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Effectiveness and safety of anticoagulant versus antiplatelet therapy in patients after endovascular revascularisation of the lower limb

Primerjava učinkovitosti in varnosti antikoagulacijskega in antiagregacijskega zdravljenja pri bolnikih po znotrajžilnem posegu na spodnjem udu

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Abstract

Background: After revascularisation, patients with peripheral arterial disease (PAD) are routinely prescribed antiplatelet treatment (APT). Patients who receive anticoagulant treatment (ACT) due to comorbidity are an exception. We set out to determine possible differences in the effectiveness and safety between ACT and APT in patients after endovascular revascularisation of the lower limb arteries.

Methods: In a single-centre retrospective cohort study, we analysed the data of 1,587 PAD patients who underwent successful endovascular revascularisation of the lower limb arteries due to disabling intermittent claudication or chronic critical limb ischemia over a 5-year period. Patients were divided into the ACT and APT groups based on their prescribed treatment. After balancing both groups' baseline characteristics with propensity score matching, we compared the effectiveness and safety of both treatment regimens in the first year after revascularisation.

Results: Compared to patients with APT, patients with ACT were older, and more often reported arterial hypertension, diabetes, chronic kidney disease, congestive heart failure, ischaemic heart disease, and prior stroke or transient ischaemic attack. After matching, the odds ratio (OR) for an effective outcome with ACT versus APT was 0.78 (95% CI 0.39–1.59; p=0.502), while the OR for a safe outcome with ACT versus APT was 4.12 (95% CI 0.82–20.73; p=0.085).

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Key words: peripheral arterial disease; percutaneous transluminal angioplasty; antithrombotic agents; treatment outcome; propensity score matching

Ključne besede: periferna arterijska bolezen; znotrajžilna angioplastika skozi kožo; antitrombotična zdravila; izidi zdravljenja; uravnoteženje z nagnjenjem

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Conclusions: Patients who required ACT were elderly, had more cardiovascular risk factors and had more advanced PAD than patients with APT. After matching, we found no statistically significant difference in the effectiveness and safety of both treatment regimens; however the wide OR confidence intervals warrant further research.

Izvleček

Izhodišča: Bolniki s periferno arterijsko boleznijo (PAB) po revaskularizaciji običajno prejemajo antiagregacijsko zdravljenje. Izjema so bolniki, ki zaradi pridruženih bolezni potrebujejo antikoagulacijsko zdravljenje. Namen raziskave je bil prepoznati morebitne razlike v učinkovitosti in varnosti med antikoagulacijskim in antiagregacijskim zdravljenjem pri bolnikih po skozikožni znotrajžilni revaskularizaciji arterij spodnjega uda.

Metode: V enocentrični retrospektivni kohortni raziskavi smo analizirali podatke o 1.587 bolnikih s PAB, pri katerih je bila v 5-letnem obdobju zaradi omejujoče intermitentne klavdikacije ali kronične kritične ishemije uda opravljena uspešna znotrajžilna revaskularizacija arterij spodnjega uda. Bolnike smo na podlagi predpisanega zdravljenja razdelili v antikoagulacijsko in antiagregacijsko skupino. Po usklajevanju osnovnih značilnosti obeh skupin z metodo usklajevanja nagnjenja smo primerjali učinkovitost in varnost obeh režimov zdravljenja v prvem letu po revaskularizaciji.

Rezultati: Bolniki v antikoagulacijski skupini so bili v primerjavi s tistimi v antiagregacijski skupini starejši ter so imeli pogosteje arterijsko hipertenzijo, sladkorno bolezen, kronično ledvično bolezen, zastojno srčno popuščanje, ishemično bolezen srca in anamnezo možganske kapi ali tranzitorne ishemične atake (TIA). Po usklajevanju je bilo razmerje obetov za uspešen izid ob antikoagulacijskem zdravljenju glede na antiagregacijsko zdravljenje 0,78 (95-odstotni interval zaupanja 0,39–1,59; p=0,502), razmerje obetov za varen izid ob antikoagulacijskem glede na antiagregacijsko zdravljenje pa 4,12 (95-odstotni interval zaupanja 0,82–20,73; p=0,085).

