

Case Report

A durable limb salvage and functional recovery after prolonged prostaglandin E1 therapy following femoro-popliteal bypass graft thrombosis: a one-year follow-up case report

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ABSTRACT

Infrainguinal bypass graft thrombosis can cause recurrent limb ischemia, tissue loss, and major amputation. A 65-year-old man with diabetes, hypertension, and previous cigarette smoking developed complete thrombosis of a Dacron femoropopliteal bypass graft six months after surgery. Pharmacogenetic testing identified a CYP2C19 intermediate-metabolizer phenotype associated with reduced clopidogrel responsiveness. Clopidogrel was discontinued, while aspirin and rivaroxaban were continued, and intravenous prostaglandin E1 (PGE1; alprostadil) therapy was initiated. Following three previously reported cycles, he completed six total cycles, each administered over three consecutive days at approximately four-week intervals. At one-year follow-up after treatment completion, he remained free of ischemic pain, ulceration, gangrene, and tissue loss, avoiding major amputation and repeat revascularization. He could walk more than 200 m and had Rutherford category 0 status. Follow-up computed tomography angiography demonstrated collateral vessels from the deep femoral circulation. This case highlights sustained limb preservation following prolonged PGE1 therapy despite graft thrombosis.

Keywords: Prostaglandin E1, Femoropopliteal bypass, Graft thrombosis, Chronic limb-threatening ischemia, Collateral circulation, Limb salvage

INTRODUCTION

Peripheral arterial disease is a major cause of lower-extremity disability and chronic limb-threatening ischemia. Surgical bypass can improve limb perfusion in appropriately selected patients, but graft thrombosis remains an important complication that may cause recurrent ischemia, tissue loss, repeat intervention, or major amputation.^{1,2}

Management of thrombosed infrainguinal bypass grafts depends on ischemia severity, graft characteristics, thrombosis mechanism, distal runoff, and available

facilities. Thrombectomy, thrombolysis, graft revision, replacement, or endovascular intervention may be considered; however, repeat revascularization is not always feasible or undertaken. In such circumstances, maintaining tissue perfusion and preventing ischemic progression are important therapeutic goals.^{1,3,4}

Prostaglandin E1 (PGE1; alprostadil) has vasodilatory, antiplatelet, endothelial-protective, and rheological effects that may improve peripheral microcirculation. PGE1 therapy has been associated with symptomatic and tissue-healing benefits in selected patients with advanced peripheral arterial disease and limited revascularization options, although durable limb-salvage benefit remains

uncertain and it should not replace feasible revascularization.^{5,6,7}

Antithrombotic therapy remains an important component of secondary prevention following lower-extremity revascularization, with treatment strategies influencing graft patency and cardiovascular outcomes.^{8,9}

We previously reported a 65 year old man with diabetes, hypertension, and smoking history who developed Dacron femoropopliteal bypass thrombosis with CYP2C19 intermediate-metabolizer status and reduced clopidogrel responsiveness. The initial report described three cycles of PGE1 therapy and early clinical improvement.¹⁰ The present report focuses on the subsequent one-year outcome after completion of six PGE1 cycles, documenting sustained symptom resolution, functional recovery, limb preservation without tissue loss or amputation, and collateral vessels on follow-up computed tomography angiography.

CASE REPORT

A 65-year-old Bangladeshi man with type 2 diabetes mellitus, hypertension, and a history of cigarette smoking had presented with progressive ischemic symptoms involving the right lower limb. Before his initial surgical intervention, he had experienced intermittent claudication and rest pain for approximately five months. On examination, the right lower limb was cold and clammy, with absent below-knee arterial pulses. Brittle nails, hair loss, and dry skin were present below the knee. Sensory function remained preserved. The ankle-brachial pressure index was 0.65.

Duplex ultrasonography demonstrated monophasic arterial flow, while computed tomography angiography showed occlusive disease involving the distal superficial femoral artery. The clinical presentation was classified as Rutherford stage 4 and Fontaine stage III chronic limb ischemia. Because optimal medical treatment did not adequately control his symptoms and endovascular facilities were unavailable at the treating institution, he underwent a mid-superficial femoral artery-to-infrageniculate popliteal artery bypass using a Dacron graft. His immediate postoperative recovery was uncomplicated, with substantial improvement in ischemic symptoms.

Following bypass surgery, the patient received aspirin, clopidogrel, and rivaroxaban. Six months after surgery, rivaroxaban was discontinued while aspirin and clopidogrel were continued. Approximately one week after discontinuation of rivaroxaban, the patient developed recurrent ischemic symptoms involving the operated limb. Duplex ultrasonography demonstrated absence of flow through the bypass graft, and computed tomography angiography confirmed complete graft thrombosis.

