Hybrid Techniques versus Thrombolysis Associated with Completion Angioplasty in Treatment of Acute on Top of Chronic Lower Limb Ischemia

Mohamed M. Zaki, MD; Hamdy A. AboElNeel, MD; Amr Nabil Kamel, MD
Department of Vascular Surgery, Faculty of Medicine, Ain Shams University, Egypt

Introduction: Acute on top of chronic ischemia, is an acute dramatic deterioration of symptoms in a chronic peripheral arterial disease (PAD) patient. The clinical presentation may be less pronounced compared to patients with pure acute embolic occlusion. Catheter directed thrombolysis (CDT) has been added to the armamentarium of treatment for acute limb ischaemia since the STILE and TOPAS trials. Hybrid techniques for treating acute limb ischemia, usually at different levels, are done by combining both open surgical and endovascular techniques.

Patients and methods: A retrospective 2 arm comparative study was conducted on patients presented with limb threatening ischemia over the course of 18 months between September 2022 to March 2024 by comparing hybrid thrombectomy followed by completion angioplasty to catheter directed thrombolysis (CDT) followed by completion angioplasty regarding limb salvage, complication rates and patency.

Results: A total 53 patients were divided into 2 groups. The primary outcome was the technical success that was achieved in 21 cases (91.3%) in hybrid group compared to 23 cases (76.7%) in CDT group. The secondary outcome was the limb salvage that was obtained in 21 cases (91.3%) in hybrid group and in 23 (76.7%) in CDT group. Procedure related adverse events were mostly in the CDT group as distal embolization (3 cases). Both groups had equal 30 days mortality 3 patients.

Conclusion: Although the total endovascular approach shows a slightly higher incidence of distal embolization and bleeding complications compared to the hybrid approach, both approaches demonstrate comparable rates of limb salvage in correlation with the stage of acute ischemia.

Key words: Hybrid techniques, thrombolysis, acute on top of chronic, lower limb ischemia.

Introduction

Limb ischemia can be defined as decreased blood perfusion to the extremities and is classified according to presentation and rate of development into acute and chronic limb ischemia. Peripheral arterial disease (PAD) is the main cause of both classes.[1]

The hallmark of chronic limb ischemia is the development of significant flow-limiting stenosis and occlusive segments by atherosclerotic plaques leading to symptoms for more than 2 weeks. Chronic ischemia is not common under 50 years of age, but it increases in prevalence to approximately twenty percent in octogenarians.[2]

On the other hand, acute limb ischemia (ALI) is defined as the sudden decrease in limb blood perfusion that compromise the viability of the limb.[3] ALI is mostly caused by either embolic or thrombotic occlusion of the limb arteries producing sudden and acute symptoms of less than 2 weeks duration. Acute on top of chronic ischemia, is an acute symptomatic deterioration of a chronic peripheral arterial disease (PAD) patient.[4]

In 70% of patients, ALI occurs due to arterial thrombosis on top of a pre-existing arterial lesion. In these situations, the clinical presentation may be less severe and minimally overt compared to patients with pure embolic occlusion, which is attributed to the presence of a well-developed network of collaterals, and is subsequently called acute on top of chronic ischemia or in situ thrombosis. Consequently, treatment of acute on top of chronic ischemia is more challenging than pure ALI.[4]

Historically, the cornerstone of treatment of acute embolic limb ischemia has been surgical arterial thromboembolectomy (TE) by using balloon catheter, which was originally devised and used by Thomas Fogarty in 1963.[5] It has many advantages in management of limb-threatening ischemia due to embolic occlusion as it can be quickly utilized through a femoral artery exposure and may be done under local anesethia, constituting a simple and rapid way for thrombus and/or embolus extraction.[6]

Percutaneous systemic thrombolysis was described to be a less invasive approach than surgery. In 1974, Dotter was the first to use systemic thrombolysis for dissolving peripheral arterial thrombosis, but his results were not encouraging owing to low success rate and high incidence of bleeding complications. Therefore, catheter-directed thrombolysis (CDT) emerged to improve the results, and is now an established treatment alternative to mechanical thromboembolectomy in patients with no contra-indications to thrombolysis and whose state of limb presentation adequate time for thrombolytic therapy.[7]

Catheter directed thrombolysis (CDT) has been introduced as a line of treatment for acute limb ischaemia since the STILE and TOPAS trials in the

DOI: 10.21608/ASJS.2024.368162

1990s.[8] It has been adopted as an alternative to surgery in Rutherford stages I and IIA acute limb ischemia (Class I, Level A) as well as stage IIb (Class IIb, Level B) by the most recent European Society of Vascular Surgery (ESVS) in patients who have no contraindication for thrombolysis or major risk of bleeding (0.4% incidence of fatal intracranial haemorrhage).[9] It carries the advantage of thrombus removal while maintaining intraluminal orientation and restoring luminal flow without disruption of collaterals.

Hybrid techniques for treating acute limb ischemia, usually as a result of multilevel affection, are performed by combining both open mechanical thrombo-embolectomy and completion angioplasty to the affected vessels. This approach been used more popular among patients with late presentation of symptoms whose limbs' clinical condition on presentation does not provide a luxury of time to perform CDT (Mainly Rutherford stages IIB) or those who have a contraindication for administration of thrombolytic agents, especially that it gives an added benefit of minimalizing hospital stay and expenses.[10]

Patients and methods

This is a retrospective 2 arm comparative study conducted on patients presented to ER with acute limb threatening ischemia at Ain Shams University Hospitals (EL Demerdash and ASUH) and Egyptian Railway Medical Center over the course of 18 months between September 2022 and March 2024. Inclusion criteria were patients above 18 years of age presented with acute limb threatening ischemia Rutherford stages I, IIa, and IIb, with associated history and investigations suggesting chronic ischemia, and having no history of renal impairment, contrast allergy, thrombophilia, and lacking any absolute contra-indication for thrombolytic therapy (Recent gastrointestinal bleeding within less than 10 days from presentation, neurosurgical intracranial or spinal intervention within 3 months from presentation, history of recent cerebrovascular event within 2 weeks of presentation, active bleeding diathesis, and serious head trauma within 3 months from presentation) or relatively major contra-indication for thrombolysis (Severe uncontrolled hypertension >180mmHg systolic or >110 diastolic, cardiopulmonary resuscitation within the last 10 days, major non-vascular surgery trauma within 10 days from presentation, puncture of a non-compressible vessel, intracranial neoplasia, and recent eye surgery).[9]

A total sample of 53 patients were included and divided into two groups, 23 patients underwent mechanical thrombectomy followed by completion angioplasty (Hybrid group), and 30 patients underwent CDT followed by completion angioplasty (CDT - catheter directed thrombolysis group).

