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PERSPECTIVES

Emerging imaging techniques after cardiac transplantation

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Improvements in survival after cardiac transplantation have in part been driven by improved graft surveillance. Graft surveillance relies mainly on 3 techniques: coronary angiography, endomyocardial biopsy and echocardiography. Developments in invasive and non-invasive imaging technology have revolutionized assessment of the heart in both health and disease, offering new insights into tissue composition and myocardial metabolism. Herein we aim to review the strengths and weaknesses of these techniques, and summarize the evidence in the following 5 fields of cardiac imaging after transplantation: cardiovascular magnetic resonance; computed tomography; positron emission tomography; single-photon emission computed tomography; and optical coherence tomography and molecular imaging techniques.
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Echocardiography, coronary angiography and endomyocardial biopsy are the mainstays of post-transplant graft surveillance. They are integral to the long-term survival of cardiac transplant recipients and provide assessment of graft function and detect manifestations of both acute rejection and cardiac allograft vasculopathy (CAV). Current International Society for Heart and Lung Transplantation (ISHLT) guidelines recommend that graft function be monitored with echocardiography, both as surveillance and to assess response to therapy in the treatment of acute cellular rejection (ACR) (Class I B and Class I C, respectively). For diagnosis and detection of CAV, coronary angiography may be performed early at 4 to 6 weeks, with or without intravascular ultrasound (IVUS) to exclude donor CAV (Class IIa C), and either annually or biannually to detect and stage CAV (Class I B). For cases in which invasive assessment is not possible, both exercise and dobutamine echocardiography, or myocardial perfusion imaging, are recommended for the detection of CAV (Class IIa B).

Evolving invasive and non-invasive imaging techniques now applied after cardiac transplantation offer new insights into graft metabolism, structure and tissue composition. Although currently predominantly research techniques, these modalities may offer advantages over current methods and potentially allow for either less invasive monitoring or a more tailored approach to post-transplant surveillance.

In this review we summarize the literature regarding the use of cardiac magnetic resonance (CMR) imaging, positron emission tomography (PET), computed tomography (CT), single-photon emission tomography (SPECT), optical coherence tomography (OCT) and molecular imaging after cardiac transplantation.

Technique overview

CMR imaging

Cine CMR produces high-resolution images that allow accurate and reproducible measurement of cardiac chamber size and systolic function. Diastolic function, regional myocardial mechanics and strain may be assessed with a range of dedicated acquisitions and post-processing techniques.

The use of vasodilator (e.g., adenosine) or inotropic (e.g., dobutamine) stress enables ischemia detection and

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quantification. Dynamic contrast-enhanced myocardial perfusion CMR, typically performed during vasodilator-induced hyperemia, allows delineation of myocardium with reduced perfusion reserve with an in-plane spatial resolution of typically <3 mm. Functional assessment during inotropic stress allows ischemia detection similar to that of stress echocardiography.

A major strength of CMR is the ability to characterize specific tissue properties. The use of gadolinium-containing contrast agents and subsequent late gadolinium enhancement (LGE) imaging may demonstrate cavity thrombus, microvascular obstruction, myocardial scar or focal fibrosis. Patterns of LGE enhancement are diagnostic in a range of pathologies, including endocardially based enhancement in infarction and epicardially based enhancement in myocarditis. Quantification of T1 and T2 relaxation times provides surrogates for myocardial fibrosis and tissue edema.

CT

Cardiac CT provides high-resolution images of cardiac anatomy that may be reconstructed in any axis. With the addition of cardiac gating and intravenous iodinated contrast agent it is possible to examine the health of coronary arteries. Both CT coronary calcium score and CT angiography are validated for screening and diagnosis of coronary artery disease in the non-transplanted heart. CT calcium scoring has a typical radiation dose of around 1.0 mSv, whereas gated angiography has historically been associated with a radiation dose in the range of 10 to 15 mSv, but with modern CT systems can now be performed with 1 to 2 mSv exposure.[1]

SPECT

SPECT assesses myocardial perfusion and, with the addition of electrocardiographic (ECG) gating, systolic function, and is both well established and widely available. SPECT has a spatial resolution of 5 to 10 mm^3 with perfusion assessed either visually or semi-quantitatively; diagnostic accuracy may be reduced in balanced or multivessel ischemia.

In a range of cardiac and systemic disease processes there is alteration in the substrate of myocardial metabolism. The disturbance in the normal balance of fatty acid and carbohydrate metabolism may reflect, or precipitate, abnormalities of cardiac health. Previously the preserve of PET imaging, improved SPECT technology has made imaging of alternate tracers possible, including those of glucose and fatty acid metabolism.

PET

PET perfusion techniques allow absolute quantification of myocardial blood flow with a spatial resolution of 4 to 7 mm^3. Both nitrogen-13 ammonia (^{13}N) and rubidium-82 (^{82}Rb) are commonly used, although oxygen-15 water (^{15}O-water) is now established as the reference tracer. Myocardial perfusion may be quantified as an absolute (myocardial blood flow, MBF) or as a function of response to vasodilator challenge (myocardial perfusion reserve, MPR). PET assessment of absolute perfusion remains the most accurate non-invasive modality.

PET also allows non-invasive characterization of myocardial metabolism. ^{18}F-2-deoxy-2-fluro-D-glucose (^{18}F-FDG) provides accurate quantification of cellular glucose metabolism, and is standard in clinical PET. The incorporation of radionucleotides into a range of metabolically active compounds allows quantification of specific physiologic processes, including fatty acid and lactate metabolism. However, the need for an on-site cyclotron to generate isotopes significantly limits availability and use. Integration of multiplanar imaging techniques with PET (e.g., CMR or CT) allows "hybrid" imaging with integration of PET findings and anatomic studies (Figure 1).

OCT

OCT is an invasive procedure conducted during coronary angiography. The technique is similar to intravascular ultrasound (IVUS) but relies on the signal derived from the backscatter of light from a near-infrared frequency beam. The reflection time to the probe of light is measured, and the characteristics of structures inferred. The short wavelength of light results in images with a better resolution than IVUS (10 to 20 nm vs 100 to 150 nm). The different properties of tissue, and subsequent effect on backscatter, mean that it is possible to develop "virtual histology" of the vessel wall. However, the superior resolution of OCT comes at the expense of decreased tissue penetrance (2 mm vs 8 mm with IVUS). An additional limitation is the need to exclude red blood cells from the coronary lumen during acquisition, which mandates balloon occlusion of the coronary artery and increases the complexity of the procedure as compared with IVUS and standard angiography.

Molecular imaging

Rather than referring to specific tools or techniques, molecular imaging allows sub-cellular, cellular and tissue processes to be studied in vivo, often with existing imaging modalities. To gain new insights into the biologic process studied, target processes and molecules are identified and specific agents developed to facilitate their study. Agents may range from non-specific contrast to labeled proteins

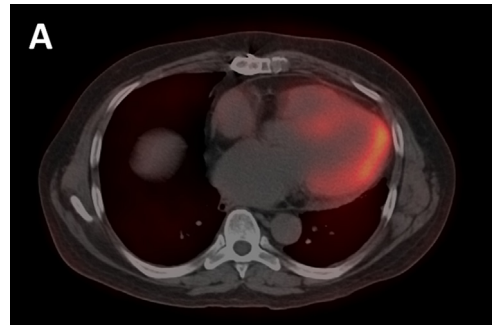

Figure 1 Unusual use of PET/CT fusion imaging after cardiac transplantation. There is increased uptake on FDG imaging in the LV, particularly of the lateral wall and apex, in a patient with recurrence of sarcoidosis in the graft.