

Thrombotic Risk after Peripheral Revascularization in Chronic Limb-Threatening Ischemia under Different Therapeutic Regimens

Irakli Popkhadze*, Teimuraz Mosiava**, Teona Lazishvili*,
Manana Gobejishvili*, Davit Abramishvili*

* Tbilisi Heart Center, Georgia

** National Center of Surgery, Tbilisi, Georgia

(Presented by Academy Member Zurab Kevanishvili)

Abstract. Chronic limb-threatening ischemia in patients with diabetic angiopathy is associated with severe infrapopliteal arterial involvement and a high risk of thrombotic complications after revascularization. This study evaluated thrombotic and vascular outcomes after infrapopliteal peripheral revascularization under different antithrombotic regimens. A total of 120 patients were divided into four equal groups receiving aspirin plus clopidogrel, aspirin plus rivaroxaban 20 mg once daily, aspirin plus rivaroxaban 2.5 mg twice daily, or triple therapy with aspirin, clopidogrel, and rivaroxaban 2.5 mg twice daily. During the 12-month follow-up, thrombotic events occurred in 15 patients, with the lowest rate observed in the group treated with aspirin plus low-dose rivaroxaban. This regimen was also associated with the highest ankle-brachial index at 12 months, the highest primary patency rate, and the lowest restenosis rate. These findings suggest that aspirin combined with low-dose rivaroxaban may provide the most favorable long-term vascular outcomes after infrapopliteal revascularization in patients with diabetic chronic limb-threatening ischemia.
© 2026 Bull. Georg. Natl. Acad. Sci.

Keywords: chronic limb-threatening ischemia, diabetic angiopathy, peripheral revascularization, thrombosis, rivaroxaban

Introduction

Diabetes mellitus is associated with progressive vascular injury involving both macrovascular and microvascular arterial beds. In patients with chronic limb-threatening ischemia (CLTI), arterial lesions are often distal, multisegmental, and accompanied by impaired collateral circulation, which contributes to poor limb perfusion and complex

revascularization outcomes (Conte et al., 2019; Gerhard-Herman et al., 2017; Norgren et al., 2007). These pathophysiological features substantially increase the risk of postprocedural thrombosis following peripheral arterial revascularization.

The diabetic vascular environment is characterized by endothelial dysfunction, platelet hyperactivity, increased fibrinogen concentration, redu-

ced fibrinolytic activity, and activation of inflammatory pathways. As a result, even technically successful revascularization may be complicated by early thrombotic occlusion, restenosis, or recurrent ischemia (Aboyans et al., 2018; Beckman & Creager, 2016; Hess & Hiatt, 2020). Preservation of long-term vessel patency therefore depends not only on procedural success but also on effective postprocedural antithrombotic management.

Although antiplatelet therapy remains a central component of treatment after peripheral revascularization, the optimal pharmacological strategy after infrapopliteal intervention remains incompletely defined, particularly in patients with diabetic angiopathy and concomitant atherosclerosis. Recent evidence suggests that dual-pathway inhibition with aspirin and low-dose rivaroxaban may reduce vascular and thrombotic events in patients with peripheral arterial disease after revascularization, but its role in diabetic CLTI with infrapopliteal lesions requires further evaluation (Anand et al., 2019; Bonaca et al., 2020; Secemsky et al., 2019).

The present work evaluates thrombotic complications and vascular outcomes under different therapeutic regimens after infrapopliteal peripheral revascularization in patients with diabetic CLTI. Specifically, the study compared antiplatelet therapy, aspirin-based anticoagulant combinations, and triple antithrombotic therapy with respect to thrombosis, reocclusion, restenosis, ankle-brachial index improvement, and primary patency during a 12-month follow-up period.

