# **Short Communication**

# Intraluminal Filling Defects on Coronary Angiography: More than Meets the Eye

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#### Summary

Intraluminal filling defects are occasionally encountered on coronary angiography and often related with coronary thrombi. However, other conditions affecting the coronary arteries may present with similar angiographic findings causing diagnostic uncertainty. Accurate characterization of the angiographic filling defect is critical, particularly in patients planned for a percutaneous coronary intervention (PCI), as diagnosis of a coronary thrombus not only increases the risk of post procedural adverse events but also requires a specific therapeutic approach. In this paper, we report three patients in whom coronary angiography revealed intraluminal filling defects mimicking coronary thrombi. When further investigated with intravascular ultrasound (IVUS) as a part of the planned PCI, the thrombus was excluded and alternate etiology of the filling defect was confirmed in all patients. The angiographic "pseudothrombi" were produced by coronary dissection in one and by heavy calcification within the atherosclerotic plaque in two patients. The use of IVUS allowed accurate characterization of the angiographic filling defect and provided important information to guide management and optimize therapeutic approach.

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Coronary angiography is a common investigation performed in patients suspected with coronary artery disease.<sup>1</sup> Intraluminal filling defects are occasional findings on coronary angiography and may present a diagnostic and a therapeutic dilemma. Although they are often associated with intra coronary thrombi, particularly in the setting of an acute coronary syndrome, several other pathologies such as coronary artery dissection, emboli, mural calcification and unopposed stent struts in a previously stented segment may also result in similar angiographic findings. As the treatment markedly differs for these diverse conditions, it is imperative to characterize the true nature of these filling defects for proper diagnosis and management. In this paper, we report three cases with intraluminal filling defects that mimicked thrombi on coronary angiography. However, further interrogation with IVUS revealed alternate causes for the angiographic appearance. The accurate identification of the underlying pathology allowed application of a specific treatment strategy with good clinical outcome.

### Case 1

An 85-year-old man with past medical history of hypertension, dyslipidemia and peripheral vascular disease was hospitalized after an inferior ST-elevation myocardial infarction. He did not receive thrombolytic therapy due to late presentation, but experienced further angina after admission to the coronary care unit. Coronary angiography revealed moderate disease in the left coronary artery and two intraluminal filling defects in the mid-segment of the right coronary artery (RCA), Fig. 1(A), suggesting presence of thrombi. An IVUS



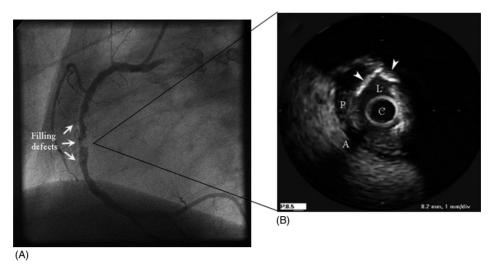


FIG. 1 Filling defects (arrows) noted in the mid segment of the right coronary artery on angiography in a patient presenting with inferior ST elevation myocardial infarction (A). IVUS showed extensive calcification at the site of the angiographic filling defects (B). Arrow heads–superficial calcification of the atherosclerotic plaque, A–arterial adventitia, C–IVUS catheter, L–arterial lumen, P–atherosclerotic plaque.

employing 40 MHz, Atlantis<sup>®</sup> SR catheter and Galaxy Imaging system (Boston Scientific Corp. Natick, MA) was performed before the planned percutaneous intervention (PCI) to better characterize the lesion and guide the therapeutic approach. IVUS demonstrated an area of atherosclerotic plaque with extensive superficial calcification at the site of the angiographic filling defects (Fig. 1(B)). No thrombus was detected at the site of the intraluminal filling defect or elsewhere in the right coronary artery. The lesion was successfully dilated with high pressure non compliant balloon inflations and placement of a Taxus (Boston Scientific, Canada) stent with good angiographic result.

