VASCULAR AND ENDOVASCULAR TECHNIQUES

Thomas L. Forbes, MD, Section Editor

First results of clampless distal anastomosis in peripheral vascular bypass with LeGoo, a thermoreversible polymer

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Background: **We report our initial experience with LeGoo (Pluromed Inc, Woburn, Mass), a temporary thermoreversible occlusive gel, in peripheral vascular revascularization.**

Methods: **Between 2007 and 2010, LeGoo was used to occlude target vessels during bypass surgery in 14 patients who required infrainguinal revascularization.**

Results: **Proximal occlusion of the target vessel was obtained with a mean quantity of 0.25 mL of LeGoo. Distal occlusion of the vessel was obtained with a mean quantity of 0.28 mL. One injection of LeGoo was sufficient to prevent backbleeding in 11 of 14 patients. The mean occlusion time was 13.4 ± 3.3 minutes. An injection of saline through the graft or better directly into the arteries was used to dissolve the gel. For our first case, a Fogarty catheter was used to remove residual gel from the anterior tibial artery.**

Conclusions: **LeGoo gel can be used to stop blood flow in small-bore arteries in the lower limbs to allow anastomoses to be performed. (J Vasc Surg 2012;55:1821-5.)**

Creating distal anastomoses in peripheral vascular bypass surgery requires clamping of the target vessel. Ideally, clamping should allow the surgeon to work in a blood-free operating field, without damaging the arterial wall and without reducing the surgeon's visual field.

External mechanical occlusion is generally achieved by using vascular clamps, and arterial occlusion is generally obtained, but sometimes at the price of irreversible damage to the vascular wall.[1,2] Compression of the limb using tourniquets, with or without an Esmarch bandage to empty venous blood from the limb, may help prevent direct vessel trauma.[3-5] The drawbacks of these techniques include (1) adequate occlusion is not always achieved, (2) total occlusion of the arterial network of the limb below the tourniquet, which can aggravate the ischemia by occluding collateral supply, (3) injury to nerves, muscle, and skin, and (4) induced spasm of the distal vessel.[6] Use of the Esmarch bandage may also lead to embolism and skin trauma.

Internal vascular occlusion is achieved by using a balloon catheter that is positioned in the arterial lumen and kept inflated. This solution is useful because it precludes the risks associated with lesions due to clamping. It does, however, make the intervention more complex for the surgeon.

LeGoo (Pluromed Inc, Woburn, Mass) is a P407 thermosensitive poloxamer polymer that has shown its efficacy in small-vessel occlusion in preclinical experiments[7-9] and more recently in humans for off-pump coronary artery revascularization.[10] It has been used for >20 years, in different contexts, including transdermal applications and collyrium. The only demonstrated toxicity is hypercholesterolemia for a dose of more than 2000 times that used for vascular occlusion.

LeGoo is a viscous liquid at room temperature that immediately solidifies when it is warmed to body temperature.[9] Consequently, when it is injected into a blood vessel at body temperature, the viscous liquid is instantaneously transformed into an occlusive plug that marries the contours of a lumen, even when the lumen is distorted by arterial disease. The plug maintains the cylindrical shape of the target vessel, making it easier to insert sutures precisely, and can be pierced easily with a surgical needle.

The LeGoo plug dissolves spontaneously after 10 to 20 minutes in situ or can be dissolved at will by injecting cold saline into the vessel or by using an instrument to disrupt the plug. Once dissolved, LeGoo cannot form a new plug because the concentration is too low, and it is excreted

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Author conflict of interest: Pluromed Inc provided the LeGoo to the unit at no cost. The authors declare no conflict of interest with Pluromed Inc. The authors had full control of data analysis and manuscript preparation.