This study also evaluates the effectiveness and safety of different antithrombotic and anticoagulant treatment strategies after peripheral arterial revascularization in patients with chronic limb-threatening ischemia caused by diabetic angiopathy. The study aims to determine the optimal pharmacological management strategy that ensures reduction of thrombotic and reocclusive complications, improvement of long-term revascularization outcomes, limb preservation, and prolongation of patient survival. Special attention is paid to the comparative

analysis of antiplatelet therapy and dual-pathway treatment (combined antiplatelet and anticoagulant therapy) in diabetic patients under conditions of coexistence and absence of atherosclerosis. This approach will allow formulation of evidence-based recommendations for optimal post-revascularization management.

Study population. The study included 120 patients hospitalized with different clinical forms of chronic arterial insufficiency of the lower extremities. All patients were diagnosed with peripheral arterial disease involving hemodynamically significant lesions of the infrapopliteal segment. The mean age of the study group was 64.8 ± 8.7 years, reflecting the higher prevalence of the disease in older age groups (Table 1).

Table 1. Characteristics of patients

Parameter	Number (n=120)	Percentage (%)
Age (mean $\pm$ standard deviation)	64.8 ± 8.7 years	–
Age distribution		
45–54 years	18	15.0%
55–64 years	36	30.0%
65–74 years	44	36.7%
≥ 75 years	22	18.3%
Sex distribution		
Male	82	68.3%
Female	38	31.7%
Comorbid conditions		
Arterial hypertension	94	78.3%
Type 2 diabetes mellitus	71	59.2%
Dyslipidemia	83	69.2%
Coronary artery disease	49	40.8%
Chronic kidney disease	21	17.5%
Smoking	67	55.8%

Sex distribution was as follows: Males – 68.3%, Females – 31.7%.

The predominance of male patients corresponds to the epidemiological characteristics of peripheral arterial disease, since atherosclerotic vascular lesions are more frequently observed in men. A significant proportion of patients had the following comorbid conditions:

- arterial hypertension,
- diabetes mellitus,

- dyslipidemia,
- coronary artery disease,
- chronic kidney disease.

Patient grouping. A total of 120 patients were divided into four equal study groups according to the antithrombotic treatment regimen, with 30 patients in each group. This stratification was performed to enable comparative evaluation of the effectiveness of different antithrombotic strategies during the post-procedural period after endovascular intervention of the infrapopliteal segment. During patient allocation, not only the prescribed antithrombotic treatment but also the underlying pathological background was taken into account, since it significantly influences both progression of vascular lesions and revascularization outcomes. The main underlying diseases were classified into three principal categories:

- Type 2 diabetes mellitus,
- Combination of diabetes mellitus and atherosclerotic vascular lesions,
- Isolated atherosclerotic vascular disease.

The study demonstrated that the most frequent clinical background was the combined form of diabetes mellitus and atherosclerosis, accounting for nearly half of the study population. This distribution is clinically expected, since infrapopliteal arterial lesions occur particularly frequently in patients with multiple vascular risk factors. According to antithrombotic regimens, the study groups were formed as follows (Table 2):

- Group I: dual antiplatelet therapy – aspirin + clopidogrel.
- Group II: aspirin + rivaroxaban 20 mg once daily.

- Group III: aspirin + low-dose rivaroxaban (2.5 mg twice daily).
- Group IV: triple therapy – aspirin + clopidogrel + low-dose rivaroxaban.

Thrombotic events. Evaluation of thrombotic events during the post-revascularization period represented one of the principal directions of the study, since the major threats to long-term vascular patency become evident precisely during the post-interventional phase. In patients with diabetic angiopathy, the risk of thrombotic complications is significantly increased due to chronic hyperglycemia, endothelial dysfunction, platelet hyperactivity, activation of the coagulation system, and impaired microvascular hemodynamics. During clinical follow-up, the most frequently observed thrombotic event was partial or complete reocclusion of the revascularized arterial segment. This finding was especially frequent after infrapopliteal interventions, where small arterial diameter, severe calcification, and poor distal runoff created additional difficulties for maintaining adequate blood flow. The tendency toward reocclusion was particularly pronounced in cases where complete obliteration of the posterior tibial artery was initially present and recanalization was achieved in only a single arterial vessel. In such cases, distal perfusion depended entirely on the functional patency of one arterial channel. The early phase of thrombotic events was predominantly observed during the first weeks after intervention, when vascular wall trauma, endothelial injury, and local coagulation activation are most pronounced.