Hybrid procedures were conducted through common femoral artery surgical exposure and Fogarty catheter thrombectomy followed by completion angiography and balloon angioplasty and stenting if needed. Catheter directed thrombolysis was performed through a duplex guided placement of a 6 French sheath in the designated appropriate access vessel, direct angiography and positioning of a multi-side pore infusion catheter (Uni-Fuse™ Infusion Catheter, Angiodynamics, NY, USA and Fountain® Infusion System, Merit, Utah, USA) within the thrombus material followed by infusion of Alteplase (Actilyse®, Boehringer Ingelheim International GmbH, Ingelheim, Germany) as an initial pulse spray 10mg followed by continuous infusion of 40mg in the rate of 1 to 1.5 mg/hour for 24 to 48 hours.[11] Patients were taken to the Angio suite after thrombolysis to perform an on-table angiogram and completion balloon angioplasty and stenting if needed.

Primary end point was technical success defined as restoration of the luminal patency in completion angiography. Secondary endpoints included clinical success defined as relief of the acute ischemic symptoms and signs as regaining restoration of distal pulsations, relief of rest pain and improvement of the capillary refill time along with warmth of the limb, in addition to limb salvage, as well as freedom from peri-procedural complications.Statistical analysis was performed using SPSS version 28.0.0 (SPSS, IBM, Chicago, IL, USA).

Results

In total, 53 patients were included in this study, 23 in the hybrid group, 13 (56.5%) of which were males and 30 patients in the CDT group 19 (63.3%) of which were males (p-value 0.62). Mean age was 61.09 years (SD15.914) in the hybrid group compared to 57.2 years (SD10.82) in the CDT group (p-value 0.04).

There was no association between any of the pre-existing medical conditions between the 2 groups **(Table 1)** with exception of hypertension which was significantly higher in the total endovascular group (p=.001); however, systolic arterial pressure had to be less than 180 mmHg for the patient to qualify for CDT, and therefore this finding was considered a confounding factor. Most patients in the hybrid group had general or spinal anesethia (owing to the fact that surgical cut-down was performed) compared to predominance of local anesethia in the CDT group (p-value <0.0001). Lesion and access sites were also significantly different between the 2 groups with p-values of 0.004 and 0.001 respectively **(Fig. 1).** Rutherford presentation of both groups was not found to be statistically significant (p-value 0.06) **(Fig. 2)**.

Procedure characteristics and outcomes are detailed in **(Table 2).** Technical success was achieved in 21/23cases (91.3%) in the hybrid group compared to 23/30 cases (76.7%) in CDT group (p-value 0.16). Stent placement was needed in one case in the hybrid group compared to 4 cases in CDT group (p-value 0.27), fasciotomy was performed in 16 cases in the hybrid group versus 14 cases in CDT group (p-value 0.96). Limb salvage was achieved in 21 cases (91.3%) in the hybrid group and in 23 cases (76.7%)in the CDT group, limb salvage was detailed in each stage of acute ischemia in **(Figs. 4,5).** Major amputations were done in a total of 9 cases, the majority of which were in the CDT group (7/30 cases) compared to (2/23 cases) in the hybrid group (p value 0.06). All major amputations were done in patients presenting with stages IIa and IIb acute ischemia **(Table 3)**, and the mean time to major amputation **(Fig. 6)** was longer in the hybrid group (45.48 days) compared to (36.83 day) in CDT group.

As regards complications **(Fig. 3),** 8 procedure related adverse events occurred in the CDT group as 3 cases had distal embolization, one case of minor intracranial haemorrhage that did not require surgical evacuation or result in neurological insult, one case of pseudoaneurysm formation at the access site, 3 access site hematomas, and although more complications occurred in the CDT group compared to hybrid group that had one mild access site haematoma and 2 cases of mild surgical wound infection that improved on antibiotics , it was not statistically significant (p-value 0.078).

None of the patients in either of the 2 groups had renal impairment requiring dialysis, and 30 days mortality was not significantly different between the 2 groups with 3 mortality cases in each group and a p-value of 1.

The ABPI increased **(Fig. 7)** from 0.1 (0.093 SD) to 0.71 (0.2 SD) in hybrid group and from 0.087 (0.09 SD) to 0.63 (0.28 SD) in the CDT group with no statistically significant differences in baseline and postoperative ABPIs between the 2 groups (P-values 0.48 and 0.24 respectively).

During a follow up period of 12 months, from a total of 44 patients who did not have an amputation and were not lost for follow up, binary restenosis (BS) was found in 11/21 (52.4%) cases in hybrid group versus 11/23 (47.8%) of cases in CDT group, with a mean time of 37.23 days (15.14 SD) and 38.96 days (12.22 SD) (P=<.0001) **(Fig. 9).**

Target lesion revascularization (TLR) was found in a 6 out of 21patients in the hybrid group compared to 9 out of 23 patients in the CDT group (P=0.46) and the time to TLR **(Figs. 8,10)** was slightly longer in the hybrid group averaging 44 days (10.9 SD) compared to 42.3 days (11.18 SD) in the CDT group; and neither was statistically significant (P-value .61).The follow up of lesion site patency and time to re-stenosis is detailed in **(Table 4).**

From the total study group population during follow up for one-year, primary patency was 77.4%, 50.9%, and 35.8% at 3, 6 and 12 months respectively, primary assisted patency was 81.1%, 60.4%, and 45.3% at 3, 6 and 12 months respectively, and secondary patency was 81.1%, 66%, 53.8% at 3, 6 and 12 months respectively.