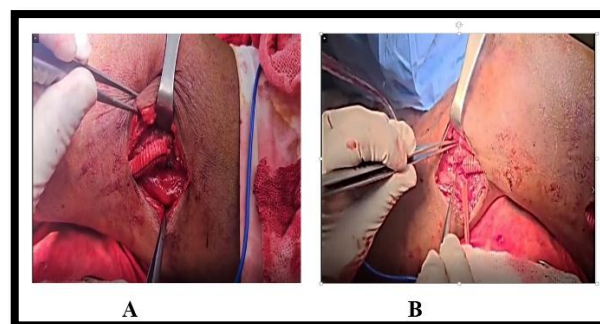


**Figure 1: Showing per-operative view of the patient.
A: Proximal anastomosis; B: Distal anastomosis**

Pharmacogenetic testing using polymerase chain reaction identified a CYP2C19 variant corresponding to an intermediate-metabolizer phenotype, consistent with reduced responsiveness to clopidogrel. Aspirin resistance was not identified. Clopidogrel was therefore discontinued, and aspirin and rivaroxaban were continued. The original presentation, bypass procedure, graft thrombosis, pharmacogenetic investigation, and initial response to PGE1 have been reported previously. The present report concerns the subsequent treatment course and long-term follow-up of the same patient.

PGE1 (Alprostadil) therapy was initiated as an adjunctive limb-preservation strategy following graft thrombosis. The initial report documented symptomatic improvement after three cycles. Treatment was subsequently continued, and the patient completed a total of six PGE1 cycles. Each cycle consisted of three consecutive days of intravenous PGE1 infusion, with treatment cycles administered at approximately four-week intervals. Therapy was delivered under clinical and hemodynamic monitoring, and no clinically significant adverse effects were documented.

During the treatment course, the patient's ischemic symptoms progressively improved. Ischemic pain gradually resolved, clinical limb perfusion improved, and walking capacity increased. Importantly, there was no development of ulceration, gangrene, or clinically evident tissue loss. No repeat bypass operation, thrombectomy, thrombolytic procedure, endovascular intervention, or other surgical revascularization was performed during this period.

The patient was followed for one year after completion of the six-cycle PGE1 regimen. At the one-year assessment, he reported complete resolution of his previous ischemic pain. He was able to walk more than 200 m and had resumed routine daily activities. There was no recurrent rest pain, ulceration, gangrene, or clinically apparent tissue loss. The patient had not undergone major amputation and had not required repeat surgical or endovascular revascularization during the follow-up period. Clinical assessment demonstrated Rutherford category 0 status, indicating the absence of symptomatic

limb ischemia at the time of evaluation. Follow-up computed tomography angiography demonstrated development of collateral vessels arising from the deep

femoral arterial circulation, providing an alternative arterial pathway toward the distal limb.

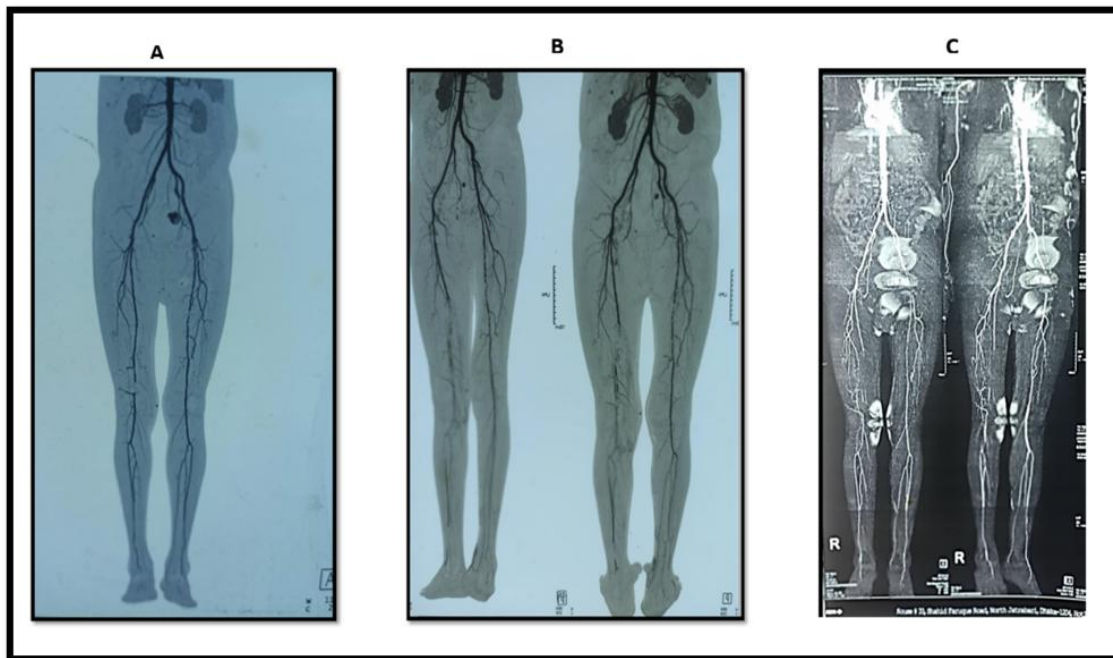


Figure 2: Showing angiographic findings of the patient. A: before surgery; B: after graft thrombosis; C: after prostaglandin therapy with development of collateral vessels

The temporal association between treatment, clinical improvement, and collateral development was notable. However, because this was a single-patient observation

without serial quantitative assessment of collateral flow, a direct causal relationship between PGE1 treatment and collateral formation could not be established.