Table 2. Distribution of patients according to antithrombotic regimen and underlying disease (n = 120)

Antithrombotic Regimen	Diabetes Mellitus	Atherosclerosis + Diabetes	Atherosclerosis	Total
Aspirin + Clopidogrel	10	14	6	30
Aspirin + Rivaroxaban 20mg once daily	9	15	6	30
Aspirin + Rivaroxaban 2.5 mg twice daily	8	14	8	30
Aspirin + Clopidogrel + Rivaroxaban 2.5 mg twice daily	9	16	5	30
Total	36	59	25	120

The first clinical signs of reocclusion included:

- recurrence or intensification of rest pain,
- decrease in foot temperature,
- progression of ulcerative lesions,
- reduction of flow velocity on duplex ultrasonography.

Duplex monitoring primarily demonstrated:

- reduction of peak systolic velocity,
- turbulent flow,
- conversion of biphasic flow into monophasic flow.

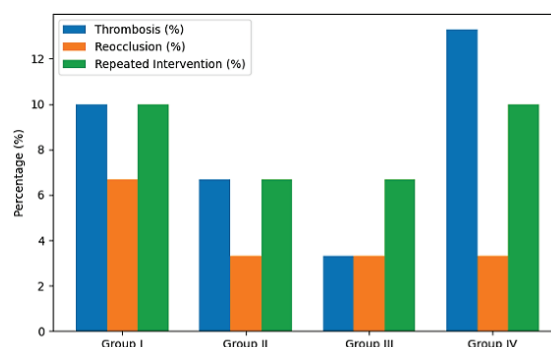
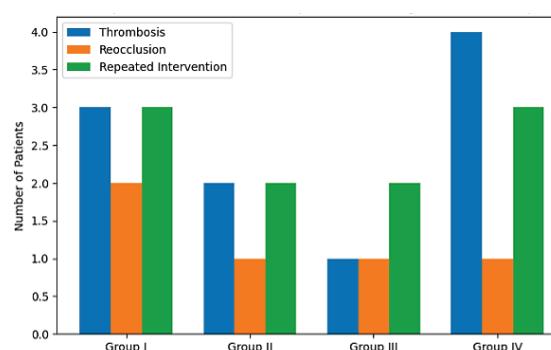
Thrombotic outcomes during a 12-month follow-up. During the 12-month follow-up period, thrombotic events were identified in 15 patients (12.5%). Among these, the most frequent complication was target vessel thrombosis, observed in 10 patients (8.3%), while acute reocclusion developed in 5 patients (4.2%). According to treatment groups, thrombotic events were distributed as follows (Table 3, Diagram 1,2):

- Group I – 5 cases.
- Group II – 3 cases.
- Group III – 2 cases.
- Group IV – 5 cases.

The lowest thrombotic frequency was observed in Groups II and III, where combined antithrombotic regimens based on aspirin and rivaroxaban were used. These findings were fully consistent with the superior hemodynamic results obtained in the same groups. Repeated endovascular intervention was required in 10 patients (8.3%). Minor amputation was performed in 8 patients (6.7%), while major amputation was necessary in 4 patients (3.3%).

Table 3. Thrombotic events by treatment group

Group	Thrombosis	Reocclusion	Repeated Intervention
Group I	3	2	3
Group II	2	1	2
Group III	1	1	2
Group IV	4	1	3

**Fig. 1.** Comparison of thrombotic complications across treatment groups.**Fig. 2.** Percentage of major vascular complications across treatment groups.

