

Type of thrombus, no reflow and outcomes of coronary intervention in ACS patients: OCT-guided study

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Thrombus is the main finding in most patients with acute coronary syndrome (ACS), the type of which potentially impacts the end result of the interventional procedure in terms of no reflow and edge dissection. Optical coherence tomography (OCT) is considered a precise intra-vascular tool to image thrombi and characterise its properties. We aimed to study the impact of thrombus type, as defined by OCT, on procedural outcome in ACS patients. In this retrospective study we enrolled 100 patients who were treated by percutaneous coronary intervention (PCI) with the guidance of OCT. We recorded demographic and clinical data of the whole studied cohort. Angiographic details and procedural data were noted. Baseline OCT study was performed before intervention and repeated post-intervention. Plaque characterisation was identified, and thrombi were defined as red or white thrombi. Acute angiographic outcome was defined with special emphasis on no reflow.

Male patients and ST-elevation myocardial infarction (STEMI) patients more often had white thrombi (58.1% and 71.2%, respectively). Cases with red thrombi had longer pain duration, which was statistically significant. Edge dissection was more frequent with red thrombus, 44.7% versus 32.1% with white thrombus, but the difference is not statistically significant, while 17% of patients with white thrombi were complicated by no-reflow phenomenon versus only 4.3% in patients with red thrombi, and this difference was statistically significant.

In conclusion, OCT-guided PCI is

feasible and safe in ACS settings. OCT-guided intra-procedural differentiation of thrombus type is potentially beneficial in predicting acute procedural outcome.

Introduction

Acute coronary events are commonly caused by plaque rupture, erosion and, infrequently, calcific nodules. In the majority of patients with acute coronary syndrome (ACS), occlusive or sub-occlusive thrombus on top of plaque deformation is the main angiographic finding. Resolving acute thrombotic occlusion remains the cornerstone step in restoring adequate coronary perfusion. Blind dealing with thrombi, depending only on angiography, may be an obstacle to optimal myocardial perfusion and increase in-hospital morbidity and mortality.¹⁻⁴

In the past, intravascular ultrasound (IVUS) and, more recently, optical coherence tomography (OCT) were frequently used for percutaneous coronary intervention (PCI) optimisation. Pre-PCI intra-vascular imaging, paved the way to precisely assess lesion significance, plaque features, necessity of lesion preparation and proper stent choice regarding width and length.⁴⁻⁶

Frequency domain OCT, as compared with IVUS, has 10 times better axial resolution, weak penetration capability (1–2 mm) and requires clearance of luminal blood. IVUS utilises ultrasound waves, in contrast to OCT, which depends on infrared light with minimal wavelength (1–3 µm) yielding magnificently higher resolution, but without satisfactory tissue penetration. The wavelength of red blood corpuscle is much greater than OCT wavelength, so backscattering occurs if luminal blood is not cleared first, before starting pullback. The combination of fine resolution with minimal penetration allows smooth distinction between plaque and abluminal surface, promoting OCT to

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be more superior in luminal measurements and clarifying thrombus composition.⁵⁻⁷

Frequency-domain OCT gives the privilege of going through the pathophysiology of unstable plaque, to differentiate between plaque rupture and erosion. Thrombi were defined as protrusions into the vessel lumen, and characterised according to their signal characteristics. White thrombus was identified as a signal-rich, low-backscattering thrombus, while red thrombus was identified as high-backscattering protrusions, with signal-free shadowing.⁸⁻¹⁴

PCI success might be hindered by the presence of intra-coronary thrombi, which influences acute procedural success in terms of improving coronary flow, thrombus prolapse and distal edge dissection. Impact of thrombus morphology and histology on procedural outcome has not been clearly studied. Depending on the physical characteristics of OCT, it is the most expected to precisely clarify thrombus type and study its impact on outcome.

We aimed to study the impact of thrombus type as defined by OCT on procedural outcome in ACS patients.

