Experience on Mechanical Thrombectomy for Acute Stroke Treatment in a Brazilian University Hospital

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Background: Brazil is a developing country struggling to reduce its extreme social inequality, which is reflected on shortage of health-care infrastructure, mainly to the low-income class, which depends exclusively on the public health system. In Brazil, less than 1% of stroke patients have access to intravenous thrombolysis in a stroke unit, and constraints to the development of mechanical thrombectomy in the public health system increase the social burden of stroke. *Objective:* Report the feasibility of mechanical thrombectomy as part of routine stroke care in a Brazilian public university hospital. *Methods:* Prospective data were collected from all patients treated for acute ischemic stroke with mechanical thrombectomy from June 2011 to March 2016. Combined thrombectomy was performed in eligible patients for intravenous thrombolysis if they presented occlusion of large artery. For those patients ineligible for intravenous thrombolysis, primary thrombectomy was performed as long as there was no evidence of significant ischemia for anterior circulation stroke (Alberta Stroke Program Early CT score >6) within a 6-hour time window, and also for those patients with wake-up stroke or posterior circulation stroke, regardless of the time of symptoms onset. *Results:* A total of 161 patients were evaluated, resulting in an overall successful recanalization rate of 76% and symptomatic intracranial hemorrhage rate of 6.8%. At 3 months, 36% of the patients had modified Rankin Scale score less than or equal to 2. The overall mortality rate was 23%. *Conclusion:* Our study, the first ever large series of mechanical thrombectomy in Brazil, demonstrates acceptable efficacy and safety results, even under restricted conditions outside the ideal scenario of trial studies. **Key Words:** Stroke—mechanical thrombectomy—stent-retriever—public health—stroke unit—stroke center—developing country—Brazil.

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Introduction

Stroke is the world's leading cause of adult disability and the second-leading global cause of death behind ischemic heart disease.[1,2] According to the World Health Organization, 89% of the deaths caused by stroke occur in low- and middle-income countries.[2] In the last decade there has been significant progress in the education, care, and research on stroke throughout the Brazilian territory. Much of this breakthrough has been a result of measures adopted by nongovernmental medical societies through the implementation of the National Stroke Project.[3] In 2012, the campaign against stroke earned political support from the Ministry of Health, becoming a national health-care priority. Among the main elements of this political action were investments in the creation of stratified stroke centers, which were classified in 3 levels of care according to hospital complexity, and provision of centralized funding for thrombolytic medication by the Brazilian Ministry of Health.[3] However, despite new overwhelming evidence of the effectiveness of mechanical thrombectomy in the treatment of ischemic stroke caused by large vessel occlusion,[4-8] it is still scarcely available in comprehensive stroke centers in the country because endovascular therapy is not reimbursed within the Brazilian public health-care system. On the other hand, a public health-care policy proposal for financing the availability of mechanical thrombectomy across the country would be weakened if not supported by a large case series confirming its feasibility in a public Brazilian stroke center.

In this study, we sought to evaluate the efficacy, safety, and feasibility of mechanical thrombectomy for acute ischemic stroke treatment in a comprehensive stroke center at a Brazilian public university hospital.

Methods

We reviewed prospectively collected data from all patients with acute ischemic stroke treated with mechanical thrombectomy at our center from June 2011 to March 2016. The primary end points related to safety were death in the first 3 months after stroke and occurrence of symptomatic intracerebral hemorrhage (European Cooperative Acute Stroke Study (ECASS) II criteria)[9]—defined as parenchymal hematoma within 36 hours, associated with increase of 4 or more points on the National Institutes of Health Stroke Scale (NIHSS; range, 0-42, with higher scores indicating more severe neurologic deficits).[10] Regarding the efficacy of the endovascular treatment, cerebral reperfusion was assessed using the thrombolysis in cerebral infarction (TICI) score (which ranges from 0 [no reperfusion] to 3 [complete reperfusion]). Successful reperfusion was defined as a TICI 2b-3.[11] Good clinical outcome was defined as functional independence in 90 days after stroke, assessed by the modified Rankin Scale (mRS, a 7-point scale ranging from 0 [no symptoms] to 6 [death], considering a score of 2 or less as functional independence).