Zaključki: Bolniki, ki so potrebovali antikoagulacijsko zdravljenje, so bili starejši in so imeli bolj številčne srčno-žilne dejavnike tveganja ter bolj napredovalo PAB kot bolniki z antiagregacijskim zdravljenjem. Po usklajevanju nismo ugotovili statistično pomembne razlike v učinkovitosti ali varnosti obeh režimov zdravljenja, vendar širina intervalov zaupanja za razmerje obetov zahteva nadaljnje raziskave.

1 Introduction

Peripheral arterial disease (PAD) indicates severe systemic atherosclerotic involvement, resulting in an increased risk of both major adverse limb events (MALE) and major adverse cardiovascular events (MACE) (1). Patients with symptomatic PAD are routinely prescribed antithrombotic therapy to lower the risk of atherothrombotic events. Except for patients for whom anticoagulant therapy (ACT) is indicated due to concomitant illness, antiplatelet therapy (APT) is generally considered to be the treatment of choice (1,2).

In patients with advanced PAD, presenting as disabling intermittent claudication or chronic critical limb ischaemia (CLI), a revascularisation procedure is usually performed to restore perfusion of the lower limb. At present, endovascular procedures, namely percutaneous transluminal angioplasty (PTA) with or without stent placement, are the preferred way of revascularisation (1,2). After revascularisation, the risk of atherothrombotic events increases as the procedure causes trauma to the vascular wall, exposes the endothelium, and induces a local inflammatory response (3), which stimulates platelet adhesion and clot formation. Meanwhile, activated platelets are also likely to promote vascular smooth muscle cell proliferation and thus cause neointimal hyperplasia (4). Preventing reocclusion and thus reducing the need for additional revascularisations is therefore one of the aims of antithrombotic treatment after endovascular procedures (1,2,5-7).

After revascularisation, the optimal antithrombotic treatment regimen is yet to be determined (1,2). While patients are mainly prescribed APT, the role of anticoagulants has not yet been fully established. Recent studies suggest better efficacy of the combination of low-dose rivaroxaban and acetylsalicylic acid compared to acetylsalicylic acid alone, but with an increased risk of bleeding (8,9). As some patients will continue to require therapeutic doses of anticoagulants after interventional revascularisation due to comorbidities, understanding their effectiveness and safety in preventing MACE and MALE is crucial. This retrospective cohort study compares the effectiveness and safety of ACT and APT in patients after endovascular revascularisation of the lower limb arteries.

2 Methods

Included in this retrospective cohort study were all patients with advanced PAD presenting as disabling intermittent claudication or CLI who underwent successful endovascular revascularisation at the Catheter Laboratory of the Clinical Department of Vascular Diseases, University Medical Centre Ljubljana, between January 2014 and December 2018. Patient data were non-concurrently obtained from electronic hospital medical records and supplemented with information received from the patients' primary care physicians, when available. We collected data on patient demographics, PAD characteristics at the time of the procedure, comorbidities (cardiovascular risk factors and risk factors for bleeding), and procedural characteristics. Diagnoses of comorbidities were based on established diagnoses in the patients' documentation, laboratory values, and prescribed medication. Data were matched by the hospitalisation identifier and anonymised for analysis.

The exclusion criteria were: a simultaneously performed surgical bypass procedure, subsequently performed additional procedures due to previously undetected stenosis of a more proximal arterial segment, and insufficient data on post-procedural antithrombotic therapy. Treatment protocols and post-procedural antithrombotic treatment were based on the ESC guidelines (1). Patients were generally prescribed APT, while in patients with comorbidity, which called for therapeutic doses of anticoagulants, ACT was continued after the procedure, sometimes with the addition of an antiplatelet agent for a limited time of usually 1 or 3 months. Patients were divided into two groups based on their prescribed antithrombotic treatment upon discharge from the hospital. Those who received ACT (excluding prophylactic doses of anticoagulants and low-dose rivaroxaban) with or without APT comprised the ACT group, while patients who received APT alone comprised the APT group. Adherence and potential changes in therapy were not considered.