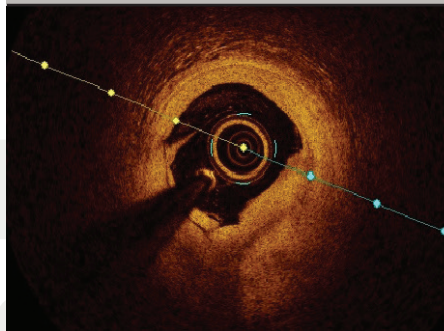
Method

Between January and June 2022, 760 cases of myocardial infarction were admitted to our centre, an invasive strategy including primary PCI was adopted in 524 patients. Of these, 131 patients underwent OCT-guided interventions based on operator experience and availability of probes; however, 31 patients were excluded either due to inappropriate image acquisition or due to excessive percutaneous transluminal coronary angioplasty (PTCA) with possible thrombus deformation. The remaining 100 patients met our inclusion criteria and were enrolled retrospectively. The exclusion criteria were: end-stage nephropathy, post-coronary artery bypass graft (CABG) patients, poor OCT image and patients with totally occlusive thrombi, even after wiring and thrombus aspiration. Written consent was achieved from every patient before participation.

Study population

Full history taking and precise clinical examination were done for all subjects. ST-

Figure 1. Optical coherence tomography (OCT) image of white thrombus



elevation myocardial infarction (STEMI) was defined as typical chest pain for 30 minutes at least, arrival to centre with primary PCI facilities within 24 hours from onset of chest pain, ST-segment elevation >0.1 mV in two or more contiguous leads or newly detected left bundle-branch block. Non-ST-elevation myocardial infarction (NSTEMI) was defined as prolonged chest pain with positive cardiac biomarkers without ST-segment elevation. We defined the culprit vessel by electrocardiogram (ECG) criteria, or during angiogram as thrombus-containing vessel.¹³

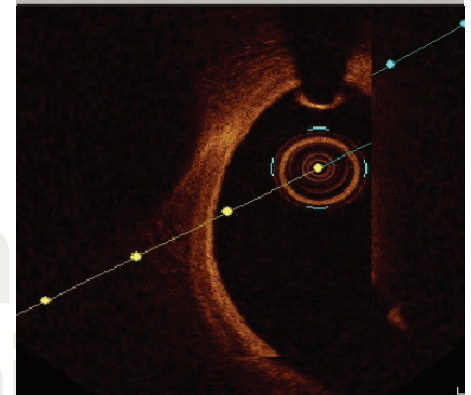
During hospital course, serum creatinine was serially withdrawn. Duration of hospital course was recorded and early post-PCI negative outcomes were mentioned. Patients were followed in outpatient clinic for six months to detect major adverse cardiovascular events (MACE).

Patient preparation and OCT procedure

Antithrombotics were administered matching the latest universal guidelines. Drug-eluting stents were deployed. Lesion measurements were done in two orthogonal views and end-diastolic frames were selected, after giving at least 200 μ g of nitrates. Post-OCT study, thrombotic lesions were categorised according to thrombus type into white and red thrombi.

A widely used frequency domain OCT system (Illumien System, Inc., St. Jude Medical, USA) and a 0.014 inch wire (Image Wire, St. Jude Medical, USA) were used. Motorised wire pull-back at 10 mm/s was done during contrast injection. OCT measurements were mentored by an OCT specialist.^{2,15}

Figure 2. OCT image of red thrombus



Plaque morphology was defined through every frame; plaque rupture was defined as discontinuity of the fibrous capsule with plaque cavitory formations. Plaque erosion was defined as irregular lumen with thrombosis overlying intact cap. Thrombus was categorised to red and white thrombi according to composition, attenuation degree and backscattering. White thrombus was defined as a signal-rich, low-backscattering mass, while red thrombus was defined as high-backscattering protrusions inside the lumen, with signal-free shadowing as shown in **figures 1 and 2**.^{2,16,17}

The OCT analysis included luminal areas at the proximal and distal referenced segments, minimal lumen areas (MLA), minimal stent area (MSA). MSA exceeding 90% was considered optimal and $\geq 80\%$ was acceptable. Dissection was defined as disruption of luminal intimal surface at the stent edges, and tissue prolapse was defined as protrusion of tissue through stent struts. Thrombolysis in Myocardial Infarction (TIMI) flow grade was recorded with special emphasis on occurrence of no reflow.^{11-14,18}

