Impact of Vascular Calcifications on Long Femoropopliteal Stenting Outcomes

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Original article

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ABSTRACT (word count: 391)

Objective: Vascular calcifications (VCs) may be a prognostic factor for outcome after endovascular treatment of peripheral arterial disease (PAD). Semi-quantitative analysis with X-ray imaging is the main limiting factor for assessing VCs. The aim of the present study was to find a correlation between the amount of VC with a CT scan quantification and mid-term results of endovascular treatment of TASC C/D femoropopliteal (FP) lesions.

Methods: Patients belonging to two previously published registries (STELLA and STELLA PTX) and who underwent a preoperative CT scan were retrospectively included in the study. VC quantification was performed with a dedicated workstation (EndoSize, Therenva) on the basis of Hounsfield units (HU). The VC percentage was calculated as the ratio between VC volume and the volume of the region of interest. For the analysis, patients were divided into three groups according to VC percentage, from lowest to highest: group 1 (G1) included the 1st quartile of VCs, group 2 (G2) included the 2nd and 3rd quartiles and group 3 (G3) included the 4th quartile. Risk of in-stent thrombosis was analysed using a multivariate model.

Results: Thirty-nine patients were included (10 in G1, 19 in G2, 10 in G3) and mean follow-up duration was 24±14.6 months. Patients in G1 and G3 had, respectively, a VC rate of <1% (no VC) and >20% (severe VC). In G2, VC was considered to be intermediate. There was no statistical difference in the cardiovascular risk factors and preoperative medication. A significant difference was found for the healthy FP diameter between G1 (4.6±0.8 mm) and G3 (6.8±0.8 mm, $p<0.0001$) and between G2 (5.2±1 mm) and G3 ($p<0.0001$). The rate of drug-eluting stents was similar in all groups. There was no difference between groups

concerning the rate of in-stent restenosis, target lesion revascularisation and target extremity revascularisation. There was a higher rate of in-stent thrombosis for G1 vs. G2 (p=0.037) and no difference was noted between G1 vs. G3 (p=0.86) or G2 vs. G3 (p=0.12). G3 was associated with early stent thrombosis (<1 month), while G1 was associated with late stent thrombosis (6-24 months). On multivariate analysis, only one predictive factor for stent thrombosis was found: patients with intermediate VC seemed to be protected against in-stent thrombosis (OR=0.27, 95% CI: 0.1-0.77; p=0.014).

Conclusion: The study showed that VC quantification with CT imaging is feasible and useful for comparing outcomes following PAD endovascular revascularisation. Below a certain threshold, the presence of VC might be necessary for plaque stability and may protect against in-stent thrombosis.

Key words: Vascular calcification, quantification, CT scan, peripheral arterial disease, in-stent thrombosis

Introduction

The most common cause of peripheral arterial disease is atherosclerosis. Despite being exposed to similar risk factors, peripheral arteries develop heterogeneous atherosclerotic lesions. Our previous work showed that carotid arteries develop predominantly lipid-rich lesions and microcalcifications, while femoral arteries develop fibrotic lesions, with extensive vascular calcification (VC) and frequent presence of osteoid tissue (1-4). These differences may have major clinical implications. Firstly, VC may destabilise atheromatous plaques and contribute to plaque rupture (5-7). Moreover, advanced and extensive VC contributes to arterial stiffness and hypertension, an important risk factor for plaque rupture (8, 9). Secondly, the presence of VC may influence the technical success rate and outcomes of peripheral endovascular procedures (10). It is noteworthy that severe VC is often considered an exclusion criterion in femoropopliteal clinical study protocols. Moreover, balloon angioplasty of severe calcified lesions is limited by early elastic recoil and poor acute and long-term outcomes (11). Although nitinol stents are designed to prevent elastic recoil and constrictive remodelling, severe VC may prevent stent expansion, resulting in poorer outcomes when compared to fully expanded stents (12). Also, it seems that VC may influence the efficacy of drug-eluting balloons during revascularisation of femoropopliteal lesions, mainly in cases of circumferential distribution (13).

Nevertheless, few data are available to determine the influence of VC on femoropopliteal endovascular treatment outcomes. In the present study, we sought to determine the perioperative and mid-term outcomes following long femoropopliteal stenting according to preoperative VC burden.

