Original Article

Thrombus age, clinical presentation, and reperfusion grade in myocardial infarction

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A B S T R A C T

Introduction: Autopsy studies show that dynamic coronary thrombosis leads to infarction. We studied intracoronary thrombus age in ST-segment elevation myocardial infarction (STEMI) and its relationship with clinical presentation and epicardial reperfusion grade.
Methods and results: Intracoronary thrombectomy was performed in 131 STEMI patients within 24 h after symptom onset, and material sufficient for pathological analysis was retrieved from 81 patients. Thrombus age was classified as fresh (<1 day), lytic (1 to 5 days), or organized (>5 days). A fresh thrombus was found in 48 patients (60%), whereas the thrombus showed lytic or organized changes in 33 patients (40%). Both thrombus and plaque material were aspirated in 40% of cases. Lytic or organized thrombi were aspirated in one third of the cases early (<12 h) after symptom onset, and fresh thrombi were also aspirated in one third of STEMI of > 12 h evolution. In multivariable analysis, fresh thrombus was associated with both persistent ST-segment elevation (even after 12 h of onset) during percutaneous coronary intervention [odds ratio (OR) 4.23, 95% confidence interval (CI) 1.05–17.42, $P = .042$) and a previous history of ischemic heart disease (OR 4.54, 95% CI 1.41–14.64, $P = .011$). There were no associations between thrombus composition and epicardial reperfusion grade or the presence of the no-reflow phenomenon. Plaque components were found in all cases of distal embolization (5%).
Conclusion: Intracoronary thrombi aspirated in STEMI frequently show more than one stage of maturation. Fresh thrombi predominate in patients with known ischemic heart disease or persistent ST-segment elevation.
Summary: In STEMI, thromboaspiration revealed thrombi at different stages of maturation, supporting a dynamic process of rupture and repair of the atherosclerotic plaque. Fresh thrombi were present more frequently within 12 h of infarction onset but also in patients with symptoms beyond 12 h. When containing plaque material, thrombi were often associated with macroscopic distal embolization during angioplasty.

1. Introduction

Exposure of a previously ruptured or eroded atherosclerotic plaque to the vessel lumen can lead to the formation of thrombi and development of ST-segment elevation myocardial infarction (STEMI). If duration of coronary occlusion is extended beyond 20 min, myocardial necrosis begins to occur [1]. Primary percutaneous coronary intervention (PCI) is the therapy of choice in the first 12 h of evolution, although patients can also benefit beyond 12 h if chest pain persists or there is evidence of ongoing ischemia or signs of heart failure [1]. The procedure may be complicated by the no-reflow phenomenon or distal embolization [2,10,12]. Further, data show that intracoronary thrombus composition in terms of age may be an independent predictor of outcome during PCI [3]. The use of thrombectomy systems that facilitate

suction of the intracoronary thrombi before implanting a stent during primary PCI allows the pathological analysis of the material retrieved by aspiration in vivo [5,9].

The objective of this study was to prospectively analyze the pathological composition of intracoronary thrombi obtained from patients with STEMI treated with PCI within the first 24 h of symptom onset and to analyze the relationship between thrombus age, clinical presentation, and epicardial reperfusion grade.

2. Methods

2.1. Study population

Between May 2006 and September 2007, we treated 186 consecutive patients with PCI within the first 24 h after the onset of STEMI. Patients with chest pain and symptoms for ≤ 12 h were eligible for primary PCI if the admission 12-lead electrocardiogram (ECG) showed ≥ 1 mm ST-segment elevation in ≥ 2 contiguous inferior or lateral leads or ≥ 2 mm in ≥ 2 contiguous precordial leads. Rescue

angioplasty was performed in patients treated with fibrinolysis without clinical and/or ECG criteria of reperfusion at 90 min [1]. In patients with STEMI presenting 12–24 h after symptom onset, PCI was performed if chest pain was still present upon admission, or if ECG showed persistent ST-segment elevation or Killip–Kimball classification ≥ II [1] upon admission. The study complies with the Declaration of Helsinki and was approved by the hospital's ethics committee, and informed consent was obtained from participants.

2.2. Coronary intervention and thrombus aspiration

Prior to initiation of PCI, all patients received a loading dose of 500 mg aspirin, 600 mg of clopidogrel orally, and 5000 IU of heparin. Thrombolysis in Myocardial Infarction (TIMI) flow grades were classified using previously established criteria [1]. The procedure was considered a success if the final TIMI flow grade was 3 and residual stenosis was < 20%. Glycoprotein IIb–IIIa blockers were used at the discretion of the operator. Thrombectomy was performed in cases with angiographically visible thrombus burden in which the coronary artery was suitable for passage of the catheter and was considered successful when a TIMI grade flow ≥ 2 was achieved after using the device. Aspirated blood and intracoronary material were collected and filtered to retrieve the thrombotic material (Fig. 1A). Distal embolism was defined as distal migration of the thrombus or as macroscopic distal occlusion of the treated vessel or one of its branches after completing the procedure. No-reflow was defined as a TIMI flow grade < 2 that was not attributed to dissection or epicardial coronary vasospasm plus no evidence of macroscopic distal embolism upon angiography. ST-segment recovery, an indicator of coronary reperfusion, was considered if there was a ≥ 50% reduction post-PCI [1,9]. Ischemic heart disease was defined as history of previous myocardial infarction or angina or history of previous coronary artery bypass grafting or PCI.