No reflow is defined as inadequate tissue perfusion through a given segment of the coronary circulation without angiographic evidence of major vessel obstruction.¹⁹

The management protocol of no-reflow phenomenon was primarily pharmacological through the intra-coronary injection of glycoprotein IIb/IIIa inhibitors, verapamil, sodium nitroprusside, adenosine and, infrequently, epinephrine.²⁰

It is worth mentioning that thrombus

Table 1. Demographics and risk profile

N=100	Number	%
Male gender	86	86
Female gender	14	14
Smokers	79	79
Hypertension	60	60
Diabetes mellitus	34	34
Hyperlipidaemia	48	48
Peripheral vascular disease	0	0
Cerebrovascular accident	6	6
Previous MI	7	7
Previous PCI	23	23
	Mean ± SD	Range
Age, years	53.3 ± 11.3	28–85
Duration of symptoms, hours	9.7 ± 8.6	2–48

Key: MI = myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation

Table 2. Culprit lesion morphology by optical coherence tomography (OCT)

N=100	Number	%	95%CI
STEMI cases	66	66	55 to 75%
NSTEMI cases	34	34	24 to 44%
No-reflow phenomenon	11	11	5 to 18%
Plaque rupture group	67	67	56 to 76%
Plaque erosion group	33	33	23 to 43%
Fibrous plaque	24	24	
Calcific plaque	12	12	
Necrotic fibrous plaque	64	64	
Thrombus type			
Red thrombi	47	47	36 to 57%
White thrombi	53	53	42 to 63%
	Mean ± SD	Range	
Reference vessel diameter, mm	3.3 ± 0.5	2.2–4.7	
Lesion dimensions, mm	1.52 ± 0.3	0.9–3	
MLA in mm ²	2.65 ± 1.0	0.8–8	

Key: CI = confidence interval; MLA = minimal luminal area; NSTEMI = non-ST-elevation myocardial infarction; SD = standard deviation; STEMI = ST-elevation myocardial infarction

identification by OCT is highly subjective and operator dependent.²¹

Statistical analysis

Statistical testing was done using the Statistical Package for Social Sciences (SPSS) version 20. Continuous variables were presented as mean ± standard deviation (SD). Categorical variables were presented as numbers and percentages. Kolmogorov-Smirnov test for normal distribution was used to delineate between parametric and non-parametric data. Analysis of variance (ANOVA) test was used to assess relations between different variables. Univariate and multi-variate analysis was done. For all tests, a p value less than 0.05 was considered a significant difference.

Results

Demographic data and risk factors

One hundred patients were enrolled in this study. Patients' demographic and clinical data are summarised in **table 1**. The mean age of studied patients was 53.3 years with males representing 86% of the studied cohort.

Mean duration of chest pain was 9.7 hours. The most encountered risk factors were: cigarette smoking (79%), hypertension (60%), hyperlipidaemia (48%) and diabetes (34%), respectively. Six subjects had previously experienced cerebrovascular stroke.

Culprit lesion characteristics

Most of the patients in this study were STEMI patients (66%), two patients had acute pulmonary oedema and one patient was in cardiogenic shock. Of culprit lesions, 67% showed plaque rupture versus 33% with plaque erosion. Culprit vessel showed white thrombus in 53 subjects while 47 patients had red thrombus. No reflow was managed successfully using intra-coronary medications in 11 patients. Culprit lesion features are shown in **table 2**.

Procedural outcome

Drug-eluting stents were implanted in all subjects. Culprit vessel was left anterior descending (LAD) 73%, right coronary artery (RCA) 18%, left circumflex (LCx) 10%, left main trunk 3%, and diagonal 3%. OCT study post-intervention revealed mean stent expansion of

Table 3. OCT study post-intervention

N=100	Number	%
Edge dissection	6	6
Tissue prolapse	38	38
Significant mal-apposition	56	56
	Mean ± SD	Range
Stent expansion, %	93.2 ± 4.5	86–114
Final MSA, mm ²	8.0 ± 2.7	3.7–15.8

Key: MSA = minimal stent area; SD = standard deviation

93.2% and mean MSA of 8 mm². Limiting edge dissection was detected in six patients, tissue prolapse encountered in 38 cases and relevant mal-apposition necessitating optimisation in 56 patients (**table 3**).

