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Comparative Outcomes of Catheter-Directed Thrombolysis and Open Surgical Revascularization in Early-Stage Acute Limb Ischemia: Real-World Evidence from a Retrospective Cohort Study

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Comparative Outcomes of Catheter-Directed Thrombolysis and Open Surgical Revascularization in Early-Stage Acute Limb Ischemia: Real-World Evidence from a Retrospective Cohort Study

Running Header: CDT vs OSR in Early-Stage Acute Limb Ischemia

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Abstract

Background: Acute limb ischemia (ALI) is a vascular emergency where timely revascularization is crucial for limb salvage and survival. While open surgical revascularization (OSR) has been the traditional standard, catheter-directed thrombolysis (CDT) has emerged as a minimally invasive alternative. Comparative real-world evidence in early-stage ALI (Rutherford I–IIa) remains limited. Methods: We conducted a retrospective single-center cohort study including 36 patients with ALI treated between 2019 and 2023 (OSR: n=24; CDT: n=12). Demographics, comorbidities, procedural details, and outcomes were analyzed. The primary endpoint was a composite of in-hospital mortality, primary patency, and secondary patency. Secondary endpoints included amputation, cerebrovascular events, renal function, and hospital stay. Effect sizes with 95% confidence intervals were reported alongside p-values to address type II error risk. Results: Baseline characteristics were comparable between groups. Both OSR and CDT significantly improved ankle-brachial index (0.64 ± 0.43 to 0.93 ± 0.33, $p<0.001$) and postoperative arterial patency. At 12 months, primary patency was 66.7% (OSR) vs. 50.0% (CDT), and secondary patency was 79.2% vs. 75.0% ($p>0.05$). Major amputation (12.5% vs. 16.7%) and mortality (8.3% vs. 16.7%) rates did not differ significantly. Hospital stay was longer after OSR (7.29 ± 4.58 vs. 6.08 ± 8.75 days, $p=0.038$). Fibrinogen levels decreased significantly during CDT, but no major bleeding events occurred. Conclusion: Both OSR and CDT provide effective revascularization in early ALI, with comparable limb salvage and survival outcomes. CDT offers a minimally invasive alternative with acceptable safety when accompanied by careful monitoring, whereas OSR remains a reliable option with immediate reperfusion. Larger multicenter studies are needed to refine patient selection and optimize treatment algorithms.

Keywords: acute limb ischemia; catheter-directed thrombolysis; surgical revascularization; limb salvage

Introduction

Acute limb ischemia (ALI) is a vascular emergency characterized by a sudden reduction in limb perfusion that, if untreated, may rapidly progress to limb loss and life-threatening complications [1]. The severity of ischemia is commonly classified using the Rutherford system [2]. Patients with Rutherford class I–IIa ischemia represent an early and potentially reversible stage, where timely

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intervention can restore perfusion before irreversible neuromuscular damage occurs. This subgroup is clinically important because outcomes are more favorable when revascularization is achieved promptly, and treatment choice in these patients may determine long-term limb salvage and functional recovery [3,4].

Traditionally, open surgical revascularization (OSR) with thromboembolectomy has been the standard approach, offering immediate flow restoration [5]. However, it carries important drawbacks: surgical trauma, anesthesia-related risk, and reduced effectiveness in distal or atherosclerotic disease [6]. More recently, catheter-directed thrombolysis (CDT) has emerged as a minimally invasive alternative, allowing gradual clot dissolution and preservation of distal branches [7]. Long-term clinical data have also shown favorable outcomes with endovascular therapy, including improved survival compared to open surgery in selected patients [8]. Yet, CDT entails longer treatment duration, risk of hemorrhage, and potential contrast-related renal complications [9,10].

Despite increasing adoption of CDT, the optimal strategy for ALI management remains unresolved [11]. Prior studies report conflicting findings on long-term outcomes, limb salvage, and complication rates [12,13]. Moreover, there is no consensus on thrombolytic dosing protocols, anticoagulation regimens, or post-procedural surveillance, leading to wide practice variations across centers [14]. This uncertainty underscores a critical knowledge gap, highlighting the need to determine how the clinical outcomes of OSR and CDT compare when these treatments are applied in routine practice, particularly in early Rutherford stages (I–IIa). Addressing this question is essential to guide treatment selection and inform standardization efforts.

