EuroIntervention

Evaluation of stents and grafts

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KEYWORDS

Cardiac imaging, stent, graft

Abstract

In the management of patients with obstructive coronary artery disease (CAD), percutaneous coronary intervention (PCI) with stent implantation is routinely performed. In patients with left main or three-vessel disease, however, coronary artery bypass grafting (CABG) may be the preferred therapeutic strategy. Importantly, both after PCI or CABG a small but non-negligible risk of restenosis remains. Early detection and treatment of in-stent restenosis or graft disease is of great clinical importance. Accordingly, accurate non-invasive methods to identify patients who would benefit from subsequent invasive coronary angiography (ICA) would be highly beneficial. Besides ICA, several non-invasive cardiac imaging techniques may be used to assess patients after revascularisation. In the present article, an overview of various anatomic and functional imaging techniques available to assess patients after revascularisation is provided.

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Introduction

In developed nations, coronary artery disease (CAD) is the main cause of morbidity and mortality. In the treatment of patients with acute myocardial infarction, primary percutaneous coronary intervention (PCI) with stent implantation is routinely performed[1]. Moreover, in patients with symptoms of stable CAD and evidence of ischaemia, elective PCI with stent implantation is increasingly performed. Indeed, it has been shown that PCI in combination with medical therapy has resulted in a significantly larger reduction in myocardial ischaemia in comparison with medical treatment alone[2]. In patients with left main or three-vessel disease, however, coronary artery bypass grafting (CABG) may be the preferred revascularisation therapy. Importantly, in patients after PCI or CABG a slight but non-negligible risk of restenosis remains. In case of PCI, stent implantation may be followed by early thrombosis or later occurring in-stent neointimal hyperplasia[3,4]. Considering CABG, graft disease may occur[5], with venous grafts being more frequently affected by graft occlusion than arterial grafts[6]. Early detection and treatment of in-stent restenosis or graft failure is of great clinical importance. Presently, invasive coronary angiography (ICA) is considered to be the standard of reference for the evaluation of CAD. Due to its invasive nature this procedure is associated with a small risk of complications. Accordingly, accurate noninvasive methods to identify patients who would benefit from subsequent ICA would be beneficial. In this review, an overview is provided of several anatomic and functional imaging techniques available to assess patients after revascularisation.

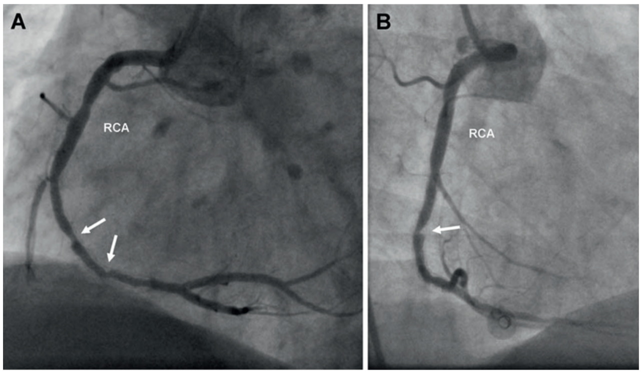

Figure 1. ICA evaluating the presence of in-stent restenosis in a 61 year-old man with previous PCI. Panel A and B show an ICA of the RCA. Two partially overlapping stents are present in the mid to distal RCA (Driver 3.5 x 30 mm, Orbus 3.5 x 18 mm). Severe in-stent restenosis is observed (arrows). ICA: invasive coronary angiography; PCI: percutaneous coronary intervention; RCA: right coronary artery

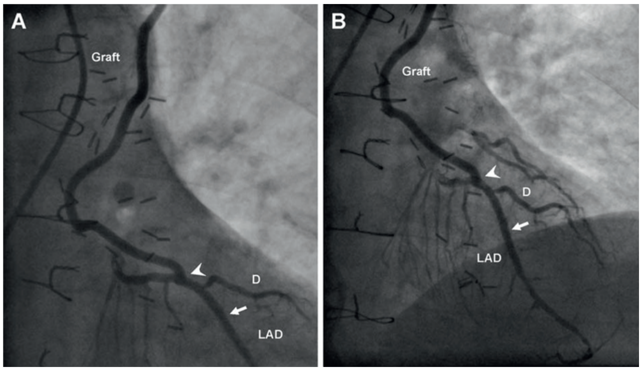

Figure 2. ICA evaluating the presence of graft patency in a 86 year-old man with previous CABG. Panels A and B show the ICA a patent single LIMA graft, with a patent anastomosis on the LAD (arrowheads) and good distal run-off. In addition, a patent stent is present in the LAD, distal from graft anastomosis (arrows). D: diagonal branch; ICA: invasive coronary angiography; LAD: left anterior descending artery; LIMA: left internal mammary artery

