Peripheral Artery Disease

Management of Patients After Endovascular Interventions for Peripheral Artery Disease

Piotr Sobieszczyk, MD; Andrew Eisenhauer, MD

Endovascular therapy to relieve intermittent claudication or critical limb ischemia in patients with lower-extremity peripheral artery disease is now firmly established as an alternative to surgical revascularization. The advent of novel technologies allows percutaneous interventions of increasingly complex arterial disease previously reserved for surgical interventions. Although the durability of aortoiliac interventions rivals that of surgical bypass, restenosis after femoropopliteal interventions remains the Achilles’ heel of endovascular therapies.

Despite the growth of endovascular procedures, the optimal postprocedural care is not well established. Moreover, it is not clear how surveillance strategies influence health resource use and whether they can prolong the durability of vascular interventions and affect the patient’s cardiovascular health. The following recommendations are therefore extrapolated from clinical experience gained in medical and surgical management of patients with peripheral artery disease and patients undergoing percutaneous coronary interventions. In the absence of data derived from randomized, controlled trials, these recommendations necessarily reflect an interpretation of “best clinical practice” of an understudied clinical area. In this article, we attempt to outline a clinically sound strategy for long-term postprocedural care.

Preventing New and Recurrent Disease

Aggressive cardiovascular risk factor reduction is a key component of postprocedural care to prevent cardiovascular events in patients with peripheral artery disease such as myocardial infarction or stroke. Regular exercise should be an integral part of postprocedural care both because of its well-established clinical benefit and because it provides a gauge for detecting the progression of obstructive arterial disease. Formal exercise therapy is a potent treatment for claudication and may offer additional benefits after femoral artery revascularization. The details and justification for risk factor modification and regular exercise are discussed in published national guidelines.

Postprocedural care and surveillance also aim to optimize the durability of endovascular procedures by combining appropriate pharmacotherapy, periodic assessment of vessel patency, and targeted reintervention. Postprocedural care may vary, depending on which arterial segment was treated and what symptoms prompted the index intervention. Recurrent symptoms may be masked in patients with multilevel interventions and those with vigorous collaterals and may not be apparent until the stent or angioplasty segment is occluded.

In clinical practice, the most frequently used pharmacotherapeutic strategy involves a 4-week course of dual antiplatelet therapy and subsequent indefinite therapy with aspirin. Clinical assessment is usually performed more frequently soon after an intervention, when restenosis is more common, for example, 1 month after the procedure, 6 and 12 months later, and annually thereafter. Adjunctive vascular studies at each visit can assess procedural success and define vessel patency (Table 1). The standard surveillance tools augmenting physical examination and symptom review are ankle-brachial index (ABI) measurement, segmental Doppler pressure (SDP) testing, exercise ABI, and Duplex arterial ultrasound. The exercise ABI may be a more sensitive method of identifying restenosis after aortoiliac interventions, particularly if claudication returns with relatively normal resting ABIs.

The fundamental rationale for close postprocedural surveillance rests on the premise that detection of threatened patency can be effectively and durably treated by another therapeutic intervention. Although widely practiced, the utility and cost-effectiveness of such surveillance programs have not been tested in randomized, clinical trials.

Wound prevention education and, when appropriate, wound care are equally essential to long-term clinical success after peripheral arterial procedures, especially with critical limb ischemia. A simple discussion of appropriate footwear and avoidance of trauma can save limbs in a patient with diabetes mellitus and peripheral artery disease. Advanced wound care can involve coordination with podiatrists, wound care nurses, and surgeons to minimize tissue loss and to maximize functional integrity.

Pharmacotherapy After Endovascular Procedures

Postprocedural pharmacotherapy is designed to reduce the incidence of cardiovascular events, to prevent acute vessel thrombosis, and to maintain long-term vessel patency. Cerebrovascular and cardiac events are prime causes of morbidity and mortality of patients with peripheral artery disease, whether they are treated by medical or endovascular means. Endovascular therapies may affect functional capacity and quality of life, but lipid-lowering therapy, control of

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hypertension, and the use of antiplatelet agents reduce cardiovascular mortality and morbidity among patients with peripheral artery disease.\textsuperscript{5,6,7} Contemporary antiplatelet therapy after peripheral interventions is thought to prevent stent thrombosis and occlusion but is poorly studied, and this practice is extrapolated from trials testing antiplatelet therapy after coronary interventions in the bare metal stent era.