Outcomes were assessed during the first year after revascularisation or until a second intervention on the same limb if performed sooner. If the only follow-ups were more than one year after the procedure, the earliest subsequent follow-up was used to assess the outcomes after one year. In this interval, all events were evaluated equally, regardless of when in the observed interval they occurred. If the patient had no follow-ups or if it was not possible to assess the outcome one year after the procedure, the patient was excluded from further analysis (Figure 1).

We defined two observed outcomes – an effectiveness outcome and a safety outcome. Treatment was considered effective if the patient experienced:

- an improvement of symptoms as defined by the Fontaine classification (10) or
- the successful healing of a stump after a previously

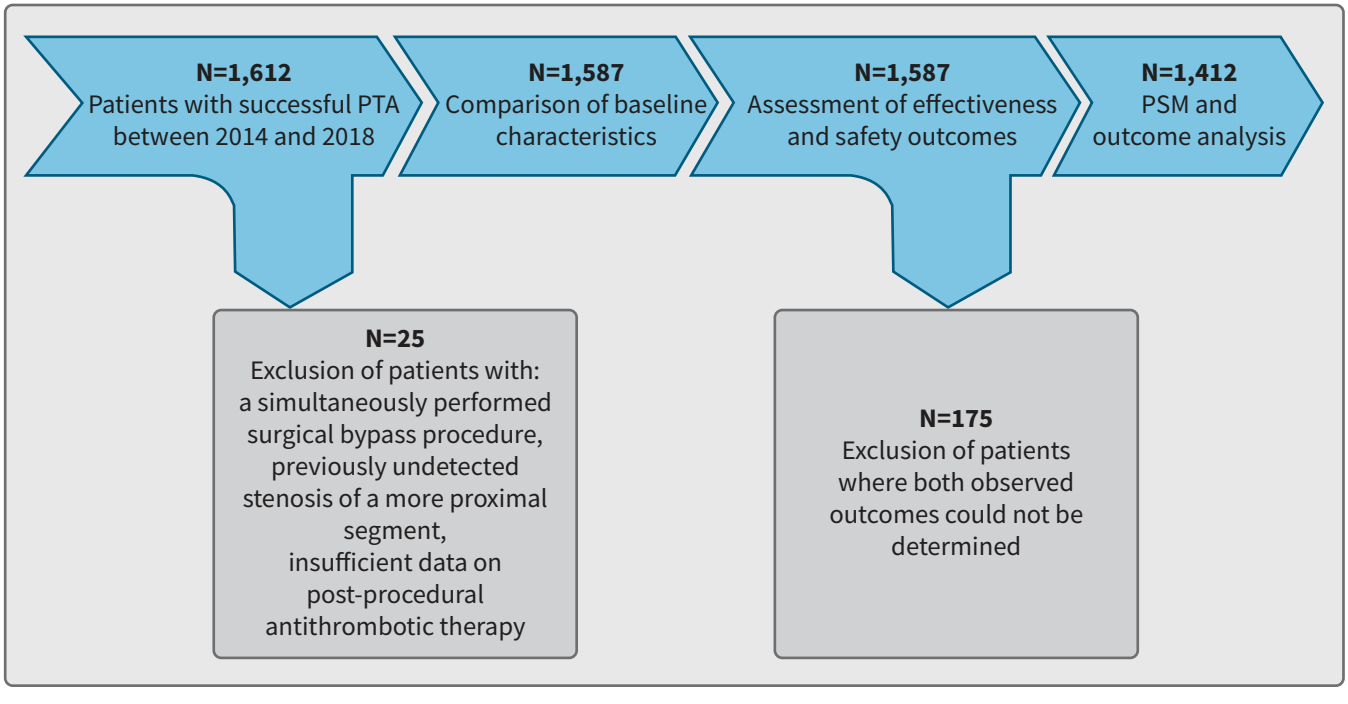

Figure 1: Patient selection process and statistical analysis.
Legend: PTA – percutaneous transluminal angioplasty; PSM – propensity score matching.

planned amputation, performed shortly before or after the revascularisation.

