Outcomes of mechanical thrombectomy at a single-centre tertiary level public health care hospital in South Africa

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DECLARATION

I, ***Martin Kiriinya***, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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DEDICATION

ACKNOWLEDGEMENTS

I would like to thank and acknowledge the assistance, guidance and support I received from my supervisors: Prof. Allan Taylor, Prof. David Le Feuvre and Dr. Kathleen Bateman; Dr. Michelle Henry for statistics support and Dr. Christel Arnold-Day for assistance in editing.

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CERTIFICATION

The undersigned certify that they have read and thereby recommend for examination the dissertation titled ***Outcomes of mechanical thrombectomy at a single-centre tertiary level public health care hospital in South Africa***, in partial fulfilment of the requirements for the degree of Master of Medicine (Neurosurgery) of the University of Cape Town.

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LIST OF ABBREVIATIONS

ADAPT	Direct Aspiration First Pass Technique
ASPECT	Alberta Stroke Program Early CT Score
AT	Allan Taylor
CI	95% Confidence Interval
CT	Computerised Tomography
CTA	Computed Tomographic Angiography
DLF	David Le Feuvre
DSA	Digital Subtraction Angiogram
GSH	Groote Schuur Hospital
HREC	Human Research Ethics Committee
ICA	Internal Carotid Artery
IQR	Interquartile Range
IVT	Intravenous Thrombolysis (With Alteplase)
KB	Kathleen Bateman
LMIC	Low-and Middle-Income Country
LVO	Large Vessel Occlusion
M1	First segment of middle cerebral Artery
MMK	Martin Muthinja Kiriinya
LVO	Large Vessel Occlusion
MT	Mechanical Thrombectomy
mTICI	Modified Thrombolysis in Cerebral Infarction Scale
NIHSS	National Institute of Health Stroke Scale
RCT	Randomized controlled trial
RESILIENT	Martin et al, 2020(RCT, Brazil)

Chapter 1 Introduction

1.1 Context

Ischaemic stroke accounts for a large amount of disability (95,000 years lived with disability) and mortality (25,000 deaths/year) in South Africa (1). Management strategies are directed at prevention by controlling major risk factors like hypertension, diabetes, dyslipidaemia and heart disease. Direct treatment aimed at reopening occluded cerebral vessels became available with the introduction of tissue plasminogen activator. Thrombolysis has potential benefit if offered within 4,5 hours of symptom onset and prevents disability and death in 143 patients for every 1000 treated. If trial inclusion and exclusion criteria for lysis are adhered to then 30% of all ischaemic stroke patients could benefit (2). Access to thrombolysis in public South African hospitals is limited. Strategies aimed at improving outcomes further and expanding the time window of treatment have focused on intra-arterial approaches, initially with thrombolytics and later mechanical clot removal. This applies mostly to patients with large vessel occlusion (LVO) where the clot burden makes intravenous thrombolysis less successful. Endovascular treatment trials had variable results until 2015 when five randomized controlled trials (RCTs) were completed. They demonstrated a high treatment effect of patients treated with mechanical thrombectomy (MT) having better functional outcomes at three months compared to best medical therapy alone (3). Mechanical thrombectomy is however resource intensive requiring trained endovascular interventionalists, cath lab resources and costly endovascular devices. Not surprisingly, all five RCTs were done in high income countries. Limited data is available to determine if similar outcomes could be achieved in lower resourced settings where time delays may be longer, device access restricted and after care and rehabilitation limited. In 2018 an acute stroke treatment guideline based on recommendations from the American Stroke Association (4) was implemented to improve referral and treatment pathways for acute stroke at Groote Schuur Hospital (GSH). The GSH stroke treatment guideline aims to rapidly select patients with large vessel occlusion and expedite treatment with mechanical thrombectomy. All patients get a computerised tomography (CT) scan at 24 hours after treatment and are clinically reviewed at 90 days post treatment. Outcome is recorded using the modified Rankin score (mRS). We conducted an audit of the clinical and interventional outcomes of patients who underwent mechanical thrombectomy from the 1st of January 2018 to the 1st of January 2022. We describe our disability, mortality, and recanalization outcomes of MT for acute LVO stroke to assess its efficacy and safety in a South African public health care system, and analyse factors associated with these outcomes. We also compared our results to published data from a RCT in a comparable LMIC (5) and other published trials.

1.2 Ethical considerations

The research protocol was presented and approved by the Surgical Department Research Committee for approval (Project 2019/073), followed by ethics approval by the University of Cape Town's Human Research Ethics Committee (HREC REF 444/2019) and finally an application to Groote Schuur Hospital for institutional approval.

