Accessibility and effectiveness of mechanical thrombectomy for ischaemic stroke in Latin American countries: a rapid review of the literature

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Abstract

Introduction. Stroke constitutes a major cause of death and disability in Latin America. Although the number of stroke survivors has increased in recent decades, a small proportion receives the appropriate treatment. Mechanical thrombectomy (MT) revolutionised stroke management by treating patients within a 24-hour window period, compared to the usual 4.5 hours with intravenous recombinant tissue plasminogen activator (IV rtPA).

Objective. To evaluate the current status of mechanical thrombectomy in Latin American countries regarding availability, accessibility, effectiveness, and cost-utility.

Methods. A rapid review of the literature was performed by identifying papers published in MEDLINE in English or Spanish from 2015 to current. Reference list search complemented the database research. Included studies were randomised controlled trials and observational studies. Data extraction was performed by one reviewer, and data synthesis was performed following the SWIM guidelines.

Results. 10 studies were included. Only one study was a randomised controlled trial. Studies reported that MT is available in Latin American countries. The proportion of treated patients varied from 3% to 19.9%. Recanalisation rates were above 69% in all studies, while functional independence (mRS 0-2) varied from 25% to 50%. Financial barriers were considered as the main limiting factor to access MT. No study realised a cost-utility analysis.

Conclusion. Evidence of the efficacy and effectiveness of MT and its main barriers to access is consistent among Latin American countries. Further research is needed, mainly from a robust economic analysis, to evaluate the economic impact of MT.

Introduction

Stroke is the second cause of death in Latin America.^[1] It is the consequence of the sudden stop of cerebral blood flow due to the rupture (haemorrhage) or blockage (ischaemia) of a cerebral artery, the latter representing over 80% of strokes.^[2] In 2013, 75% of deaths and 81% of disabilities due to stroke occurred in low- and middle-income countries (LMICs) such as those from Latin America.^[3] Recently, a decline in the stroke death rate has been observed in high-income countries (HICs) and LMICs due to improved stroke care.^[4] From 1990 to 2019, the number of stroke survivors increased by 80%^[5] in the Latin American region.

Intravenous thrombolysis with recombinant tissue plasminogen activator (IV rtPA) is the gold standard treatment for acute ischemic stroke (AIS) and is associated with improved functional independence after stroke.^[6] This treatment is widely available in Latin American countries, and its accessibility has increased since it was introduced in the region. Further, a recent multinational stroke registry in Latin America revealed that the proportion of AIS patients receiving IV rtPA is similar to that of HICs.^[7] Nonetheless, the main limitation of IV rtPA is that its administration is limited to the first 4.5 hours from stroke onset, thus hindering patients receiving this therapy.

Stroke treatment was revolutionised after the publication of randomised clinical trials (RCTs) demonstrating the efficacy of mechanical thrombectomy (MT) to improve recanalisation and clinical outcomes compared to standard treatment^[8], allowing eligible stroke patients to be treated within a 24-hour time window.^[4] However, MT is not broadly available in Latin America, and less than 1% of stroke patients from these countries are treated with MT.^[7] According to Martins et al.,^[1] MT is scarcely accessible in the region and mostly limited to private health care institutions. Studies from Latin America have described effectiveness and efficacy similar to RCTs from HIC and have also described some limitations to access MT.^[9-14] However, no systematic approach has been conducted to evaluate the status of MT in the region.

Due to the similarity in the socioeconomic context among Latin American countries, a systematic review of the literature would provide relevant information for stakeholders in the region by presenting a robust evaluation of MT's effectiveness and the limitations of its availability and the cost-utility of this treatment. Therefore, a rapid review of the literature was developed to evaluate the current status of mechanical thrombectomy in Latin American countries in terms of availability, accessibility, effectiveness, and cost-utility.

Material and methods

A rapid review was considered as an adequate method to address the aim of this study as it assesses what is already known about a policy or practice issue, uses systematic review methods to search and critically appraise existing research.^[15]

2.1 Eligibility criteria

2.1.1 Study types

RCTs provide information on the efficacy of an intervention under ideal, experimental conditions; this type of study allows the comparison with other RCTs; on the other hand, observational studies, mainly from clinical registries, offer information about the 'real-life' effect of the intervention and allow the identification of the core barriers to access MT. Therefore, both RCTs and observational studies will be included.