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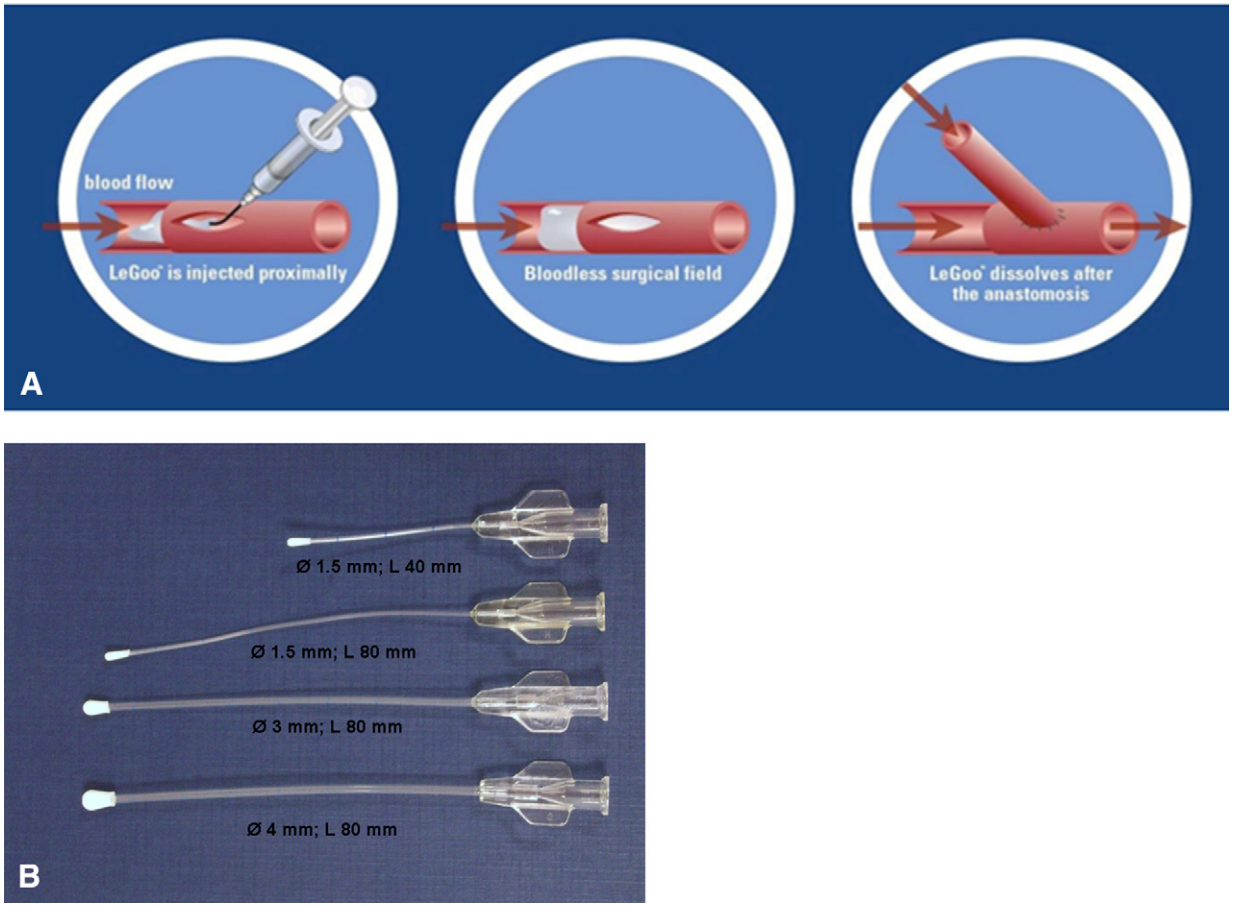

Fig 1. Use of LeGoo. **A,** The surgeon creates an arteriotomy and injects LeGoo retrograde while withdrawing the cannula. LeGoo dissolves slowly when in contact with blood. LeGoo is fully dissolved with ice or cold saline. **B,** Cannulas with outer diameters of from 1.0 mm × 4 cm long to 4.0 mm × 8 cm long.

through the kidneys.[9] If the LeGoo plug dissolves spontaneously before completion of the anastomosis, additional injections can reconstitute the occlusion (Fig 1, *A*).

Experimental studies have analyzed the thermoreversible proprieties of Poloxamer P407 and shown that it is impossible for the solution to form a gel when the concentration is below 12%.[7-9] Preclinical experiments showed that LeGoo is nontoxic. The plug dissolves from its micellar form into unimeric molecules.[9] We report our initial experience with LeGoo in peripheral revascularization surgery.

METHODS

Between 2007 and 2010, LeGoo was used in 14 patients (9 men, 5 women) with peripheral vascular disease (PVD) by one surgeon (O.B.) at Le Bocage Hospital, Dijon, France. During the same period, 102 revascularizations with distal bypasses using conventional clamping were performed. The standard method used in our department is a vascular clamp placed on a noncalcified area. A completion angiogram is systematically done at the end of the procedure.

The inclusion criteria were symptomatic patients, according to Fontaine stages, with infrainguinal lesions that required distal bypasses. LeGoo was used when calcifications of the target vessel foreshadowed the difficulties of clamping. Bypasses were done with the great saphenous vein, when available, or with a Dacron prosthesis.

Surgical procedures. Surgery was performed under general anesthesia. Heparin (50 IU/kg of body weight), was administered once the surgical approaches had been completed. A 4 mm arteriotomy was made in the target artery. A specially designed catheter of the appropriate diameter and length, with a soft olive-shaped tip (Pluromed Inc Fig 1, *B*) and attached to a syringe prefilled with LeGoo, was inserted through the arteriotomy and pushed to a position 1.5 to 2 cm proximal to the arteriotomy. The viscous liquid LeGoo was injected by hand while the cannula was slowly withdrawn. To stop back-bleeding, LeGoo was injected distally in a manner similar to the proximal injection.