Patients and Methods

Population

Patients included in this study belong to two published prospective registries (14, 15). Briefly, the patients presented with femoropopliteal lesions ≥ 15 cm (TASC II C and D) and were enrolled as soon as the guide crossed the lesion. The first patient cohort (STELLA study) was treated with a LifeStent® bare metal stent (Bard Peripheral Vascular, Tempe, AZ, USA) and was enrolled between November 2008 and October 2009. The second patient cohort was treated with a Zilver® PTX® paclitaxel-eluting stent (STELLA PTX study) (16) (16) (16) (16) (16) (16) (Cook Peripheral Vascular, USA) and was enrolled between March 2011 and April 2012. The inclusion/exclusion criteria and the endovascular procedures were identical for both groups and have already been reported in the STELLA and STELLA PTX studies. Protocols were approved by local ethics committees and all patients gave their informed consent.

CTA analysis and quantification of VC

All computed tomography angiograms (CTAs) were analysed with a dedicated workstation (17-20) (EndoSize®, Therenva, France) by one investigator blinded to outcomes. Centrelines from the common femoral artery to the end of the popliteal artery (Fig. 1A) were manually extracted for femoropopliteal occlusions, otherwise automatic extraction was used (in case of stenosis). A region of interest (ROI) was determined as a cylinder centred around centrelines (Fig. 1B) whose diameter was manually adjusted to ensure all VC was included. Within the ROI, a dedicated program allowed segmentation of both arterial lumen (ALu) and VC (Fig. 1C-D) with a thresholding tool. The difference between ALu and VC was based on HU density (21-23): voxels in the range 400-3000 HU were considered VC (and quantified in mm^3) whereas voxels in the range 100-400 HU were considered ALu (Fig. 1C-D). Volume of

VC and ALu were calculated for the entire femoropopliteal artery but also at the level of the treated segment. The percentage of VC and ALu at the level of the treated segment was determined by the ratio between the volume of VC and ALu and the volume of the ROI. The other CTA parameters analysed were the length of lesions and the diameter of the healthy superficial femoral artery.

Definition of groups

In order to compare pre-, peri- and post-operative data according to the amount of VC, 3 groups were established. The overall population was divided according to the rate of VC, from the lowest to the highest percentage of VC: group 1 (G1) included the 1st quartile of VC, G2 included the 2nd and 3rd quartiles and G3 included the 4th quartile.

Follow-up

Follow-up consisted of a clinical examination, measurement of ankle-brachial index (ABI) and a duplex scan at 1, 3, 6, 9, 12, 18 months then annually thereafter. An X-ray of the thighs with two separate incidences of at least 45° was taken after 12 months in order to test for stent fracture. All of the data were entered in a prospective follow-up register.

Endpoints

The primary endpoint compared between groups was in-stent thrombosis during follow-up. Secondary endpoints were target lesion revascularisation (TLR), target extremity revascularisation (TER) and in-stent restenosis (ISR). Endpoint definitions have already been described in articles reporting on the respective results recorded for both cohorts, and comply with international definitions.

Statistical analysis

Continuous variables were presented as mean ± SD and categorical variables as count and percentages. Pearson's chi-square test was used for comparisons of continuous variables, and one-way factorial ANOVA for categorical data after testing the normality of the data, and then differences among means were analysed using post-hoc Tukey-HSD or Games-Howell multiple comparison tests depending on the results of the assumption of homogeneity of variances (Levene test). A correlation between SFA diameter and amount of VC was calculated by use of the Pearson correlation coefficient. Postoperative outcomes were compared between groups using the log-rank test. A predictive model was developed to demonstrate any correlation between pre/perioperative factors and stent thrombosis. Inclusion of variables in the model with $p<0.1$ (or forced-in) were based on the Pearson's chi-square test for categorical variables and ANOVA for continuous variables. A multivariate analysis implemented using a Cox model with a stepwise descending procedure was fitted. A p value < 0.05 was considered statistically significant. Data were analysed using SPSS software (SPSS Inc., Chicago, IL, USA).

Results

Demographic data

Of the 103 patients of both registries, only those with preoperative computed tomography angiography (CTA) were included. Patients with only a duplex scan (n=29), magnetic resonance angiography (n=25) or without a CTA (n=10) were excluded from the study. Thirty-nine patients were therefore included for analysis. Every patient in group 1 had a VC rate in the lesion area of <1%; this group was therefore considered the non-calcified group (n=10). Patients in group 3 had a VC rate >20%; this group was considered the heavily calcified group (n=10). Group 2 consisted of patients with a VC rate in the range 1-20% and was considered as the intermediate calcification group (n=19).

