Results from a multicenter registry of heparin-bonded expanded polytetrafluoroethylene graft for above-the-knee femoropopliteal bypass

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ABSTRACT

Objective: The aim of the study was to retrospectively analyze early and follow-up results of above-the-knee femoropopliteal bypasses (AKb) performed with a bioactive heparin-bonded expanded polytetrafluoroethylene (HB-ePTFE) graft in patients with peripheral arterial obstructive disease in a multicentric retrospective registry involving seven Italian vascular centers.

Methods: During a 14-year period ending in March 2016, an HB-ePTFE graft was used in 1401 interventions performed for peripheral arterial obstructive disease. Comorbidities, risk factors, and follow-up outcomes were collected in a multicenter registry with a dedicated database. A post hoc analysis of the database was performed to identify 364 (25.9%) patients who underwent AKb. Early (intraoperative and <30 days) results were analyzed in terms of death, thrombosis, amputations, reinterventions, and the occurrence of major local and systemic complications. Follow-up results were analyzed by life-table analysis (Kaplan-Meier test) in terms of primary and secondary graft patency, assisted primary patency, limb preservation, and amputation-free survival. The analysis of follow-up results was stopped in December 2016.

Results: In 61 (16.7%) patients, AKb was performed after the failure of a previous ipsilateral revascularization. Critical limb ischemia was present in 164 (45%) cases; the remaining patients had life-limiting intermittent claudication. Perioperative mortality occurred in three (0.8%) patients: in the hospital (n = 2) due to acute myocardial infarction and after discharge (n = 1) due to fatal arrhythmia. Early thromboses occurred in six (1.6%) patients; all these patients had primary AKb for critical limb ischemia. The cumulative rate of perioperative amputations was 0.5% (2 cases), whereas the cumulative rate of early reinterventions was 3% (11 cases). Median duration of follow-up was 28 months (range, 1-168 months); the median cumulative follow-up index for survival was 0.75 (range, 0.05-1). Estimated survival at 5 years was 75.3% (standard error [SE], 0.03). Estimated 5-year primary patency was 64% (SE, 0.04); the corresponding figure in terms of assisted primary patency was 65% (SE, 0.035). Secondary patency rate at 5 years was 74.5% (SE, 0.03). The rate of limb preservation at 5 years was 95% (SE, 0.02); the corresponding figure in terms of amputation-free survival was 74% (SE, 0.04).

Conclusions: In an era of endovascular enthusiasm, with conflicting results for the treatment of long or complex lesions of the superficial femoral artery, AKb with the use of HB-ePTFE graft remains an effective option, with low rate of perioperative complications and satisfactory long-term results. (J Vasc Surg 2018;67:1463-71.)

In recent years, meta-analyses showed that endovascular treatments have supplanted bypass surgery as the preferred first technique for the treatment of peripheral arterial obstructive disease (PAOD), especially in the femoropopliteal segment.[1-4] Nevertheless, results were not completely satisfactory; costs increased fourfold in the last decades, and considering a composite end point that includes death and major amputation, this was significantly worse for endovascular revascularization compared with bypass surgery.[5] These data are noteworthy because the majority of recent endovascular series have been mainly weighted toward treatment of short femoropopliteal lesions, also using different techniques.[7-11] Most important, robust long-term data in the endovascular arm are questionable, especially for complex lesions, and evidence from randomized clinical trials has already shown that bypass surgery has better patency in the long-term outcomes.[12-16] When it comes to open surgery, short-segment autologous great saphenous vein (GSV) has been reported to provide better long-term outcomes than prosthetic grafts for above-the-knee femoropopliteal bypass (AKb).[17-20] However

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*A full list of the PROPATEN Italian Registry Group is given in the Appendix (online only).

Author conflict of interest: none.

Additional material for this article may be found online at www.jvascsurg.org.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2017.09.017

this preferred conduit is not available or suitable in almost half of patients, and conflicting data still exist as to either alternative vein options or the best material to be used for prosthetic graft bypass.[21,22]

The aim of this study was to evaluate early and long-term results of AKb performed with a bioactive heparin-bonded expanded polytetrafluoroethylene (HB-ePTFE) graft in patients with PAOD in a multicentric retrospective registry involving seven Italian vascular centers.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective analysis of a multicenter registry
- **Take Home Message:** Femoral to above-knee popliteal artery bypass with heparin-bonded polytetrafluoroethylene was used in 364 patients (45% with critical limb ischemia) and resulted in 0.8% early mortality and an estimated 5-year survival of 75.3%, 5-year primary patency of 64%, and 5-year rate of amputation-free survival of 74%.
- **Recommendation:** This study suggests that heparin-bonded polytetrafluoroethylene can be used in femoral to above-knee popliteal artery bypasses with a 5-year primary patency of 64%.

METHODS

Population of patients. During a 14-year period ending in March 2016, an HB-ePTFE graft (Gore Propaten; W. L. Gore & Associates, Flagstaff, Ariz) was used in 1401 interventions performed for PAOD in seven Italian hospitals. The registry was created in 2006; at the very beginning, it included three centers at which this type of graft was used for the first time in Italy.[23-25] Then, starting from 2008, four other high-volume centers with a large use of this graft were invited to join the registry. Comorbidities, risk factors, and follow-up outcomes were collected in a multicenter registry with a dedicated database. The registry was approved by the local ethical committee of each center; all subjects gave informed consent to the treatment of their personal data. Data were collected in a multicenter registry with a dedicated database. Data collection was retrospective until 2008; it was prospective thereafter. Each center was asked to send its updated data to the coordinating center twice a year, where they were transformed into SPSS files and elaborated for the analyses. The reliability of the data contained in the registry was certified by an external independent commission (Castalia Group, ICT and Quality Management, Aosta, Italy) in two different sessions (2009 and 2013). A post hoc analysis of the database was performed to identify 364 (25.9%) patients who underwent AKb. In the same period, in the same centers, AKb with single-segment autologous GSV was performed in seven patients. Some ($n = 101$) of the AKb patients included in this study have been part of one previous study of the registry[26]; however, although above-the-knee anastomosis was one of the variables included in both the univariate and multivariable analyses, AKb was not analyzed separately in that paper. The modalities of the choice of the type of graft and of data collection and insertion have already been described.[26,27]

