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1 **Original article**

2 **Impact of vascular calcifications on long femoropopliteal stenting**

3 **outcomes**

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22

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24

25 **ABSTRACT (word count: 391)**

26

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

32

33 **Methods:** Patients belonging to two previously published registries (STELLA and STELLA
34 PTX) and who underwent a preoperative CT scan were retrospectively included in the study.
35 VC quantification was performed with a dedicated workstation (EndoSize, Therenva) on the
36 basis of Hounsfield units (HU). The VC percentage was calculated as the ratio between VC
37 volume and the volume of the region of interest. For the analysis, patients were divided into
38 three groups according to VC percentage, from lowest to highest: group 1 (G1) included the
39 1st quartile of VCs, group 2 (G2) included the 2nd and 3rd quartiles and group 3 (G3)
40 included the 4th quartile. Risk of in-stent thrombosis was analysed using a multivariate
41 model.

42

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

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

57

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

62

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

65

66 Introduction

67 The most common cause of peripheral arterial disease is atherosclerosis. Despite being
68 exposed to similar risk factors, peripheral arteries develop heterogeneous atherosclerotic
69 lesions. Our previous work showed that carotid arteries develop predominantly lipid-rich
70 lesions and microcalcifications, while femoral arteries develop fibrotic lesions, with extensive
71 vascular calcification (VC) and frequent presence of osteoid tissue (1-4). These differences
72 may have major clinical implications. Firstly, VC may destabilise atheromatous plaques and
73 contribute to plaque rupture (5-7). Moreover, advanced and extensive VC contributes to
74 arterial stiffness and hypertension, an important risk factor for plaque rupture (8, 9).
75 Secondly, the presence of VC may influence the technical success rate and outcomes of
76 peripheral endovascular procedures (10). It is noteworthy that severe VC is often considered
77 an exclusion criterion in femoropopliteal clinical study protocols. Moreover, balloon
78 angioplasty of severe calcified lesions is limited by early elastic recoil and poor acute and
79 long-term outcomes (11). Although nitinol stents are designed to prevent elastic recoil and
80 constrictive remodelling, severe VC may prevent stent expansion, resulting in poorer
81 outcomes when compared to fully expanded stents (12). Also, it seems that VC may influence
82 the efficacy of drug-eluting balloons during revascularisation of femoropopliteal lesions,
83 mainly in cases of circumferential distribution (13).
84 Nevertheless, few data are available to determine the influence of VC on femoropopliteal
85 endovascular treatment outcomes. In the present study, we sought to determine the
86 perioperative and mid-term outcomes following long femoropopliteal stenting according to
87 preoperative VC burden.

88

89 **Patients and Methods**

90 *Population*

91 Patients included in this study belong to two published prospective registries (14, 15). Briefly,
92 the patients presented with femoropopliteal lesions ≥ 15 cm (TASC II C and D) and were
93 enrolled as soon as the guide crossed the lesion. The first patient cohort (STELLA study) was
94 treated with a LifeStent® bare metal stent (Bard Peripheral Vascular, Tempe, AZ, USA) and
95 was enrolled between November 2008 and October 2009. The second patient cohort was
96 treated with a Zilver® PTX® paclitaxel-eluting stent (STELLA PTX study) (16) (16) (16)
97 (16) (16) (16) (Cook Peripheral Vascular, USA) and was enrolled between March 2011 and
98 April 2012. The inclusion/exclusion criteria and the endovascular procedures were identical
99 for both groups and have already been reported in the STELLA and STELLA PTX studies.
100 Protocols were approved by local ethics committees and all patients gave their informed
101 consent.

102

103 *CTA analysis and quantification of VC*

104 All computed tomography angiograms (CTAs) were analysed with a dedicated workstation
105 (17-20) (EndoSize®, Therenva, France) by one investigator blinded to outcomes. Centrelines
106 from the common femoral artery to the end of the popliteal artery (Fig. 1A) were manually
107 extracted for femoropopliteal occlusions, otherwise automatic extraction was used (in case of
108 stenosis). A region of interest (ROI) was determined as a cylinder centred around centrelines
109 (Fig. 1B) whose diameter was manually adjusted to ensure all VC was included. Within the
110 ROI, a dedicated program allowed segmentation of both arterial lumen (ALu) and VC
111 (Fig. 1C-D) with a thresholding tool. The difference between ALu and VC was based on HU
112 density (21-23): voxels in the range 400-3000 HU were considered VC (and quantified in
113 mm^3) whereas voxels in the range 100-400 HU were considered ALu (Fig. 1C-D). Volume of