1.3 Author guidelines of the Journal

Chosen journal: Interventional Neuroradiology (INR) – SAGE Journals

INR is a peer-reviewed clinical practice journal documenting the current state of interventional neuroradiology worldwide. INR publishes original clinical observations, descriptions of new techniques or procedures, case reports, and articles on the ethical and social aspects of related health care. Original research published in INR is related to the practice of interventional neuroradiology. This journal is a member of the Committee on Publication Ethics (COPE). It has a 5-year impact factor. The ISSN is 1591-0199 for print and 2385-2011 for the electronic version. The online link is: https://journals.sagepub.com/home/ine,

Journal Instructions to Authors for Original Papers (also see appendix 4)

Abstract: No more than 300 words; 3 to 5 keywords; no references.

Main Body: The manuscript is written in Helvetica or Times New Roman (12-point size) font. References are written in the Vancouver style; numbered in order they appear.

The manuscript adheres to the word limits and reference limits:

Original research 4000 words; 40 references.

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Chapter 2 Publication-ready manuscript

Outcomes of mechanical thrombectomy at a single-centre tertiary level public health care hospital in South Africa

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Abstract:

Introduction:

Mechanical thrombectomy (MT) is standard of care for acute ischaemic stroke from large vessel occlusion (LVO) following randomized controlled trials performed largely in high-income countries. Limited data exists on its effectiveness in the setting of low- and middle-income countries (LMIC). We aimed to evaluate the safety and efficacy of MT in a tertiary level public hospital in Cape Town, South Africa.

Methods:

Patients with acute ischaemic stroke presenting consecutively to Groote Schuur Hospital between 01 January 2018 to 01 January 2022 with proximal intracranial occlusion in the anterior circulation treated with MT within 6 hours from onset using CT and CTA imaging-based protocols were evaluated. Demographic, clinical, radiological, and procedural data were obtained from the stroke unit database. Recanalization was evaluated post-procedure by modified Treatment in Cerebral Infarction score (mTICI). Functional independence (modified Rankin scores (mRS) 0-2) and mortality at 90 days were also assessed.

Results:

Thrombectomies were performed in 84 patients during the study period. The median age was 56 years (IQR) and 51% of participants were female. Median National Institute of Health Stroke Score was 18 and median baseline Alberta Stroke Programme Early CT score was 8. Bridging thrombolysis was given to 65% of participants. Median time from symptom onset to reperfusion was 339 minutes (IQR). Successful recanalization (mTICI 2b/3) was obtained in 62%. At 90 days, 34 % of participants gained functional independence and mortality was 34%.

Conclusion:

This study demonstrated similar rates of recanalization and functional independence to that seen in trials in high-income countries using basic imaging despite a higher mortality and longer median time to reperfusion. This data supports the effectiveness of MT in a tertiary level public hospital in South Africa despite the challenges of providing emergent stroke care in a resource-constrained setting.

Key words: *mechanical thrombectomy, low-and-middle-income country, outcomes, south africa*

INTRODUCTION

The benefit of mechanical thrombectomy (MT) in the treatment of acute ischaemic stroke due to large vessel occlusion (LVO) of the anterior circulation was established following five major randomized clinical trials in 2015, which demonstrated better functional outcomes at three months compared to best medical therapy alone (1, 2, 3, 4, 5). Pooled analysis of these trials by Hermes group. showed that MT was effective overall and within sub-groups under-represented in the individual trials, such as the elderly, patients not receiving IV alteplase and those treated later than 300 minutes after stroke onset (6). Subsequent trials have shown consistent superiority of MT compared to best medical treatment alone. Favorable outcomes have moreover been reported in the extended time periods up to 24 hours for patients carefully selected using advanced imaging (7, 8), in patients undergoing MT without thrombolysis (9) and in resourced constrained healthcare systems compared to the earlier trials (10, 11).

At Groote Schuur Hospital, we conducted a retrospective review of the clinical and interventional outcomes of patients who underwent MT from 1st January 2018 to 1st January 2022, utilizing protocol-based recommendations from the updated American Stroke Association guidelines of 2015(12) for the management of acute ischemic stroke due to LVO of the anterior circulation. We describe our disability, mortality, and recanalization outcomes of MT for acute LVO stroke to assess its efficacy and safety in a South African public health care system, and analyse factors associated with these outcomes. We thereafter compare our results to published data from a randomized control trial in a comparable LMIC, namely Brazil (10), as well as other similar published trials.

METHODOLOGY

Study Design

A single centre retrospective review study. The study was approved and overseen by the Department of Surgery Research Committee (Project 2019/073) and Human Research Ethics Committees at Groote Schuur Hospital (GSH) (HREC ref 444/2019).

Data Collection Methods

Neurovascular procedural reports for all patients undergoing MT for LVO from the 1st January 2018 to the 1st January 2022 were identified and cross-referenced with the GSH Stroke Unit clinical database. Data was extracted from the clinical database, and missing data obtained from folders, imaging, and telephonic interviews. All digital subtraction angiograms, pre- and post-procedure, were independently reviewed by the author (MMK) and stroke neurologist (KB) to determine the location of the initial large vessel occlusion and mTICI score. Discrepancies were resolved by consensus decision with an interventional neurosurgeon (AT/DLF).

