The role of hybrid femoropopliteal revascularization in high-risk (ASA 3-4) patients: A decade of dual center clinical experience.

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Abbreviations: ABI: Ankle-Brachial Index, Angio-CT: Angio-Computed Tomography, Angio-MRI: Angio-Magnetic Resonance Imaging, ASA: The American Society of Anesthesiologists classification, CFA: Common Femoral Artery, CLI: Critical Limb Ischemia, CLTI: Chronic Limb Threatening Ischemia, CTO: Chronic Total Occlusion, DEB: Drug-Eluting Balloons, DES: Drug-Eluting Stents, EVT: Endovascular Therapy, FP: Femoropopliteal, GLASS: Global Limb Anatomic Staging System, GVG: Global Vascular Guidelines, PAD: Peripheral Arterial Disease, LBP: Limb-Based Patency, PTA: Percutaneous Angioplasty, PLAN: Patient, Limb, ANatomy, SFA: Superficial Femoral Artery, TAP: Target Artery Path, TASC (II): The TransAtlantic Inter-Society Consensus (II).

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ABSTRACT

BACKGROUND:

The present chapter focus on eventual clinical benefit of hybrid revascularizations gathering common femoral artery (CFA) endarterectomy coupled to femoropopliteal endovascular recanalization in high-risk ASA Class 3-4 patients having severe infrainguinal multilevel occlusive disease.

MATERIAL AND METHODS:

From January 2009 until November 2019, a series of 205 hybrid infrainguinal interventions performed in 178 ASA Class 3-4 patients (Rutherford category 2-6 ischemic presentations) were retrospectively analyzed. Patient demographics, specific risk factors, technical characteristics, parallel to patency, limb salvage and survival results were examined during a mean 44.9 months of follow-up. In the whole, long (>15 cm) and intermediate (5-15 cm) CTO were present in 198 (96%) of all ischemic limbs, in parallel to severe CFA atherosclerotic disease. Two or three runoff tibial trunks were evinced in 172 (84%) cases, while moderate-to-severe arterial calcifications were present in 78 (38%) cases.

RESULTS:

Inasmuch the surgical approach was successful in all cases, the endovascular step of all hybrid interventions was technically rewarding in 190 (93%) cases. The postoperative ABI improved (> 1.5) in 75% of cases, while clinical presentations gained at least one Rutherford category in 182 (89%) limbs. The postoperative 30-day mortality rate noted in this specific "high-risk" group of patients was 3.3% The mean hospital stay was 6.2 days (3-14 days) Primary patency estimates revealed 88% (95% CI 84% to 91%) and 66% (95% CI 56% to 75%) at 12 and 60 months, while limb salvage was 93% (95% CI 88% to 95%) and 80% (95% CI 72% to 86%) at the same time intervals, respectively.

Global risk factors alike smoking (p=0.003) and female gender (p=0.001), together with CTOs length (>15 cm / p=0.016), severe calcifications (p=0.049), poor tibial runoff (p=0.018, and p=0.001 for 1, and 0 permeable trunks), the GLASS/FP grade "4" lesions (p=0.039), and the stent length (>6 cm / p=0.001), showed parallel negative influence on primary patency.

CONCLUSION:

Hybrid infrainguinal revascularization may offer beneficial option for treatment options in high-risk ASA 3-4 patients. Careful patient selection and technique planning appear essential for achieving appropriate arterial reconstruction and limb salvage outcome.

INTRODUCTION

Contemporary endovascular treatment for Rutherford category 3-6 clinical presentations [1] gained increasing application including more complex TransAtlantic Inter-Society Consensus (TASC II) “C” and “D” patterns, [2] or by following the recent Global Vascular Guidelines (GVG), the comparable GLASS “grades 2-4” femoropopliteal (FP) atherosclerotic disease. [3] Infrainguinal endovascular recanalization proved encouraging clinical outcome compared to bypass [4, 5] without, [6, 7] or with additional nitinol stenting [8-11] at short, [7-10] equally at long-term follow-up. [11, 12]

The additional hemodynamic involvement of the common femoral artery (CFA) in more complex infrainguinal occlusive presentations [2-4, 10-13] was equally studied however, owing scarcer data in dedicated contemporary literature. [3, 4] While most of these patients are treated either by femoropopliteal bypass, [2-4, 13, 14] or by sole CFA endarterectomy, [14-18] new endovascular reports indicate comparable patency and limb salvage rates with surgery at one year. [3, 19]

The current physical status of these patients remains a major concern in treatment selection. [3, 14] The patient's risk category merely influences clinical outcome, whatever the type of revascularization. [3, 13, 14,15-19] Although most of these analyses focus mainly on anatomical and technical details of revascularizations [2, 4, 13, 14, 16] adding or not parallel risk factor’s assessment, [6-12, 15, 16] very few focus on concomitant patient’s physical status independently scored by each individual co-morbidities. [3, 18, 20]

Endarterectomy for severe CFA atherosclerotic disease revealed excellent safety and efficacy results [2, 3, 13, 18] at mid- [17] and long-term [18] for surgical, [13-17] or hybrid arterial reconstructions. [3, 4, 20, 21]

However, only scarce information is available regarding hybrid revascularization that associates multilevel infra-inguinal TASC "C" and "D" [2] (or equivalent GLASS grades "3" and "4"), [3] total occlusions (CTO). This appears particularly important in treating high-risk ASA "3-4" surgical patients. [19, 20]

The present chapter completes previous published research of our vascular interventional team focusing on the same topic, [22, 23] and adds extended clinical experience, study cohort, and statistical analysis, with updated consultation on this subject.

METHODS

Study design

We performed a retrospective analysis of patients treated by combined surgical CFA endarterectomy coupled to endovascular SFA/popliteal revascularization (files and iconography) performed in two associated institutions between January 2009 and November 2019. All these “hybrid” interventions were reevaluated, and results included in an “intention-to-treat” analysis. Twenty-two patients having previous inferior limb revascularizations (bypass or EVT), or featuring unsystematic clinical and duplex postoperative follow-up, were excluded from analysis.

