# Cardiac imaging for the detection of ischemia after percutaneous coronary intervention

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## Abstract

Percutaneous coronary intervention (PCI) is increasingly used to treat coronary heart disease. Despite major technologic advances, however, not even drug-eluting stents confer long-term immunity from cardiac events, as disease progression causes significant morbidity after PCI. Myocardial perfusion imaging (MPI) accurately detects ischemia and stratifies risk when performed 2 months or more after PCI. Coronary computed tomography angiography may also have an important role in the assessment of patients after PCI: it permits direct imaging of restenotic lesions and obstructive plaque, and facilitates assessment of non obstructive plaque, which is not detectable with MPI, but is frequently responsible for hard cardiac events.

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## Introduction

Coronary heart disease (CHD), the single largest killer in Europe and the US, accounted for 1.95 million deaths in Europe each year during the most recent years for which data are available [1] and was the underlying or contributing cause of death for 653 000 in the US in 2003 [2]. Since its development in 1977 [3] and the introduction of bare-metal [4,5] and drug-eluting stents [6,7], percutaneous coronary intervention (PCI) has become a mainstay for treating CHD. For selected patients with acute coronary syndromes, acute myocardial infarction, and cardiogenic shock, PCI is the treatment of choice. With restenosis rates at an all-time low [6,7], increasing numbers of patients with multivessel disease, chronic total occlusions, complex lesions, small-diameter vessels, and diseased bypass conduits are undergoing PCI. In Europe, PCI rates ranged from 77 to 2194 per million population in 2000; stents were implanted in 38–1501 per million [1]. In the US, 664 000 PCI procedures were performed in 2003; 84% involved placement of a stent [2]. As life expectancy increases and additional technological improvements occur, PCI use will likely increase still further.

## Adverse events, restenosis, and disease progression

Despite significant advances, cardiac event rates in patients after successful PCI are greater than in the general population. A meta-analysis of 29 randomized studies comparing outcomes after balloon angioplasty and coronary stenting found combined rates of death and myocardial infarction were 5% in both groups over 6–16 months [8]; stent deployment did not decrease hard events. As restenosis rarely causes

hard events, it follows that the ability of stents to decrease restenosis does not necessarily translate into a reduction in hard events. In clinical trials of the drug-eluting stents now commercially available, rates of major adverse events at 6–12 months were 3–10%, despite restenosis rates of 0–9% [9].

As drug-eluting stents almost eliminate restenosis, disease progression assumes increased importance. Obstructive disease in untreated vessel segments was found in 44% of 87 patients undergoing angiography 2 years or more after PCI [10]; 45% of asymptomatic persons had such disease. During 1-year follow-up, 6% of 3747 post-PCI patients in the National Heart, Lung, and Blood Institute Dynamic Registry underwent clinically-driven, non-target lesion revascularization [11]; 59% presented with unstable angina and 9% with non-fatal myocardial infarction.

## Myocardial perfusion imaging, symptom status, and prognosis

The specificity of myocardial perfusion imaging (MPI) early after PCI is poor [12]. Reversible defects were observed in 17% of patients undergoing exercise stress single-photon emission computed tomography (SPECT) within 1 week of coronary stent implantation [13] and in 36% of those undergoing adenosine SPECT 4 days after stenting [14]. In the latter study, defects persisted in 50% of those who underwent reimaging at 1.5 months [14]. The ability of MPI to detect stenoses depends on regional differences in tracer uptake resulting from impaired relative coronary flow reserve (the ratio of maximal blood flow in stenotic arteries to that in patent arteries). However, microvascular function also affects perfusion and, thus, MPI. Hypoperfusion occurs in the absence of obstruction if absolute myocardial flow reserve (the ratio of blood flow during maximal vasodilatation to resting blood flow), is impaired. Early after PCI, absolute myocardial flow reserve is decreased secondary to endothelial dysfunction and medial injury at the treated site or abnormal microvascular and resistive vessel function distal to the site, or both [15,16]. Consequently, regional perfusion can be impaired, despite epicardial arterial patency.

