Interventional Cardiology

Early drug eluting stent thrombosis in acute coronary syndromes

Alaa Solaiman Algazzar*, Ahmed Abd ElMoez ElSayed, Azza Ali Katta, Khaled S. Ahmed
National Heart Institute, Egypt
*Author for correspondence:
Tel.: 01148145561
goodminds@hotmail.com
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Plaque rupture and thrombus formation play a key role in the pathogenesis of acute coronary syndrome (ACS) [1]. The etiology of early stent thrombosis (ST) (within 30 days) after stent implantation is multifactorial. Clinical studies implicate multiple factors comprising clinical demographics such as diabetes mellitus, renal failure, angiographic lesion characteristics (greater burden of coronary atherosclerosis), interventional procedure-related factors (smaller final stent minimal lumen diameter) and pharmacotherapeutic conditions (pre-procedural inconsistent antiplatelet drug use) as predictors of early ST [2,3]. The discontinuation of dual antiplatelet therapy was a powerful predictor of ST during the first 6 months following stent implantation in a cohort of over 3,000 patients (HR 13.74; 95% CI 4.04–46.68; P<0.001) [4]. This was confirmed by a study by Schulz et al. in over 6,000 patients with 4-years follow up [5].

Intravascular ultrasound (IVUS) has been the standard imaging modality for evaluating the status of a coronary stent. However, it is limited in evaluating neointimal tissue within the stented segment due to its low resolution. Contrary to IVUS, optical coherence tomography (OCT) has a resolution of 10-20 μm, which is about 10 times higher than that of IVUS (80-120 μm). Previous studies have shown the superiority of OCT over IVUS in relation to resolution capacity [6]. Currently different types of stent related vessel damage can be clearly identified with help of OCT as shown in Table 1.

Table 1: Quantitative OCT parameters for suboptimal stent deployment.

Parameter	Definition
Edge dissection	Presence of a linear rim of tissue with a maximal width ≥200 μm and a clear separation from the vessel wall or underlying plaque that was adjacent (<5 mm) to a stent edge [7,8].
Reference lumen narrowing	Lumen area <4.5 mm^2 in the presence of significant residual plaque adjacent to stent edges [8].
Stent Strut Malapposition	Distance from Stent strut to adjacent vessel wall >200 μm (Figure 1) [8-10].
Residual stenosis	In-stent minimum lumen area <70% of the average reference lumen area [8].
Intrastent plaque/thrombus protrusion	Plaque/thrombus prolapsing between stent struts into the vessel lumen ≥500 μm in thickness (Figure 2) [7,9,11,12].
intra-stent dissection flaps	Defined as a disruption of the luminal vessel surface in the stent segment with a dissection flap protruding in the lumen. Significant if dissection flap tip to the joint point with the vessel wall extending ≥200 μm into the lumen (Figure 3) [13].
intra-stent dissection cavities	Defined as a disruption of the luminal vessel surface in the stented segment with an underlying cavity in the vessel wall [13].
Tissue prolapse	Defined as convex-shaped tissue with a regular surface protruding between adjacent stent struts towards the lumen, without disruption of the continuity of the luminal vessel surface. The maximal prolapse of tissue was measured and was defined as the distance from the arc connecting adjacent stent struts to the greatest extent of prolapse into the lumen (TP length) ≥200 μm in the lumen [14].
Red thrombus	Defined as an intraluminal mass discontinuing of the surface of the vessel wall with a signal free shadow behind the structure [15].

Previous IVUS studies in patients with mostly stable angina have reported small stent [7-15], underexpansion, stent edge dissection, and residual reference segment disease as the strongest IVUS predictors of ST [16-18]. In the IVUS sub study from the HORIZONS-AMI trial, the 2 strongest predictors of definite/probable early ST were the minimum lumen cross sectional area because of tissue protrusion after stenting and inflow/ outflow disease (residual stenosis or dissection) as well as a higher incidence of TIMI grade 0/ flow at baseline and after stenting [19].

An autopsy registry investigated the histopathology features of early (ST) in 67 stented coronary lesions from 59 patients who presented with acute coronary syndrome (ACS) and died within 30 days. The investigator found that prolapse of necrotic core (NC) was significantly greater in thrombosed compared to patent lesions (70% *vs.* 43%, p=0.045); plaque rupture as precedent of ACS was significantly greater in sections with thrombosis compared to patent sections; and the extent of NC prolapse, medial tear, and incomplete strut apposition were significantly greater in thrombosed compared to patent sections [20].

In CLI-OPCI ACS Sub study, stent malapposition (>200 μm) in the acute setting, was not associated to a worse outcome. Device oriented cardiovascular events (DoCE) rate was very similar in patients with or without OCT-detected acute stent malapposition (ASM) (12.8% *vs.*11.4%; P=0.730). Unlike previous findings in the stable setting, significant residual intrastent plaque/thrombus protrusion after PCI was associated with an increased risk of DoCE recurrence at follow-up in ACS patients [21]. These results confirmed the previous IVUS and OCT findings failed to relate acute stent–vessel wall malapposition with clinical outcome (Figure 1) [22,23].