As shown in Table 1, there was no difference in demographic characteristics between groups, except a significantly higher rate of hyperlipidaemia in group 3 (p=0.008). Statin therapy rates were not different.

Lesions and intraoperative data (Table 2)

With regard to anatomical characteristics of the femoropopliteal segment, it was noted that the diameter was different between groups with the ANOVA test, and post-hoc tests revealed that this difference was significant between group 1 and 3 (p<0.0001) and between group 2 and 3 (p=0.0002). There was no difference between group 1 and 2 (p=0.217). A significant correlation was found between femoropopliteal segment diameter and the amount of VC (Fig. 2). Given the fact that groups were determined according to VC rate, a significant difference was found between them for Ca and ALu volume in the lesion area and for the overall femoropopliteal segment. With regard to endovascular treatment, no difference was observed for characteristics of implanted stents nor for use of X-ray and contrast load.

Perioperative results

During follow-up, 10 (25.6%) stent thromboses occurred (Table 3): 4 (40%) in group 1, 2 (10.5%) in group 2 and 4 (40%) in group 3. According to the log rank test, this rate was statistically different between group 1 vs. 2 but not between group 2 vs. 3 and group 1 vs. 3. When the date of occurrence of stent thrombosis was analysed (Fig. 3), a trend was shown: heavy Ca was associated with early stent thrombosis, while no Ca was associated with late stent thrombosis. More precisely, heavy Ca presented a stent thrombosis at 1 month while every patient with no Ca presented a stent thrombosis between the 6th and the 24th months. All patients with intermediate Ca presented a stent thrombosis after the 48th month. Rates of in-stent restenosis, TLR and TER are provided in Table 3 and were not statistically different between groups.

Risk factor for in-stent thrombosis

Results of the univariate/multivariate analysis are provided in Tables 4 and 5. On univariate analysis, the femoropopliteal diameter was higher in the in-stent thrombosis population (6.1± 1.3 mm vs. 5.2 ± 1.1, p=0.05) but on multivariate analysis it did not appear to be significant, although a trend towards a protective effect of the femoropopliteal diameter on in-stent thrombosis was noted (Table 5). The other variables included in the multivariate analysis were sex, hypercholesterolaemia and calcification (according to groups). Only VC appeared to significantly influence in-stent thrombosis. Patients belonging to group 2, i.e. with an intermediate calcification rate, seemed to be protected from in-stent thrombosis with an odds ratio of 0.27 (95% confidence interval: 0.1-0.77; p=0.014).

Discussion

In this study, we report that the rate of VC has a high impact on endovascular treatment outcomes after long femoropopliteal stenting. Given that a high amount of VC is frequently an exclusion criterion, few data are available concerning results of endovascular therapies in calcified arteries because it is assumed that outcomes are poor with this specific arterial feature. In this paper, we sought to determine the role of VC after stent implantation. It seems that, as assumed, a high rate of VC is at risk of technical failure and poor outcomes but also arteries with no calcification. An intermediate rate of VCs may protect against in-stent thrombosis.

Classification

Currently, neither quantitative nor qualitative preoperative VC assessment is available in routine practice. Indeed, current VC quantitative grading is based on subjective, semi-quantitative, angiographic- and fluoroscopic-based assessments. Furthermore, VC nature and composition cannot be determined by current non-invasive methods. Among non-invasive preoperative imaging methods, CTAs are still more available and cheaper than magnetic resonance angiographies and are widely used in current practice. Two previously published grading systems are often used in studies to assess VC but the quantification is based on angiographic images and remains subjective (24, 25). In 2014, Rocha-Singh *et al.* (25) proposed a peripheral arterial calcium scoring system (PACSS) and a method for its clinical validation. In this classification, the scoring system takes into account the pathological location of calcification (intima, media, combined) along with the location and length of the affected segment and is based on angiographic assessment. Correlation of this grading system with procedure and patient outcomes is currently under evaluation. Dattilo *et al.* reported an angiographic calcium score and used fluoroscopic images to quantify VC but the circumference of VC was determined by an anteroposterior view, raising the question of the

accuracy of this quantification. In cardiology literature, optical coherence tomography (OCT) has been reported to assess VC and stent expansion. In this particular study, a high rate of VC was found to be a factor for stent underexpansion (26). Although algorithms for segmenting VC on CT images have existed for decades, they have only been reported in clinical papers since Ohana *et al.* (23). They proposed an alternative to the Trans-Atlantic Inter-Society Consensus Document II on Management of Peripheral Arterial Disease classification (TASC II)(27) based on the mean occluded diameter and percentage of calcifications. Calcification volume determined by a colour-coded map provided an accurate estimate but no correlation with clinical or morphological outcomes was given. Our assessment method was similar to that of Ohana *et al.* but, in both cases, CTA did not allow intimal and medial calcifications to be distinguished. Medial calcifications, known as Mönckeberg's medial calcinosis, are associated with type II diabetes and chronic kidney disease and represent a specific pattern of VC with a distinct pathological type of calcification that may contribute to arterial stiffness (28).