Two months or more after PCI, both the sensitivity and specificity of SPECT for detecting myocardial ischemia are approximately 80% and are essentially equivalent in all three vascular territories [12]. After PCI, SPECT is a more powerful prognostic indicator than angina. Up to 58% of patients with restenosis after bare-metal stenting remain asymptomatic [17]. In the Emory Angioplasty versus Surgery Trial (EAST) [18], 46% of 165 patients who underwent PCI for multivessel disease had ischemia on SPECT 1 year after revascularization; at least 43% were asymptomatic. After 3 years, myocardial infarction, death or both occurred in 29% of those with ischemia, but in only 14% of patients without ischemia. Cottin et al [19] observed reversible SPECT perfusion defects in 31% of 152 patients 5 months after stent implantation;

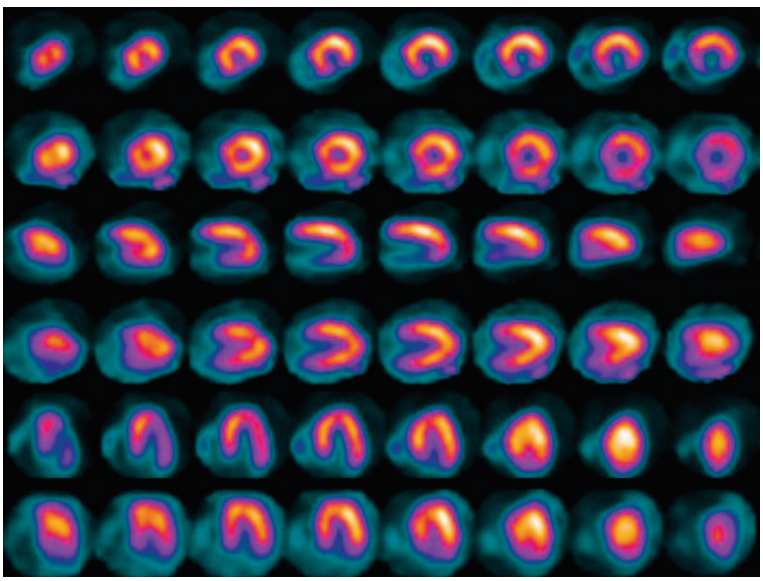

*Figure 1. Exercise single photon emission computed tomography (SPECT) images from a patient who underwent stenting of the left anterior descending coronary artery 8 months previously. At the time of stent implantation, non-obstructive disease was evident in the mid left circumflex artery. The patient was asymptomatic until 2 weeks before stress testing. There is a medium-sized, severe, reversible perfusion defect involving the inferolateral wall of the left ventricle. Perfusion appears normal in the left anterior descending artery territory. The patient underwent repeat coronary angiography. The lesion in the mid left circumflex artery was found to have progressed to 90% diameter stenosis; the left anterior descending artery stent was patent.*

ischemia was silent in 70%. Death or myocardial infarction occurred in 28% of patients with ischemia, including death in 15%, but in only 3% of ischemia-free patients. Angina did not predict adverse events. Zhang et al [20] followed 318 patients who had undergone PCI, for a period of 38 months. The annual rate of death and non-fatal myocardial infarction was 3.9% in those with reversible SPECT defects, despite a 10.7% annual late revascularization rate, compared with 0.2% in patients with normal MPI. Among patients with ischemia, hard events occurred equally often in symptomatic and asymptomatic individuals; hard events were best predicted by the summed stress score [20]. Exercise SPECT images from a patient who underwent stenting of the left anterior descending coronary artery 8 months previously are shown in *Figure 1*.

## Other imaging modalities after PCI

Stress echocardiography can be used to detect restenosis. A review of 13 studies involving 989 patients found the mean sensitivity to be 74% and specificity 87% [21]. In-stent restenosis is detected with excellent accuracy by multidetector computed tomography angiography (CTA). In one study, 16 of 18 in-stent lesions $\geq$ 60% by quantitative coronary angiography and 75 of 93 patent stents were correctly identified with a 40-slice scanner [22]. Only five of 111 stents were not assessable. Sensitivity, specificity, and negative predictive value were 89%, 81%, and 97%, respectively. Examples of fully patent, partially restenotic, and completely obstructed stents are shown in *Figure 2*.

Although the role of CTA in the management of CHD has not yet been defined, the ability to image both the arterial lumen and wall confers potential advantages on CTA compared with other imaging modalities. Factitious perfusion defects occur when MPI is performed early after PCI [12]. Myocardial stunning after PCI [23] may similarly yield false-positive echocardiographic findings. Properly performed, it is unlikely CTA will yield factitious results, because coronary arteries and stents are imaged directly. Secondly, among patients with normal