### Antithrombotic and Antiplatelet Therapies

The initial antithrombotic therapy used after pioneering transluminal catheter dilation of the superficial femoral artery (SFA) consisted of several days of injectable unfractionated heparin but evolved quickly to include antiplatelet therapy with sulfinpyrazone.\textsuperscript{8,9} With the advent of balloon angioplasty, the postprocedural care used a combination of short-term antiplatelet therapy and long-term warfarin therapy. The importance of antithrombotic agents in long-term vessel patency after balloon dilation of the femoral and iliac arteries was quickly and firmly established, with several series showing a 50% increase in midterm patency.\textsuperscript{10,11} Aspirin monotherapy and dual antiplatelet therapy replaced anticoagulants as the standard postprocedural treatment after percutaneous interventions of peripheral arteries around the time this regimen was adopted for coronary stents.\textsuperscript{12,13}

There are no modern randomized trials defining optimal antiplatelet therapy after peripheral endovascular interventions. In contemporary clinical practice, indefinite aspirin therapy is deemed sufficient after peripheral balloon angioplasty. Similarly, aspirin monotherapy is probably sufficient after atherectomy procedures. Recent trials of novel drug-eluting balloons required long-term aspirin and clopidogrel therapy, but “real-world” European registries used a simpler regimen of indefinite aspirin and a 3-month course of clopidogrel.\textsuperscript{14,15} Patients with more complex anatomy are often treated with prolonged dual antiplatelet therapy, but again, there is no evidence to determine the risks and benefits of this approach.

The advent of balloon-expandable and self-expanding stents introduced the potential for rapid artery occlusion resulting from stent thrombosis. In contemporary clinical trials of femoropopliteal stenting, aspirin is continued for a minimum of 6 months or indefinitely and clopidogrel is continued for 1 to 3 months.\textsuperscript{16-18} Most practitioners favor indefinite aspirin therapy and a minimum 4-week course of a second thienopyridine antiplatelet agent after stent placement in the upper or lower extremities. This common approach is extrapolated from randomized, controlled trials that defined the optimal antiplatelet therapy for bare metal coronary stents.

The early and ultimately unsuccessful trials of self-expanding, drug-eluting stents mandated dual antiplatelet therapy for only 3 to 4 months.\textsuperscript{19} More recent experience with paclitaxel-eluting femoropopliteal stents suggests that 2 months of dual antiplatelet therapy followed by indefinite aspirin course is associated with low rates of acute stent thrombosis.\textsuperscript{20} Because of the similarity in vessel diameter, coronary drug-eluting stents placed in the tibial vessels could have a similar thrombosis risk. However, it is not certain whether a year-long dual antiplatelet therapy is necessary. In patients who have a low bleeding risk, it may be reasonable to mirror the year-long course of dual antiplatelet therapy used after coronary interventions with drug-eluting stents. Preliminary data suggest that for the new-generation drug-eluting coronary stents, this time course may be shortened.

The duration and intensity of antiplatelet therapy must be balanced against the individual bleeding risk. For example, more intensive or prolonged therapy may be justified in a younger patient with complex disease compared with older patients who are at higher risk of bleeding. The incremental safety and effectiveness of the newer oral antiplatelet agents such as ticagrelor and prasugrel compared with clopidogrel are uncertain after noncoronary interventions.

### Antirestenotic Therapies

The optimal postprocedural medical regimen would include an agent that retards neointimal proliferation at the site of intervention. Unfortunately, such an antirestenotic agent is elusive.

The lipid-lowering agent probucol can reduce restenosis after coronary and femoropopliteal balloon angioplasty.\textsuperscript{21-23} However, prolongation of the QT interval with the risk of cardiac arrhythmia precludes its clinical use.