Lesions and intraoperative data

With regard to lesions and intraoperative data, we observed that VCs were associated with a larger femoropopliteal diameter. Enlargement of femoropopliteal arteries was probably linked to positive vessel remodelling. Indeed, during the atherosclerotic process, femoral arteries may locally develop compensatory enlargement to compensate for lumen narrowing by plaque formation (29). Consequently, we can assume that positive femoropopliteal remodelling could be associated with a greater amount of VCs.

Severe VC is associated with perioperative in-stent thrombosis

Occurrence of in-stent thrombosis at 1 month is significantly higher in most calcified groups. Vascular calcifications are known to represent a technical challenge for interventionalists as they may make artery recanalisation difficult and may promote technical failure leading to a perioperative in-stent thrombosis. Different types of technical failure were observed during long femoropopliteal recanalisation such as non-expansion of self-expandable stents, stent malapposition or plaque fracture leading to local thrombosis. It is noteworthy that severe VC is often considered an exclusion criterion for femoropopliteal clinical trials (30, 31) but, so far, few data have been available to state that severe VCs are a predictive factor for poor morphological success at 1 month.

Mid-term in-stent thrombosis and restenosis with soft plaques

The multivariate analysis concluded that patients with intermediate VCs are less likely to present an in-stent thrombosis during follow-up in comparison to others. Indeed, patients with severe VC presented in-stent thrombosis during the perioperative period and patients with soft plaques were at risk of in-stent thrombosis at mid-term. Analysis of in-stent thrombosis timing suggests that the in-stent thrombosis mechanism may be different. Technical failure, as described above, may be the main cause of perioperative in-stent thrombosis. However, for a longer follow-up, a biological factor may explain in-stent thrombosis. Therefore, this observation may suggest that lesions with a low amount of VC are an entity at risk of complications following endovascular revascularisation. This hypothesis derives from fundamental research where it was recently found that osteoprotegerin (OPG) and osteoid metaplasia (OM) were associated with carotid plaque stability (1). In this study, a significantly higher presence of OM, OPG and pericytes was noted in asymptomatic compared to symptomatic plaques. Without femoropopliteal plaque analysis, these results cannot be transposed and a plaque accident is not similar to a stent thrombosis but it can be

assumed that femoropopliteal VC could have the same behaviour on the stented plaque as the carotid plaque. An interesting study on coronary arteries failed to show that severely calcified arteries have a lower rate of in-stent restenosis whereas the working assumption was based on previous histological findings (32). The authors noted that restenosis is composed of neointimal hyperplasia derived from smooth muscle cells and fibroblasts migrating from the vessel wall. Since normal components of calcific arterial walls are largely replaced by calcium deposits and fibrosis, the authors suggested that stented calcific arteries would restenose less than non-calcified arteries. Finally, despite the potential role played by calcifications, it has been shown also in coronary artery disease that a pathophysiological process characterized by impaired endothelial coverage, persistent fibrin deposition, and ongoing vessel wall inflammation contribute to late in stent thrombosis(33).

Limitations

The main limitation of this study is obviously the number of patients enrolled. Although statistical tests designed for small samples were used, a greater number of patients would probably have highlighted other differences between the groups. For that reason, the results of the multivariate analysis should be interpreted with caution. It is probably more appropriate to conclude that we found a trend more than there is clearly a significant difference between groups. Moreover, the rate of stent thrombosis is especially high in this study but does not reflect the rate found in both registries. As a reminder, the rate if in-stent thrombosis at one year was 11.3% and 14.6% in STELLA and STELLA PTX registries respectively. But in the paper of Bosier et al(34), this rate was 24% at one year, almost similar to our study (25.6%). Grouping of both registries may also be interpreted as a bias because bare metal stent (BMS) and drug-eluting stent (DES) outcomes have been mixed. However, it can be observed that the DES rate was similar in all groups and recently, we have shown with a propensity score-

