolysis. World Neurosurg 2017;108:850-800.
9. Froehler MT, Saver JL, Zaidat OO, Jahan R, Aziz-Sultan MA, Klucznik RP, *et al.* Interhospital transfer before thrombectomy is associated with delayed treatment and worse outcome in the STRATIS registry (Systematic evaluation of patients treated with neurothrombectomy devices for acute ischemic stroke). Circulation 2017;136:2311-21.
10. Gupta R, Horev A, Nguyen T, Gandhi D, Wisco D, Glenn BA, *et al.* Higher volume endovascular stroke centers have faster times to treatment, higher reperfusion rates and higher rates of good clinical outcomes. J Neurointerv Surg 2013;5:294-7.
11. Grigoryan M, Chaudhry SA, Hassan AE, Suri FK, Qureshi AI. Neurointerventional procedural volume per hospital in United States: Implications for comprehensive stroke center designation. Stroke 2012;43:1309-14.
12. Adeoye O, Albright KC, Carr BG, Wolff C, Mullen MT, Abruzzo T, *et al.* Geographic access to acute stroke care in the United States. Stroke 2014;45:3019-24.
13. Menon BK, Almekhlafi MA, Pereira VM, Gralla J, Bonafe A, Davalos A, *et al.* Optimal workflow and process-based performance measures for endovascular therapy in acute ischemic stroke: Analysis of the Solitaire FR thrombectomy for acute revascularization study. Stroke 2014;45:2024-9.
14. Cao Y, Wang S, Sun W, Dai Q, Zhu W, Yin Q, *et al.* Lack of improvement following endovascular therapy in patients with acute ischemic stroke. Int J Neurosci 2017;127:176-82.
15. Prabhakaran S, Ward E, John S, Lopes DK, Chen M, Temes RE, *et al.* Transfer delay is a major factor limiting the use of intra-arterial treatment in acute ischemic stroke. Stroke 2011;42:1626-30.
16. Nikoubashman O, Pauli F, Schürmann K, Othman AE, Bach JP, Wiesmann M, *et al.* Transfer of stroke patients impairs eligibility for endovascular stroke treatment. J Neuroradiol 2017. pii: S0150-9861(16)30209-7.
17. Rinaldo L, Brinjikji W, Rabinstein AA. Transfer to high-volume centers associated with reduced mortality after endovascular treatment of acute stroke. Stroke 2017;48:1316-21.

18. Rai AT, Seldon AE, Boo S, Link PS, Domico JR, Tarabishy AR, *et al.* A population-based incidence of acute large vessel occlusions and thrombectomy eligible patients indicates significant potential for growth of endovascular stroke therapy in the USA. J Neurointerv Surg 2017;9:722-6.
19. Fargen KM, Fiorella DJ, Mocco J. Practice makes perfect: Establishing reasonable minimum thrombectomy volume requirements for stroke centers. J Neurointerv Surg 2017;9:717-9.
20. Brinjikji W, Kallmes DF, Lanzino G, Cloft HJ. Carotid revascularization treatment is shifting to low volume centers. J Neurointerv Surg 2015;7:336-40.
21. Panezai S, Gezmu T, Kirmani J, Chukwuneke F, Bitra R, Mammo A, *et al.* Compliance with joint commission measures in state-designated stroke centers. J Hosp Med 2014;9:88-93.
22. Eesa M, Menon BK, Hill MD, Demchuk A, Goyal M. Achieving faster recanalization times by IA thrombolysis in acute ischemic stroke: Where should we direct our efforts? Interv Neuroradiol 2011;17:228-34.