Preoperative workup, indications for surgery, surgical details, and follow-up protocol. In all the cases, preoperative diagnostic assessment consisted of ankle-brachial index (ABI) measurement, duplex ultrasound scanning, and computed tomography angiography of the aortoiliac axis and of the lower limbs. Patients were operated on in the presence of severe lifestyle-limiting intermittent claudication after the failure of other conservative measures or in the presence of critical limb ischemia (CLI). Apart from a native distal popliteal artery free from severe stenosis, anatomic indication for AKb has substantially changed during the years. In the first years of the registry experience, it was performed in patients with ≥10 cm of occlusion of the superficial femoral artery (SFA). In the most recent years, it was reserved for patients with ≥20 cm of occlusion or chronic total occlusion of the SFA starting from just below its origin, severe and diffuse calcifications of the SFA, and less complex lesions after the failure of a previous endovascular treatment.

The interventions were performed in the operating room under general anesthesia with standard technique, which consisted of a longitudinal approach to the femoral bifurcation and to the distal SFA-proximal popliteal artery. The anastomoses were performed in an end-to-side fashion at the level of the distal common femoral artery and of the distal SFA. In selected patients with concomitant occlusive disease of the femoral bifurcation, endarterectomy was accomplished with patching. Similarly, we considered an AKb feasible even in the presence of a diseased proximal popliteal artery, but with a good-quality distal popliteal artery as well as tibial vessels. In case of severely diseased above-knee popliteal artery, we performed an endarterectomy and an adjunctive Linton patch at the distal anastomosis. In case of tibial vessel disease, an adjunctive procedure in the form of angioplasty has been left to the surgeon's judgment. All the patients had intraoperative intravenous administration (30-40 units/kg) of sodium heparin at arterial clamping. At the end of the intervention, completion angiography or duplex ultrasound was routinely performed. Postoperative antithrombotic treatment consisted of single or double antiplatelet treatment or oral anticoagulation; it was determined on the basis of the surgeon's preference as well as according to the patient's comorbidities and risk factors, or it was driven by some particular technical aspects performed during the intervention. In general,

those patients who presented already taking warfarin continued with such medical treatment in the postoperative period. Follow-up was always performed at 1 month and 12 months and on a yearly basis thereafter. Follow-up visits consisted of clinical examination, ABI measurements, and duplex ultrasound examination. During ultrasound examinations, the patency of the bypass and the status of the inflow and outflow arteries were assessed. If symptoms suggested a recurrent femoropopliteal obstruction, computed tomography angiography or digital subtraction angiography was used to confirm or eventually to treat this lesion.

Definitions and end points. Comorbidities and risk factors were defined as previously described.[28] The clinical status was defined according to the Rutherford classification, and the anatomic characteristics of the SFA obstructive lesions were divided according to the TransAtlantic Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II) classification.[29] Early (intraoperative and <30 days) results were analyzed in terms of death, thrombosis, amputations, reinterventions, and the occurrence of major local and systemic complications, defined according to recommended standards for reports dealing with lower extremity ischemia.[29] Significant (>70%) anastomotic restenosis was defined as a significant increase of the peak systolic velocity at the stenotic site higher than 250 cm/s; occlusion was defined as absence of flow into the graft. Follow-up results were analyzed in terms of primary (the possibility of maintaining a functioning graft without adjunctive interventions) and secondary (the possibility of restoring graft patency when a thrombosis occurred) graft patency, assisted primary patency (defined as the success of procedures carried out on a still patent bypass to prevent its thrombosis), limb preservation (the absence of amputation at above-knee or below-knee level), and amputation-free survival (freedom from above-the-ankle amputation and from all-cause mortality). The analysis of follow-up results was stopped at December 2016. The follow-up index for late survival in the study group was assessed; it was defined as the ratio between the investigated follow-up period and the theoretically possible follow-up period up to December 2016.[30]

Statistical analysis. Clinical data were prospectively recorded and tabulated in a Microsoft Excel (Microsoft Corp, Redmond, Wash) database. Statistical analysis was performed by means of SPSS 24.0 for Windows (IBM Corp, Armonk, NY). Categorical variables were presented using frequencies and percentages, and continuous variables were presented with mean ± standard deviation or median and ranges on the basis of data distribution. Continuous variables were analyzed with χ^2 test and Fisher exact test, when necessary. Independent samples Student *t*-test was used for continuous variables; Wilcoxon signed rank test was used to evaluate the difference in ABI measurement before and after intervention. Follow-up data were analyzed by life-table analysis (Kaplan-Meier test). A univariate analysis to identify potential significant predictors of graft primary patency was performed with Kaplan-Meier survival estimates ± standard error (SE) and log-rank test for each covariate. Associations that yielded a P value < .20 on univariate screen were then included in a forward Cox regression analysis; the strength of the association of variables with postoperative outcomes was estimated by calculating the hazard ratio and 95% confidence intervals (significance criterion of 0.25 for entry, 0.05 for removal). The discrimination of the model was obtained by calculating the area under the receiver operating characteristic curve. All reported P values were two sided; P value < .05 was considered significant.

