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RESEARCH ARTICLE

INTRACORONARY EXPLORATION IN ACUTE CORONARY SYNDROME BY OPTICAL COHERENCE TOMOGRAPHY (OCT): EXPERIENCE OF NORD FRANCHE-COMTÉ HOSPITAL.

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Abstract

Purpose: We evaluated the impact of the thrombus burden measured by optical coherence tomography (OCT) on the occurrence of peri-procedural myocardial infarction among patients included undergoing percutaneous coronary intervention (PCI) in non ST elevation acute coronary syndrome.

Methods: Prospective multicenter study including patients treated for NSTE-ACS (<72 h) undergoing PCI of the infarct related artery. OCT was performed before and after PCI. Thrombus burden was measured quantitatively by planimetry, and semi quantitatively by the OCT thrombus score. Secondary endpoints evaluated the correlation between the OCT characteristics of the infarct related artery and the volume of thrombus, post PCI outcome of the thrombus, and the impact of thrombus volume on fractional flow reserve (FFR) measured at the end of the procedure.

Results: 20 patients aged 62±6 years from Nord Franche-comté hospital were included. Thrombus was more frequently present on OCT (14 patients (69%)) than on angiography (6 patients (31%)). There was no significant difference in the loading dose of aspirin, P2Y12 inhibitors or GPIIb/IIIa inhibitors between groups. Type IVa MI occurred in 7 patients (33%). The presence of thrombus was not associated with periprocedural MI (5 (39%) vs 2 (18%) p=0.93). Mean thrombus volume evaluated either by planimetry or semi-quantitavely was not predictive of type IVa MI. The presence of a plaque erosion or a plaque rupture was correlated with the presence of thrombus. There was a strong correlation between the presence of thrombus pre PCI and the presence of tissue prolapse post PCI. The volume of thrombus was significantly correlated with the volume of tissue prolapse (p=0.03 and p=0.01), this suggests that tissue prolapse is at least partly composed of thrombus. The presence of thrombus and its volume measured pre PCI did not affect the functional outcome of the angioplasty post pci (FFR = 0.94±0.04 vs 0.93±0.04 p=0.51).

Conclusion: OCT enables better visualization of thrombus than angiography in NSTE-ACS. In patients receiving optimal antiplatelet therapy, neither the presence nor the volume of thrombus impacts on the rate of periprocedural myocardial infarction. Thrombus burden as measured pre-PCI is correlated with post PCI intra-stent tissue

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protrusion, but does not influence the functional outcome of the angioplasty as measured by FFR.

Introduction:-

guided group due to the severity of the stenosis or the presence of thrombus, and required predilatation to enable an OCT run suitable for analysis.

Plaque rupture (figure 16) was present in half of all lesions and intact fibrous cap (figure 17) in the other half. Three quarters had mainly lipid-rich plaque composition, and the other 25% had fibrous plaque (Table 3).

Thrombus was visible in 14 patients (69%) on OCT. The thrombus was white in 6 patients (42.2%), red in 3 patients (19.3%) and mixed in 5 patients (38.6%).

The median thrombus volume was 1.07mm³ [0.09; 3.40], median thrombus length was 2.95 mm [0.50; 5.50], median thrombus area was 0.42 mm ² [0.12; 0.79] and median thrombus height was 0.50 mm [0, 27; 0.80].

57% of patients with thrombus received glycoprotein (GP) IIb/IIIa inhibitors, versus 42% of patients without thrombus (p=0.10). There was no significant difference in the loading dose of aspirin and P2Y12 inhibitors between the 2 groups (p=0.14). Necrotic core or intraplaque hemorrhage was observed in 70% of cases, and a calcium nodule in only 16.8% of cases. The mean OCT thrombus score was 9.67 ± 9.40.

OCT was more accurate to detect thrombus (14 patients) than angiography (9 patients), with an angiographic sensitivity of 63%, specificity of 97%, positive predictive value of 98% and a negative predictive value of 54% (Table 4). Thrombus TIMI Score was correlated to thrombus volume measured by planimetry (p<0.004) (figure 18). OCT thrombus score was also correlated to thrombus volume measured by planimetry (p<0.001) (figure 19).

None of the patient characteristics, and no variable among troponin at admission, troponin at 24 hours or creatinine at admission was predictive of the presence of thrombus (Table 5). The number diseased vessels, the infarct related artery, and the ACC/AHA lesion type were also not found to be associated with the presence of thrombus. Plaque rupture and plaque erosion were significantly associated with the presence of thrombus (p= 0.004 and p<0.001). The volume of thrombus was not significantly different in both cases (figure 20).

