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Clinical paper

Thrombus composition in sudden cardiac death from acute myocardial infarction☆

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ABSTRACT

Background and aim: It was hypothesized that the pattern of coronary occlusion (thrombus composition) might contribute to the onset of ventricular arrhythmia and sudden cardiac death (SCD) in myocardial infarction (MI).

Methods: The TIDE (Thrombus and Inflammation in sudden DEath) study included patients with angiographically-proven acute coronary occlusion as the cause of a ST elevation MI (STEMI) complicated by Sudden Cardiac Death (SCD group) or not (STEMI group). Thrombi were obtained by thrombo-aspiration before primary percutaneous coronary stenting and analyzed with a quantitative method using scanning electron microscopy. We compared the composition of the thrombi responsible for the coronary occlusion between the two groups and evaluated factors influencing its composition.

Results: We included 121 patients and found that thrombus composition was not different between the SCD group (n = 23) and the STEMI group (n = 98) regarding content of fibrin fibers (60.3 ± 18.4% vs. 62.4 ± 18.4% respectively, p = 0.68), platelets (16.3 ± 19.2% vs. 15.616.7 ±%, p = 0.76), erythrocytes (14.6 ± 12.5% vs. 13 ± 12.1%, p = 0.73) and leukocytes (0.6 ± 0.9% vs. 0.8 ± 1.5%, p = 0.93). Thrombus composition did not differ between patients receiving upstream-use of glycoprotein IIb/IIIa platelet receptor inhibitors (GPI) and patients free of GPI. The only factor found to influence thrombus composition was the ischemic time from symptom onset to primary PCI, with a decreased content in fibrin fibers (57.8 ± 18.5% vs. 71.9 ± 10.1%, p = 0.0008) and a higher platelet content (19.2 ± 19.1% vs. 7.9 ± 5.7% p = 0.014) in early presenters (<3 h of ischemic time) vs. late presenters (>6 h of ischemic time).

Conclusion: Composition of intracoronary thrombi in STEMI patients does not differ between those presenting with and without SCD. Time from symptom onset to coronary reperfusion seems to be the strongest factor influencing thrombus composition in MI.

Introduction

Sudden cardiac death (SCD) accounts for 4 million deaths every year worldwide.[1] A frequent cause of SCDs is ventricular fibrillation or fast ventricular tachycardia in the setting of an acute coronary artery occlusion.[2,3] Several risk factors of SCD have been identified in previous studies, however the relationship between an acute coronary artery occlusion and the onset of ventricular arrhythmia is unknown.[4–9]

Abbreviations: STEMI, ST-elevated myocardial infarction; SCD, sudden cardiac death; TIDE study, Thrombus and Inflammation in sudden DEath study; GPI, glycoprotein IIb/IIIa inhibitors; IQR, interquartile range.

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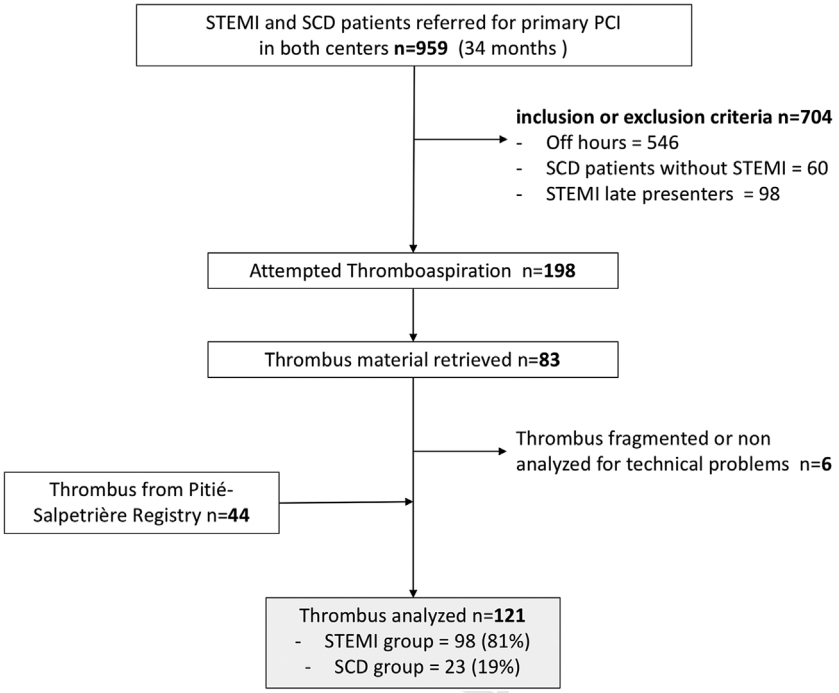