matched analysis that, according to both registries, paclitaxel-eluting stents do not seem to provide benefits in terms of clinical and morphological outcomes for TASC C/D lesions compared to bare metal stent(35). Moreover, there is an heterogeneity in the dual antiplatelet therapy (DAPT) prescription in the present cohort and even though there is no high level of evidence for DAPT after peripheral endovascular stenting, coronary studies recommended DAPT systematically for a minimum duration of 6 months to prevent in stent thrombosis(36). Our working hypothesis needed to focus on two different lesions in terms of plaque composition: these were no VC and severe VC. The rate of VC according to median values ultimately showed that group composition was appropriate to our objective to compare essentially no Ca and severe Ca. The intermediate VC group including the 2nd and 3rd quartiles of the entire population corresponds to the “moderate” group in many studies using a 3-grade VC classification. We do not support that four grades of VC classification would be relevant since our hypothesis was that no and severe VC groups are of interest and leads to different outcomes with different mechanisms.

Conclusion

This study showed that an accurate quantification of VC is interesting to assess endovascular outcomes after stenting of FP lesions. It seems that both absence and heavily calcifications are at risk of in-stent thrombosis. Calcification of a certain quantity and quality may be necessary for plaque stability. Additional data with a larger population are mandatory to confirm these results.

326 **Conflict of interest**

327 Yann Gouëffic: Boston Scientific, Cook, Hexacath, Medtronic, Perouse.

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Table 1. Demographic data

	Total Population (n=39)	Non calcified group (n=10)	Intermediate calcifications group (n=19)	Heavily calcified group (n=10)	P value
Age (mean ± SD)	71 ± 12	70.5 ± 11.2	71 ± 12.8	71.4 ± 12.7	0.96
Gender (male, n, %)	24 (61.5%)	4 (40%)	12 (63.2%)	8 (80%)	0.181
Body Mass index (mean ± SD)	24.2 ± 5	24.1 ± 4.3	23.2 ± 5.4	26.6 ± 4.5	0.25
Active smoking (n, %)	12 (30.8%)	5 (50%)	6 (31.6%)	1 (10%)	0.152
Hypertension (n, %)	25 (64.1%)	6 (60%)	14 (73.7%)	5 (50%)	0.428
Diabetes mellitus (n, %)	8 (20.5%)	0	5 (26.3%)	3 (30%)	0.198
Renal failure* (yes, n, %)	5 (12.8%)	1 (10%)	2 (10.5%)	2 (20%)	0.733
Hyperlipidemia (n, %)	21 (53.8%)	3 (30%)	10 (52.6%)	8 (80%)	0.080
Double antiplatelet therapy (n, %)	13 (33.3%)	4 (40%)	7 (36.8%)	2 (20%)	0.759
Anti-vitamin K therapy (n, %)	1 (2.6%)	0	1 (5.3%)	0	0.583
Statin therapy (n, %)	30 (76.9%)	8 (80%)	13 (68.4%)	9 (90%)	0.409
ACE inhibitor or ATA II * (n, %)	64.1 (25%)	6 (60%)	11 (57.9%)	8 (80%)	0.475
Rutherford stages					
3 (n, %)	14 (35.9%)	4 (40%)	6 (31.6%)	4 (40%)	
4 (n, %)	16 (41%)	4 (40%)	10 (52.6%)	2 (20%)	0.461
5 (n, %)	9 (23.1%)	2 (20%)	3 (15.8%)	4 (40%)	

* defined as an estimated glomerular filtration rate 30<ml/min/1.73m^{-2} according to MDRD formula