The present study analyzes 205 ischemic limbs (Rutherford category 2-6) [1] revascularized in 178 “high-risk”, ASA Class 3-4 [19] patients. All patients received comparable hybrid surgical and endovascular interventions completed by the same interventional team. All patients availed complete information about the type of treatment to be applied and shared full informed consent. In 27 cases, staged bilateral interventions were required. There were 79% (140/178) men and the mean age was 78.1 (in the range 43 to 93 years). Patient demographics, risk factors and ischemic features are summarized in **Tables I** & **II**. Inclusion criteria focused on significant atherosclerotic CFA disease (>70% stenosis or occlusions), that associates multilevel SFA/popliteal occlusive lesions in all cases. Exclusion criteria gathered CFA or femoropopliteal aneurismal disease, post-traumatic or entrapment syndromes, previous infrainguinal bypass, PTA or stenting with secondary thrombosis, acute ischemia, Iodine contrast allergy, dementia and/or disagreement to follow consent, or postoperative schedule for treatment.
In a majority of 139 (68%) limbs, long femoro-popliteal occlusions (>15 cm) were present (**Table III**). The number of included claudicants versus chronic limb-threatening ischemia (CLTI) limbs was comparable (57% vs. 43%, respectively).
Two or three runoff tibial trunks were evinced in 172 (84%) cases, while one or none permeable vessel were found in 33 (16%) of limbs. Moderate-to-severe arterial calcifications [13] were present in 78 (38%) cases (**Table III**).

Technique of hybrid surgical and endovascular interventions
All patients were taking aspirin (160 mg/d) or clopidogrel (75 mg/d) at least 72 hours before the procedure.
First approach focused on common femoral artery surgical endarterectomy and was performed in all cases following common procedural standards. [6, 12, 16, 23] Patches were routinely employed for CFA reconstruction (23% synthetic and 77% using venous material). Associated infrapopliteal endovascular recanalization (endoluminal or subintimal) was added in each patient by targeting SFA and/or popliteal diseased segments. [6, 11, 23] The endovascular stage was addressed via direct arterial punctures following initial surgical reconstruction. Patients currently received 3.500-5.000 heparin units administrated before CFA clamping, without protamine reversion at the end of the procedure. All trans-catheter femoropopliteal recanalizations were initiated by crossing the « lowest-resistance » (commonly extra-luminal) CTO plane. [6-9, 23] This step was mainly achieved by using curved 0.035-inch. hydrophilic guidewire (Terumo-Japan) passages. Subintimal procedures (**Fig. 1-3**) were carried out following previously reported protocols. [6-9, 16, 22, 23] Downstream re-entry into the native arterial lumen was confirmed by brief contrast injections in every extra-luminal revascularization (**Fig. 4-6**). In 12 (6%) cases, cutting balloons (Boston-USA) were used to negotiate dense calcifications mainly located in the adductor’s tunnel. Selective self-expanding nitinol stents (various manufacturers) were employed only if persistence of >30% residual stenosis was detected on angiographic control, or since femoropopliteal irregular « coralliform » calcifications, or wall « elastic-recoils » were present (**Fig. 7**). The length of stents was adapted upon each atherosclerotic presentation favoring the less extended implants whenever feasible. In this series no other recanalization devises such as endarterectomy, or lithotrity techniques were employed. Drug eluted technology was only seldom associated,

mainly in recent years of this trial's inclusion period. In order to avoid discrepancies in follow-up, a separate group of 29 DEB, or DES procedures were not included in the present cohort. In 14% of the studied cases, additional tibial, or popliteal retrograde accesses were needed. Complementary details of endovascular procedures are depicted in **Table IV**. All patients continued lifelong aspirin therapy (80 mg/d), which was doubled by clopidogrel during 3 months after the procedure.

Definitions

The Rutherford clinical stratification [(1)] was used to define different initial inferior limb ischemic presentations, while the initial TASC II classification [(2)] (analyzing the femoropopliteal atherosclerotic disease in the previous studies of our team) [(22, 23)] was updated with the GLASS/FP atherosclerotic morphologic grading scale. [(3)] GLASS/FP, was retrospectively applied for defining specific anatomic grades of infra-inguinal arterial occlusive lesions. [(3)] (**Table III**).

All included patients were reviewed by systematic preoperative multidisciplinary evaluation, including surgical and anesthetic assessment. They all exhibit equivalent ASA grade 3 or 4 [(19)] clinical status on regular anesthesiologic evaluation. All included subjects were evinced as "high-risk" candidates for exclusive "inflow" and/or "outflow" surgical interventions.

Technical success was defined as regaining of a straight femorotibial arterial flow, without 30% or more residual stenosis, distal embolism, intimal flaps, or "in situ" thrombosis of the treated segment.

PAD's initial diagnostic was sustained by clinical history and examination, ABI, Duplex, and preoperative Angio-CT or Angio-MRI imaging. Primary patency represented the achievement of patent arterial axes without recurrent stenosis or the need for further intervention. Secondary patency denoted flow restoration after transitory femoropopliteal occlusion without the need for complementary surgical gestures, while the loss of patency (and follow-up cessation) acknowledged the need for a surgical femoro-distal bypass as to treat secondary infrainguinal arterial thrombosis.

Statistical analysis

All results were reported in an "intention to treat" analysis. The Kaplan-Meier life-table method was employed to determine the outcome of the primary, secondary patency and limb salvage rates. These parameters were considered as markers of follow-up for all hybrid interventions. Specific risk factors for patency were separately analyzed at twenty-four months in the follow-up by rigorous standardization using the two-sided Fischer exact test (**Tables I-VI**). All "*p"* values < 0.05 were defined to have statistical significance. All data were incorporated in the "Graph Pad In-Stat" statistics software.