If there was no improvement or symptoms worsened, if the patient required another procedure or even major amputation of the treated limb, or if the patient died regardless of cause, treatment was deemed ineffective.

Safety of treatment was defined as the absence of major bleeding according to the ISTH criteria (11).

Statistical analysis of baseline characteristics was performed using the SPSS statistical package (version 25, IBM SPSS Statistics, USA). Propensity score matching (PSM) and logistic regression were performed in the R programming language (12). Descriptive statistics were used to report the patients' baseline characteristics, with categorical variables presented as frequency and percentage, and continuous variables presented as mean and standard deviation. The groups' characteristics were compared using Pearson's χ^2 or Fisher's exact tests for categorical variables and independent samples t-tests for continuous variables. We used PSM to select the subgroup of patients whose baseline characteristics and risk were comparable, making the observed outcomes dependent only on the treatment group and not on the patients' other characteristics. We matched the patients in the APT group to the patients in the ACT group. Included in the matching process were all patients for whom the effectiveness and safety outcomes could both be determined. A propensity score was calculated for each patient based on demographics, PAD severity, procedural characteristics, and comorbidities, signifying the probability that a patient would be prescribed ACT based on the included covariates (13). We also calculated the standardised mean differences (SMD) before and after matching, indicating an individual covariate's balance between the treatment groups. Covariates were considered well balanced when SMD was <0.05. After calculating propensity scores, matching was performed with three matching algorithms (nearest neighbour, full, and optimal). The nearest neighbour 1:5 algorithm with replacement enabled the inclusion of a sufficient number of patients and yielded adequate balance. After applying this algorithm, the data had the smallest number of covariates where SMD was >0.05 and the largest final effective sample size (patients from the ACT group were matched to multiple patients from the APT group). Further analysis was thus conducted using this method. The final sample included all patients from the ACT group and only the matched patients from the APT group. To assess the relative effectiveness and safety of both treatment regimens, we fit two logistic models to the matched sample, with the treatment group, the calculated propensity scores, and atrial fibrillation (previously not included in the PSM) as predictors, and the effectiveness or safety as the outcome. We then calculated the odds ratio (OR) and the corresponding confidence intervals (CI) for the effectiveness and safety outcomes for ACT versus APT.

The study was conducted according to the guidelines of the Declaration of Helsinki. The study design was approved by the National Medical Ethics Committee (0120-623/2019/4; February 10, 2020).

3 Results

We reviewed the data of all 1,612 patients who had undergone technically successful revascularisation between the years 2014 and 2018. After excluding ineligible patients, we included 1,587 patients in the analysis of baseline characteristics, 233 (14.7%) of whom received ACT. In the ACT group, the majority of patients (173; 74.2%) were prescribed warfarin, 21 patients (9.0%) received rivaroxaban, and 17 (7.3%) received dabigatran. The remaining patients received apixaban, low-molecular-weight heparin, or acenocoumarol. About two-thirds of patients in the ACT group (156; 67.0%) were temporarily prescribed antiplatelet agents in addition to ACT for an average duration of 2.3 months. The comparison of the patients' baseline characteristics for the ACT and APT groups is presented in Table 1.

In the unmatched groups, the effectiveness of ACT was 58.5% (120/205 patients), while the effectiveness of APT was 77.3% (933/1,207 patients). Within one year after endovascular revascularisation, all-cause mortality was 22.4% in the ACT group (46/205 patients) and 7.9% in the APT group (95/1,207 patients). The incidence of major bleeding was 4.4% in the ACT group (9/205 patients) and 1.2% in the APT group (15/1,207 patients). Bleeding was fatal for one patient in the ACT group (0.5%) and two in the APT group (0.2%). Of the 24 major haemorrhages recorded, 13 (54.2%) occurred within the first two months after revascularisation. Three of them directly resulted from the procedure, as there was bleeding at the procedural access site.

