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Role of Intravascular Ultrasound in Patients with Acute Myocardial Infarction

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Rupture of a vulnerable plaque and subsequent thrombus formation are important mechanisms leading to the development of an acute myocardial infarction (AMI). Typical intravascular ultrasound (IVUS) features of AMI include plaque rupture, thrombus, positive remodeling, attenuated plaque, spotty calcification, and thin-cap fibroatheroma. No-reflow phenomenon was attributable to the embolization of thrombus and plaque debris that results from mechanical fragmentation of the vulnerable plaque by percutaneous coronary intervention (PCI). Several grayscale IVUS features including plaque rupture, thrombus, positive remodeling, greater plaque burden, decreased post-PCI plaque volume, and tissue prolapse, and virtual histology-IVUS features such as large necrotic core-containing lesion and thin-cap fibroatheroma were the independent predictors of no-reflow phenomenon in AMI patients. Non-culprit lesions associated with recurrent events were more likely than those not associated with recurrent events to be characterized by a plaque burden of ≥70%, a minimal luminal area of ≤4.0 mm^2, or to be classified as thin-cap fibroatheromas. **(Korean Circ J 2015;45(4):259–265)**

KEY WORDS: Myocardial infarction; Atherosclerosis; Ultrasonography, interventional.

Introduction

   Acute myocardial infarction (AMI) results from spontaneous plaque rupture or erosion and subsequent thrombosis.[1][2] Intravascular ultrasound (IVUS) has a pivotal role in detecting plaque characteristics and periprocedural complications, and assessing plaque evolution after medical therapy. Pre-percutaneous coronary intervention (PCI) provides measures of vessel sizes, lumen, plaque and plaque length; assesses plaque morphology, calcium, and remodeling pattern; detects vulnerable plaque

including plaque rupture, thrombus, attenuated plaque, and thin-cap fibroatheroma (TCFA); detects dissection and aneurysm; and determines stent size and length.[3] IVUS can predict post-PCI distal embolization or no-reflow. Many IVUS predictors of peri-procedural myocardial infarction (MI) have been demonstrated, including thrombus formation,[4][5] greater plaque burden,[4][5] positive remodeling,[6][7] and decreased post-PCI plaque volume,[5][8] and TCFA.[9] IVUS is very useful to assess plaque changes and its impact on long-term clinical outcomes.[10-12] Recently, Singh et al.[13] reported that IVUS guidance in patients with AMI is associated with reduced in-hospital mortality, similar length of hospital stay, and increased cost of care and vascular complications, as compared with conventional angiography-guided PCIs.

   The authors have reviewed pre- and post-PCI IVUS findings and predictors of peri-procedural MI and plaque progression/regression in patients with AMI.

Pre-Percutaneous Coronary Intervention Intravascular Ultrasound Findings in Acute Myocardial Infarction

