

Thrombus Burden In ST-Elevation Myocardial Infarction

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Abstract:

Background: Acute ST-elevation myocardial infarction (STEMI) remains one of the leading causes of morbidity and mortality worldwide. Thrombus formation plays a central role in the pathogenesis of STEMI, resulting from plaque rupture and subsequent activation of platelets and the coagulation cascade. The amount of thrombus within the infarct-related artery—known as thrombus burden—is a key determinant of procedural success, distal embolization, and short- and long-term clinical outcomes. Assessing thrombus burden during primary percutaneous coronary intervention (PPCI) is therefore essential for risk stratification and guiding interventional strategies.

Keywords: STEMI, thrombus burden, primary PCI, TIMI flow, myocardial blush, no-reflow phenomenon, MACE

Introduction:

Primary percutaneous coronary intervention (PCI) represents the gold standard therapy for coronary revascularization during ST-segment elevation myocardial infarction (STEMI) and a timely reperfusion strongly correlates with clinical outcomes. However, despite the restoration of the epicardial coronary artery patency, the perfusion of the infarcted myocardium might be incomplete, due to microvascular obstruction and dysfunction (1).

The presence of large thrombus burden (LTB) in the infarct related artery (IRA) might increase the risk of distal embolization, microvascular obstruction, and no-reflow phenomenon leading to contractile dysfunction and irreversible myocardial damage. Thrombus burden is classified by visual angiographic assessment in LTB defined as thrombus equal or greater than two vessel diameters and in small thrombus burden (STB) less than two vessel diameters. In case of occluded IRA, thrombus burden is reclassified after guidewire crossing or small (diameter 1.5 mm) deflated balloon passage or dilation (2).

In patients with STEMI, the anterior localization of the infarction is often associated with greater myocardial dysfunction, heart failure and increased mortality, mostly due to the larger myocardial territory supplied by the left anterior descending artery (LAD) (1).

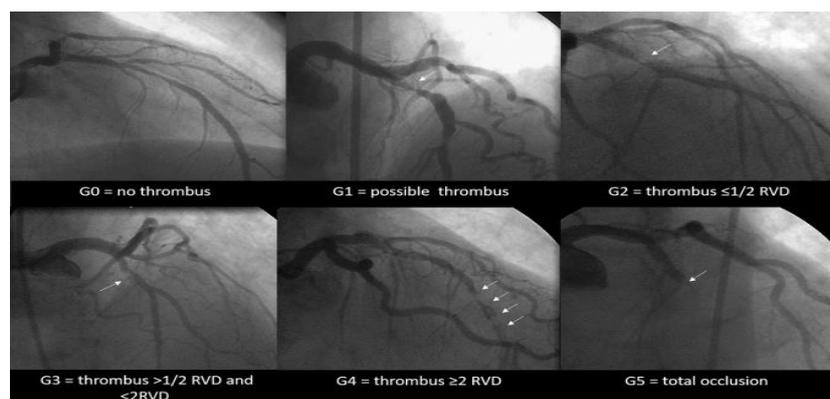


Fig 1. Thrombus burden classification. *RVD* reference vessel diameter. The Thrombolysis In the Myocardial Infarction (TIMI) thrombus classification consists of six grades from grade 0 (no thrombus) to grade 5 (total

occlusion). Grade 5 represents an occluded infarct related artery and prevents thrombus size assessment. Grade 5 was reclassified after guidewire crossing or small (diameter 1.5 mm) deflated balloon passage. After G5 reclassification, large thrombus burden (LTB) was defined as being greater than or equal to two vessel diameters or greater (G4) and small thrombus burden (STB) defined by thrombus grade < G4 (2)

Definition and Measurement of Thrombus burden

Defined as the size and extent of clot formation in coronary arteries during ST-segment elevation myocardial infarction (STEMI), is a critical factor influencing procedural success and long-term prognosis. In diabetic patients, metabolic factors, including stress hyperglycemia, amplify thrombus burden, leading to increased risks of adverse outcomes. This chapter provides a detailed examination of thrombus burden, covering its definition, measurement techniques, prevalence, risk factors, clinical impact, management strategies, and its association with stress hyperglycemia in diabetic STEMI patients (2).

