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Antithrombotic therapy following revascularization for chronic limb-threatening ischaemia: a European survey from the ESC Working Group on Aorta and Peripheral Vascular Diseases

Short title: **Antithrombotic therapy following revascularization for chronic limb-threatening ischaemia**

Marco De Carlo[1*], Oliver Schlager[2*], Lucia Mazzolai[3], Marianne Brodmann[4], Christine Espinola-Klein[5], Daniel Staub[6], Victor Aboyans[7], Henrik Sillesen[8], Sebastian Debus[9], Maarit Venermo[10], Jill Belch[11], Mauro Ferrari[1], and Raffaele De Caterina[1]

* M. De Carlo and O. Schlager equally contributed to this manuscript

1- Cardiothoracic and Vascular Department, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy
2- Division of Angiology, 2nd Department of Medicine, Medical University of Vienna, Austria
3- Division of Angiology, Heart and Vessel department, Lausanne University Hospital (CHUV), Lausanne, Switzerland
4- Division of Angiology, Medical University Graz, Austria
5- Section Angiology, Department of Cardiology, Cardiology I, University Medical Center Mainz, Mainz, Germany
6- Division of Angiology, University Hospital Basel, University of Basel, Basel, Switzerland
7- Department of Cardiology, Dupuytren University Hospital, and INSERM 1094 & IRD 270, University of Limoges, Limoges, France
8- Department of Vascular Surgery, Rigshospitalet, University of Copenhagen, and Department of Clinical Medicine, University of Copenhagen, Denmark
9- Department of Vascular Medicine, University Heart Centre Hamburg, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany
10- Department of Vascular Surgery, Helsinki University Hospital and University of Helsinki, Helsinki, Finland
11- The Institute of Cardiovascular Research, University of Dundee, Ninewells, Scotland, UK

Correspondence:

Marco De Carlo, MD, PhD, FESC
Cardiac Catheterization Laboratory
Cardiothoracic and Vascular Department, Azienda Ospedaliero-Universitaria Pisana
via Paradisa, 2 – 56124 Pisa, Italy
Phone: +39 050995326 - Fax: +39 050995325
E-mail: marcodecarlo@gmail.com

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ABBREVIATIONS

AT: antithrombotic therapy

DAPT: dual antiplatelet treatment

DPI: dual pathway inhibition

CLTI: chronic limb-threatening ischemia

LEAD: lower extremity arterial disease

LER: lower extremity arterial revascularization

LMWH: low-molecular weight heparin

MACE: major adverse cardiovascular events

MALE: major adverse limb events

OAC: oral anticoagulation

SAPT: single antiplatelet treatment

ABSTRACT

Aims: Chronic limb-threatening ischaemia (CLTI) entails dismal outcomes and is an absolute indication to lower extremity revascularization (LER) whenever possible. Antithrombotic therapy is here crucial, but available evidence on best strategies (choice of drugs, combinations, duration) is scarce. We conducted a European internet-based survey on physicians' use of antithrombotic therapy after revascularization for CLTI, under the aegis of the ESC Working Group on Aorta and Peripheral Vascular Disease in collaboration with other European scientific societies involved in CLTI management and agreeing to send the survey to their affiliates.

Methods and Results: 225 respondents completed the questionnaire. Antithrombotic therapy following surgical/endovascular LER varies widely across countries and specialties, with dedicated protocols reported only by a minority (36%) of respondents. Dual antiplatelet therapy with aspirin and clopidogrel is the preferred choice for surgical (37%) and endovascular (79%) LER. Dual pathway inhibition (DPI) with aspirin and low-dose rivaroxaban is prescribed by 16% of respondents and is tightly related to the availability of reimbursement (OR 6.88; 95%CI 2.60-18.25; P=0.0001) and to the choice of clinicians rather than of physicians performing revascularization (OR 2.69; 95%CI 1.10-6.58; P=0.03). A ≥6 months-duration of an intense (two-drug) postprocedural antithrombotic regimen is more common among surgeons than among medical specialists (OR 2.08; 95%CI 1.10-3.94; P=0.024). Bleeding risk assessment is not standardised and likely underestimated.

Conclusion: Current antithrombotic therapy of CLTI patients undergoing LER remains largely discretional, and prescription of DPI is related to reimbursement policies. An individualised assessment of thrombotic and bleeding risks is largely missing.

Keywords: Antithrombotic therapy; chronic limb-threatening ischemia; lower-extremity artery disease; peripheral revascularization; vascular surgery; dual pathway inhibition.

INTRODUCTION

Chronic limb-threatening ischaemia (CLTI) is a severe disease characterised by unrelenting limb pain, poor quality of life and a high risk of limb amputation.[1,2] CLTI is also characterised by an extremely high risk of major adverse cardiovascular events (MACE), comprising cardiovascular death, myocardial infarction and stroke. Historically, CLTI patients have been managed by physicians of different specialties, including vascular surgeons, vascular medicine specialists and cardiologists, with relevant differences among European countries. Such variability, together with the poor awareness of lower extremity arterial disease (LEAD)[3] and with a paucity of randomised trials, has led to major disparities in management and clinical outcomes. Recently, efforts have been made to standardise the management of CLTI through an inter-society collaboration producing the *Global Vascular Guidelines*.[2]

