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Original Article

Characteristics, clinical profiles, and outcomes of patients undergoing endovascular thrombectomy: A retrospective study, Saudi Arabia☆

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الملخص

أهداف البحث: السكتة الدماغية هي أحد الأسباب الرئيسية للوفاة وضعف الوظيفة الجسدية. أصبحت عملية استئصال الخثرة داخل الأوعية الدموية الآن هي المعيار المعترف به لعلاج السكتة الدماغية الإقفارية الحادة في الدورة الدموية الأمامية مع انسداد الأوعية الدموية الكبيرة، وخاصة عندما تكون صور الدماغ المواتية واضحة في غضون 24 ساعة من ظهور الأعراض. تهدف هذه الدراسة إلى توضيح الخصائص والملامح السريرية ونتائج المرضى الذين خضعوا لاستئصال الخثرة داخل الأوعية الدموية للسكتة الدماغية الإقفارية الحادة.

طريقة البحث: في تصميم مجموعة مستندة إلى السجلات بأثر رجعي، قمنا بمراجعة السجلات الطبية للأفراد الذين خضعوا لاستئصال الخثرة داخل الأوعية الدموية بسبب السكتة الدماغية الإقفارية الحادة في مستشفى الملك فهد العام في جدة، المملكة العربية السعودية. شملت الدراسة، التي أجريت من يوليو 2022 إلى نهاية أكتوبر 2023، تحليلا شاملا للعوامل السريرية والإشعاعية والعوامل المرتبطة بالوقت والنتائج المتنوعة.

النتائج: في مجموعة مكونة من 117 مريضا بمتوسط عمر 58.5 عاما، كان 81 مريضا (69.2%) من الذكور. كان ارتفاع ضغط الدم والسكري من أكثر عوامل الخطر شيوعا، حيث أثرا على 48.7% و41% من المجموعة على التوالي. كان لدى ما يقرب من نصف المرضى درجة مواتية وفق برنامج ألبرتا للسكتة الدماغية للتصوير المقطعي المبكر (7-10)، وتلقى 45.3% منهم منشط البلازمينوجين عن طريق الوريد. حقق ما يقرب من ثلثي المرضى درجة 2ب في العلاج المعدل للاحتشاء الدماغي أو أعلى، وأظهر 39.3% انسداد الشريان الدماغي الأوسط-إم1. كان معدل حدوث التحول النزفي المصحوب بأعراض حوالي 13%، بينما حقق ثلث المرضى نتيجة مواتية حسب مقياس رانكين المعدل (0-2). ارتبطت عوامل مثل التقدم في السن، وارتفاع درجات مقياس السكتة الدماغية للمعاهد الوطنية للصحة، والإقامة الطويلة في المستشفى بنتائج أسوأ. وعلى العكس من ذلك، فإن غياب ارتفاع ضغط الدم والرجفان الأذيني، إلى جانب ارتفاع مقياس انحلال الخثرة في احتشاء دماغي، زاد بشكل كبير من احتمالية تحقيق نتائج إيجابية.

الاستنتاجات: في دراستنا، أظهر مرضى استئصال الخثرة من الأوعية الدموية الذين تم فحصهم فئة عمرية أصغر سنا، حيث أظهرت النتائج السريرية والشعاعية درجة معينة من التشابه مع المنشورات الأخرى. ومن الجدير بالذكر أن غياب ارتفاع ضغط الدم والرجفان الأذيني، جنبا إلى جنب مع درجة أعلى في اختبار انحلال الخثرة في احتشاء دماغي، كان مرتبطا بزيادة احتمالية تحقيق نتيجة إيجابية

الكلمات المفتاحية: السكتة الدماغية الإقفارية الحادة؛ استئصال الخثرة داخل الأوعية الدموية؛ مقياس رانكين المعدل؛ برنامج ألبرتا للسكتة الدماغية للتصوير المقطعي المبكر؛ درجة العلاج المعدل للاحتشاء الدماغي

Abstract

Background: Stroke is a significant contributor to both mortality and compromised physical function. Endovascular thrombectomy (EVT) is now the recognized standard of care for anterior circulation acute ischemic stroke

☆ The study was conducted in the stroke unit at King Fahad Hospital in Jeddah, Saudi Arabia from July 1, 2022 through October 2023.