Clinical and Radiological Assessment

The stroke severity was assessed by the NIHSS upon hospital admission. A brain computed tomography (CT) scan was promptly performed, followed by additional imaging methods to assess the artery occlusion site, depending on their availability (transcranial color Doppler, carotid ultrasound, and CT angiography). The brain CT scan was assessed, in joint analysis with a general radiologist, using the Alberta Stroke Program Early CT score (ASPECTS)[12] to quantify the presence of early signs of ischemic injury. Brain CT scan control was performed immediately after the thrombectomy as well as 24-48 hours after treatment. Clinical outcome was assessed at 3-month follow-up by certified examiners, considering independent functional outcome as mRS less than or equal to 2. We collected clinical and radiological data from all of the study subjects.

Acute Stroke Protocol

All patients were treated according to our institution's acute stroke protocol, which is based on Brazilian Guidelines for Acute Ischemic Stroke Treatment.[13,14] Essentially, the protocol includes 2 strategies for endovascular recanalization: either primary thrombectomy or combined treatment with intravenous thrombolysis. For all patients who were eligible for standard intravenous recombinant tissue plasminogen activator thrombolysis and presented with occlusion of large artery (proximal middle cerebral artery, proximal posterior or anterior cerebral artery, carotid or basilar occlusion), endovascular treatment was considered as a combined treatment, and patients were taken to the angiography room for mechanical thrombectomy immediately after the initiation of the intravenous thrombolysis as possible. For patients who were ineligible for intravenous thrombolysis[13,14] and had an acute stroke of the anterior circulation, endovascular recanalization was considered the primary reperfusion strategy as long as there was no evidence of early signs of ischemia involving more than one third of the middle cerebral artery territory on brain CT scan or ASPECTS greater than 6, and provided that patients were within a 6-hour window since symptoms onset. Primary thrombectomy was also performed, regardless of the time of symptoms onset, for those patients who were admitted to our hospital with a wake-up stroke of anterior circulation, but seen last time well within 24 hours, if ASPECTS is greater than 6, and for patients with posterior circulation stroke, when intravenous thrombolysis was contraindicated.

Neurointerventional Procedure

All mechanical thrombectomy procedures were performed by a member of the neurointerventional team,

staffed with 4 interventional neuroradiologists providing 24/7 on-call coverage for emergency care. In addition to acute ischemic stroke, this team was also responsible for attending emergencies such as ruptured brain aneurysm and acute hemorrhagic events that were also treatable by endovascular approach.

Type of anesthesia (local, sedation, or general anesthesia) for each case was determined according to the patient's clinical condition and agreed upon by the anesthesiologist and performing interventional neuroradiologist.

All procedures were performed through a 6F or 7F guiding catheter, continuously perfused with a solution of 40 mg of verapamil hydrochloride or 10 mg of milrinone, diluted in 1000 mL of saline solution (.9%). The following thrombectomy devices were available: Solitaire stent-retriever (Covidien, Irvine, CA), Penumbra aspiration system (Penumbra, Alameda, CA), ACE aspiration system (Penumbra), and Trevo stent-retriever (Stryker, Kalamazoo, MI). If proximal carotid or vertebral occlusion was identified, either a Wallstent or an Express stent (both by Boston Scientific, Marlborough, MA), respectively, was used to perform angioplasty and stenting before the distal mechanical thrombectomy procedure. Stent-retrievers have a preset quota within the annual purchase of hospital materials, so its use was systematized since the beginning of the study. The use of thrombus-aspiration device had a lower sampling because its acquisition by the hospital had been only recently authorized.

