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Intra-coronary thrombus evolution during acute coronary syndrome: regression assessment by serial optical coherence tomography analyses

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Aims We investigated the feasibility of thrombus quantification by frequency-domain optical coherence tomography (FD-OCT) methods in patients with highly thrombotic acute coronary syndrome (ACS) treated by deferred stenting strategy.

Methods and results Patients were suitable for inclusion if they presented (i) an ACS that was successfully revascularized by manual thrombo-aspiration and (ii) a large residual thrombus on coronary angiography and initial FD-OCT analysis. These patients underwent a second procedure including FD-OCT analysis after several days of optimal antithrombotic therapy. Serial area measurements within the athero-thrombotic culprit lesion were performed to evaluate the OCT-thrombus score, volume, and length. Sixteen patients (88% men/age = 59.3 ± 4.1 years/94% STEMI) were included in the study. The mean delay between OCT analyses was 3.9 ± 0.3 day. No adverse event was observed during this interval. We observed a reduction of thrombus burden between the two analyses, as assessed by the significant reductions in OCT-thrombus score (22.3 ± 2.6 vs. 10.3 ± 1.3, $P < 0.001$), OCT-thrombus volume (9.6 ± 2.3 vs. 3.6 ± 0.9 mm^3, $P = 0.003$), and OCT-thrombus length (11.1 ± 1.4 vs. 7.4 ± 0.8 mm, $P = 0.01$). The percentages of OCT-thrombus score and volume reduction were highly correlated with the inter-OCT analyses delay (respectively $\rho = 0.65$ and $\rho = 0.84$, $P < 0.01$ for both).

Conclusion FD-OCT assessment of thrombus volume in selected ACS patients is feasible, safe, and could allow clot regression monitoring *in vivo*.

Keywords acute coronary syndromes • thrombus • optical coherence tomography

Introduction

The restoration of epicardial coronary blood flow by percutaneous coronary intervention (PCI) has dramatically improved the prognosis of patients with acute coronary syndrome (ACS) during the past decades.[1] However, PCI success might be limited by the presence of intra-coronary thrombus, which is a prominent compound of the unstable coronary atherosclerotic lesion.[2,3] Although the use of intra-coronary stent is mandatory according to the European Society of Cardiology (ESC) guidelines (Class IA recommendation),[1] a growing number of publications recently challenged this paradigm and proposed a two-step strategy in selected patients, including an initial efficient thrombus removal followed by a deferred stent implantation.[4–9] This approach might improve the PCI success rate by decreasing the thrombotic load within the culprit lesion and potential embolization.[10] However, thrombus regression pattern and its timing under optimal medical therapy during ACS are partially unknown *in vivo*, although this parameter is crucial to determine the best timing for stent placement.

Different optical coherence tomography (OCT) methods have been proposed to quantify thrombus burden, but the use of these techniques for thrombus regression monitoring has never been

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reported.[11] The present pilot study evaluated the feasibility of repeated thrombus quantification by OCT and investigated its evolution in patients with ACS.

Methods

Patient selection and study design

The study global design is given in *Figure 1*. Patients were suitable for inclusion if they fulfilled the following criteria: (i) ACS (STEMI or NSTEMI) with high thrombus burden (TIMI thrombus grade $\geq$3) on initial coronary angiography, (ii) successful revascularization (final TIMI 3 flow, no chest pain and ST segment normalization) by manual thrombo-aspiration and the presence of a large residual thrombus, and (iii) decision of deferred coronary stenting by the operator.

These patients underwent initial culprit lesion documentation by frequency-domain OCT (FD-OCT) analysis and were then treated by optimal antithrombotic therapy. A second procedure was then scheduled and the subjects underwent repeated coronary angiography and culprit lesion FD-OCT analysis. Given the absence of consensus regarding the optimal delay between procedures in the literature, the control time point was left at the operator discretion. Our local Ethics Committee approved the study and informed consent was obtained.

PCI and ACS medical management

All procedures were performed through radial access. PCI was performed with a 6-Fr guiding catheter in all patients. A 0.014-inch guide wire was placed distally in the target vessel. Thrombo-aspiration was performed using a manual thrombectomy device (Eliminate. TERUMO, Tokyo, Japan). The number of passes was left at the operator discretion.

All the patients were treated in accordance with the ESC guidelines for management of patients with STEMI and NSTEMI,[1] including double antiplatelet therapy, low molecular weight heparin, and use of abciximab or bivalirudin.