Participants

All patients undergoing MT for LVO at GSH from the 1st January 2018 to the 1stJanuary 2022 were included. Eligible patients were above 18 years of age, pre-stroke score of 0 or 1 on modified Rankin scale (mRS), a clinical baseline of 6 or higher on the National Institutes of Health stroke Scale (NIHSS), with an arterial occlusion of the internal carotid artery (ICA), the first segment of middle cerebral artery (M1) or both confirmed by Computed Tomographic Angiography (CTA) who had a baseline Alberta Stroke Program Early CT Score (ASPECT) above five and treatment initiated within 6 hours from stroke onset.

Intervention

After triage in the emergency department, the stroke team reviewed and identified patients who met the clinical and radiological criteria for MT according to local hospital acute stroke protocols (Appendix 5). Patients who arrived within 4.5 hours and without contraindication to thrombolysis were given 0.9mg/kg of IV alteplase (IVT).

MT was performed by experienced neuro-interventionalists: 2 neurosurgical consultants, 1 neurosurgical endovascular fellow and 1 consultant interventional radiologist. All cases were done under general anesthesia. Neuro-interventional techniques included both Direct Aspiration First Pass Technique (ADAPT) and use of stent retriever with Aspiration (SOLUMBRA), at the discretion of the treating neuro-interventionalist. After the procedure, patients were admitted to a neurocritical care unit for at least 24hrs for monitoring and optimized blood pressure management before transfer to a specialized post-acute stroke ward for continued best medical therapy and rehabilitation.

Outcome Variables

The primary outcome was the proportion of MT patients achieving a mRS of 0-2 (no or mild disability) or 6 (death) at 90-days post-stroke. The mRS is routinely evaluated at follow-up either in-person or telephonically by the attending neurologists at the post-reperfusion stroke clinic. For those patients with missing outcome data, telephonic assessment was carried out by a study investigator (MMK). The secondary outcome was the proportion of MT patients achieving successful post-procedure recanalization defined by a modified Thrombolysis in Cerebral Infarction Scale (mTICI) grade of 2b, 2c or 3.

Statistical analyses

Descriptive data were generated as median and interquartile ranges for continuous variables, and frequencies and proportions for categorical variables. Analyses were run with SPSS Version 26, with the threshold for statistical significance set at $p = 0.05$.

Comparison of the current dataset to RESILIENT, 2020 (Brazil):

Our data was compared to the RESILIENT trial, 2020(Brazil). One sample Wilcoxon rank tests were used to compare continuous variables to the RESILIENT data, and one sample binomial tests were used for the categorical variable comparisons.

Predictors of modified Rankin scale scores and successful recanalization:
Three separate logistic regression analyses were used to assess the predictors of (a) a mRS of 0-2; (b) a mRS of 6 (which indicates the patient died), and (c) successful recanalization defined as a mTICI Grade of 2b–3. Univariate analyses were run for between-group comparisons (independent sample t-tests for continuous variables and chi-square for categorical variables). Variables identified as having a significant difference/association with the outcome variables in the univariate analyses were entered into the regression model as predictors. Backwards stepwise logistic regression analyses were run to determine which variables from the univariate analyses remained significant predictors of the outcome variables.

RESULTS

Participants

From the 1st January 2018 to the 1st January 2022, a total of 84 patients had MT done. The median age was 55.5years, 43 (51.1%) were female. The median NIHSS score was 18 (IQR, 15-21). The baseline median ASPECT was 8 (IQR, 7-9) and 7 (8.3%) of whom had ASPECT score of less than 6. 55 (65.5%) received IV thrombolysis. Occlusion sites included M1 in 41 (48.8%), Carotid terminus in 21 (25%), Tandem ICA in 18 (21.4%) and M2 & M3 level in 4 (4.8%) patients respectively (Figure 1).
When comparing patient baseline characteristics between our study and RESILIENT, the following significant differences were found. Our patient group was younger (p= < .001), and we had a significantly lower proportion of patients with stroke in the left hemisphere (p = .039), significantly higher proportion of patients with M1 and extracranial(tandem) occlusion (p=<.001) and a significantly higher proportion of patients with atrial fibrillation (p = .005) but significantly fewer patients with congestive cardiac failure (p = .002). (Table 1).