Table I. Comorbidities and risk factors for above-the-knee bypass (AKb) patients

Variable	(N = 364)
Female gender	53 (14.5)
Age, years	71 ± 9
History of smoking	216 (59)
Hyperlipemia	224 (61.5)
Arterial hypertension	294 (81)
Ischemic heart disease	125 (34)
End-stage renal disease	8 (2)
Diabetes mellitus	141 (39)
Rutherford class	
3	200 (55)
4	86 (24)
5	68 (18)
6	10 (3)

Categorical variables are presented as number (%). Continuous variables are presented as mean ± standard deviation.

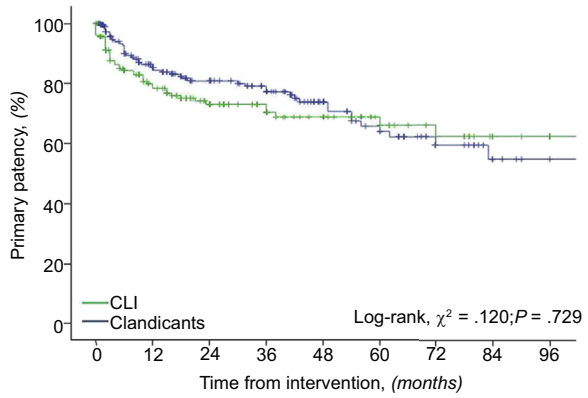
RESULTS

Clinical and anatomic characteristics. Demographic data, comorbidities, and common risk factors for atherosclerosis of the study group are reported in Table I. In 61 (16.7%) patients, AKb was performed after the failure of a previous ipsilateral revascularization (endovascular, n = 44; open surgery, n = 17). CLI was present in 164 (45%) cases; the remaining patients had life-limiting intermittent claudication, defined as class 3 of the Rutherford classification (Table I). At preoperative imaging, according to the TransAtlantic Inter-Society Consensus II classification, 102 (28%) SFA lesions were classified as type C and 262 (78%) as type D; 83 (22.8%) patients had three patent tibial vessels, 184 (50.5%) had two patent tibial vessels, and the remaining 97 (26.6%) had only one vessel with direct inflow to the foot. Median preoperative ABI at the affected limb was 0.4 (range, 0-0.8).

Surgical details. The site of the proximal anastomosis was the common femoral artery in 358 (98.3%) patients; the remaining 6 had the anastomosis at the level of the proximal SFA. The site of the distal anastomosis was the proximal popliteal artery in 295 (81%) patients and distal SFA in 69 (19%). Adjunctive procedures were performed at both runin and runoff levels; as far as runin is concerned, 15 (4.1%) patients had a concomitant endovascular treatment of the ipsilateral iliac axis, whereas 62 (17%) patients had a concomitant open procedure (endarterectomy with patching, n = 57 [15.6%]; femorofemoral crossover bypass, n = 4 [1.1%]; common to deep femoral artery bypass, n = 1 [0.3%]). Adjunctive procedures at the distal level were performed in 56 (15.4%) patients: endarterectomy with patching in 26 (7.1%), endarterectomy with vein cuff in 7 (1.9%), and endovascular treatment of concomitant distal popliteal and tibial disease in 23 (6.3%). The mean duration of the intervention was 122 ± 62 minutes (range, 50-540 minutes).

Early results. Perioperative mortality occurred in three (0.8%) patients: in the hospital (n = 2) due to acute myocardial infarction and after discharge (n = 1) due to fatal arrhythmia. Early thromboses occurred in six (1.6%) patients; all these patients had primary AKb for CLI, in three cases with more than one patent tibial vessel and in three cases with only one patent tibial vessel. Thrombosis rate in CLI was significantly higher than for claudicants (3.5%; $P = .006$). Urgent reintervention was performed in all cases, consisting of surgical thrombectomy in five patients (with concomitant endovascular procedures at popliteal and tibial level in two patients) and below-the-knee composite autologous saphenous vein-HB-ePTFE bypass in one patient. In this last case, recurrent thrombosis occurred, leading to irreversible ischemia and major amputation; in the other five cases, the reintervention was successful. Another major amputation was necessary in the presence of a patent AKb in a patient with sepsis due to infected gangrene of the foot. The cumulative rate of perioperative amputations was 0.5% (1.2% in CLI patients; $P = .1$ in comparison with claudicants). No major systemic complications occurred; there were six (1.6%) major local complications requiring surgical revision in five cases (drainage of hematoma, n = 3; dehiscence of the distal anastomosis with redo anastomosis, n = 1; dehiscence of the inguinal surgical wound with secondary closure, n = 1). The remaining patient developed a severe lymphangitis of the limb, requiring a prolonged hospitalization for medical treatment and physiotherapy. The cumulative rate of early reinterventions was 3% (11 cases). Mean hospital stay was 7.1 ± 5.1 days. Median ABI value at discharge was 0.8 (range, 0-1; $P < .001$ in comparison with preoperative values). Medical treatment at discharge consisted of single antiplatelet therapy in 153 (42%) patients, double antiplatelet therapy in 164 (45%), and oral anticoagulants in 47 (13%). Anticoagulants were more frequently used in patients with CLI ($P = .01$ in comparison with claudicants), and there was a trend toward a more frequent use in patients undergoing reintervention ($P = .07$ in comparison with patients operated on for primary intervention).