Anatomic imaging after revascularisation

Invasive cardiac imaging

ICA has since long been regarded to be the gold standard for the assessment of CAD. With superior resolution, this technique provides a direct and accurate assessment of the coronary arteries, including a detailed anatomical overview enabling the precise evaluation of the degree of stenosis. As a result, ICA is extensively employed to guide further treatment, such as PCI or CABG. Also in the assessment of patients after revascularisation, ICA is the gold standard for the detection of restenosis. Figure 1 illustrates the use of ICA in the assessment of in-stent restenosis. Figure 2 shows an ICA of an arterial graft in a patient with previous CABG.

In many cases, however, ICA is used for diagnostic evaluation only, and is not followed by intervention. Since ICA is inevitably linked to patient discomfort as well as a small risk of complications, these patients could potentially benefit from a noninvasive approach to visualise the coronary arteries.

Noninvasive cardiac imaging

Several noninvasive imaging modalities have been developed allowing the direct visualisation of the coronary arteries. Early studies on the direct noninvasive assessment of recurrent coronary or graft failure after revascularisation used electron-beam computed tomography (EBCT) technology[7]. More recently, however, multidetector computed tomography coronary angiography (CTA) technology has evolved and this technique is increasingly used for the noninvasive diagnosis of CAD. In addition, the feasibility of magnetic resonance imaging (MRI) to noninvasively assess coronary and graft patency has recently been demonstrated[8].

CTA

CTA has been shown to be a valuable imaging modality for the assessment of CAD. Besides the assessment of degree of stenosis, this technique allows to some extent also assessment of plaque type and atherosclerotic changes in the vessel wall. Although 64-row CTA is the currently most widely used system, 265-row and 320-row CTA have recently been introduced. With these CTA systems a volumetric scanning technique is used, enabling faster image acquisition as the entire heart is covered in a single gantry rotation[9]. Owing to a high negative predictive value, CTA is particularly valuable in the exclusion of CAD in patients with a low-to-intermediate pre-test likelihood[10]. Nevertheless, CTA may also be used in carefully selected patients with prior revascularisation[10]. Sun et al performed a meta-analysis of 14 studies using 64-row CTA, including a total of 1,398 stents[11]. Pooled estimates of the sensitivity and specificity for the detection of in-stent restenosis after the inclusion of the 11% uninterpretable stents were 79% and 81%. However, it is important to note that the value of CTA in the assessment of in-stent restenosis remains limited in small stents (<3 mm) and stents with thick struts (≥140 µm)[12]), as high-density artefacts may obscure part of the stent lumen. An example of the effect of stent diameter on stent interpretability on CTA is shown in Figure 3. Furthermore, the positive predictive value remains low, and in-stent restenosis is frequently overestimated on CTA. Importantly however, consistently high negative predictive values have been reported, indicating that in carefully selected patients the technique may be particularly useful to rule out in-stent restenosis1[1]. CTA scans revealing stent patency and in-stent restenosis are shown in Figures 4 and 5, respectively.

Patients with prior CABG may also be assessed using CTA. As compared to the coronaries, grafts have a relatively large diameter and are reasonably free of cardiac motion. As a result, grafts tend to be more easily visualised on CTA as compared to native coronary arteries, although high-density artefacts caused by metal clips implanted during graft surgery may locally disturb graft assessment