## Case 2

A 48-year-old-man with past medical history of smoking, dyslipidemia, hypertension, diabetes mellitus, obesity and a remote history of myocardial infarction was referred for coronary angiography after hospitalization for an acute coronary syndrome. Coronary angiography revealed sequential significant stenoses in the mid and distal segments of the left anterior descending (LAD) artery, occlusion of the obtuse marginal branch of the left circumflex artery and a significant stenosis in the distal segment of the RCA. He underwent PCI of the mid and distal LAD with placement of three Cypher (Johnson & Johnson, Canada) stents with excellent angiographic result. He was treated with aspirin and clopidogrel after the procedure and was scheduled for PCI on the RCA as a staged procedure. Selective left coronary angiography performed at the time of the staged intervention on the RCA eight weeks later demonstrated an intraluminal filling defect in the mid LAD a few millimeters before the previously stented segment (Fig. 2(A)). IVUS was performed to better characterize the nature of the angiographic filling defect. IVUS demonstrated the presence of an intimal dissection flap (Fig. 2(B)) extending proximally from the edge of the stent resulting in significant narrowing of the arterial lumen. No thrombus was noted either within or proximal to the stent. This was treated with additional Cypher (Johnson & Johnson, Canada) stent placement to cover the entire length of dissection. The patient also underwent an uneventful PCI of the RCA at the same sitting with good clinical outcome.

# Case 3

A 62-year-old man with past medical history of dyslipidemia was hospitalized following a non-ST-elevation myocardial infarction. Coronary angiography demonstrated a significant stenosis in the proximal left circumflex artery and an intraluminal filling defect in the proximal RCA (Fig. 3(A)) suggestive of coronary thrombus. A PCI to the culprit lesion in the RCA was planned but deferred in view of the angiographic findings, and the patient was treated with aspirin, clopidogrel, intravenous heparin and eptifibatide. Coronary angiography performed 48 h later showed no significant change in the angiographic findings. An IVUS performed for bettercharacterization of the angiographic filling defect demonstrated a heavily calcified plaque with no evidence of thrombus (Fig. 3(B)). In view of the IVUS findings, rotational atherectomy was performed followed by balloon angioplasty and placement of a Driver<sup>®</sup> (Medtronic, Canada) stent with good angiographic and clinical outcome.

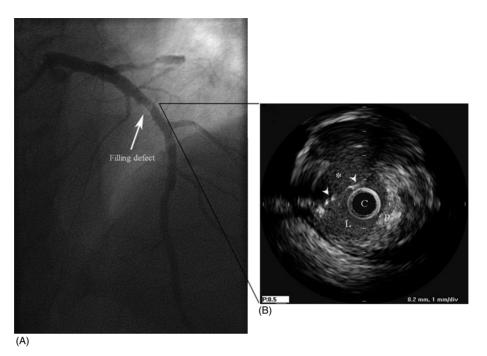
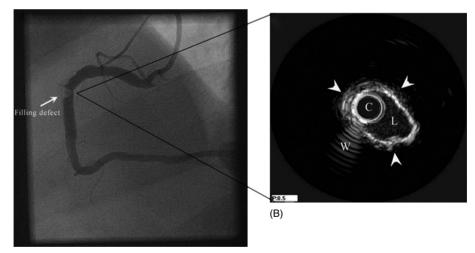


FIG. 2 Intraluminal filling defect noted on coronary angiography proximal to an LAD segment stented 8 weeks earlier (A). IVUS revealed an intimal flap at the site of the filling defect with compromise of the arterial lumen. Arrow heads-dissection flap, \*-false lumen, L-true lumen, P-plaque, C-IVUS catheter.



(A)

FIG. 3 A filling defect in the proximal RCA that persisted despite 48 h treatment with aspirin, clopidogrel, heparin and eptifibatide (A). IVUS demonstrated a heavily calcified atherosclerotic plaque at the site of the angiographic filling defect. Arrow heads–extensive superficial calcification of the atherosclerotic plaque, C–IVUS catheter, L–arterial lumen, W–guide wire artifact.