The presence of a lipid-rich plaque, a fibrous plaque, a necrotic core, a calcium nodule or neo vessels was not associated with the presence of thrombus (Table 5).

Primary end point: impact of thrombus volume measured quantitatively or semi quantitatively on periprocedural myocardial infarction:-

Periprocedural myocardial infarction occurred in 7 patients (40%). The presence of thrombus was not associated with the occurrence of periprocedural myocardial infarction (p=0.93) (Table 6).

The volume of thrombus assessed either by planimetry or in a semiquantitative manner was not associated with the occurrence of type IVa myocardial infarction. Patients who presented type IVa MI had a mean thrombus volume of 3.28 ± 4.92 mm³, whereas the volume was 2.72 ± 4.04 mm³ among patients who did not present periprocedural MI (p=0.52) (Table 7).

Among patients with periprocedural MI, OCT thrombus score was 10.33± 10.11, vs 9.23±8.94 among patients without periprocedural MI (p=0.56). The results were the same after adjustment for pretreatment with aspirin and P2Y12 inhibitors and for the use of GP IIb/IIIa inhibitors. Only 1 (5%) patients suffered from no reflow.

OCT analysis post PCI:-

Tissue protrusion was present in all cases with varying volume (range 0.23 - 14.5 mm³). The median protrusion volume was 2.29 mm³ [1.31; 4.20]. The median protrusion length was 6.90 mm [4.35; 9.80], median height was 0.46 mm [0.32; 0.62], and median protrusion area was 8.76 mm ² [5.44; 11.95] (Table 8).

Irregular protrusion was seen in 68% of cases (14 patients), smooth in 13% of cases (3 patients) and disrupted in 18 % of cases (4 patients). Among patients with thrombus on OCT, the protrusion volume was 3.75± 4.71, vs 0.34± 1.13 among patients without thrombus (p=0.0007). Thrombus volume measured by planimetry was correlated to the volume of protrusion (p=0.03) (figure 21). OCT thrombus score was also correlated to the volume of protrusion (p=0.01) (figure 22).

Impact of thrombus mass on post PCI FFR:-
Regardless of the method used for thrombus measurement, the thrombus burden did not affect the post PCI FFR.
Among patients with thrombus on OCT, FFR post PCI was 0.94±0.04 vs 0.93±0.04 in those with no thrombus on OCT (p=0.51).

The correlations were respectively R^2=0.005 (p=0.49) for OCT Thrombus score, and R^2=0.0014 (p=0.70) for planimetry.

Discussion:-

Thrombus is more frequently visualized on OCT than on angiographic images. The presence of thrombus is frequent in NSTE-ACS (70% of cases). The nature of the underlying layer is not correlated with the presence of thrombus, whereas plaque rupture and plaque erosion are associated with thrombus presence. The volume of thrombus is approximately the same, whatever the nature of the underlying lesion (rupture or erosion). In our study, neither the presence nor the volume of thrombus was associated with the occurrence of periprocedural myocardial infarction. Conversely, the thrombus volume was significantly correlated with the volume of tissue protrusion, but this had no impact on the final FFR measures at the end of the procedure.

Defining the appropriate management for patients with acute myocardial infarction requires careful assessment of the risk of mortality and adverse ischemic events. In this context determining the morphology of the targeted plaque and its composites is essential for carrying out percutaneous coronary intervention (PCI). Thrombus is frequently encountered on angiography in patients with unstable angina and acute myocardial infarction (AMI). Ross et al. (17) found that among patients with stable angina, those showing thrombus on in angiography were at higher risk of ischemic outcomes. Marieke et al. (18) investigated the incidence and repercussions of angiographically visible distal embolization (AVDE) after primary PCI in ST-elevation MI patients, and found that the presence of thrombus impacted the presence of thrombus post PCI, and was associated with impaired myocardial reperfusion and poor outcome.

New techniques for intracoronary imaging are much more efficient for the detection of thrombus. Indeed, in our study of patients with NSTE-ACS, the correlation between the TIMI Thrombus Score and the volume of thrombus measured by OCT by planimetry was excellent. However, angiography was able to detect thrombus in only 44% of the cases, whereas thrombus was visualized in almost 70% of cases by OCT.

The OCT Thrombus Score was first described by Prati et al in the COCTAIL trial (15). It is routinely used for the quantification of thrombus. Its simplicity, rapidity and reproducibility make it a top-grade tool for this task. In this context, the OCT Thrombus Score is recommended by the expert review for OCT of the European Cardiology Society. However, it was never validated in a large-scale study, although Amabile et al (19) reported that it was correlated with the volume of thrombus in a sample of 3 patients. Our study, comprising a larger number of patients, confirms these results, and shows good correlation with the thrombus volume as measured by planimetry.