White thrombus versus red thrombus

The studied cohort was categorised according to thrombus type to two groups: white thrombus (53%) versus red thrombus

Table 4. Comparison between demographic and clinical variables as regards thrombus type

	Red thrombus Number (%)	White thrombus Number (%)	p value
Male gender N=86	36 (41.9)	50 (58.1)	0.009
Young (<55.3 years) N=50	17 (34)	33 (66)	0.009
Smoker N=79	33 (41.8)	46 (58.2)	0.04
Hypertensive N=60	32 (53.3)	28 (46.7)	0.1
Diabetic N=34	18 (52.9)	16 (47.1)	0.3
Dyslipidaemic N=48	26 (54.2)	22 (45.8)	0.1
STEMI N=66	19 (28.8)	47 (71.2)	
NSTEMI N=34	28 (82.4)	6 (17.6)	0.000
	Red thrombus Mean ± SD	White thrombus Mean ± SD	
Pain time in hours	13.7 ± 9.4	6 ± 4.6	0.000

Key: NSTEMI = non-ST-elevation myocardial infarction; SD = standard deviation; STEMI = ST-elevation myocardial infarction

Table 5. Comparison between type of thrombus as regards negative outcomes detected by OCT

	Red thrombus Number (%)	White thrombus Number (%)	p value
Prolapse	3 (6.4)	3 (5.7)	0.8
Dissection	21 (44.7)	17 (32.1)	0.1
No reflow	2 (4.3)	9 (17)	0.04
Combined negative outcome	23 (48.9)	23 (43.3)	0.5

(47%). Both groups were compared according to demographic and clinical data as shown in **table 4**. White thrombus was found to be significantly more evident (58.1%) among male patients (p=0.009). Younger age at presentation was significantly related to white thrombi, while smokers only showed a trend for that. There is no statistically relevant difference regarding thrombus type among hypertensive, diabetic, or dyslipidaemia patients. White thrombi were significantly evident in STEMI patients (71.2%, p=0.000 with odds ratio 11.5) while in NSTEMI patients, white thrombi represented a minority. Cases with red thrombi had longer pain duration before presentation as compared with white thrombi, which was significant statistically (13.7 ± 9.4 vs. 6 ± 4.6 hours) as shown in **table 4**.

Composite negative procedural outcome in relation to thrombus type

Thrombus prolapse shows no statistically significant difference between both types of thrombi. Edge dissection was noticed more frequently with red thrombus 44.7% versus 32.1% among cases with white thrombus and the difference is not statistically significant. No-reflow phenomenon complicated 17% of patients with white thrombi versus only 4.3% of patients with red thrombi, and this difference was statistically significant. Collectively, a higher percentage of combined negative outcomes was witnessed among cases of red thrombi, but with no statistical significance (**table 5**).

Confirming the previous data in **table 5**, a logistic-regression model was conducted

Table 6. Logistic-regression model of thrombus type and the no-reflow phenomenon as a negative outcome during intervention

	Exp(B)	No reflow 95%CI	Wald	p
Thrombus type (Red as having risk)	0.22	0.05 to 1.1	3.5	0.059

p>0.05 not significant

Key: CI = confidence interval

supporting that no reflow was not statistically related to red thrombi as compared with white thrombi with an odds ratio of 0.22, as shown in **table 6**.

Six-month follow-up

Recruited subjects were followed for six months in outpatient departments, no MACE were encountered in terms of cardiovascular-related mortality, myocardial infarction or target vessel re-intervention, apart from minor bleeding in a single subject and two patients' admission with decompensated heart failure.

Discussion

The essential target of this study was to check the feasibility of OCT guidance in differentiating red and white thrombi within culprit lesions of ACS, thereafter, which type is more related to negative procedural outcomes such as no reflow, edge dissection, thrombus prolapse and their combined end point.