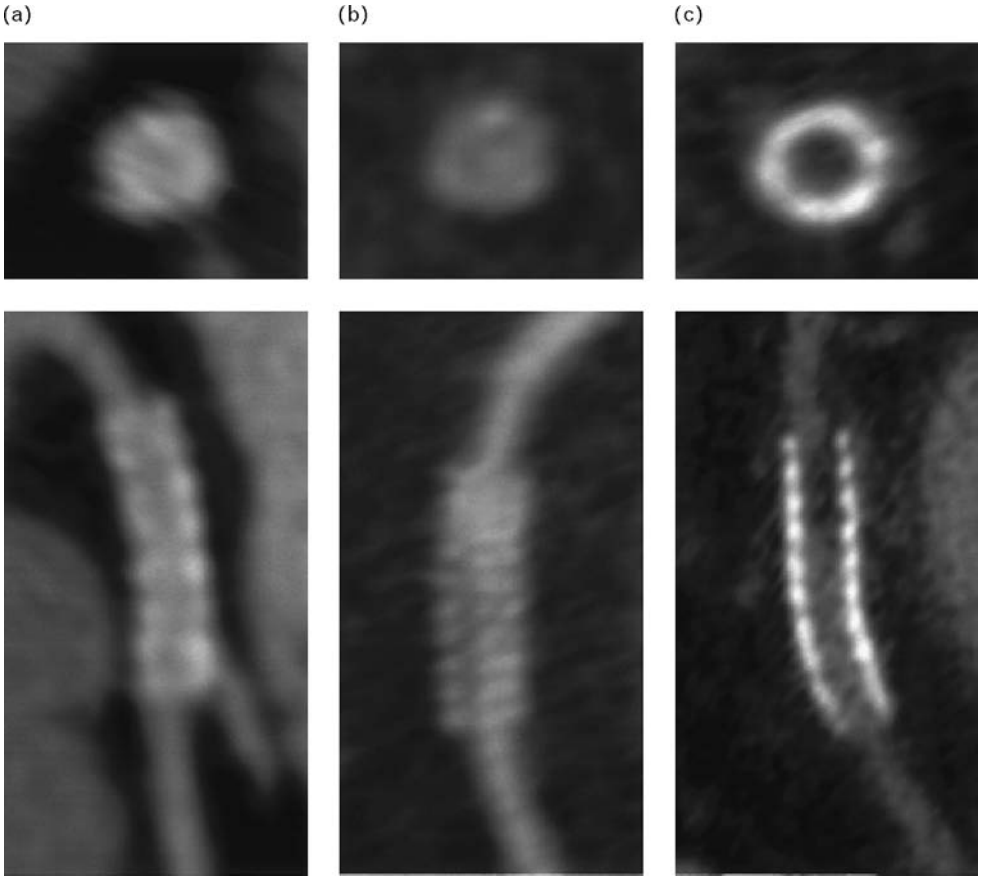


*Figure 2. Two-dimensional reconstruction of three stents in curved multiplanar reformatted format in long-axis (below) and short-axis perpendicular to the center line (above). (a) Stent fully patent, with homogeneous contrast enhancement throughout the long- and short-axis images (quantitative coronary angiography [QCA] 0%). (b) Partially restenosed stent showing lack of contrast enhancement in lower left portion of long-axis image and in crescent-shaped portion of short-axis image taken from lower part of stent (QCA 39%). (c) An obstructed stent, showing lack of contrast enhancement throughout long- and short-axis images (QCA 100%). (From Gaspar et al [22], with permission.)*

SPECT, those with known CHD have greater annual rates of hard events than those without disease (1.4% compared with 0.4%; $P < 0.001$) [24]. This is consistent with the fact that hard events frequently result from rupture of non-obstructive coronary plaques not detectable with SPECT. Patients with CHD have plaque; those without disease do not. As both obstructive and non-obstructive plaque are detected with CTA, more accurate assessment of cardiac risk may be possible. Finally, coronary artery calcium can be quantified in conjunction with CTA or as a stand-alone technique. In patients who have not undergone PCI, changes in coronary artery calcium over time predict myocardial infarction [25]. Although coronary artery calcium scoring is generally not recommended for patients with stents, because stented vessel segments cannot be evaluated, serial measurements of coronary artery calcium in non-stented segments may facilitate assessment of risk and response to medical therapy and lifestyle modifications.

## Conclusion

Despite major technologic advances, not even drug-eluting stents confer long-term immunity from cardiac events, as disease progression causes significant morbidity after PCI. Performed 2 months or more after PCI, SPECT accurately detects ischemia and stratifies risk, whereas angina is an unreliable indicator. Coronary CTA accurately and directly assesses arterial patency and has tremendous potential for assessing prognosis after PCI. ■

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