

Breaking the breach in Latin America: A pilot study of mechanical thrombectomy in the public healthcare system in Chile

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Abstract

Background: Mechanical Thrombectomy (MT) is the standard of care for treatment of large vessel occlusion stroke. Until the beginning of 2020 MT was not funded nor widely implemented at the public healthcare level in Chile.

Objective: To describe the results of a pilot program created to provide access to public MT in Santiago - Chile.

Methods: Analysis from a prospectively collected database of MT cases performed between September 2017 and September 2019 in one center. A stroke network was developed with a single MT capable stroke center and five primary stroke centers. The primary efficacy endpoint was the rate of functional independence (mRS 0-2) at 90 days. Successful reperfusion was defined as 2 b-3 according to the thrombolysis in cerebral infarction scale. Safety outcomes include the rates of symptomatic intracranial hemorrhage and 90-day mortality.

Results: A total of 100 patients were treated over the study period. Their mean age was 62.8 ± 11.8 years and median baseline National Institute of Health Stroke Scale (NIHSS) measurement was 17. Seventy-seven percent of the patients received intra venous thrombolysis. Successful reperfusion was achieved in 95% of the cases. NIHSS at 24 hours showed a median drop of 7 points from baseline ($p < 0.00001$) and 50% of the follow-up patients were functionally independent at 90 days. Symptomatic Intracerebral hemorrhage occurred in 5% of the patients and 90-day all case mortality was 11%.

Conclusions: We demonstrated the feasibility of a publicly funded MT program in Chile, with similar results as other international randomized control trials.

Keywords

Stroke, mechanical thrombolysis, thrombectomy, public health, cerebral revascularization

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Introduction

Acute ischemic stroke (AIS) due to large vessel occlusion (LVO) is a severe and devastating disease with poor outcomes in approximately 75% of the patients despite intravenous thrombolysis (IVT).^{1,2} In 2015, five randomized controlled trials (RCT) were published demonstrating that functional outcomes were remarkably better after IVT followed by mechanical thrombectomy (MT) than with IVT alone. Thus, IVT and MT is the standard of care in the treatment of AIS secondary to LVO.¹⁻⁷ Although MT was quickly adopted in developed countries as a first-line therapy, Latin American countries have not yet been able to implement nationwide programs.⁸

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Chile has become the first Latin American nation to climb into the category of high-income country. Nevertheless, there are significant inequities in terms of access to medical care with a large difference between the private and public healthcare systems. In Chile, approximately 75% of the population is affiliated to a public insurance system (FONASA: Fondo Nacional de Salud). Public stroke programs have been based in a centrally organized program under the Ministry of Health, offering neurological assessment and IVT.⁹ Although MT has been provided by various public hospitals for some years, up to 2019 there were still no official government reimbursement policies. The purpose of the current study is to evaluate the 2-year results of a publicly funded pilot program for MT in AIS in Santiago - Chile.

Patients and methods

This is a cohort study of 100 consecutive patients treated within our MT pilot program between September 2017 and October 2019. Data was prospectively recorded and retrieved from the hospital database. This study was approved by the local ethic committee and informed consent was obtained in all cases.

The program was based in a stroke health network with a single MT-capable stroke center and five primary stroke centers (PSC) in the metropolitan area of Santiago, using a drip and ship model, encompassing 4 different metropolitan health system areas with a total of 4.5 million inhabitants. Inclusion criteria were patients of age 18 years or older presenting with AIS due to anterior circulation LVO as confirmed by computed tomography angiography (CTA) within 6 hours from symptoms onset. Patients with Alberta Stroke Program Early Computed Tomography Score (ASPECTS) <6 on baseline non-contrast Computer Tomography (CT) were excluded from this protocol. Initial clinical assessment was performed by a neurologist at the PSCs and if eligible received IV Alteplase (Actilyse – Boehringer Ingelheim GmbH) within the first 4.5 hours as per standard guidelines. MT was performed at the main center using a proximal balloon guiding catheter (Corail, Balt Montmorency France; Celo, Medtronic Fridley MN USA) and stentriever (Catch and Catch Mini, Balt Montmorency France; Solitaire, Medtronic Fridley MN USA) as primary strategy. Contact aspiration (Fargo Aspi, Balt Montmorency France) was used mainly as a rescue therapy after stentriever fail. All cases were done in a Siemens Biplane Angiography Suite Artis Zee (Siemens, Erlanger Germany) under general anesthesia (GA). After treatment, patients were managed in a Stroke Unit at the MT-capable center for at least 24-48 hours and then transferred back to the referring PSC for stroke etiology workup, secondary prevention and rehabilitation. We collected all demographic,