Most of the ACS patients in our study were presenting with STEMI (n=66). Plaque rupture was encountered in 77% of patients, where it represented 83% of STEMI cases, while plaque erosion represented 64% of NSTEMI patients. This finding is considered a rehearsal of what Guagliumi *et al.*, Fang *et al.*, and Dai *et al.* found in their studies.²²⁻²⁴

Before discussing our targeted differentiation of thrombus types to red and white, a very important clarification has to be done, because of which a lot of ACS patients were not recruited to our study. OCT-guided thrombus and plaque analysis was done only if at least TIMI flow ≥2 was achieved after culprit lesion wiring ± thrombus aspiration,

but not after PTCA, fearing that PTCA may alter plaque morphology or add to negative outcomes as no reflow before our analysis. This pathway was also done by Amabile *et al.* when they studied thrombus burden by OCT before and after deferral of PCI in STEMI patients in 2014.²⁵

White thrombus was more evident in male gender (58.1%) and also in young age (<53 years, our mean age) whereas smokers only trended for that. This can be attributed to early time of presentation in young male smoker patients who are not preconditioned to ischaemia at the time of presentation, when the thrombus is mainly formed of platelets, before fibrin meshwork is well established and red blood cells profoundly settle in the clot. Other atherosclerotic risk factors such as hypertension, diabetes or dyslipidaemia were not statistically different between the two types of thrombi.

White thrombi were consistently present in STEMI patients (71.2% of STEMI patients) but they represented a minority in NSTEMI patients, while the reverse was encountered with red thrombi. The group of patients with red thrombi had a longer duration of pain before presentation (13.7 ± 9.4 hours) compared with the group with white thrombi (6 ± 4.6 hours), which may be a dart to our point that fibrin mesh maturation and red blood cell settlement present after a longer time.

Despite a paucity of data about thrombus type in relation to different demographic, clinical and angiographic presentations, shades of our data were echoed in a review of literature published by Khandkar *et al.* in 2021 about the mechanistic differences among ACS patients, how to

detect by imaging (where OCT surely was recommended as the best) and how this can affect the targeted procedure plan.²⁶

As for acute procedural negative outcomes, our study focused on no reflow, thrombus prolapse and dissection. White thrombi were found to be strongly related to occurrence of no reflow, which happened in 17% of white thrombi patients versus only 4.3% of red thrombi patients. Again, this was not stated as solidly as we state before, but suggested by Khandkar *et al.* by relating ruptured fibrous cap to STEMI patients to white thrombi, then relating no reflow to STEMI patients.²⁶

Logically, if no-reflow phenomenon is mostly due to micro-thrombi dislodgement to distal circulation after PTCA or stent deployment, as stated in almost all literature discussing this phenomenon, this shall happen more commonly with the platelet-rich white thrombi than with the fibrin and red blood cell-rich red thrombi. This could also explain the good response of no reflow to intracoronary glycoprotein IIb/IIIa inhibitors to stop platelet aggregation and white thrombus propagation.^{20,22}

Regarding thrombus prolapse, there was no significant difference between the two types of thrombi, while dissection was encountered more with red thrombi patients but without statistical significance. Also, the combined negative outcome showed no difference between the two thrombi types.

This study is not a limitation-free study, being a non-randomised study, selection bias and other forms of bias cannot be excluded. Moreover, the study was not empowered to detect differences in MACE or other clinical outcomes. So, larger randomised clinical

Key messages

- Optical coherence tomography (OCT) is feasible in setting of acute coronary syndrome (ACS) when used by experienced hands
- OCT can perfectly optimise angiographic outcome post-percutaneous coronary intervention (PCI)
- White thrombus is a major risk factor of no reflow
- Anticipation of no reflow is possible with intravascular imaging

studies are needed to clarify these gaps of evidence. Despite these limitations, we do believe that our data are potentially adding to the body of evidence supporting the use of OCT as the best intra-vascular imaging modality to optimise acute procedural outcomes in ACS patients.

Conclusion

OCT-guided PCI is feasible and safe among patients with ACS. OCT-guided intra-procedural differentiation of thrombus type is potentially beneficial in predicting acute procedural outcome ●

Conflicts of interest

None declared.

Funding

None.

Study approval

The study had ethical approval number FMASU R 162 2022.

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