CLTI is an absolute indication to lower extremity arterial revascularization (LER), either surgical or endovascular, aiming at relieving pain, allowing for wound healing, preventing amputation, and ultimately reducing mortality. After endovascular LER, current guidelines recommend dual antiplatelet therapy (DAPT) with aspirin and clopidogrel for at least one month,[1,2] often extended to 3-6 months in clinical practice.[4] In patients with infrapopliteal disease, as well as in those undergoing implantation of drug-eluting or covered stents, a longer DAPT duration may be adopted, although without supporting evidence.[5] Single antiplatelet therapy (SAPT) is recommended following surgical LER, while DAPT for up to 24 months is proposed for patients undergoing infrainguinal prosthetic bypass surgery.[2] A comprehensive review of antithrombotic therapy (AT) for revascularization in CLTI patients is being published in this issue of the *Journal*.[6]

Recently, the "*Vascular Outcomes studY of Aspirin alonG with rivaroxaban in EndovasculaR or surgical limb revascularization for peripheral artery disease"* (VOYAGER-PAD) trial demonstrated the efficacy of a novel regimen of low-dose rivaroxaban and low-dose aspirin – "dual pathway inhibition" (DPI) – in patients undergoing LER, independent of revascularization modality.[7] Since the publication of this trial, the heterogeneous reimbursement criteria for DPI across Europe have further increased variability in the treatment of CLTI. Importantly, DPI has been proposed as the default strategy for both endovascular and surgical LER by the 2021 Consensus Document on antithrombotic therapies in aortic and peripheral arterial diseases authored by the ESC Working Group on Aorta and Peripheral Vascular Diseases (WG A&PVD) in collaboration with the Working Groups on Thrombosis and Cardiovascular Pharmacotherapy.[5] Following its publication, the ESC WG A&PVD promoted a survey on AT in patients undergoing infrapopliteal LER for CLTI in collaboration with various European and National scientific societies across Europe, according to its mission of promoting collaboration

among different specialties taking care of patients with vascular diseases.[8] We hereby present the results of this survey.

METHODS

We designed a web-based questionnaire to obtain a photography of the type and duration of AT prescribed by European specialists to CLTI patients undergoing surgical or endovascular revascularization of infrapopliteal arteries, isolated or associated with above-the-knee revascularization (**Supplementary Annex S1**). We also investigated the choice of AT in patient at high bleeding risk and in those with a compelling indication for oral anticoagulants (OAC). Additional information collected included an estimate of the number of infrapopliteal revascularization procedures performed at the respondents' hospitals, and the presence of therapeutic protocols. The survey was in English and designed to be completed in less than 10 min. An e-mail invitation to complete the questionnaire was sent to 500 members of the WG A&PVD on May 14, 2021, and a link to the survey was published on the WG web page. In addition, the link was also published on the web pages of the European Society for Vascular Medicine and of the European Society for Vascular and Endovascular Surgery. Finally, an e-mail invitation to solicit response to the survey was sent to all the members of the National Societies of Vascular Surgery of Austria, Denmark, Italy and Switzerland, the National Society of Angiology of Germany, and the National Societies of Vascular Medicine of Austria and Switzerland. The survey was closed on 27 June 2021.

Categorical variables were expressed as frequency and percentages. Assuming that SAPT with aspirin is the standard therapy in current clinical practice, we performed a multivariable logistic regression analysis to identify predictors of use of alternative therapies (DPI, DAPT, SAPT with clopidogrel), and of a longer duration of the intensified postprocedural antithrombotic regimen (defined as any association of two or more antithrombotic drugs), both for surgical and endovascular revascularization, including all candidate variables (defined as those featuring a $P < 0.10$ at univariable analysis) into the model. A significance level of $P < 0.05$ was required for a variable to be retained in the model. A two-sided $P < 0.05$ was considered statistically significant. All analyses were performed using the SAS version 9.4 statistical software (SAS Institute, Inc., Cary, NC, USA).

Primary data for this article and not shown in the main manuscript are available in the Online Supplementary Material.

RESULTS

A total of 268 specialists responded to the questionnaire. Of these, 23 did not complete the survey, and 22 declared they did not work in a centre performing revascularization. Therefore, we collected a complete questionnaire from a total of 225 physicians from 17 European countries (n=215; 95.6%) and 6 non-European countries (n=10; 4.4%; these received the invitation as members of the WG A&PVD). Among European responders, 74.0% were from Western Europe, 16.3% from Southern Europe, 7.0% from Northern Europe, and 2.8% from Eastern Europe (**Figure 1** and **Supplementary Table S1**). Most responders (44.0%) were specialists in vascular medicine, 38.2% were vascular surgeons, 16.0% cardiologists, and the remaining 1.8% radiologists or internists (**Figure 1**). Vascular medicine specialists represented 58.3% of respondents in German-speaking countries and 19.8% in other countries, reflecting the different role of this specialty across Europe. In the respondents' hospitals, endovascular and surgical revascularization were performed in 96.8% and 87.1%, respectively, with 13.6% of the centres performing endovascular revascularization only. At the time of this survey, DPI was reimbursed only in Denmark, Germany and Switzerland.

Most respondents reported that AT following revascularization is decided by physicians performing revascularization (77.3%), rather than by clinicians in charge of patients during hospitalization (20.4%) – if different from the one performing revascularization –, or the local Vascular Team (2.2%). On the other hand, a decision to de-escalate AT during follow-up was taken by physicians from the team performing revascularization in a lower percentage (54.2%), with a larger role for other stakeholders, including clinicians in charge of patients during hospitalization (20.4%), specialists in charge of patients' follows-up (vascular medicine specialists 17.8%, cardiologists 3.6%) and by general practitioners (4.0%) (**Figure 2**).