In the hybrid group, primary patency was found in 11 (47.8%) cases compared to 12 (40%) cases in the CDT group (P-value 0.57). Assisted primary patency was found in 15/23 (65.2%) cases in the hybrid group and 15/30 (50%) cases in the CDT group (p-value 0.27). Secondary patency was higher in the CDT group [20/30 (66.7%) cases] compared to 15/23 (65.2%) cases in the hybrid group (p-value 0.91) **(Table 5).**

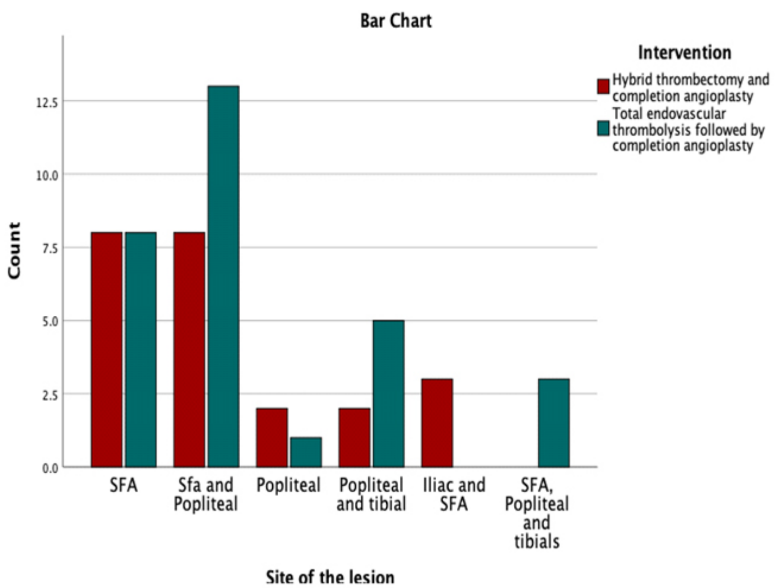

Fig 1: Site of the lesion.

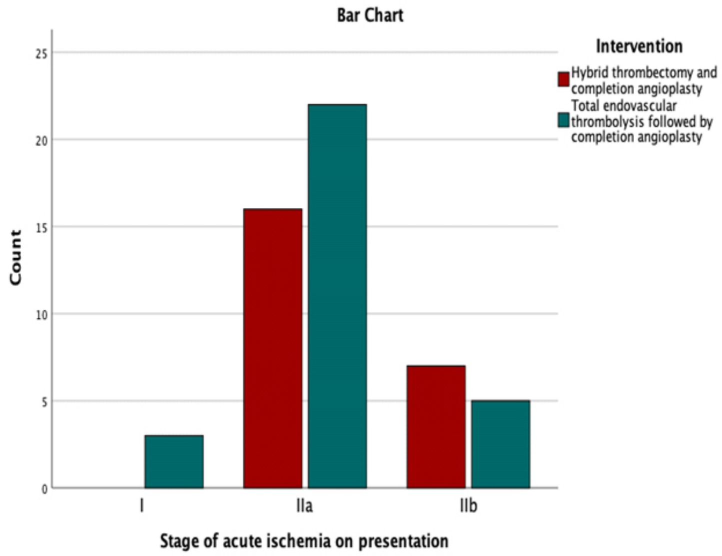

Fig 2: Stage of acute ischemia on presentation.

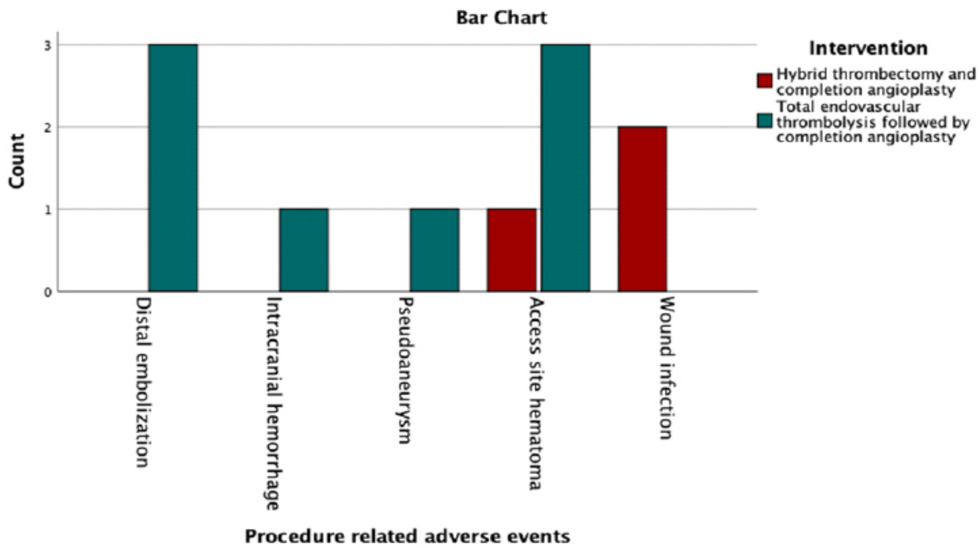

Fig 3: Procedure related adverse effects.