Comparison between treatment groups. A comparative analysis of different antithrombotic treatment regimens was performed to evaluate hemodynamic effectiveness, maintenance of primary patency, restenosis frequency, and development of thrombotic events (Table 4).

During the 12-month follow-up period, the highest ankle-brachial index (ABI) values were observed in Groups II and III, where combined antithrombotic regimens were used, whereas comparatively lower values were recorded in Group I.

The primary patency rate was also highest in Group III (86.7%), while in Group I it reached 76.7%.

The lowest restenosis frequency was identified in Group III, whereas the highest frequency was observed in Groups I and IV.

Analysis of thrombotic events also demonstrated that Group III had the lowest complication burden.

Table 4. Comparative hemodynamic and clinical outcomes across treatment groups

Parameter	I Group	II Group	III Group	IV Group	p-value
ABI at 12 months	0.71 ± 0.13	0.78 ± 0.12	0.80 ± 0.13	0.74 ± 0.13	0.032
Primary patency (%)	76.7	83.3	86.7	80.0	0.041
Restenosis (%)	16.7	13.3	10.0	16.7	0.048
Thrombotic events (%)	16.7	13.3	6.7	13.3	0.037

The difference between Group III and Group I in terms of ABI improvement and maintenance of primary patency was statistically significant ($p < 0.05$).

Comparative analysis demonstrated that the combined antithrombotic regimen provided superior hemodynamic and clinical outcomes, reflected by: higher ABI values, lower restenosis frequency, lower incidence of thrombotic events.

These findings suggest that intensified combined therapy after infrapopliteal endovascular intervention may be considered a more effective strategy for improving long-term outcomes.

Thus, the performed comparative analysis indicates that in diabetic chronic limb-threatening ischemia (CLTI), the frequency of thrombotic events is directly associated with: baseline hemodynamic severity, extent of infrapopliteal arterial lesions, degree of calcification, subsequent antithrombotic management.

The obtained data confirm that clinical prognosis should be assessed using an integrated model rather than isolated individual parameters.

Statistical evaluation of thrombotic events. During the 12-month follow-up period, thrombotic events were recorded in 15 patients (12.5%) (Table 5).

The distribution by treatment groups was as follows: Group I – 16.7%; Group II – 13.3%; Group III – 6.7%; Group IV – 13.3%.

The difference between treatment groups was statistically significant ($p = 0.037$).

The lowest thrombotic frequency was observed in Group III, confirming the superior protective effect of this antithrombotic regimen.

Table 5. Statistical analysis

Group	Thrombotic events (%)	p-value
I	16.7	
II	13.3	
III	6.7	0.037
IV	13.3	

Conclusion

The present study demonstrated that postprocedural thrombotic complications remain one of the principal determinants of long-term outcomes after infrapopliteal revascularization in patients with diabetic chronic limb-threatening ischemia.

Comparative analysis of four antithrombotic regimens showed that Group III (aspirin plus low-dose rivaroxaban 2.5 mg twice daily) achieved the most favorable clinical and hemodynamic results.

This regimen was associated with the lowest thrombotic event frequency (6.7%), the highest ankle-brachial index (ABI) at 12 months (0.80 ± 0.13), the highest ankle-brachial index (ABI) at 12 months (0.80 ± 0.13), the highest primary patency (86.7%), and the lowest restenosis rate (10.0%).

The superiority of Group III became especially evident in patients with coexistence of diabetes mellitus and atherosclerosis, suggesting that dual pathway inhibition provides greater benefit under combined thrombotic burden.

These findings indicate that aspirin plus low-dose rivaroxaban may be considered the most effective postprocedural antithrombotic strategy for improving long-term vascular outcomes after infrapopliteal intervention in diabetic CLTI.