For 175 patients, both the effectiveness and safety outcome could not be determined. After their exclusion from further analysis, PSM was performed on 1,412 patients (Figure 1). The characteristics of both patient groups before and after matching are shown in Table 2. All variables presented in Table 2 were used as covariates in the PSM procedure. After matching, the sample size was 655 patients, namely 205 patients in the ACT group

Table 1: Comparison of baseline characteristics of the anticoagulant group and the antiplatelet group of patients.

	Anticoagulant group (N=233)	Antiplatelet group (N=1,354)	p value
Patient characteristics			
Age (years)	76.1 ± 10.1	69.0 ± 10.4	**<0.001**
Female sex	93 (39.9)	569 (42.0)	0.546
Arterial hypertension	215 (92.3)	1,141 (84.3)	**0.001**
Dyslipidemia	154 (66.1)	1,077 (79.5)	**<0.001**
Diabetes mellitus	122 (52.4)	581 (42.9)	**0.007**
Ischaemic heart disease	74 (31.8)	293 (21.6)	**0.001**
Atrial fibrillation	188 (80.7)	34 (2.5)	**<0.001**
Congestive heart failure	103 (44.2)	133 (9.8)	**<0.001**
History of stroke or TIA	54 (23.2)	150 (11.1)	**<0.001**
Chronic kidney disease	91 (39.1)	292 (21.6)	**<0.001**
Liver disease	3 (1.3)	6 (0.4)	0.134
Bleeding diathesis	9 (3.9)	38 (2.8)	0.380
Smoking			**<0.001**
current or abstinence of <1 year	26 (11.2)	534 (39.4)	
abstinence of >1 year	74 (31.8)	368 (27.2)	
Excessive alcohol intake	9 (3.9)	63 (4.7)	0.592
PAD characteristics and procedural characteristics			
Fontaine classification grade			**<0.001**
2b	96 (41.2)	996 (73.6)	
3	30 (12.9)	82 (6.1)	
4	107 (45.9)	276 (20.4)	
ABI before the procedure	0.61 ± 0.26	0.59 ± 0.21	0.267
TASC II classification*			**0.001**
A	36 (15.5)	382 (28.2)	
B	76 (32.6)	495 (36.6)	
C	60 (25.8)	333 (24.6)	
D	12 (5.2)	35 (2.6)	
Treated arterial segment†			**<0.001**
infrapopliteal	46 (19.7)	98 (7.2)	
femoropopliteal	85 (36.5)	616 (45.5)	
femoropopliteal and infrapopliteal	74 (31.8)	276 (20.4)	
iliac	25 (10.7)	352 (26.0)	
iliac and femoropopliteal	3 (1.3)	12 (0.9)	

	Anticoagulant group (N=233)	Antiplatelet group (N=1,354)	p value
Previous amputation			**0.001**
none	198 (85.0)	1,248 (92.2)	
below the ankle	22 (9.4)	74 (5.5)	
above the ankle	13 (5.6)	32 (2.4)	
Previous revascularisation			0.754
of the same segment	39 (16.7)	211 (15.6)	
of a different segment	30 (12.9)	197 (14.5)	

Data are shown as frequency and percentage (%) for categorical variables and as mean ± standard deviation for continuous variables (age and ankle-brachial index). Due to rounding, totals may be different from 100%. Bold values denote statistical significance at the p<0.05 level.*TASC II was not assessed if revascularisation was performed on the infrapopliteal segment only. †All groups include percutaneous transluminal angioplasty with or without stent placement.
Legend: ABI – ankle-brachial index; TIA – transient ischaemic attack.

and 450 in the APT group. The effective sample size was 430.6 patients.

We found no statistically significant difference between the matched ACT and APT groups, neither in the effectiveness outcome (OR for ACT versus APT 0.78; 95% CI 0.39–1.59; p = 0.502) nor in the safety outcome (OR for ACT versus APT 4.12; 95% CI 0.82–20.73; p = 0.085).

4 Discussion

Current recommendations for the antithrombotic treatment of PAD patients after endovascular procedures are mainly extrapolated from evidence-based recommendations for the antithrombotic treatment of patients with coronary heart disease (5). Antiplatelet drugs represent a cornerstone of antithrombotic treatment after

Table 2: Results of nearest neighbour 1:5 propensity score matching for the anticoagulant group and the antiplatelet group of patients.