Statistical Analysis

The mean and standard deviation (SD), median, and interquartile range (IQR) were calculated for the descriptive statistics of numeric variables as appropriate. Percentage and mode were used to describe categorical variables. We used Student's *t*-test, Mann–Whitney test, and Fisher's exact test as appropriate for univariate analyses. The percentage of recanalization, percentage of mRS scores less than or equal to 2 at 3 months, symptomatic hemorrhage rates, and mortality rates in the present study were compared with those in the earlier large trials. A P value <.05 (2-sided) was used as the threshold for statistical significance. All of the statistical analyses were performed with SPSS version 20.0 (IBM Corp., Armonk, NY).

Results

One hundred sixty-one patients subjected to mechanical thrombectomy for endovascular treatment in acute stroke were evaluated. The mean patient age was 65 ± 14 (SD) years (range 21-89 years) and the patients' median NIHSS score was 19 (IQR, 15-24) at admission. Demographic characteristics of the patients treated are shown in Table 1. Vessel imaging (either transcranial color Doppler US: duplex ultrasonography (TCCD) plus cervical US or computed tomography angiography (CTA)) was performed in all patients. Median ASPECTS score was 10 (IQR, 9-10).

Table 1. *Demographic data of study*

Total number of patients	161
Male : female	93:68
Hypertension	125 (77.6%)
Atrial fibrillation	47 (29.2%)
Diabetes	30 (18.6%)
Renal chronic disease	8 (5%)
Pulmonary chronic obstructive disease	21 (13%)
Coronary artery disease	50 (31.1%)

Vessel occlusions were located in the middle cerebral artery in 42.3% of cases (38.5% M1, 3.8% M2), distal internal carotid artery in 26%, tandem carotid occlusion in 12.5%, cervical carotid artery alone in .5%, posterior cerebral artery (P1) in .5%, multiple locations in 3%, and basilar artery in 15%.

General anesthesia was performed in 68% of procedures. Primary thrombectomy and combined approach were performed in 54.2% and 45.8% of cases, respectively. The mean time from symptom onset to recanalization was 378 ± 132 (SD) minutes. The mean procedure length was 62.5 ± 43 (SD) minutes. We obtained an overall recanalization rate (TICI scores of 2b and 3) of 76% and a symptomatic intracranial hemorrhage rate of 7%. At 3 months, 36% of the patients had mRS score less than or equal to 2. The overall mortality rate was 23%. The results were compared with the primary outcomes of the latest major international clinical trials that analyzed the results of mechanical thrombectomy over medical therapy alone (Table 2).

Regarding the type of thrombectomy material used, the Solitaire stent-retriever was the most used device, having been adopted in 86.5% of cases. Of those, the stent-retriever has been intentionally detached inside the occluded vessel in 7 cases as the only strategy to keep the artery patent after unsuccessful prior attempts of clot retrieval. Thrombus-aspiration system was used as the primary thrombectomy device in 10% of cases (5MAX ACE and Penumbra System, Penumbra, Alameda, CA). Carotid artery stenting with the Wallstent stent was performed in 18.7% of cases.

Discussion

The Brazilian National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária) only approved thrombolytic therapy with recombinant tissue plasminogen activator for treatment of ischemic stroke in 2001, 5 years after approval by the American regulatory agency (Food and Drug Administration). Initially, thrombolytic therapy was available only in private hospitals and some university hospitals that could afford the

Table 2. *The outcomes of the present study compared with 5 large trials assessing intra-arterial treatment for acute ischemic stroke*

Trial (year)	Endovascular sample (n)	Recanalization (TICI = 2b/3) n (%)	3 Months mRs ≤2 n (%)	sICH n (%)	3 Months mortality n (%)	Median NIHSS (IQR)
MR-CLEAN (2014)	233	115/196 (58.7) $P < .001$	76 (32.6) $P = .516$	14 (6) $P = .834$	49 (21) $P = .710$	17 (14-21)
ESCAPE (2015)	165	113/156 (72.4) $P = .703$	87 (53) $P = .002$	6 (3.6) $P = .220$	17/164 (10.4) $P = .002$	17 (12-20)
SWIFT-PRIME (2015)	98	73/83 (88) $P = .019$	59 (60) $P < .001$	0 (0) $P = .007$	9 (9) $P = .006$	17 (13-20)
EXTEND-IA (2015)	35	25/29 (86) $P = .236$	25 (71) $P < .001$	0 (0) $P = .218$	3 (9) $P = .064$	17 (13-20)
REVASCAT (2015)	103	67 (65) $P = .126$	45 (43.7) $P = .244$	2 (1.9) $P = .085$	19 (18.4) $P = .441$	17 (14-20)
Present study (2016)	161	120/158 (75.9)	58 (36)	11 (6.8)	37 (23)	19 (15-24)