Follow-up results. All patients who survived the operation entered the follow-up. Median duration of follow-up was 28 months (range, 1-168 months); 358 (99.2%) patients had regular postoperative follow-up visits. The median cumulative follow-up index for survival was 0.75 (range, 0.05-1). During follow-up, 58 (16.1%) deaths were recorded; the cause of death was cardiac in 28 cases and cancer in 12 patients. Two patients suffered from fatal sepsis, whereas pulmonary embolism, stroke, and car accident were the causes of death in one patient each. Finally, the cause of death was unknown in 13 patients. Estimated survival at 5 years was 75.3% (SE, 0.03). Significant restenosis at the distal anastomotic site was found in 10 (2.8%) patients who underwent endovascular treatment of their anastomotic lesions; the treatment was successful in two patients, whereas in the remaining eight cases, late thrombosis of the bypass occurred. Overall, there were 85 (23.5%) thromboses during follow-up. Estimated 5-year primary patency was 64% (SE, 0.04; Fig 1); the corresponding figure in terms of assisted primary patency was 65% (SE, 0.035). In 37 cases, a secondary intervention to treat graft thrombosis was required using open thrombectomy plus patch or angioplasty of the anastomosis (n = 12), intra-arterial locoregional thrombolysis with eventual additional angioplasty of the anastomosis (n = 10), redo bypass using autologous vein (n = 8), or redo bypass using HB-ePTFE graft again (n = 7). In another 41 patients, the occlusion led to mild to moderate intermittent claudication, and medical treatment was decided on. In this subgroup of patients, eight had had a procedural adjunct at the inflow site that was still performing well at the time of the AKb thrombosis detection. In seven patients, the occlusion was caused by graft infection, for an overall infection rate of 1.9%; in five, HB-ePTFE graft was excised without replacement, whereas in two cases, an autologous saphenous vein bypass was performed after graft excision. Secondary patency rate at 5 years was 74.5% (SE, 0.03; Fig 2). Eleven (3%) major amputations occurred during follow-up, in all but one case at the thigh level. The primary intervention had been performed for CLI in nine of those patients (in one case with patent bypass for severe foot and leg infection; 5.5%) and for claudication in the remaining two (1%). The rate of limb preservation at 5 years was 95% (SE, 0.02); the corresponding figure in terms of amputation-free survival was 74% (SE, 0.04). Limb preservation rates at 5 years were 97.5% in claudicants and 91.5% in CLI patients ($P = .008$, log-rank = 7). The clinical status, the type of



No. at risk	360	239	172	135	89	61	37	20	13
Patency, (%)	98	82	77.5	74	71	64	60	58	58
S.E.	0.7	2	2	3	3	4	4	5	5
95%CI	96.2-99.2	77.7-85.9	72.5-81.8	68.6-79.1	65.6-76.9	57.7-71.3	51.9-68.1	48.2-66.7	48.2-66.7

Fig 1. Kaplan-Meier estimate of primary patency stratified for clinical status: critical limb ischemia (*CLI*) vs claudicants. At the bottom of the figure, the overall rate of primary patency for the entire cohort is reported. *CI,* Confidence interval; *S.E.,* standard error.

intervention, and the proximal or distal adjuncts were not significant parameters of AKb failure. In contrast, gender, diabetes, the runoff status, and the kind of postoperative medical treatment entered the multivariable analysis for primary patency during follow-up (Table II); only postoperative medical treatment was independently associated with that outcome at multivariable analysis (Table III).

DISCUSSION

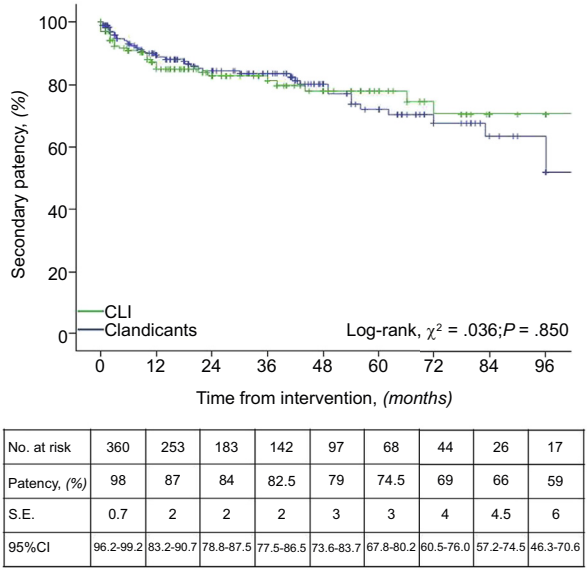
The optimal management of chronic obstructive disease of the SFA is still debatable. Historically, open surgical treatment with AKb represented for many years the only available option, providing excellent results in the perioperative period and in the long-term setting. In more recent years, endovascular techniques have been increasingly used also in the femoropopliteal region, at the beginning only for the treatment of short and anatomically favorable lesions and then also in the presence of long, complex occlusions, to the point that in many centers, they are used as the first-line treatment strategy in all patients with SFA disease.

However, the longer and the more complex lesions treated with endovascular surgery are, the poorer the results tend to be in the long-term period, independent of the strategies and the devices used. Data from recent reports with the use of different devices (drug-eluting balloons, drug-eluting stents, covered and uncovered stents) in the treatment of SFA lesions longer than 20 cm showed a significant paucity of results at a follow-up time longer than 1 year, whereas the few studies with a longer follow-up yielded poor results in terms of patency of the treated segment.[9,14,15,31]

As a consequence, there is agreement also from "endo-enthusiastic" interventionalists that the real challenge for endovascular surgery is the treatment of long lesions and chronic total occlusions of the SFA.[13] In such situations, a surgical bypass at the above-the-knee level can still represent an effective option, with satisfactory follow-up results in terms of graft patency as reported in Table IV, symptom relief, and limb preservation.[3,4,32]

