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Relationship between thrombus age in aspirated coronary material and mid-term major adverse cardiac and cerebrovascular events in patients with acute myocardial infarction

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ABSTRACT

Background and aims: Recent studies have shown that coronary thrombus histopathology is associated with impaired myocardial reperfusion and poor clinical outcome in patients with acute myocardial infarction (AMI). We sought to investigate the age of thrombi aspirated during percutaneous coronary intervention (PCI) in patients with AMI and evaluate the relationship between histopathologic findings and major adverse cardiac and cerebrovascular events (MACCEs) defined as all-cause death, stroke, or myocardial infarction within 6 months of PCI.

Methods: In this prospective 2-center observational study, coronary material was obtained during PCI from 305 patients with AMI within 24 h of symptom onset. Thrombi were morphologically classified as either only fresh or older (lytic changes or organization).

Results: MACCE occurred in 38 (12.5%) patients. Only fresh thrombi were observed in 114 (37%) of 305 patients; older thrombi were identified in 191 (63%). The rate of MACCE was significantly higher among patients with older thrombus ($p = 0.011$). Multivariate analysis also showed the presence of older thrombus [odds ratio (OR) 3.03, 95% confidence interval (CI) 1.122–9.522] is an independent predictor of MACCE within 6 months of PCI, as well as age (OR 1.051, 95% CI 1.013–1.094) and creatine kinase concentration (OR 1.025, 95% CI 1.013–1.037). The prevalence of slow flow or distal embolization during PCI and peak creatine kinase concentration were significantly higher in the older thrombus group ($p < 0.05$, respectively).

Conclusions: Older thrombus found in aspirated coronary material is associated with impaired myocardial reperfusion and is an independent predictor of mid-term MACCE in patients with AMI.

1. Introduction

Thrombus propagation on a disrupted or eroded atherosclerotic plaque is a potentially life-threatening event that leads to acute myocardial infarction (AMI) [1,2]. Primary percutaneous coronary intervention (PCI) to achieve immediate restoration of blood flow and limit the extent of myocardial necrosis is the preferred treatment for AMI [3]. Thrombus aspiration during primary PCI has commonly been performed to reduce distal embolization and improve microvascular perfusion, which might affect short-term and long-term clinical outcomes [3–5]. However, recent large trials have questioned its safety and value [6,7]. On the other hand, thrombus aspiration enables the evaluation of the coronary thrombus causing AMI *in vivo*. This practice has provided a better understanding of the pathophysiology of coronary thrombosis. Several retrospective pathologic studies of aspirated coronary material have shown that plaque disruption and thrombus formation occur significantly earlier than symptom onset, coronary thrombi are days or weeks old in many patients, and the presence of an older thrombus is an independent predictor of long-term mortality in patients with ST-elevation myocardial infarction (STEMI) [8,9]. Others have also described a significant relationship

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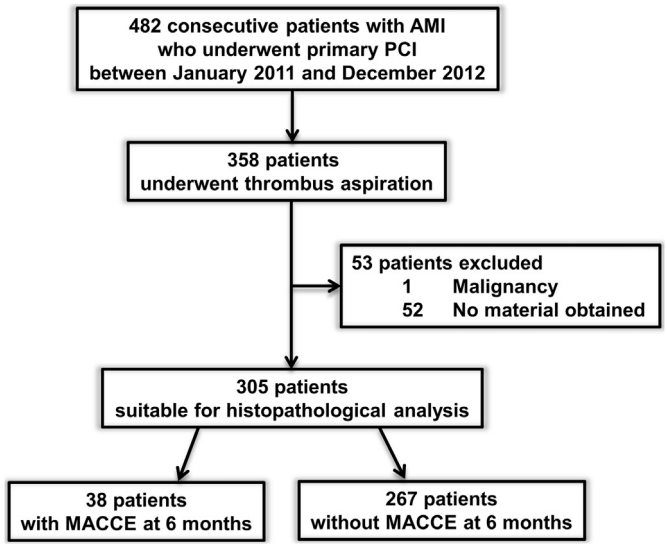

Fig. 1. Study flow chart.
AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; MACCE, major adverse cardiac and cerebrovascular event.

between pathologic findings in coronary thrombus and myocardial reperfusion grade during PCI [10,11]. In addition, we have previously reported that the presence of organized thrombus independently predicts in-hospital death in patients with AMI, who underwent thrombus aspiration during primary PCI [12]. These studies imply an association between histopathologic findings in aspirated coronary material and mid-term adverse events. However, little is known about this association. Therefore, we prospectively investigated the age of thrombi aspirated during PCI in patients with AMI and evaluated whether histopathologic findings are related to major adverse cardiac and cerebrovascular events (MACCEs), defined as all-cause death, stroke, or myocardial infarction, within 6 months of PCI.