Oral administration of rapamycin can reduce in-stent restenosis after coronary intervention.\textsuperscript{24-27} However, its use has not been studied as adjunctive therapy after lower-extremity interventions, and concerns about long-term immunosuppression limited further investigations of this agent.

More recently, there has been increasing interest in cilostazol as an oral agent for reducing in-stent restenosis after peripheral interventions. The largest experience comes from Japan, and it is not clear whether the effects of cilostazol can be generalized to other populations. In a small randomized study of 127 patients treated with femoropopliteal stents, Iida et al\textsuperscript{28} showed that treatment with cilostazol resulted in a 3-year primary patency rate of 73% compared with 51% in patients receiving placebo (P=0.013). In another randomized study, Soga et al\textsuperscript{29} showed the efficacy of cilostazol in reducing restenosis after balloon angioplasty or stenting in femoropopliteal interventions. After 2 years, freedom from revascularization was 85% in the cilostazol arm compared

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<th>Table 1. Definitions of Successful Endovascular Intervention Used in Research Studies Versus Suggested Criteria for Clinical Care</th>
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<td><strong>Research Definitions of Success of Endovascular Interventions</strong></td>
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<tr>
<td>Acute hemodynamic success</td>
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ABI indicates ankle-brachial index; and PSVR, peak systolic velocity ratio comparing the stenosis with a proximal reference segment.
with 62% in the placebo arm \( (P=0.038) \). Long-term data from prospective registries also suggest some beneficial effect of cilostazol. In a cohort of patients with anatomically less complex TransAtlantic Inter-Societal Consensus (TASC) II A– and B–type SFA lesions, the use of stenting and cilostazol was associated with a 4-year primary patency rate of 80%.30 Soga et al31 showed that treatment with cilostazol predicts freedom from restenosis in a cohort of patients undergoing SFA stenting with 5-year secondary patency rates of 86%. More recently, a propensity-matched analysis of >500 patients showed that 5-year restenosis rates after femoropopliteal stenting are 31% in patients treated with cilostazol and 43% in those not receiving cilostazol. This effect was more pronounced in patients at high risk of in-stent restenosis: those with anatomically complex TASC II C and D lesions, patients with poor infrapopliteal runoff, and those requiring chronic hemodialysis.32

Although therapy with 3 antiplatelet agents poses concerns about bleeding complications, the later addition of cilostazol to aspirin may be reasonable in selected patients at high risk of in-stent restenosis. Although the effect of cilostazol on restenosis is modest, the clinical benefit of cilostazol in preventing recurrent symptoms requires more rigorous study before it can be routinely recommended.

### Surveillance of Vessel Patency

Most vascular specialists agree that patients undergoing percutaneous revascularization should be followed up at regular intervals to address cardiovascular risk factor modification, to screen for disease progression in other arterial beds, and to monitor the patency of the treated vessel. The premise behind close surveillance of vessel patency is simple: It is much easier to treat restenosis than complete occlusion. Identifying restenosis before it leads to an occlusion could therefore reduce the complexity and risk of subsequent procedures.

This clinically rational argument has not been tested in randomized, clinical trials. Moreover, the degree of restenosis at which reintervention offers the optimal clinical result has not been defined. Thus, the strategy outlined in this section is based on clinical experience and suggests the use of a higher peak systolic velocity threshold compared with that used to define binary restenosis in randomized trials of femoropopliteal stents (Table 1).17,18 It must be emphasized that the decision to treat restenosis incorporates the ultrasonographic assessment of restenosis in the context of clinical symptoms and the ABI. The potential benefit of repeat intervention should also be weighed against the patient’s functional status, comorbidities, and periprocedural risk.

In most patients, restenosis will present with recurrent symptoms of claudication or a decrease in ABI, both easily detected on clinical examination. Because the within-person variability of the ABI is 0.10 to 0.15, changes in ABI greater than this magnitude are associated with initial success of treatment or restenosis.33 In others, particularly in patients with SFA disease and with well-established profound femoris collaterals, symptoms may return only after the vessel has reclosed. In these patients, arterial ultrasound surveillance is a particularly useful surveillance tool. The presence of infrapopliteal arterial disease limits the utility of clinical examination in monitoring the patency of SFA. Thus, ultrasound imaging of the infraguinal vessels, in addition to ABI and SDP, is a mainstay of surveillance. Computed tomographic angiography is not commonly used for routine surveillance because of the risks associated with contrast exposure and cumulative radiation dose. Magnetic resonance angiography is not a reliable tool for investigating stent patency because of inherent ferromagnetic artifact, which obscures the stent lumen. The baseline values are established within 4 weeks after the intervention and followed up serially thereafter (Table 2).