clinical, and procedural data including baseline NIHSS, angiographic outcome based on the modified Thrombolysis in Cerebral Infarction (mTICI) scale and NIHSS at 24 h post treatment. Patients were followed-up at 90 days with a validated phone questionnaire for modified Rankin scale (mRS) score evaluation.^{10,11} The questionnaire was answered by patients or their caregivers. The primary efficacy endpoint was the rate of independency (mRS 0-2) at 90 days (good outcome). Successful reperfusion was defined as mTICI 2 b-3. Safety outcomes include the rates of symptomatic intracranial hemorrhage (sICH, defined as \geq four-point increase in NIHSS associated with Parenchymal Hematoma Type II, PH2)¹² and 90-day mortality. We used Stata SE 13.0 for statistical analysis. Chi2 Pearson, T-student and Mann-Whitney tests were used to compare clinical variables and functional outcome (mRS) at 90 days control. Spearman rank correlation was used to compare the time from symptoms onset and successful recanalization with the 24 h NIHSS and mRS at 90 days.

Results

A total of 100 patients were treated over the study period. The mean age was 62.8 ± 11.8 years and median baseline NIHSS was 17 [11-20]. Fifty-six percent of the patients were male, and seventy-seven percent received IV thrombolysis. Occlusion sites most often included the M1- (53%) or M2- (20%) segment of middle cerebral artery (MCA) or the intracranial Internal Cerebral Artery (ICA) terminus (12%). Twelve percent of the patients had cervical tandem lesions. Successful reperfusion was achieved in 95% of the cases after a median number of one pass [1,3]. The median procedural duration (groin puncture to recanalization) was 36 minutes. The NIHSS at 24 hours showed a median reduction of 7 points from baseline ($p < 0.00001$). sICH occurred in 5% and 90-day mortality was 11% (Table 1).

Seventy-six patients were available for answering the 90-day follow-up phone questionnaire, of which 50% were functionally independent (mRS ≤ 2). When we analyzed factors related to good (mRS ≤ 2) versus bad (mRS ≥ 3) outcome at 90 days, we found statistically significant differences in the following variables: NIHSS at presentation, change from baseline to 24 h NIHSS and number of SR passes (Table 2). (Chi2 Pearson, T-student, Man-Whitney).

The time from symptoms onset and successful recanalization was directly related to a better 24 h NIHSS (Spearman corr, $\rho = 0.29$, $p = 0.009$) and to a better functional outcome (mRS) at 90 days (Spearman corr, $\rho = 0.29$, $p = 0.02$).

Discussion

Stroke is the second leading cause of death and disability in Latin American countries. Even though the

Table 1. Clinical data, treatment and outcome of patients treated within a MT pilot program (n = 100).