Table 1. **Baseline patient characteristics of cohorts from Cape Town and Brazil**			
Variable	**Cape Town N = 84**	**Brazil N = 111**	**p-value**
Age – Years – no. (%)	84 (100%)		
median (IQR)	55.5 (46.3-66)	65 (54-77)	< .001
Female – no. (%)	43 (51.2)	51 (45.9)	
NIHSS – no. (%) ‡	77 (91.6)		
median (IQR)	18 (15-21.5)	18 (14–21)	.979
Location of stroke in left hemisphere – no. (%)	40 (47.6)	64 (57.7)	.039
Medical History – no. (%)			
History of stroke or TIA	12 (14.2)	14 (12.6)	.393
Atrial Fibrillation	20 (23.8)	15 (13.5)	.005
Diabetes Mellitus	24 (28.6)	23 (20.7)	.050
Hypertension	60 (71.4)	70 (63.1)	.071
Current or Past Tobacco use	44 (52.4)		
Ischemic Heart Disease	13 (15.5)		
Congestive Cardiac Failure	6 (7.1)	22 (19.8)	.002
Systolic Blood Pressure (mmHg) – no. (%)	77 (91.7)		
median (IQR)	144 (128-160)	144 (130–162)	.445
Glucose level at hospital arrival – no. (%) -	75 (89.2)		
median(mmol/L)	7 (5-9)	6.9 (6–8.2)	
Baseline ASPECTS – no. (%) †	83 (98.8)		
median (IQR)	8 (7-9)	8 (7–9)	.072
CT or CTA Performed - no. (%)	83 (98.8)	110 (99.1)	.195
Level of Occlusion ‖			
M1 – no. (%)	28 (33.3)	88 (79.3)	< .001
Carotid T – no. (%)	20 (23.8)	23 (20.7)	.192
Tandem – no. (%)	17 (20.2)	9 (8.1)	< .001
M2 or M3 – no. (%)	9 (10.7)		
IV Thrombolysis Done – no. (%)	51 (60.7)	76 (68.5)	.078

‡ Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher scores indicating more severe neurologic deficits

† The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) ranges from 0 to 10, with higher scores indicating smaller infarct core.

‖ Level of Occlusion was determined based on digital subtraction angiogram.

Procedural Outcome

Intravenous thrombolysis was started at a median of 175 minutes (IQR, 135.8-210) for 32 (65.5%) of the eligible patients. Median time of stroke onset to groin was 297 minutes, (IQR, 236-350). Median procedural duration (groin puncture to recanalization) was 39 minutes (IQR, 23-58). Median time of onset to reperfusion was 339 minutes (IQR, 287 – 394). (Table 2)

Table 2. **Treatment pathway time variables***

Variable	**Cape Town N = 84**	**Brazil N =111**	**P - value**
Prehospital delay – no. (%)	82 (97.6)		
median (IQR)	120 (75.8-181.8)	136 (107-160)	.223
Door to scan – no. (%)	77 (91.7)		
median (IQR)	56 (32.5-95)	27 (9 – 78)	< .001
Scan to groin - no. (%)	79 (94.0)		
median (IQR)	80 (59-134)	96 (70 -141)	.711
Door to groin -no. (%)	82 (97.6)		
median (IQR)	168 (117.8-218)	116 (89-213)	< .001
Groin to recanalization – no. (%)	82 (97.6)		
median (IQR)	39 (22.8-58.25)	41 (31-69)	.961
Onset to groin -no. (%)	81 (96.4)		
median(IQR)	297 (234.5-352.5)		
Onset to recanalization -no. (%)	81 (96.4)		
median (IQR)	339 (285-394)	300 (217 – 448)	< .001
Onset to needle -no.(%)	32(65.5)		
median	175(135.3-210)	170(132-213)	.594
Door to needle -no.(%)	31(56.4)		
median	54(37-100)		

* Time measured in minutes

The table shows workflow metrics, measured in time spent on consecutive steps from stroke onset to recanalization, in comparison to RESILIENT study metrics.

When comparing time with RESILIENT, we had a significantly longer door to scan time and door to groin ($p < 0.001$) and a proportionately longer time to recanalization ($p =< 0.001$).

Primary and Secondary Outcomes

The primary outcome, mRS at 90 days was collected from seventy-four patients, of which 25(33.9%) were functionally independent with mRS 0,1 or 2 and 25(33.8%) died (mRS 6). Successful recanalization, mTICI 2b,2c, and 3 was achieved in 52(61.9%) The procedure failed in 2 patients; 1 due to stenosis of cervical segment of ICA limiting access to the clot and the second patient had a blister aneurysm that bled. Both patients were included in the study as a mTICI 0.

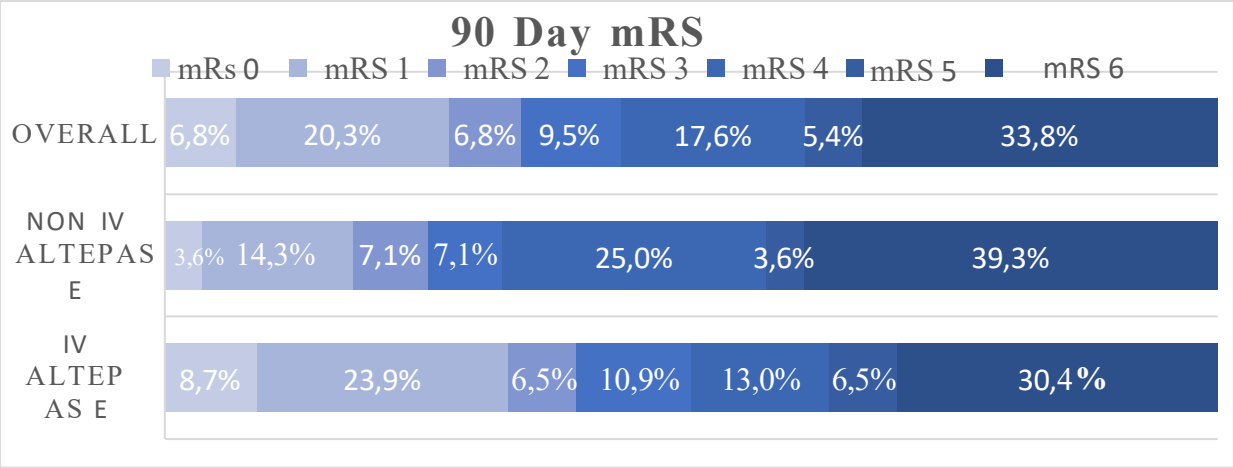
Comparative statistical analysis done with a one sample binomial test on primary and secondary outcomes indicated that proportion of patients with mRS of 0-2 was similar between our study and RESILIENT study(p=0.488), proportion of patients who died, mRS of 6 was significantly higher in our sample and proportion of patients with successful recanalization was significantly higher in RESILIENT study compared to ours (P<0.001). (Table 3)