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(AIS) with large vessel occlusion (LVO), especially when favorable brain images are evident within 24 h of symptom onset. This study elucidated the characteristics, clinical profiles, and outcomes of patients who underwent EVT for AIS.

Methodology: In this retrospective record-based cohort study, we reviewed the medical records of individuals who underwent EVT for AIS at King Fahad General Hospital in Jeddah, Saudi Arabia. The study, conducted from July 2022 through October 2023, encompassed a comprehensive analysis of clinical, radiological, and time-related factors and diverse outcomes.

Results: In a cohort of 117 patients with a mean age of 58.5 years, 81 (69.2%) were male. Hypertension and diabetes mellitus were the most common risk factors, affecting 48.7% and 41% of the cohort, respectively. Approximately half of the patients had a favorable ASPECT Score (7−10), and 45.3% received intravenous tissue plasminogen activator (tPA). Nearly two-thirds achieved a modified thrombolysis in cerebral infarction (mTICI) score of 2b or higher, and 39.3% exhibited M1-middle cerebral artery (MCA) occlusion. The incidence of symptomatic hemorrhagic transformation was about 13%, whereas one-third of the patients attained a favorable mRs outcome (0−2). Factors such as advanced age, higher NIH Stroke Scale (NIHSS) scores, and prolonged hospital stays were associated with poorer outcomes. Conversely, the absence of hypertension and atrial fibrillation, along with higher TICI scores, significantly increased the likelihood of favorable outcomes, with P values of 0.015, 0.0490, and 0.025, respectively.

Conclusions: In our study, the examined patients who underwent EVT were younger in age, with clinical and radiological outcomes showing some degree of comparability to other publications. Notably, the absence of hypertension and atrial fibrillation, combined with a higher TICI score, was associated with an increased likelihood of achieving a favorable outcome.

Keywords: Acute ischemic stroke; Alberta Stroke Program Early Computed Tomography (ASPECT) score; Endovascular thrombectomy; modified Rankin Scale (mRS); Modified thrombolysis in cerebral infarction (mTICI)

Background

Globally, stroke is a leading cause of both mortality and morbidity. The utilization of early reperfusion therapy has demonstrated its effectiveness in enhancing stroke outcomes by diminishing both mortality rates and disability. The management of acute ischemic stroke (AIS) attributed to large vessel occlusion (LVO) has experienced notable progress in recent years. Numerous randomized clinical trials have underscored the efficacy and safety of endovascular thrombectomy (EVT) in specific cases involving anterior circulation LVO.[1,2] Currently, EVT stands as the established standard of care for anterior circulation AIS characterized by LVO, mainly when advanced favorable brain images are observed within 24 h from the onset of symptoms. The prevalence of LVO in published studies exhibits variability, ranging from less than 10% to approximately two-thirds of patients with stroke. This variance is influenced by diverse factors such as the study protocol, LVO definition, and the geographical region where the study was conducted. A comprehensive systematic review of 16 studies, primarily from North America and Europe, revealed an average LVO prevalence of one-third across the studies.[3−5] In our kingdom and region, the EVT is still developing and not yet widely available in all cities. There is a pressing need to better understand the patient population affected by and eligible for this treatment, as well as the factors that may influence its outcomes.

This study delineated the characteristics, clinical profiles, and outcomes of patients undergoing EVT for AIS at King Fahad General Hospital in Jeddah, Saudi Arabia.