2.3. Thrombus analysis and pathological classification

The aspirated intracoronary material was fixed immediately in 10% formalin and was considered appropriate for pathological analysis if it had a minimum size of 2 mm. After it was embedded in paraffin, the retrieved material was cut into 4-μm serial sections and stained with hematoxylin and eosin (HE). Thrombi were classified by pathology into three groups according to the accepted definitions of thrombus age [4]: (a) fresh thrombus (<1 day), comprised of platelet aggregates, erythrocytes, intact granulocytes, and fibrin (Fig. 1B); (b) lytic thrombus (1 to 5 days), characterized by areas of colliquative necrosis and granulocytes with karyorrhexis (Fig. 1C); and (c) organized thrombus (>5 days), characterized by the presence of smooth muscle cells, homogeneous or hyaline fibrin, and depositions of connective tissue and capillary vessel ingrowth (Figs. 1D and 2A). For the purpose of the current analysis, lytic and organized thrombi were combined into one group and compared against the fresh thrombus group. We also analyzed the degree of thrombi heterogeneity identifying components of another type of thrombus, i.e., fresh thrombus components in a predominantly organized thrombus or vice versa.

To better identify smooth muscle cells and neovascularization within thrombi, additional immunohistochemistry was performed on specimens that contained lytic/organized thrombi. Primary monoclonal antibodies included anti-smooth muscle α-actin (1A4, Dako, Denmark), which labels smooth muscle cells (Fig. 2B), and anti-CD34 (QBEnd10, Dako), which labels endothelial cells (Fig. 2C). Plaque components were identified based on the presence of inflammatory cells, cholesterol crystals, collagen tissue, and/or calcification (Fig. 3A–D).

2.4. Statistical analysis

Continuous variables were expressed as means and standard deviations, and categorical variables were expressed as absolute frequency. The Student's t test was used to compare means, and the χ^2 test, or Fisher's Exact Test, if necessary, was used to evaluate the relationship between dichotomous variables. Multivariable logistic regression analysis was performed using the backward stepwise method to estimate odds ratios (ORs) for the variables associated with fresh thrombus (all variables with a P value < .1 in the univariate analysis were incorporated into the model). SPSS 15 software (SPSS,
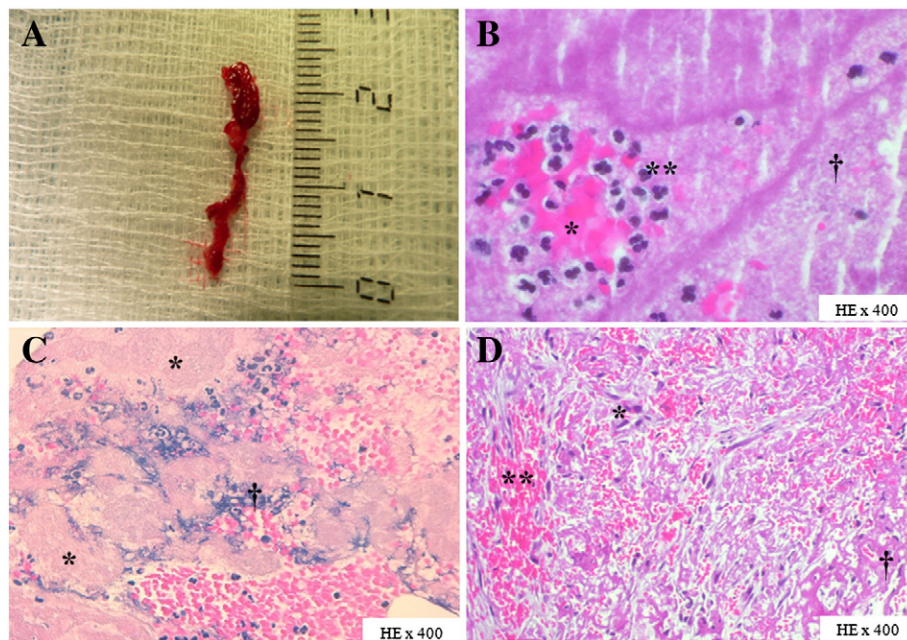

Fig. 1. (A) Macroscopic appearance of the aspirated thrombus after thrombectomy. (B) Microphotograph of a fresh thrombus (HE staining, ×400). *Nonhomogeneous fibrin, **leukocytes, †platelet aggregates. (C) Microphotograph of a lytic thrombus (HE staining, ×400). *Colliquative necrosis, †granulocytes with karyorrhexis. (D) Microphotograph of an organized thrombus (HE staining, ×400). *Endothelial cells, **erythrocytes, †hyaline and homogenized fibrin.