IVUS analysis of TAXUS IV, V and VI and TAXUS ATLAS Workhorse, Long Lesion and Direct Stent studies showed that routinely detected ASM in bare metal stent (BMS) or TAXUS patients was not associated with early- and long-term adverse clinical events, in particular any early or late stent thrombosis [24]. However, late stent malapposition may be the consequence of chronic inflammation and delayed healing, resulting in tissue necrosis and erosion around the stent. It is suggested that delayed re-endothelialization, impaired vasomotion and chronic inflammation, allow for platelet adhesion, initiation of the coagulation cascade and subsequent thrombotic stent occlusion [25].

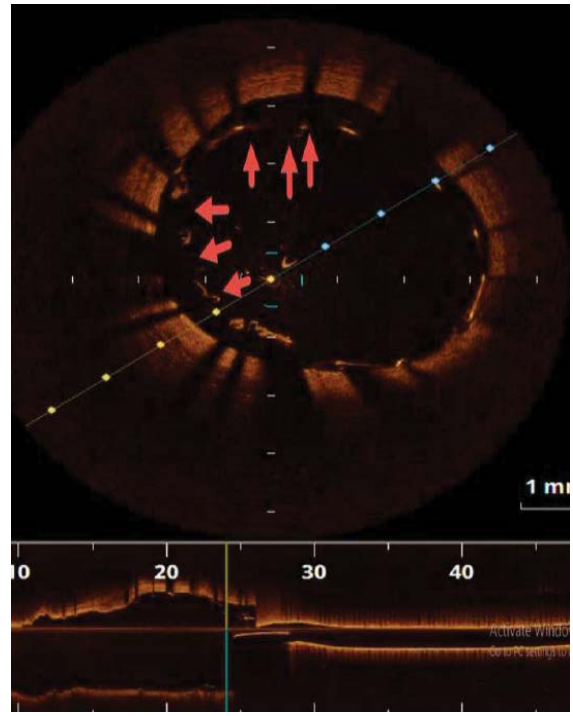

Figure 1: Stent Strut Malapposition. Look for space between Stent strut to adjacent vessel wall (red arrows).

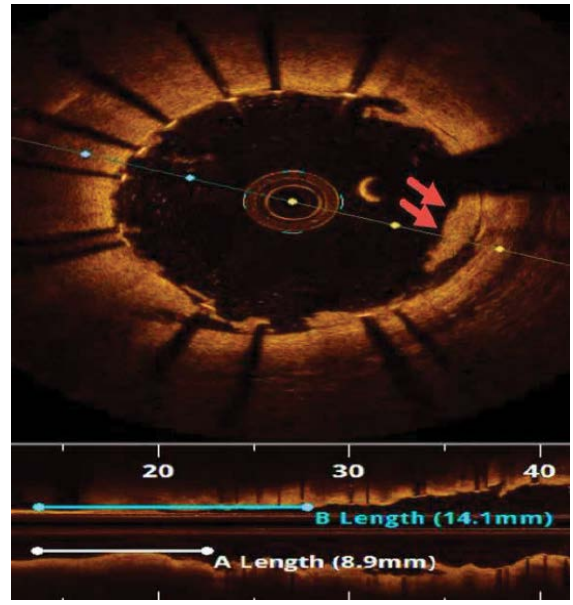

Figure 2: Intrastent plaque/thrombus protrusion through stent struts (red arrows).

Another hidden cause of acute stent thrombosis is Intra-stent dissection which is disruption of the luminal vessel surface in the stent segment. It can appear in two forms: (a) dissection: the vessel surface is disrupted and a dissection flap is visible; (b) cavity: the vessel surface is disrupted and an empty cavity can be seen. The pathophysiology of Intra-stent dissection is speculative

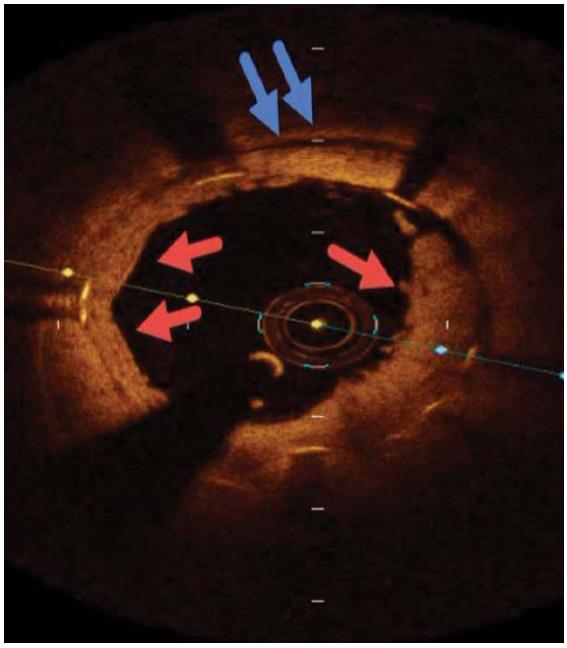

Figure 3: Intrastent dissection (blue arrows) and acute intraluminal stent thrombus red arrow.

but likely involves rupture of new plaque within the stent, with propagation of the dissection plane along the interface between the stent and intima. Assessment of OCT in some studies has revealed that vessel wall injury (tissue prolapse 97.5%, intra-stent dissection flap 86.3%, edge dissection 25.0%) after DES deployment occurs more frequently than previously expected [13,26]. However, most of these injuries heal at 9-month follow up period [14].The use of OCT in percutaneous coronary procedures represents a step ahead for understanding atherosclerotic disease and the response of the intima to stent placement.

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