Autologous saphenous vein is considered the material of choice in infrainguinal surgical revascularizations; however, although there is general agreement on its use in the below-knee and tibial setting, in AKb, a large proportion of interventions are performed with a prosthetic graft in other European countries, also in the presence of an available saphenous vein.[33] Furthermore, the recent guidelines from the Italian Society for Vascular and Endovascular Surgery suggested a primary role of prosthetic graft for above-the-knee revascularization, thus preserving the autologous GSV for eventual further distal interventions. Having said that, despite a large meta-analysis of the Cochrane society showing that ePTFE is outscored by the autologous GSV, several reports published conflicting data regarding the performance of ePTFE for AKb, with patency rate at 5 years ranging from 39% to 50% at best in the most recent analyses. Moreover, significantly better results were reported with the use of Dacron graft than with the use of ePTFE in at least three multicentric randomized studies, with patency rates for ePTFE ranging from 50% at 3 years to 35% at 5 years.[35-37] A recent meta-analysis confirmed these results, showing a nonsignificant trend toward better performance for Dacron graft in the midterm and long-term setting.[38] However, none of them included the new-generation HB-ePTFE graft, which was the focus of our registry. Because of the limited number of AKb grafts with the use of autologous GSV performed in the participating centers, we were not able to compare the results of HB-ePTFE with those of vein; anyway, our 67% primary patency rate looks promising, and it is not so far away from a historical comparison focusing on the long-term outcomes of the GSV reported in the literature.[39,40] Furthermore, we should take into account that we treated patients with CLI (eg, nearly half of the cases in our registry), who otherwise have been excluded from the most recent comparative analysis with Dacron.[37] Last but not least, our data compare favorably with the recent series reporting the use of new grafts, which yielded satisfactory results only in the early follow-up.[41,42]

When it comes to the identification of independent risk factors, several variables have been reported to influence graft patency. In our experience, the only independent risk factor for primary patency was the type of postoperative regimen; specifically, antiplatelet therapy did better



No. at risk	360	253	183	142	97	68	44	26	17
Patency, (%)	98	87	84	82.5	79	74.5	69	66	59
S.E.	0.7	2	2	2	3	3	4	4.5	6
95%CI	96.2-99.2	83.2-90.7	78.8-87.5	77.5-86.5	73.6-83.7	67.8-80.2	60.5-76.0	57.2-74.5	46.3-70.6

Fig 2. Kaplan-Meier estimate of secondary patency stratified for clinical status: critical limb ischemia (*CLI*) vs claudicants. At the bottom of the figure, the overall rate of secondary patency for the entire cohort is reported. *CI,* Confidence interval; *S.E.,* standard error.

in comparison to warfarin. Being a registry, we did not have strict criteria for the choice of the postoperative type of treatment, and our result could be the consequence of the inclusion bias (patients with more advanced clinical status and undergoing reintervention were preferentially treated with oral anticoagulants). However, this result finds translational support from large trials to single-center experience. All these studies have already proven that prosthetic bypasses benefit from postoperative antiplatelet therapy, whereas in venous bypasses, better results may be achieved with postoperative oral anticoagulation.[43,44] We did not find any other factor significantly affecting long-term graft patency; there was a trend toward poorer results in patients with poor runoff, whereas surprisingly, the clinical status was not associated with a worse graft patency. As far as the rate of limb preservation is concerned, we had excellent 5-year results, not only in claudicants but also in patients with CLI, who suffered from major amputation in about 5% of the cases. This is, in our opinion, an important finding from either a clinical or a technical point of view. First, in most of the published series, the rates of amputations in CLI largely exceed 10%.[18,44] Second, the major amputation occurred in almost all CLI patients with poor runoff, whereas amputation rate among claudicants was negligible, similar to that reported in other studies, confirming the long-term safety of the procedure also in non-CLI patients.[34] In our experience, only about 50% of late thromboses caused a worsening of preoperative clinical status and required a reintervention, whereas the other 50% of the patients developed only mild to moderate symptoms and were medically managed. Similarly, Bosma et al[32] concluded in their study that the necessity of graft revision after thrombosis in the absence of CLI seems to be questionable. Furthermore, the fact that major amputation was required after multiple thrombectomies in most of the cases suggests

Table II. Univariate analysis for 5-year primary patency

Variable	Primary patency, %	Log-rank	*P*
Gender			
Female	42	1.8	.1
Male	67		
Type of intervention			
Primary	68	0.6	.4
Reintervention	57		
Hypertension			
Yes	66	0.01	.9
No	63.5		
Coronary artery disease			
Yes	63	0.01	.9
No	64.5		
Diabetes			
Yes	64.5	1.8	.1
No	72		
Clinical status			
Intermittent claudication	63	0.7	.4
CLI	65		
Runoff status			
1 vessel	53.5	3.8	.05
>1 vessel	67		
Runin adjunctive procedures			
Yes	66.5	0.3	.5
No	63.5		
Runoff adjunctive procedures			
Yes	64.5	0.2	.6
No	63		
Postoperative medical treatment			
Single antiplatelet	70.5	8.5	.01
Double antiplatelet	65		
Oral anticoagulants	48		

CLI, Critical limb ischemia.

Table III. Multivariable analysis for primary patency

Variable	95% CI	HR	*P*
Gender	0.8-2.3	1.3	.2
Diabetes	0.9-2.2	1.4	.08
Runoff status	1.1-2.9	1.8	.06
Postoperative medical treatment	1.2-2.1	1.6	.01

CI, Confidence interval; *HR,* hazard ratio.