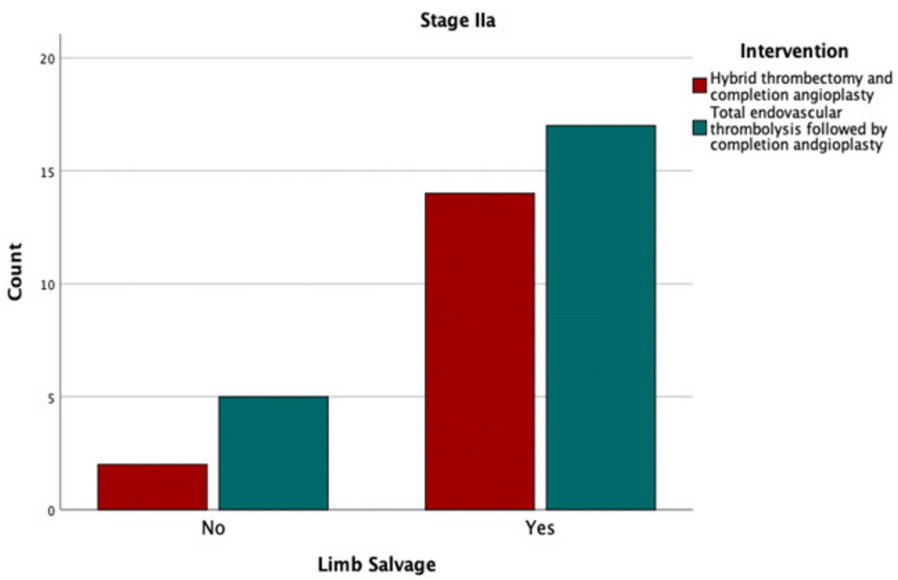

Fig 4: Limb salvage in Stage IIa acute ischemia.

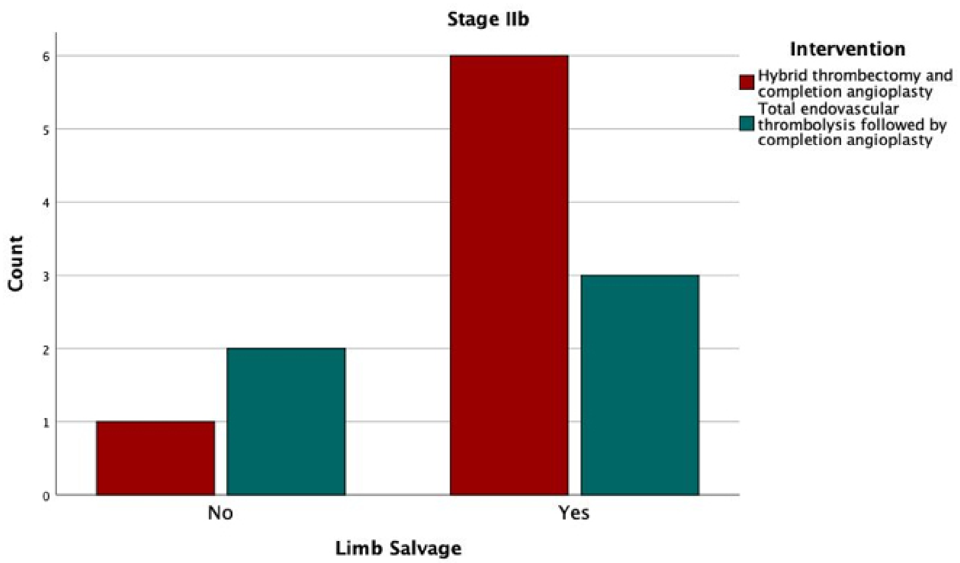

Fig 5: Limb salvage in stage IIb acute ischemia.

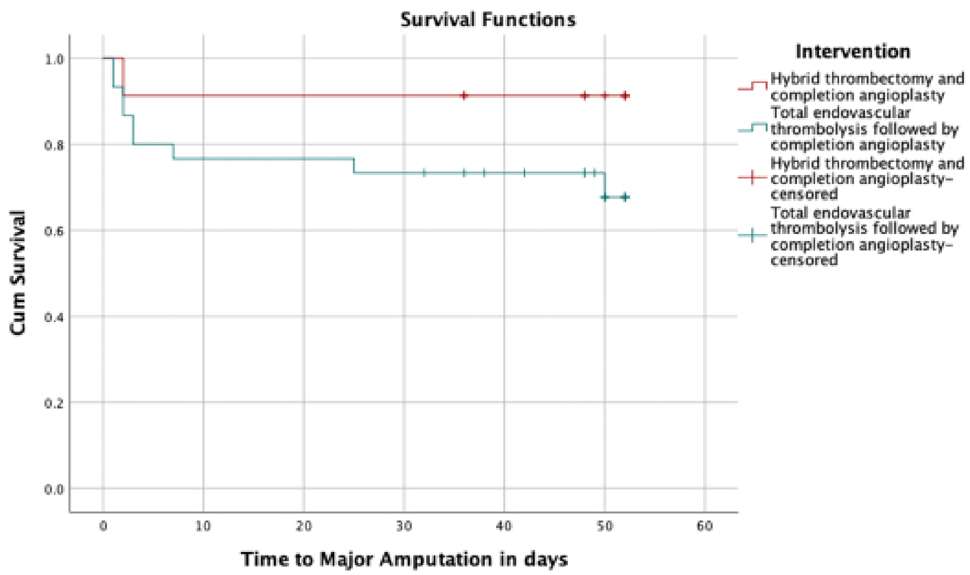

Fig 6: Time to major amputation in days in both groups.