Porto et recently studied the predictive factors on OCT for the occurrence of periprocedural myocardial infarction, in which half of the patients were treated for stable angina and the other half for NSTE-ACS. The presence of thrombus was not associated with periprocedural myocardial infarction; however, the thrombus was not quantified. The OCT characteristics of the culprit lesion in patients treated with non-urgent angioplasty, mainly in the context of stable angina, studied by Lee et al (20) were also not correlated with the occurrence of a type IVa MI. The thrombus was not quantified in this study either. Yonetsu and al. (21) did not find that thrombus on OCT was predictive of creatine kinase-MB elevation in patients with elective stent implantation. In 2014, Souteyrand et al. performed OCT control in patients with an infarct presenting a high thrombotic load on angiography (22). After 30 days, thrombus was only visible in 30% of cases. Taking account of these contradictory results, our study is, to the best of our knowledge, the first to evaluate the impact of the volume of thrombus on periprocedural myocardial infarction in patients with non ST elevation acute coronary syndrome.Patients received optimal treatment as recommended by the

European Society of Cardiology and the American college of Cardiology. Patients received the same pre-angioplasty treatment (dual antiplatelet therapy, unfractionated heparin). Similarly, the majority of patients with a high thrombotic load received GP IIb/IIIa inhibitors.

Thus, in our study concerning non-ST elevation acute coronary syndromes, thrombus was present in most cases, patients received optimal treatment with at least DAPT, leading to an identical occurrence of type IVa myocardial infarction, irrespective of whether thrombus was present or not, and regardless of the thrombus volume. Thus, the optimal treatment decreased the complications related to myocardial infarction, indeed only 1 patients suffered from no reflow.

Our results are therefore contradictory with those performed by angiography. The reasons are probably due to the fact that firstLy, a large part of the thrombus was not seen on angiography (in one third of cases). Secondly, existing angiographic studies date from several years ago, when treatment options were not the same as now. Thirdly, the population studied concerned patients with and without ST elevation. However, we know that the volume of thrombus in STEMI is much higher than in NSTEMI and that the prognosis is much less favourable.

Our study showed that the predictive lesion characteristics of thrombus formation were plaque rupture and plaque erosion. These results are in line with the previous pathology (23) or OCT (24) studies. Indeed, in plaque rupture, a structural defect, or a gap in the fibrous cap exposes the highly thrombogenic core to the blood. The mechanism of plaque erosion is less obvious. It is likely due to the loss of the antithrombotic properties of the plaque surface resulting in thrombus formation. In both cases, the thrombus volume was the same (25). Hu et al found a higher thrombus volume on OCT in patients with plaque rupture compared to plaque erosion. However, the antiplatelet treatment was not specified.

The plaque type, the presence of a necrotic core, the presence of calcium nodule or neo vessels were not associated with the presence of thrombus. We did not find any other OCT studies that analyzed these characteristics.

Finally, OCT provided clearer and more frequent visualization of tissue protrusion. However, its mechanism remains unclear and debated. Young et al. showed a greater incidence of tissue protrusion on IVUS in patients presenting with myocardial infarction as compared to patients with stable angina (26). Sugiyama et al. recently showed that the presence of thrombus pre-angioplasty was predictive of the occurrence of tissue protrusion (27). However, the volume of thrombus was not quantified. Our study confirms these results showing a very good correlation between the volume of thrombus present pre angioplasty (measured by planimetry or semi quantitatively) and the volume of tissue protrusion post angioplasty. Moreover, we showed that the volume of thrombus is associated with the presence of irregular protrusion in non ST elevation acute coronary syndrome. Thus, we assume that tissue protrusion in NSTEMI is mostly of thrombotic origin.

Study limitations:-

The main limitation of our study is that we did not evaluate the impact in terms of clinical events. The number of patients included was higher than in most OCT studies. However, considering the occurrence of Major Cardiovascular Events in NSTEMI (28), a much higher number of patients would have been required to show potential clinical differences.

Table 1:-Baseline Characteristics of the Study Population.