The existence of a dedicated written protocol for AT following revascularization was reported by 36.0% of the respondents, while an informal protocol was reported by 42.2%; the remaining 21.8% reported that the choice is left at the physician's discretion (**Figure 2**). The assessment of bleeding risk in these patients was based on clinical judgement according to 72.3% of respondents, while bleeding scores were used by 27.7%.

Surgical revascularization

Among the 196 respondents working in centres performing surgical revascularization, the median of the reported monthly range of procedures was 11-20, with 25.0% each operating more than 20 patients (high-volume centres). The routine postprocedural regimen was DAPT with aspirin and clopidogrel for 36.6% of respondents, SAPT for 20.9% (aspirin 16.3%, clopidogrel 4.6%), DPI for 13.7%, SAPT associated with short-term (1-6 months) LMWH for

15.7%, and full-dose OAC (either vitamin K-antagonists or direct oral anticoagulants) for 13.1% (short-term for 9.8%, long-term for 3.3%) (**Figure 3**). Prescription of DPI was associated with high-volume centres (23.7% vs 10.8%, P=0.049), as well as the presence of a written antithrombotic protocol (21.1% vs 9.4%, P=0.040), the choice of therapy by the clinician rather than by the surgeon (23.7% vs 10.4%, P=0.040), and the availability of reimbursement (25.4% vs 6.4%, P=0.0009). At multivariable analysis, the availability of reimbursement was the only independent predictor of DPI usage (odds ratio [OR] 3.80; 95% confidence interval [CI] 1.33-10.87; P=0.01). Among the 79.1% of respondents reporting an intensified postprocedural regimen, duration of the initial antithrombotic regimen was 1 month for 13.3%, 3 months for 36.7%, 6 months for 19.2%, and ≥1 year for 30.8% of them (**Figure 3**).

The proportion of patients deemed at high bleeding risk was reported to be <15% by 45.0% of respondents, 15-30% by 32.9%, and >30% by 22.1%. The routine postprocedural AT for those patients was generally less intense, with SAPT for 67.1% (aspirin 44.1%, clopidogrel 23.0%), SAPT and short-term LMWH for 11.2%, DAPT for 9.9%, DPI for 6.6%, and OAC for 5.3% (short-term 4.0%, long-term 1.3%). According to the 32.9% of respondents describing an early intensified postprocedural AT, de-escalation to SAPT was prescribed earlier in high-risk than in non-high bleeding risk patients (de-escalation occurring at 1 month for 39.6% of respondents, at 3 months for 33.3%, at 6 months for 6.3%, and at ≥1 year for 20.8% of them). Finally, among patients with concomitant indication for OAC, the routine postprocedural antithrombotic regimen was OAC associated with short-term SAPT (1-6 months) for 60.9% (aspirin 43.7%, clopidogrel 17.2%), OAC monotherapy for 35.8%, OAC associated with long-term aspirin for 2.7%, and DAPT without OAC for 0.7%.

Endovascular revascularization

The 218 respondents working in centres performing endovascular revascularization reported a median monthly range of endovascular procedures of 11-20, with 41.5% treating more than 20 patients per month. The routine postprocedural AT was DAPT for 79.2% of respondents, DPI for 11.6%, SAPT associated with short-term LMWH for 5.2%, SAPT for 2.9% (aspirin 2.3%, clopidogrel 0.6%), and short-term OAC for 1.1% (**Figure 4**). Prescription of DPI was associated with choice by a clinician rather than the interventionist (22.7% vs 7.8%, P=0.007), and with reimbursement availability (27.5% vs 1.0%, P<0.0001). Reimbursement availability (OR 37.0; 95%CI 4.8-286; P=0.0005) and choice by a clinician (OR 3.1; 95%CI 1.05-8.84; P=0.04) were independent predictors of DPI usage. Among the 97.1% of respondents reporting a postprocedural regimen more intense than SAPT, duration of intensified AT was 1 month for 18.5%, 3 months for 45.2%, 6 months for 19.6%, and ≥1 year for 16.7% (**Figure 4**).

Among recipients of endovascular procedures, the proportion of patients deemed at high bleeding risk was reported to be <15% by 41.7% of respondents, 15-30% by 34.5%, and >30% by 23.8%. The preferred postprocedural antithrombotic regimen for those patients was SAPT for 53.5% (aspirin 25.6%, clopidogrel 27.9%), DAPT for 30.2%, SAPT and short-term LMWH for 8.7%, DPI for 6.4%, and OAC for 1.1%. Among the 46.5% of respondents reporting an initial intensified postprocedural regimen, the duration of such regimen was 1 month for 52.6%, 3 months for 29.2%, 6 months for 10.2%, and ≥1 year for 8.0%.

The preferred postprocedural AT for patients with concomitant indication for OAC was OAC with short-term SAPT for 77.1% (aspirin 42.4%, clopidogrel 34.7%), and OAC monotherapy for 22.9%.