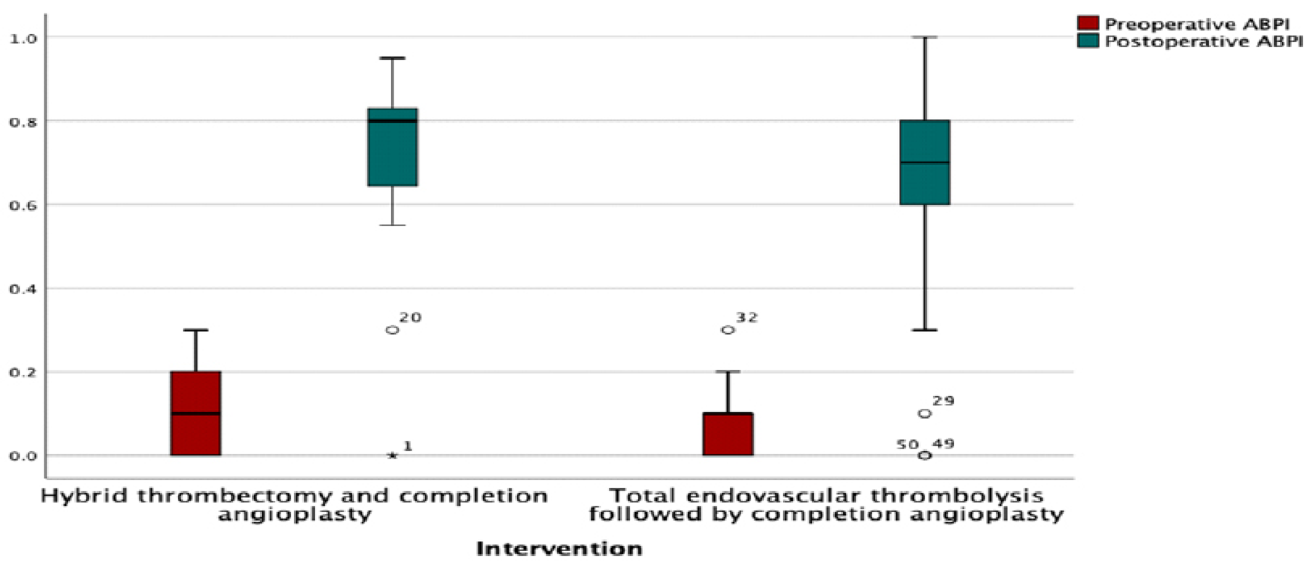

Fig 7: Pre and post-operative ABPI.

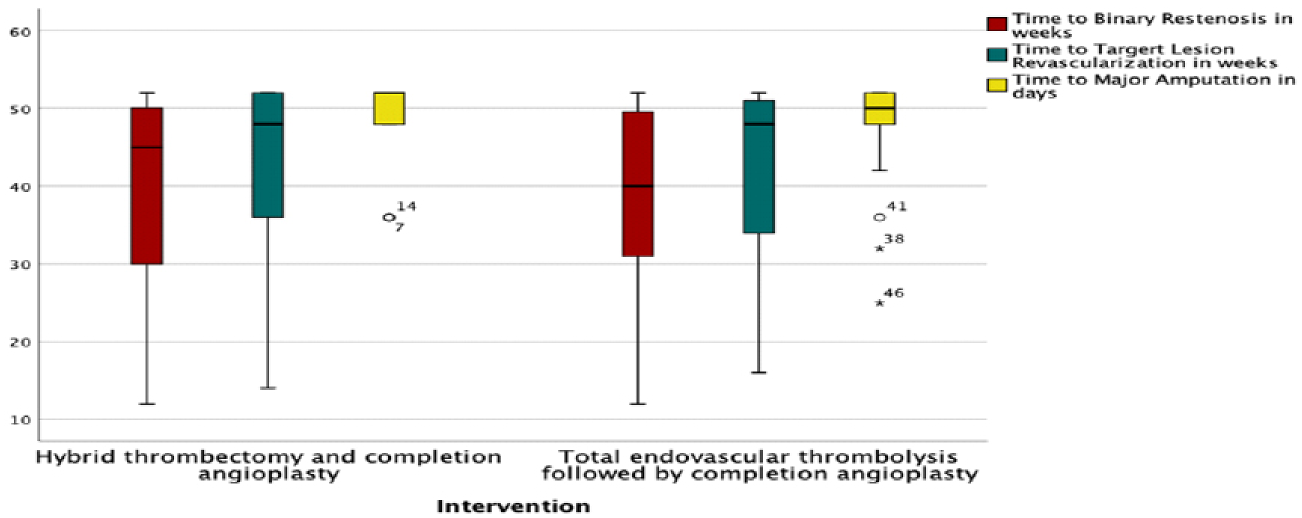

Fig 8: Time to Binary stenosis, TLR and Major amputation.

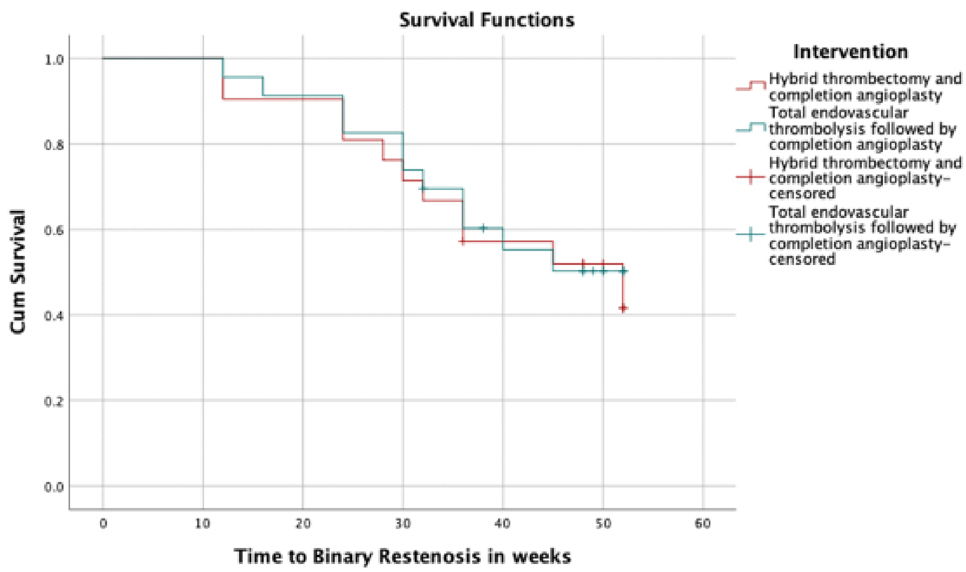

Fig 9: Time to Binary Restenosis in weeks.