	N=20
Age	62 ±6
Male (%)	16 (80)
Diabetes Mellitus (%)	13 (65)
Obesity (%)	10 (50)
Hypercholesterolemia (%)	7 (35)
Hypertension (%)	11 (55)
Current Smokers (%)	13 (65)
Family history of CAD (%)	8 (40)
History of myocardial infarction (%)	9(45)
History of Heart failure (%)	2(10)

History of stroke (%)	1(5)
History of Peripheral artery disease (%)	1(5)
History of kidney injury (%)	3(15)
History of PCI	7(35)
History of CABG	1(5)
History of valvular heart disease (%)	2(10)
Infarct-related artery	0(0)
Right coronary artery (%)	6 (30)
Circumflex artery (%)	3 (15)
Left anterior descending artery (%)	4(20)
ACC/AHA lesion type	
A (%)	5 (25.0)
B1 (%)	11 (55.0)
B2 (%)	2 (10)
C (%)	1 (5)
Troponin at admission ng/L	0.54[0.15;1.72]
Troponin at 24h ng/L	1.30[0.52;3.58]
Hemoglobin at admission g/dl	14.8[1.85;15.8]
Creatinine at admission µmol/l	82.5[70.87;95.65]
LVEF (%)	60[53;66]
Duration of procedure, min	56[49;78]
Volume of contrast medium, ml	190[140;250]

Table 2:-Pretreatment, periprocedural treatment, and treatment at discharge.

N=20	
Pre-Procedure	
Loading dose of P2Y12 inhibitor	16 (80%)
Loading dose of aspirin	16 (80%)
Anticoagulant during PCI	17 (85%)
Unfractionated heparin	19 (95%)
Enoxaparin	1 (5%)
Bivalirudin	0 (0%)
Periprocedural GP IIb/IIIa inhibitor	10 (50%)
Discharge treatment	
ACEI/ARB	18 (90%)
Beta blocker	17 (85%)
Statin	19 (95%)
Diuretics	3 (15%)
Aspirin	19 (95%)
P2Y12 inhibitor	20(100%)
Clopidogrel	2 (10%)
Prasugrel	2 (10%)
Ticagrelor	16 (80%)

Table 3:-OCT findings before angioplasty.

N=20	
Plaque rupture (%)	20/10 (50%)
Intact fibrous plaque (%)	20/10 (50%)
Lipid-rich plaque (%)	15 (75%)
Fibrous plaque (%)	4 (20%)
Thin-cap fibroatheroma (%)	11 (55%)
Calcifications (%)	9 (45%)
Calcium nodule (%)	3 (15)

Necrotic core/ or Intraplaque hemorrhage(%)	14(70)
>Semi-circular	2 (10%)
Thrombus	14 (70%)
White thrombus	3(15%)
Red thrombus	4(20%)
Mixed thrombus	7(35%)
Thrombus Volume mm^3	1.07[0.09;3.40]
Thrombus length mm	2.95[0.50;5.50]
Thrombus area mm^2	0.42[0.12;0.79]
Thrombus height mm	0.50[0.27;0.80]
OCT Thrombus Score	9.69±9.40

Table 4:-Sensitivity, specificity, positive predictive value and negative predictive value of thrombus detection with angiography.

	Thrombus OCT yes N=14	Thrombus Oct no N=6
Thrombus angiography yes		1
Thrombus angiography no	6	2
Sensitivity	63.86%	
Specificity	97.29%	
PPV	98.15%	
NPV	54.54%	

Table 5:-Protrusion characteristics.

	N=20
Protrusion volume mm^3	2.29[1.31;4.20]
Protrusion length mm	6.90[4.35;9.80]
Protrusion height mm	0.46[0.32;0.62]
Protrusion area mm^2	8.76[5.44;11.95]
Irregular protrusion	14(70%)
Smooth protrusion	2(10%)
Disrupted protrusion	3(15%)

Table 6:-Impact of thrombus presence and volume on periprocedural (type 4a) myocardial infarction.

	Type IVa MI (+) N=8	No Type IVa MI N=12	p
Thrombus (+)		8	0.93
Thrombus (-)	3	4	
Thrombus volume	3.28 ± 4.92	2.72±4.04	0.52
OCT thrombus score	10.33±10.11	9.23±8.94	0.56

Table 7:-TIMI Thrombus Score by angiography.

	N=20
Timi Thrombus 0(%)	6 (30%)
Timi Thrombus 1(%)	4 (20%)
Timi Thrombus 2(%)	5 (25%)
Timi Thrombus 3(%)	4 (20)
Timi Thrombus 4(%)	2 (10%)
Timi Thrombus 5(%)	1 (5%)