2.1.2 Participants

Included studies must involve adult patients (>18 years) with AIS defined by neuroimaging (computed tomography or magnetic resonance imaging). Studies addressing haemorrhagic stroke will be excluded.

2.1.3 Intervention

The intervention evaluated in this review is the use of MT.

2.1.4 Comparator

For this rapid review, studies comparing outcomes with a control group will be included. Also, studies only reporting no comparators will be included for the purposes of a narrative synthesis.

2.1.5 Outcome measure

This rapid review defined as primary outcomes organised in four main areas (i) availability of MT, (ii) accessibility of MT, (iii) effectiveness of MT and (iv) cost-utility of MT.

2.2 Information sources

A search of the literature was performed in December 2020. The literature search was limited to one database: MEDLINE. However, the review of the bibliography of each of the included articles was used as an additional search technique.

The approval of MT in the American Stroke Association guidelines, which are used as the primary reference for

most Latin American countries, was published in 2015.^[16] Thus, the literature search strategy was limited to papers published from 2015 onwards. Articles published in English and Spanish were considered for inclusion.

2.3 Selection of studies

One reviewer (AGA) was responsible for selecting the studies, which was initiated by downloading all titles and abstracts retrieved by the search strategy to a reference management database software (Mendeley) to remove duplicates, followed by the screening of titles and abstracts for inclusion. The full text of the potentially included studies was retrieved to assess inclusion and exclusion criteria. The studies that met the criteria were included.

2.4 Data extraction

Key data were extracted using a defined data extraction template presented in supplementary material 1.

2.5 Summary measures and evidence synthesis

The summary measures obtained from the included articles were organised as follows:

i) Availability:

a. Number of hospitals in which MT is available in the country.

ii) Accessibility:

a. Proportion of stroke patients that receive MT treatment.

b. Main barriers to access MT.

iii) Effectiveness:

a. Proportion of successful recanalisation, and

b. Proportion of functionally independent (considered as a modified Rankin Scale (mRS) of 0 to 2) patients 90 days after hospital discharge.

iv) Cost-utility:

a. QALYs reduced with MT compared to usual care.

Due to the heterogeneity of the included studies in terms of study design, a meta-analysis was not considered, and the synthesis without meta-analysis (SWIM) guidelines were followed.^[17] Synthesis was performed around the outcomes of the included studies with a focus on the primary objectives.

3. Results

Ten studies were included in the final analysis (figure. 1), and a summary of these studies is shown in table 1.



NA: non-applicable; ‡: information complemented by the author of this review. Functional independence was considered as a mRs of 0-2.

3.1 Availability

The availability of MT was restricted to hospitals located in the capital cities in 3 (Argentina, Chile, and Colombia) out of 5 of the countries. Only Mexico^[9] and Brazil^[20] described MT availability in hospitals from cities other than the country's capital. Chile^[22,23] and Mexico^[9] reported having MT available mainly in private hospitals, while the rest reported MT availability in public hospitals.

3.2 Accessibility

a. Proportion of stroke patients that receive MT treatment.

Mexico and Colombia reported results from a cohort of stroke patients treated with MT;^[9,13] thus, accessibility could not be described. In Argentina, accessibility varied from 3% to 19.9% (10,18,19), while in Brazil was 12%^[25], and Chile reported the lowest accessibility with 5.5%.^[22]

b. Main barriers to access MT.

Financial barriers (lack of public funding and high MT cost) were the main limiting factor to access MT in 4 out of the five countries. Only the report from Colombia did not recognise an economic barrier.^[13] Additionally, Brazil and Colombia identified as a barrier the lack of the required infrastructure to perform MT^[13,24] Only the study from Colombia mentioned geographical, administrative (bureaucracy) and lack of trained specialists as further barriers.^[13]

3.3 Effectiveness:

a. Proportion of successful recanalisation

Successful recanalisation was above 70% in all countries except Mexico, which reported 69.4%.^[9] Studies from Chile reported a recanalisation rate of 90.3% and 95%^[22,23], while those from Brazil varied between 76% to 92.6%^[20, 21, 24], and the ones from Argentina between 73% to 78%.^[10, 19, 20] The study from Colombia did not describe the percentage of successful recanalisation.^[13]

b. proportion of functionally independent patients 90 days after hospital discharge.