Fig. 1. Flow chart of the study. STEMI: ST-segment elevated myocardial infarction; SCD: sudden cardiac death; PCI: percutaneous coronary intervention.

In ST-elevation myocardial infarction (STEMI) patients, a hypothesis is that differences in patterns of STEMI development leading to more rapid coronary occlusion could trigger SCD. In the TIDE (Thrombus and Inflammation in sudden DEath) microparticle study, we reported higher concentrations of intracoronary endothelial microparticles in STEMI with SCD at presentation versus those without SCD, suggesting that ventricular arrhythmia in the setting of acute myocardial ischemia is not entirely explained by rhythmic vulnerability.[10] A vascular vulnerability related to a specific pattern of abrupt coronary occlusion may also be involved. The TIDE Thrombus study (NCT00748111) was designed to investigate this hypothesis. Our aim was to assess whether thrombus architecture per se could affect the occurrence of SCD in myocardial infarction and characterize the independent correlates of thrombus composition.

Methods

Study design

We prospectively screened all the STEMI and SCD patients referred to the catheterization laboratory of the Pitié-Salpêtrière and Cochin Hospital in Paris France for primary percutaneous coronary intervention (PCI). In the thrombus analysis of the TIDE study, we included SCD patients with documented STEMI (SCD group) and STEMI patients without ventricular arrhythmias (STEMI group) meeting the following inclusion criteria: age >18 years; documented acute coronary artery occlusion with thrombolysis in myocardial infarction (TIMI) flow of 0, 1, or 2; coronary blood sampling using an aspiration catheter available; a time delay from symptom onset to ventricular arrhythmia or pulseless condition of less than 1 h; successful out-of-hospital resuscitation with Return Of Spontaneous Circulation (ROSC) after SCD. Due to logistical constraints, we evaluated only patients presenting during 'on hours'. Our aim was to include 4 STEMI for each SCD. Based on our previous experience in the analysis of thrombus composition in STEMI presenters, we estimated a sample size of 100 STEMI and 25 SCD to be reasonable although no sample size calculation could be performed due to the lack of available data.[11] Recruitment of the TIDE study was slower than expected and patients with STEMI from the thrombus registry of the Pitié-Salpêtrière hospital who matched the inclusion criteria of the TIDE study were included in the present analysis as explained in Fig. 1.

Thrombus collection

Thrombo-aspiration during primary PCI was performed by a low-profile catheter (Export 6F, Medtronic, Santa Rosa, California). Collected thrombi were immediately washed with saline and fixed with 2% glutaraldehyde in 50 mmol/l Na Cacodylate buffer (pH 7.3). Patients received 250 mg of aspirin intravenously; 600 mg of clopidogrel (crushed and administrated in the nasogastric tube if necessary for SCD patients) and the use of glycoprotein IIb/IIIa platelet receptor inhibitors (GPI) were administered before and/or during the procedure at the discretion of the physicians.

Study oversight

The study was reviewed and accepted by the ethics committee of the Institutional Review Board of the Cochin Hospital, Paris, France and the thrombus registry of the Pitié-Salpêtrière is declared as part of the ePARIS STEMI registry which was reviewed and accepted by the ethics committee of the Institutional Review Board of the Pitié-Salpêtrière Hospital. Informed consent was obtained before the procedure in all STEMI patients without SCD. The ethics committee allowed blood sampling and thrombus collection without consent during PCI procedures in case of SCD. However, the data could be used only if informed consent was obtained from the next of kin before or after the procedure and from the patient if s/he survived.

Scanning electron microscope analysis

Sample fixation, dehydration, and preparation were performed according to a previously published method.[12] High-definition photographs (×3000 magnification) were obtained using a