Therefore, in this study we retrospectively compared OSR and CDT in patients with ALI, focusing on efficacy, safety, and key prognostic parameters—including renal function, thrombolytic dosage, and arterial patency. By clarifying these real-world outcomes, we aim to contribute evidence toward individualized decision-making in ALI management, particularly given the current lack of standardized protocols and the heterogeneous outcome reporting in previous studies, as highlighted by Veenstra et al [15].

Methods

This study was designed as a retrospective, single-center cohort analysis, focusing on 36 patients diagnosed with ALI who underwent either OSR (n=24) or CDT (n=12) between January 1, 2019, and December 31, 2023. Patient data were obtained from electronic medical records and institutional databases. All procedures included in the analysis were performed by board-certified cardiovascular surgeons with extensive experience in the management of ALI.

Patient Selection and Inclusion Criteria:

Eligible patients were those aged 18 years and older who were diagnosed with ALI based on clinical examination and imaging findings (e.g., Doppler ultrasound, computed tomography angiography), and subsequently underwent either OSR or CDT as a primary intervention. Exclusion criteria included patients with chronic limb ischemia, incomplete medical records, prior major lower limb amputation, or those who received hybrid or purely endovascular treatments not involving thrombolysis (Figure 1).

Treatment allocation was not randomized but was determined by the cardiovascular surgeon based on ischemia severity, comorbidities, anatomical factors, and contraindications to thrombolysis. As such, physician judgment inherently introduced a potential source of selection bias. To mitigate this, baseline demographics and comorbidities were compared between groups to ensure clinical comparability.

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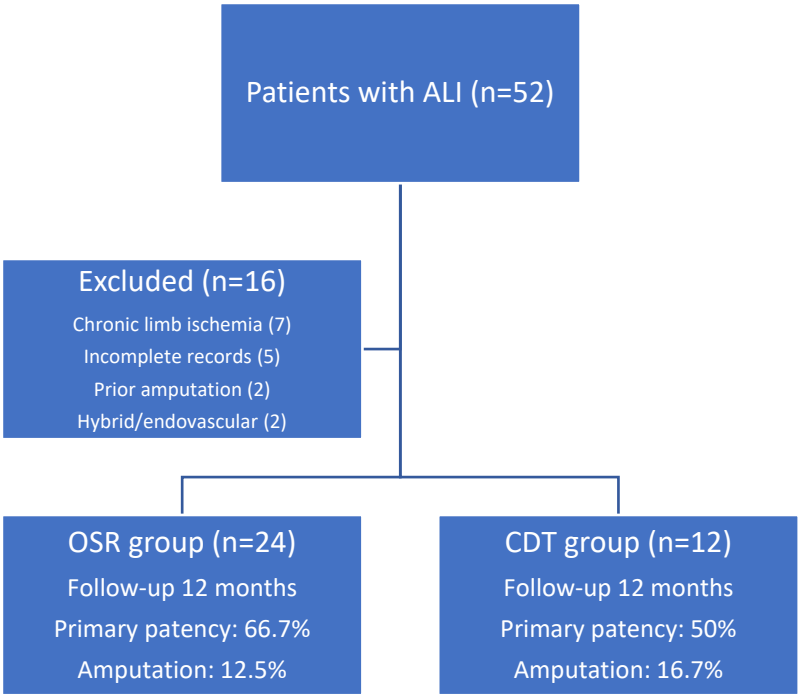

Figure 1. Study consort diagram of patient selection and treatment allocation.

Intervention Details

CDT Protocol

CDT was performed by intra-arterial administration of thrombolytic agents (e.g., alteplase) through percutaneously inserted catheters under fluoroscopic guidance. The infusion was typically initiated at a rate of 0.5–1.0 mg/h, with subsequent dose and duration adjustments made at the discretion of the physician, based on individual patient characteristics, angiographic findings, and bleeding risk. Plasma fibrinogen levels were systematically monitored before initiation and following completion of therapy to guide dosage modifications and ensure procedural safety.

Anticoagulation

During CDT, all patients received concomitant low-dose unfractionated heparin infusion (typically 500–1,000 IU/h) through the sheath to maintain catheter patency and reduce peri-procedural thrombosis risk. Activated clotting time was not routinely measured, but infusion rates were adjusted if bleeding tendency was suspected [16].

After completion of CDT or OSR, all patients were transitioned to systemic anticoagulation (either low-molecular-weight heparin-LMWH or intravenous unfractionated heparin, followed by oral anticoagulation where indicated, such as atrial fibrillation) [12,17]. While the general principle of peri- and post-procedural anticoagulation was standardized, exact drug choice and duration were tailored according to comorbidities, bleeding risk, and prior antithrombotic therapy.