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

119

120 *Definition of groups*

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

125

126 *Follow-up*

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

131

132 *Endpoints*

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

138

139 *Statistical analysis*

140 Continuous variables were presented as mean \pm SD and categorical variables as count and
141 percentages. Pearson's chi-square test was used for comparisons of continuous variables, and
142 one-way factorial ANOVA for categorical data after testing the normality of the data, and
143 then differences among means were analysed using post-hoc Tukey-HSD or Games-Howell
144 multiple comparison tests depending on the results of the assumption of homogeneity of
145 variances (Levene test). A correlation between SFA diameter and amount of VC was
146 calculated by use of the Pearson correlation coefficient. Postoperative outcomes were
147 compared between groups using the log-rank test. A predictive model was developed to
148 demonstrate any correlation between pre/perioperative factors and stent thrombosis. Inclusion
149 of variables in the model with $p < 0.1$ (or forced-in) were based on the Pearson's chi-square
150 test for categorical variables and ANOVA for continuous variables. A multivariate analysis
151 implemented using a Cox model with a stepwise descending procedure was fitted. A p value
152 < 0.05 was considered statistically significant. Data were analysed using SPSS software
153 (SPSS Inc., Chicago, IL, USA).

154

155

156 **Results**

157 *Demographic data*

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

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

169 *Lesions and intraoperative data (Table 2)*

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

179

180 *Perioperative results*

181 During follow-up, 10 (25.6%) stent thromboses occurred (Table 3): 4 (40%) in group 1, 2
182 (10.5%) in group 2 and 4 (40%) in group 3. According to the log rank test, this rate was
183 statistically different between group 1 vs. 2 but not between group 2 vs. 3 and group 1 vs. 3.
184 When the date of occurrence of stent thrombosis was analysed (Fig. 3), a trend was shown:
185 heavy Ca was associated with early stent thrombosis, while no Ca was associated with late
186 stent thrombosis. More precisely, heavy Ca presented a stent thrombosis at 1 month while
187 every patient with no Ca presented a stent thrombosis between the 6th and the 24th months.
188 All patients with intermediate Ca presented a stent thrombosis after the 48th month. Rates of
189 in-stent restenosis, TLR and TER are provided in Table 3 and were not statistically different
190 between groups.

191

192 *Risk factor for in-stent thrombosis*

193 Results of the univariate/multivariate analysis are provided in Tables 4 and 5. On univariate
194 analysis, the femoropopliteal diameter was higher in the in-stent thrombosis population ($6.1 \pm$
195 1.3 mm vs. 5.2 ± 1.1 , $p=0.05$) but on multivariate analysis it did not appear to be significant,
196 although a trend towards a protective effect of the femoropopliteal diameter on in-stent
197 thrombosis was noted (Table 5). The other variables included in the multivariate analysis
198 were sex, hypercholesterolaemia and calcification (according to groups). Only VC appeared
199 to significantly influence in-stent thrombosis. Patients belonging to group 2, i.e. with an
200 intermediate calcification rate, seemed to be protected from in-stent thrombosis with an odds
201 ratio of 0.27 (95% confidence interval: 0.1-0.77; $p=0.014$).

202

203

204 Discussion

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

213 Classification

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

229 accuracy of this quantification. In cardiology literature, optical coherence tomography (OCT)
230 has been reported to assess VC and stent expansion. In this particular study, a high rate of VC
231 was found to be a factor for stent underexpansion (26). Although algorithms for segmenting
232 VC on CT images have existed for decades, they have only been reported in clinical papers
233 since Ohana *et al.* (23). They proposed an alternative to the Trans-Atlantic Inter-Society
234 Consensus Document II on Management of Peripheral Arterial Disease classification (TASC
235 II)(27) based on the mean occluded diameter and percentage of calcifications. Calcification
236 volume determined by a colour-coded map provided an accurate estimate but no correlation
237 with clinical or morphological outcomes was given. Our assessment method was similar to
238 that of Ohana *et al.* but, in both cases, CTA did not allow intimal and medial calcifications to
239 be distinguished. Medial calcifications, known as Mönckeberg's medial calcinosis, are
240 associated with type II diabetes and chronic kidney disease and represent a specific pattern of
241 VC with a distinct pathological type of calcification that may contribute to arterial stiffness
242 (28).