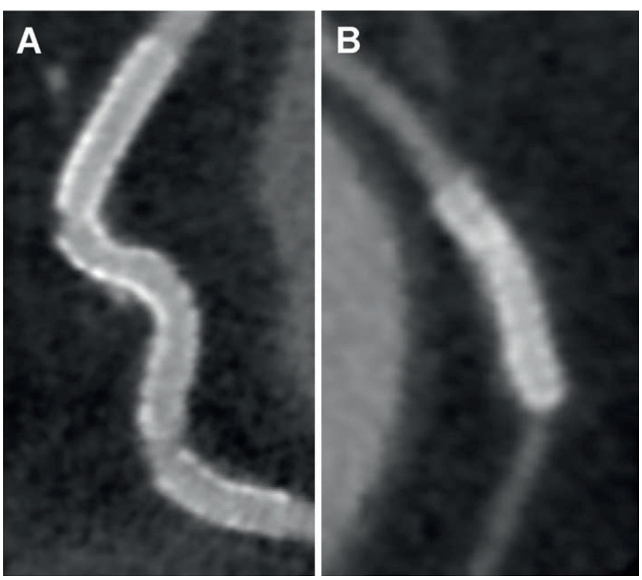

Figure 3. Example of the effect of stent diameter on CTA image quality in a 79-year-old patient with prior PCI with stent implantation. Panel A shows a curved multiplanar reconstruction of four partially overlapping stents (from proximal to distal: S7 3.5 x 18 mm, S7 3.5 x 18 mm, S7 3.5 x 23 mm, S7 3.5 x 12 mm) with a large diameter (≥3.0 mm) in the RCA. All stents are patent without the presence of significant in-stent restenosis. In panel B, a stent (Promus 2.5 x 15 mm) with a small stent diameter (<3.0 mm) is shown in the LCx. The presence of in-stent restenosis cannot be reliably excluded due to poor in-stent visibility in the presence of high-density artefacts which render the stent uninterpretable. CTA: computed tomography coronary angiography; ICA: invasive coronary angiography; LCx: left circumflex coronary artery; PCI: percutaneous coronary intervention; RCA: right coronary artery

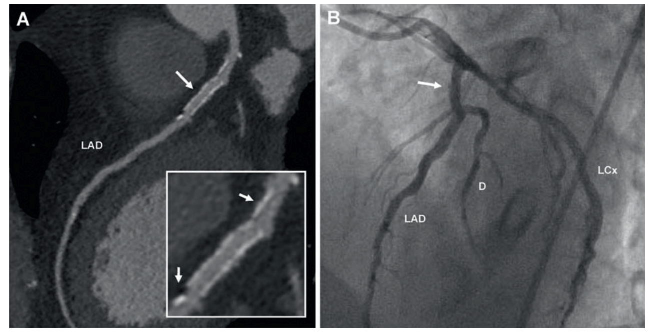

Figure 4. CTA of a 52-year-old man with a history of PCI of the LAD revealing stent patency. Panel A shows a curved multiplanar reconstruction of the LAD showing a patent stent in the proximal LAD (long arrow). In the lower right corner, an enlarged curved multiplanar reconstruction of the patent stent is shown. Proximal and distal to the stent, two lesions are observed without significant luminal narrowing (short arrows). Stent patency was confirmed on ICA (arrow). ICA: invasive coronary angiography; LAD: left anterior descending coronary artery; PCI: percutaneous coronary intervention; LCx: left circumflex coronary artery; RCA: right coronary artery

(Figure 6, panel D). In a meta-analysis by Hamon and colleagues, including 15 studies with a total of 2,023 grafts, the diagnostic performance of 16-row and 64-row CTA was assessed in patients with a history of CABG[13]. On average, graft assessability was 92%, while average sensitivity and specificity in the detection of ≥50% graft stenosis were 96% and 97%. These data demonstrate a good performance of CTA for the noninvasive assessment of graft integrity. However, the native coronary arteries of patients with previous CABG are considerably more difficult to assess using this technique[10] due to extensive calcifications and small vessel calibre in the presence of long standing CAD. An example of a CTA investigation in a patient with prior venous and arterial CABG is shown in Figure 6. Thus, although it is presently not justified to routinely use this technique in the assessment of patients after revascularisation, CTA may be an attractive alternative to ICA for graft visualisation in carefully selected patients.

MRI

With respect to patients after previous revascularisation, MRI has been mostly investigated in patients after prior CABG. Coronary stents can generally not be assessed using this modality as a result of image degradation due to radiofrequency shielding and susceptibility artefacts. Even though this phenomenon may also be observed in the presence of metallic clips which are implanted during CABG surgery, these artefacts are usually less pronounced. Although early studies investigating MRI in the evaluation of graft patency after CABG reported good diagnostic accuracy[14], with the introduction of 3-dimensional navigator and contrast enhanced techniques, further improvement in image quality and overall procedural success was achieved. In the assessment of 34 patients with a total of 79 bypass grafts using gadolinium enhanced 3-dimensional MR angiography for the assessment of graft patency, Bunce et al showed a sensitivity and specificity of 85% and 73%[15]. Moreover, Langerak and co-workers determined the diagnostic