Plaque rupture

   Rupture of vulnerable plaque and/or endothelial erosions with subsequent thrombus formation are the main mechanisms implicated
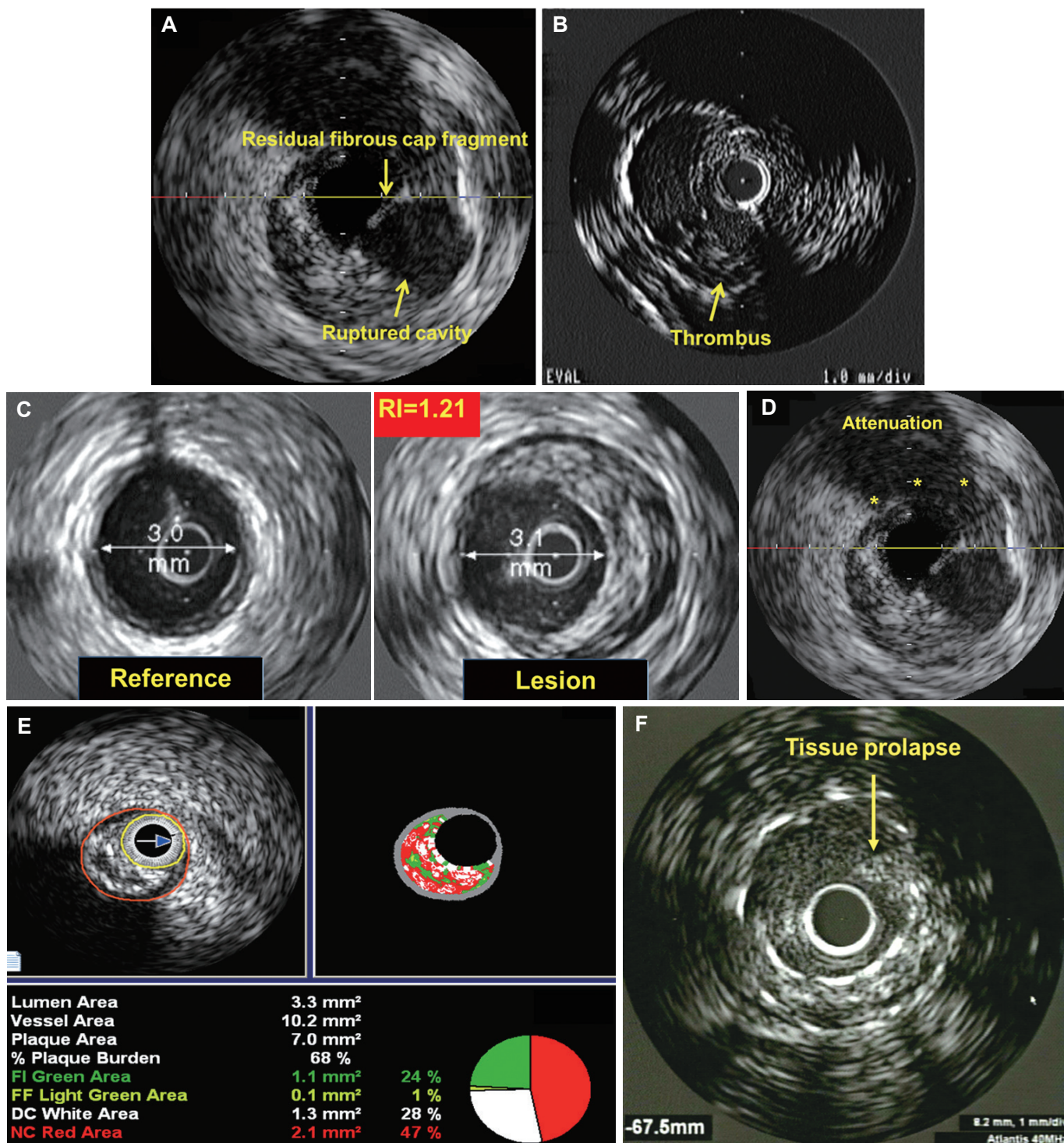
Fig. 1. Intravascular ultrasound findings in patients with acute myocardial infarction. (A) Plaque rupture with a cavity that communicated with the lumen with an overlying residual fibrous cap fragment, (B) intracoronary thrombus shows a distinct hypoechoic mass, (C) positive remodeling with a remodeling index of 1.21, (D) attenuated plaque shows hypoechoic plaque with deep ultrasound attenuation without calcification or very dense fibrous plaque, (E) thin-cap fibroatheroma with a necrotic core of 35.4% of plaque area in the presence of 83.3% of plaque burden, and (F) tissue prolapse shows an intraluminal tissue extrusion through the stent struts.

in the pathogenesis of AMI. Fig. 1A showed a ruptured plaque containing a cavity that communicated with the lumen with an overlying residual fibrous cap fragment.[14] Rupture sites separated by a length of artery containing smooth lumen contours without cavities represent multiple plaque ruptures. In the our previous study,[15] ruptured plaque was observed in 46% patients with

ST-segment elevation myocardial infarction (STEMI) and 29% patients with non-ST-segment elevation myocardial infarction (NSTEMI) (p=0.002); furthermore, multiple plaque ruptures tended to be more frequent in patients with STEMI, as compared with those with NSTEMI (19% vs. 13%, p=0.14). However, plaque cavity cross-sectional area (CSA) and ruptured plaque length were not different between patients with STEMI and those with NSTEMI (2.34±1.16 mm^2 vs. 2.33±1.58 mm^2, p=0.9, and 2.69±1.11 mm vs. 2.67±1.67 mm, p=0.9, respectively). Kusama et al.[16] reported that plaque rupture was associated with morphologic characteristics of vulnerable lesions with a higher incidence of soft plaque and positive remodeling. Plaque rupture is closely related to obstructive thrombus formation and the longitudinal morphology of plaque rupture also affects the coronary flow. The presence of thrombi may obscure IVUS detection of plaque rupture.