OSR Anticoagulation & Adjunctive Therapies

OSR consisted of standard thromboembolectomy performed under general or regional anesthesia. Systemic intravenous unfractionated heparin (3,000–5,000 IU bolus) was administered intraoperatively after vascular control was obtained, in line with routine surgical practice, to minimize thrombus propagation. Adjunctive maneuvers, such as intraoperative flushing with heparinized saline, were also employed at the discretion of the operating surgeon [18].

Postoperatively, patients were continued on systemic anticoagulation (LMWH or intravenous unfractionated heparin) with transition to oral anticoagulants or dual antiplatelet therapy, depending on comorbidities, underlying atrial fibrillation, or atherosclerotic burden.

Outcome Measures

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The primary outcome of the study was a composite endpoint consisting of:

1. In-hospital mortality,
2. Primary patency, defined as uninterrupted patency of the treated vessel without need for further intervention, and
3. Secondary patency, defined as patency restored after a reintervention following an initial occlusion.

Secondary outcomes included:

- Major amputation rates (above the ankle),
- Incidence of cerebrovascular events (e.g., stroke or transient ischemic attack) during hospitalization, and
- Length of hospital stay, measured in days from admission to discharge.

Statistical Analysis

Descriptive statistics were represented as mean (standard deviation), median (minimum–maximum), and frequency (%) for continuous and categorical variables, respectively. The normality assumption was evaluated using the Shapiro–Wilk test, boxplots, histograms, and Q–Q plots. Independent groups were compared with the independent samples t-test or the Mann–Whitney U test, depending on parametric assumptions. Associations among categorical variables were assessed with the chi-square test or Fisher's exact test. Longitudinal changes were analyzed using repeated measures ANOVA with one fixed factor, and binary changes over time were evaluated with McNemar's test.

Given the small sample size and the risk of type II error, effect sizes were reported alongside p-values. For continuous outcomes, we present mean differences with 95% confidence intervals (Welch method) and Cohen's d where appropriate. For binary outcomes, group proportions are reported with Wilson 95% CIs, risk differences with Newcombe 95% CIs, and risk ratios with log (Katz) 95% CIs. Effect sizes for nonparametric tests are given as r, and categorical associations as Phi (φ). Statistical significance was set at $p \leq 0.05$, but estimates with 95% CIs are emphasized to aid interpretation. All analyses were conducted using SPSS version 23 (IBM SPSS, 2015).

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Ankara University 2025000665-1 on 22/08/2025.

Results

A total of 36 patients were included in the study, of whom 24 (66.7%) underwent OSR and 12 (33.3%) received CDT. The mean age of the entire cohort was 62.56 ± 13.39 years, with a range of 32 to 100 years. Most patients were male (75%), while 25% (n=9) were female. Demographical data are shown in **Table 1**.

Table 1. Baseline demographic and clinical characteristics of patients with ALI undergoing OSR or CDT. Data are presented as mean ± standard deviation, median (minimum–maximum), or n (%).

Variable	OSR	CDT
Age	60.21±11.76 61.00 (32.00 – 78.00)	67.25±15.66 67.50 (50.00 – 100.00)
Gender, K	7 (29.17)	2 (16.67)
Hypertension	13 (54.17)	6 (50.00)
Diabetes Mellitus	14 (58.33)	6 (50.00)
Heart Failure	5 (20.83)	3 (25.00)
Coronary Artery Disease	10 (41.67)	4 (33.33)
Stroke	4 (16.67)	2 (16.67)

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Atrial Fibrillation	8 (33.33)	7 (58.33)
Hyperlipidemia	14 (58.33)	7 (58.33)
COPD	4 (16.67)	2 (16.67)
Renal Disease	4 (16.67)	4 (33.33)
Smoking	18 (75.00)	6 (50.00)
Previous Vascular Intervention	13 (54.17)	4 (33.33)
Rutherford Class (I-IIa)	20 (83.33)	8 (66.67)

Preoperative and Postoperative Clinical Parameters

The mean preoperative ankle-brachial index (ABI) was 0.64 ± 0.43, which improved significantly to 0.93 ± 0.33, postoperatively ($p < 0.001$). Similarly, preoperative creatinine level was 1.12 ± 1.02 mg/dL, and increased slightly in postoperative period but it was not significant (1.22 ± 0.94 mg/dL, $p = 0.103$). The mean duration of hospitalization was 6.89 ± 6.18 days (median: 5 days, range: 1–32 days).