Overall revascularization analyses

When considering AT for combined surgical and endovascular revascularization, the prescription of DPI (15.9% of responders) tended to be associated with the presence of a written antithrombotic protocol (21.7% vs 12.4%, P=0.09), the choice of therapy by a clinician rather than the physician performing revascularization (28.9% vs 11.7%, P=0.006), and reimbursement availability (31.1% vs 5.6%, P<0.0001). Reimbursement availability (OR 6.88; 95%CI 2.60-18.25; P=0.0001) and choice of therapy by a clinician (OR 2.69; 95%CI 1.10-6.58; P=0.03) were independent predictors.

Similarly, the prescription of clopidogrel rather than aspirin as SAPT (44.1% of responders) was associated with the choice performed by a clinician rather than by the interventionist/surgeon, both at univariable (57.6% vs. 39.8%; P=0.07) and multivariable analysis (OR 2.29; 95%CI 1.00-5.27; P=0.05).

The choice of a prolonged duration (≥6 months) of the postprocedural intensified AT (47.5% of responders) was associated with the respondent being a surgeon, both in univariable (57.5% vs 41.1%, P=0.055) and at multivariable analysis (OR 2.08; 95%CI 1.10-3.94; P=0.024).

DISCUSSION

Although CLTI exhibits the worst outcomes within the spectrum of atherosclerotic disease, and although its global burden appears to be increasing worldwide,[2] scientific evidence supporting treatments, and hence evidence-based guidelines, remain scanty.[6] Even more, the evidence specifically regarding the type and duration of AT following revascularization is minimal. Therefore, current recommendations are mainly based on extrapolations of evidence regarding

LEAD in general, and on expert consensus.[1,2] In this context of lack of evidence and of lack of standardised assessments of thrombotic and bleeding risks, AT is largely discretional. The present survey provides original insights on the contemporary management of AT in these patients and documents the heterogeneity in the management of CLTI across Europe, reflecting both the variety of different specialties involved, and the ample variability of AT strategies.

The main findings are:

1. Antithrombotic therapy following surgical revascularization for CLTI varies widely, without a dominant default strategy, and includes the discretional prescription of parenteral or oral anticoagulation for 30% of respondents. Conversely, a default strategy with DAPT following endovascular LER is prescribed according to 80% of respondents, with anticoagulation limited to 6% of cases.
2. An intensified AT is prescribed by 97% of respondents following endovascular LER and by 79% following surgical LER. Duration of the intensified regimen varies widely; a longer duration (≥6 months) is twice more common among vascular surgeons than among medical specialists (vascular medicine specialists, internists and cardiologists), probably related to a perceived risk of graft thrombosis extending beyond 6 months. A longer duration is preferred by 50% of respondents for surgical LER vs 36% for endovascular LER in standard-bleeding-risk patients. In high-bleeding-risk patients, a longer duration is preferred by 27% and 18% of respondents for surgical and endovascular LER, respectively.
3. The presence of an estimated high bleeding risk makes an intensified postprocedural AT less likely (46% and 27% of respondents for endovascular and surgical LER, respectively). In case of concomitant indication to OAC, add-on SAPT is prescribed by 77% and 64% of respondents following endovascular and surgical LER, respectively.
4. The prescription of DPI is tightly related to national reimbursement policies: in countries with reimbursement, the use of DPI among respondents is 6-fold higher.
5. The choice of AT by a clinician in charge of the patient during hospitalization (when different from the physician performing revascularization), is strongly associated with prescription of DPI and of clopidogrel as SAPT. This greater adherence to guideline recommendations likely reflects – in our interpretation – a stronger interest for medical therapy by clinicians who are not focussed on the technicalities of revascularization.
6. Over 40% of respondents estimates the prevalence of high bleeding risk to be lower than 15%, presumably underestimating patients' bleeding risk, since published in-hospital bleeding rates during hospitalization for CLTI are above 15%.[9]

In recent years, various registries consistently reported that a more potent AT with DAPT vs. SAPT in CLTI patients reduces ischaemic adverse events, both MACE and major adverse limb events (MALE), a composite of chronic and acute limb ischemia, and major amputation due to vascular causes.[10-13] In the lack of dedicated trials on AT for CLTI, useful hints may derive from trials on AT for LEAD in general. A meta-analysis of randomised trials comparing more intense vs. less intense AT (more vs less intense SAPT; DAPT vs SAPT; DPI vs SAPT) found that intensified AT is associated with a significant reduction in the risk of subsequent LER [relative risk (RR) 0.89, 95%CI 0.83–0.94], of amputation (RR 0.63, 95%CI 0.46–0.86), and of stroke (RR 0.82, 95%CI 0.70–0.97), at the cost of increased risk of major bleeding (RR 1.23, 95%CI 1.04–1.44).[14] It may be argued that the absolute benefit of an intensified AT on ischaemic outcomes should be magnified in CLTI patients, being these at the highest ischaemic risk within the spectrum of LEAD. Paradoxically, there are CLTI patients who are still receiving no AT at all, according to a recent analysis of German health insurance records including 199,953 patients hospitalized for CLTI between 2010 and 2017 (63% of whom undergoing LER).[9] The proportion of patients not receiving any AT on admission throughout the study period was unacceptably high, at 51%, although the rate at 1 year after the index hospitalization was lower and decreased from 37% in 2011 to 27% in 2018. The use of AT in academic centres is definitely higher, as reported by the "*COhorte de Patients ARTériopathes" (COPART)* registry, a French prospective multicentre registry of hospitalizations for symptomatic LEAD. Among 1,981 patients (41% of whom with CLTI), 91% were prescribed AT at discharge, including any antiplatelet agent or OAC.[15]

The under-prescription of AT might be related to the perception that many CLTI patients are at high bleeding risk. Indeed, the above-mentioned German study reported a bleeding rate of 18.8% during hospitalization.[9] Importantly, CLTI is an independent predictor of in-hospital major bleeding in patients undergoing LER (OR 1.61; 95%CI 1.40–1.86), as reported by a US registry enrolling 25,382 patients.[16] In turn, the same registry identified major bleeding as an independent predictor of in-hospital mortality (OR 10.87; 95%CI: 6.95-17.02).[17] However, no data are available regarding the bleeding risk of CLTI patients beyond hospitalization.