Thrombus

The identification of thrombus requires at least 2 of the following: distinct hypoechoic mass, brightly speckled plaque, channeling within the plaque, evacuated plaque cavity, or detached mobile mass (Fig. 1B).[17] The detection rate of thrombus by IVUS is not high due to the limited resolution of IVUS. Injection of contrast or saline may disperse the stagnant flow, clear the lumen, and allow differentiation of stasis from thrombosis. However, none of these features is pathognomic for thrombus, and the diagnosis of thrombus by IVUS should always be considered presumptive.[3] In our previous study,[15] IVUS-detected thrombus was observed in 34% patients with STEMI and 21% patients with NSTEMI (p=0.006).

Positive remodeling

Coronary artery remodeling is assessed by comparing the lesion site to the reference external elastic membrane (EEM) CSA. Remodeling index is the lesion site EEM CSA divided by the average of the proximal and distal reference EEM CSA. Positive remodeling is defined as a remodeling index >1.05 (Fig. 1C), intermediate remodeling as a remodeling index between 0.95 and 1.05, and negative remodeling as a remodeling index <0.95.[18] In patients with AMI, Hasegawa et al.[19] reported that 55% cases showed positive remodeling on IVUS, whereas negative remodeling was observed in 25% cases; in addition, patients with positive remodeling were significantly older than those with negative remodeling, and the frequency of calcifications was higher and soft plaque with small calcifications was the more frequent in patients with positive remodeling than those with negative remodeling.

Attenuated plaque

Attenuated plaque is defined as hypoechoic plaque with deep ultrasound attenuation without calcification or very dense fibrous plaque (Fig. 1D).[20] Wu et al.[21] reported that 78% of the AMI patients had attenuated plaques in the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial. Lee et al.[22] reported that attenuated plaque was observed in 39.6% of STEMI and 17.6% of NSTEMI (p<0.001). Furthermore, the level of C-reactive protein (CRP) was higher and angiographic thrombus and initial Thrombolysis In Myocardial Infarction (TIMI) flow grade <2 were more common; IVUS lesion site plaque burden and remodeling index were significantly greater; lesion site luminal dimensions were significantly smaller; and thrombus, positive remodeling, and plaque rupture were more common in AMI patients with attenuated plaque, as compared with those without attenuated plaque.

Thin-cap fibroatheroma

Plaque composition plays a role in plaque disruption and thrombosis that leads to acute coronary events.[23] Lesions with a large lipid core have a higher risk for disruption than sclerotic plaques.[24] TCFA by virtual histology (VH)-IVUS is defined as a necrotic core (NC) ≥10% of plaque area in at least 3 consecutive frames without overlying fibrous tissue in the presence of ≥40% plaque burden (Fig. 1E).[25] TCFA is the precursor of plaque rupture that accounts for a majority of coronary thrombi and coronary death.[22] Previous study has shown that VH-IVUS identified TCFA is a more prevalent finding in patients with AMI than in stable angina patients.[26]

Plaque characteristics according to age

Cardiovascular disease is highly prevalent among the elderly who constitute an increasing segment of the population, accounting for most of their morbidity and mortality. Compared with the general population, elderly patients undergoing coronary revascularization are more likely to present with more complex lesions, unstable angina, comorbid conditions and a lower ejection fraction.[27][28] Hassani et al.[29] reported that rupture/dissection were observed more frequently (32% vs. 9%, p=0.009) and culprit lesions contained more thrombus (14% vs. 2%, p=0.04) in the <65-year-old group; conversely, in octogenarians, lesions were predominantly calcified (57% vs. 10%, p<0.001) and longer (20.9±7.8 mm vs. 16.6±6.1 mm, p=0.004) with less positive remodeling (19% vs. 56%, p<0.001), and age was the only independent predictor of calcified plaque (p=0.02) and remodeling (p=0.005) in AMI patients.