ექსპერიმენტული მედიცინა

თრომბოზული რისკი პერიფერიული რევასკულარიზაციის შემდეგ კიდურის ქრონიკული, სიცოცხლისთვის საშიში იშემიის დროს სხვადასხვა თერაპიული რეჟიმის პირობებში

ირაკლი ფოფხაძე*, თეიმურაზ მოსიავა**, თეონა ლაზიშვილი*,
მანანა გობეჯიშვილი*, დავით აბრამიშვილი*

* თბილისის გულის ცენტრი, თბილისი, საქართველო

** ქირურგიის ეროვნული ცენტრი, თბილისი, საქართველო

(წარმოდგენილია აკადემიის წევრის ზურაბ ქევანიშვილის მიერ)

კიდურის ქრონიკული, სიცოცხლისთვის საშიში იშემია დიაბეტური ანგიოპათიის მქონე პაციენტებში ასოცირებულია ინფრაპოპლიტური არტერიების მძიმე დაზიანებასა და რევასკულარიზაციის შემდგომ თრომბოზული გართულებების მაღალ რისკთან. კვლევის მიზანი იყო ინფრაპოპლიტური პერიფერიული რევასკულარიზაციის შემდეგ თრომბოზული და სისხლძარღვოვანი გამოსავლების შეფასება სხვადასხვა ანტითრომბოზული თერაპიული რეჟიმის პირობებში. კვლევაში ჩართული იყო 120 პაციენტი, რომლებიც დაიყო ოთხ თანაბარ ჯგუფად, რომლებიც ღებულობდნენ ასპირინს და კლოპიდოგრელს; ასპირინი და რივაროქსაბანი 20 მგ დღეში ერთხელ; ასპირინი და დაბალდოზიანი რივაროქსაბანი 2,5 მგ დღეში ორჯერ და სამმაგი თერაპია ასპირინით, კლოპიდოგრელითა და დაბალდოზიანი რივაროქსაბანით. 12-თვიანი დაკვირვების პერიოდში თრომბოზული მოვლენები გამოვლინდა 15 პაციენტში, ყველაზე დაბალი სიხშირით ასპირინისა და დაბალდოზიანი რივაროქსაბანის ჯგუფში. აღნიშნული რეჟიმი ასევე ასოცირებული იყო 12 თვეზე კოჭ-მხრის ინდექსის ყველაზე მაღალ მაჩვენებელთან, პირველადი გამავლობის საუკეთესო მაჩვენებელსა და რესტენოზის ყველაზე დაბალ სიხშირესთან. მიღებული შედეგები მიუთითებს, რომ ასპირინისა და დაბალდოზიანი რივაროქსაბანის კომბინაციამ შესაძლოა, უზრუნველყოს ყველაზე ხელსაყრელი გრძელვადიანი სისხლძარღვოვანი გამოსავლები ინფრაპოპლიტური რევასკულარიზაციის შემდეგ დიაბეტური ანგიოპათიის ფონზე განვითარებული კიდურის ქრონიკული იშემიის მქონე პაციენტებში.