The concept of surveillance after endovascular interventions is borrowed from the widely accepted practice of periodic clinical examination, interval ultrasound imaging of femoropopliteal bypass grafts, and hemodynamic assessment with SDP testing after surgical revascularization. Close clinical surveillance of surgical conduits can identify threatened grafts, allow revision before graft failure, and improve long-term graft patency.34 However, the incremental benefit of ultrasonographic surveillance on short-term graft patency and clinical outcomes has been challenged in more recent randomized trials.35 No randomized trials have assessed the clinical benefit and cost-effectiveness of various surveillance methods after endovascular interventions. Clinical series suggest that meticulous surveillance and “maintenance” after femoropopliteal stenting can yield promising durability even in the most challenging lesion types.36,37 The duration of ultrasonographic surveillance is also unknown. Most SFA restenosis occur in the first 12 months, but de novo disease jeopardizing stent patency may arise at any time.

### Physical Examination

The physical examination is the simplest and most important part of postprocedural follow-up and should start at the

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**Table 2. Examples of Surveillance Strategies Available in Vascular Laboratories After Endovascular Intervention in Different Arteries of the Lower Limb**

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<th>Arterial Segment</th>
<th>Time Intervals</th>
<th>Vascular Laboratory Studies</th>
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<td>Aortoiliac arterial segment</td>
<td>1, 6, and 12 mo and annually thereafter</td>
<td>ABI or SDP testing, Exercise ABI if inconclusive resting studies, Iliac artery ultrasound in suitable body habitus</td>
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<tr>
<td>Femoropopliteal arterial segment</td>
<td>1, 6, and 12 mo and annually thereafter</td>
<td>ABI measurement, Duplex ultrasound assessment of PSVR</td>
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<tr>
<td>Tibial arteries</td>
<td>1, 6, and 12 mo and annually thereafter</td>
<td>Duplex ultrasound in case of infrapopliteal stenting</td>
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ABI indicates ankle-brachial index; PSVR, peak systolic velocity ratio; and SDP, segmental Doppler pressures.

*These supplement clinical assessment of symptoms and physical examination.*
completion of the procedure. Thus, initial assessment of the femoral, popliteal and pedal pulses should document a new baseline. Increased arterial perfusion to the foot will often result in a hyperemic, hot, red foot. It is not uncommon to observe transient pedal and ankle edema, which usually resolves within several days to weeks. The emergence of livido reticularis and painful digital ischemia within a day or two after the procedure may suggest cholesterol embolization and the need for more intensive medical therapy or less enthusiasm for repeat endovascular procedures. Each follow-up visit should include careful examination of the feet to confirm the presence of pedal pulses, capillary refill, and new skin ulceration and any change from the baseline examination. Newly discovered pallor, decreased temperature, pain at rest, and loss of pedal pulses should raise concerns about acute ischemia caused by thrombosis of a stent or angioplasty site. Similarly, nonhealing wounds and digital ulcers should prompt evaluation of critical limb ischemia caused by progression of arterial insufficiency. Patients having revascularization for critical limb ischemia may require more frequent clinical examination to monitor wound healing, to provide wound debridement, and to monitor adequacy of arterial perfusion in the healing period.

The ABI

The ABI is easily obtained during physical examination by calculating the ratio between the highest of the ankle pressures measured in the dorsalis pedis or posterior tibial artery on each side and the higher of the 2 brachial pressures.39 A value <0.9 is consistent with hemodynamically significant arterial obstructive disease between the aorta and ankle. A decrease in the ABI of >0.15 relative to the baseline value obtained after the procedure suggests restenosis at the site of intervention or emergence of de novo disease outside the treated segment. Thus, a change in ABI indicates a change in arterial perfusion but does not determine its location. The magnitude of the decline when reintervention should be considered has not been studied. In our practice, a 20% decline compared with baseline ABI immediately after the procedure triggers careful review of the ultrasound and symptoms. The ABI is also not helpful in calcified and noncompressible vessels, which may falsely elevate ABI, masking a drop in ankle perfusion.