Table IV. Summary of the available literature reporting on long and complex femoropopliteal lesions

Author	Year of publication	Study type	Procedure type	Lesion length, cm or TASC II type	1 year		3 years		5 years		10 years	
					PP, %	LS, %	PP, %	LS, %	PP, %	LS, %	PP, %	LS, %
Endovascular surgery												
Zeller et al[6]	2014	Prospective, multicenter, single-arm	HB-SG	TASC C, D	67	NA	NA	NA	NA	NA	NA	NA
Scheinert[13]	2012	Prospective, multicenter, single-arm	PTA-DEB	26.4	91.1	100	NA	NA	NA	NA	NA	NA
Schmidt et al[15]	2016	Retrospective, single center	PTA-DEB	24 ± 10	89.2	100	53.7	97.9	NA	NA	NA	NA
Davaine et al[8]	2015	Prospective, single center	DES	TASC C, D	52.5	NA	NA	NA	NA	NA	NA	NA
Palena et al[9]	2017	Prospective, single center	Stenting	TASC C, D	94.1	100	NA	NA	NA	NA	NA	NA
Bypass surgery					77	NA	57.6	NA	38.6	NA	NA	NA
Devine et al[35]	2004	Multicenter, randomized trial	PTFE (vs Dacron)	NSR	66	NA	49	NA	41	74	NA	NA
van Det et al[37]	2009	Multicenter, randomized trial	PTFE (vs Dacron)	NSR	NA	NA	NA	NA	36	NA	28	94
Assadian et al[42]	2015	Prospective, multicenter, single-arm	Double-layer (PTFE + polyester)	NSR	85.6	100	NA	NA	NA	NA	NA	NA
Present study	2017	Multicenter registry	HB-ePTFE	TASC C, D	82	97	74	95	64	95	58	95

DES, Drug-eluting stent; *HB-ePTFE*, heparin-bonded expanded polytetrafluoroethylene graft; *HB-SG*, heparin-bonded stent graft; *LS*, limb salvage; *NA*, not available; *NSR*, not specifically reported; *PP*, primary patency; *PTA-DEB*, percutaneous transluminal angioplasty with drug-eluting balloon; *PTFE*, polytetrafluoroethylene; *TASC II*, TransAtlantic Inter-Society Consensus II.

that this graft might offer better opportunity to be reopened more easily the previous-generation ePTFE grafts. Actually, we are not able to demonstrate it on a scientific basis; nevertheless, this may have been due to the thrombogenicity reduction of heparin at the anastomotic sites. Our position finds support in a previous study. In an experimental study, thrombogenicity reduction was reported to be related to the reduction of the development of intimal hyperplasia because heparin is known to reduce the migration of smooth muscle cells that are responsible for the formation of intimal hyperplasia.[45] All these data seem to contradict what was suggested by other authors, that is, that the late failure of the graft can precipitate the clinical evolution, leading a stable intermittent claudication to an unstable CLI.[18] A limited number of thromboses were caused by graft infection; the overall infection rate was about 2%, comparing well with that reported in the literature, ranging from 3% to 12% of all infrainguinal revascularizations.[18,46] However, infections remain a fearful complication of synthetic grafts in infrainguinal interventions, considering that a major amputation was necessary in the presence of a patent graft in two cases of infection.

Limitations. This analysis has some limitations. All of the analyzed data were derived from a registry and analyzed retrospectively; furthermore, it lacks comparative groups of patients treated with endovascular treatment or GSV. Second, because all patients enrolled in this registry underwent surgical bypass, it is supposed they have been deemed fit surgical candidates. Last, criteria for selection of patients and postoperative treatment varied among the different centers. However, these limitations are present in all previous similar studies. In contrast, follow-up was performed consistently at 3 years and included clinical visits and radiologic examinations. Moreover, outcomes adhered systematically to the proposed guidelines, and we present long-term outcomes analyses that compare well with other studies.

CONCLUSIONS

In our experience, the following clinically relevant findings could be made:

- In a "daily practice" real-world setting, AKb showed satisfactory long-term results for long or complex lesions of the SFA.

- A significant positive trend on primary patency rate was observed in patients who received antiplatelet therapy; this is a finding that could not be generalizable to all patients who undergo AKb. Indeed, a prospective cohort of patients would be needed to define which patients, in terms of anatomic and surgical characteristics, will benefit from dual antiplatelet therapy.
- In a cohort that includes half of patients at high risk for limb loss (eg, CLI), the low rate of major amputations makes it a satisfactorily safe and effective intervention.

For all these reasons, in our opinion, AKb is a valid and viable first-line alternative to endovascular surgery in long or complex lesions of the SFA.

AUTHOR CONTRIBUTIONS

Conception and design: GP, WD, RP, PC, CP
Analysis and interpretation: GP, WD, RP, PC, CP
Data collection: GP, WD, RP, PC, CP
Writing the article: GP, WD, RP, PC, CP
Critical revision of the article: GP, WD, RP, PC, CP
Final approval of the article: GP, WD, RP, PC, CP
Statistical analysis: GP, WD
Obtained funding: Not applicable
Overall responsibility: GP
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REFERENCES

