Novel imaging aspects in the management of patients with acute coronary syndromes

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The Feasibility of Optical Coherence Tomography Guided Thrombus Aspiration in Patients With Non-ST-Elevation Myocardial Infarction After Initial Conservative Therapy – a Pilot Study

8

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During percutaneous coronary intervention (PCI) in patients with acute coronary syndrome balloon inflation or stent deployment leads to fragmentation of thrombus causing microembolization and myocardial damage [1]. Manual thrombus aspiration (TA) allows effective retrievement of thrombus in 70% to 80% of patients with ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) [2,3]. TA use in STEMI patients enhances myocardial perfusion, reduces the incidence of microvascular obstruction and improves prognosis [2,4,5]. However, data on TA in NSTEMI patients are scarce. One small study investigating TA in NSTEMI patients who underwent early revascularization demonstrated that TA is associated with high retrieval rates of thrombus with a marked reduction in Thrombolysis In Myocardial Infarction (TIMI) thrombus score and an increased rate of TIMI-flow grade 3 [3]. No data are available on thrombus aspiration in initially conservatively treated NSTEMI patients. TA is frequently performed when thrombus is visible on coronary angiography (CAG) although it is known that its accuracy in thrombus detection is limited. Intravascular imaging with optical coherence tomography (OCT) enables superior assessment of thrombus [6]. In this pilot study we investigated the efficacy of TA involving imaging with OCT in patients presenting with NSTEMI after initial conservative therapy.

Thirty NSTEMI patients who were conservatively treated the first 72 hours and had a clinical indication for PCI were prospectively included. Exclusion criteria were: electrocardiographic ST-segment elevation, hemodynamic instability, renal dysfunction (serum creatinine >2,26 mg/dL), and inability to perform OCT (TIMI flow grade 0 or 1, target vessel diameter <2.5 mm). Before PCI, all patients were treated with low molecular weight heparin, aspirin, and clopidogrel [7]. PCI was performed in the following order: first, OCT acquisition was performed (C7 imaging system, DragonFly catheter St. Jude/LightLab Imaging); second, TA was performed (6F Export Aspiration Catheter, Medtronic), followed by a second OCT acquisition; third, the culprit lesion was treated with stenting, followed by a third OCT acquisition. Effective TA was defined as the presence of atherothrombotic material in the aspirated samples and the material was analyzed as previously described [2].

Angiographic analysis involved assessment of TIMI flow grade and TIMI thrombus score. OCT images were analyzed off-line using dedicated software (QIvus 2.1, Medis medical imaging systems). Identical regions of interest (ROI) of the three OCT pullbacks were identified using landmarks of the coronary arteries. Quantitative analyses were performed by detection of lumen areas, diameters and volumes of the ROI were calculated. Differences in pullback lengths between the patients were compensated by calculating a normalized ROI [8]: Normalized ROI = [ROI volume/ no. slices in ROI pullback] x median no. slices in ROIs of the population. Thrombus was visually scored as a mass protruding into the coronary vessel lumen [6].

The study was approved by the Ethics Committee of the University Medical Centre Groningen and all participants provided written informed consent.

Continuous variables are presented as means±standard deviation or as medians with interquartile range, ANOVA with repeated measures followed by Bonferroni's

Table 1. Baseline and histopathologic characteristics

	N = 30
Demographics	
Age, years	65.0±11.0
Male gender	24 (80)
Body mass index, kg/m2	29.0±4.7
Risk factors	
Diabetes	6 (20)
Hypertension	17 (57)
Hyperlipidemia	17 (57)
Current smoker	10 (33)
Family history	11 (37)
Previous CABG	1 (3)
Previous myocardial infarction	4 (13)
Previous PCI	4 (13)
Peak Troponin I, µg/L	1.07 (0.20–12.02)
Peak Troponin T, µg/L	0.14 (0.06-0.45)
Time from last complaints to PCI, days	4.4 (3.2–6.0)
Multivessel disease	12 (40)
Anterior infarction	16 (54)
Probability of in-hospital death (GRACE risk score)	
Low (<1%)	15 (50)
Intermediate (1-3%)	12 (40)
High (>3%)	3 (10)
Histopathologic analysis	
Effective thrombus aspiration	6 (20)
Thrombus	
White platelet thrombus	6 (20)
Red erythrocyte rich thrombus	0 (0)
Plaque	
Thrombus with plaque component	6 (100)
Thrombus without plaque component	0 (0)
Size	
None	2 (3)
Casts	22 (67)
Small (<0.5 mm)	3 (10)
Medium (0.5 - 2 mm)	3 (10)
Large (>2 mm)	0 (0)

The data are mean±SD, median, IQR, or numbers (%). CABG = coronary artery bypass graft; IQR = interquartile range; mm = millimeter; SD = standard deviation. Casts were defined as fragmental filter casts of loosely cohesive platelets which may not be defined as thrombus.

post-hoc test was used to compare continuous variables. Categorical variables are presented as numbers and percentages and were compared using the χ2 test. Statistical significance was defined as a two-sided p-value of <0.05.