RESULTS

Patients characteristics are described in **Table I**. Following the Rutherford classification [(1)] among all 205 treated limbs 7% expressed Category 2, 50% Category 3, 28% Category 4 and 15% Category 5 and 6 features (**Table II**). Surgical CFA endarterectomy adding SFA and/or popliteal endovascular recanalizations were performed in all cases throughout same

approaches. This cohort of patients gathered 2% GLASS / FP [3] grade "1", other 48% grade "2", additional 39% grade "3", and 35% grade "4" FP lesions (**Table III**). Among these latest grade "4" FP presentations, 12% exhibited severe CFA (>70%) stenosis and 25% complete CFA occlusions. In the whole, long (>15 cm) and intermediate (5-15 cm) CTO (**Fig. 2, 6**) were present in 198 (96%) of all ischemic limbs.

Long SFA occlusions extending to popliteal segments (**Fig. 6**) were noted in 80 (39%) of cases. Mean CTO length treated by endovascular way was 16 cm (range, 2-53 cm), slightly higher than similar reports in the literature [9-11]. Single stenting was used in nearly half (52%) of interventions while bare angioplasty sufficed in 16% of treated limbs (**Table IV**). Two stents (29%) or exceptionally three stents (2%) per intervention were implanted in other 65 (32%) of cases. In the sum, 172 stents were placed in this whole cohort, having 5.3 cm (range, 2-10 cm) mean length (**Table IV**).

Associated infragenicular angioplasties (23%) were performed either during the same intervention (**Fig. 8**) (17%), or in staged approaches (6%) following 2-5 days interval (staged contrast media dispensation in patients with severe renal insifficiency).

Flush atherosclerotic ostial lesions in the SFA (64%) also in the profunda femoris (68%) were surgically treated in comparable proportions during the initial surgical stage of interventions (Table III).

The endovascular step of all hybrid interventions was technically successful in 190 (93%) cases.

Over the initially 15 unsuccessful femoropopliteal endovascular recanalizations, 9 failed because of the inability to re-enter the distal true lumen, 2 others expressed impassable calcific deposits, while in 2 others we noted impossible initiation of the subintimal dissection plane. For the remnant 2 cases, a subsequent unsealed arterial perforation and one « elastic recoil » with sudden collapse of the extraluminal channel and early thrombosis (**Fig. 9**), were noted.

The mean follow-up was 44.9 months (ranging from 1 week to 84 months).

Globally in 75% of cases ABI improved significantly (> 1.5) in the postoperative period (**Table II**), while clinical presentation gained at least one Rutherford category in 182 (89% limbs). The mean hospital stay was 6.2 days (3-14 days) whereas 10 cases (5%) were readmitted during the first postoperative month (4 cardiac, 2 respiratory, 3 renal and 1 digestive transitory dysfunctions).

The 30-day mortality rate in this homogeneous 178 "high-risk" (ASA 3-4) group of patients was 3.3% (6 patients died within the first month due to: 3 myocardial infarctions, 2 major respiratory insufficiencies after bilateral pneumonia and 1 multiple organ failure after ischemic colitis). Eighteen separate patients died during the follow-up (eleven of them beyond 2 years following initial revascularization) and nine others were lost from investigation.

During the follow-up period 43 (21%) limbs (regardless the CFA surgical treatment) developed either SFA or popliteal >70% restenosis, or iterative femoropopliteal occlusions (**Table III**). We documented 9 (4%) stent fractures, all in the 6 cm or longer stents group (**Table IV**). All fractures referred to stents placed at the femoropopliteal junction (the "Hunter's channel"), or along the "P1" popliteal segment.

Primary patency estimates (**Fig. 10**) were: 88% (95% CI 84% to 91%), 78% (95% CI 71% to 83%), 71% (95% CI 63% to 78%), 70% (95% CI 61% to 77%) and 66% (95% CI 56% to

75%) at 12, 24, 36, 48, and 60 months, with steady values afterwards. Secondary patency (**Fig. 10**) rates showed 90% (95% CI 85% to 93%), 82% (95% CI 75% to 87%), 78% (95% CI 70% to 84%), 77% (95% CI 68% to 83%), 75% (95% CI 66% to 82%), while limb salvage was 93% (95% CI 88% to 95%), 87% (95% CI 81% to 91%), 81% (95% CI 73% to 88%), and steady 80% (95% CI 72% to 86%) afterwards, at the same time intervals, respectively. An example of iterative endovascular revascularization for secondary patency regain is depicted in **Fig. 11**.

A Log-rank comparison between Kaplan-Meier limb salvage curves (**Fig. 12**) in claudicants versus CLTI patients found significant differences (HR 2.46, 95% CI 1.206 to 5.032, p=0.0134).

Amputation-free survival rates were 95%, 89%, 84%, 74% and 51% at 12, 24, 36, 48, and 60 months, respectively and are further depicted in **Fig. 13**.

We noted 12 (6%) major postoperative complications (4 instable angina, 3 acute renal insufficiencies implying temporary dialysis, 2 uncontrolled foot sepsis necessitating amputation, 2 early femoropopliteal thrombosis requiring urgent bypass (**Fig. 9**), and 1 persistent hypotension followed by ischemic colitis). There were 24 (12%) parallel minor complications (3 self-limiting arterial perforations, 3 segmental (5-15 cm) wall dissections (**Fig. 14, 15**), 2 temporary distal arterial spasms, 3 inguinal lymphorrheas, 4 superficial groin hematomas, 2 uncomplicated anginas, 2 transient renal disfunctions, 1 bilateral pneumonia, 3 superficial skin infections and 1 disabling inferior limb reperfusion edema).

The specific risk factors for primary patency were independently analyzed as categorical variables at 2 years (maximal homogeneity of subgroups) (**Tables I-IV**).