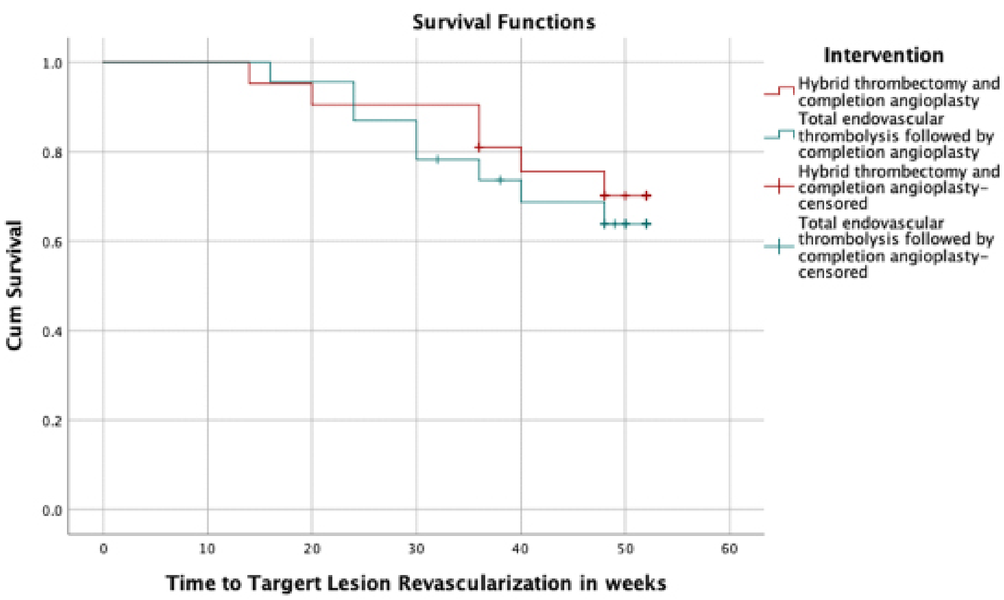

Fig 10: Time to Target Lesion Revascularization in weeks.

Table 1: Association of demographics, co-morbidities, and clinical characteristics in both groups

Variable		Intervention: Hybrid thrombectomy and completion angioplasty	Intervention: Total endovascular thrombolysis followed by completion angioplasty	p-value
Age	Mean (/- SD)	61.09 (15.914)	57.2 (10.82)	.043
Gender	Male	13 (56.5%)	19 (63.3%)	.62*
	Female	10 (43.5%)	11 (36.7%)	
Smoking		12 (52.2%)	18 (60%)	.57*
Diabetes		21 (91.3%)	22 (73.3%)	.16**
Hypertension		20 (87%)	13 (43.3%)	.001*
Stage of Acute Ischemia on presentation	Stage I	0 (0%)	3 (10%)	.1***
	Stage IIa	16 (69.9%)	22 (73.3%)	
	Stage IIb	7 (30.4%)	5 (16.7%)	
Site of the lesion	SFA	8 (34.8%)	8 (26.7%)	0.064***
	SFA and Popliteal	8 (34.8%)	13 (43.3%)	
	Popliteal	2 (8.7%)	1 (3.3%)	
	Popliteal and Tibial	2 (8.7%)	5 (16.7%)	
	Iliac and SFA	3 (13%)	0 (0%)	
	SFA, Popliteal and Tibials	0 (0%)	3 (10%)	

p-value calculated using Pearson's Chi-Square. **p-value calculated using Fisher's Exact Test. ***p-value calculated using Likelihood Ratio.
SFA (Superficial femoral artery).

Table 2: Procedure characteristics and outcome

Variable		Intervention: Hybrid thrombectomy and completion angioplasty	Intervention: Total endovascular thrombolysis followed by completion angioplasty	p-value
Anesethia	General	9 (39.1%)	1 (3.3%)	<.0001***
	Spinal	7 (30.4%)	0 (0%)	
	Local	7 (30.4%)	29 (96.7%)	
Access Site	Ipsilateral Antegrade	22 (95.7%)	16 (53.3%)	.001*
	Contralateral Retrograde	1 (4.3%)	14 (46.7%)	
Stent Placement	No	22 (95.7%)	26 (86.7%)	.269**
	Yes	1 (4.3%)	4 (13.3%)	
Technical Success	No	2 (8.7%)	7 (23.3%)	.16**
	Yes	21 (91.3%)	23 (76.7%)	
Procedure related adverse events	Distal Embolization	0 (0%)	3 (37.5%)	.078***
	Intracranial Haemorrhage	0 (0%)	1 (12.5%)	
	Pseudoaneurysm	0 (0%)	1 (12.5%)	
	Access site hematoma	1 (33.3%)	3 (37.5%)	
	Wound infection	2 (66.7%)	0 (0%)	
30 days mortality	No	20 (87%)	27 (90%)	1**
	Yes	3 (13%)	3 (10%)	
Need for Fasciotomy	No	7 (30.4%)	16 (53.3%)	.096*
	Yes	16 (69.6%)	14 (46.7%)	
Major amputation	No	21 (91.3%)	23 (76.7%)	.06*
	Yes	2 (8.7%)	7 (23.3%)	
Time to major amputation in days	Mean (/- SD)	45.48 (14.46)	36.83 (20.17)	.07
Limb Salvage	No	2 (8.7%)	7 (23.3%)	.06*
	Yes	21 (91.3%)	23 (76.7%)	

*p-value calculated using Pearson's Chi-Square. **p-value calculated using Fisher's Exact Test. ***p-value calculated using Likelihood Ratio.

Table 3: Limb salvage in different acute ischemia stages

	Stage	Total Number		Intervention		p-value
				Hybrid thrombectomy and completion angioplasty	Total endovascular thrombolysis followed by completion angioplasty	
Limb Salvage	I	3	Yes	0 (0%)	3 (100%)	-
	IIa	38	Yes	15 (46.9%)	17 (53.1%)	.37*
	IIb	12	Yes	6 (66.7%)	3 (33.3%)	.31*

*p-value calculated using Fischer's Exact Test.