Abbreviations: ESCAPE, Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimising CT to recanalisation times; EXTEND-IA, Extending the Time for Thrombolysis in Emergency Neurological Deficits—Intra-Arterial; IQR, interquartile range; MR CLEAN, Multicenter Collaboration for Endovascular Treatment of Acute Ischaemic Stroke in The Netherlands; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; REVASCAT, Randomized Trial of Revascularization with Solitaire FR Device versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting within Eight Hours of Symptom Onset; sICH, symptomatic intracranial hemorrhage; SWIFT-PRIME, Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment; TICI, thrombolysis in cerebral infarction.

medication. In 2008, the National Stroke Project was created by conjoint efforts from the Brazilian Stroke Society, the Brazilian Academy of Neurology, the Brazilian Medical Association, the Brazilian Society of Cardiology, and the Brazilian Emergency Network. The main objectives of the National Stroke Project included improvement in stroke awareness through educational campaigns, training of health-care professionals in stroke care, development of stroke centers across the country, improvement in primary and secondary stroke prevention, and implementation of programs for early rehabilitation and family support.

Implementation of the National Stroke Project enabled several academic medical centers across the country to verify the efficacy and safety of intravenous thrombolysis for the treatment of ischemic stroke.[3] The results of those studies were fundamental in mobilizing public health policy, culminating with the publication in 2012 of the Brazilian National Stroke Policy Act by the Brazilian Ministry of Health.[3] This Act established the battle against stroke as a national health priority.

The Ministry of Health then provided financial resources for investment in stroke units and for reimbursement of thrombolytic medication within the public health system. Despite the budget increase for intrahospital expenses related to stroke care, no specific investment was directed to the development and implementation of mechanical thrombectomy in the stroke centers. In the same year of 2012, the Brazilian Guidelines for Acute Ischemic Stroke Treatment[13,14] was published, as a result of several scientific meetings of the Brazilian Stroke Society, intended to guide specialists and nonspecialists in stroke care on managing patients with acute ischemic stroke. However, at that time, efficacy of mechanical thrombectomy for acute ischemic stroke treatment was still based on results of early studies, and therefore, the procedure was considered as level 2 evidence, class B recommendation.[14] Even if current trial results were available at that time, the demand for governmental support for implementation of mechanical thrombectomy would have faced a national shortage of centers qualified for this type of procedure, raising questions about the viability of its implementation within both public and private health systems.[15,16] Furthermore, there was still not enough techno-scientific national data to support any calls on the government for direct investments in the development of mechanical thrombectomy in these centers.[15,16]

The results obtained in this series of 161 cases of ischemic stroke from large vessel treated with mechanical thrombectomy showed a recanalization success rate (TICI 2b-3) in 75.9% of cases and a 36% rate of favorable outcome at 3-month follow-up (considered as mRS ≤2). Incidence of death in the first 3 months after stroke and occurrence of symptomatic intracerebral hemorrhage were 23% and 6.8%, respectively.