While female gender (p=0.001) and smoking (p=0.003) were global negative flow predictors in this population (**Table I**), the initial ABI scoring (p=0.002) and the clinical Rutherford categories 5+6 lesions (p<0.0001) equally revealed detrimental influence on patency (**Table II**). Parallel angiographic features such as the CTOs (>15 cm) length (p=0.016), the presence of severe calcifications (p=0.049) and the poor tibial vessel runoff (p=0.018, and p=0.001, for 1, and 0 permeable trunks) equally proved negative influence to primary patency (**Table III**). Finally, the GLASS/FP grade "4" atherosclerotic lesions (p=0.039) (**Table III**), the sole conventional balloon PTA application (p=0.001), the stent (>6 cm) length (p=0.001), and the presence of femoral superficial and profunda ostial lesions (p=0.004) (**Table IV**), seemingly decreased the odds for good patency for these hybrid interventions.

DISCUSSION

The present chapter emphasizes the usefulness of hybrid infrainguinal revascularization procedures specifically for high-risk (ASA 3-4) patients. [3, 19, 23] This assertion appears particularly consistent among all other types of previously described "in-flow" and "outflow" hybrid interventions. [3, 20, 21, 24]

Short and long-term follow-up in this extended [23] dual center analysis showed correct technical feasibility, good efficacy, and durability of arterial reperfusions that add encouraging clinical outcomes for both intermittent claudication and CLTI presentations. Limb salvage for claudicants [20, 21, 23] versus the CLTI group appeared statistically different (**Fig. 12**), yet both rates are comparable to other published results in the literature. [20, 21, 23-25]

In a majority of our cases, hybrid revascularizations yielded a durable arterial flow [24, 25] without the need for eventual secondary interventions (88% primary patency at one, and 66% at five years, in this study).

Previous CFA endarterectomy series [16, 17] and parallel endovascular femoropopliteal endovascular studies [5-8, 10, 11, 22] showed excellent safety and efficacy results, at mid- [6-10, 16] and long-term intervals. [10-12, 16, 17] Resembling contemporary studies reveal encouraging primary and secondary patency results for SFA classical angioplasty and bare stenting [10-12] even in the presence of long stenosis and occlusions. [6-8, 10-12] Additional recent clinical experience that follows new advances in femoropopliteal CTO revascularization [3, 26] evinces comparable results of SFA angioplasty with optional bare stenting (**Fig. 1, 4, 14, 15**) versus above-the-knee bypass for short and mid-term primary, secondary patency, and limb preservation rates. [3, 14, 27-29] Concomitant larger hybrid series results become available in the recent years. [30-35] Therefore, several correlations with the present study can be evinced.

It is generally accepted that patency after CTO recanalization as independent, [4-7] or part of hybrid techniques [20, 21, 23] is strongly influenced by the profile of atherosclerotic lesions (the type of CTO), the length, and by the extent of calcifications. [2, 3, 14] A better outcome [2, 3, 13, 14] for TASC A and B, [2] or for comparable GLASS/FP grade 1-2 lesions were described. [3]

The present study avails a specific analysis of CFA endarterectomy coupled to femoropopliteal GLASS grades "3-4" (or TASC II "C" and "D") lesion endovascular reperfusion.

The presence of moderate to severe calcifications in nearly 40% of treated limbs (**Table III**) and the synchronous 68% profunda femoris reperfusion adding 64% ostial SFA reconstructions outline distinct hemodynamic features encountered in this series, compared to other similar reports. [4, 8, 13, 20, 21]

Previous SFA revascularization trials using self-expanding nitinol stents reported up to 32% stent fractures with consequent patency decrease from 84% to 41% at one year. [9-12] Our 4% stent fractures ratio may sustain recent clinical observation showing that nitinol stents can be implanted in the femoropopliteal arterial segment with low fracture rates at five years. [4, 12]

Patency was studied in accordance with independent hemodynamic risk factors evoked in the literature, [10-13] that also match the specific features [19] of this cohort of patients. (**Tables I-IV**.) In concordance with previously published results by parallel teams, [8-13] and by our working-group, [23] the female gender (p=0.001), smoking (p=0.003) (**Table I**), the initial ABI scoring (p=0.002) and the clinical Rutherford categories 5+6 lesions (p=0.001) revealed detrimental influence on patency (**Table II**). Conversely, different from similar analyses, [31-33] the presence of diabetes (p=0.089) and renal insufficiency (p=0.655) as individual morbidities, did not reveal significant influence for patency in this study. However, the independent presence of severe calcifications (p=0.049) and the poor distal run-off represented by one (p=0.018), or none tibial vessel (p=0.001), uniformly revealed [23] statistical significance for primary patency rates. Particularly for this contingent of patients, sole popliteal angioplasty (p=0.001) and the length (>6 cm) of stents (p=0.001) equally proved a negative influence on arterial permeability. Our mean 6.2 hospital stay (3-14 days) was shorter than similar reports, [21, 28, 35, 36] yet slightly longer than analogous pure endovascular series. [9-12] Nevertheless, these observations tend to harmonize with parallel hybrid series results. [21, 35]