SAPT, most commonly with aspirin, has remained the mainstay of AT of CLTI for decades. The COPART registry reported that, among 939 patients hospitalised for CLTI between 2006 and 2016, AT remained unvaried throughout the decade.[18] In particular, the 71% rate of patients receiving antiplatelet therapy on admission (84% SAPT, 16% DAPT) and the 34% rate of patients on OAC remained unchanged.

On the other hand, short-term DAPT with aspirin and clopidogrel has been the standard of care after endovascular LER and after surgical LER with prosthetic grafts.[1,2] A retrospective

analysis of the Vascular Quality Initiative reported that, among 12,117 patients undergoing surgical LER for CLTI between 2003 and 2016, DAPT was prescribed to 39% of patients, and was associated with a 5-year survival benefit (70% vs 66%; P=0.04).[13] A similar benefit (71% vs 67%; P=0.01) was observed with DAPT against SAPT among 22,991 CLTI patients undergoing endovascular LER, while no benefit was found among those revascularized for claudication, independent of LER modality.[13] A retrospective analysis of the Swedish National Vascular Registry reported a much lower use of DAPT (31%) following endovascular LER among 1,941 CLTI patients.[12] Interestingly, DAPT was associated with a lower rate of amputation only in patients receiving a stent (HR 0.56; 95%CI 0.36-0.86). A recent British registry enrolling 625 patients (67% CLTI) reported that endovascular LER (mostly balloon angioplasty) was followed by SAPT in 77% of cases and by DAPT in 23%.[19]

A major breakthrough for AT in patients undergoing LER recently came from the results of VOYAGER-PAD,[7] consistent with those of the LEAD subgroup of the "*Cardiovascular Outcomes for People Using Anticoagulation Strategies*" (COMPASS) trial.[20] The significant benefit on ischaemic endpoints supports the proposal of DPI as the default strategy following surgical or endovascular LER.[5] Importantly, in both trials DPI was associated with a significant (but limited) increase in non-fatal bleeding events in the first year of treatment, which became non-significant in the following years. The safety of DPI has been confirmed by the long-term open-label extension of the COMPASS trial, encompassing 12,964 patients followed-up for an additional median time of 1 year.[21] The incidence rates for major bleeding was 1.01 (95%CI 0.86-1.19) compared with 1.67 (95%CI 1.48-1.87) during the randomized treatment phase. Consistent results were reported by the multicentre prospective "*Xarelto plus acetylsalicylic acid: treatment patterns and outcomes in patients with atherosclerosis*" (XATOA) registry, enrolling patients with CAD and/or LEAD who received DPI in clinical practice.[22] Among 5,532 patients (58.9% with LEAD), major bleeding rates were 0.95 per 100 patient-years, as compared to 1.67 per 100 patient-years in COMPASS. Conversely, the incidences of MACE and MALE were higher in XATOA (2.26 and 3.57 per 100 patient-years, respectively), as compared to COMPASS (2.18 and 0.19 per 100 patient-years), probably related to a higher prevalence of LEAD in XATOA (58.9% vs. 15.1%, respectively).

The applicability of VOYAGER-PAD findings to the real world was retrospectively analysed in the COPART registry.[23] Among 2,259 patients evaluated (66% with CLTI), only 30.1% resulted eligible for DPI, mainly because of concomitant need for OAC (45%), presence of malignancy (24%), history of stroke (20%), need for DAPT (16%), high bleeding risk (13%), or severe renal failure (12%). Similar to XATOA, patients in COPART were at higher ischaemic risk than those enrolled in VOYAGER-PAD. In the VOYAGER-PAD-eligible subset of COPART, the 1-year

MALE rate was 27.9% (95%CI 19.9-38.3) vs 6.0% (95%CI 5.3-6.9) in the control arm of VOYAGER-PAD. The applicability of VOYAGER-PAD was also assessed in the Danish Vascular Registry: out of 32,911 patients (47% CLTI), only 27.1% were eligible.[24] Consistently, the 3-year rate of the primary efficacy outcome as defined in VOYAGER-PAD was higher in the eligible cohort of the registry than in the control arm of the trial (24.1% vs 19.9%). In summary, although the majority of real-world patients undergoing LER would have been excluded from the DPI trials, their higher cardiovascular risk may potentially lead to a greater absolute benefit with DPI.

The evidence favouring DPI should lead to a decline in the non-evidence-based use of both parenteral and oral anticoagulants in patients undergoing surgical LER, still amounting to 30% in our survey. A wider reimbursement availability would certainly boost the application of DPI, as highlighted by our findings. Nevertheless, further evidence is needed to better define the risk/benefit profile of DPI as compared to AT different from aspirin monotherapy, the comparator chosen in VOYAGER-PAD. In particular, a direct comparison of DPI vs DAPT with aspirin and clopidogrel in patients undergoing endovascular LER would be warranted.