Comorbidities and Baseline Characteristics

The most prevalent comorbid conditions were hyperlipidemia (58.33%), diabetes mellitus (55.56%), hypertension (52.78%), smoking history (66.67%), and atrial fibrillation (41.67%). Other common comorbidities included atherosclerotic heart disease (38.89%), heart failure (22.22%), kidney disease (22.22%), and prior vascular interventions (47.22%).

Patency and Outcomes

Preoperatively, the popliteal artery was patent in only 13.89% of patients whereas anterior tibial artery in 8.33%, and posterior tibial artery in 22.22%. These rates demonstrated a significant postoprative improvement to 94.44%, 66.67%, and 80.56%, respectively (all $p < 0.001$).

Primary patency at 6 and 12 months was observed in 69.4% and 61.1% of patients, respectively. Secondary patency rates were higher, with 83.3% at 6 months and 77.8% at 12 months. The overall amputation rate was 13.9%, mortality rate was 11.1%, and one patient (2.8%) experienced a procedure-related cerebrovascular event. According to Rutherford classification, 22.2% of patients presented with Class I ischemia, while 77.8% had Class IIa ischemia (Figure 2). No patients with Rutherford class IIb or III ischemia were included in the present cohort.

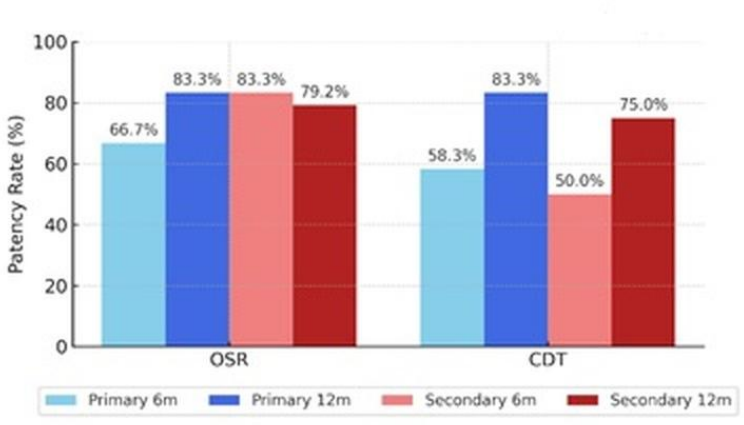

Figure 2. Primary and secondary patency rates at 6 and 12 months following OSR and CDT.

Comparison Between OSR and CDT Groups

There were no statistically significant differences between the OSR and CDT groups in terms of age (60.21 ± 11.76 vs 67.25 ± 15.66 years, $p = 0.139$), preoperative ABI (0.63 ± 0.45 vs 0.66 ± 0.39, $p = 0.540$), or preoperative creatinine (1.19 ± 1.24 vs 0.99 ± 0.16 mg/dL, $p = 0.120$). Hospital stay was longer

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in the OSR group (7.29 ± 4.58 vs 6.08 ± 8.75 days, p = 0.038). The mean difference with 95% CI is illustrated in Figure 3.

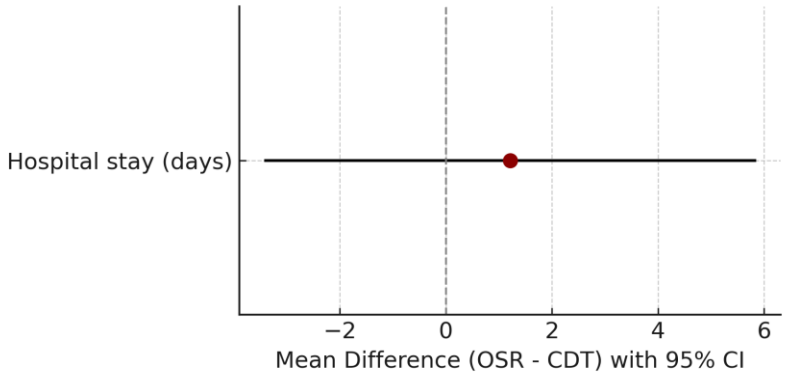

Figure 3. Mean difference in hospital stay (OSR – CDT) with 95% confidence interval.