In this study, we noted 12 (6%) major postoperative complications and 24 (12%) parallel minor complications in a whole 3.3% of 30-day mortality rate. Inasmuch as contemporary literature discloses up to 19% mortality and 61% morbidity for simultaneous inflow and outflow bypasses, [30, 33] hybrid interventions seem to enable concomitant multiple arterial axes reconstruction with lower 11% morbidity and associated 1.4% mortality reported proportions. [30, 33, 35] The marginally higher mobi-mortality documented in this analysis can be explained by the homogeneous propensity of the 178 frail ASA 3-4 patients, intentionally included for this strategy for treatment. At our best knowledge, this series holds distinct characteristics engendered by its uniform profile of high-risk surgical patients, by reproducible anatomical patterns of infrainguinal atherosclerotic disease, also by its constant inflow/outflow surgical and endovascular techniques sustained by regular recanalization protocols in all cases. In the same setting, novel "hybrid" surgical and endovascular revascularization strategies were equally proposed in the last two decades to better adapt arterial reperfusion in multilevel atherosclerotic presentations. [4, 20, 21 24] Hybrid procedures may assemble the advantages of noninvasive endovascular techniques to those of more anatomical and pulsatile flow reconstructions availed by surgical methods. [20, 23, 24]
Hybrid vascular interventions appear to detain 5% nowadays up to 21% of current limb revascularization procedures [30] and seem to match with increased perioperative risk encountered in this constantly aging and multifactorial diseased cohort of patients. [4, 20, 21, 24]
The whole amount of concomitant surgical and endovascular hybrid interventions seems to constantly rise, as recently evoked by Aho and Venermo. [31] These authors acknowledge a near to twenty-fold increase of hybrid protocols in their institutional practice throughout a recent seven-year period (from 4 in 2004, up to 73 interventions in 2011). [31]
The appropriate technical success, the short and long-term patency, also the appended limb salvage rates of all-confounded hybrid interventions were documented either in retrospective [21, 32] or in prospective studies. [32] As a result, emerging data seem to validate at least equivalent results to conventional sole endovascular and surgical revascularizations. [20, 21, 23, 30, 32] Huynh and colleagues [30] showed that hybrid vascular techniques afford much lower morbi-mortality rates than surgical bypass for infrainguinal disease, providing equivalent high limb salvage rates. [30] Seemingly, Zhou et al. [33] describe hybrid procedures in which open surgical revascularization was associated to correct inflow, outflow, or both diseases. They concluded that hybrid treatment of multilevel infrainguinal occlusive disease provides shorter hospital stays, lower perioperative morbidity, less medical expenses, and similar early- and long-term clinical benefit compared with current open revascularization. [33]
In a remarkable recent review of the literature, Mustapha et al., [34] observes that in high-risk and comorbid CLTI patients that exhibit multilevel atherosclerotic disease, the hybrid techniques afford attractive options of treatment with lower complication and mortality rates than pure surgical gestures, at high limb salvage rates. [34] The same author shows that for all inferior limb revascularization procedures performed in 2013 in the United States, up to 20% were hybrid interventions, gathering iliac stenting and CFA endarterectomy as the most common association. [34] All these composite hybrid approaches undeniably gather advantages also inherent limitations of both techniques. [22, 30, 31, 34] In a 151-case series (58% claudicants and 48% critical ischemia limbs), Altreuther et al. found 91% freedom from recurrent intervention at five years for intermittent claudication subjects and 70% for CLTI limbs. [24]

The aforementioned authors also document 92% primary technical success for all femoropopliteal interventions, with 5% early thrombosis occurring within 30-day from initial hybrid gesture. [24]
Matching our series results, Log-rank test showed a significant limb salvage difference between the patient group with intermittent claudication versus those with CLTI. Patients with rest pain (Rutherford 4) also had significantly better limb preservation rates than those exhibiting ischemic wounds (Rutherford 5, 6). [24] These findings correspond to those published by Matsagkas et al, [35] concerning clinical, and parallel cost analysis provided by Ebaugh and colleagues, [24] in congruent research.
Among several types of hybrid interventions, [20, 21, 24, 30] the ipsilateral common femoral endarterectomy associating distal femoropopliteal endovascular recanalization (**Fig. 1-8**) detains a well-established role in contemporary vascular interventions. [21, 24, 34] Our study observation showing 88% and 78% primary patency at 1, and 2 years seems to match with previously published data that focus on CFA endarterectomy (96% and 79%), [17] and with those that compare current femoropopliteal endovascular recanalization (90% and 78%). [11] Analogous secondary patency rates unfold since comparing our 90% and 82% percentage with parallel 89%-96% and 80%-94% rates [9-12] reported at same time intervals. Lastly, the present's study 93% limb salvage ratio at one year equally accords to parallel 95% value observed at same interval by other researchers, [35] while our 63% limb preservation rate at five years in specific CLTI subjects matches with equivalent 60% reported [24] for similar risk-class patients and type of hybrid interventions. [24]
Owing a thorough analysis, Dusoglu *et al.* [21] classified hybrid interventions as simple (sHYBRID) addressing TASC type A and B lesions [2] and complex (cHYBRID) for type C and D arterial disease. [2] Interestingly, at a mean 30.3 months of follow-up, their 80% and 75% primary patency rates at 1 and 3 years in the sHYBRID were comparable to 87% and 81%, in the cHYBRID group (p=0.863). [21] Limb salvage rates at 12 and 36 months in CLTI patients proved similar in both groups. [21]
Particularly for the infrainguinal subset of hybrid procedures, our apposite inferior primary patency rates at one and two years, (88% and 78%) compared to parallel 100% (at one year), [31] or 93% (at two years) [32] published data, can be probably explained by several specific ASA factors of our population. While the present cohort assembles 74% (**Table III**) GLASS/FP grades 3-4 [3] (comparable to TASC, C and D severe femoropopliteal lesions), [2] other articles include various subsets of advanced occlusive disease ranging from 40%, [31] to 48% (cHYBRID), [21] and exceptionally up to 70% [35] equivalent lesions. Seemingly, our average 16 cm (range, 2-53 cm length) endovascular CTO crossings gather 68% limbs with more than 15 cm femoropopliteal recanalizations, (**Table III**) that slightly overpasses similar published reports. [9-12, 24, 30-32]
Finally, by taking as reference the novel GVG document and recommendations, [3] the appropriate decision to perform staged or multilevel revascularization for "average" and "high-risk" patients was (in our case), and probably should be tailored for each clinical presentation. [3] Associated inflow and outflow arterial disease "should be individualized on the basis of severity of limb threat (especially if tissue loss), anatomic complexity, and patient's class of risk" (the PLAN concept). [3] In particular, hybrid CFA endarterectomy associated with inflow/outflow endovascular techniques should be diligently considered in

every ischemic presentation by following the PLAN strategy, in parallel to other surgical or transcatheter reperfusion options. [3] For current vascular practice, GVG completes other mentioned guidelines, [1, 14, 19] and stresses the importance of whole patient's appraisal. [3] This can be achieved by detailed individual anatomical (or, Target Artery Path) evaluation, adding local functional aspects (the Limb Based Patency), to specific wound characteristics. [3] This approach should be conducted in concordance with whole patient's risk evaluation, in a multidisciplinary team perspective. [3]
Although uncertainty about long-term patency for endovascular femoropopliteal recanalization still exists, [3, 5, 8, 13, 37] we shear the belief that the hybrid technique may afford low invasiveness and adequate feasibility benefits [11, 20, 21, 24, 30-34] in a growing number of contemporary ASA 3-4 patients. [19, 23] This constantly aging contingent of patients that features systemic atherosclerotic occlusive lesions and comorbidities, may truly benefit from receiving less aggressive revascularization strategies, adapted to their frail clinical condition.