Coronary angiography analysis

Two operators retrospectively reviewed coronary angiography and analysed pre- and post-thrombectomy culprit lesion characteristics, including antegrade angiographic flow and thrombus grade in the culprit vessel according to the TIMI criteria (angiographic thrombus score).[12] The degree of stenosis (before and after thrombectomy) was calculated by a dedicated quantitative coronary angiography (QCA) software (Centricity CA1000/GE Healthcare, Buc, France).

FD-OCT images acquisition

FD-OCT images were acquired with a commercially available system (C7 System; LightLab Imaging, Inc./St Jude Medical, Inc., Westford, MA, USA). The OCT catheter (C7 Dragonfly; LightLab Imaging, Inc./St Jude Medical, Inc.) was first advanced to the distal end of the target lesion after successful completion of the thrombectomy and direct intra-coronary injection of 1 mg nitrates. The entire length of the target area was then scanned using the integrated automated pullback device at 20 mm per second and rotation speed of 100 MHz. During image acquisition, coronary blood flow was replaced by continuous flushing of contrast media directly from the guiding catheter at a rate of 4 mL per second with a power injector to create a virtually blood-free environment.

FD-OCT images analysis

All images were recorded digitally, stored, and each frame read by two independent investigators blinded to timing of the analysis (initial vs.

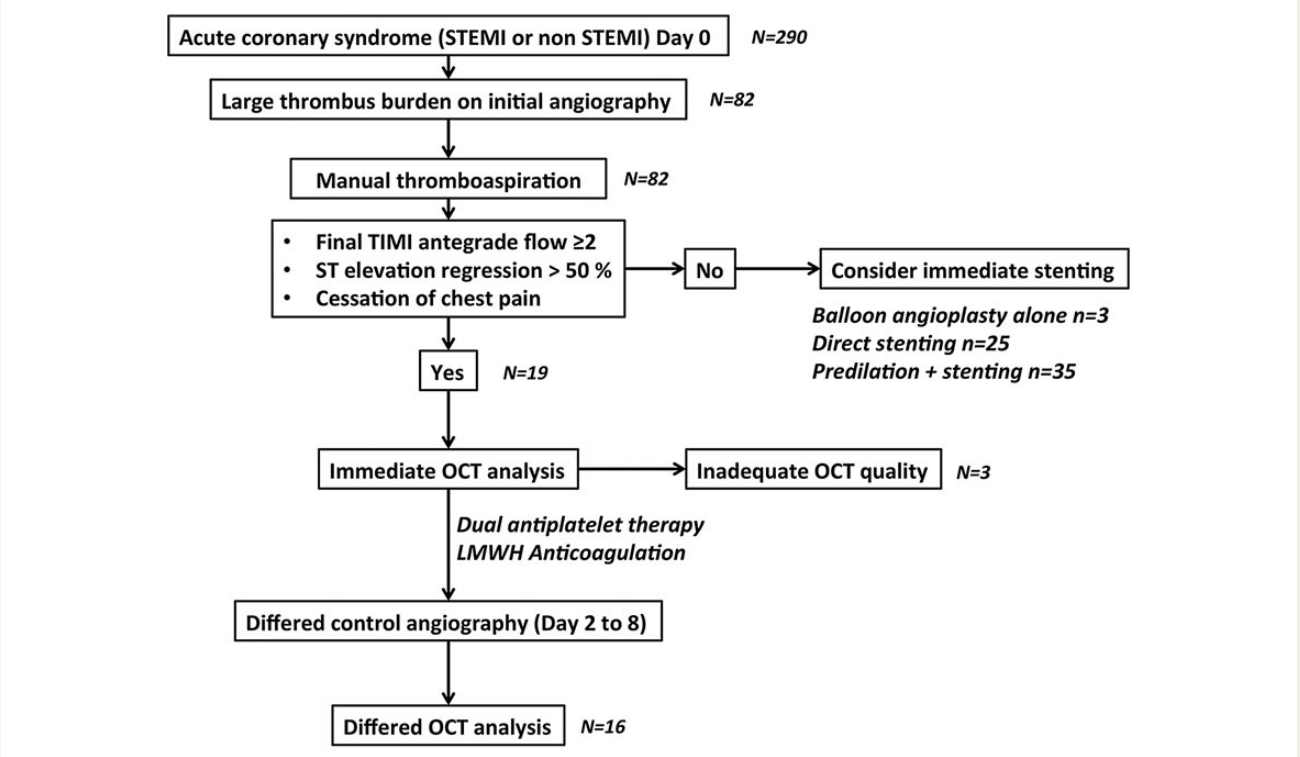


Figure 1: Flow chart of the study.

subsequent analysis), and angiographic features. Systematic images analysis was performed in 1-mm intervals. Offline analysis was performed with proprietary software (Lightlab Imaging, Inc./St Jude Medical, Inc.) after confirming calibration settings of the Z-offset.