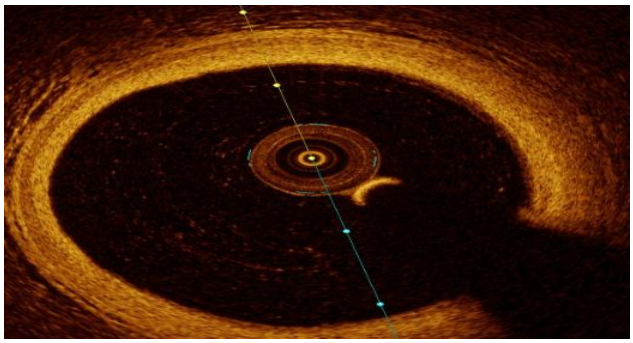


Figure 1:-Normal artery wall showing intima media and adventis

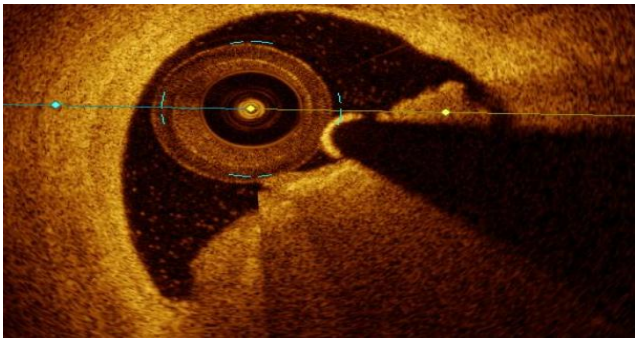


Figure 2: red thrombi

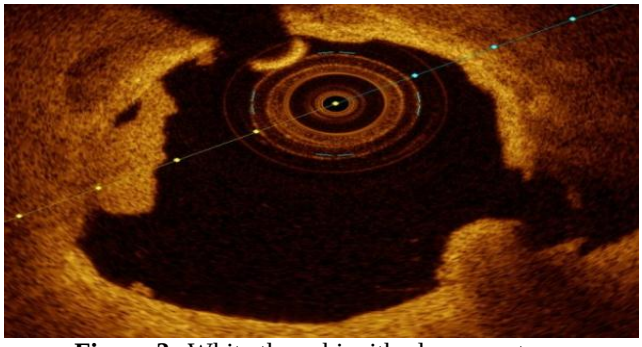


Figure 3:-White thrombi with plaque rupture.

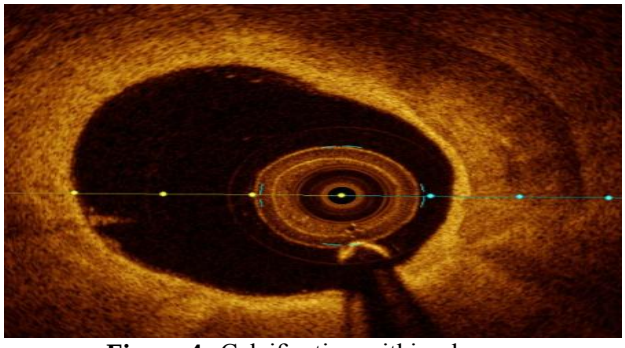


Figure 4:-Calcification within plaque.

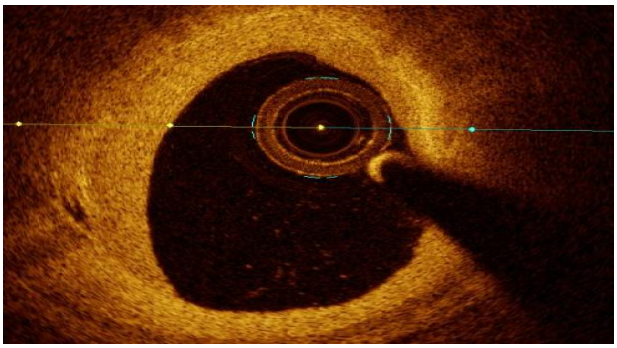


Figure 5:-Fibrous plaque.