Table 4: Follow up lesion patency and time to restenosis

Variable	Hybrid thrombectomy and completion angioplasty	Total endovascular thrombolysis followed by completion angioplasty	p-value
	Mean (/- SD)	Mean (/- SD)	
Preoperative ABPI	0.1 (0.093)	0.087 (0.09)	.48*
Postoperative ABPI	0.71 (0.2)	0.63 (0.28)	.24*
Time to Binary Restenosis in weeks	37.23 (15.14)	38.96 (12.22)	<.0001*
Time to Target Lesion Revascularization in weeks	44 (10.9)	42.3 (11.18)	.61*
Time to major amputation in days	45.48 (14.46)	36.83 (20.17)	.07*
Duration of the procedure in hours	2.6 (0.9)	3.9 (1.03)	.9*
Time to major amputation in days	**Median (IQR)** 47.65 (41.89 – 53.41)	**Median (IQR)** 39.48 (32.012 – 46.96)	.06*
Time to Target Lesion Revascularization in weeks	46.28 (41.6 – 50.9)	44.57 (39.86 – 49.27)	.62*
Time to Binary Restenosis in weeks	40.49 (34.29 - 46.7)	41.04 (35.72 – 46.36)	.84*

*p-value calculated using Independent samples t-test.

Table 5: Both groups patency rates

Variable	Intervention		p-value
	Hybrid thrombectomy and completion angioplasty	Total endovascular thrombolysis followed by completion angioplasty	
Binary Restenosis	11 (52.4%)	11 (47.8%)	.76*
Target Lesion Revascularization	6 (28.6%)	9 (39.1%)	.46**
Primary Patency	11 (47.8%)	12 (40%)	.57*
Primary Assisted Patency	15 (65.2%)	15 (50%)	.27*
Secondary Patency	15 (65.2%)	20 (66.7%)	.91*

*p-value calculated using Likelihood ratio. **p-value calculated using Chi Square.

Discussion

Acute limb ischemia poses a severe threat to both life and limb, leading to significant morbidity and mortality. It complicates approximately 15–20% of cases of chronic limb ischemia,[12,13] and carries a 30-day mortality rate of around 26%.[14]

The 2012 guidelines from the American College of Chest Physicians recommend a hybrid surgical approach for revascularization over a solely endovascular approach in cases of both thrombotic and embolic acute limb ischemia.[15] However, many of the studies supporting this recommendation were conducted before recent advancements in catheter-directed therapy techniques. Consequently, these findings may be biased towards favouring the hybrid approach.

The ESVS guidelines recommendations have undergone revisions since the 2017 guidelines, which advocated for surgical thrombectomy over catheter-directed thrombolysis in cases with neurological deficits. Conversely, catheter-directed thrombolysis was deemed more suitable for less severe cases without neurological deficits.[16]

In contrast, the 2020 guidelines propose considering catheter-directed thrombolysis, if promptly initiated, for patients with Rutherford grade IIb acute limb ischemia.[9] This approach may be combined with recently developed devices of percutaneous aspiration or thrombectomy, which has been associated with 6-month amputation rates of less than 10%.[17]

In our study, we discovered that there were no statistically significant differences between the two approaches concerning limb salvage, the rate and timing of major amputations, overall procedure-related adverse events, and 30-day mortality. However, we observed a higher incidence of distal embolization and bleeding complications in the total endovascular group.

These findings align with a systematic review by Enezate et al., which also found no significant difference in mortality and amputation rates between the two treatment options at a 1-year follow-up.[18] Similarly, Ouriel and colleagues concluded that there was an equal cumulative amputation risk at 1 year between both groups, but with lower mortality in the thrombolysis group.[8]

However, in contrast to our results, the STILE (Surgery versus Thrombolysis for Ischaemia of the Lower Extremity) trial reported significantly better limb salvage and amputation-free survival among acute ischemia patients randomized to thrombolysis.[19] Additionally, Grip et al. found no difference in stroke/intracranial haemorrhage rates between acute ischemia patients managed with an endovascular approach compared to those treated with open surgery.[20]

A recent systematic review and meta-analysis of surgical and endovascular revascularization approaches for acute ischemia patients concluded that there were no differences in limb salvage between thrombectomy and thrombolysis, although there was a higher risk of haemorrhagic complications in the thrombolysis group.[21]

Analysing our patients' pre- and post-intervention mean ankle-brachial pressure index (ABPI) increases and technical success, we found comparable, albeit statistically insignificant, differences between both groups. These results echo those observed by Taha et al., who found similar overall technical success rates between open surgery and endovascular approaches for revascularizing acute limb ischemia, despite a higher rate of failed graft bypass revascularization in open surgery.[22]

While there were no significant differences between both groups regarding binary restenosis, we did observe a statistically significant difference in the time to binary restenosis, which was longer in the total endovascular approach group. Additionally, although there were non-significant differences in primary, primary-assisted, and secondary patencies, the mean time to target lesion revascularization (TLR) was slightly longer in the hybrid group.

These findings align with those of Taha et al., who reported comparable non-significant differences in primary, primary-assisted, and secondary patencies at 1 and 2 years of follow-up between open and endovascular revascularization.[22] However, Grip et al. found better patency rates at a 30-day follow-up in the endovascular group.[20]

Contrary to the previous recommendations of the Society for Vascular Surgery (SVS) and other vascular societies, which suggest urgent surgery for severe ischemia patients with motor deficits (Rutherford class IIb),[23,24] our study's data analysis indicates that there are no significant differences in limb salvage concerning the intervention approach used and the stage of acute ischemia presented.

As there was a lack of reporting on the severity stage of acute ischemia, the only study that utilized Rutherford classification of acute limb ischemia, conducted by Taha et al., suggested that endovascular management could be the preferred first-line management for Rutherford class II native and stented artery cases, while surgery is preferred for Rutherford class II bypass graft failures.[22]

Conclusion

Although the total endovascular approach shows a slightly higher incidence of distal embolization and bleeding complications compared to the hybrid approach in patients with acute limb ischemia, both approaches demonstrate comparable rates of limb salvage relative to the approach used and the stage of acute ischemia. Future randomized controlled trials are needed to advocate for the widespread adoption of the total endovascular approach, even in Rutherford class IIb cases, for the most optimal approach.