Thrombi were defined as masses protruding into the vessel lumen, discontinuous from the surface of the vessel wall, and characterized according to the signal characteristics. White thrombus was identified as a signal-rich, low-backscattering mass, while red thrombus was identified

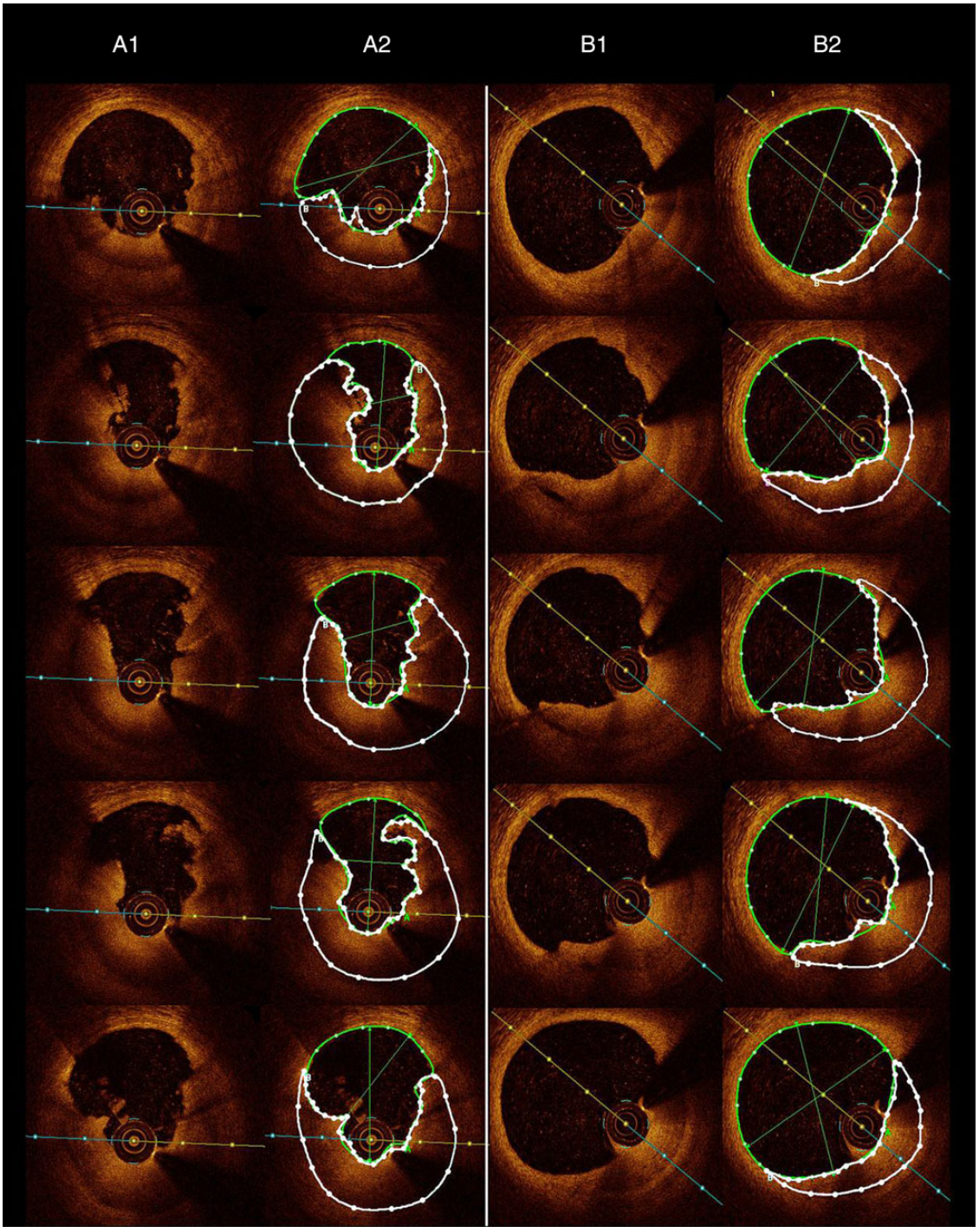


Figure 2: Example of thrombus burden optical coherence tomography analysis in a mid-left anterior descending artery lesion. The first (A1 and A2) and second optical coherence tomography runs (B1 and B2) were acquired, respectively, following thrombo-aspiration and after 5 days of antithrombotic therapy. Both sets of images (1-mm intervals) are displayed head to head, from proximal to distal part of the lesion (top to bottom), with (columns A2 and B2) and without (columns A1 and B1) thrombus area and intra-lumen area delimitations. Each row depicts the thrombus burden reduction on the exact same position within the culprit lesion, which was determined by longitudinal view analysis.