Materials and Methods

The retrospective record-based cohort study investigated the medical records of individuals who experienced AIS and were eligible for EVT at King Fahad General Hospital. The study spanned the first of July 2022 to the end of October 2023. Data collection involved structured data sheets encompassing sociodemographic and the following clinical details: age; sex; nationality, National Institutes of Health Stroke Scale (NIHSS), which is a reliable, valid, and responsive tool for measuring stroke severity, with scores ranging from 0 to 42, where higher scores indicate greater severity and are associated with poorer outcomes; and pre-morbid modified Rankin Scale (mRS), which evaluates the degree of disability or dependence in daily activities of people who have suffered a stroke. Scores on the mRS range from 0 to 6, with higher scores indicating worse functional outcomes; a score of 6 represents death. It is used for both initial assessment and post 3-month evaluation to determine the patient's degree of disability and functional status. Additionally, we obtained information on radiological characteristics, including baseline Alberta Stroke Program Early Computed Tomography (ASPECT) score and the posterior circulation Acute Stroke Prognosis Early CT Score (pc-ASPECTS), quantitative scores that measure the extent of early ischemic changes, ranging from 0 to 10. A score of 10 represents no early ischemic changes and is associated with better outcomes. We also obtained the modified treatment in cerebral infarction (mTICI) score, which evaluates the intracranial angiographic flow and various clinical and radiological outcomes, and ranges from 0 to 3; 0 indicates no perfusion and 3 indicates complete reperfusion. A positive outcome was defined as an mRs of 0−2, while successful recanalization was characterized by an mTICI score of 2b−3.[6−8]

Hemorrhagic transformation (HT) was classified based on the European Cooperative Acute Stroke Study II (ECASS II) criteria in the CT scan conducted 24 h post-intervention; the ECASS classification includes no HT,

hemorrhagic infarction (HI), or parenchymal hematoma (PH). HI is further divided into type 1 and type 2, whereas PH is also divided into type 1 and type 2, with PH2 being the most severe, characterized by blood clots covering over 30% of the infarct area and causing significant space-occupying effects.[9,10] The research protocol underwent thorough review and approval by the ethics and research committee of King Fahad General Hospital, Ministry of Health, Jeddah, Saudi Arabia.

The information was systematically collected, thoroughly reviewed, and then input into Statistical Package for Social Sciences version 26 (SPSS; IBM Co., Armonk, NY, USA). All statistical analyses were two-tailed, with a significance level set at alpha 0.05. $P \leq 0.05$ was considered statistically significant. Descriptive analysis entailed presenting frequency distribution and percentage for various study variables, encompassing patients' biodemographic data, clinically relevant stroke data, procedural characteristics, reported complications among the study patients, and clinical outcomes. The occlusion sites in the cases were visually represented. Quantitative variables, such as time lapse, were conveyed as mean and standard deviation (SD), along with median and interquartile range. To identify factors associated with mRs on discharge among patients undergoing EVT, we used the chi-squared and exact probability tests, followed by multivariate logistic regression to detect independent predictors of good outcomes. Odds ratios (ORs), confidence intervals (CIs), and p values were derived. A stepwise logistic regression model was employed to determine predictors of positive outcomes among patients with stroke.

Results

A comprehensive cohort of 117 patients, all of whom experienced AIS and underwent EVT, were enrolled in our study. The mean age was 58.5 ± 14.9 years. Among them, 81 (69.2%) were male, and 64 (54.7%) were non-Saudi individuals. The identified risk factors for stroke were diverse, with hypertension being the most prevalent at 48.7%, followed by diabetes mellitus (DM) at 41%, smoking at 21.4%, previous transient ischemic attack/stroke at 14.5%, dyslipidemia at 12%, and atrial fibrillation at 12.9% (as detailed in Table 1). The ASPECT score exhibited a range from 4 to 10, with an average value of 7.8 ± 1.6. Approximately half of the patients demonstrated a favorable ASPECT score in the range of 7−10. Intravenous tissue plasminogen activator (tPA) was administered to 53 (45.3%) of the patients. Regarding the mTICI score, nearly two-thirds of the cohort achieved a TICI score of 2b or higher, while approximately 10% experienced failed recanalization. Additionally, 106 (90.6%) of the patients exhibited no symptoms on their pre-stroke mRS (as outlined in Table 2).