Patency of the arterial iliac interventions is commonly monitored by assessment of the perfusion pressure distal to the site of the intervention, and ABIs and SDP testing are routinely used for that purpose. Exercise ABIs are particularly useful after aortoiliac interventions when symptoms recur in the absence of detectable change in resting ABI or SDP (Figure 1). Ultrasound imaging of the iliac vessels can be difficult because of their depth and the presence of bowel gas. Iodinated contrast exposure makes computed tomographic angiography an impractical tool for routine or repeated aortoiliac surveillance, although it may be helpful when physiological tests are inconclusive.

ABI measurement is also the mainstay of vascular surveillance after femoropopliteal interventions and tibial angioplasty. The presence of tibial artery stents, especially distal to the proximal calf, is considered by many operators to be a contraindication to ABI because of concern about deforming the stents by application of blood pressure cuff. In this case, arterial ultrasound may be useful for surveillance of distal tibial stents.

SDP and Pulse Volume Recording

The SDP test, an expanded form of the ABI, measures pressures along the thigh and calf and calculates a ratio at each
location relative to the brachial pressure. This test helps to localize a hemodynamically significant lesion. It is also used to monitor the outcome of iliac interventions and to assess vessel patency after femoropopliteal balloon angioplasty and atherectomy. The thigh-brachial index provides direct assessment of pressure gradients across the aortoiliac segment, and gradients along the thigh and upper calf assess the femoropopliteal segment. SDP testing is generally avoided in patients with stents in the infrainguinal arteries because of theoretical concerns about stent deformation (Figure 2). Pulse volume recording, commonly obtained with SDP testing, records the change in volume of a limb segment with each arterial pulse and is helpful in the assessment of arterial flow in the presence of calcified arteries, which cannot be occluded by pressure cuff.

**Duplex Arterial Ultrasound**

Arterial duplex ultrasound can assess restenosis of the common femoral, superficial femoral popliteal, and proximal tibial interventions. Duplex ultrasound is a widely accepted and well-validated tool for the assessment of infrainguinal arterial anatomy. Duplex ultrasound identifies narrowing in arteries by an increase in maximum blood flow velocity (peak systolic velocity) compared with the nearest proximal reference segment. Two-dimensional ultrasound is used to identify the artery for Doppler interrogation.

A >2.0- to 2.5-fold increase in the peak systolic velocity compared with the adjacent proximal segment generally indicates a ≥50% stenosis. Values in this range have been used in clinical trials to define the presence or absence of restenosis. In our practice, however, clinical symptoms and risk of stent failure are usually associated with a >3-fold increase in the peak systolic velocity ratio, which indicates a stenosis exceeding 70% (Table 1 and Figure 3). This value is commonly used in clinical practice as a threshold above which reintervention is considered. Ultrasound can also identify femoropopliteal stent fractures, which may increase the risk of stent failure.

**Figure 2.** Segmental Doppler pressure (SDP) and pulse volume recording (PVR) test in a patient 5 years after placement of a right superficial femoral artery stent. SDP and PVR indicate a widely patent stent. SDP is generally avoided after femoropopliteal stenting to avoid deforming the stent by pressure cuff inflation.
of restenosis and occlusion. However, recent data suggest that this may be a less frequent phenomenon in newer compared with older stent designs, with later studies reporting rates of 2% to 3% at 12 months after implantation.\textsuperscript{16,20,43,44}

In patients undergoing infrapopliteal interventions for critical limb ischemia, patency of the tibial vessels and thus their surveillance may be clinically less important after the wound heals and metabolic requirements of the pedal tissues return to a low level. Nevertheless, duplex ultrasound can be useful in imaging tibial stents and assessing their patency (Figure 4).