#### Discussion

The assessment of coronary anatomy by conventional angiography plays an important role in the diagnosis and treatment of patients with coronary artery disease. However, there are important limitations to this technique, most notable of which is the lack of tissue characterization for the atherosclerotic plaque or the vessel wall. The intraluminal filling defects are occasionally noted on coronary angiography and often diagnosed as coronary thrombi based on nonspecific findings such as the presence of a filling defect, luminal haziness or alterations in the density of the intraluminal contrast media, i.e. staining. However, other vascular pathology such as mural calcification, emboli, aneurysm, coronary dissection or collateral blood flow may also produce similar angiographic findings and result in diagnostic uncertainty. Several studies have shown that coronary angiography has poor sensitivity for the detection of coronary

calcification,<sup>2</sup> thrombi<sup>3-5</sup> or dissection<sup>5,6</sup> and offers limited ability to differentiate between these conditions.<sup>5,7–9</sup> Although fluoroscopy alone may detect mural calcification in heavily calcified coronary arteries, it does not provide information about the location (superficial or deep) of calcification within the arterial wall. IVUS on the other hand provides superior image resolution (axial resolution of 100 to 200µm and a lateral resolution of 250 µm with 20 to 40 MHz catheter<sup>10</sup>) with tissue characteristics of the luminal contents and morphology of the arterial wall. Although, IVUS affords excellent sensitivity for the detection of mural calcification<sup>2,11,12</sup> and coronary dissection,<sup>8,13</sup> no pathognomonic features of thrombi on IVUS examination have been described and coronary angioscopy remains the gold standard for its diagnosis.<sup>3,4,13</sup> However, the use of angioscopy is limited to research applications in most catheterization laboratories due to the associated technical challenges. These include obstruction of blood flow with an occluding balloon in the proximal coronary artery or continuous saline flush for keeping a blood-free field of view during angioscopic examination and difficulty of use in small vessels or across narrow lesions. Despite its lower sensitivity in the detection of plaque surface erosions or small thrombi<sup>13,14</sup> compared to angioscopy, IVUS remains the most common supplementary tool used for coronary imaging and provides adequate resolution for diagnosis of clinically significant intraluminal, plaque and stent associated thrombi.<sup>11</sup> Several features characteristic of thrombi have been described on IVUS examination<sup>11,15,16</sup> and validated both *in-vitro*<sup>17,18</sup> and *in-vivo*.<sup>19</sup> The criteria most commonly used for the diagnosis of thrombus on IVUS include the presence of an echodense structure within the lumen or adjacent to the arterial wall or a stent without any evidence of blood flow inside.4,8,11,17

As highlighted by the reported cases, the accurate characterization of the angiographic filling defects with IVUS examination not only renders an accurate diagnosis but also allows for a targeted therapy specific to the underlying pathology. A calcified atherosclerotic plaque seen on IVUS requires aggressive lesion dilatation with a noncompliant balloon or plaque modification with a cutting balloon or rotational atherectomy, techniques that would be contraindicated in the presence of a thrombus or a dissection. Similarly, a diagnosis of dissection by IVUS would prompt additional stent deployment, a strategy that may be associated with increased risk of stent thrombosis in the presence of coronary thrombi. Moreover, the presence of intracoronary thrombus during PCI increases the risk of periprocedural adverse events<sup>20</sup> and may necessitate the use of mechanical thrombectomy, distal protection devices or systemic/local antithrombotic and anticoagulant therapy to reduce procedural complications.<sup>21</sup>

In most catheterization laboratories, IVUS is not frequently used due to the associated cost, time and unproven benefit for routine procedures, but a more liberal approach is suggested in patients with ambiguous lesions on coronary angiography or undergoing complex interventions to improve diagnostic accuracy and guide therapy to improve clinical outcomes.<sup>15,16,22</sup>

#### Conclusions

All intraluminal filling defects on coronary angiography do not represent thrombi. Although a patient's clinical presentation in conjunction with angiographic findings may suggest the likely etiology of an angiographic filling defect in many cases, further characterization with IVUS particularly in those planned for a PCI can provide complementary information with important therapeutic implications.

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