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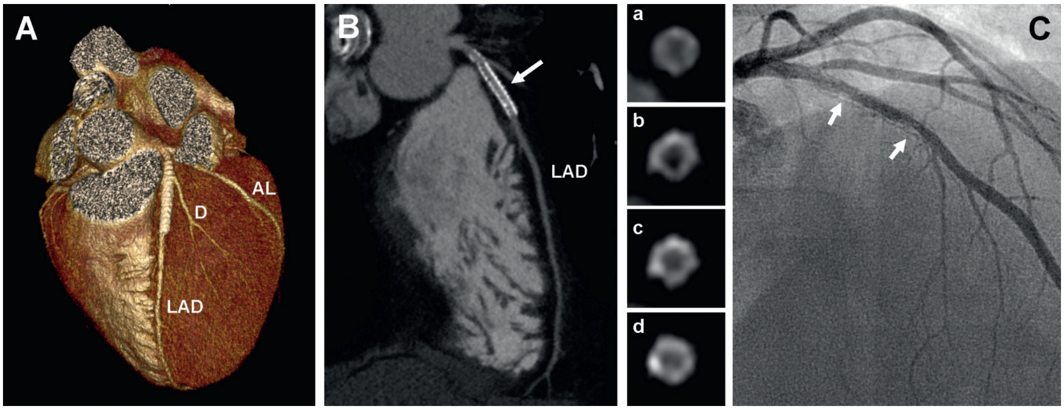

Figure 5. CTA of a 39-year-old man with prior PCI of the LAD revealing in-stent restenosis. Panel A shows a three-dimensional volume rendered reconstruction of the heart, giving an overview of the LAD, D1 and a large AL. A curved multiplanar reconstruction in Panel B shows two partially overlapping stents (Cypher 3.5 x 33 mm, Zeta 3.5 x 23 mm) in the proximal LAD (arrow) with severe in-stent hyperplasia. On the right hand side, four transverse sections of the stent indicate low-attenuating neointimal hyperplasia corresponding to non-calcified (transverse section b) and mixed-plaque (transverse section d). Transverse sections of the proximal (a) and mid stents sections (c) show a normal contrast-enhanced lumen. On ICA, the patient was diagnosed with in-stent neointimal proliferation (arrows) with severe lumen reduction of the distal stent. AL: anterolateral branch; D1: first diagonal branch; ICA: invasive coronary angiography; LAD: left anterior descending coronary artery; PCI: percutaneous coronary intervention