| | |
|-------------------------------------|-------------|
| Age | 62.8 ± 11.8 |
| Sex (male) | 56% |
| NIHSS at arrival | 17 (11, 20) |
| Occluded vessel | |
| - MCA M1 | 53% |
| - MCA M2 | 20% |
| - Carotid terminus (T occlusion) | 12% |
| - Tandem | 12% |
| - Basilar | 2% |
| - Non-T intracranial ICA | 1% |
| Occluded side | |
| - Left | 53% |
| - Right | 45% |
| - Basilar | 2% |
| IV thrombolysis | 77% |
| mTICI scale | |
| - 3 | 66% |
| - 2B | 29% |
| - 2A | 2% |
| - 0 | 2% |
| - 1 | 1% |
| Successful reperfusion (mTICI 2B-3) | 95% |
| Number of device passes | 1 (1, 3) |
| NIHSS at 24h | 7 (3, 15) |
| Change in NIHSS from baseline | 5.9 ± 5.8 |
| Decompressive craniectomy | |
| - No | 98% |
| - Yes | 2% |
| sICH | 5% |
| 90-Day mortality | 11% |
| mRS at 90 days | |
| - 0 | 16% |
| - 1 | 13% |
| - 2 | 9% |
| - 3 | 15% |
| - 4 | 4% |
| - 5 | 8% |
| - 6 | 11% |
| - Not available | 24% |

Note: Data presented in mean ± SD, percentage % or P₅₀ (P₂₅, P₇₅), as appropriate.

ICA: internal carotid artery; IV: intravenous; MCA M1: middle cerebral artery M1 segment; MCA M2: middle cerebral artery M2 segment; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; SD: standard deviation; sICH: symptomatic intracerebral hemorrhage; mTICI: modified thrombolysis in cerebral infarction.

incidence, prevalence, mortality and disability adjusted life years (DALYs) have declined from 1990 to 2017, the absolute number of patients suffering a stroke has increased by 81% during the same period.⁸ In Chile, stroke has an incidence of 160 per 100.000 inhabitants and is the leading cause of death accounting for approximately 8000 cases per year.¹³ There are many reasons for the high stroke burden in Latin America countries: dietary, genetic and environmental factors, deficiencies in healthcare access, acute treatments being less available, and problems in the primary care health system for prevention

and early detection of the disease.⁸ In Chile it has become mandatory by law for all hospitals to admit any patient presenting with AIS (AUGE-GES guarantees).¹⁴ However, IVT is not yet fully implemented as it is not widely available, nor equally administrated within our nation's territory, as it depends on the presence of a trained neurologist or neurological telestroke set up. Private healthcare centers for AIS are well developed in some restricted areas with several centers that could qualify for a Comprehensive Stroke Center certification. However, there is still a large gap in the availability of MT for the remaining 75% of the population who depend on the public healthcare system. We showed in a recent publication good results in MT for AIS in a single private stroke center in Santiago - Chile,¹⁵ which encouraged us to start a pilot program in 2017 to reduce the breach of stroke care standards between private and public healthcare and to increasingly provide a timely and effective treatment for as many patients as possible.

We achieved similar results to prior large published stroke studies including the meta-analysis performed by Goyal et al.⁴ Compared to the meta-analysis intervention population, our patients were slightly younger in age (63 vs 68 years) but had similar NIHSS on presentation and achieved comparable rates of independent outcomes at 90 days (50% vs 46%). The safety endpoints of sICH and 90-day mortality were also similar (Table 3).⁴

We have chosen to develop the stroke network with a Drip and Ship model due to the singularities of our local reality including technical and human resources availability. Nevertheless, we are evaluating models for direct transfer of patients to our center, from home or Emergency Medical Services (EMS), in order to reduce time to MT reperfusion as "mothership" strategy.¹⁶ The recent DIRECT-MT trial showed non inferiority of MT alone vs alteplase + MT, which could favor the direct MT strategy without IVT. Nevertheless, these results should be considered carefully because in the drip and ship model there is still no strong data to omit IVT.¹⁷ We are now in the process of including patients in late window (from 6 up to 24 hours) and implement the use of artificial intelligence-based software for standardization and improvement of the decision-making process.^{18,19}

The importance of our results is that they represent a real-life scenario that well reflect the reality of many public healthcare networks in Latin America, fighting against stroke with similar economic and cultural barriers. Moreover, our series showed similar results to the prior MT RCTs and Meta-Analysis,⁴ confirming that these results can be replicated in other settings. The recent published results from the RESILIENT study confirmed that MT in the Public Healthcare in Brazil is feasible, safe and effective.²⁰ Our study shows also that these results are reproducible in another Latin America public care system.