The significance of thrombus burden lies in its direct impact on coronary blood flow and myocardial perfusion, particularly during primary percutaneous coronary intervention (PCI). Diabetic patients are particularly vulnerable due to their prothrombotic state, necessitating a thorough understanding of this phenomenon. This section sets the foundation for an in-depth analysis, linking thrombus burden to metabolic stress (3).

Thrombus burden is quantified using the Thrombolysis in Myocardial Infarction (TIMI) thrombus grading scale, which ranges from 0 (no thrombus) to 5 (complete vessel occlusion). Grades 1–3 indicate small thrombus burden (STB, thrombus diameter <2 times the vessel diameter), while grade 4 represents large thrombus burden (LTB, ≥ 2 times the vessel diameter), and grade 5 requires flow restoration for accurate grading (4).

Advanced imaging techniques enhance measurement precision. Optical coherence tomography (OCT) provides high-resolution images of thrombus structure, while intravascular ultrasound (IVUS) assesses thrombus volume and vessel wall characteristics. These methods offer detailed insights into thrombus composition, aiding in risk stratification and treatment planning. This section elaborates on these techniques and their clinical applications (5).

Prevalence and Risk Factors

In a cohort of 806 STEMI patients, 28.0% exhibited large thrombus burden (LTB), while in diabetic patients, the prevalence rises to 33.9%. Key risk factors include diabetes mellitus, which increases thrombogenicity due to chronic hyperglycemia, and age, with older patients showing higher LTB rates. Elevated troponin and leukocyte levels also correlate with increased thrombus burden. (6)

Other factors, such as the SYNTAX score (indicating coronary artery disease complexity) and smoking history, contribute to prevalence variations. Diabetic patients are particularly affected due to their altered coagulation profiles, making thrombus burden a significant concern (7).

Impact on Clinical Outcomes

Large thrombus burden is associated with worse clinical outcomes, particularly in anterior STEMI. Studies report higher 10-year mortality (adjusted hazard ratio [aHR] 2.27; 95% CI: 1.42–3.63; $P=0.001$) and 30-day mortality (aHR 5.60; 95% CI: 2.49–12.61) in patients with LTB (Russo et al., 2022). Additionally, 10-year major adverse cardiac event (MACE) rates are increased (aHR 1.46; 95% CI: 1.03–2.08; $P=0.033$). LTB also correlates with higher rates of no-reflow (4.0% vs. 0.5% in STB, $P<0.01$) and distal embolization (17.3% vs. 3.4%, $P<0.001$) (8). These complications impair myocardial perfusion, worsening prognosis. This section provides an extensive analysis of these outcomes, supported by statistical evidence. (2)

Thrombus Burden in Diabetic Patients

Diabetic patients exhibit larger, more resistant thrombi due to altered composition, including higher fibrin and glycated protein content. Chronic hyperglycemia enhances a prothrombotic state by increasing platelet activation and coagulation factor expression. Stress hyperglycemia further amplifies this effect, contributing to larger thrombus burdens in acute settings. The interplay of metabolic and inflammatory factors in diabetes creates a unique thrombotic profile, necessitating tailored therapeutic approaches. This section explores these mechanisms in detail, highlighting the challenges in managing thrombus burden in this population. (9)

Pathophysiology of Intracoronary Thrombus Formation

In the majority of cases, the nidus for thrombogenesis is erosion of an underlying atherosclerotic plaque and subsequent exposure of thrombogenic subendothelial matrix and plaque to circulating platelets. Plaque rupture initiates the coagulation cascade in one of two distinct but ultimately synergistic pathways (Fig. 2). In the first pathway, platelet glycoprotein VI binds directly with collagen exposed by the denuded endothelium. Concurrently platelet glycoprotein Ib-V-IX interacts with collagen-bound von Willebrand factor (vWf). (10)

This process triggers platelet activation, adherence and accumulation to the vessel wall leading to formation of ‘white’ thrombi. In contrast, the second pathway leads to formation of ‘red’ thrombi where tissue factor initiates a proteolytic cascade which leads to generation of thrombin which in turn converts fibrinogen to fibrin while also triggering activation and accumulation of platelets through release of various agonists including adenosine, thromboxane A₂ and serotonin. These agents activate other platelets, thereby amplifying the thrombogenic process. Coronary thrombus consists of platelets, erythrocytes, inflammatory cells and fibrin. The thrombin-generating process leads to denser, more fibrin-rich thrombus which becomes progressively more difficult to disrupt (both pharmacologically and mechanically) with time. (11)