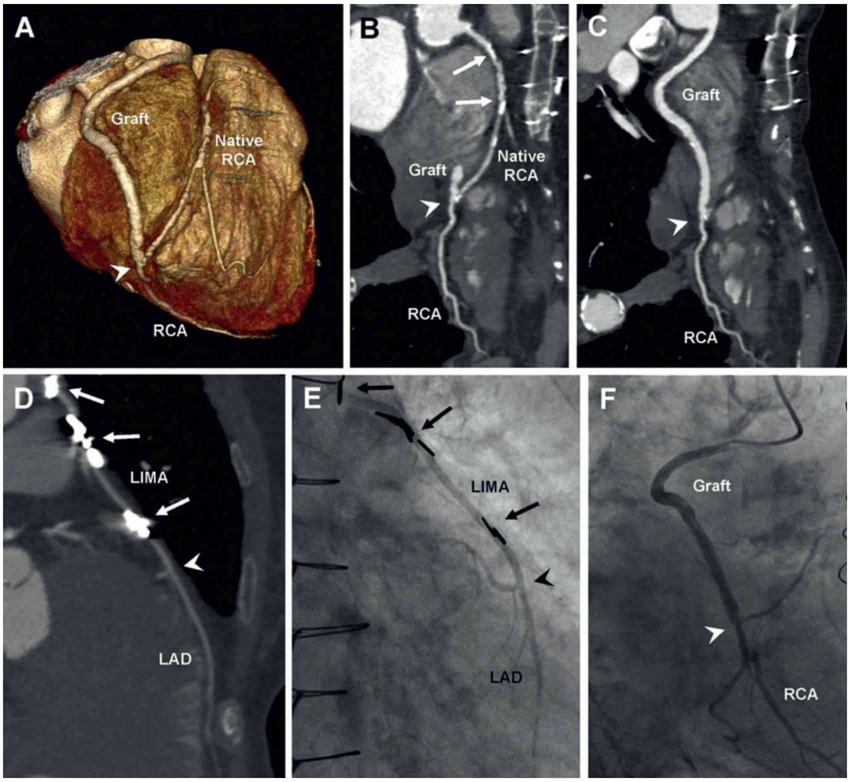

Figure 6. CTA of a patient in a 77-year-old woman with a history of venous and arterial CABG. A three-dimensional volume rendered reconstruction of the heart is shown in Panel A. A single venous graft is identified with an anastomosis on the distal RCA (arrowhead). Panel B shows a curved multiplanar reconstruction of a heavily diseased native RCA, with severely calcified and non-calcified lesions proximal to the graft anastomosis (arrows). A curved multiplanar reconstruction of a patent venous graft is depicted in Panel C. Although diffuse atherosclerosis with calcified plaque is visible in the venous graft, no significant luminal narrowing is observed. Furthermore, a patent anastomosis with the RCA is present (arrowhead) with good distal run-off. In Panel D, a LIMA graft is shown with a patent anastomosis on the mid-LAD. The graft appears to be patent with good distal run-off, although high-density artefacts caused by metal clips locally hamper graft visibility. Patency of the venous and LIMA grafts and anastomoses (arrowheads), as well as good distal run-off in the grafted vessels was confirmed on ICA (Panels E and F). CTA: computed tomography coronary angiography; ICA: invasive coronary angiography; LAD: left anterior descending coronary artery; LIMA: left internal mammary artery; PCI: percutaneous coronary intervention; RCA: right coronary artery

accuracy of high-resolution 3-dimensional MRI in the identification of ≥50% vein graft stenosis in 38 patients with a total of 56 grafts[16]. While sensitivity and specificity were 83% and 100% for the assessment of graft occlusion, sensitivity and specificity were lower for the detection of significant graft stenosis (73% and 80%, respectively).

MRI is a versatile imaging modality that has some important benefits over other imaging techniques, such as its noninvasive nature and the lack of ionising radiation exposure. Furthermore, MRI enables anatomic and functional analysis in a single acquisition. Nevertheless, procedural difficulties as well as its time consuming nature limit the routine use of MRI in clinical practice. Additionally, the magnetic field associated with MRI imaging excludes the assessment of patients with pacemakers, defibrillators and intracranial metal clips.

Functional imaging after revascularisation

While anatomical imaging techniques are used to determine the severity of CAD and degree of stenosis, the haemodynamic consequences of an obstructive lesion remain uncertain using this approach. Nevertheless, therapeutic decision making, such as assessing the need for repeat revascularisation, is largely based on the extent of complaints as well as the severity of ischaemia on functional imaging. Several noninvasive functional imaging modalities are available, such as single photon emission computed tomography (SPECT), stress echocardiography and MRI. Furthermore, the use of computed tomography (CT) perfusion imaging is under investigation. An overview of the (potential) use of these modalities to assess myocardial function after revascularisation will be given in the following paragraphs.

Myocardial perfusion imaging with SPECT

Myocardial perfusion imaging using SPECT is one of the most commonly used modalities in the identification of myocardial ischaemia. During SPECT image acquisition, ECG gating is used, allowing the concurrent evaluation of global and regional LV function[17]. In the assessment of patients after revascularisation, Giedd and colleagues performed a meta-analysis including eight studies with 940 patients, who underwent both stress SPECT and ICA within two to 48 years after PCI[18]. Sensitivity and specificity of SPECT in the assessment of myocardial ischaemia were both 79%, indicating that this is a feasible technique in the assessment of patients with prior PCI. However, it is important to note that when SPECT is performed early, within two months of PCI, the sensitivity of this technique is decreased.

The assessment of graft disease using SPECT has also been investigated. In a study by Lakkis and colleagues in 50 symptomatic patients with a total of 119 grafts, SPECT was performed late (51±47 months) after CABG. The sensitivity of this technique in the assessment of any graft stenosis in patients with typical recurrent angina was 84%, whereas in patients with atypical symptoms the sensitivity was 70%[19]. Furthermore, for both groups of patients exercise SPECT was superior to exercise ECG alone[19]. In patients who are unable to exercise, Dobutamine-atropine stress SPECT may also be performed to assess myocardial perfusion with good diagnostic accuracy (sensitivity and specificity of 81% and 79%)[20]. These data suggest that SPECT is a valuable imaging modality for the assessment of graft disease late after bypass surgery. Overall it may be stated that SPECT is a robust imaging modality in the evaluation of myocardial perfusion in patients with a history of revascularisation.

Myocardial perfusion imaging using stress echocardiography

Stress echocardiography is a readily available clinical tool for the noninvasive assessment of myocardial perfusion. During exercise or pharmacological stress echocardiography, the occurrence of wall motion abnormalities indicates the presence of flow limiting CAD. In addition, stress echocardiography using contrast agents may also be performed to assess myocardial perfusion[21]. An example of myocardial contrast echocardiography during rest and dobutamine stress is provided in Figure 7.