Table 3. **Primary and Secondary Outcomes**

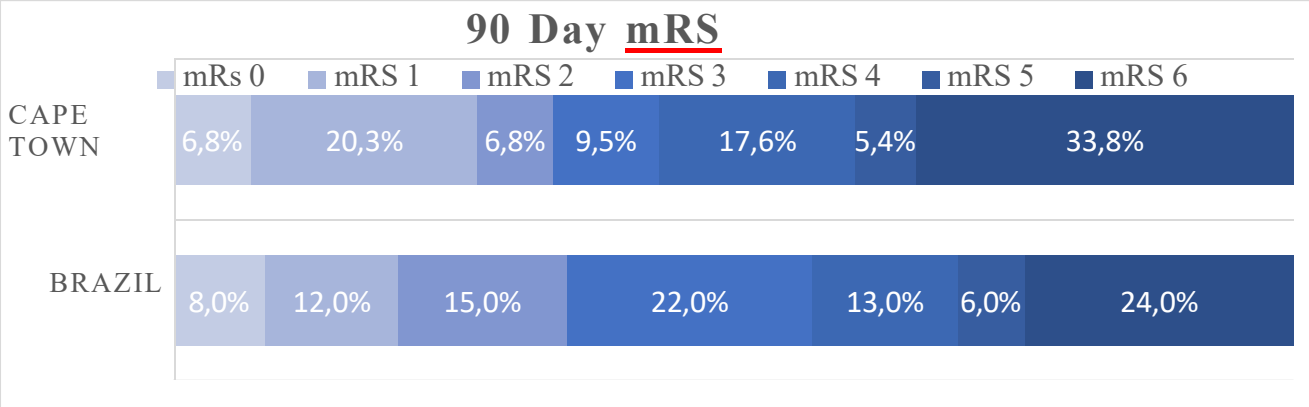
	Cape Town N= 84	**Brazil N= 111**	**p-value**
Primary Outcomes at 90 days:			
Functional independence (mRS 0-2) - no. (%)	25 (33.8)	39 (35.1)	.488
Mortality rate (mRS 6) – no. (%)	25 (33.8)	27 (24.3)	.039
Secondary Outcome:			
Successful post-procedural recanalization (mTICI 2B-3) – no. (%)	52 (61.9)	91 (82.0)	< .001

Figure 1. Scores on Modified Rankin Scale at 90days

A. Patients in our study according to use or non-use of IV alteplase and the overall outcome (Cape Town)



B. Comparison between overall outcome in our study and Intervention Group of RESILIENT(Brazil) trial



Scores on the modified Rankin Scale range from 0 to 6: **0** indicating no symptoms at all; **1**, No significant disability despite symptoms; **2**, slight disability; **3**, moderate disability; **4**, moderately severe disability **5**, severe disability and **6**, death.

Panel A; Shows mRS percentages of patients eligible for IV altepase, those not eligible and overall, in our study. IV altepase group had better functional outcome and less mortality compared to those not eligible.

Panel B: Shows mRS percentages of patients in our study compared to the RESILIENT trial.

Predictors of disability, mortality, and successful recanalization

Predictors of modified Rankin scale scores 0-2

Univariate variate analyses found a significant association between a mRS of 0-2 and Carotid T, NIHSS, and ASPECT (see Table 4). There was a trend towards a significant association with age and NIHSS. These significant variables were entered into a logistic regression model. The final model was statistically significant ($\chi^2 = 13.13$, $p = 0.004$), correctly classified 76.1% of patients, and had a Nagelkerke R^2 of 0.248. Patients with a mRS score of 0-2 were less likely to have Carotid T occlusion site, were younger in age, and had a higher ASPECT score. (Table 4)