Examining the location of stroke based on occluded arteries (Figure 1), the prevalent sites were M1-middle cerebral artery (MCA) (39.3%), internal carotid artery (ICA) (20.5%), tandem occlusion (16.2%), basilar artery (11.1%), M2-MCA (10.3%), and vertebral artery (2.6%). Furthermore, 73 cases (62.4%) had occlusion on the right side. The procedural timeline among the study patients, outlined in Table 3, revealed key intervals: the average time from the last

Table 1: Biodemographic characteristics of patients with endovascular thrombectomy (n = 117).

Characteristics	No	%
Age in years		
<50	33	28.2%
50−69	62	53.0%
70+	22	18.8%
Mean ± SD	58.5 ± 14.9	
Sex		
Male	81	69.2%
Female	36	30.8%
Nationality		
Saudi	53	45.3%
Non-Saudi	64	54.7%
Risk factors		
Hypertension	57	48.7%
Diabetes mellitus	48	41.0%
Ischemic heart disease	28	23.9%
Heart failure	27	23.1%
Smoking	25	21.4%
Previous TIA/stroke	17	14.5%
Dyslipidemia	14	12.0%
Atrial fibrillation	15	12.9%

TIA: Transient ischemic attack.

Table 2: Clinical and radiological data of patients who underwent endovascular thrombectomy (n = 171).

Stroke data	No	%
ASPECTS core or pc-ASPECTS		
4	5	4.3%
5	4	3.4%
6	16	13.7%
7	17	14.5%
8	35	29.9%
9	20	17.1%
10	20	17.1%
Mean ± SD	7.8 ± 1.6	
Intravenous tPA		
Yes	53	45.3%
No	64	54.7%
mTICI score		
0	11	9.4%
1	5	4.3%
2a	14	12.0%
2b	16	13.7%
2c	56	47.9%
3	15	12.8%
NIHSS at arrival		
Moderate stroke (5−15)	57	48.7%
Moderate to severe stroke (16−20)	43	36.8%
Severe stroke (21−42)	17	14.5%
Pre-stroke mRs		
0	106	90.6%
1	6	5.1%
2	2	1.7%
3	3	2.6%

ASPECTS: Alberta Stroke Program Early Computed Tomography Score; Intravenous tPA: Intravenous tissue-type plasminogen activator; mRS: Modified Rankin Scale; mTICI: Modified thrombolysis in cerebral infarction; NIHSS: National Institutes of Health Stroke Scale; pc-ASPECTS: Posterior Circulation Acute Stroke Prognosis Early CT Score.