These results are in line with the evolution of the new thrombectomy devices, improved from those observed during the era of the Merci Retriever, the first reperfusion therapy device specifically for use in acute ischemic stroke, which during the first trial showed a 48% recanalization rate, a 7.8% rate of symptomatic intracerebral hemorrhage, and a 44% 3-month mortality rate.[17] By the time the Brazilian National Stroke Policy Act was published in 2012, the use of stent-retrievers in mechanical thrombectomy for stroke therapy had just been ap-

proved by the Brazilian National Health Surveillance Agency, and only a few national case reports were available.[18]

The efficacy and safety end points analyzed in our study showed similar results to those observed for mechanical thrombectomy in Multicenter Collaboration for Endovascular Treatment of Acute Ischaemic Stroke in The Netherlands (MR CLEAN),[4] Extending the Time for Thrombolysis in Emergency Neurological Deficits—Intra-Arterial (EXTEND-IA),[5] and Randomized Trial of Revascularization with Solitaire FR Device versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting within Eight Hours of Symptom Onset (REVASCAT)[7] recent trials. All compared end points showed no statistically significant differences from those 3 studies, except for successful vessel revascularization, which was higher in our study compared with the MR CLEAN trial, and for functional independence at 3 months, which had a higher incidence at the EXTEND-IA trial. We presented higher rates of mortality and clinical disability at 3-month follow-up compared with the results of the Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimising CT to recanalisation times (ESCAPE)[6] and Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME)[8] trials. However, patient selection in those trials was subject to more refined imaging criteria with the disposal of CT perfusion and magnetic resonance imaging (MRI) (SWIFT PRIME), which were not available in our study. Moreover, our patient population included patients with posterior circulation stroke and unknown time window (including wake-up stroke) cases, which are known to have worse clinical course and were not included in any of the referenced trials. Less than 1% of stroke patients in the Brazilian public health system have access to intravenous thrombolysis and admission to a stroke unit, and regular availability of CT perfusion and MRI for stroke acute care is still far from routine practice. In addition to less selective criteria (inclusion of patients with posterior circulation stroke, unknown time window stroke, and no functional imaging studies—Perfusion CTA or MRI), which are expected to lead to worse clinical outcomes, the patients in this study were not systematically referred to stroke rehabilitation centers nor did they have access to home care assistance. The probable negative impact on death rates and clinical recovery from the public health postdischarge infrastructure was not within the scope of this study and could not be analyzed.

Our aim was to analyze the feasibility of mechanical thrombectomy for the treatment of acute ischemic stroke in this context of limited resources. Despite all limitations, we obtained results fully comparable with the MR CLEAN and REVASCAT trials. Considering only those patients with anterior circulation strokes treated within 6 hours, we obtained a successful recanalization rate (TICI 2b/3) of 88.7%, with no statistically significant difference from the rates observed at the ESCAPE and SWIFT PRIME trials, and higher than those at the MR CLEAN, EXTEND-IA, and REVASCAT trials.

The in-hospital data were obtained from the routine practice in a comprehensive stroke center, using the resources already available in a tertiary public university hospital structure, after reorganization of the working conditions for the inclusion of mechanical thrombectomy within its therapeutic options.

The establishment of this restructure had the cooperation between the clinical staff of Interventional Radiology and Neurology services, alongside the administrative direction of the university hospital, which met the demands of the medical staff listed below.

1. Availability of clinical vascular neurologist on duty 24/7.
2. Availability of interventional neuroradiologist on call 24/7.
3. Strong and consistent involvement of neuroradiologists in providing CT data to rule out hemorrhage, but more importantly in providing prompt advanced imaging-based decision-making data, including on stroke volume, penumbra, status of collateral circulation, size and location of thrombus, and status of arterial access to cerebral circulation.
4. Inclusion of thrombectomy devices in the annual budget of hospital supplies, with the possibility of material consignment in case of exceeding the annual purchase.

There was no need for additional medical recruitment because the hospital already had an active interventional neuroradiology staff providing emergency coverage for ruptured brain aneurysm and incoercible bleeding treatable by endovascular interventions.

Conclusion

The lack of large records showing the feasibility of mechanical thrombectomy in Brazilian stroke centers weakened political actions toward the development of this type of treatment in the public health system. Our study confronts this issue, demonstrating the efficacy and safety of mechanical thrombectomy performed in a Brazilian public university hospital, even under limited conditions outside the ideal scenario of the trial studies.

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