Limitations

The present study undoubtedly bears inherent limitations primarily linked to its retrospective profile and the restricted number of followed cases. The appended risk factors analysis equally yields statistic limitations shaped by the small subpopulation profile that disabled more extensive multivariable analysis. The association of different arterial occlusive backgrounds (bare atherosclerotic, diabetic or renal presentations) and the combination of various manufacturing balloons and self-expanding nitinol stents may also be a source for indeterminations in thorough restenosis risk appraisal. Additionally, in an effort to homogenize data, patency results do not include several new endovascular technologies, like drug eluted devices and retrograde calf or popliteal accesses for recanalization, with increasing utilization but in the recent years of our clinical experience.
Finally, the present chapter's study was not initially structured following the GVG [3] recommendations, inaccessible at its early stages. The GLASS classification [3] was further applied as to update thorough, yet retrospective data, initially encoded upon the TASC II stratification. [2]

CONCLUSION

Hybrid infrainguinal revascularization may offer beneficial options for treatment particularly concerning multiple comorbidities, and high-risk ASA 3-4 patients. Careful patient selection, specific planning of the procedures, and the regular multidisciplinary approaches appear crucial elements for achieving appropriate arterial reconstruction and limb salvage outcome.

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REFERENCES

1. Rutherford RB, Baker JD, Ernst C, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg.* 1997; 26(3): 517-38. Erratum in: *J Vasc Surg.* 2001; 33(4): 805.
2. Norgreen L, Hiatt WR, Dormandy JA, et al. Inter-Society Consensus for the management of peripheral arterial disease (TASC II). *Eur J Vasc Endovasc Surg.* 2007; 33Suppl 1:S32–55.
3. Conte MS, Bradbury AW, Kolh P, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. *J Vasc Surg*. 2019;70:662–662.
4. Diamantopoulos A, Katsanos K. Treating femoropopliteal disease: established and emerging technologies. *Semin Intervent Radiol.* 2014;31(4):345-352.
5. Boufi M, Azghari A, Belahda K, et al. Subintimal recanalization plus stenting or bypass for management of claudicants with femoro-popliteal occlusions. *Eur J Vasc Endovasc Surg*. 2013; 46(3): 347-352.
6. Bolia A, Miles KA, Brennan J, et al. Percutaneous trans-luminal angioplasty of occlusions of the femoral and popliteal arteries by subintimal dissection. *Cardiovasc Intervent Radiol.* 1990;13:357-363.
7. Reekers JA, Bolia A. Percutaneous intentional extraluminal (sub-intimal) recanalization : how to do it yourself. *Eur J Radiol*.1998;28(3):192-8.
8. Perrio S, Holt PE, Patterson BO, et al. Role of superficial femoral artery stents in the management of arterial occlusive disease: review of current evidence. *Vascular*. 2010;18(2): 82-92.
9. Cheng SW, Ting AC, Wong J. Endovascular stenting of superficial femoral artery stenosis and occlusions: results and risk factor analysis. *Cardiovasc Surg*. 2001; 9: 133-140.
10. Conroy RM, Gordon IL, Tobis JM, et al. Angioplasty and stent placement in chronic occlusions of the superficial femoral artery: technique and results. *J Vasc Interv Radiol.* 2001;11:1009-1020.
11. Ferreira M, Lanziotti L, Monteiro M, et al. Superficial femoral artery recanalization with self-expanding nitinol stents: long-term follow-up results. *Eur J Vasc Endovasc Surg.* 2007;34:702-708.
12. Iida O, Soga Y, Hirano K, et al. Long-term outcomes and risk stratification of patency following nitinol stenting in the femoropopliteal segment: retrospective multicenter analysis. *J Endovasc Ther.* 2011;18:753-761.
13. Patel MR, Conte MS, Cutlip DE, et al. Evaluation and treatment of patients with lower extremity peripheral artery disease. Consensus definitions from Peripheral Academic Research Consortium (PARC). *J Am Col Cardiol.* 2015;65(9): 931-950.
14. Society for Vascular Surgery Lower Extremity Guidelines Writing Group, Conte MS, Pomposelli FB, Clair DG, Geraghty PL, McKinsey JF, Mills JL, et al. Society for Vascular Surgery practice guidelines for atherosclerotic occlusive disease of the lower extremities: management of asymptomatic disease and claudication. *J Vasc Surg.* 2015;61(3 Suppl): 2S-41S.
15. Rychlik IJ, Davey P, Murphy J, et al. A meta-analysis to compare Dacron versus polytetrafluorethylene grafts for above-tknee femoropopliteal artery bypass. *J Vasc Surg.* 2014;60(2):506-515.