243

244 **Lesions and intraoperative data**

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

251

252 **Severe VC is associated with perioperative in-stent thrombosis**

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

262

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

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

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

289

290 **Limitations**

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

303 matched analysis that, according to both registries, paclitaxel-eluting stents do not seem to
304 provide benefits in terms of clinical and morphological outcomes for TASC C/D lesions
305 compared to bare metal stent(35). Moreover, there is an heterogeneity in the dual antiplatelet
306 therapy (DAPT) prescription in the present cohort and even though there is no high level of
307 evidence for DAPT after peripheral endovascular stenting, coronary studies recommended
308 DAPT systematically for a minimum duration of 6 months to prevent in stent thrombosis(36).
309 Our working hypothesis needed to focus on two different lesions in terms of plaque
310 composition: these were no VC and severe VC. The rate of VC according to median values
311 ultimately showed that group composition was appropriate to our objective to compare
312 essentially no Ca and severe Ca. The intermediate VC group including the 2nd and 3rd
313 quartiles of the entire population corresponds to the “moderate” group in many studies using a
314 3-grade VC classification. We do not support that four grades of VC classification would be
315 relevant since our hypothesis was that no and severe VC groups are of interest and leads to
316 different outcomes with different mechanisms.

317

318 **Conclusion**

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

324

325

326 **Conflict of interest**

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

328

329

330

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332 None

333

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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 \pm SD)	71 \pm 12	70.5 \pm 11.2	71 \pm 12.8	71.4 \pm 12.7	0.96
Gender (male, n, %)	24 (61.5%)	4 (40%)	12 (63.2%)	8 (80%)	0.181
Body Mass index (mean \pm SD)	24.2 \pm 5	24.1 \pm 4.3	23.2 \pm 5.4	26.6 \pm 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 $30 < \text{ml/min/1.73m}^2$ 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).