Limitations

This survey offers a photograph of prescription patterns by a number of health practitioners dealing with CLTI and willing to reply to a questionnaire solicited by Scientific Societies. Several limitations have to be considered. Firstly, we cannot estimate the response rate to the survey, as the invitation was sent not only through e-mailing, but also via hyperlinks published on webpages of scientific societies; therefore, a selection bias of respondents cannot be excluded. Secondly, we cannot assume that views of the respondents are representative of those of all physicians involved in the management of CLTI patients undergoing revascularization in their centres and beyond. Thirdly, we did not directly investigate reasons underlying the choice of type and duration of treatment.

Conclusions

With the limitations of self-reported perceptions, the current survey offers an overview of contemporary management of AT in patients undergoing LER for CLTI in Europe. The survey points to the high heterogeneity of treatments, arguing for the need of a better evidence base to guide amid the several alternative therapeutic options in such patients.

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LEGEND TO FIGURES

Figure 1. Pie chart depicting the distribution of nationality (right panel) and specialty (left panel) of respondents.

Figure 2. Pie chart depicting the distribution of antithrombotic protocols (right panel) and of physicians who are in charge of deciding when to de-escalate antithrombotic treatment following revascularization (left panel).

Figure 3. Pie chart depicting the distribution of type (right panel) and duration (left panel) of initial, more intense antithrombotic regimen following surgical revascularization. LMWH, low-molecular weight heparins; OAC, oral anticoagulants.

Figure 4. Pie chart depicting the distribution of type (right panel) and duration (left panel) of initial, more intense antithrombotic regimen following endovascular revascularization. LMWH, low-molecular weight heparins; OAC, oral anticoagulants.

Graphical Abstract: We conducted a European survey to appraise on the current use of antithrombotic therapies after revascularization for chronic limb-threatening ischemia. Two-hundred and twenty-five centres responded to a web-based questionnaire documenting the choice of antithrombotic therapies regimens, and the use of intensified antithrombotic therapies after revascularization, either endovascular or surgical. Results of this survey document the heterogeneity of antithrombotic approaches and highlight the several unmet needs in this area.

Figure 1

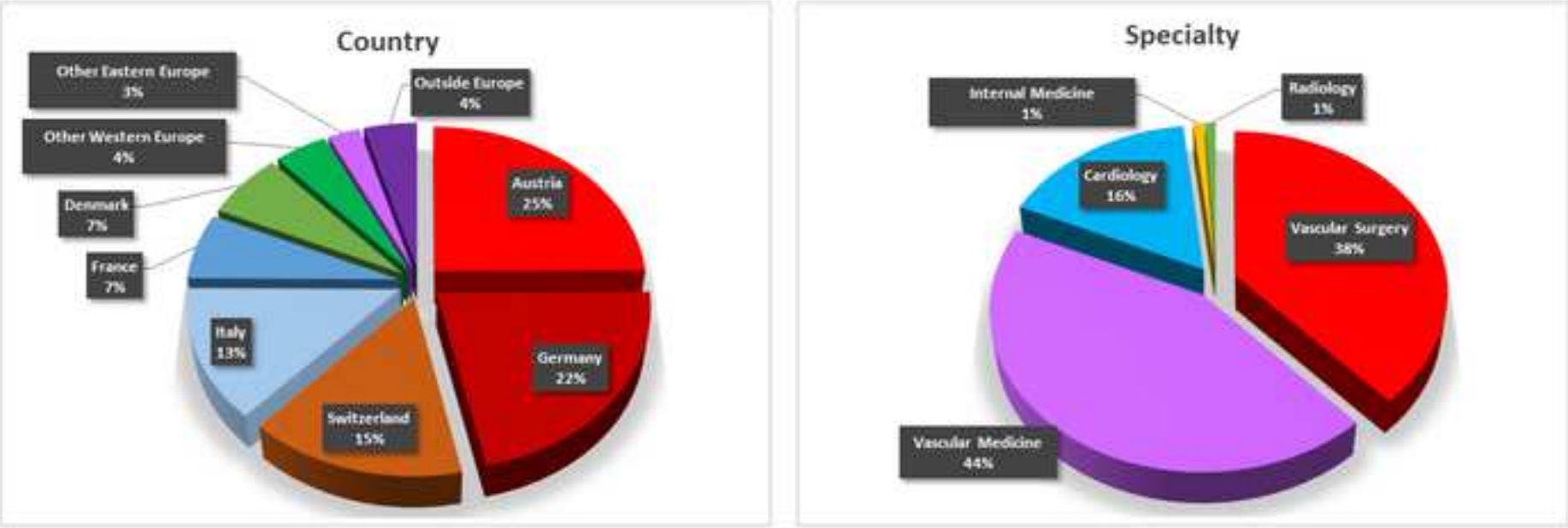
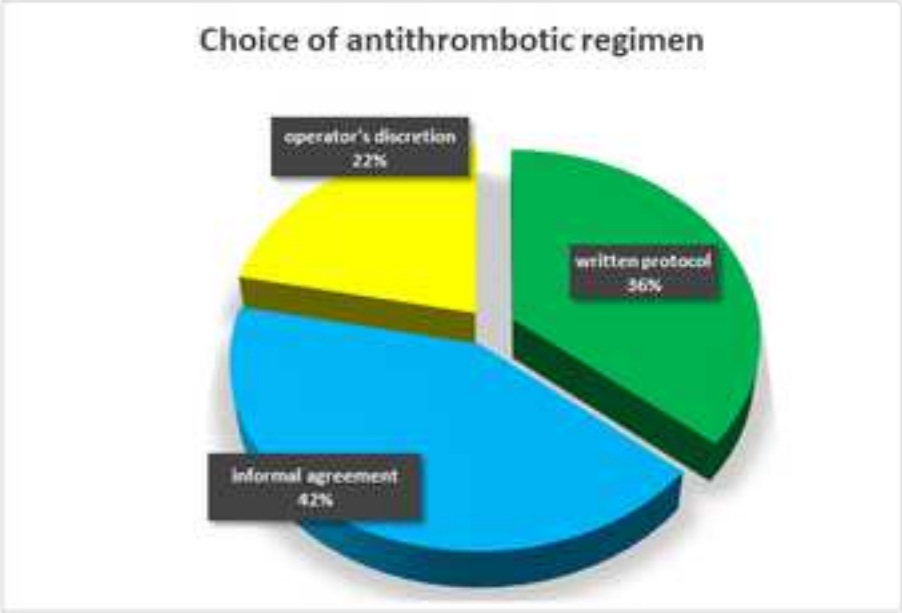