Table 4. Associations with mRS of 0-2

Variable	B	p	OR	95% CI
Univariate analysis				
Carotid T	4.78	0.029*	0.20	0.04 – 0.95
Age	-0.04	0.075	0.97	0.93 – 1.00
NIHSS	-0.10	0.062	0.90	0.81 – 1.01
ASPECT	0.41	0.037*	1.51	1.03 – 2.21
Multivariate analysis				
Carotid	-1.42	0.094	0.24	0.05 – 1.27
Age	-0.06	0.023*	0.95	0.90 – 0.99
ASPECT	0.46	0.050*	1.59	1 – 2.53

*$p < 0.05$

Predictors of modified Rankin scale scores of 6

Univariate variate analyses found a significant association between mRS of 6 and hypertension, Carotid T, and time from scan to groin (see Table 5.). There was also a trend in a significant association with time from door to scan. These variables were entered into a logistic regression model. The final model was statistically significant ($\chi^2 = 24.12$, $p < 0.001$), correctly classified 83.3% of patients, and had a Nagelkerke R^2 of 0.475. Patients with a mRS score of 6 were more likely to have Carotid T occlusion site, more likely to have hypertension, had a longer Door to scan time but a shorter scan to groin time. (Table 5)

Table 5. Associations with mRS of 6

Variable	B	P	OR	95% CI
Univariate analysis				
Hypertension	2.12	0.040*	8.31	1.11 – 62.44
Carotid T	1.94	0.035*	6.93	1.15 – 41.97
Door to scan	0.01	0.095	1.01	0.99 – 1.02
Scan to groin	-0.15	0.014*	0.99	0.97 – 0.99
Multivariate analysis				
Hypertension	1.94	0.045*	6.94	1.05 – 46.03
Carotid T	2.19	0.013*	8.98	1.59 – 50.64
Door to scan	0.02	0.023*	1.02	1.00 – 1.04
Scan to groin	-0.02	0.018*	0.98	0.96 – 1.00

*$p < 0.05$

Predictors of successful recanalization (Grade 2b-3)

Univariate variate analyses found a significant association between successful recanalization and previous stroke, Atrial Fibrillation, and time from groin to perfusion (see Table 6). These significant variables were entered into a logistic regression model. The final regression model was statistically significant ($\chi^2 = 15.39$, $p < 0.001$), correctly classified 68.3% of patients, and had a Nagelkerke R^2 of 0.234. Patients with successful recanalization were less likely to have had a previous stroke, but more likely to have atrial Fibrillation. (Table 6)

Table 6. Associations with Grade 2b-3

Variable	B	P	OR	95% CI
Univariate analysis				
Previous stroke	-3.65	0.015*	0.03	0 – 0.49
Atrial fibrillation	2.29	0.032*	9.91	1.22 – 80.38
Groin to perfusion time	-0.02	0.043*	0.98	0.96 – 0.99
Multivariate analysis				
Previous stroke	-3.69	0.012*	0.03	0 – 0.45
Atrial fibrillation	2.43	0.022*	11.37	1.42 – 91.33

*$p < 0.05$

DISCUSSION

South Africa is one of the most highly populated countries in Sub-Saharan Africa with a population of 56million people(13). Just like many Lower- and Middle-Income Countries (LMICs), stroke is a major cause of morbidity and mortality; and was declared a catastrophic illness in South Africa in October 2007(14). Although the incidence is not known, the age-standardized prevalence of stroke is estimated at 290 per 100,000(15). Ischaemic stroke accounts for a large amount of disability (95,000 years lived with disability) and mortality (25,000 deaths/year) in South Africa(16). GSH is one of two tertiary level public hospitals with endovascular capabilities in Cape Town, a city with an estimated population of 3.7 million people(17).

Standardized stroke protocols were implemented at GSH in 2018 utilising uncontrasted CT brain and CT angiography to select patients with acute ischemic stroke due to LVO for MT (Appendix 5), using criteria similar to that used in the Mr CLEAN study performed in the Netherlands (2015). This retrospective analysis of data from 01 January 2018 reveals recanalization rates and 3-month disability outcomes comparable to Mr CLEAN and RESILIENT(Brazil) studies, supporting the effectiveness of MT in middle-income countries despite the challenges facing health systems in this setting.

Our primary outcome was evenly distributed in thirds, -one third of the patients achieved functional independence (mRS 0-2), one third dependant (mRS 3-5) and a third mortality (mRS 6) at 90days. Young age and higher ASPECT scores had positive predictive value for mRS 0-2. Our study had a younger population, with a median age of 55 years at presentation compared to currently published trials from RESILIENT and HERMES Collaboration where their median age was 65 and 68 years respectively. No specific factors were identified in our study as likely cause of stroke at younger age compared to population in other trials. Seven (8.3%) of the patients included in this study had APECT scores lower than 6 and therefore were likely to have had a larger a much larger ischaemic core prior to treatment. MT in patients with a larger ischaemic core may be effective in improving overall disability but fewer patients with large core infarcts achieve functional independence compared to those with small ischaemic core. (18).

The secondary outcome, mTICI 2b-3 was achieved in 62% of the patients. Success of recanalization has been identified as one of the most important modifiable factors affecting disability (19) however it did not reach statistical significance in this study.