Comorbidity profiles were similar, with no significant differences in hypertension, diabetes mellitus, atrial fibrillation, or smoking. Likewise, procedural outcomes did not differ significantly: amputation (12.5% OSR vs 16.7% CDT, p = 1.000), mortality (8.3% OSR vs 16.7% CDT, p = 0.588), and cerebrovascular events (0% OSR vs 8.3% CDT, p = 0.333). Effect sizes with 95% confidence intervals for binary outcomes are summarized in Figure 4**.**

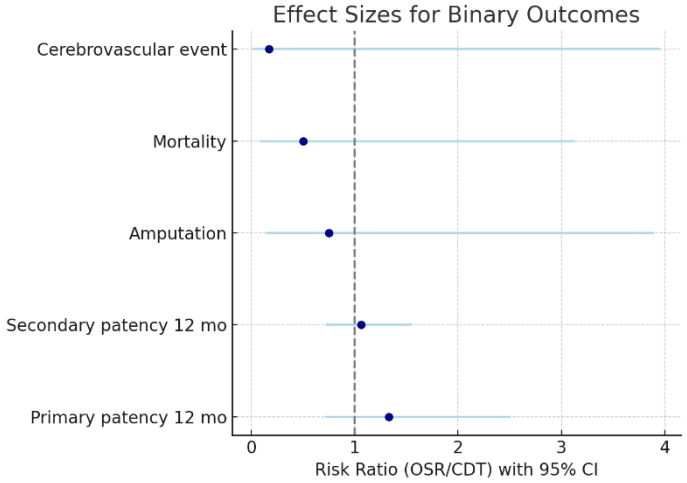

Figure 4. Risk ratios with 95% confidence intervals for binary outcomes (primary and secondary patency at 12 months, amputation, mortality, cerebrovascular events).

However, given the unequal group sizes (24 vs 12) and the overall small cohort, these comparisons are underpowered. The absence of statistical significance should therefore be interpreted cautiously, as clinically meaningful differences may not have been detectable. To address type II error risk, effect sizes with 95% confidence intervals (CIs) are reported. The mean difference in hospital stay was +1.21 days (95% CI −3.43 to +5.85). At 12 months, primary patency was 66.7% vs 50.0% (risk difference +0.17; 95% CI −0.13 to +0.42; risk ratio 1.33; 95% CI 0.69–2.59), and secondary patency 79.2% vs 75.0% (risk difference +0.04; 95% CI −0.24 to +0.32; risk ratio 1.06; 95% CI 0.72–1.57). For major amputation and in-hospital mortality, 95% CIs were wide and included clinically relevant effects, again underscoring limited power. At 12 months, primary patency was 66.7% vs 50.0% and secondary patency 79.2% vs 75.0% for OSR and CDT, respectively. **Figure 5** illustrates the Kaplan–

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Meier survival curve comparing cumulative survival rates between the two groups during the 12-month follow-up period log-rank p =0.653).