	Unmatched groups			Matched groups		
	Anticoagulant group (N=205)	Antiplatelet group (N=1,207)	SMD	Anticoagulant group (N=205)	Antiplatelet group (N=450)	SMD
Patient characteristics						
Age (years)	76.1 ± 10.1	68.7 ± 10.3	0.727	76.1 ± 10.1	75.8 ± 9.6	0.026
Female sex	85 (41.5)	503 (41.7)	0.004	85.0 (41.5)	188.3 (41.9)	0.008
Arterial hypertension	189 (92.2)	1,020 (84.5)	0.241	189.0 (92.2)	407.4 (90.5)	0.059
Dyslipidemia	132 (64.4)	969 (80.3)	0.361	132.0 (64.4)	283.2 (62.9)	0.030
Diabetes mellitus	108 (52.7)	520 (43.1)	0.193	108.0 (52.7)	244.1 (54.2)	0.031
Ischaemic heart disease	63 (30.7)	262 (21.7)	0.206	63.0 (30.7)	150.6 (33.5)	0.059
Congestive heart failure	90 (43.9)	117 (9.7)	0.837	90.0 (43.9)	188.3 (41.9)	0.041
History of stroke or TIA	48 (23.4)	136 (11.3)	0.325	48.0 (23.4)	105.4 (23.4)	<0.001
Chronic kidney disease	80 (39.0)	258 (21.4)	0.392	80.0 (39.0)	193.6 (43.0)	0.081
Liver disease	3 (1.5)	5 (0.4)	0.109	3.0 (1.5)	5.7 (1.3)	0.017

	Unmatched groups			Matched groups		
	Anticoagulant group (N=205)	Antiplatelet group (N=1,207)	SMD	Anticoagulant group (N=205)	Antiplatelet group (N=450)	SMD
Bleeding diathesis	9 (4.4)	35 (2.9)	0.080	9.0 (4.4)	21.1 (4.7)	0.014
Smoking			0.703			0.050
non-smoker	116 (56.6)	390 (32.3)		116.0 (56.6)	245.4 (54.5)	
current or abstinence of <1 year	25 (12.2)	487 (40.3)		25.0 (12.2)	53.6 (11.9)	
abstinence of >1 year	64 (31.2)	330 (27.3)		64.0 (31.2)	151.0 (33.6)	
Excessive alcohol intake	7 (3.4)	54 (4.5)	0.054	7.0 (3.4)	16.2 (3.6)	0.011
PAD characteristics and procedural characteristics						
Fontaine classification stage			0.735			0.077
2b	83 (40.5)	900 (74.6)		83.0 (40.5)	166.8 (37.1)	
3	27 (13.2)	73 (6.0)		27.0 (13.2)	58.0 (12.9)	
4	95 (46.3)	234 (19.4)		95.0 (46.3)	225.2 (50.0)	
TASC II			0.509			0.059
A	30 (14.6)	344 (28.5)		30.0 (14.6)	61.0 (13.6)	
B	65 (31.7)	439 (36.4)		65.0 (31.7)	140.9 (31.3)	
C	55 (26.8)	299 (24.8)		55.0 (26.8)	126.9 (28.2)	
D	12 (5.9)	31 (2.6)		12.0 (5.9)	30.7 (6.8)	
TASC II was not assessed	43 (21.0)	94 (7.8)		43.0 (21.0)	90.4 (20.1)	
Treated arterial segment*			0.617			0.021
infrapopliteal	40 (19.5)	84 (7.0)		40.0 (19.5)	85.6 (19.0)	
femoropopliteal	76 (37.1)	558 (46.2)		76.0 (37.1)	165.1 (36.7)	
femoropopliteal+infrapopliteal	66 (32.2)	240 (19.9)		66.0 (32.2)	146.6 (32.6)	
iliac	20 (9.8)	314 (26.0)		20.0 (9.8)	46.1 (10.2)	
iliac+femoropopliteal	3 (1.5)	11 (0.9)		3.0 (1.5)	6.6 (1.5)	
Previous amputation			0.263			0.101
none	174 (84.9)	1,117 (92.5)		174.0 (84.9)	365.3 (81.2)	
below the ankle	21 (10.2)	67 (5.6)		21.0 (10.2)	58.8 (13.1)	
above the ankle	10 (4.9)	23 (1.9)		10.0 (4.9)	25.9 (5.8)	
Previous revascularisation			0.077			0.057
none	141 (68.8)	832 (68.9)		141.0 (68.8)	312.6 (69.5)	
of the same segment	37 (18.0)	191 (15.8)		37.0 (18.0)	86.0 (19.1)	
of a different segment	27 (13.2)	184 (15.2)		27.0 (13.2)	51.4 (11.4)	