1. Goodney PP, Beck AW, Nagle J, Welch HG, Zwolak RM. National trends in lower extremity bypass surgery, endovascular interventions, and major amputations. J Vasc Surg 2009;50:54-60.
2. Bisdas T, Borowski M, Torsello G; First-Line Treatments in Patients With Critical Limb Ischemia (CRITISCH) Collaborators. Current practice of first-line treatment strategies in patients with critical limb ischemia. J Vasc Surg 2015;62:965-73.
3. Antoniou GA, Chalmers N, Georgiadis GS, Lazarides MK, Antoniou SA, Serracino-Inglott F, et al. A meta-analysis of endovascular versus surgical reconstruction of femoropopliteal arterial disease. J Vasc Surg 2013;57:242-53.
4. Abu Dabrh AM, Steffen MW, Asi N, Undavalli C, Wang Z, Elamin MB, et al. Bypass surgery versus endovascular interventions in severe or critical limb ischemia. J Vasc Surg 2016;63:244-53.
5. Sachs T, Pomposelli F, Hamdan A, Wyers M, Schermerhorn M. Trends in the national outcomes and costs for claudication and limb threatening ischemia: angioplasty vs bypass graft. J Vasc Surg 2011;54:1021-31.
6. Zeller T, Peeters P, Bosiers M, Lammer J, Brechtel K, Scheinert D, et al. Heparin-bonded stent-graft for the treatment of TASC II C and D femoropopliteal lesions: the Viabahn-25 cm trial. J Endovasc Ther 2014;21:765-74.
7. Tepe G, Laird J, Schneider P, Brodmann M, Krishnan P, Micari A, et al. Drug-coated balloon versus standard percutaneous transluminal angioplasty for the treatment of superficial femoral and popliteal peripheral artery disease: 12-month results from the IN.PACT SFA randomized trial. Circulation 2015;131:495-502.
8. Davaine JM, Querat J, Kaladji A, Guyomarch B, Chaillou P, Costargent A, et al. Treatment of TASC C and D femoropoliteal lesions with paclitaxel eluting stents: 12 month results of the STELLA-PTX registry. Eur J Vasc Endovasc Surg 2015;50:631-7.
9. Palena LM, Diaz-Sandoval LJ, Sultato E, Brigato C, Candeo A, Brocco E, et al. Feasibility and 1-year outcomes of subintimal revascularization with Supera stenting of long femoropopliteal occlusions in critical limb ischemia: the "Supersub" study. Catheter Cardiovasc Interv 2017;89:910-20.
10. Müller-Hülsbeck S, Keirse K, Zeller T, Schroë H, Diaz-Cartelle J. Twelve-month results from the MAJESTIC trial of the Eluvia paclitaxel-eluting stent for treatment of obstructive femoropopliteal disease. J Endovasc Ther 2016;23:701-7.
11. Bontinck J, Goverde P, Schroë H, Hendriks J, Maene L, Vermassen F. Treatment of the femoropopliteal artery with the bioresorbable REMEDY stent. J Vasc Surg 2016;64:1311-9.
12. Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FG, Gillespie I, et al. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: analysis of amputation free and overall survival by treatment received. J Vasc Surg 2010;51(Suppl):18S-31S.
13. Scheinert D. Treatment paradigms for the superficial femoral artery: are they a-changin? JACC Cardiovasc Interv 2012;5:339-40.
14. Lammer J, Zeller T, Hausegger KA, Schaefer PJ, Gschwendtner M, Mueller-Huelsbeck S, et al. Sustained benefit at 2 years for covered stents versus bare-metal stents in long SFA lesions: the VIASTAR trial. Cardiovasc Intervent Radiol 2015;38:25-32.
15. Schmidt A, Piorkowski M, Görner H, Steiner S, Bausback Y, Scheinert S, et al. Drug-coated balloons for complex femoropopliteal lesions: 2-year results of a real-world registry. JACC Cardiovasc Interv 2016;9:715-24.
16. Dake MD, Ansel GM, Jaff MR, Ohki T, Saxon RR, Smouse HB, et al. Durable clinical effectiveness with paclitaxel-eluting stents in the femoropopliteal artery: 5-year results of the Zilver PTX randomized trial. Circulation 2016;133:1472-83.
17. Klinkert P, Post PN, Breslau PJ, van Bockel JH. Saphenous vein versus PTFE for above-knee femoropopliteal bypass. A review of the literature. Eur J Vasc Endovasc Surg 2004;27:357-62.
18. Berglund J, Björck M, Elfström J; SWEDVASC Femoropopliteal Study Group. Long-term results of above knee femoro-popliteal bypass depend on indication for surgery and graft-material. Eur J Vasc Endovasc Surg 2005;29:412-28.
19. Pereira CE, Albers M, Romiti M, Brochado-Neto FC, Pereira CA. Meta-analysis of femoropopliteal bypass grafts for lower extremity arterial insufficiency. J Vasc Surg 2006;44:510-51.
20. Twine CP, McLain AD. Graft type for femoro-popliteal bypass surgery. Cochrane Database Syst Rev 2010;5:CD001487.
21. Schanzer A, Hevelone N, Owens CD, Belkin M, Bandyk DF, Clowes AW, et al. Technical factors affecting autogenous vein graft failure: observations from a large multicenter trial. J Vasc Surg 2007;46:1180-90.
22. Conte MS. Critical appraisal of surgical revascularization for critical limb ischemia. J Vasc Surg 2013;57(Suppl):8S-13S.
23. Battaglia G, Tringale R, Monaca V. Retrospective comparison of a heparin bonded ePTFE graft and saphenous vein for infragenicular bypass: implications for standard treatment protocol. J Cardiovasc Surg (Torino) 2006;47:41-7.
24. Dorigo W, Di Carlo F, Troisi N, Pratesi G, Innocenti AA, Pulli R, et al. Lower limb revascularization with a new bioactive