Advantages of stress echocardiography are that it is easily performed, noninvasive, free of radiation as well as being associated with low costs. Also, the value of stress echocardiography in the detection of restenosis after revascularisation has been well tested. Scherhag et al recently performed a meta-analysis including 13 studies, comparing stress echocardiography and ICA in 989 patients 3-6 months after primary intervention[22]. The investigators reported an average sensitivity and specificity of 74% and 87%, showing good value of this technique in the detection of significant restenosis after PCI. Furthermore, Kafka and colleagues evaluated the value of exercise echocardiography in predicting the presence of stenosis on ICA[23]. In a study including 128 patients with previous CABG who underwent exercise echocardiography, positive and negative predictive values of 85% and 81% were shown. Importantly, the accuracy of stress echocardiography was increased in patients who had significant stenosis in multiple regions as compared to one region. Furthermore, Hoffmann et al determined the values of transthoracic and transoesophageal dobutamine stress echocardiography to detect significant graft or coronary stenosis in 60 patients with prior CABG[24]. Although acceptable diagnostic accuracy was shown for transthoracic dobutamine stress echocardiography (with a sensitivity of 78%), higher accuracy could be obtained by transoesophageal echocardiography (with a sensitivity of 93%). Together, these data suggest that, in the follow-up of patients after revascularisation, stress echocardiography is a useful imaging modality for the noninvasive diagnosis for obstructive CAD.

Myocardial perfusion imaging with MRI

In addition to the assessment of graft stenosis and occlusion, MRI may also be used for the assessment to graft function by means of MR flow velocity measurements, or flow mapping. Blood flow through the graft is measured in rest and during pharmacologically induced stress, after which the coronary flow reserve is derived. Indeed, in an investigation by Langerak and co-workers, flow mapping during rest and stress was performed in 69 patients who were referred for ICA[25]. Although a sensitivity and specificity for MRI in the detection of ≥50% single vein graft stenosis of 94% and