References

1. Waton S, Johal A, Heikkila K, Cromwell D: National Vascular Registry Report 2017. London: The Royal College of Surgeons of England; 2017. Available from: https://www.annualreports.com/HostedData/AnnualReportArchive/W/TSX_WJA_2017.pdf. [Last accessed on 2021 Oct 01].

2. Fowkes FG, Aboyans V, Fowkes FJ, McDermott MM, Sampson UK, Criqui MH: Peripheral artery disease: Epidemiology and global perspectives. ***Nat Rev Cardiol.*** 2017; 14(3): 156-70.

3. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG: Inter-society consensus for the management of peripheral arterial disease (TASC II). ***J Vasc Surg.*** 2007; 45(1): 5-67.

4. Nickinson A, Bown MJ: Acute and chronic limb ischaemia. ***Surg (United Kingdom).*** 2019; 37(2): 93-101.

5. Gianmarco D, Edoardo P, Francesco S, Giancarlo P, Laura N, Cecilia F, et al: Acute on chronic limb ischemia: From surgical embolectomy and thrombolysis to endovascular options. ***Seminars in Vascular Surgery.*** 2018; 31(2–4): 66-75.

6. Palfreyman S, Booth A, A Michaels A: A Systematic review of intra-arterial thrombolytic therapy for lower-limb ischaemia. ***European Journal of Vascular and Endovascular Surgery.*** 2000; 19(2): 143-157.

7. Falluji N, Mukherjee D: Critical and acute limb ischemia: An overview. ***Angiology.*** 2014; 65(2): 137-146.

8. Ouriel K, Veith FJ, Sasahara AA: For the TOPAS investigators. Thrombolysis or peripheral arterial surgery (TOPAS): phase 1 results. ***J Vasc Surg.*** 1996; 23: 64–75.

9. Björck M, Earnshaw JJ, Acosta S, Bastos G, Cochennec F, Debus ES, et al: Editor's Choice - European Society for Vascular Surgery (ESVS) 2020 Clinical practice guidelines on the management of acute limb ischaemia. ***Eur J Vasc Endovasc Surg***. 2020; 59(2): 173-218.

10. Aho P, Venermo M: Hybrid procedures as a noveltechnique in the treatment of critical limb ischemia. ***Scandinavian Journal of Surgery.*** 2012; 101(2): 107-13.

11. Chan J, Chet R, Andrew K, Sonny P: Usefulness of catheter directed thrombolysis using alteplase in peripheral vascular occlusion. ***Baylor University Medical Center Proceedings.*** 2001; 14(1): 3–7.

12. Lyden SP: Endovascular treatment of acute limb ischemia: Review of current plasminogen activators and mechanical thrombectomy devices. ***Perspect Vasc Surg Endovasc Ther.*** 2010; 22: 219-22.

13. Creager MA, Kaufman JA, Conte MS: Clinical practice. Acute limb ischemia. ***N Engl J Med.*** 2012; 366: 2198-206.

14. Clason AE, Stonebridge PA, Duncan AJ, et al: Morbidity and mortality in acute lower limb ischaemia: A 5-year review. ***Eur J Vasc Surg.*** 1989; 3: 339-43.

15. Alonso-Coello P, Bellmunt S, McGorrian C, et al: Antithrombotic therapy in peripheral artery disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. ***Chest.*** 2012; 141: e669S-90S.

16. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, et al: ESC Scientific Document Group. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). ***Eur Heart J.*** 2018; 39(9): 763-816.

17. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG: Inter-society consensus for the management of peripheral arterial disease (TASC II). ***J Vasc Surg.*** 2007; 45(Suppl. S): S5e67.

18. Enezate TH, Omran J, Mahmud E, Patel M, Abu-Fadel MS, White CJ, et al: Endovascular versus surgical treatment for acute limb ischemia: A systematic review and meta-analysis of clinical trials. ***Cardiovasc Diagn Ther.*** 2017; 7(3): 264-271.

19. Results of a prospective randomized trial evaluating surgery versus thrombolysis for ischemia of the lower extremity. The STILE trial. ***Ann Surg.*** 1994; 220(3): 251-66; discussion 266-8.

20. Grip O, Wanhainen A, Michaëlsson K, Lindhagen L, Björck M: Open or endovascular revascularization in the treatment of acute lower limb ischaemia. ***Br J Surg.*** 2018; 105(12): 1598-1606.

21. Veenstra EB, Van der Laan MJ, Zeebregts CJ, de Heide EJ, Kater M, Bokkers RPH: A systematic review and meta-analysis of endovascular and surgical revascularization techniques in acute limb ischemia. ***J Vasc Surg.*** 2020; 71(2): 654-668.e3.

22. Taha AG, Byrne RM, Avgerinos ED, et al: Comparative effectiveness of endovascular versus surgical revascularization for acute lower extremity ischemia. ***J Vasc Surg.*** 2015; 61: 147-54.

23. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL et al: American Association for Vascular Surgery/Society for Vascular Surgery; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society of Interventional Radiology; ACC/AHA task force on practice guidelines. ACC/AHA guidelines for the management of patients with peripheral arterial disease (Lower extremity, renal, mesenteric, and abdominal aortic): A collaborative report from the American Associations for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA task force on practice guidelines (Writing committee to develop guidelines for the management of patients with peripheral arterial disease)-summary of recommendations. ***J Vasc Interv Radiol.*** 2006; 17: 1383–1397.

24. Baril DT, Patel VI, Judelson DR, Goodney PP, McPhee JT, Hevelone ND, et al: Vascular Study Group of New England. Outcomes of lower extremity bypass performed for acute limb ischemia. ***J Vasc Surg.*** 2013; 58: 949–956.