Once the operative field was bloodless, the conduit (prosthesis or great saphenous vein) was anastomosed to

Table I. Clinical data

Variable	*Mean ± SD (range) No. (ratio) (N = 14)*
Demographics data	
Age, years	73 ± 13 (35-90)
Men/women	9/5 (1.8)
Cardiovascular risk factors	
Smoking	5
Hypertension	10
Dyslipidemia	10
Diabetes	10
Body mass index >30 kg/m^2	3
Comorbidities	
COPD	0
Coronaropathy	0
Cerebrovascular disease	4
Renal disease[a]	3

COPD, Chronic obstructive pulmonary disease; *SD,* standard deviation.
[a]Assessed at creatinine >200 μmol/L.

the arteriotomy with continuous 6-0 or 7-0 polypropylene sutures. If the LeGoo plug dissolved before completion of the anastomosis and bleeding into the surgical field resumed, additional LeGoo was injected to reconstitute the plug and re-establish a bloodless field. When the suture line was completed and before snugging the continuous suture, the gel plug was allowed to dissolve spontaneously or was dissolved by injecting cold saline into the artery. When blood flow through the anastomosis was strong, the continuous suture was tightened and tied.

The quality of the hemostasis was defined as grade 1, no bleeding; grade 2, minimal bleeding, but the anastomosis could be performed without additional aid; grade 3, moderate bleeding, the anastomosis could be performed with directed additional saline flow; grade 4, profuse bleeding and the anastomosis could not be performed with the use of LeGoo gel.

RESULTS

The patients were an average age of 73 years (range, 35-90 years). The symptomatic PVD was acute leg ischemia in 4 patients, Fontaine stage IV in 8, Fontaine stage III in 1, and Fontaine stage II in 1. Cardiovascular risk factors and comorbidities are listed in Table I.

LeGoo was used to occlude 5 anterior tibial arteries, 4 peroneal arteries, 2 posterior tibial arteries, 1 superficial femoral artery, 1 popliteal artery, and 1 tibioperoneal trunk. The conduit vessel used was a great saphenous vein in six patients and a Dacron prosthesis in eight.

The proximal occlusion of the target vessel was obtained with a mean quantity of 0.25 mL of LeGoo (range, 0.1-0.5 mL). A standard clamp was not required for any of these patients. Four patients did not need a proximal injection because there was no bleeding from the proximal side (occluded arteries). When an injection was given, one injection of LeGoo on the proximal side was sufficient in 8 of 10 cases. Two patients required a second injection of LeGoo. Distal occlusion of the vessel was obtained with a mean quantity of 0.28 mL (range, 0.0-0.8 mL). One injection of LeGoo was sufficient to stop back-bleeding in 11 patients, 3 required a second injection of LeGoo, and a third distal injection was needed in 1 patient due to bleeding from collateral branches.

The mean occlusion time was 13.4 ± 3.3 minutes (range, 2-18 minutes). The total quantity of LeGoo needed per case was 0.6 ± 0.3 mL (range, 0.3-1.3 mL). After completion of the anastomoses, the LeGoo plug was dissolved with saline by direct injection into the arteries in 13 of 14 patients.

After the completion angiogram in the first of our cases, a Fogarty balloon was used to remove a residual plug in an anterior tibial artery rather than waiting for the gel to dissolve naturally. In this case, saline had been injected through the proximal end of the graft rather than directly into the gel, leading to a longer-than-expected dissolution time. Operative data are presented in Table II.

The quality of hemostasis was grade 1 in 10 patients, grade 2 in 2, grade 3 in 1, and grade 4 in 1. Grafts were patent in 12 of 14 patients (85.7%) at 30 days.

Two postoperative deaths occurred in patients who were operated on for acute ischemia. One patient died of multiple organ failure on day 12. This patient suffered from polyvascular disease, with myocardial infarction and limb ischemia, and underwent concomitant revascularization of coronary and leg arteries. The second patient needed a second intervention for thrombosis of a Dacron prosthesis bypass on the peroneal artery[6] and died on day 2 of low cardiac output.

DISCUSSION

Ideally, clamping of calcified small-bore arteries should provide an atraumatic blood-free field at the site of the arteriotomy, without hampering the surgeon. LeGoo gel seems to have these qualities. This polymer, which was initially used as an excipient for various medicines, is a nontoxic, nonthrombotic occlusive gel. LeGoo gel uses a concentration of 20% of fractionated poloxamer P407. This concentration falls progressively when the polymer is in contact with the blood both upstream and downstream, which explains why blood flow sometimes resumes prematurely before completion of the anastomosis, requiring the injection of more gel. The gel can be dissolved rapidly by injecting physiologic saline directly into the arteries.