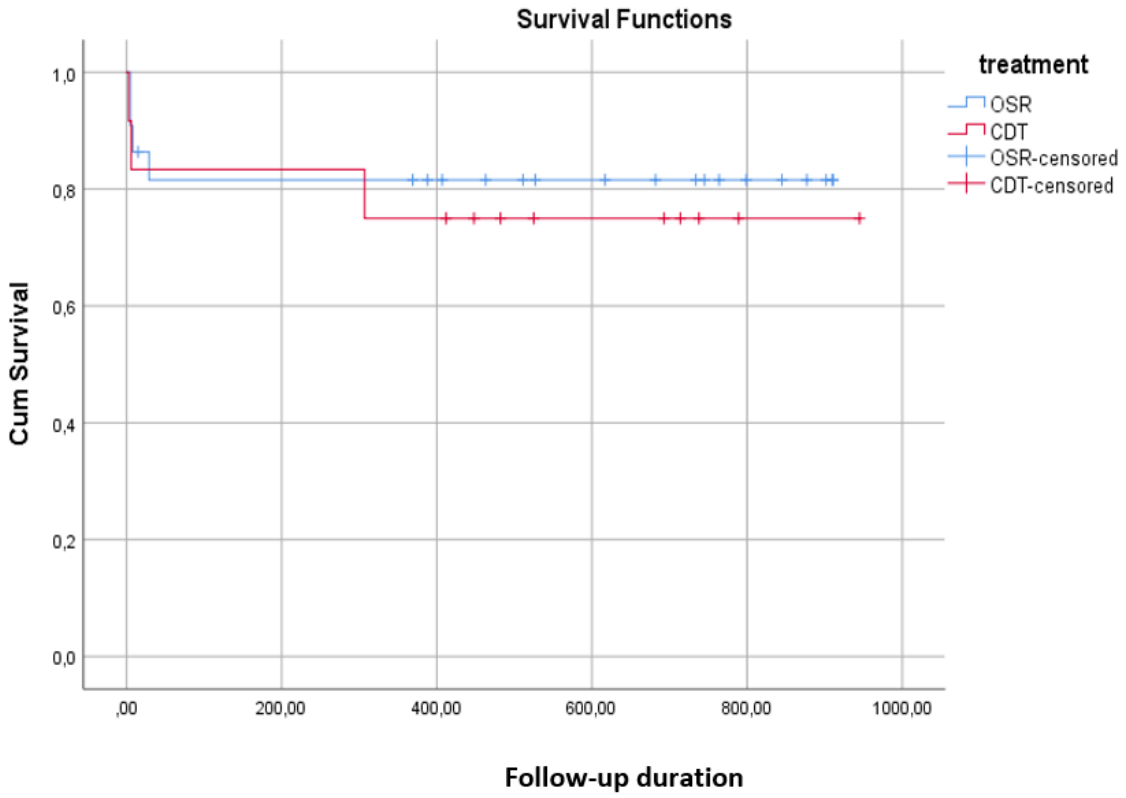

Figure 5. Kaplan–Meier survival curve comparing cumulative survival rates between the OSR and CDT groups during the 12-month follow-up period.

Thrombolytic Infusion

In the CDT cohort, the duration of thrombolytic infusion and the total administered dose of alteplase demonstrated considerable variability. The median infusion duration was 24 hours (range: 15–32 hours), while the median total dose was 19.5 mg (range: 12–28 mg). Most patients received infusion periods of 15 to 24 hours, with total doses generally aligned with the treatment duration, reflecting standardized yet patient-tailored dosing strategies. **Figure 6** presents individual patient data, showing that although infusion times tended to cluster within the 24-hour range, total doses exhibited greater variability, likely due to adjustments for body weight, clinical response, and bleeding risk. These findings underscore the individualized nature of CDT protocols in real-world practice and highlight the importance of flexible dosing regimens tailored to patient characteristics.

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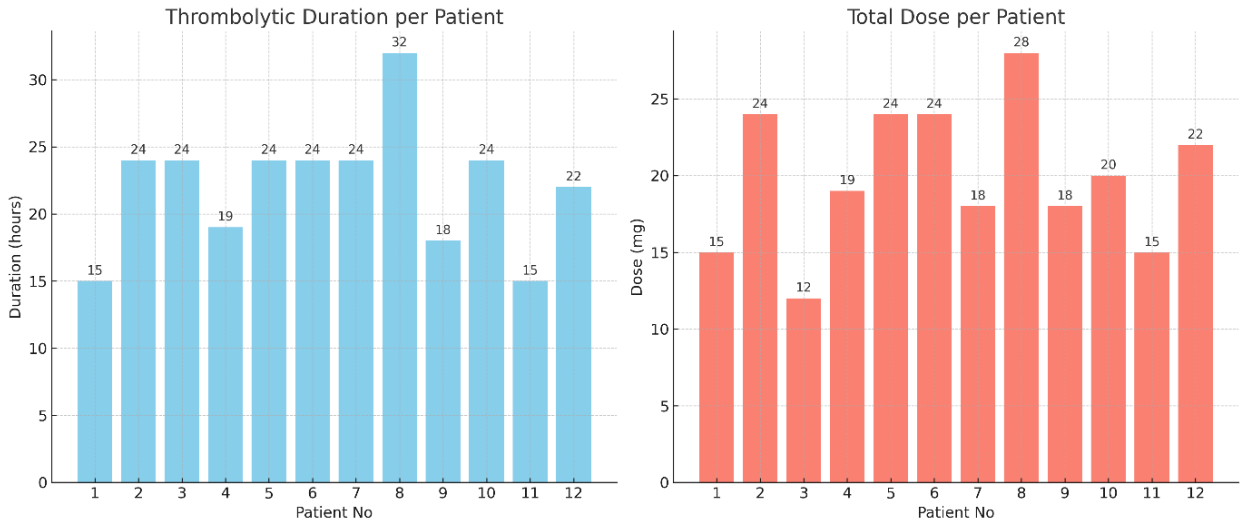

Figure 6. *Thrombolytic infusion duration and total dose administered per patient undergoing CDT.*

Fibrinogen Levels

Peri-procedural fibrinogen levels significantly decreased after intervention compared with baseline values (3.48 ± 1.33 g/L vs. 2.42 ± 1.36 g/L, p = 0.003), with a large effect size (r = 0.861). This reduction was more pronounced in patients undergoing CDT, reflecting the pharmacodynamic effect of thrombolysis. Despite the decline, no major bleeding events were observed, suggesting that close monitoring of fibrinogen remains important for procedural safety [19–21].