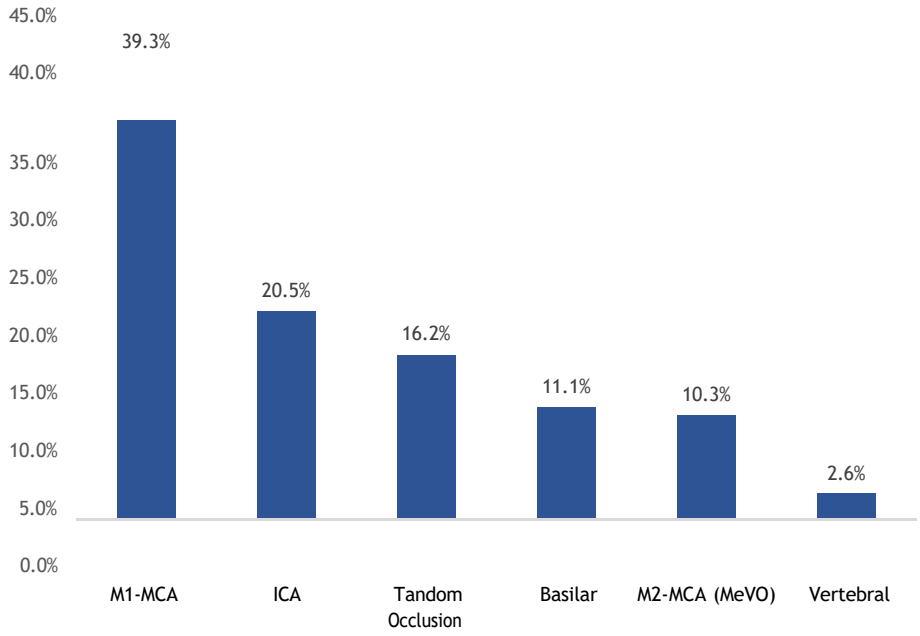

Figure 1: Location of occluded artery among study patients with acute ischemic stroke.

Table 3: Time lapse for procedures among study patients.

Time factors	Range	Mean	SD	Median (IQR)
Time from last seen well to presentation (in min)	30–600	195.8	120.9	180 (100–275)
Door to scan (min)	5–330	40.1	59.8	24 (19–37)
Door to Needle (min)	15–310	81.9	53.6	67 (40–97)
Door to puncture (min)	30–400	115.2	58.8	106.5 (82–134.25)
Puncture to reperfusion (min)	3–136	39.5	28.2	30 (20–51.5)
Door to reperfusion (min)	33–420	155.9	67.33	146 (113.25–174.5)

seen well to presentation was 180 min (with a range of 100–275 min), Door to Scan took 24 min (19–37 min), Door to Needle (DTN) was 67 min (40–97 min), Door to Puncture was 106 min (82–134 min), Puncture to Reperfusion was 30 min (20–51 min), and Door to Reperfusion was 146 min (113–174 min). These time intervals offered insights into the procedural efficiency and timelines associated with EVT for AIS in our study cohort.

Regarding certain clinical outcomes within our patient cohort. The incidence of symptomatic HT, including parenchymal hemorrhage grades 1 and 2 (PH1-2), was estimated to be approximately 13%. Approximately one-third of the patients achieved a favorable mRS outcome falling within the range of 0–2, as detailed in Table 4. To determine the predictors of a positive outcome among patients with stroke in our study, we employed a univariant and multiple stepwise logistic regression model. Among all of the factors analyzed, advanced age, higher initial NIHSS score, and longer hospital stays were significantly associated with lower chances of a positive outcome. By contrast, patients

Table 4: Clinical outcome of patients who underwent endovascular thrombectomy (n = 171).

Outcome	No	%
Length of hospital stay		
<1 week	49	41.9%
1–2 weeks	26	22.2%
>2 weeks	42	35.9%
Hemorrhagic transformation ECASS II		
Yes, asymptomatic HI grade 1	12	10.3%
Yes, asymptomatic HI grade 2	8	6.8%
Yes, symptomatic PH grade 1	11	9.4%
Yes, symptomatic PH grade 2	5	4.3%
No	81	69.2%
90-day mRS		
Good outcome (mRS 0–2)	40	34.1%
Poor outcome (mRS 3–6)	77	65.8%

ECASS II: European Cooperative Acute Stroke Study II; HI: Hemorrhagic infarction; mRs: Modified Rankin Scale; PH: Parenchymal hematoma.

Table 5: Univariate analysis of factors associated with good and poor outcomes.