as high-backscattering protrusions inside the lumen of the artery, with signal-free shadowing in the OCT.[13] The longitudinal view was used to mark and measure the length of the athero-thrombotic culprit lesion. The distance between the most distal and the most proximal frame that showed intraluminal material suggestive of thrombus defined the thrombus length.[11]

The OCT-thrombus score was graded, according to the method proposed by the ESC OCT expert review document.[14] Thrombus score grading was based on the semi-quantitative assessment of thrombus (number of involved quadrants in the cross-sectional OCT images) and the longitudinal extension of the thrombus itself. By applying this method, in each cross-section, a thrombus was classified as absent or subtending 1, 2, 3, or 4 quadrants. The global OCT-thrombus score was then calculated as the sum of each cross-section score.[14,15]

The outlines of lumen and thrombus were drawn for area measurements on cross-sectional image by multiple points trace function (*Figure 2*). Intra-lumen area (LA) and thrombus area (TA) were measured for each interval within the lesion, and the OCT-thrombus volume (TV) was calculated as follows[11]:

$$\text{TV} = \text{mean TA} \times \text{Thrombus length}.$$

Proximal and distal reference LAs, as well as minimal lumen area (MLA), were measured for each lesion. References were defined as the most 'normal-appearing' segments 5 mm proximal and distal to the lesion shoulders by OCT. The reference LA was the average of proximal and distal reference LAs. Percent area stenosis was calculated as follows:[16]

$$100 \times \frac{(\text{reference LA} - \text{MLA})}{\text{reference LA}}.$$

Statistical analysis

Statistical analysis was performed with SPSS 16.0 (SPSS software, Chicago, IL, USA) software. Data are expressed as mean and standard error to the mean. Continuous and categorical variables were compared using the Mann–Whitney U-test (for independent samples), Student's *t*-test (for paired samples), and the χ^2 test or Fisher's exact test. Univariate correlations were assessed by Pearson's correlation or Spearman's rho (ρ) test after log transformation of variables. The inter-observer reproducibility of TV and score measurements was prospectively assessed in patients, using Pearson's correlations, the Bland–Altman plot analysis, and the coefficient of variation.[17] A two-sided alpha level of 0.05 was used for all superiority testing.

Results

Baseline characteristics

A total of 290 NSTEMI + STEMI patients were screened for inclusion between September 2011 and December 2012. Eighty-two of these patients presented initial TIMI thrombus grade ≥3 and benefited from manual thrombectomy. Nineteen of these subjects fulfilled the inclusion criteria and underwent initial OCT analyses. Three out of these (16%) subjects were excluded for inadequate image quality related to abundant red thrombus on initial analysis (inducing inability to accurately delimitate TAs and LAs); 16 patients (i.e. 32 OCT runs) were finally analysed. The baseline characteristics of the study patients are given in *Table 1*. Patients were predominantly men and suffered from STEMI in 94% of the cases. A previous thrombolysis was given in 25% of patients.

Table 1 Population baseline characteristics ($n = 16$)

Age (years)	59.3 ± 4.1
Male gender, *n* (%)	13 (88)
STEMI, *n* (%)	15 (94)
Stent thrombosis, *n* (%)	3 (19)
Initial TIMI flow grade	
Grade 0, *n* (%)	6 (37)
Grade 1, *n* (%)	5 (32)
Grade 2, *n* (%)	4 (25)
Grade 3, *n* (%)	1 (6)
Initial thrombus TIMI grade	
Grade 3, *n* (%)	2 (13)
Grade 4, *n* (%)	8 (50)
Grade 5, *n* (%)	6 (37)
Culprit lesion localization	
LAD, *n* (%)	11 (69)
RCA, *n* (%)	2 (12)
Cx, *n* (%)	3 (19)
Pre- and Per thrombo-aspiration management	
Previous thrombolysis, *n* (%)	4 (25)
Initial bivalirudin infusion, *n* (%)	4 (25)
Initial abciximab infusion, *n* (%)	8 (50)
Post thrombo-aspiration management	
Aspirin, *n* (%)	16 (100)
Clopidogrel, *n* (%)	3 (19)
Prasugrel, *n* (%)	12 (75)
Ticagrelor, *n* (%)	1 (6)
Low molecular weight heparin, *n* (%)	16 (100)

Cx, circumflex artery; LAD, left anterior descending artery; RCA, right coronary artery.