REFERENCES

- Aboyans, V, Ricco, JB, Bartelink, MEL, Björck, M, Brodmann, M, Cohnert, T, Collet, JP, Czerny, M, De Carlo, M, Debus, S, Espinola-Klein, C, Kahan, T, Kownator, S, Mazzolai, L, Naylor, AR, Roffi, M, Röther, J, Sprynger, M, Tendera, M, Tepe, G, ... Desormais, I. (2018). ESC Guidelines on the diagnosis and treatment of peripheral arterial diseases. *Eur Heart J.*, 39(9), 763-816.
- Anand, SS, Bosch, J, Eikelboom, JW, Connolly, SJ, Diaz, R, Widimsky, P, Aboyans, V, Alings, M, Kakkar, AK, Keltai, K, Maggioni, AP, Lewis, BS, Störk, S, Zhu, J, Liang, Y, Maggiono, A, Lopez-Jaramillo, P, O'Donnell, M, Commerford, P, Vinereanu, D, ... Yusuf, S. (2019). Rivaroxaban with or without aspirin in patients with stable peripheral or carotid artery disease. *J Am Coll Cardiol.*, 73(3), 327-340.
- Beckman, JA, Creager, MA. (2016). Vascular complications of diabetes. *Circ Res.*, 118(11), 1771-1785.
- Bonaca, MP, Bauersachs, RM, Anand, SS, Debus, ES, Nehler, MR, Patel, MR, Fanelli, F, Capell, WH, Diao, L, Jaeger, N, Hess, CN, Pap, AF, Kittelson, JM, Gudzi, I, Mátyás, L, Krievins, DK, Diaz, R, Brodmann, M, Muchlhofer, E, Haskell, LP, ... Hiatt WR. (2020). Rivaroxaban in peripheral artery disease after revascularization. *N Engl J Med.*, 382(21), 1994-2004.
- Conte, MS, Bradbury, AW, Kolh, P, White, JV, Dick, F, Fitridge, R, Mills, JL, Ricco, JB, Suresh, KR, Murad, MH, Aboyans, V, Aksoy, M, Alexandrescu, VA, Armstrong, D, Azuma, N, Belch, J, Bergoeing, M, Björck, M, Chakfé, N, Cheng, S, ... Wang, S. (2019). Global vascular guidelines on the management of chronic limb-threatening ischemia. *J Vasc Surg.*, 69(6S), 3S-125S.
- Dormandy, JA, Rutherford, RB. (2000). TASC Working Group. Management of peripheral arterial disease (PAD). TransAtlantic Inter-Society Consensus (TASC). *J Vasc Surg.*, 31(1, Pt 2), S1-S296.
- Gerhard-Herman, MD, Gornik, HL, Barrett, C, Barshes, NR, Corriere, MA, Drachman, DE, Fleisher, LA, Fowkes, FGR, Hamburg, NM, Kinlay, S, Lookstein, R, Misra, S, Mureebe, L, Olin, JW, Patel, RAV, Regensteiner, JG, Schanzer, A, Shishehbor, MH, Stewart, KJ, Treat-Jacobson, D, Walsh ME. (2017). 2016 AHA/ACC guideline on management of patients with lower extremity peripheral artery disease. *Circulation*, 135(12), e726-e779.
- Hess, CN, Hiatt, WR. (2020). Antithrombotic therapy for peripheral artery disease in 2020. *JAMA*, 324(9), 853-855.
- Hiatt, WR, Fowkes, FGR, Heizer, G, Berger, JS, Baumgartner, I, Held, P, Katona, BG, Mahaffey, KW, Norgren, L, Jones, WS, Blomster, JI, Millegård, M, Reist, C, Patel, MR. (2017). Ticagrelor versus clopidogrel in symptomatic peripheral artery disease. *N Engl J Med.*, 376(1), 32-40.
- Norgren, L, Hiatt, WR, Dormandy, JA, Nehler, MR, Harris, KA, Fowkes, FG. (2007). TASC II Working Group. Inter-society consensus for the management of peripheral arterial disease (TASC II). *J Vasc Surg.*, 45(Suppl S), S5-S67.
- Patel, MR, Mahaffey, KW, Garg, J, Pan, G, Singer, DE, Hacke, W, Breithardt, G, Halperin, JL, Hankey, GJ, Piccini, JP, Becker, RC, Nessel, CC, Paolini, JF, Berkowitz, SD, Fox, KAA, Califf, RM. (2011). ROCKET AF Steering Committee; ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med.*, 365, 883-891.
- Secemsky, EA, Kundi, H, Weinberg, I, Jaff, MR, Krawisz, A, Parikh, SA, Beckman, JA, Yeh RW. (2019). Association of long-term antithrombotic therapy with outcomes after peripheral artery revascularization. *J Am Coll Cardiol.*, 73(25), 3271-3280.

Received May, 2026