2. Materials and methods

2.1. Study population

All patients provided written informed consent. The study protocol complies with the Declaration of Helsinki. It was approved by the hospital ethics committee.

This prospective 2-center observational study included 482 consecutive patients with AMI who underwent primary PCI within 24 h of symptom onset at Miyazaki Medical Association Hospital and Miyazaki Prefectural Nichinan Hospital, between January 2011 and December 2012. Of these, 358 patients underwent manual thrombus aspiration during primary PCI. The diagnosis of AMI was based on a history of prolonged ischemic chest pain, characteristic electrocardiogram changes, new regional wall motion abnormalities, and elevated creatine kinase (>2 times above the normal range) within 24 h of symptom onset. Exclusion criteria included no material obtained by aspiration (n = 52) and other disease, resulting in a life expectancy of less than 6 months (n = 1). Ultimately, 305 patients with AMI were enrolled according to the eligibility criteria (Fig. 1), of whom 140 were included in our previous study [12].

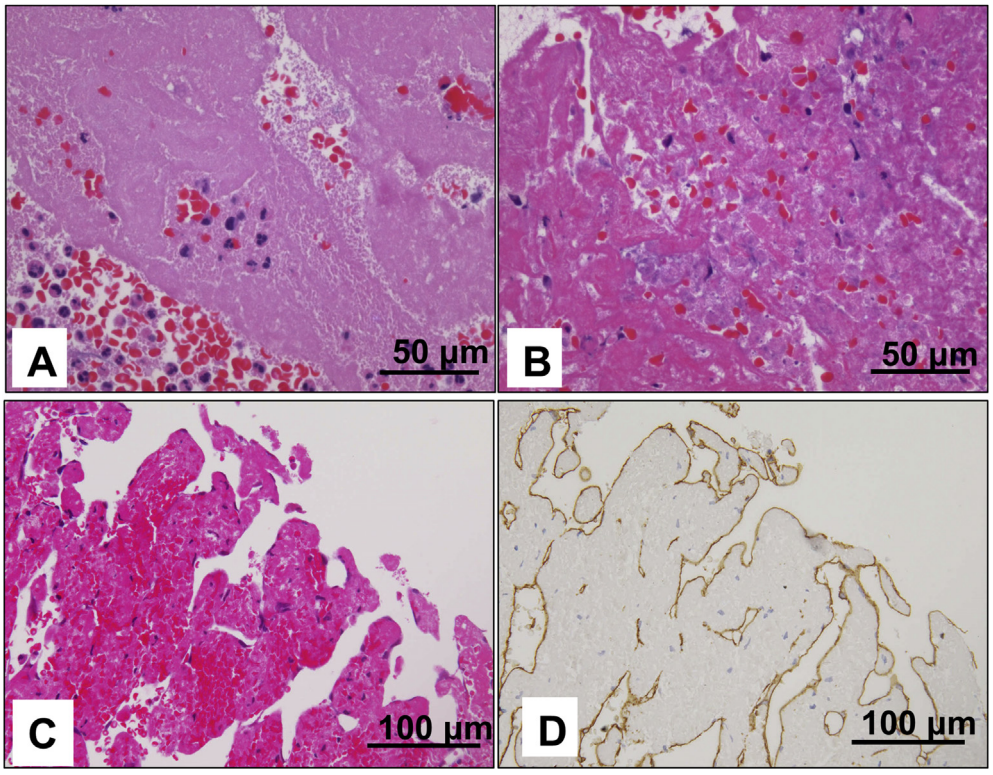

Fig. 2. Representative photomicrographs of coronary thrombi aspirated from patients with AMI.
(A) Fresh thrombus appears as layers of fibrin and intact blood cells (platelets, erythrocytes, and granulocytes). (B) Lytic thrombus has features of homogeneous structural elements with nuclear swelling, fragmentation, and nuclear dust. (C) Organized thrombus shows endothelialization and capillary vessel ingrowth with collagen deposition. (D) Immunostaining for CD34, a marker of endothelial cells, clearly illustrates endothelialization and capillary vessel ingrowth in organized thrombus. AMI, acute myocardial infarction.