Data are shown as frequency and percentage (%) for categorical variables and as mean ± standard deviation for continuous variables (age). Due to the selected algorithm, patient frequencies may be shown with decimals. Due to rounding, totals may be different from 100%. *All groups include percutaneous transluminal angioplasty with or without stent placement.
Legend: SMD – standardised mean difference.

revascularisation, while the role of anticoagulants has not yet been completely established. The COMPASS and VOYAGER-PAD trials found the addition of low-dose rivaroxaban to acetylsalicylic acid to reduce the incidence of MACE and MALE in patients with stable PAD as well as in patients after a revascularisation procedure. However, a slightly increased risk of bleeding, excluding fatal and intracranial haemorrhage, was noted in both trials (8,9). Other studies were less conclusive, with some of them failing to demonstrate any difference between the combination of ACT with APT and APT alone (14-17).

After an endovascular procedure, patients are generally prescribed APT. In patients who require therapeutic doses of anticoagulants due to comorbidity, transient addition of APT is always considered, with the final decision hinging on the patient's risk for bleeding (1,2). In our study, two-thirds of patients in the ACT group were simultaneously prescribed at least one antiplatelet drug. Atrial fibrillation is one of the most common indications for anticoagulant use (18), which explains why the prevalence of atrial fibrillation in our study was more than 80% in the ACT group and only 2.5% in the APT group. The presence of atrial fibrillation typically indicates higher age, and, therefore, a higher probability of comorbidity, including a more severe course of PAD with a poorer outcome (19). Our results are in concordance with these expectations. Compared to patients in the APT group, patients with ACT were more than 7 years older and more likely to have arterial hypertension, diabetes mellitus, chronic kidney disease, ischaemic heart disease, congestive heart failure, and a history of stroke or TIA. As expected, the higher age and more frequent comorbidities of patients in the ACT group were also reflected in more advanced PAD in these patients. Patients with ACT had more complex atherosclerotic lesions according to the TASC II classification. Furthermore, previous amputations were twice as common in the ACT group as in the APT group, while CLI was present in almost 60% of patients in the ACT group compared to just over a quarter of patients in the APT group.

Interestingly, despite a significantly higher prevalence of CLI in the ACT group, no difference in the pre-procedural ankle-brachial index (ABI) was found. This could be explained by a potentially higher prevalence of medial arterial calcification in ACT group patients, which was not yet as pronounced as to increase the ABI above 1.4. Diabetes mellitus and chronic kidney disease, relevant risk factors for the development of medial arterial calcification, were more common in our patients with ACT (2,20). Both diseases also are independent risk factors for infrapopliteal PAD (21,22). In our study, this is reflected in the higher frequency of treatment of infrapopliteal arteries in patients in the ACT group compared to those in the APT group.