prosthetic graft: early and late results. Ann Vasc Surg 2008;22:79-87.
25. Dorrucci V, Griselli F, Petralia G, Spinamano L, Adornetto R. Heparin-bonded expanded polytetrafluoroethylene grafts for infragenicular bypass in patients with critical limb ischemia: 2-year results. J Cardiovasc Surg (Torino) 2008;49:145-9.
26. Pulli R, Dorigo W, Castelli P, Dorrucci V, Ferilli F, De Blasis G, et al. Midterm results from a multicenter registry on the treatment of infrainguinal critical limb ischemia using a heparin-bonded ePTFE graft. J Vasc Surg 2010;51:1167-77.
27. Dorigo W, Pulli R, Piffaretti G, Castelli P, Griselli F, Dorrucci V, et al. Results from an Italian multicentric registry comparing heparin-bonded ePTFE graft and autologous saphenous vein in below-knee femoro-popliteal bypasses. J Cardiovasc Surg (Torino) 2012;53:187-94.
28. Dorigo W, Piffaretti G, Pulli R, Castelli P, Pratesi C; PROPATEN Italian Registry Group. A multicenter predictive score for amputation-free survival for patients operated on with an heparin-bonded ePTFE graft for critical limb ischemia. World J Surg 2017;41:306-13.
29. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG; TASC II Working Group. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Eur J Vasc Endovasc Surg 2007;33(Suppl 1):S1-75.
30. von Allmen RS, Weiss S, Tevaearai HT, Kuemmerli C, Tinner C, Carrel TP, et al. Completeness of follow-up determines validity of study findings: results of a prospective repeated measures cohort study. PLoS One 2015;10:e0140817.
31. Tran K, Ullery BW, Kret MR, Lee JT. Real-world performance of paclitaxel drug-eluting bare metal stenting (Zilver PTX) for the treatment of femoropopliteal occlusive disease. Ann Vasc Surg 2017;38:90-8.
32. Bosma J, Turkçan K, Assink J, Wisselink W, Vahl AC. Long-term quality of life and mobility after prosthetic above-the-knee bypass surgery. Ann Vasc Surg 2012;26:225-33.
33. Lees T, Troëng T, Thomson IA, Menyhei G, Simo G, Beiles B, et al. International variations in infrainguinal bypass surgery—a VASCUNET report. Eur J Vasc Endovasc Surg 2012;44:185-92.
34. Peinetti F, Bellandi G, Cappelli A, Castagnola M, Dorigo W, Gargiulo M, et al. Patologia ostruttiva cronica aorto-iliaca e delle arterie degli arti inferiori. Ital J Vasc Endovasc Surg 2015;22(Suppl 2):25-68.
35. Devine C, McCollum C; North West Femoro-Popliteal Trial Participants. Heparin-bonded Dacron or polytetrafluorethylene for femoropopliteal bypass: five-year results of a prospective randomized multicenter clinical trial. J Vasc Surg 2004;40:924-31.
36. Jensen LP, Lepäntalo M, Fossdal JE, Røder OC, Jensen BS, Madsen MS, et al. Dacron or PTFE for above-knee femoropopliteal bypass. A multicenter randomised study. Eur J Vasc Endovasc Surg 2007;34:44-9.
37. van Det RJ, Vriens BH, van der Palen J, Geelkerken RH. Dacron or ePTFE for femoro-popliteal above-knee bypass grafting: short- and long-term results of a multicentre randomised trial. Eur J Vasc Endovasc Surg 2009;37:457-63.
38. Takagi H, Goto SN, Matsui M, Manabe H, Umemoto T. A contemporary meta-analysis of Dacron versus polytetrafluoroethylene grafts for femoropopliteal bypass grafting. J Vasc Surg 2010;52:232-6.
39. AbuRahma AF, Robinson PA, Holt SM. Prospective controlled study of polytetrafluoroethylene versus saphenous vein in claudicant patients with bilateral above knee femoropopliteal bypasses. Surgery 1999;126:594-601.
40. Johnson WC, Lee KK. A comparative evaluation of polytetrafluoroethylene, umbilical vein, and saphenous vein bypass grafts for femoral-popliteal above-knee revascularization: a prospective randomized Department of Veterans Affairs cooperative study. J Vasc Surg 2000;32:268-77.
41. Lumsden AB, Morrissey NJ; Comparison of Safety and Primary Patency Between the FUSION BIOLINE Heparin-Coated Vascular Graft and EXXCEL Soft ePTFE (FINEST) Trial Co-investigators. Randomized controlled trial comparing the safety and efficacy between the FUSION BIOLINE heparin-coated vascular graft and the standard expanded polytetrafluoroethylene graft for femoropopliteal bypass. J Vasc Surg 2015;61:703-12.
42. Assadian A, Eckstein HH; Peripheral Bypass Grafting: Prospective Evaluation of FUSION Vascular Graft for Above Knee Targets (PERFECTION) Study Group. Outcome of the FUSION vascular graft for above-knee femoropopliteal bypass. J Vasc Surg 2015;61:713-39.
43. Belch JJ, Dormandy J; CASPAR Writing Committee. Results of the randomized, placebo-controlled clopidogrel and acetylsalicylic acid in bypass surgery for peripheral arterial disease (CASPAR) trial. J Vasc Surg 2010;52:825-33.
44. Klingelhoefer E, Bergert H, Kersting S, Ludwig S, Weiss N, Schönleben F, et al. Predictive factors for better bypass patency and limb salvage after prosthetic above-knee bypass reconstruction. J Vasc Surg 2016;64:380-8.
45. Heyligers JM, Lisman T, Verhagen HJ, Weeterings C, de Groot PG, Moll FL. A heparin-bonded vascular graft generates no systemic effect on markers of hemostasis activation or detectable heparin-induced thrombocytopenia-associated antibodies in humans. J Vasc Surg 2008;47:324-9.
46. Brothers TE, Robison JG, Elliott BM. Predictors of prosthetic graft infection after infrainguinal bypass. J Am Coll Surg 2009;208:557-61.

Submitted Jun 21, 2017; accepted Sep 7, 2017.

Additional material for this article may be found online at www.jvascsurg.org.

APPENDIX (online only).

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