Association between inflammatory marker and plaque characteristics

Plaque rupture frequently occurs at the site of thinnest fibrous

cap with heavy infiltration of activated macrophage foam cells, indicating ongoing inflammation at the site of plaque disruption. Inflammation plays an important role in both atherogenesis and atherothrombotic events. High-sensitivity CRP is associated with increased risk for coronary artery disease, and myocardial necrosis further promotes the synthesis of CRP. Sano et al.[30] reported that plaque rupture was observed more frequently in the elevated CRP group (≥3 mg/L) than in the normal CRP group (70% vs. 43%, p=0.01) and the presence of ruptured plaque alone correlated with elevation of serum CRP {p=0.02; odds ratio (OR), 3.35; 95% confidence interval (CI), 1.22 to 9.18}. Tanaka et al.[31] reported that high-sensitivity CRP levels had a positive correlation with the number of plaque ruptures (p<0.01). Therefore, multiple plaque rupture is associated with systemic inflammation, and patients with multiple plaque rupture can be expected to show a poor prognosis.

Post–Percutaneous Coronary Intervention Intravascular Ultrasound Findings in Acute Myocardial Infarction

Tissue prolapse after stent implantation

Tissue prolapse is characterized by an intraluminal tissue extrusion through the stent struts, and is easily detectable using IVUS (Fig. 1F). Several pre-PCI IVUS factors such as soft (rather than fibrous or calcified) plaque, smaller minimal lumen diameter, and larger plaque burden are related to tissue prolapse. The risk of tissue prolapse is known to be higher during aggressive stenting procedures.[32][33] In our previous study,[34] we assessed the incidence, predictors, and outcome of tissue prolapse after stent implantation in patients with AMI. The tissue prolapse was detected in 27% patients after stent implantation, and stent length, plaque rupture, and positive remodeling were independently associated with the development of tissue prolapse. We also showed that tissue prolapse, plaque rupture, and thrombus were independently associated with post-stenting creatine kinase-myocardial band elevation.

Stent malapposition after stent implantation

Stent malapposition may be a sign of impaired healing or the result of suboptimal stent implantation. Stent malapposition may increase the thrombotic risk due to the presence of intraluminal stent struts. van der Hoeven et al.[35] studied acute and late stent malapposition after implantation of bare-metal stents (BMS) and sirolimus-eluting stents (SES) in STEMI patients who were enrolled in the MISSION! Intervention Study. Acute stent malapposition was found in 38.5% SES patients and 33.8% BMS patients (p=0.51); and late stent malapposition in 37.5% SES patients and 12.5% BMS

patients (p<0.001). Acquired stent malapposition was found in 25.0% SES patients and 5.0% BMS patients (p<0.001). Predictors of acute stent malapposition were reference diameter (SES: OR 3.49, 95% CI 1.29 to 9.43; BMS: OR 28.8, 95% CI 4.25 to 94.5) and balloon pressure (BMS: OR 0.74, 95% CI 0.58 to 0.94). Predictors of late stent malapposition were diabetes mellitus (SES: OR 0.16, 95% CI 0.02 to 1.35), reference diameter (BMS: OR 19.2, 95% CI 2.64 to 139.7), and maximum balloon pressure (BMS: OR 0.74, 95% CI 0.55 to 1.00). After SES implantation, acquired stent malapposition was caused by positive remodeling in 84% and plaque reduction in 16% of patients.