Longitudinal Analysis

Repeated measures ANOVA showed a significant improvement in ABI over time ($F = 16.549$, $p < 0.001$), but no significant interaction between treatment group and time ($F = 0.053$, $p = 0.819$), suggesting that both OSR and CDT led to comparable improvements in ABI. No significant differences were found over time or between groups for creatinine levels.

Arterial Segment Patency Comparison

Within-group analysis showed significant improvement in arterial patency (popliteal, anterior tibial, and posterior tibial arteries) from preoperative to postoperative assessments in both groups. However, between-group comparisons of postoperative patency rates did not reach statistical significance.

Discussion

In this retrospective single-center analysis comparing OSR and CDT in patients with early-stage ALI (Rutherford I–IIa), both modalities demonstrated comparable short and mid-term outcomes. Primary and secondary patency rates at 6 and 12 months did not differ significantly between groups, consistent with prior studies reporting similar limb salvage and survival outcomes in early ischemia [22,23]. This finding supports the role of CDT as a clinically valid alternative to OSR when applied in appropriately selected patients [24].

Our results align with previous randomized trials, meta-analyses, and large-scale registries that have compared CDT and OSR. Landmark trials such as STILE and TOPAS demonstrated similar limb salvage rates between modalities, albeit with higher bleeding risks in the CDT arm [22,25]. Meta-analyses, including those by Enezate et al. and Veenstra et al., confirmed that while OSR achieves immediate reperfusion, CDT avoids surgical trauma and is particularly advantageous in patients with higher operative risk [15,26]. More contemporary evidence from Yang et al. and Kolte et al.

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reported no differences in mortality, amputation, or long-term patency between endovascular and surgical approaches [13,23]. Systematic reviews and guideline recommendations also reinforce that both modalities remain valid, stage-dependent options in modern practice [12,26]. These findings, together with recent data from large national cohorts (e.g., Ozawa et al., Ugwumba et al.), are summarized in **Table 2**, which highlights the overall consistency of outcomes across diverse patient populations and practice settings [1,6].

Table 2. Summary of landmark trials, meta-analyses, large cohort studies, guidelines, and the present study comparing CDT and OSR in ALI.

Study (Year)	Design / Setting	Population (ALI stage)	Interventions	Primary/Key Outcomes	Main Findings	Notes / Limitations
TOPAS (Ouriel et al., 1998, NEJM)	RCT, multicenter	Acute arterial occlusion (mixed)	CDT (urokinase) vs Surgery	Limb salvage, complications	Comparable limb salvage; higher bleeding with thrombolysis	Early protocols; outdated drugs/devices
STILE (Comerota et al., 1996, JVS)	Prospective randomized	Acute limb ischemia	CDT vs Operative therapy	Limb salvage, patency, bleeding	Similar limb salvage; increased bleeding in CDT	Older technology; limited generalizability
Enezate et al., 2017 (Cardiovasc Diagn Ther)	Meta-analysis	ALI (pooled)	Endovascular vs Surgery	Mortality, amputation, recurrent ischemia (1–12 mo)	No significant differences; trend toward lower short-term amputation with endovascular	Heterogeneity across included studies
Veenstra et al., 2020 (EJVES)	Systematic review & meta-analysis	ALI	CDT vs Surgery	Composite clinical endpoints	Comparable endpoints when appropriately selected	Supports individualized treatment selection
Yang et al., 2022 (J Thromb Thrombolysis)	Large cohort (Taiwan)	ALI	CDT vs Surgical thrombectomy	In-hospital mortality, amputation	No difference in mortality or amputation	Observational; potential selection bias
Kolte et al., 2020 (Circ Cardiovasc Interv)	Propensity-matched analysis	ALI	Endovascular vs Surgical	Limb salvage, mortality	Better in-hospital outcomes for endovascular therapy	Residual confounding possible
ESVS Guideline (Björck et al., 2020)	Guideline synthesis	ALI	—	Evidence-based recommendations	Both OSR and CDT valid depending on stage/anatomy	Emphasizes expertise & timely reperfusion
Ozawa et al., 2024 (EJVES, Japan)	Large-scale analysis	Acute lower-limb ischemia	Endovascular vs OSR	Clinical outcomes (national dataset)	Comparable results in modern practice	Administrative dataset; limited detail
Ugwumba et al., 2025 (Ann Vasc Surg)	Systematic review	Modern endovascular vs Surgery	Contemporary CDT vs OSR	Comparative effectiveness	No consistent superiority; selection matters	Highlights need for standardized protocols
Maheta et al., 2024 (Cardiol Rev)	Narrative review	ALI	Spectrum of CDT	Management/complications	Modern CDT feasible with careful monitoring	Bleeding/renal risks remain
This study (2019–2023)	Retrospective cohort (single-center)	Rutherford I–IIa (n=36; OSR 24 vs CDT 12)	OSR vs CDT (alteplase; heparin)	6–12 mo patency, amputation, mortality, LOS	Comparable outcomes; OSR	Small sample, non-randomized,