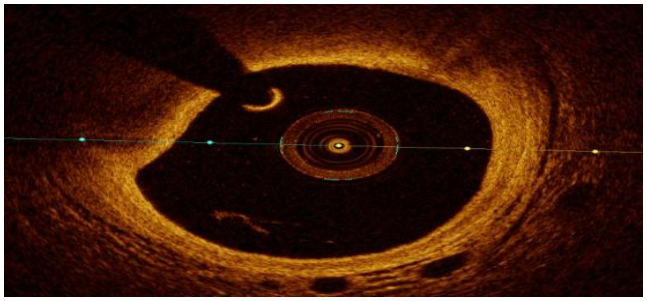


Figure 6:-necrotic pool

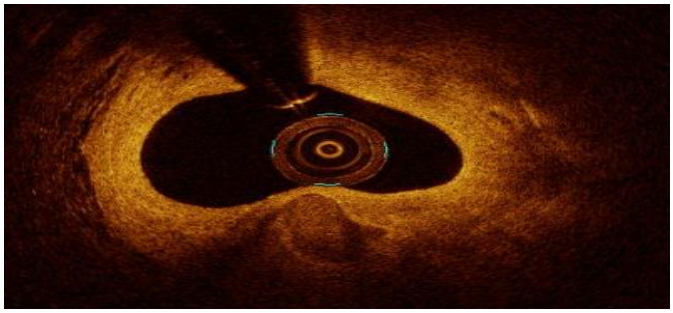


Figure 7:-Calcium Nodule

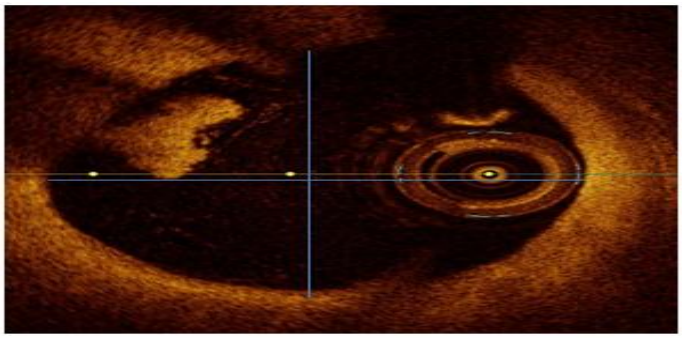


Figure 8:-OCT Thrombus score 1

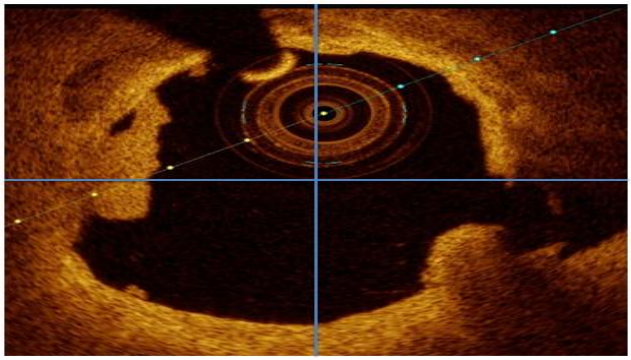


Figure 9:-OCT Thrombus score 2

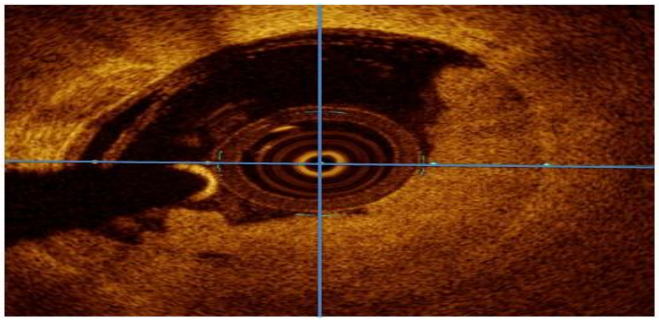


Figure 10:-OCT Thrombus Score 3

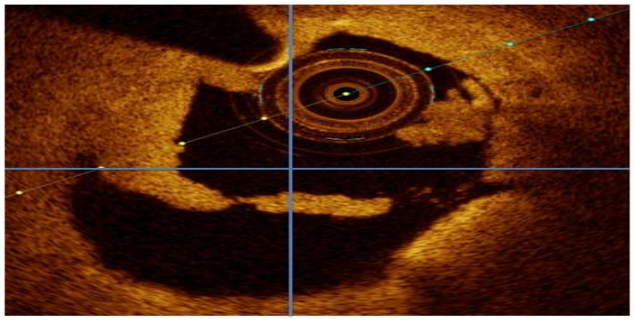


Figure 11:-OCT Thrombus score 4

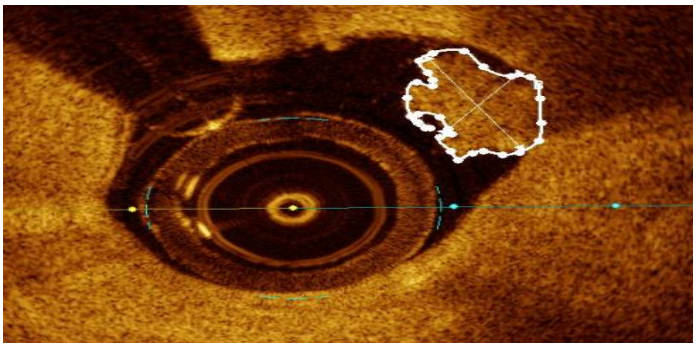


Figure 12:-thrombus volume assessed by planimetry

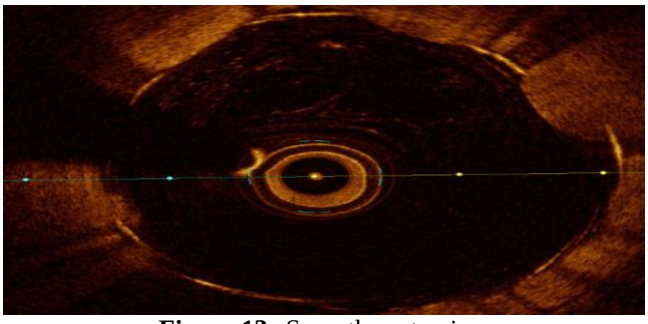