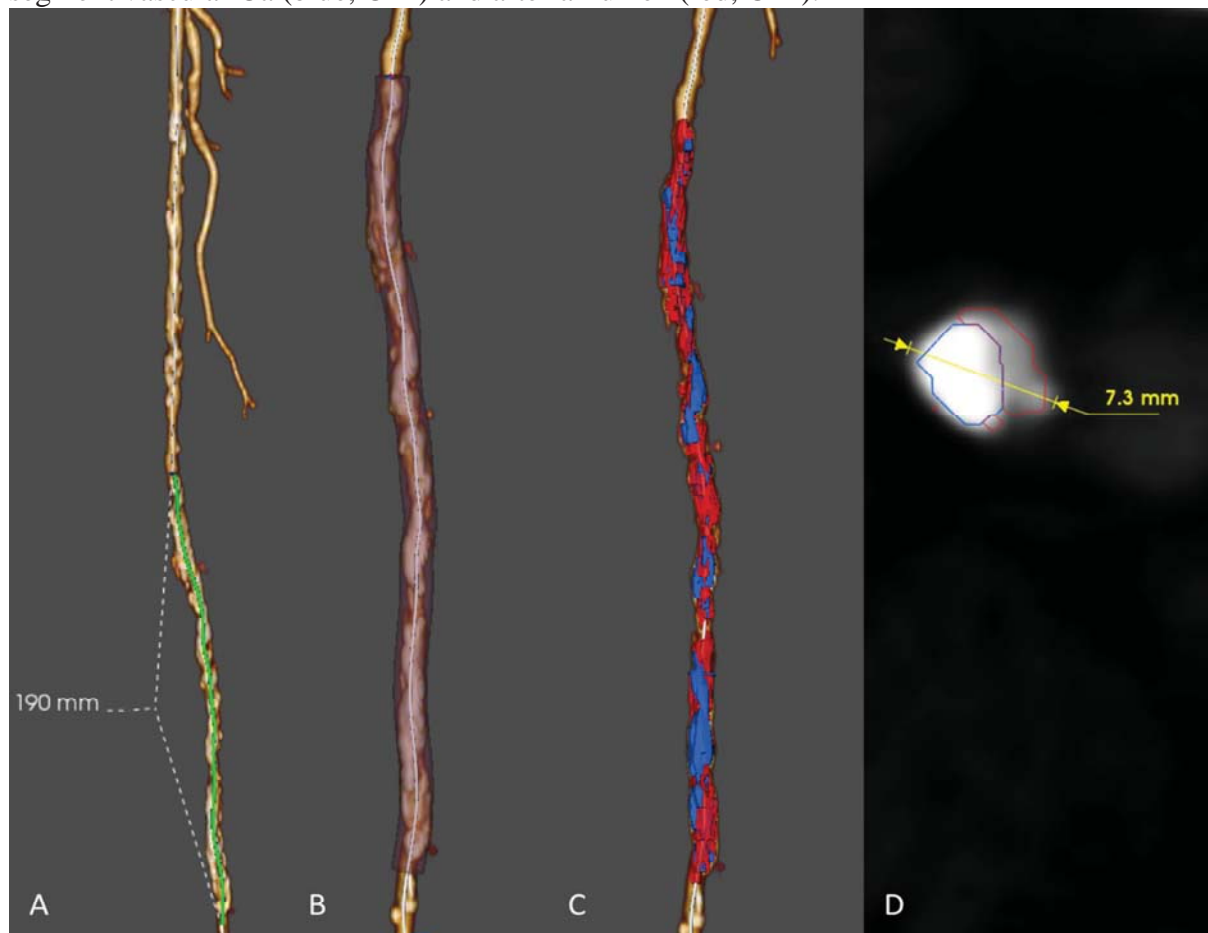


Fig. 2. Correlation between SFA diameter and percentage of Ca

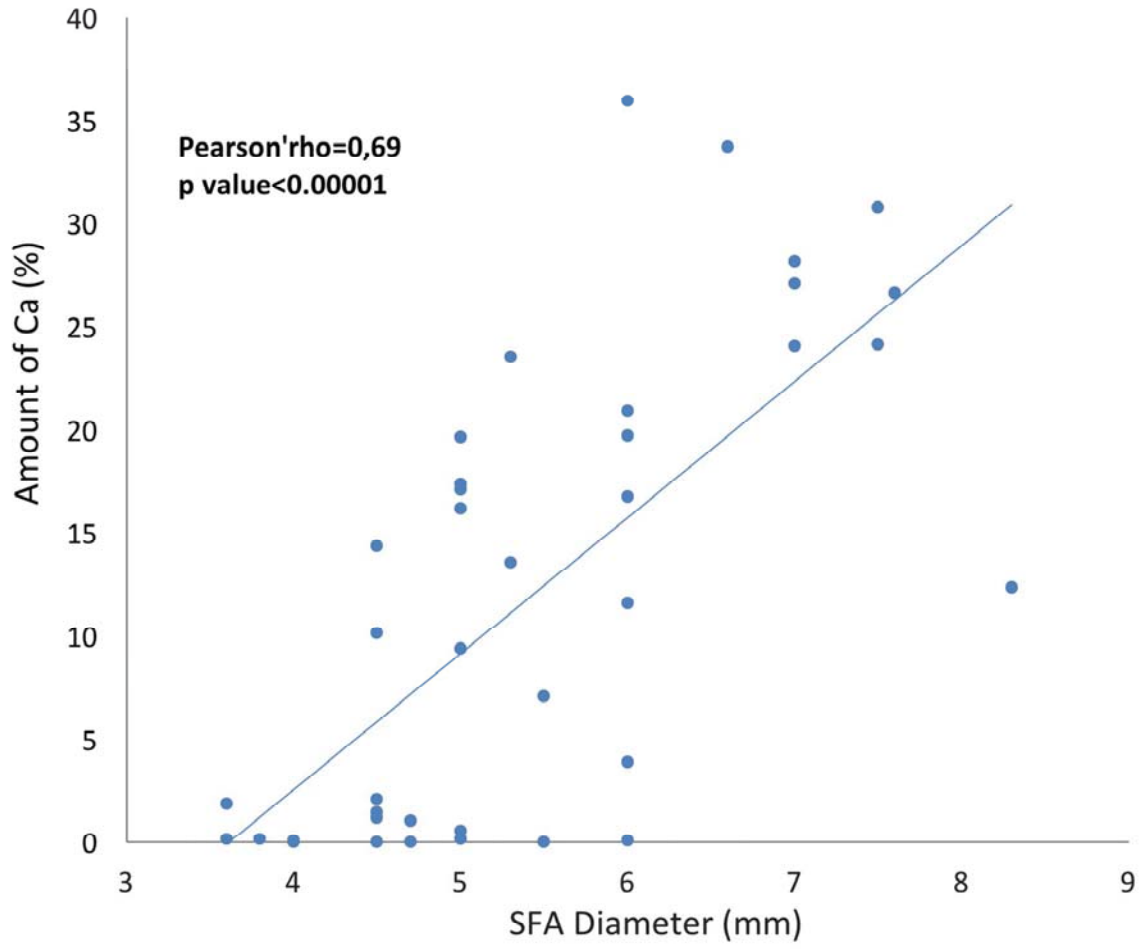


Fig. 3. Analysis of date of thrombosis according to Ca rate.