Only studies from 3 countries described the proportion of patients with functional independence 90 days after hospital discharge: in Argentina varied between 25% to 47.5%^[10,18,19], in Brazil was between 34% to 35%^[20, 21, 24], and in Chile of 50%.^[23] Colombia reported functional independence of 50% of stroke patients 365 days after hospital discharge^[13], while Mexico presented the shortest follow up (59 days) and a proportion of 64% of functionally independent patients.^[9]

3.4 Cost-utility

None of the included studies reported results from a cost-economic analysis.

Discussion

4.1 Summary of evidence

This rapid review identified ten studies that reported information about the availability, accessibility and/ or effectiveness of MT in AIS, with none of the studies performing a cost-utility analysis. Only one study was an RCT, while the rest were observational studies; all studies reported offering IV rtPA before MT according to national and international guidelines. The RCT by Martins et

Table 1. Summary of included studies.				
Study ID	Study design	City, country and setting	Participants	Outcomes:
Alet et al, 2020 (18)	Observational, clinical registry	Buenos Aires, Argentina; comprehensive stroke centre	891	 Availability: only the reporting centre. Accessibility: Proportion of patients receiving MT: 3%. Barriers to access: not reported. Effectiveness: Recanalization rate: 78%. Functional independence: 37% at 90 days after hospital discharge.
Cirio et al, 2020 (19)	Observational, clinical registry of treated patients	Buenos Aires, Argentina; comprehensive stroke centre.	699	Availability: only the reporting centre. Accessibility: Proportion of patients receiving MT: 19.9%. - Barriers to access: not reported. Effectiveness: - Recanalization rate: 74.8%. - Functional independence: 47.5% at 90 days after hospital discharge.
Colla Machado et al, 2016 (10)	Observational, case series	Buenos Aires, Argentina; university hospital.	11	 Availability: only the reporting centre. Accessibility: Proportion of patients receiving MT: NA. Barriers to access: resources (asymmetric distribution of resources). Effectiveness: Recanalization rate: 73%. Functional independence: 27% at 90 days after hospital discharge.
Gonzalo Muñoz et al, 2017 (13)	Observational, case series	Medellin, Colombia; com- prehensive stroke centre.	10	 Availability: only the reporting centre. Accessibility: Proportion of patients receiving MT: NA. Barriers to access: geographical, administrative (bureaucracy), limited number of trained professionals, lack of comprehensive stroke care services. Effectiveness: Recanalisation rate: not reported. Functional independence: 50% at 535 days after hospital discharge.
Mar- quez-Rome- ro et al, 2020 (9)	Observational, clinical registry of treated patients	Multiple cities, Mexi- co; public and private hospitals	49	 Availability: ca 35, mostly private‡. Accessibility: Proportion of patients receiving MT: NA Barriers to access: financial (lack of public funding). Effectiveness: Recanalization rate: 69.4%. Functional independence: 64% at 59 days after hospital discharge.
Martins et al, 2020 (20)	Randomised controlled trial	Multiple cities, Brazil; 12 public hospitals.	300	 Availability: Multiple centres for the purpose of the RCT. Accessibility: Proportion of patients receiving MT: NA. Barriers to access: lack of public funding. Effectiveness: Recanalization rate: 82%. Patients receiving MT had a functional independence at 90 days of OR 2.28 (95%CI 1.41 – 3.69) compared to the control group.
Nakiri et al, 2017 (21)	Observational, clinical registry of treated patients	Sao Paolo, Brazil; public university hospital.	161	 Availability: only the reporting centre. Accessibility: Proportion of patients receiving MT: NA. Barriers to access: not reported. Effectiveness: Recanalization rate: 75.9%. Functional independence: 36% at 90 days after hospital discharge.
Reyes et al, 2018 (22)	Observational, clinical registry	Santiago, Chile; private hospital.	1875	 Availability: only the reporting centre. Accessibility: Proportion of patients receiving MT: 5.5%. Barriers to access: not reported. Effectiveness: Recanalization rate: 90.3%. Functional independence: 62.5% at hospital discharge.
Rivera et al, 2020 (23)	Observational, clinical registry of treated patients	Santiago, Chile; public and private hospitals.	100	 Availability: only the reporting centre. This was a pilot program to evaluate the feasibility of public funding to MT.
Thays Beck- hauser et al, 2020 (24)	Observational, clinical registry	Sao Paolo, Brazil; public university hospital.	1739	 Availability: only the reporting centre. Accessibility: Proportion of patients receiving MT: 12%. Barriers to access: lack of public funding for MT, low availability of advanced multimodal neuroimaging.