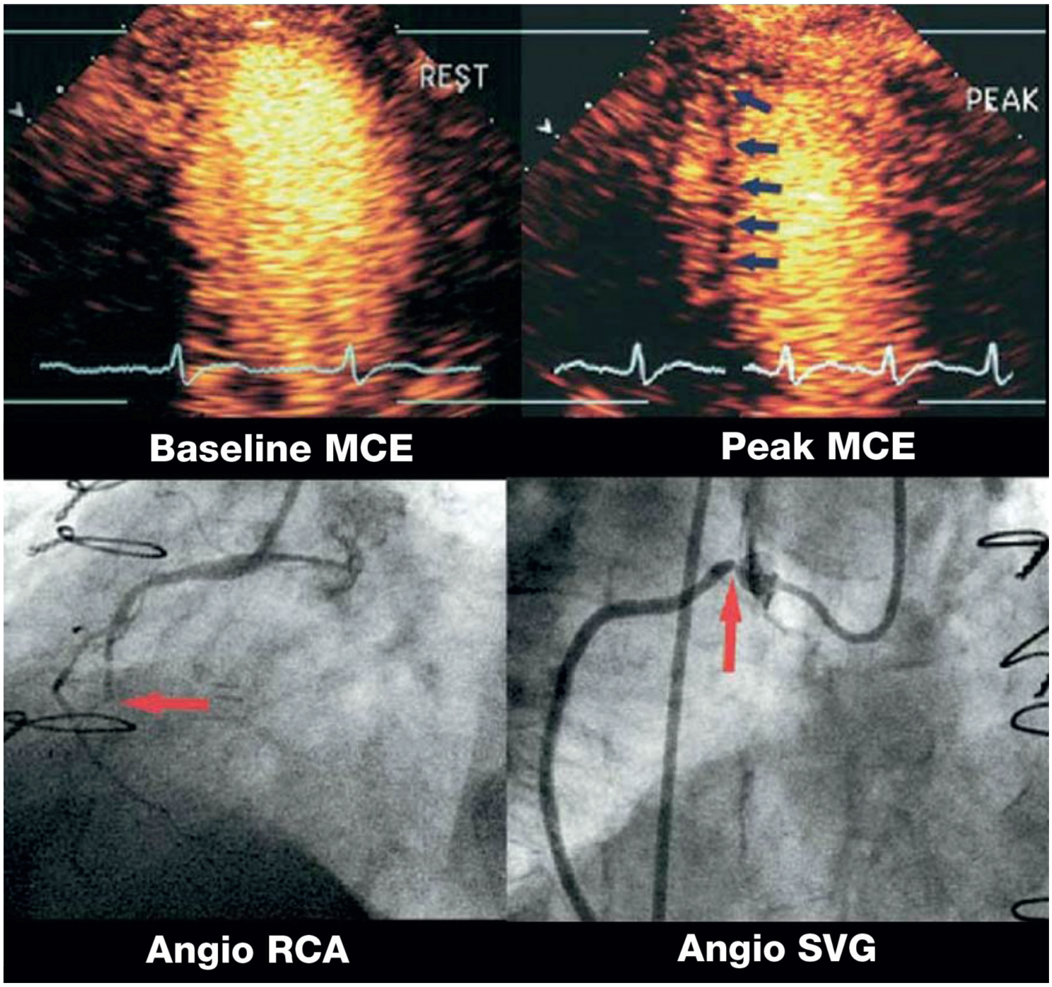

Figure 7. Example of myocardial contrast echocardiography during rest and dobutamine stress. Myocardial contrast echocardiographic images from apical 2-chamber view at rest (top right) and peak dobutamine stress (top left) of a 73-year-old woman who presented with exertional dyspnoea three years after coronary artery bypass grafting. A reversible perfusion abnormality can be observed in the inferior wall (arrows). Subsequent angiography (angio) demonstrated an occluded right coronary artery (RCA) (bottom right) and severe proximal stenosis of related saphenous vein graft (SVG) (bottom left). Reprinted with permission from reference 21.

63% were reported, 20% of the examinations were uninterpretable. Figure 8 shows an example of an MR imaging examination of grafts.

Importantly, MRI also enables the identification of myocardial ischaemia due to obstructive CAD by allowing the assessment of myocardial perfusion as well as motion abnormalities. During MRI pharmacological stress is usually applied. Subsequently, image acquisition is performed during the first-pass of a bolus of gadolinium, revealing perfusion defects as areas of lower signal density. Relatively few studies have been conduced identifying the use of MRI in the assessment of patients after revascularisation. Recently, Klein et al investigated the diagnostic accuracy of combined adenosine stress perfusion using MRI and late gadolinium enhancement in patients with prior CABG[26]. In a total 78 patients, MRI perfusion imaging was performed resulting in a sensitivity and specificity of 77 and 90% on a patient level, in the detection of significant stenosis in grafts and coronaries. If only areas supplied by grafts were taken into account, the sensitivity and specificity would be similar (78 and 94%). Furthermore, Doesch and co-workers showed that the diagnostic value of adenosine stress MRI in patients with prior revascularisation was comparable to that in patients without prior revascularisation. Regarding patients with prior revascularisation, in a total of 88 patients with prior PCI, sensitivity and specificity were 92% and 75%, while in a total of 21 patients with previous CABG, sensitivity and specificity were 88% and 67%[27]. Similarly, good diagnostic accuracy was shown using dobutamine-atropine stress MRI in patients with a history of revascularisation and wall motion abnormalities at rest. The sensitivity and specificity of obstructive disease were 89% and 84%, providing further support for the use of MRI in the identification of in-stent restenosis and graft disease[28].

CT myocardial perfusion imaging

CTA is sometimes difficult to perform in patients after revascularisation, as this technique frequently overestimates the degree of stenosis. Consequently, patients with an obstructive lesion