Patients who received thrombolysis had trend towards higher functional independence and lower mortality rate at 90days. All patients who received thrombolysis, barring two patients referred from a private Hospital, were administered intravenous alteplase at our facility. Both ‘mothership’ and ‘drip-and-ship’models of acute stroke are employed in the state-funded hospital referral networks in Cape town but the ‘mothership’ model predominates, particularly after hours where services and expertise may not be available at smaller facilities.

Due to limited resources, less established stroke triage and response systems compared to higher income countries, there were pre-hospital and in-hospital delays, and ultimately longer time to treatment. Median time from symptom onset to recanalization was 339minutes, which is much higher than what has been reported in other centres -including RESILIENT trial who had median time of 300minutes (10). Onset to groin time has been shown to be an independent factor that affects success of recanalization (20), and our results indicate the need for improved in-hospital management protocols and performance to optimise outcomes. Some of the factors that contributed to in-hospital delays included lack of pre-hospital

notification, delay in folders retrieval and triage, time to scan and the time to assemble the on-call stroke teams after decision is made. Long door to scan time was one of the factors associated with mortality in our study. (Table 5)

The long onset to groin time also highlighted the potential benefit for having advanced perfusion-based imaging which would improve patient selection, as well as be used to evaluate and add on patients who arrive to hospital during the extended window period with clinical deficit infarct volume mismatch (7, 8).

Despite, a higher mortality rate, we achieved comparable results to other trials. The percentage of patients with mRS of 0-2 of 33.8% in our study was comparable to MR CLEAN, 32.6%, and RESILIENT trial 39% which even though was slightly higher, a one-sample binomial test showed the difference was not significant. Whilst RESILIENT trial selection criteria was more accommodative, extending eligibility time of stroke onset to treatment up to eight hours; 50(45%) of their participants in the intervention group were selected based on advanced CT perfusion imaging. They also achieved an overall significantly higher recanalization rate of 82% and lower mortality of 24.3%. The mortality rate of 33.8% found in our study, is the highest compared to the currently published randomized control trials. Hypertension, Carotid T level of occlusion, longer time to scan, and scan to groin were found to have significant association. Even though no clear statistically significant mortality benefit is established in previous outcome studies of MT compared to the best standard medical therapy alone, there is a trend in favour of MT. (21) Our study being retrospective and non-randomized we were not able to compare our outcomes to standard medical therapy alone.

Conclusion

Our study represents a real-life scenario and outcome in a public healthcare system in Sub-Saharan Africa. We achieved similar rates of recanalization (61.9%) and functional independence (33.9%) to that seen in published trials from high-income and other LMICs using basic imaging despite a higher mortality and longer median time to reperfusion. These data support the effectiveness of MT in a public hospital in south Africa despite the challenges of providing emergent stroke care in a resource-constrained setting.

Strengths

The data is from a high-volume state hospital that offers comprehensive stroke care in South Africa.

Limitations

Some of the limitations of our study included loss to follow up of 10(12%) of the patients by the 90th day. Being a real life retrospective non-randomized study, with MT as standard of care for eligible patients, there was no control group with standard medical therapy alone to compare our outcomes to. The outcomes were assessed by the investigators who are part of the stroke team involved in the management of the patients.

Author contributions:
MMK, AT, KB assisted with data collection. MMK, KB, AT and DLF analyzed the data. All authors had access to the data set, assisted with data review and manuscript preparation, and approved the final manuscript.

Declaration of conflict of interests:
None

Funding
None

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Appendix 1: Department of Surgery Research Committee Approval

UNIVERSITY OF CAPE TOWN

Department of Surgery
Departmental Research Committee
Dr Timothy Pennel
D24 Office, Groote Schuur Hospital
Observatory 7925
South Africa
Tel (021) 404 3430
Email: tim.pennel@uct.ac.za

17 Jun 2019

Ass. Prof. A Taylor

Department of Surgery
University of Cape Town

Dear Ass. Prof. Taylor

RE: Project 2019/073

PROJECT TITLE: An Audit Of 90 Day Clinical Outcome In Stroke Patients Treated With Mechanical Thrombectomy At Groote Schuur Hospital

The above protocol has been reviewed by the Department of Surgery Research Committee. I am pleased to inform you that the committee approved the scientific merit of the study, and endorse the protocol for submission to the relevant ethics committee.

Although this letter serves as confirmation that the above protocol has successfully passed through the surgical DRC, respective ethics committees still require DRC chair signature before submission.

Please use the above project number in all future correspondence,

Yours sincerely

Signed by candidate

DR TIMOTHY PENNEL
CHAIRMAN: RESEARCH COMMITTEE

"OUR MISSION is to be an outstanding teaching and research university, educating for life and addressing the challenges facing our society."