Table 1: Clinical timeline of the case report.

Clinical stage	Event
Initial presentation	Chronic right lower-limb ischemia with intermittent claudication and rest pain
Initial assessment	ABI 0.65; Rutherford stage 4; Fontaine stage III
Revascularization	Mid-SFA-to-infrageniculate popliteal Dacron bypass
Postoperative period	Marked clinical improvement
First 6 months	Aspirin + clopidogrel + rivaroxaban
Month 6	Rivaroxaban discontinued
Approximately 1 week later	Recurrent ischemia and complete bypass graft thrombosis
Subsequent investigation	CYP2C19 intermediate-metabolizer phenotype identified
Medication modification	Clopidogrel discontinued; aspirin + rivaroxaban continued
Initial PGE1 therapy	Three cycles reported in the previous publication
Subsequent treatment	Additional PGE1 cycles administered
Total treatment	Six PGE1 cycles completed
Post-treatment	Progressive symptomatic and functional improvement
One-year follow-up	Pain-free; Rutherford category 0; walking >200 m
One-year follow-up	No wound, tissue loss, amputation, or repeat revascularization
Follow-up CTA	Development of collateral vessels from the deep femoral circulation

DISCUSSION

The present case provides a longitudinal observation of sustained limb preservation and functional recovery

following femoropopliteal bypass graft thrombosis and prolonged PGE1 therapy. The principal contribution is the one-year clinical course after completion of six

treatment cycles rather than the previously reported CYP2C19 finding or graft thrombosis.¹⁰

The initial graft thrombosis occurred after discontinuation of rivaroxaban despite continued aspirin and clopidogrel. CYP2C19 intermediate-metabolizer status may have contributed to reduced clopidogrel responsiveness; however, graft failure was likely multifactorial, with diabetes, hypertension, smoking, graft-related factors, distal runoff, and other thrombotic mechanisms potentially contributing.

Following thrombosis, aspirin and rivaroxaban were continued and PGE1 was administered as an adjunctive limb-preservation therapy. The initial report documented improvement after three cycles, while the present follow-up demonstrates completion of six cycles and persistence of benefit for one year.¹⁰ The patient remained free of ischemic pain, ulceration, gangrene, tissue loss, and major amputation, achieved Rutherford category 0 status, and could walk more than 200 m without repeat revascularization.

Follow-up CTA demonstrated collateral vessels arising from the deep femoral circulation. Collateralization may help maintain distal tissue perfusion despite occlusion of the primary arterial pathway.¹¹ PGE1 may potentially improve peripheral perfusion through vasodilation, antiplatelet and endothelial effects, and effects on microvascular flow and tissue perfusion.¹² However, collateral development is multifactorial and cannot be attributed to PGE1 in this individual case. Evidence for PGE1 in severe limb ischemia suggests potential symptomatic and tissue-healing benefits, but consistent reduction in major amputation has not been established.¹³

The favorable outcome may also reflect continued aspirin and rivaroxaban therapy, risk-factor modification, smoking cessation, glycemic control, and surveillance.^{14,15} Therefore, the observed recovery should be considered multifactorial rather than evidence of an isolated PGE1 effect.

This case is particularly relevant where repeat surgical or endovascular revascularization is unavailable or not undertaken. Nevertheless, PGE1 should not be considered a substitute for revascularization, which remains the preferred treatment when feasible. The case instead suggests that prolonged PGE1 may warrant further investigation as an adjunctive limb-preservation strategy in carefully selected patients with limited revascularization options.

CONCLUSION

Six cycles of intravenous PGE1 were followed by durable limb preservation, complete symptom resolution, and functional recovery one year after femoropopliteal bypass graft thrombosis. Although collateral development cannot be causally attributed to PGE1, this case highlights its

potential as an adjunctive limb-preservation strategy in carefully selected patients with severe ischemia when repeat revascularization is not undertaken.

Patient perspective

At one-year follow-up, the patient reported complete resolution of his previous ischemic pain and substantial improvement in his walking ability and routine daily activities. He expressed satisfaction with preservation of his limb and avoidance of amputation and further vascular intervention.

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Ethical approval: Not required

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