Reproducibility of the data

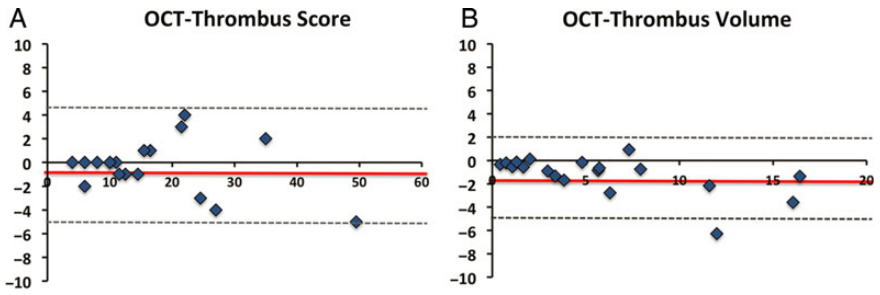
Both observers independently analysed the first 18 pullbacks to determine inter-observer variability of thrombus score and volume measurement. Bland–Altman plots for inter-observer variability are illustrated in *Figure 3*. The variability and limits of agreement showed acceptable reliability for these parameters according to the definitions.[17]

OCT-thrombus parameters correlation

There was a high degree of correlation between all the thrombus parameters on the 32 OCT analyses: the OCT-thrombus score correlated to the OCT-thrombus volume (Spearman's $\rho = 0.85$, $P < 0.01$; *Figure 4*) and the thrombus length ($\rho = 0.77$, $P < 0.001$), whereas thrombus length and volume were also correlated ($\rho = 0.81$, $P < 0.01$). These correlations remained highly significant using the Pearson's *r* correlation. However, there was no significant correlation between any thrombus OCT parameters and thrombus angiographic TIMI grade.

Thrombus regression on serial OCT analyses

The delay between OCT analyses ranged from 2 to 6 days, with an average value of 3.94 ± 0.3 days. During this period, all patients



	OBSERVER 1	OBSERVER 2	ABSOLUTE DIFFERENCE	RELATIVE DIFFERENCE	Coeff. of Correlation	Coeff. of Variation	Limits of agreement	
							Upper	*Lower*
OCT-THROMBUS SCORE	16.8±2.6	17.1±2.8	0.3 ± 0.5	0.98	0.96	2 %	-4.8	4.2
OCT-THROMBUS VOLUME	5.2±1.0	6.4±1.2	1.2 ± 0.4	0.79	0.93	21 %	-4.4	2.0

Figure 3: Inter-observer reproducibility of thrombus burden parameters. Bland–Altman plots and tables with limits of agreement are given for thrombus score (*A*) and volume (*B*).

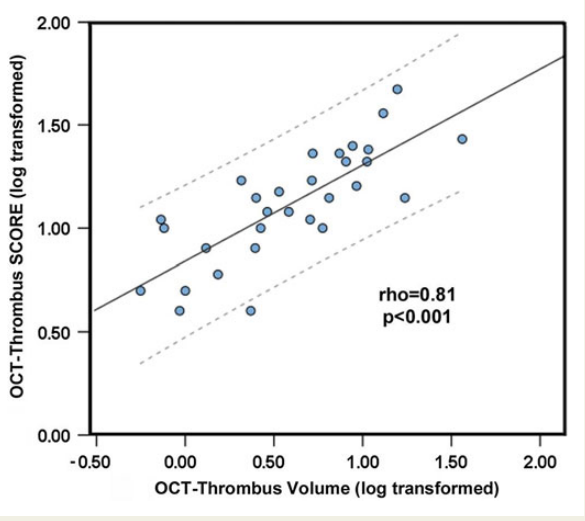


Figure 4: Correlation between thrombus volume and thrombus score in the overall population (32 optical coherence tomography runs).

were given low molecular weight heparin + double antiplatelet therapy (*Table 1*). Initial abciximab or bivalirudin infusions were, respectively, administered to 50 and 25% of the patients. There was no adverse event reported during the inter-OCT course, including no recurrence of myocardial ischaemia, ventricular arrhythmia, heart failure, target vessel re-occlusion, or significant bleeding events (BARC class $\geq$2).