* ACE: Angiotensin-converting-enzyme ARA II : angiotensin II receptor antagonist

Table 2. Anatomical and intraoperative data

	Total Population (n=39)	Non calcified group (n=10)	Intermediate calcifications group (n=19)	Heavily calcified group (n=10)	P value
SFA diameter (mm, mean±SD)	5.4 ± 1.2	4.6 ± 0.8	5.2 ± 1	6.8 ± 0.8	<0.0001
Lesion length (mm, mean±SD)	202.1 ± 103.2	176.9 ± 79	217.4 ±108.1	201.1 ± 120.8	0.616
SFA occlusion (yes, n, %)	28 (71.8%)	7 (70%)	13 (68.4%)	8 (80%)	0.796
Ca volume lesion (mm^3, mean±SD)	1076 ± 1322	5.5 ± 7.4	870 ± 701	2702 ± 1571	<0.0001
ALu volume lesion (mm^3, mean±SD)	1996 ± 1553	1194 ± 1027	1584 ± 772	3786 ± 1895	<0.0001
Ca volume SFA (mm^3, mean±SD)	1348 ± 1428	24.6 ± 44.1	1196 ± 854	3141 ± 1392	<0.0001
ALu volume SFA (mm^3, mean±SD)	5735 ± 3041	4651 ± 2425	4870 ± 2836	8769 ± 2107	0.001
Drug eluting stent (yes, n, %)	19 (48.7%)	3 (30%)	12 (63.2%)	4 (40%)	0.193
Stented length (mm, mean±SD)	250 ± 104	233 ± 90	267 ± 108	233 ± 116	0.611
Number of stents (mean±SD)	2.5 ± 1.3	2.4 ± 1	2.8 ± 1.2	2 ± 1	0.22
Stent diameter (mm, mean±SD)	6 ± 0.6	5.8 ± 0.8	6.1 ± 0.5	5.9 ± 0.6	0.391
Fluoroscopic time (min, mean±SD)	18.5 ± 12	11.1 ± 3.9	18.2 ± 8.2	27.3 ± 17.6	0.009
Surface-dose product ($mGy.m^2$, mean±SD)	2.91 ± 3.91	1.25 ± 0.61	3.55 ± 3.99	3.39 ± 3.06	0.3
Contrast load (mL, mean±SD)	69.1 ± 31.5	51.8 ± 22.3	72.4 ± 30.7	81.6 ± 37.4	0.097

* SFA: superficial femoral artery, Ca: calcifications, ALu: arterial lumen

Table. 3 Influence of calcification on postoperative outcomes during follow-up according to groups (log-rank test)

	Occurrence (n,%)	Group 1	Group 2	Group 3
Stent thrombosis (in global population)	10 (25.6%)	P value of pair comparison		
Group 1 (No Ca group)	4 (40%)		0.037	0.861
Group 2 (Intermediate Ca group)	2 (10.5%)	0.037		0.121
Group 3 (Heavy Ca group)	4 (40%)	0.861	0.121	
In-stent restenosis	9 (23.1%)	P value of pair comparison		
Group 1	4 (40%)		0.358	0.741
Group 2	4 (21.1%)	0.358		0.520
Group 3	1 (10%)	0.741	0.520	
Target lesion revascularization	17 (43.6%)	P value of pair comparison		
Group 1	19 (65.5%)		0.113	0.735
Group 2	5 (26.2%)	0.113		0.380
Group 3	5 (50%)	0.735	0.380	
Target extremity revascularization	18 (46.2%)	P value of pair comparison		
Group 1	6 (60%)		0.113	0.735
Group 2	6 (31.6%)	0.113		0.380
Group 3	6 (60%)	0.735	0.380	

Table. 4 : Factors associated with stent thrombosis by log rank test.

	No stent thrombosis (n=29)	Stent thrombosis (n=10)	P value
Age (years, mean±SD)	72.5 ± 11.1	65.9 ± 13.6	0.213
Body mass index	23.9 ± 5.2	25.2 ± 4	0.468
Gender (male, n, %))	16 (55.2%)	8 (80%)	0.155
Active smoking (n, %)	10 (34.5%)	2 (20%)	0.332
Hypertension (n, %)	18 (62 .1%)	7 (70%)	0.48
Diabetes mellitus (n, %)	5 (17.2%)	3 (30%)	0.601
Renal failure* (yes, n, %)	4 (13.8%)	1 (10%)	0.619
Hyperlipidemia (n, %)	13 (44.8%)	8 (80%)	0.058
Double antiplatelet therapy (n, %)	11 (37.9%)	2 (20%)	0.473
Anti-vitamin K therapy (n, %)	1 (3.4%)	0	0.744
Statin therapy (n, %)	22 (75.9%)	8 (80%)	0.581
ACE inhibitor or ATA II * (n, %)	18 (62.1%)	7 (70%)	0.480
Rutherford stages 3/4/5	9(31%)/13(44.8%)/7(24.1%)	5(50%)/3(30%)/2(20%)	0.549
Lesion Ca			
No Ca (group 1)	6 (60%)	4 (40%)	
Intermediate Ca (group 2)	17 (89.5%)	2 (10.5%)	0.109
Heavy Ca (group 3)	6 (60%)	4 (40%)	
SFA diameter (mm, mean±SD)	5.2 ± 1.1	6.1± 1.3	0.05
Lesion length (mm, mean±SD)	205 .6± 107.7	183.9 ± 93	0.575
SFA occlusion (yes, n, %)	7 (70%)	13 (68.4%)	0.796
Drug eluting stent (yes, n, %)	3 (30%)	12 (63.2%)	0.193
Stented length (mm, mean±SD)	250.3 ± 109.3	240 ± 91	0.790
Number of stents (mean±SD)	2.5 ± 1.2	2,60± 1.1	0.75
Stent diameter (mm, mean±SD)	6 ± 0.6	6 ± 0.7	0.885