Figure 13:-Smooth protrusion

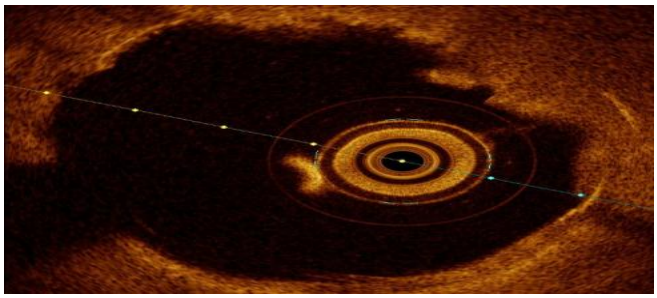


Figure 14:-Irregular protrusion

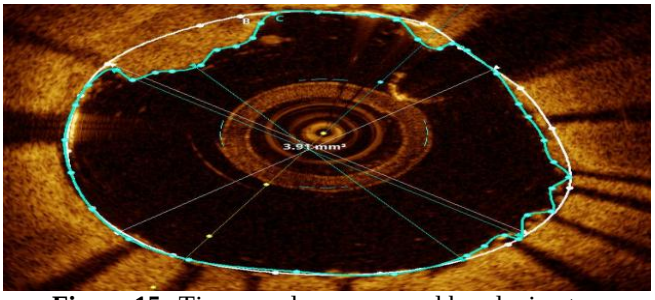


Figure 15:-Tissue prolapse assessed by planimetry

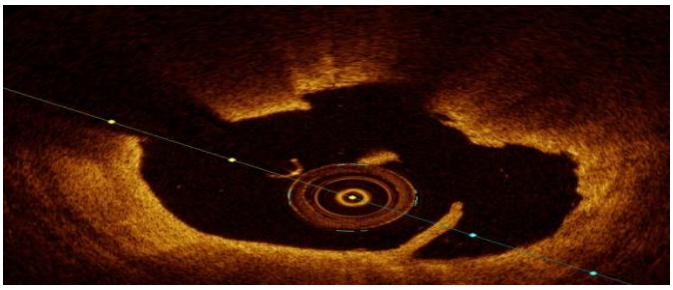


Figure 16:-plaque rupture

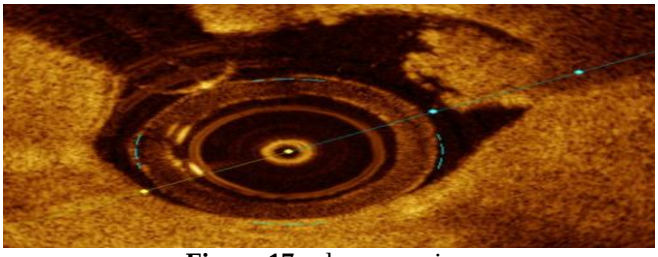


Figure 17:-plaque erosion

Figure 18:-Correlation between TIMI Thrombus Score assessed by angiography and thrombus volume measured by planimetry by OCT.

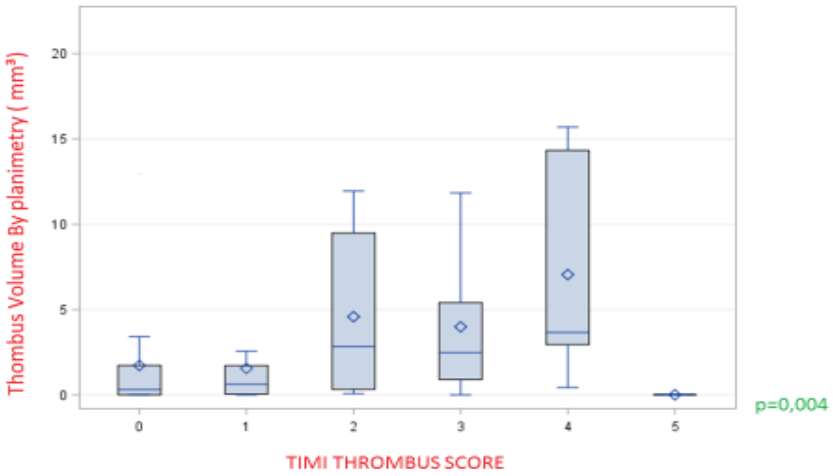


Figure 19:-correlation between OCT thrombus score and Thrombus Volume measured by planimetry.