Before matching, 175 patients for whom both observed outcomes could not be determined were excluded. These were the patients who did not have a follow-up examination within one year of their procedure and did not die. Possibly, these patients did not attend follow-up examinations because their outcomes were favourable. However, other explanations, such as treatment in other institutions, are also possible. We excluded all of them from further analysis to prevent bias, which did not affect the two groups' baseline characteristics (Table 1 and the unmatched groups in Table 2). In order to evaluate the effectiveness and safety outcomes, the two groups were balanced using PSM, after which adequate balance was achieved. PSM is increasingly used in observational studies, as it enables the comparison of groups of patients with radically different characteristics by preprocessing the groups and yielding data already controlled for the measured pre-treatment variables (i.e. confounding variables or variables that predict the outcome) (23). Compared to multiple logistic regression, PSM is very tolerant regarding the number of included covariates (24). Therefore, we were able to include a wide range of covariates that are associated with the patients' treatment regimen and might affect the observed outcomes. Since we were comparing two very different groups, PSM allowed us to match patients in the APT group to patients in the ACT group and make the final estimate of the odds ratio for the population of interest more precise. In our study, patients in the APT group were matched to their counterparts in the ACT group, meaning our findings cannot be extrapolated to the entire population but to the subset of patients with similar characteristics to those with ACT – older patients with more severe PAD and more comorbidities.

After matching, we found no statistically significant difference neither in the effectiveness, nor the safety of both treatment regimens. One can hypothesise that patients were already prescribed the most appropriate treatment considering their health status. However, our study cannot confirm the equivalence of the two treatment regimens. A possible explanation for the lack of difference may also be an insufficient number of included patients, considering that antithrombotic treatment is only one of many factors that influence the outcome of revascularisation. Furthermore, the vast majority of patients in our ACT group simultaneously received APT for a short duration, which may, to some extent, obscure the results.

Comparable studies often focus on an individual arterial segment rather than the entire limb. The treated arterial segment can significantly impact treatment outcomes, as the long-term patency after percutaneous revascularisation of the iliac segment is known to be better than that of the femoropopliteal and infrapopliteal segments (25,26).

According to previous research, increased bleeding risk would be expected in patients who received ACT (8,9,27,28). In our study, the safety analysis had a wide confidence interval, likely due to very rare bleeding events. The annual risk of major bleeding in patients with ACT is estimated at 2–5%, with fatal bleeding occurring in 0.5–1% of patients (29). Our results are consistent with these estimates as 4.4% of patients in the unmatched ACT group suffered major bleeding, with fatal bleeding occurring in 0.5% of patients. For APT, the annual risk of major bleeding is less than 0.5% (30). In our study, 1.2% of patients in the unmatched APT group suffered major bleeding in the observed period. It should be noted that these annual estimates were made for all patients who had been prescribed a specific antithrombotic treatment, while in our study patients also underwent revascularisation, which itself poses a risk of bleeding. Thus, 3 of our patients experienced bleeding at the access site due to the procedure. The somewhat higher incidence of major bleeding in the APT group could also be explained by the fact that more than 60% of our patients in the APT group temporarily received dual antiplatelet therapy, which is known to increase the risk of major bleeding 2- to 3-fold (31). This is further supported by the fact that more than half of our patients who experienced major bleeding, did so in the first two months after revascularisation.

Our single-centre study has some limitations. Its retrospective nature prevented us from assessing the patients' possible poor adherence to their prescribed treatment, which could affect the observed outcomes. In the ACT group, the majority of patients simultaneously received an antiplatelet agent for a limited duration, which could affect both the effectiveness and safety outcome. Furthermore, only the antithrombotic treatment upon discharge from the hospital was considered in the analysis, without considering the treatment before the procedure or possible changes in treatment in the observed period. Another limitation was the number of included patients. Although we analysed all successful procedures in a 5-year period to include a sufficient number of patients, the ACT group was still relatively small and was even further reduced after patients without both outcomes were excluded and PSM was performed.

5 Conclusion

Patients with PAD who required ACT significantly differed from patients in the APT group. In our study, they were 7 years older on average, had more advanced PAD, and had more comorbidities than patients in the APT group. After PSM, no statistically significant difference was found in the effectiveness and safety outcomes between the two groups. As we matched patients in the APT group to patients in the ACT group, our findings can only apply to the population of older patients with more comorbidities.

As the antithrombotic treatment patients are prescribed after revascularisation is only one of many factors that influence the outcome, we cannot confirm the equivalence of both treatment regimens using this study design. In order to provide more precise data, a large prospective study of the effectiveness and safety of treatment with therapeutical doses of anticoagulants in PAD patients after revascularisation would be required.

Conflict of interest

None declared.

Editors comment

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