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section 16 Cardiovascular disorders 3326 or pulmonary embolism, and to diagnose most valvular abnormal- ities. This is proving extremely useful in the management of critic- ally ill patients. Transducers compatible with smartphones further increase the availability of immediate ultrasound assessment; a rechargeable and fully wireless platform linked to a smartphone app by Bluetooth or Wi-Fi has recently been released. It is important to recognize that these devices cannot perform a full echocardiogram and a more detailed study is needed if the screening scan is abnormal or inconclusive. In critically ill patients with sepsis or severe metabolic derangement, left ventricular func- tion is often abnormal; however, this does not always imply that left ventricular dysfunction is the cause of the presentation. Repeat examination following treatment of the underlying illness often re- veals that this finding is transient and is not always an indication of primary cardiac

disease. The advent of portable ultrasound has prompted the development of several types of emergency ultrasound including: • FAST scan—focused assessment with sonography for trauma • FEEL scan—focused echocardiography in emergency life support • FICE scan—focused intensive care echocardiography • FATE scan—focused transthoracic echocardiography Each of these require specific training, mentoring, and accredit- ation to become proficient. Full training in transthoracic echocar- diography typically requires 2 years and over 500 scans performed and reported. Limitations of echocardiography Despite the rapid and substantial advances in ultrasound tech- nology and the widespread use of echocardiography, it is important to recognize and understand the limitations of the technique. These include reliance on acoustic windows (clear images are impossible in some patients), evaluation at rest (most echo studies are per- formed with the patient resting, so dynamic lesions such as out- flow tract gradients of mitral regurgitation can be underestimated), subjective assessments (precise quantification of cardiac function and valve disease can be challenging and often a more subjective opinion is required, which depends critically on the operator's ex- perience and training), evaluation of complex structures such as the right ventricle remains a major challenge (3D techniques are showing promise but are not in mainstream use), and the fact that the scope of an 'echo' is broad (to measure every parameter possible would take more than 60 min). Like any other test, echocardi- ography is most powerful when the pretest probability has been considered and a specific question asked; for example, 'Is there im- portant aortic stenosis to explain symptoms and signs?' FURTHER READING Cheitlin MD, et al. (2003). ACC/AHA/ASE guideline update for the clinical application of echocardiography: summary article. Circulation, 108, 1146. Douglas PS, et al. (2011). ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/ SCCM/SCCT/SCMR 2011 appropriate use criteria for echocardiog- raphy. J Am Soc Echo, 24, 229. Feigenbaum H (2004). Feigenbaum's echocardiography. Lea & Febiger, Philadelphia, PA. Flachskampf FA, et al. (2001). Recommendations for performing transesophageal echocardiography. Euro J Echocardiol, 2, 8. King A, et al. (2016). Global longitudinal strain: a useful everyday measurement? Echo Research and Practice, 3, 85–93. Leeson P, Augustine D, Mitchell ARJ, Becher H (2012). Echocardiography, 2nd edition. Oxford University Press, Oxford. Rimington H, Chambers J (2016). Echocardiography: a practical guide for reporting and interpretation, 3rd edition. CRC Press, Florida, US. Zoghbi WA, et al. (2003). Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echo, 16, 777. 16.3.3 Cardiac investigations: Nuclear, MRI, and CT Nikant Sabharwal, Andrew Kelion, Theodoros Karamitos, and Stefan Neubauer ESSENTIALS Myocardial perfusion scintigraphy Myocardial perfusion scintigraphy provides physiological informa- tion about the coronary circulation, in contrast to the anatomical information provided by angiography. Three radionuclide-labelled perfusion tracers are routinely used in single photon emission computed tomography (SPECT) imaging: thallium-201 and the technetium-99m-labelled complexes sestamibi and tetrofosmin. Imaging is performed following tracer injection during stress (exercise or pharmacological) and at rest; comparison allows determination of whether regional perfusion is normal, or if there is inducible hypoperfusion or infarction/scar. Myocardial perfusion imaging is minimally invasive, and—in con- trast to other methods of investigation—can be performed regardless of overall exercise capacity, abnormalities of the resting electrocar- diogram (ECG), pacemakers, obesity, claustrophobia, renal dysfunc- tion, iodine allergy, or acoustic windows. In the investigation of a patient with possible coronary artery dis- ease, a normal SPECT study is very reassuring, predicting a very low chance of cardiac death or nonfatal myocardial infarction over the following few years (<1% per year). High-risk markers on SPECT pro- vide additional prognostic

value to clinical, exercise test, and even angiographic variables, and decisions about revascularization can be usefully informed by SPECT imaging. ECG-gated SPECT allows images to be taken throughout the cardiac cycle, when comparison of end-systolic and end-diastolic images then allows volumetric analysis and calculation of left ven- tricular ejection fraction. Positron emission tomography (PET) Using PET, myocardial perfusion imaging can be performed with nitrogen-13 ammonia or rubidium-82, and metabolic imaging with