Figure 2



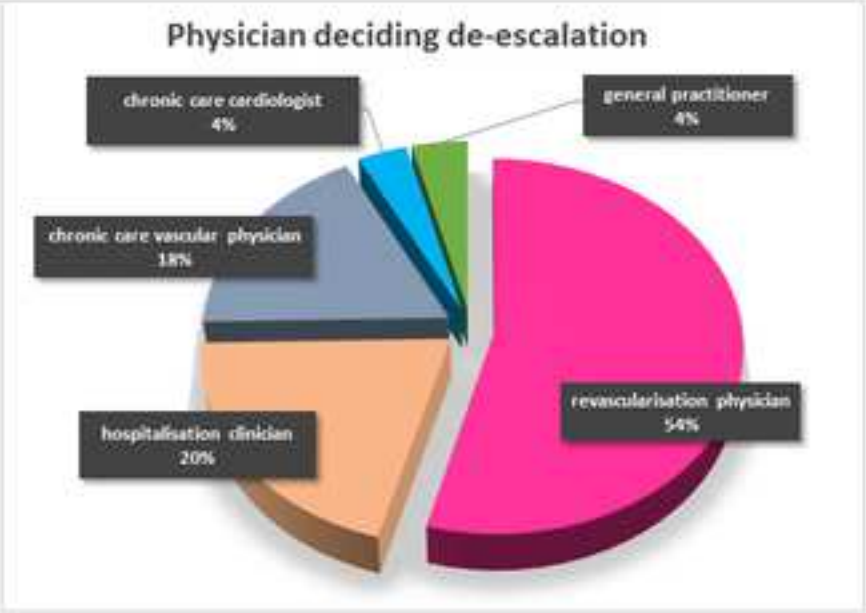
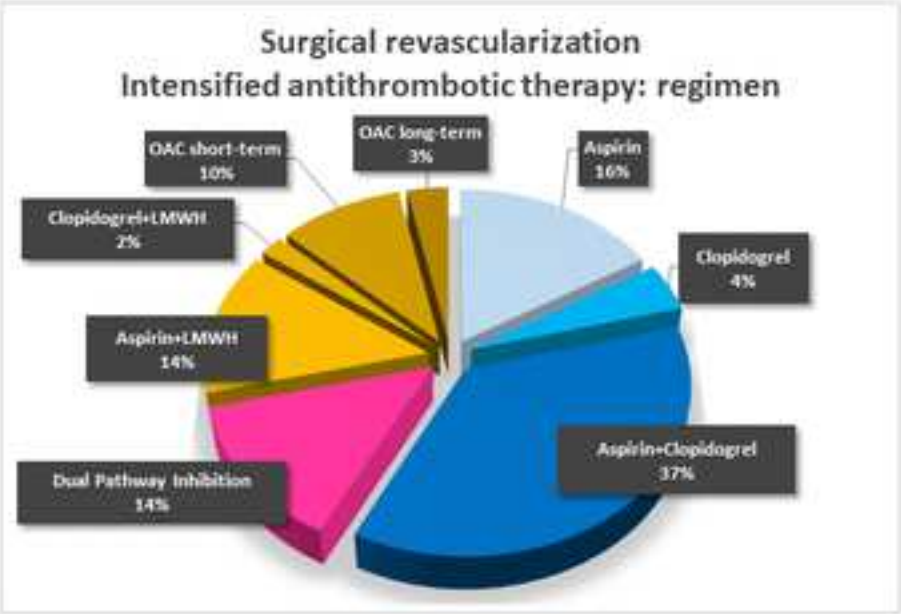