The value of serial ultrasound surveillance after balloon angioplasty without stent implantation is controversial. Investigations of the value of ultrasound surveillance in patients treated with balloon angioplasty and atherectomy without stent implantation suggested that ultrasound did not offer any additional value over clinical and ABI assessment.\textsuperscript{45} The value of ultrasound after balloon angioplasty may be influenced by the observation that some residual stenosis after percutaneous transluminal angioplasty resolves with time, a phenomenon not seen in stents.\textsuperscript{46} Others identified ultrasound as a valuable tool in identifying residual percutaneous transluminal angioplasty stenosis and found it to be predictive of future restenosis and occlusion.\textsuperscript{47}

Ultrasound surveillance after stent implantation, on the other hand, allows identification of moderate- to high-grade restenosis at a stage when reintervention may maintain patency of the stent and prevent its occlusion. Once a stent occludes, the durability of any reintervention is limited. Single-center experience suggests that vigorous surveillance and a strategy of reintervention for high-grade restenosis and threatened stents can result in superior patency, even in very long-segment SFA stents.\textsuperscript{36} The gain in patency as a result of surveillance may be greater in SFA lesions between 100 and 200 mm and those >200 mm in length.\textsuperscript{36}

The value of imaging surveillance depends on reintervention providing a lasting benefit. At present, the efficacy of reintervention is highly variable, but the low morbidity associated with repeat endovascular therapy encourages many to accept the need for periodic reintervention. Restenosis after balloon angioplasty can be treated with stent placement, but
effective therapy for restenosis of a stented segment remains elusive. Restenosis of the aortoiliac stents, although uncommon, is usually treated with balloon redilation or with covered stents. Restenosis is more common in the SFA segment where a pattern of restenosis influences the durability of subsequent reinterventions. Balloon angioplasty and atherectomy in the restenosed SFA stent can be durable in a short, focal restenosis, but its effectiveness has been variable in longer segments of restenosis. Vascular brachytherapy has not been effective in preventing restenosis when used during initial intervention. There is evidence, however, that intravascular gamma radiation and balloon angioplasty can be an effective tool for restenosis of SFA stents (Figure 5).

Although the first-generation femoropopliteal drug-eluting stents did not reduce in-stent restenosis, more recent programs of self-expanding paclitaxel-eluting stents for SFA stenosis show more encouraging results. In these studies, the 12-month rate of freedom from target lesion revascularization is >80%. Controversy over the design of the modern drug-eluting stent trials obscures their absolute benefit, and comparisons between studies suggest that the short-term results were similar to those observed in randomized trials of modern bare metal stents. It remains to be seen whether drug-eluting balloons or second-generation drug-eluting stents change the need for vigilant detection of restenosis or prove to be effective therapy for in-stent restenosis of bare metal stents.

The optimal duration of ultrasound surveillance in the femoropopliteal arteries is also unclear. Although most restenosis occurs in the first 12 months, the progression of native disease and late restenosis can certainly affect stent patency. It is not clear whether at some point clinical examination and basic ABI measurement become superior or equivalent to more elaborate ultrasound testing. However, many clinicians would viscerally favor longer imaging surveillance after complex arterial reconstruction and implantation of long stents.

Conclusions

Endovascular therapy to relieve intermittent claudication and critical limb ischemia offers durable treatments in many patients. Surveillance requires regular clinical assessment to assess the recurrence of symptoms and maintenance of antiplatelet and antiatherosclerosis medical therapy and should be supplemented by physiological tests (eg, ABIs or segmental leg pressures). Although noninvasive imaging by duplex ultrasound is not proven to provide additional benefit, in many patients, this can be a useful adjunct to assess vessel patency and to help determine whether restenosis is a cause of recurrent symptoms. However, like surgical bypass, early detection of restenosis or new disease after endovascular therapy may permit a less complicated reintervention to restore patency and to reduce symptoms. Despite the growing use of endovascular procedures, the paucity of randomized, clinical trials conducted to define the optimal long-term management of these patients is striking. Although this review may help outline a “common sense” clinical approach to postprocedural care, it should above all pose more questions than answers and thus stress the need for well-designed trials necessary to answer them.

Disclosures

None.

References


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