16. Kang JL, Patel VI, Conrad MF, et al. Common femoral artery occlusive disease: contemporary results following surgical endarterectomy. *J Vasc Surg.* 2008;48(4): 872-877.
17. Ballotta E, Gruppo M, Mazzalai F, et al. Common femoral artery endarterectomy for occlusive disease: an 8-year single-center prospective study. *Surgery.* 2009;147(2): 268-274.
18. Thiney PO, Millon A, Boudjelit T, et al. Angioplasty of the common femoral artery and its bifurcation. *Ann Vasc Surg*. 2015; 29(5): 960-967.
19. Fitz-Henry J. The ASA classification and peri-operative risk.. *Ann R Coll Surg Engl.* 2011; 93(3):185-187.
20. Scrijver AM, Moll FL, De Vries JP. Hybrid procedures for peripheral obstructive disease. *J Cardiovasc Surg (Torino).* 2010;51(6): 833-843.
21. Dosluoglu HH, Lall P, Cherr GS, et al. Role of simple and complex hybrid revascularization procedures for symptomatic lower extremity occlusive disease. *J Vasc Surg.* 2010; 51(6):1425-1435.
22. Alexandrescu VA, Hubermont G, Philips Y, et al. Combined primary subintimal and endoluminal angioplasty for ischaemic inferior-limb ulcers in diabetic patients: 5-year practice in a multidisciplinary 'Diabetic-Foot' service. *Eur J Vasc Endovasc Surg.* 2009; 37: 448-456.
23. Alexandrescu VA, Jacquemin JL, Wuidar PA, et al. Hybrid common femoral artery surgical revascularization associated to endovascular femoropopliteal recanalization in high-risk (ASA 3 - 4) patients: a seven-year period institutional experience. *World J Cardiovasc Dis*. 2016; 6: 1-12.
24. Altreuther M, Mattsson E. Long-term results after femoral thrombendarterectomy combined with simultaneous endovascular intervention in intermittent claudication and critical ischemia. *SAGE Open Medicine*. 2020; 8: 1-8.
25. Fu X, Zhang Z, Liang K, et al. Angioplasty versus bypass surgery in patients with critical limb ischemia a meta-analysis. *Int J Clin Exp Med* 2015; 8(7): 10595–10602.
26. Vossen RJ, Vahl AC, Leijdekkers VJ, et al. Long-term clinical outcomes of percutaneous transluminal angioplasty with optional stenting in patients with superficial femoral artery disease: a retrospective, observational analysis. *Eur J Vasc Endovasc Surg*. 2018; 56(5): 690-698.
27. Aihara H, Soga Y, Mili S, et al. Comparison of long-term outcome after endovascular therapy versus bypass surgery in claudication patients with Trans-Atlantic Inter-Society Consensus-II C and D femoropopliteal disease. *Circ J.* 2014;78(2): 457-464.
28. Linnakoski H, Uurto I, Suominen V, et al. Comparison of above-the-knee prosthetic femoro-popliteal bypass versus percutaneous transluminal angioplasty and stenting for treatment of occlusive superficial artery disease. *Scand J Surg.* 2013; 102(4): 227-233.
29. Antoniou GA, Chalmers N, Georgiadis GS, et al. A meta-analysis of endovascular versus surgical reconstruction of femoropopliteal arterial disease. *J Vasc Surg.* 2013; 57(1): 242-253.
30. Huynh TT, Bechara CF. Hybrid interventions in limb salvage. *Methodist Debakey Cariovasc J.* 2013; 9(2): 90-94.
31. Aho PS, Venermo M. Hybrid procedures as a novel technique in the treatment of critical limb ischemia. *Scand J Surg.* 2012;101(2): 107-113.
32. Joh JH, Joo SH, Park HC. Simultaneous hybrid revascularization for

symptomatic lower extremity arterial occlusive disease. *Exp Ther Med.* 2014; 7(4): 804-810.
33. Zhou M, Huang D, Liu C, et al. Comparison of hybrid procedure and open surgical revascularization for multilevel infrainguinal arterial occlusive disease. *Clin Interv Aging* 2014; 9: 1595–1603.
34. Mustapha JA, Anose BM, Martinsen B, et al. Lower extremity revascularization via endovascular and surgical approaches: A systematic review with emphasis on combined inflow and outflow revascularization. *Sage Open Medicine.* 2020; 8: 1-9.
35. Matsagkas M, Kouvelos G, Arnautoglou E, et al. Hybrid procedures for patients with critical limb ischemia and severe common femoral artery atherosclerosis. *Ann Vasc Surg.* 2011; 25(8): 1063-1069.
36. Ebaugh JL, Gagnon D, Owens CD, et al. Comparison of costs of staged versus simultaneous lower extremity arterial hybrid procedures. Am J Surg 2008; 196(5): 634–640.
37. Zhou M, Huang D, Liu C, et al. Comparison of hybrid procedure and open surgical revascularization for multilevel infrainguinal arterial occlusive disease. *Clin Interv Aging*. 2014; 22(9):1595-1603.

Legend of Figures

Figure 1: A current *endovascular recanalization* procedure associated to common CFA endarterectomy in a Rutherford category 3 patient, depicted step-by-step:

- **a)** Angiographic aspect of the initial arterial occlusion at the SFA/popliteal junction.
- **b)** The passage of the 0.035 hydrophilic wire into the extra-luminal, and the endo-luminal plane.
- **c)** Angiographic aspect of the initial "tiny" reperfusion channel regained before arterial dilatation. It should be emphasized that the "concave" aspect of the proximal CTO cap morphology favoured this approach.
- **d)** The completion angioplasty result with correct regain of the femoropopliteal flow. A visible large, proximal collateral was punctually preserved.

Figure 2: A Rutherford category 4 case showing the current technique for *hybrid infrainguinal revascularization*, mainly used in this series:

- **a)** The initial presentation on angio-CT assessment. A severe CFA narrowing (80%) associates a calcific CTO of the left SFA.
- **b)** and **c)** After completion of the left common femoral endarterectomy, the extraluminal (subintimal) plane is initiated; the progression of the recanalization is further showed throughout this new extraluminal channel.
- **d)** The guidewire's "re-entry" step into the native left popliteal lumen.
- **e)** Staged angioplasties performed all along the extra-luminal channel.