Role of intravascular ultrasound to predict periprocedural myocardial infarction

The periprocedural MI or no-reflow phenomenon is observed frequently after PCI for AMI. No-reflow phenomenon is attributable to the embolization of thrombus and plaque debris that results from mechanical fragmentation of the vulnerable plaque by PCI. Tanaka et al.[6] reported that lipid pool-like image and lesion EEM CSA were independent predictive factors of no-reflow phenomenon after reperfusion for AMI. Kusama et al.[36] reported that patients with plaque rupture had a higher incidence of no-reflow phenomenon (15% vs. 3%, p=0.08) and a lower myocardial blush grade (1.5 vs. 2.3, p<0.05) after PCI. Endo et al.[20] reported that ultrasound attenuation with a longitudinal length of ≥5 mm and plaque rupture correlated with no-reflow phenomenon in patients with STEMI. Our previous study[37] showed that positive remodeling, plaque rupture, IVUS-detected thrombus, and tissue prolapse were independently associated with post-stenting cardiac-specific troponin I elevation. In another previous study,[38] we demonstrated that tissue prolapse, high-sensitivity CRP, and culprit lesion multiple plaque ruptures were associated with post-PCI no-reflow in AMI patients with plaque rupture. Ohshima et al.[39] reported that cavity volume of ruptured plaque was an independent predictor for angiographic no-reflow phenomenon during primary angioplasty in patients with STEMI. Sato et al.[8] reported that the decrease in plaque volume after PCI was significantly larger in patients with inadequate reflow than in those with reflow (49.4±18.9 vs. 31.7±15.5 mm³, p=0.001) and delta-plaque volume was significantly correlated with corrected TIMI frame count after PCI in patients with AMI.

There are controversies in the association between VH-IVUS plaque components and no-reflow or slow-flow phenomenon after PCI in AMI patients.[40-43] In the largest investigation to date regarding relation between plaque composition and no-reflow,[9] we demonstrated the NC-rich plaque as assessed by VH-IVUS was independently associated with no-reflow.

Intravascular ultrasound predictors of stent thrombosis

Many IVUS predictors for early stent thrombosis (EST) including under expansion of stents, smaller final lumen area and inflow/outflow disease (residual stenosis or dissection) have been reported.[44-47] Previously, we reported that plaque burden at the minimum lumen site was significantly greater, and pre-PCI plaque rupture and IVUS-detected thrombus were observed more frequently, and post-stenting tissue prolapse was observed more frequently in patients with EST, as compared with those without EST (68.8% vs. 32.6%, p=0.003); and tissue prolapse was an independent predictor of EST.[48]

Role of Intravascular ultrasound to Detect Plaque Progression/Regression

Several IVUS studies have demonstrated the benefits of statin therapy in regression or non progression of coronary plaque. Previous IVUS studies have shown that low-density lipoprotein (LDL) cholesterol level was the independent predictor of changes in coronary plaque size.[49)50] The Providing Regional Observations to Study Predictors of Events in the Coronary Tree (PROSPECT) trial[10] demonstrated that non-culprit lesions associated with recurrent events were more likely than those not associated with recurrent events to be characterized by a plaque burden of ≥70%, a minimal luminal area of ≤4.0 mm^2, or to be classified as TCFAs. Lehman et al.[51] reported that plaque progression over time was dependent on plaque composition i.e., there was more progression in noncalcified plaque, as compared to calcified plaque. Nicholls et al.[52] reported that calcified plaques are more resistant to undergoing changes in size in response to systemic interventions targeting atherosclerotic risk factors. Our previous study,[53] indicated that NC is associated with plaque progression in patients when the LDL cholesterol level is around 80 mg/dL at 9 month follow up after treatment with rosuvastatin 10 mg/day. Events related to non-culprit lesions typically occurred at sites that were classified as TCFAs.

Conclusion

IVUS is a useful tool to assess vascular geometry and morphology, and quantitative composition of atherosclerotic plaque at pre-PCI. It is additionally used to assess post-procedural tissue prolapse and malapposition, and to predict post-PCI myonecrosis and EST and plaque progression/regression at long-term follow-up in AMI patients. Although IVUS has limited resolution, it can inform clinical decision making, especially to determine vessel size and arterial remodeling and to select stent size and length, as compared to other imaging modalities such as optical coherence tomography. IVUS guidance can reduce mortality and vascular complications, as compared with conventional angiography-guided PCI in patients with AMI. The recently developed multimodality coronary imaging catheter utilizing combination of IVUS and near-infrared spectroscopy is being used in clinical practice to interrogate the artery and determine the structure and chemistry of the plaque.

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