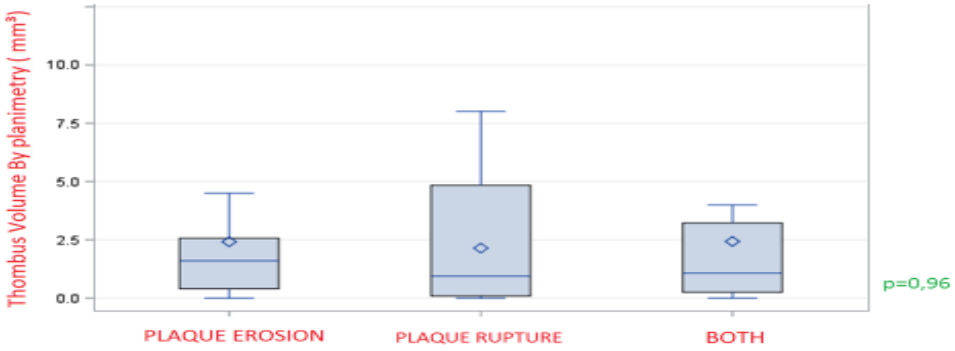


Figure 20:-Plaque volume according to the underlying plaque

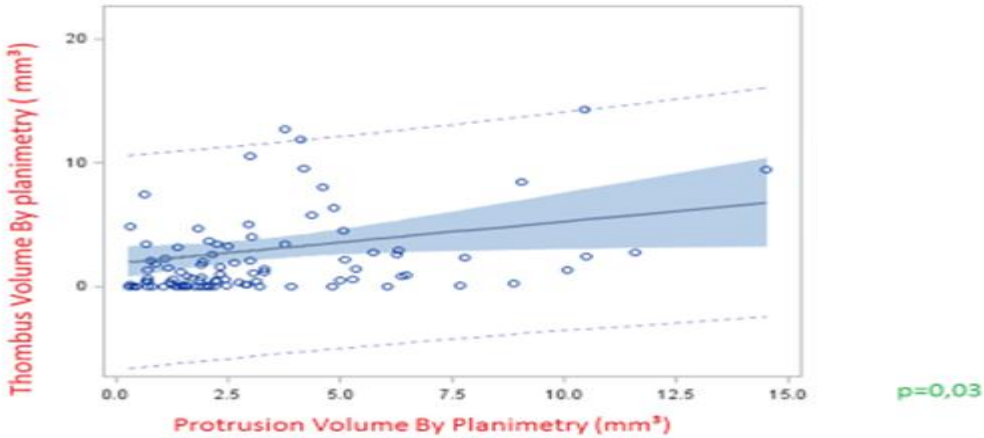
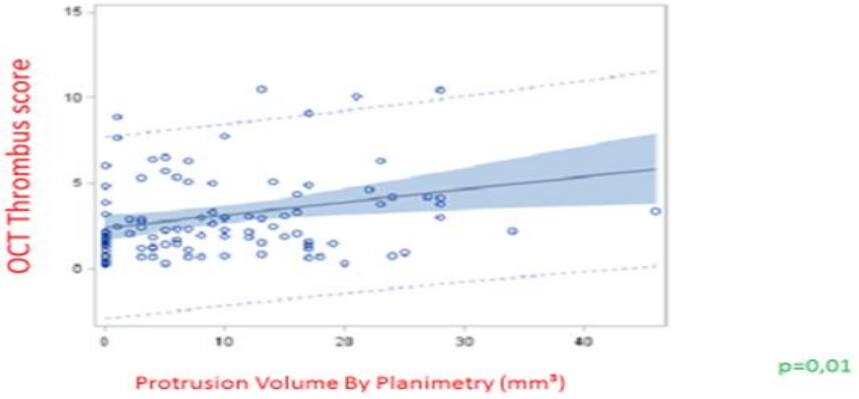


Figure 21:-Correlation between Protrusion Volume measured by planimetry and thrombus volume measured by planimetry.



Conclusion:-

OCT allows better visualization of thrombus than angiography in non–ST elevation acute coronary syndrome. In patients receiving optimal antiplatelet therapy, neither the presence nor the volume of thrombus impacts on the occurrence of periprocedural myocardial infarction. Thrombus burden as measured pre-PCI is associated with post-PCI intra-stent tissue protrusion, but does not influence the functional outcome of the angioplasty measured by FFR.

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