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		longer LOS; renal function stable	no fibrinogen monitoring

Beyond limb-related endpoints, both treatment strategies significantly improved ABI, underscoring their efficacy in restoring perfusion during early ALI [27]. Importantly, renal function remained stable in our CDT cohort, despite theoretical concerns about contrast-induced nephropathy. In addition, we observed a significant postoperative reduction in fibrinogen levels, particularly among patients undergoing CDT. This decline is consistent with the pharmacological effects of thrombolytic therapy and highlights the importance of peri-procedural coagulation monitoring. While no major bleeding complications occurred in our cohort, systematic fibrinogen assessment may help optimize CDT safety, in line with current guideline recommendations [12,28]. This observation is consistent with contemporary evidence showing that CDT, when accompanied by adequate hydration and careful patient selection, is generally safe with respect to kidney function (9, 10, 14). Moreover, the ABI improvements observed in elderly patients treated with CDT highlight its feasibility in higher-risk populations, in line with reports that endovascular approaches can achieve meaningful hemodynamic gains across diverse age groups [1,4]. Collectively, these findings support CDT not only as an effective but also as a safe therapeutic option when peri-procedural protocols are optimized. Our experience, in line with prior reports, suggests that CDT can be performed with acceptable safety and efficacy, provided peri-procedural protocols are stringently optimized [7].

Length of hospitalization was modestly longer in the OSR cohort, reflecting the invasiveness of surgical intervention and associated perioperative management. Although the absolute difference in median stay was approximately one day in our series, even small reductions may have system-level implications in high-volume centers [29]. Contemporary comparative studies report shorter hospital stays with endovascular/CDT strategies relative to OSR, albeit with the need for close monitoring during thrombolysis [6,13]. From a broader perspective, shorter admissions can improve bed turnover and patient throughput; however, effects on cost are mixed—some datasets show higher index-hospitalization costs with endovascular approaches despite shorter length of stay, underscoring the need for formal cost-effectiveness analyses [9,13].

Limitations

This study is limited by its retrospective, non-randomized design and small sample size (n = 36), which reduce statistical power and introduce the risk of type II error. Treatment allocation was based on physician discretion, introducing potential selection bias, as patients at higher operative risk or with unfavorable anatomy were more likely directed toward CDT. Confidence intervals for outcomes remained wide, underscoring the need for cautious interpretation of apparent equivalence. Furthermore, functional outcomes, and quality-of-life measures were not systematically assessed. Future multicenter prospective studies with standardized CDT protocols, real-time coagulation monitoring, and cost-effectiveness analyses are warranted to optimize treatment algorithms and improve patient-centered care in ALI.

Conclusion

In this retrospective single-center study of patients with early-stage ALI (Rutherford I–IIa), CDT and OSR demonstrated comparable short- and mid-term outcomes in terms of primary and secondary patency, amputation, and mortality. Both modalities significantly improved ABI and arterial patency, with stable renal function observed across groups. Although OSR was associated with a slightly longer hospital stay, CDT required careful peri-procedural monitoring due to thrombolysis-related fibrinogen depletion. These findings support the use of both approaches as valid, stage-dependent treatment strategies in early ALI, with CDT representing a safe and effective minimally invasive alternative when applied in appropriately selected patients. This is further supported by the 10-year single-center series from Konstantinou et al., which demonstrated lower

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mortality and prolonged survival among patients undergoing endovascular therapy compared to those treated with open surgery [8]. Larger prospective studies are warranted to validate these findings and inform standardized treatment protocols.

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