The evolution of the angiography and OCT parameters is given in *Table 2*. The angiographic thrombus score significantly decreased between the two procedures. We also observed significant 50.5 $\pm$ 4.8% reduction in OCT-thrombus score, 55.6 $\pm$ 6.3% decrease in OCT-thrombus volume, and 26. $\pm$ 7.4% diminution in thrombus length. Moreover, there were significant increases in the culprit lesion MLA, the distal reference segment cross-sectional area, and OCT area stenosis. Altogether, these data suggested a reduction in the thrombotic burden and limited vasodilation of the target vessel under optimal medial therapy. However, the degree of stenosis assessed by QCA methods did not significantly change between measurements over time (*Table 2*).

The thrombus burden reduction depended on the duration of medical therapy (as assessed by the inter-OCT analyses delay). Hence, we observed highly significant correlations between inter-OCT delay and OCT-thrombus volume (Spearman's $\rho = 0.84$, $P < 0.001$; *Figure 5*), OCT-thrombus score ($\rho = 0.65$, $P = 0.006$; *Figure 5*), and OCT-thrombus length ($\rho = 0.68$, $P = 0.01$) reductions. There was no significant difference in OCT-thrombus score or volume variations in patients with white or red thrombus on initial procedure (respectively 57 $\pm$ 7.3 vs. 49.7 $\pm$ 2.7%, $P = 0.7$, and 52.5 $\pm$ 5.3 vs. 41.6 $\pm$ 5.2%, $P = 0.44$). Finally, we did not observe significant differences in OCT-thrombus score and volume reduction percentages between patients treated with bivalirudin or abciximab infusions (respectively 65 $\pm$ 9.1 vs. 52.6 $\pm$ 11, $P = 0.37$, and 48.5 $\pm$ 6.5 vs. 53.2 $\pm$ 8.1, $P = 0.93$).

Correlations between OCT and angiographic parameters

We pooled the analyses from the 32 procedures (Post-TA and control) led in the 16 patients to assess the relationships between OCT and angiographic parameters (*Table 3*). We observed modest significant inverse correlations between OCT-thrombus volume and QCA, as

well as OCT area stenosis and QCA. Moreover, we compared OCT-derived thrombus parameters in patients with low (angiographic TIMI thrombus score ranging from 0 to 2, $n = 25$) vs. high thrombotic load (angiographic TIMI thrombus score ≥ 3, $n = 7$) on angiography. There was no significant difference in OCT-thrombus volume (9.3 ± 4.9 vs. 5.9 ± 1.1, $P = 0.69$) or OCT-thrombus score (17.6 ± 2.6 vs. 15.9 ± 2.2, $P = 0.37$) between the two groups.

Table 2 Angiography and OCT parameters evolution between analyses (mean delay: 3.9 ± 0.3 days)

	Post-TA analysis	Control analysis	*P*-value
Angiography parameters			
Lesion length (mm)	15.5 ± 1.5	14.6 ± 1.4	0.55
Reference diameter (mm)	3.0 ± 0.1	3.2 ± 0.1	0.09
Stenosis percentage by QCA (%)	54.2 ± 4.5	49.7 ± 3.5	0.33
Thrombus TIMI grade	2.3 ± 0.3	0.9 ± 0.2	<0.001
Grade 0, *n* (%)	0	4 (25)	
Grade 1, *n* (%)	4 (25)	9 (56)	
Grade 2, *n* (%)	5 (31)	3 (19)	<0.001
Grade 3, *n* (%)	6 (37)	0	
Grade 4, *n* (%)	1 (7)	0	
Grade 5, *n* (%)	0	0	
OCT parameters			
Proximal reference LA (mm^2)	7.3 ± 1.1	7.7 ± 1.1	0.14
Distal reference LA (mm^2)	6.0 ± 0.9	6.8 ± 1.1	0.03
Thrombus score	22.3 ± 2.6	10.3 ± 1.3	<0.001
TV (mm^3)	9.6 ± 2.3	3.6 ± 0.9	<0.001
Thrombus length (mm)	11.1 ± 1.4	7.4 ± 0.8	0.01
MLA (mm^2)	1.7 ± 0.2	2.6 ± 0.4	0.002
Area stenosis (%)	71.8 ± 3.4	59.4 ± 6.8	0.01
White thrombus presence, *n* (%)	88	81	0.62