Factors		Outcome				P-value
		Poor		Good		
		No	%	No	%	
Age in years	<50	21	63.6%	12	36.4%	0.049*
	50–69	40	64.5%	22	35.5%	
	70+	20	90.9%	2	9.1%	
Sex	Male	57	70.4%	24	29.6%	0.689
	Female	24	66.7%	12	33.3%	
Diabetes mellitus	Yes	37	77.1%	11	22.9%	0.125
	No	44	63.8%	25	36.2%	
Hypertension	Yes	46	80.7%	11	19.3%	0.009*
	No	35	58.3%	25	41.7%	
Hyperlipidemia	Yes	8	57.1%	6	42.9%	0.296^
	No	73	70.9%	30	29.1%	
Atrial fibrillation	Yes	13	92.9%	1	7.1%	0.041*^
	No	68	66.0%	35	34.0%	
Previous TIA/stroke	Yes	15	88.2%	2	11.8%	0.049*
	No	66	66.0%	34	34.0%	
Large vessel occlusion location	Basilar	9	69.2%	4	30.8%	0.174^
	ICA	13	54.2%	11	45.8%	
	M1-MCA	30	65.2%	16	34.8%	
	M2-MCA (MeVO)	10	83.3%	2	16.7%	
	Tandem occlusion	17	89.5%	2	10.5%	
	Vertebral	2	66.7%	1	33.3%	
mTICI score	0	11	100.0%	0	0.0%	0.249
	1	4	80.0%	1	20.0%	
	2a	9	64.3%	5	35.7%	
	2b	11	68.8%	5	31.3%	
	2c	11	73.3%	4	26.7%	
	3	35	62.5%	21	37.5%	
NIHSS at arrival	No/minor stroke	0	0.0%	0	0.0%	0.179^
	Moderate stroke	37	64.9%	20	35.1%	
	Moderate to severe stroke	29	67.4%	14	32.6%	
	Severe stroke	15	88.2%	2	11.8%	
Length of hospital stay	<1 week	29	59.2%	20	40.8%	0.147
	1–2 weeks	18	69.2%	8	30.8%	
	>2 weeks	34	81.0%	8	19.0%	

P: Pearson X^2 test; ^:Exact probability test; *P < 0.05 (significant).
ICA: Internal carotid artery; MCA: Middle cerebral artery; MeVO: Medium-sized intracranial arteries; mTICI: modified thrombolysis in cerebral infarction, NIHSS: National Institutes of Health Stroke Scale; TIA: Transient ischemic attack.

Table 6: Multiple stepwise logistic regression model for predictors of good outcomes.

Factors	P-value	AOR	95% CI	
			Lower	Upper
Age in years	0.048[a]	0.86	0.74	0.99
No hypertension	0.015[a]	3.11	1.25	7.73
No atrial fibrillation	0.049[a]	5.88	1.14	20.54
NIHSS at arrival	0.035[a]	0.90	0.82	0.99
Hospital stay	0.046[a]	0.96	0.94	0.98
mTICI	0.025[a]	2.10	1.10	4.01

AOR: Adjusted odds ratio; CI: Confidence interval; mTICI: modified thrombolysis in cerebral infarction; NIHSS: National Institutes of Health Stroke Scale.
[a] P < 0.05 (significant).

without hypertension and atrial fibrillation, as well as those with higher TICI scores, significantly increased the likelihood of favorable outcomes, with P values of 0.015, 0.0490, and 0.025, respectively (see Tables 5 and 6).

Discussion

To the best of our knowledge, local Saudi data on EVT cases and outcomes are scarce. A recently published study from the Saudi capital conducted by the King Fahad Medical City (KFMC) group addressed this gap.[10] Our study elucidated the characteristics, clinical profiles, and outcomes of patients undergoing EVT for AIS at King Fahad General Hospital. Additionally, we compared our findings with data from other local and international registries.

Stroke manifests at a younger age in Saudi Arabia and the Middle East, as evident in our cohort's median age of 58. This aligns with findings from a thrombolysis study in the Middle East and North Africa (MENA) region, which reported a median age of 55.15. Similarly, a local study in a Saudi tertiary center indicated a comparable age group for patients with thrombolysis, and most of Alhazzani et al. studied the stroke incidence is less than 60 years old. Notably, our patients were younger than the recent KFMC cohort as well as the Al Khathaami et al. group, where the median age was 61 years.[11–15] In our patient cohort, hypertension was the predominant risk factor, closely followed by DM. Our findings closely align with the Saudi Stroke Data, which reported nearly 60% of patients having hypertension, with almost half of them being diabetic. Cardioembolic strokes, constituting 20–30% of cases, tend to be more disabling, and our analysis indicated that over half of our patients had a presumed stroke mechanism related to cardiac issues based on their cardiac background. Notably, the absence of hypertension was linked to a higher likelihood of a favorable outcome in our analysis, and a similar trend was observed for the absence of DM in the Alhazmi et al. EVT cohort.[16–18,11]