Table 2. Comparison between clinical variables and outcome good (mRS ≤ 2) or bad (mRS ≥ 3) at 90 days control (n = 76).

| | Dependent/death mRS ≥ 3 (n = 38) | Independent mRS ≤ 2 (n = 38) | p |
|---|--|--------------------------------------|--------|
| Age | 64.6 \pm 10.5 | 64.3 \pm 11.9 | 0.89 |
| NIHSS at arrival | 18 (15, 22) | 13.5 (2, 7) | <0.001 |
| Change in NIHSS from baseline | 3.1 \pm 6.4 | 7.9 \pm 4.3 | <0.001 |
| mTICI ^a | | | 0.45 |
| - 3 | 22 (58%) | 26 (72%) | |
| - 2B | 12 (32%) | 9 (25%) | |
| - 2A | 1 (3%) | 1 (3%) | |
| - 1 | 1 (3%) | 0 (0%) | |
| - 0 | 2 (5%) | 0 (0%) | |
| Good recanalization (mTICI 2B-3) ^a | | | 0.18 |
| - Good | 34 (89%) | 35 (97%) | |
| - Bad | 4 (11%) | 1 (3%) | |
| Number of device passes | 2 (1, 3) | 1 (1, 2) | 0.004 |
| IVT | | | |
| - No | 12 (32%) | 7 (18%) | 0.19 |
| - Yes | 26 (68%) | 31 (82%) | |

Note: Data presented in mean \pm SD, number (%) or P₅₀ (P₂₅, P₇₅), as appropriate.

^amTICI and Good recanalization was not considered in two patients that were already open at arrival.

IVT: intravenous thrombolysis; NIHSS: National Institutes of Health Stroke Scale; SD: standard deviation; mTICI: modified thrombolysis in cerebral infarction.

Table 3. Comparison between our results and Goyal et al. meta-analysis.⁴

| | Our results | Goyal et al. ⁴ meta-analysis (intervention population) |
|--|----------------|--|
| NIHSS at 24h | 7 (3, 15) | 8 |
| Change in NIHSS. Baseline to 24h | -5.9 \pm 5.8 | -6.4 \pm 8.2 |
| NIHSS 0-2 at 24h | 17% | 21% |
| Early neurological recovery (≥ 8 pts drop in NIHSS at 24h) | 37% | 50.2% |
| sICH | 5% | 4.3% |
| Mortality | 11% | 15.3% |
| mRS at 90 days in followed up patients | 50% | 46% |

Note: Data presented in mean \pm SD, percentage % or P₅₀ (P₂₅, P₇₅), as appropriate.

NIHSS: National Institutes of Health Stroke Scale; sICH: symptomatic intracerebral hemorrhage; mRS: modified Rankin Scale; SD: standard deviation.

Our study presents some limitations. We were not able to carry out 90 days follow up control for all patients (76% follow-up), due to changes in their contact phone, no phone number or repatriation system that hindered strict control by our center. Nevertheless, we checked national databases for patient deaths during that period and included them as outcome if found. We have modified our local protocols for actively search and confirm phones numbers and contact information for proper follow up. Finally, this is a cohort study, with no control group and no randomization. Thus, as MT is considered a standard of care for LVO in the first 6 hours from symptoms onset, randomization is not considered feasible in this scenario.

At the end of the pilot study period, the Chilean government approved the financing of MT in the public health system, starting in January 2020.

In summary, our results confirmed that implementation of MT for treatment of LVO in a public health care network in a Latin American country is feasible yielding technical and clinical outcomes that are comparable with other large international series and trials.

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