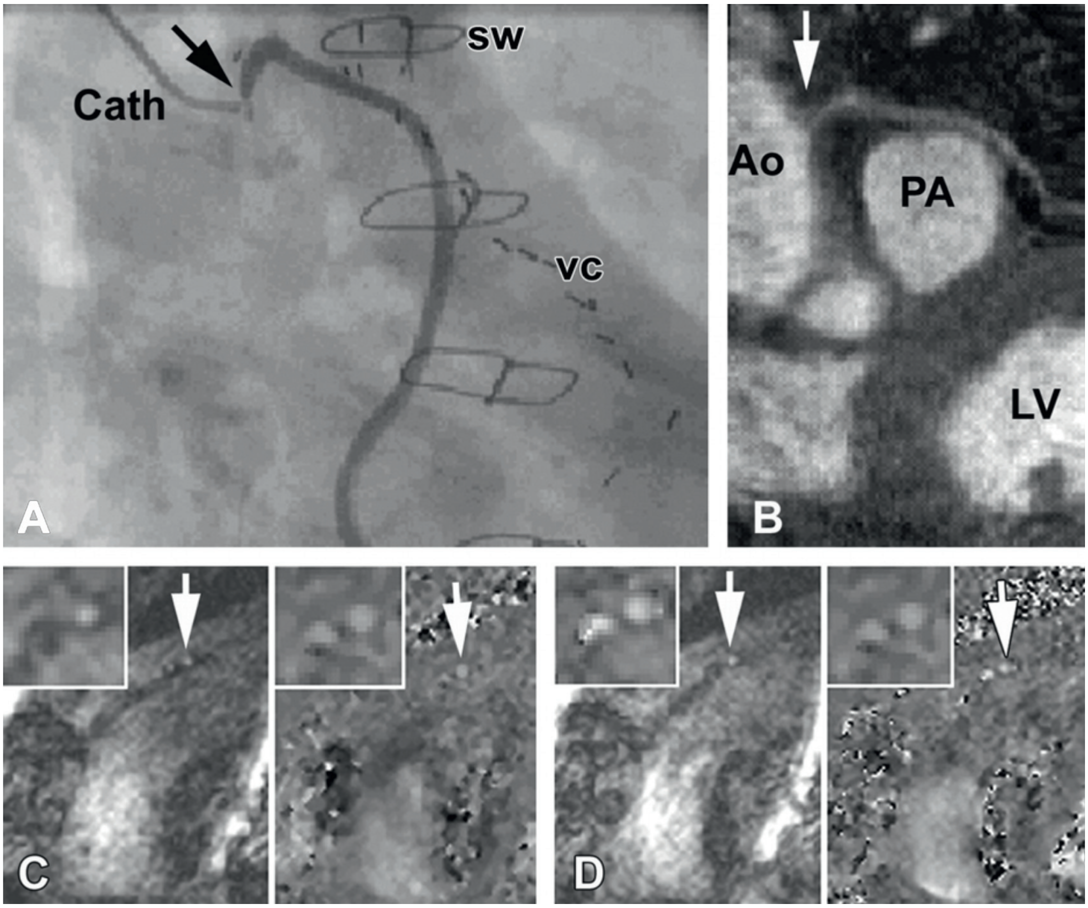

Figure 8. Results of an MR imaging examination of grafts. Panel A shows an ICA of a sequential vein graft to the LCx in a 61-year-old man with a 74% origin stenosis (arrow) in the graft. In panel B, a multiplanar reconstruction of navigator-gated three-dimensional MR angiographic data confirms the origin stenosis (arrow). In panels C and D oblique sagittal flow MR images are shown obtained at baseline (Panel C) and during stress (Panel D). Images on the left are modulus images with anatomic information; images on the right are phase images with velocity information. A detail of the graft cross section is depicted in the upper left corner of each image. Arrows indicate cross section of the graft depicted in Panels A and B. In addition and more anterior to a cross section of the stenotic vein graft, the cross section of a LIMA graft to the LAD can be seen. Reprinted with permission from reference 30. Ao: ascending aorta; Cath: catheter; LAD: left anterior descending coronary artery; LCx: left circumflex coronary artery; LIMA: left internal mammary artery; LV: left ventricle; PA: pulmonary artery; sw: sternal wire; vc: vascular clip

are frequently referred for myocardial perfusion imaging to determine the functional consequences of the stenosis. The use of combined CT myocardial perfusion imaging and CTA in a single examination is presently under investigation. Although the assessment of CT myocardial perfusion imaging has not yet been performed in patients after revascularisation, a few preliminary studies are available showing the use of this technique in the general population. In a recent study by George et al, the value of combined adenosine stress CT and CTA was tested to predict perfusion abnormalities caused by significant obstruction in 40 patients with an abnormal SPECT investigation[29]. In addition, ICA was available in 27 patients. On a patient level, the investigators reported a sensitivity and specificity for the identification of significant stenosis causing perfusion abnormalities of 86% and 92%. Furthermore, the positive and negative predictive values were 92% and 85%, respectively. These data suggest that the simultaneous assessment of CTA and CT perfusion imaging allows for the detection of CAD causing perfusion abnormalities in the general population with good diagnostic accuracy. Moreover, with the introduction of 256-row and 320-row volumetric scanning techniques, CTA and CT myocardial perfusion imaging can be performed in only one heart beat. Although limited data is currently available, large multicentre studies investigating the use of combined anatomic and functional imaging using CTA are in progress. To validate the use of these combined investigations in patients after revascularisation, future studies are warranted.

Conclusion

Despite the availability of successful revascularisation strategies, a small risk of in-stent restenosis or graft disease in patients after PCI or CABG remains. While ICA is still the gold standard in the evaluation of CAD, several noninvasive modalities in the assessment of CAD are increasingly used in patients with a history of revascularisation. As each imaging modality has different advantages and limitations, the choice of technique is dependent on patient characteristics as well as local availability and expertise.

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