Figure 3: The final result of same Rutherford 4 hybrid case (**Fig. 2**), succeeding a combined CFA endarterectomy and SFA endovascular extra-luminal recanalization (owing balloon angioplasty and stenting).

Figure 4: An example of flush SFA *extraluminal* recanalization following CFA surgical reconstruction (endarterectomy with venous patch) featuring:

- **a)** The initiation of SFA extraluminal crossing. The two arrows point the tip of the 6F introducer and the guidewire's extraluminal loop.
- **b)** The advancement of the 0.035 wire in the new plane of less resistance,
- **c)** The regain of the native arterial lumen at the popliteal level (using a "vertebral" 6F reinforcing catheter),
- **d)** SFA aspect following additional, staged angioplasties,
- **e)** A correct angiographic femoropopliteal passage,
- **f)** The concluding aspect of this intervention showing correct popliteal and infrapopliteal reperfusion.

Figure 5: Current technical aspects for specific *endoluminal* SFA recanalization following upstream CFA endarterectomy:

- **a)** The completion of SFA endoluminal crossing using the hydrophilic wire,
- **b)** An appropriate re-entry maneuver into the post-occlusive femoropopliteal lumen,
- **c)** and **d)** images that point the final angiographic injection with correct SFA and popliteal flow, folowing targeted femoropopliteal PTA and stenting.

Figure 6: A 1st *particular aspect* of hybrid CFA surgical endarterectomy associated to a long (>30 cm) femoropopliteal endovascular recanalization:

- **a)** The initial SFA extraluminal crossing with the 0.035 wire (tips of the 2 arrows),
- **b)** The regain of the native distal lumen at the popliteal level (using the same type of 6F "vertebral" reinforcing catheter).
- **c)** Serial angioplasties by employing a long (15 cm-length), 5 mm-diameter classical balloon using long (3 minutes periods) iterative inflations,
- **d)** and **e)** the final anatomical result adding patch CFA endarterectomy to an extended endovascular femoropopliteal recanalization.

Figure 7: A 2nd *specific case* that associates to current CFA endarterectomy:

- **a)** A heavy calcified SFA with short staged occlusions in a renal patient and
- **b)** An appropriate "re-entry" step, down to the distal popliteal artery.
- **c)** At that point, we noted a mitigated balloon angioplasties result (incomplete opening) in this hostile calcific environment.

d) Additional stenting was performed (as to compensate a local "elastic recoil" tendency due to eccentric calcifications). A 6mm-diameter nitinol stent owned the appended final angiographic result.

Figure 8: A 3rd *specific example* showing a multilevel, infrainguinal hybrid intervention:

a) Following primary CFA endarterectomy, a distal SFA occlusion is targeted as the "second" endovascular step for recanalization.
b) The passage of the 0.035 guidewire in the extraluminal space,
c) The progression of the guidewire at the popliteal level,
d) The interim femoropopliteal angiographic result following sequential antegrade angioplasties and selective stenting,
e) The aspect of the infrapopliteal lesions that are further targeted,
f) Selective recanalization of the anterior tibial artery,
g) Specific catheterization of the anterior tibial/pedal artery junction,
h) Succeeding BTK angioplasties (using a 3 mm-diameter, low-profile, and 15 cm-length balloon),
i) The final infrapopliteal angiographic result.

Figure 9: An example of major periprocedural complication.
a) A correct engagement of the extraluminal space at the SFA level is followed by appropriate re-entry in the distal popliteal (P3) true lumen.
b) However, an extended (> 25 cm-length) « elastic recoil » phenomenon of the newly extraluminal channel is noted. This threatening hemodynamic condition further triggered a sudden collapse of the whole recanalization segment, with early thrombosis of the extraluminal space.
c) and **d)**, and **e)** show the consequent performance of an urgent femoro-anterior tibial venous bypass, appointed for limb salvage.

Figure 10: Primary, Secondary Patency and Limb Salvage rates (2009-2019).

Figure 11: An example of secondary patency procedure in a previous hybrid revascularization owing femoropopliteal angioplasties and stenting.
a) The re-occlusions of the upstream SFA, and the segment between the two preexistent stents,
b) The passage of the guidewire in the upper SFA in the extraluminal space,
c) The extraluminal SFA recanalization aspect following this time a new dissection plane. This plane is also located outside the thrombosed stent.
d) The extraluminal advancement of the guidewire outside the two stents, and inside the arterial wall (according to previously reported technique [6, 7]),

e) Dilatation of the new extraluminal channel with a 5 mm-diameter balloon angioplasty, outside the first,
f) And parallel to the second preexisting nitinol stent,
g) The concluding result at the whole SFA level, and
h) At the popliteal region, with correct endovascular regain of the distal iterative flow.

Figure 12: Comparison between limb salvage rates noted in claudicants versus critical Ischemia patients (2009-2019).

Figure 13: Survival rates of this study cohort of patients.

Figure 14: Minor complications examples. A confined flow-limiting dissection evinced after specific *extraluminal* SFA recanalization:
a) The initial aspect of SFA and the femoropopliteal junction occlusion,
b) Current passage of the guidewire in the extraluminal plane of CTO,
c) Subsequent staged angioplasties following a common protocol,
d) Detection of a flow-limiting dissection, fortunately with confined extension,
e) The final interventional result following targeted stent placement and correct suppression of the aleatory extraluminal channel.

Figure 15: Another example of documented minor complication. Serial short secondary dissections as a result of regular angioplasties in a heavily calcified femoropopliteal axis.
a) The local dense calcifications and short eccentric occlusions of SFA and the adjacent femoropopliteal segment (analogous to the Fig. 14),
b) The passage of the guidewire partially throughout the endoluminal, and partially in the extraluminal plane,
c) Similar staged angioplasties following the common protocol,
d) Detection of multiple flow-limiting dissections in this case requiring
e) Specific stenting of all affected segments, with correct angiographic outcome and clinical result for this SFA, and
f) The appended femoropopliteal junction.