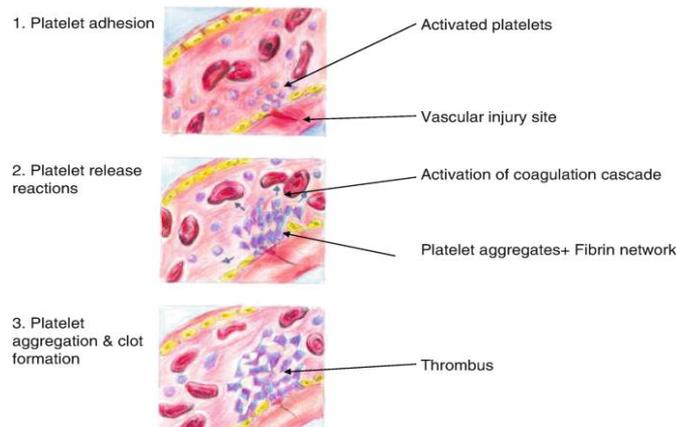


Fig 2. Intracoronary effects of coagulation cascade. (12)

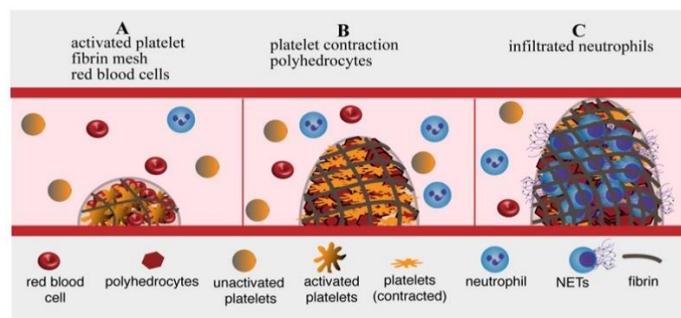


Figure 3: (A) During the initial phases, the thrombus is composed of activated platelets, red blood cells and a porous fibrin mesh. (B) As time progress, platelets contract and red blood cells compress into polyhedrocytes.

(C) Activated platelets promotes infiltration of leukocytes including neutrophils into the thrombus forming NETs and stabilising the thrombus with much smaller pores. Clot components are not drawn to scale **(13)**.

Management

The extent of ICT observed during PPCI correlates strongly with both procedural success and clinical outcome. Due to the complex nature of intracoronary thrombogenesis, a multi-faceted and systematic approach is required to achieve successful thrombus dissolution. This includes arrest of the coagulation cascade (usually achieved using pharmacotherapy), flow restoration (usually through mechanical techniques) and occasionally with the use of thrombus extraction tools. Thrombus extraction may theoretically limit distal embolization of thrombus, thereby preventing microvascular obstruction and incomplete microvascular reperfusion.**(14)**

Pharmacological Interventions

At point of initial STEMI diagnosis, patients should receive a loading dose of aspirin (e.g. 300 mg or institutional practice) and a P₂Y₁₂ antagonist (e.g. clopidogrel 600 mg, prasugrel 60 mg or ticagrelor 180 mg). Peri-procedural anticoagulation is generally achieved using unfractionated heparin or in some catheter laboratories using low-molecular weight heparin (e.g. enoxaparin), factor Xa inhibition (e.g. fondaparinux) or a reversible direct thrombin inhibitor (bivalirudin) **(15)**.

Various ancillary pharmacological therapies have been utilized to treat distal embolization as a consequence of intracoronary thrombus formation. These agents include calcium channel blockers, adenosine, nicorandil, glycoprotein IIb/IIIa inhibitors, vasodilators and nitroprusside. Calcium channel blockers may inhibit platelet aggregation and have a direct effect on calcium flux through the sarcolemmal membrane that could protect injured myocytes**(12)**.

Adenosine affects intracellular calcium and inhibits neutrophil accumulation, superoxide generation. Nicorandil, an ATP-dependent potassium channel opener, can prevent reperfusion injury and protect cardiac myocytes. Glycoprotein IIB/IIIA inhibitors have also been used in cases of no reflow and inhibit platelet aggregation. **(16)**.

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