Subsequent PCI and clinical outcome

The underlying mechanism for culprit lesion thrombosis was identified as plaque fibrous cap rupture in 11, stent thrombosis in 3, and plaque erosion in 2 patients.[18] Twelve out of 16 patients were finally treated by stent implantation during the second procedure (drug eluting stent in nine patients). No thrombus embolization or no-reflow was observed during the PCIs. The remaining four patients did not undergo stent placement because of limited residual atherosclerotic burden with MLA >4 mm^2 or the presence of stent thrombosis with uncovered struts: these patients did not receive previous thrombolysis and benefited from an initial double antiplatelet therapy that was continued after hospital discharge, including aspirin in all cases, associated to clopidogrel in 2 and prasugrel in 2. Average troponin Ic peak was 121.2 ± 37.7 IU/L, and left ventricle ejection fraction at discharge was $50.1 \pm 2.1\%$. Clinical follow-up was obtained in 15 patients (median follow-up time: 694 days/interquartile range: 90 days); there was no major adverse cardiovascular event (death + myocardial infarction + target vessel revascularization) observed during this period.

Discussion

In this pilot study, we used FD-OCT imaging techniques to identify and quantify thrombus burden in patients with ACS. The present data illustrate that (i) serial thrombus analyses by OCT following manual thrombectomy are feasible and safe in selected patients and (ii) thrombus burden diminishes over time under optimal medical therapy and this decrease can be monitored by intra-coronary imaging.

Thrombosis plays a critical role in the pathophysiology of ACS, as disruption of an atherosclerotic plaque triggers activation of platelets and formation of fibrin within the vessel lumen.[19] However, intracoronary thrombus identification remains an issue for interventional cardiologists, since angiography has limited sensitivity. FD-OCT accurately differentiates red or white thrombus from the underlying atherosclerotic plaque.[20] Previous reports showed that OCT is comparable to coronary angioscopy and histologic examinations for

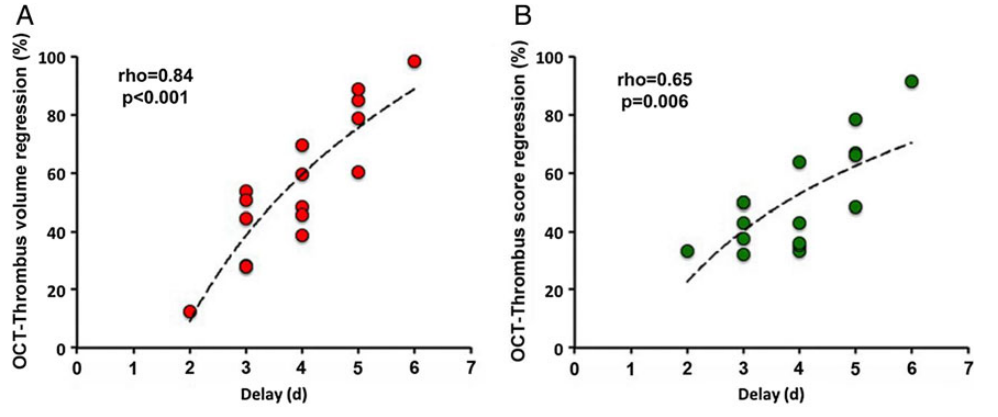


Figure 5: Time course of thrombus burden reduction in patients with acute coronary syndrome as a function of the duration of post-thrombectomy medical therapy. The thrombus volume (*A*) and score (*B*) reductions were highly correlated to the delay between analyses.

Table 3 Correlations between angiographic and OCT parameters in the 32 pooled procedures

	OCT-thrombus volume	OCT-thrombus score	OCT area stenosis	QCA	MLA
OCT-thrombus volume	X	$R = 0.69$ $P < 0.001$	$R = -0.08$ $P = 0.67$	$R = -0.37$ $P = 0.04$	$R = 0.25$ $P = 0.17$
OCT-thrombus score	$R = 0.69$ $P < 0.001$	X	$R = 0.21$ $P = 0.25$	$R = 0.007$ $P = 0.97$	$R = -0.18$ $P = 0.33$
OCT area stenosis	$R = -0.08$ $P = 0.67$	$R = 0.21$ $P = 0.25$	X	$R = 0.48$ $P = 0.01$	$R = -0.87$ $P < 0.001$
QCA	$R = -0.37$ $P = 0.04$	$R = 0.007$ $P = 0.97$	$R = 0.48$ $P = 0.01$	X	$R = -0.63$ $P < 0.001$
MLA	$R = 0.25$ $P = 0.17$	$R = -0.18$ $P = 0.33$	$R = -0.87$ $P < 0.001$	$R = -0.63$ $P < 0.001$	X