When assessing ASPECT score in comparison to other cohorts, our mean ASPECT of 7.8 was similar or slightly lower than those observed in the KFMC, MR CLEAN, German Stroke Registry, and Stroke-International Stroke Thrombectomy Registry (SITS-ISTER) registries.[11,19–21] In examining the occluded arteries contributing to stroke, we found that M1-MCA occlusion occurred in approximately 40% of our patients. This prevalence was notably lower than the KFMC group study, where M1 occlusion affected more than half of their cohort. The observed difference may be attributed to their extended window-based image selection criteria. While the definition of medium-sized intracranial arteries (MeVOs) remain subject to debate and variability, our patients with M2-MCA or MeVO occlusion constituted about 10%, a figure lower than the generally acknowledged one-third incidence and less than the Alhazmi et al. cohort.[22,11] Perfusion imaging plays a critical role in AIS management by enhancing prognosis prediction and identifying patients who may benefit from treatment, even outside traditional time limits for intravenous thrombolysis or EVT. Substantial evidence supports thrombolytic therapy for patients with a targeted mismatch ratio profile up to 9 h and clot removal for those with a targeted mismatch ratio up to 24 h after the last known time. The absence of more advanced imaging modalities, including CT perfusion during our inclusion period, may have limited the precise detection of such entities.[23]

Early administration of intravenous tPA is linked to decreased long-term disability and complications like symptomatic intracranial hemorrhage in patients with AIS. Despite proven benefits, its usage is constrained in certain countries, including Saudi Arabia, partly due to delayed emergency department presentations.[24,25] Achieving rapid recanalization is crucial for successful EVT and positive patient outcomes. Prolonged recanalization is associated with a reduced likelihood of achieving mRS scores of 0–2 at 90 days and increased complications.[26] Our median timeline, featuring DTN of about 1 h, compares favorably with other local results. In a large tertiary center in Riyadh city, the median DTN time was 70 min, and in another study, it was 82 min. The mean DTN times reported in the study from Dubai was 64.1 min. Our Door to Puncture at 107 min and Puncture to Reperfusion in 30 min aligned closely with Alhazzmi et al.'s group in Door to Puncture but showed a shorter reperfusion time. To further enhance timing, we recommend additional improvement initiatives and quality projects.[27,11,12]

This study had several limitations. Its retrospective nature introduced biases, and being single-center limits generalizability. Incomplete data and the absence of advanced imaging modalities during the inclusion period may have impacted the precision of our findings. The small sample size and lack of extensive longitudinal follow-up also constrained the robustness of our conclusions. Additionally, variability in treatment protocols and evolving stroke management guidelines during the study period might have influenced outcomes. Addressing these limitations in future multicenter, prospective studies with larger cohorts and comprehensive follow-up protocols is essential for more definitive conclusions about EVT outcomes in Saudi Arabia.

Conclusions

In our study, the examined patients who underwent EVT were younger in age, with clinical and radiological outcomes showing some degree of comparability to the most recent and only Saudi publication. Notably, the absence of hypertension and atrial fibrillation, combined with a higher TICI score was associated with an increased likelihood of achieving a favorable outcome.

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Conflict of interest

The authors have no conflicts of interest to declare.

Ethical approval

This study was approved by the ethics committee of King Fahad General Hospital, Jeddah, Saudi Arabia. All patients provided written informed consent before being enrolled in the study. The study was performed in accordance with the Declaration of Helsinki.

Authors contributions

MSA, AHA, MAA, RIM, EAA, AHA: Conceptualization, resources, data curation, formal analysis, investigation, and writing original draft. FAA, MMA, NFA, SSA: Methodology, validation, reviewing and editing draft, visualization, supervision, and project administration. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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