Figure 3



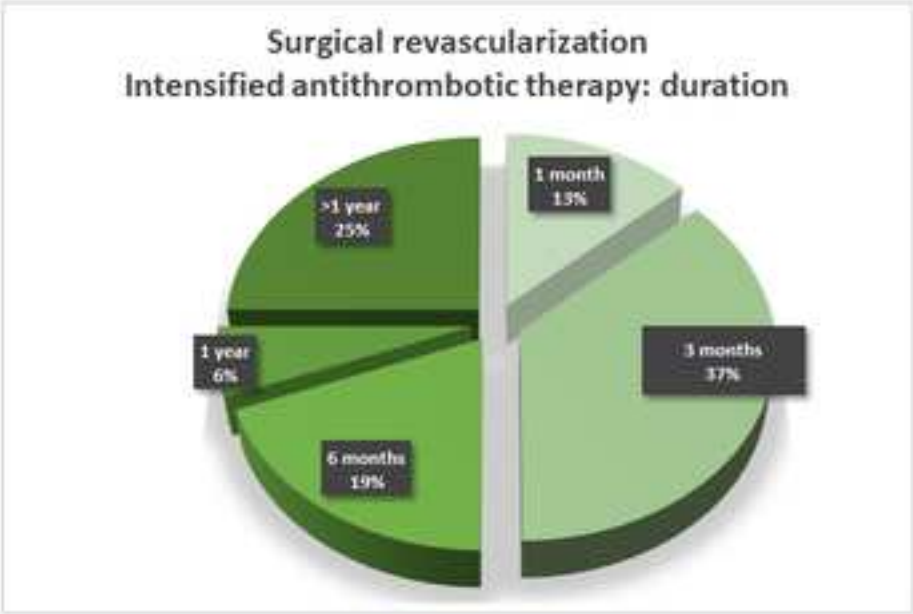
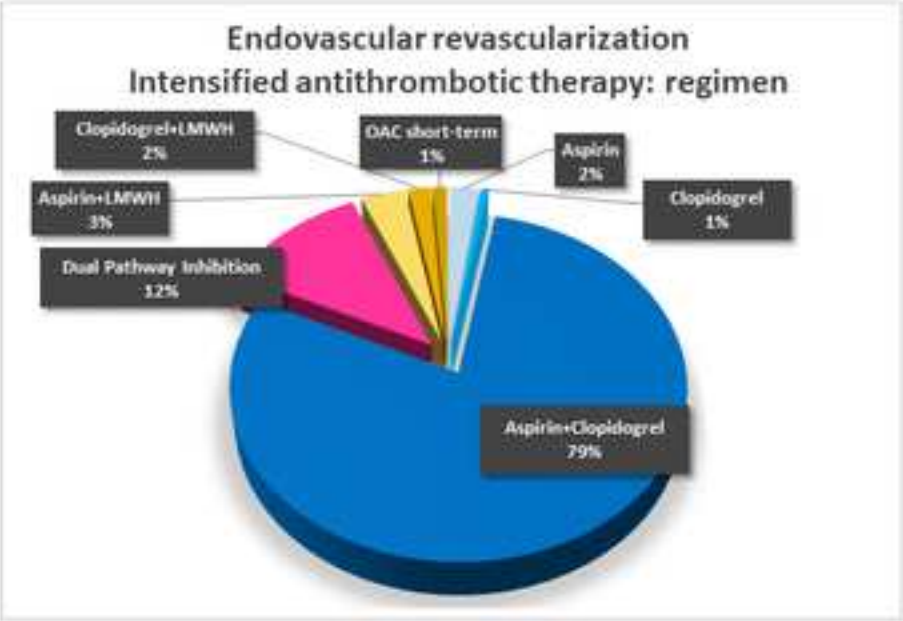
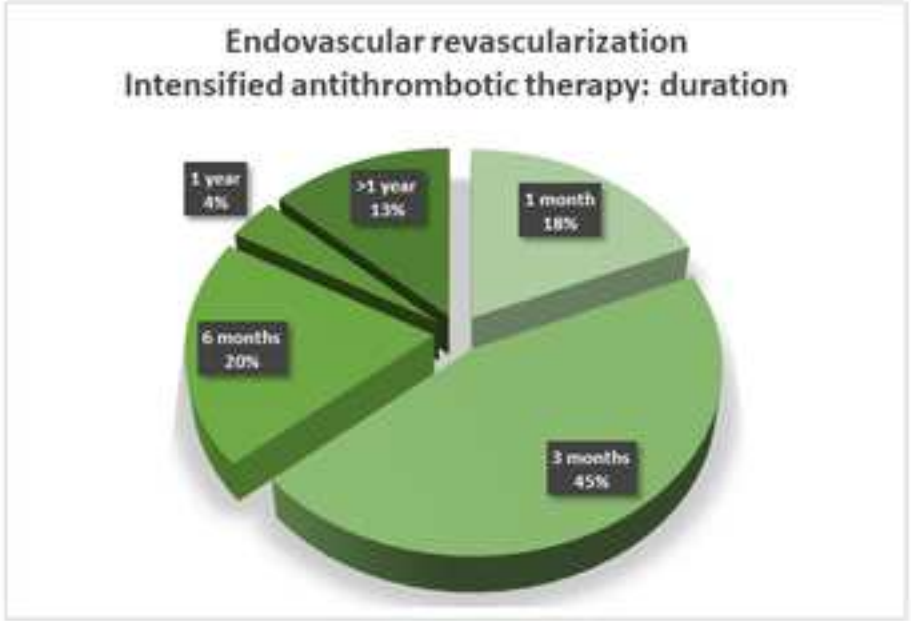


Figure 4





Graphical Abstract