R, Pearson's correlation coefficient

thrombus detection during ACS, *in vivo* and *ex vivo*.[21,22] Moreover, as FD-OCT imaging relies on consecutive cross-sectional analyses, it might allow thrombus quantification within the culprit atherosclerotic plaque. Several groups investigated FD-OCT methods for this purpose. Hence, the COCTAIL study investigators proposed a semi-quantitative thrombus score that was based on the length and quadratic extension of thrombus on cross-sectional images.[15] More recently, Magro *et al.*[11] reported the accuracy of residual athero-thrombotic burden quantification following stent implantation in STEMI. In the present study, we investigated the feasibility of repeated thrombus volumetric quantification by OCT in high-risk ACS before placement of any stent. Our results show that this method was accurate for thrombus quantification and volume variation assessment. Interestingly, the thrombus volumes we measured were highly correlated to the semi-quantitative thrombus score values, suggesting that this parameter might adequately reflect the global thrombotic load. As we did not observe any distal embolization, severe spasm, artery re-occlusion or dissection during the post-thrombectomy, and control analyses, our data confirm previous observation regarding the safety of FD-OCT during STEMI.[23]

Our results indicate that thrombus progressively decreases over time under medical treatment. Although this evolution during ACS has been previously hypothesized and observed on angiography,[6–8] our data are the first to provide indications on the thrombus load diminution rate *in vivo*. The thrombus progressive dissolution is subtended by the interaction between two main effectors. First, antithrombotic therapy (dual antiplatelet therapy + anticoagulation) given to the subjects blocks the pro-aggregatory and pro-thrombotic pathways and prevents the thrombus growth. Secondly, the endogenous fibrinolysis systems progressively dissolve the established fibrin-stabilized platelet aggregates.[24] Both actors contribute thus to the thrombus dissolution, but their respective influence is largely unknown during ACS *in vivo*. However, the differences in the initial medical therapy (including use of prasugrel or clopidogrel), the inter-individual variable response to antiplatelet drugs, as well as the differences in patients endogenous fibrinolysis status might have partially influenced our results and account for the observed variations in thrombus decrease rate.

The concept of a two-step approach (initial thrombectomy followed by deferred stenting) has been recently developed by different groups[5–9] to improve the PCI results by limiting its complications in some selected patients. Nevertheless, the deferral interval is highly variable in these different studies, and the optimal timing between the initial and subsequent procedure is still unknown.[4] Our data indicate that the thrombus disappearance is a progressive phenomenon. We thus observed that more than a half of the initial burden is resorbed after 5 days of optimal medical treatment. The results might suggest that this delay could be chosen in case of a deferred stenting procedure to minimize the culprit lesion residual thrombus, yet it might also lead to an increased hospital stay.[10]

Several limitations of the study warrant consideration. First, our results are based on data collected from a single catheterization facility, and the sample size is small. The volumetric thrombus assessment might thus provide different information in other clinical situations. Furthermore, the small sample size might explain why several angiography parameters (such as the QCA measurement) did not significantly decrease over time. Moreover, our imaging analysis was not corroborated by pathological analysis, as this procedure could not be performed *in vivo* in ACS patients, and thrombus aspiration products are not analysed routinely in our institution. Finally, our thrombus evaluation is based on FD-OCT analysis. This technique might be limited in some cases by the signal attenuation caused by large amounts of red thrombus. This might alter the lumen and thrombus outlines drawing and impeach accurate delimitation. In this series, the analysis was possible in 84% of the screened patients and revealed evidences of white thrombus in 88% of the cases. This high proportion of white thrombus might be related to the characteristics of the population we studied. Very few data are available regarding the thrombus characteristics in STEMI and the way the antithrombotic therapy could interfere with the natural evolution of thrombus from white to red. Hence, Wieringa *et al.*[25] recently observed that white thrombus was present in a vast majority of NSTEMI patients after 3 days of pre-PCI treatment and allowed correct OCT analysis of culprit lesion. Although we acknowledge that red thrombus is a limit to thrombus quantification, our data support the feasibility of the method and show adequate reproducibility compared with other published reports in the field.[11] Finally, there was no standardization of antithrombotic therapy between patients, which might have affected the inter-individual thrombus regression rate. In summary, this current pilot study shows for the first time that repeated

thrombus volumetric analyses are feasible and safe by using FD-OCT technique in selected patients with ACS. This method provides valuable information on thrombus regression *in vivo* under optimal medical therapy. Further research is needed to assess the reproducibility and the impact of these preliminary results in larger multi-centric ACS cohorts with standardized antithrombotic therapy.

Conflict of interest: N.A., G.S., P.M., and C.C. received consulting fees from St Jude Medical; G.S. and P.M. received consulting fees from Terumo.

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