al.^[20] demonstrated the safety and efficacy of recanalisation and functional independence at 90 days with MT in the context of a public hospital from a developing country, with similar results to that of developed countries.^[25] Similarly, all observational studies reported similar or higher percentages of successful recanalisation and functional independence after stroke treatment with MT compared to results from HICs.^[11]

Most of the studies reported MT availability was limited to the countries' capital cities. Only two studies mentioned that MT is available in other cities^[9,20]; however, Marquez Romero et al.^[9] reported a higher availability in private hospitals, while Martins et al.^[20] mentioned that MT was available in public hospitals through donations from manufactures of the MT devices used in their research. This finding suggests a concentration of MT services among the cities with better economic development or private hospitals. Additionally, financial barriers due to the lack of funding for MT were identified as the most common reason for eluding stroke treatment with MT; this has been recently highlighted by Gongora-Rivera et al. in a national survey among endovascular neurologists in Mexico, where over 80% of the participants reported financial barriers as the main limiting factor to access MT.^[26] Lastly, the proportion of patients receiving MT varied from 3% to 19.9%. This number is higher to the previous report from a Latin American multicentre stroke registry^[7]; nonetheless, only two studies^[19,24] had a similar or higher proportion of stroke patients accessing MT compared to the estimated 12% of eligible patients based on a report from the United Kingdom.^[27]

Among the included studies, only one reported having a drip and ship pathway of stroke care for MT^[23], which consists of first transferring the patient to the nearest stroke care hospital with the capacity to administer IV rtPA. The rest followed a mothership pathway, consisting of transferring the patient directly to a comprehensive stroke to provide IV thrombolysis and MT. Although the mothership pathway of care has proven to improve functional independence compared to drip and ship, no differences prevail in successful reperfusion, symptomatic intracranial haemorrhage, or 90-day mortality.^[28] Therefore, the high concentration of comprehensive stroke centres in the capital cities and the successful experience in the study by Rivera et al.^[23] could serve as an opportunity for stakeholders from the region to increase the availability and access for stroke patients benefiting from MT.

The following implications might be considered for policymakers: the evidence from this review supports the efficacy (experimental effectiveness) and effectiveness (practical or 'real-life' effectiveness) of MT compared to usual care under the context of Latin American countries. However, the information of most of the articles was based on observational studies, mainly from case series or clinical registries. These studies are subject to selection bias, for instance, the inclusion of patients with a better outcome. Further, financial barriers (lack of public funding or high costs of MT) were identified as the main reason for eluding patients benefiting from MT and might contribute to the access of MT limited to developed cities (i.e. capital cities) or private hospitals. Finally, increasing centres providing drip and ship stroke care might expand the availability and access of MT in the region.

4.2 Limitations

The primary limitations of this review are the characteristics of the included studies (mostly observational from case series or clinical registries). Also, the methodology of this review was that of a rapid review and articles were limited to those published from 2015 onwards. Further, the study was developed by a single reviewer; thus, the study selection was not performed with a double independent revision, and the quality assessment and robust data extraction were not realised. Despite the beforementioned limitations, we believe some strengths merit comment.

4.3 Impact for future research

There is a need for an economic analysis of MT in Latin American countries to provide more accurate information to policymakers about the economic impact and health outcomes benefits that MT could have compared to usual care. In addition, prospective observational studies with consecutive samples are needed to have a more accurate the proportion of patients treated with MT. Lastly, a critical systematic review of the literature with less restrictive criteria is needed to have a more robust analysis of the information available.

Conclusions

The evidence from this rapid review demonstrates that MT is practised in different Latin American countries with limited access, mainly to the countries capital cities and private hospitals. The effectiveness and efficacy are similar to that from high-income countries, but the lack of public funding and the higher costs of mechanical thrombectomy constitute the main barrier to benefit from this therapy. There is a need for robust economic analysis in the region to evaluate the economic impact of mechanical thrombectomy and provide accurate information to policymakers from Latin American countries.

Authors disclose no conflict of interests.

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