At the beginning of our study, one instance of residual occlusion occurred in a distal artery due to poor rinsing through the Dacron bypass once the anastomosis had been completed. After the completion angiogram, a Fogarty catheter was used to remove the gel rather than waiting for it to dissolve naturally. From this case onward, we systematically removed gel residues before completing the anastomosis by injecting cold saline solution directly into the arteries. We recommend that a completion angiogram of the anastomosis and the downstream vascular bed be performed systematically at the end of the procedure (Fig 2).

Several experimental studies have shown the efficacy of the procedure and the absence of intimal lesions in pig

Table II. Data on bypasses: number and volume of LeGoo injections

			Proximal flow		*Distal flow*		*Total*	
Pt	*Target vessel*	*Vessel conduit*	*Injections (No.)*	*Quantity (mL)*	*Injections (No.)*	*Quantity (mL)*	*Quantity (mL)*	*Occlusion time (min)*
1	Peroneal artery	GSV	1	0	3	0.7	0.7	18
2	Tibioperoneal trunk	Dacron prosthesis	1	0	1	0.2	0.2	12
3	Anterior tibial artery	Dacron prosthesis	2	0.3	2	0.3	0.6	14
4	Popliteal	Dacron prosthesis	0	0	1	0.8	0.8	9
5	Anterior tibial artery	Dacron prosthesis	1	0.2	1	0.4	0.6	12
6	Posterior tibial artery	GSV	1	0.2	1	0.3	0.5	11
7	SFA	Dacron prosthesis	2	1	1	0.3	1.3	9
8	Anterior tibial artery	Dacron prosthesis	1	0.3	1	0.2	0.5	13
9	Peroneal artery	Dacron prosthesis	1	0.2	1	0.2	0.4	14
10	Anterior tibial artery	GSV	0	0	1	0.4	0.4	18
11	Posterior tibial artery	GSV	1	0.1	1	0.2	0.3	20
12	Peroneal artery	GSV	1	0.2	1	0.2	0.4	14
13	Peroneal artery	GSV	1	0.4	2	0.5	0.9	12
14	Anterior tibial artery	Dacron prosthesis	1	0.3	1	0.4	0.7	12
Mean				0.23 ± 0.25		0.36 ± 0.18	0.6 ± 03	13.4 ± 3.3

GSV, Great saphenous vein; *SFA,* superficial femoral artery.

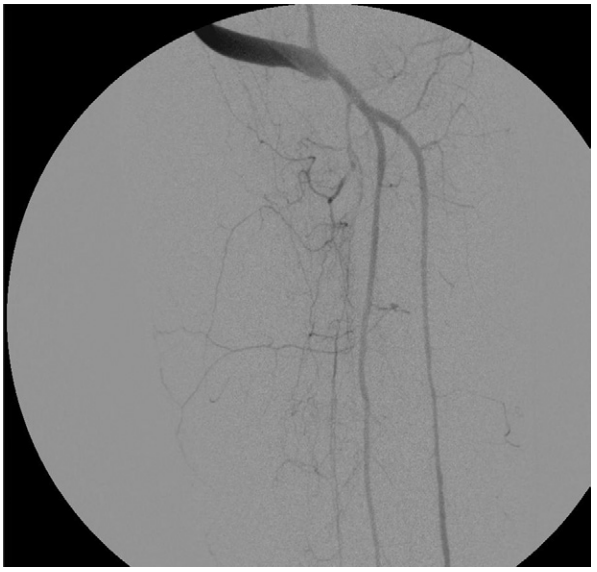

Fig 2. Final control angiogram of the first case in our experience shows the distal anastomosis and the downstream vascular bed at the end of a bypass on tibioperoneal trunk.

arteries.[7,8,11] After obtaining the European Conformity certificate in 2007, two clinical studies showed the efficacy and safety of LeGoo gel in human coronary artery surgery. The study by Bouchot et al[10] confirmed the efficacy of LeGoo in 99 coronary anastomoses without extracorporeal circulation in 50 patients. The study by Rastan et al[12] showed similar results in minimally invasive coronary artery surgery in 10 patients compared with 10 control patients.

Clamping is difficult, not only in calcified arteries but also when target arteries have been stented. This was the case for our patient 4, who had a stent in the midpopliteal artery and who required a bypass from the femoral to the upper popliteal artery, with a downstream artery that could not be clamped.

Finally, the LeGoo gel could be of interest to create arteriovenous fistulas for patients who require hemodialysis. The first results seem to be satisfactory and will be reported in a future publication.

CONCLUSIONS

This feasibility study showed that LeGoo provides temporary arterial occlusion by blocking blood flow in small-bore arteries in the lower limbs. LeGoo allows safe and atraumatic anastomosis. The plug facilitates the creation of the anastomoses by maintaining the cylindrical shape of the vessels and can be easily pierced with a surgical needle.

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