Table 5. Results of the multivariate analysis

	coeff	Wald χ^2	df*	Probability > χ^2	Odds ratio (95% CI)
Intermediate Ca	-1.315	6.025	1	0.014	0.27 (0.1 - 0.77)
Sex (male)	0.256	0.311	1	0.577	1.29 (0.53 - 3.17)
Hyperlipidemia	0.412	0.828	1	0.363	1.51 (0.62 - 3.67)
SFA diameter	-0.492	3.819	1	0.051	0.61 (0.373 – 1.001)

* CI = confidence interval, df=degree of freedom

Fig. 1. CT-images processing: after centerlines extraction (A), a region of interest (purple cylinder, B) is determined and centered around the centerlines. A threshold tool is applied to segment vascular Ca (blue, C-D) and arterial lumen (red, C-D).

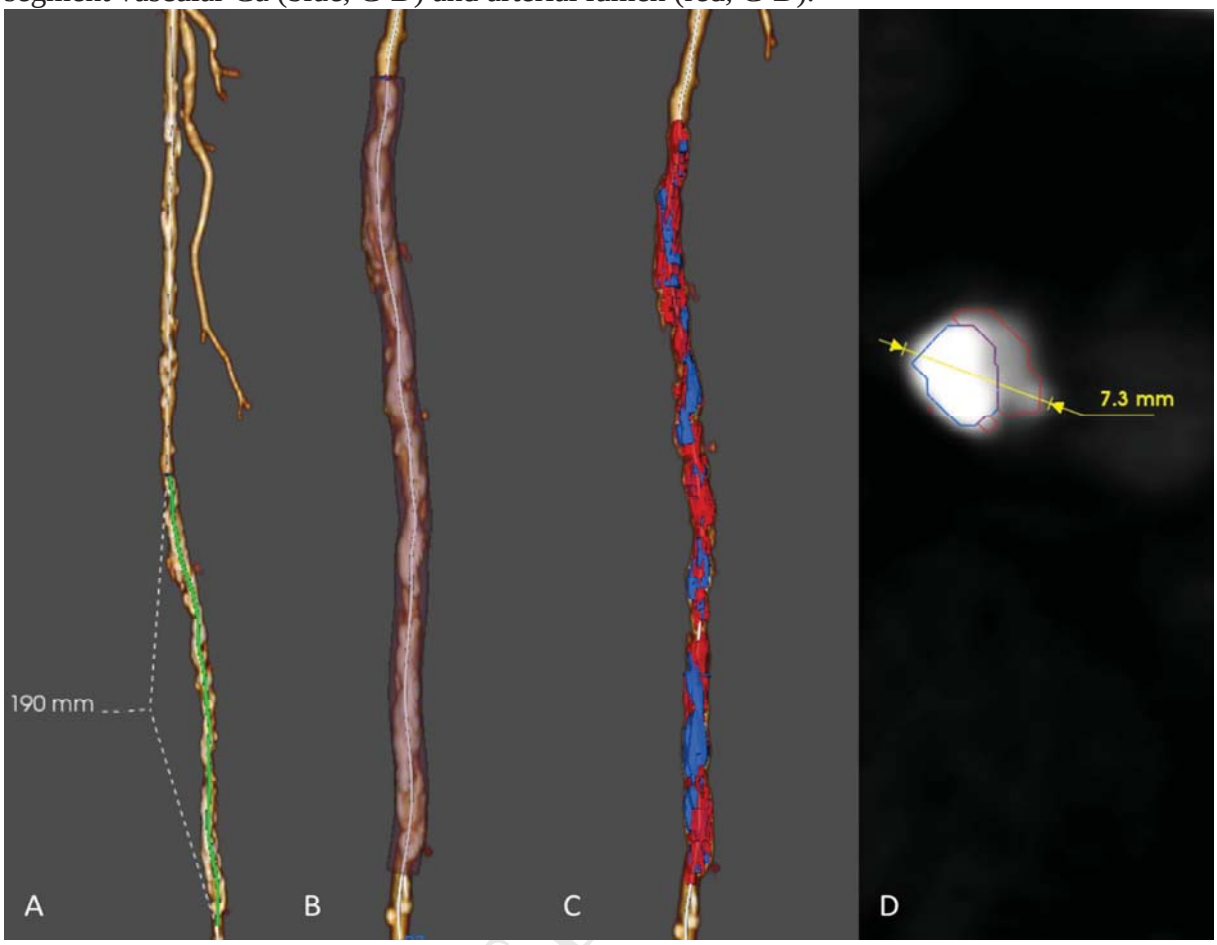

Fig. 2. Correlation between SFA diameter and percentage of Ca

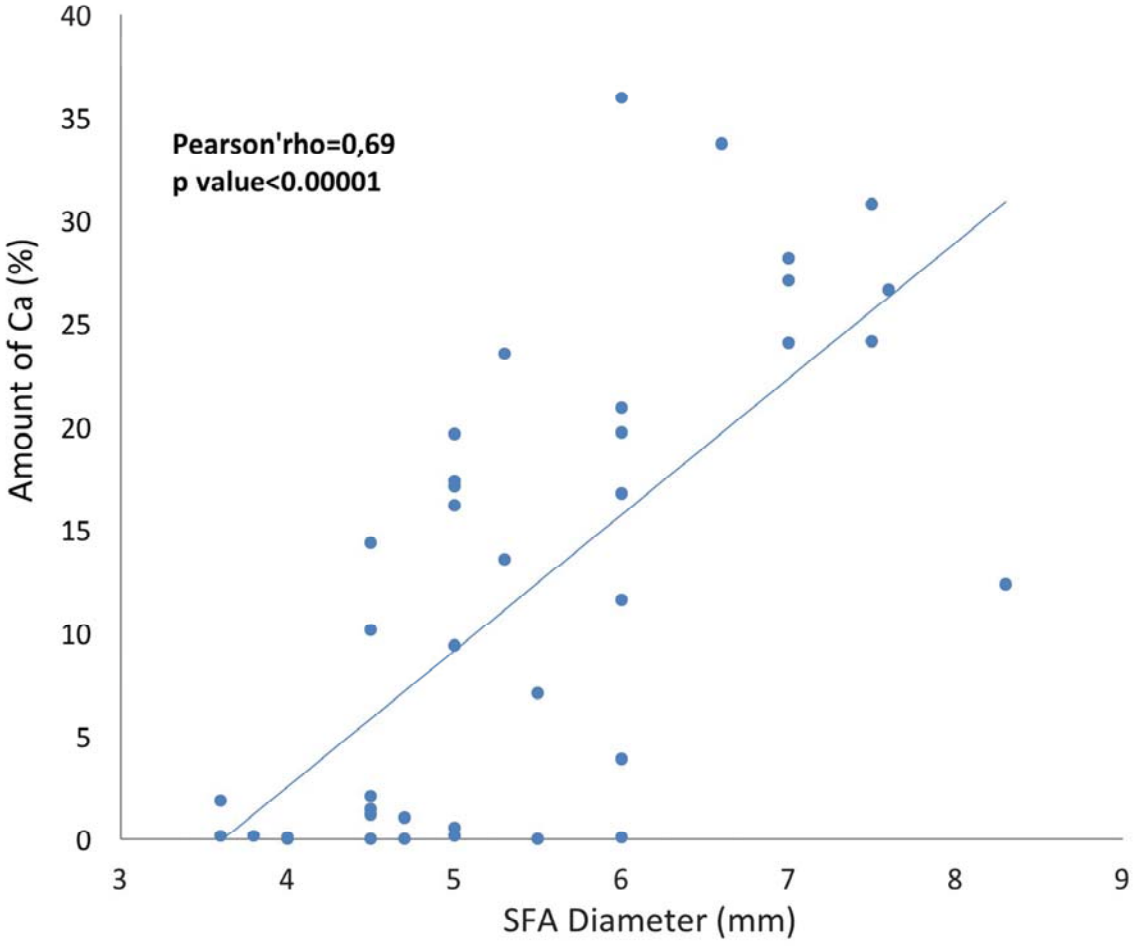

Fig. 3. Analysis of date of thrombosis according to Ca rate.