Clinical and histopathological patient characteristics are presented in Table 1. Median time after the last complaints to PCI was 4.4 days. Histopathological analysis of the aspirated material showed aspiration of thrombus in only 20% of patients,

Table 2. Angiographic and OCT characteristics

	Before TA *N=30*	**After TA** *N=30*	**After stent** *N=30*	P-value
Invasive coronary angiography				
Thrombus	18 (60)	19 (63)	0 (0)	<0.001
TIMI Thrombus score				<0.001
0	12 (40)	11 (37)	30 (100)	
1	17 (57)	19 (63)	0 (0)	
2	1 (3)	0 (0)	0 (0)	
3/4/5	0 (0)	0 (0)	0 (0)	
TIMI flow grade				0.014
0/1	0 (0)	3 (10)	0 (0)	
2	15 (50)	11 (37)	6 (20)	
3	15 (50)	16 (53)	24 (80)	
Optical coherence tomography				
Thrombus	17/30 (57)	19/30 (63)	19/30 (63)	NS
Thrombus color				
White	11/17 (65)	13/19 (68)	NA	
Red	6/17 (35)	6/19 (32)	NA	
ROI length (mm)	24.23±9.27	24.23±9.27	24.23±9.27	
ROI volume (mm)	142.90±78.58	140.77±76.17	193.25±87.53†‡	<0.001*
Normalized ROI volume (mm3)	134.35±53.65	132.90±55.77	186.10±59.60†‡	<0.001*
Average area (mm2)	5.75±2.33	5.68±2.40	8.02±2.59 †‡	<0.001*
MLA (mm2)	1.69±1.04	1.81±1.12	5.66±2.62 †‡	<0.001*
Average diameter (mm)	2.59±0.52	2.56±0.55	3.14±0.53 †‡	<0.001*
Largest diameter (mm)	3.50±0.71	3.43±0.74	3.71±0.64 †‡	<0.001*
MLD (mm)	1.41±0.40	1.46±0.42	2.61±0.62 †‡	<0.001*

** 3-way comparison (before TA, after TA, after stent)*
† p<0.05 vs. before TA
‡ p<0.05 vs. after TA

The data are mean ± SD, or numbers (%). CROI = culprit region of interest; MLA = minimal lumen area; MLD = minimal lumen diameter; mm = millimeter; NA = not available; NS = not significant; ROI = region of interest; SD = standard deviation; TA = thrombus aspiration; TIMI = thrombus in myocardial infarction.

which were small amounts of fragmented atherosclerotic debris.

The angiographic and OCT data are provided in Table 2. TIMI thrombus score of 0 and 1 was observed in 29 patients before TA and in all patients after TA. Similarly, TIMI-flow did not improve after TA (TIMI-flow <3 in 15 patients before TA versus 16 patients after TA). Thrombus on OCT was observed in 17 patients, the majority being white thrombus. In 2 patients minimal amounts of white thrombus were induced by the guide wire or manipulation with the TA catheter. Moreover, minimal amounts of thrombus with plaque protrusion were observed after stent implantation in 19 patients (mean volume 1.67±1.69 mm^3). Mean volumes, diameters and areas of the ROIs were not significantly different before and after TA.

This study provides novel insight into TA in NSTEMI patients who underwent initial conservative therapy. First, although thrombus was observed on OCT in more than half of patients, the rate of retrieval of thrombus was low and only small amounts of atherothrombotic debris were found by histopathological analysis. Second, TA did not result in improved blood flow in the culprit coronary artery or in decrease of intracoronary thrombus burden on OCT. Revascularization results in better prognosis in NSTEMI patients [7]. However, embolization of thrombus into the microvasculature in patients with acute coronary syndrome may lead to microvascular obstruction which may be of prognostic significance [9,10]. Although TA in STEMI patients and less evidently in NSTEMI patients with early revascularization resulted in better TIMI flow, in the present study though, TIMI flow after TA did not improve. Also, no clear improvement of vessel lumen volumes and areas of the vessel were observed on OCT. It is worth mentioning though, that with continuous improvements of the device technology an increased rate of effective TA may be expected with a new generation TA catheters also in NSTEMI patients with less thrombus load.

Several study limitations should be mentioned. First, the applicable guidelines at the start of the study recommended early catheterization only in NSTEMI patients with features of high risk, whereas current guidelines recommend PCI within 72 hours in all patients [7]. Second, this pilot study had a limited sample size and was designed only to investigate the principle of TA in patients with expectedly low thrombus burden. Finally, the effect of TA was assessed by measuring differences of the intraluminal volume between OCT runs since direct quantification of thrombus is limited with OCT.

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