Appendix 2: University of Cape Town's Human Research Ethics Committee approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

05 July 2019

HREC REF: 444/2019

A/Prof A Taylor
Division of Neurosurgery
H-53, OMB

Dear A/Prof Taylor

PROJECT TITLE: AN AUDIT OF 90 DAY CLINICAL OUTCOME IN STROKE PATIENTS TREATED WITH MECHANICAL THROMBECTOMY AT GROOTE SCHUUR HOSPITAL

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 July 2020.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

Signed by candidate

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
NHREC-registration number: REC-210208-007

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical

Appendix 3: Groote Schuur Hospital institutional approval

Western Cape Government
Health

GROOTE SCHUUR HOSPITAL
Enquiries: Dr Bernadette Eick
e-mail: Bernadette.Eick@westerncape.gov.za

Professor Allan Taylor
NEUROSURGERY

E-mail: allan.taylor@uct.ac.za / muthinjamartinink@gmail.com

Dear Professor Taylor,

RESEARCH PROJECT: An Audit of 90-Day Clinical Outcome In Stroke Patients Treated With Mechanical Thrombectomy At Groote Schuur Hospital

Your recent letter to the hospital refers.

You are granted permission to proceed with your research, which is valid until **30 July 2020.**

Please note the following:

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) No additional costs to the hospital should be incurred i.e. Lab, consumables or stationary. **If access to TRACK Care/NHLS is required, kindly attach our letter of approval to the application form.**
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
f) Confidentiality must always be maintained .
g) Should you at any time require photographs of your subjects, please obtain the necessary indemnity forms from our Public Relations Office (E45 OMB or ext. 2187/2188).
h) Should you require additional research time beyond the stipulated expiry date, please apply for an extension.
i) Please discuss the study with the HOD before commencing.
j) Please introduce yourself to the person in charge of an area before commencing.
k) On completion of your research, please forward any recommendations/findings that can be beneficial to use to take further action that may inform redevelopment of future policy / review guidelines.
l) Please contact Michelle Riley (Patient Fees) at ext. 2276 to ascertain if there will be charges for conducting the Research and to obtain a quote or to discuss charges
m) Kindly submit a copy of the publication or report to this office on completion of the research.
n) At no time should any posters encouraging patients to partake in research, be displayed within a clinical area.

I would like to wish you every success with the project.

Yours sincerely

Signed by candidate

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER
Date: 8 April 2020

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Appendix 4: Instructions to the author (INR - SAGE)

Checklist:

Title page	
Contains the full postal address of all authors	
The names and affiliations of all authors are correct	
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Only authors who have contributed sufficiently to the manuscript have been added	
Supplies first, middle initial, and last names, highest academic degrees, and institutional affiliations of all authors (use superscript number that corresponds to each author)	
Provides full address, telephone and fax numbers, and email address of a corresponding author	
Conflict of interest statement	
Ethical approval statement/ IRB approval number	
Number of words, figures and references are stated in the title page	
Abstract (for original research articles, systematic reviews and meta-analysis articles)	
No more than 300 words	
Does not contain any references	
3 to 5 keywords; use MeSH terms (Keywords should be searched in MeSH) supplied	
Main Body	
References are written in the Vancouver style	
References are numbered in the order in which they appear	
The ethical approval or consent is stated in the methods section	
Conflict of interest statement is provided	
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Supplementary items are cited in the main text	
The manuscript is written in Helvetica or Times New Roman (12 point size) font.	
The manuscript adheres to the word limits and reference limits: Original research 4000 words 40 references Review article 6000 words 80 references Systematic review & meta-analysis 4000 words Case report & Technical notes 2000 words 15 references Letter to the editor 1200 words 10 references	
Tables	
Each table should be placed on a separate page	
Titles of all tables should be supplied	
Definitions of all abbreviations used should be explained below each table	
Percentages should be up to 1 decimal point i.e. n(%) = 25(12.5)	
P-value should be up to 3 decimal points i.e (P=0.027)	
Other values should be to 2 decimal points i.e 20.0 0± 4.50	
Figures	
Should be at least 300 dpi resolution	
Have an adequate legend to explain the figure	
Photographs of recognizable persons require a signed release from the patient or legal guardian authorizing publication. Masking eyes to hide identity is not sufficient. (Author should be able to provide signed release forms when requested.)	
Figure legends should not exceed 300 words per figure.	

Please note that your manuscript may be returned or rejected if your manuscript does not comply with the author guidelines.

Appendix 5

GSH Acute stroke Mechanical Thrombectomy Eligibility Criteria

1.Patients eligible for intravenous r-tPA should receive intravenous r-tPA even if mechanical thrombectomy is being considered.

2.Patients should receive mechanical thrombectomy if they meet all the following criteria:

a) Prestroke mRS score 0 to 1,
b) Acute ischemic stroke receiving intravenous tPA within 4.5 hours of onset according to guidelines from professional medical societies,
c) Causative occlusion of the ICA or proximal MCA (M1),
d) Age ≥18 years,
e) NIHSS score of ≥6,
f) ASPECTS of ≥6, and
g) Treatment can be initiated (groin puncture) within 6 hours of symptom onset.

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