16.3.3 Cardiac investigations 3327 fluorine-18 fluorodeoxyglucose (FDG). Cardiac PET is expensive, but image quality is superior to SPECT and absolute flow quantification is possible. PET is gaining a significant foothold in the developed world, largely driven by the roll-out of scanners for oncological imaging and the availability of generator-supplied rubidium-82 as a perfu- sion tracer. Imaging using oxygen-15-water is considered the gold standard for absolute quantification of myocardial perfusion (though static perfusion images cannot be obtained), and metabolic imaging with FDG occupies the same position in the assessment of myocar- dial viability. Cardiac MRI MRI uses the magnetic properties of the hydrogen nucleus, radio waves, and powerful magnets, to provide high-quality still and cine images of the cardiovascular system with and without the use of exogenous contrast (gadolinium). Cardiovascular MRI is the gold standard method for the three-dimensional analysis of cardiothor- acic anatomy, the assessment of global and regional myocardial function, and viability imaging (late gadolinium enhancement tech- nique). Using first-pass perfusion imaging under vasodilator stress, cardiovascular MRI has high diagnostic accuracy for the identifica- tion of myocardial ischaemia. Oedema imaging using T2-weighted techniques is useful for the identification of acute coronary syn- dromes and myocardial inflammation. Coronary MRI is feasible, and particularly indicated for anomalous coronaries. Its spatial and temporal resolution is inferior to CT or conventional angiography, and the identification and grading of stenoses remains challenging. Molecular imaging may in future allow visualization of unstable plaque. Parametric mapping techniques such as T1 and T2 map- ping offer a quantitative measure of tissue characteristics further improving the ability to detect oedema and diffuse fibrosis. Abnormal signal can be distinguished either without contrast (native T1 or T2), or post-contrast (extracellular volume measurement). Cardiovascular MRI also provides important prognostic data for many cardiovas- cular diseases and is now an essential component of an advanced cardiovascular imaging service, and it is anticipated that its role will continue to grow. Cardiac CT Multidetector computed tomography is a fast and noninvasive method for the visualization of the coronary arteries. In comparison to CT imaging of other organs, it requires a scanner with at least 64 detectors and ECG gating. CT can be used to assess the overall burden of coronary atheroma in terms of calcification, and angio- graphic images can be obtained following power injection of iodin-ated X-ray contrast. The spatial and temporal resolution of cardiac CT remains in- ferior to invasive angiography. Its positive predictive value is limited by artefacts, particularly in relation to calcified plaques, though in experienced hands this may be less of a problem than the litera- ture suggests. However, the great strength of the technique lies in its extremely high negative predictive value, which exceeds 99% in most studies. Hence cardiac CT is an excellent test to rule out cor- onary stenoses in patients with low to intermediate likelihood of dis- ease. With further technical developments it is likely that coronary CT will replace invasive coronary angiography for many diagnostic purposes. Nuclear imaging Introduction to myocardial perfusion scintigraphy Myocardial perfusion scintigraphy (MPS) can provide information on (1) viable vs. infarcted myocardium on the resting scan; (2) in- ducible hypoperfusion on the stress scan (in comparison with rest); and (3) regional and global left ventricular function, both at rest and post-stress. The procedure is

versatile and minimally invasive, and is not limited by overall exercise capacity, abnormalities of the resting ECG, pacemakers, obesity, claustrophobia, renal dysfunction, iodine allergy, or acoustic windows. Indeed, it is very difficult to identify any patient who is not suitable for nuclear perfusion imaging, and as a result the technique has matured into a first-line procedure for the assessment of coronary artery disease in many countries. Over 5 million nuclear cardiology procedures were undertaken in the United States of America in 2001. Basic principles of MPS An intravenous injection of a radiopharmaceutical tracer is admin- istered, which enters intact myocardial cells and is retained within them to allow time for subsequent imaging. Usually, the comparison of stress and rest images determines whether regional myocardial perfusion is uniform, or if there are in- ducible or reversible perfusion defects (corresponding to inducible ischaemia) or fixed perfusion defects (corresponding to infarction; Fig. 16.3.3.1). There are currently three radiopharmaceutical perfusion tracers used in single photon emission computed tomography (SPECT) imaging: thallium-201, and two technetium-99m-labelled agents, sestamibi and tetrofosmin. All are monovalent cations, roughly the same size as a hydrated potassium ion. Following injection, they are delivered to the myocardium in proportion to blood supply and enter the cells down the electrochemical gradient. Thallous-201 chloride has been in use since the mid-1970s. It is produced in a commercial cyclotron, and has a half-life of 73 h. It emits photons of varying energies (predominantly 68–80 keV). Following myocardial uptake, thallium-201 gradually re-equilibrates with the extracellular space (redistribution). Therefore, following injection of 80 MBq during stress (exercise or pharmacological), imaging must be performed immediately (within 10 min). A redis- tribution scan 3–4 h later reflects resting viability/perfusion without the need for a second injection. Nevertheless, a second injection of thallium (40 MBq) may be administered at rest to optimize the as- sessment of myocardial viability. Sestamibi and tetrofosmin are organic complexes with technetium-99m. Technetium-99m is widely available in nuclear medicine departments from a generator and is used to label a freeze-dried product in a vial. Technetium-99m emits γ-rays at 140 keV and has a half-life of 6 h. Sestamibi and tetrofosmin bind to intracellular components, and hence their distribution at the time of imaging (typically 30–60 min after injection) reflects myocardial perfusion at the time of injection. Separate injections are required for stress and rest imaging, either on separate days (typically 400 MBq on each day) or on the same day (with a larger second dose— 750 MBq after 250 MBq—to swamp residual activity). Sublingual

 glyceryl trinitrate can be given before the resting injection of sestamibi or tetrofosmin to maximize the detection of myocardial viability. Photons emitted from the patient are imaged by a gamma camera, the head of which is essentially a large crystal of sodium iodide. Absorption of a γ-photon produces a burst of photons within the visible range (scintillation), which is detected by underlying photo- multiplier tubes. The gamma camera rotates around the patient over a 180° arc from right anterior oblique to left posterior oblique. A planar image is acquired at each of a series of 32–64 steps, and these can be gated to the patient's ECG to provide functional in- formation on the processed scan. Acquisition usually takes 15–20 min. The planar projections are reconstructed and reoriented to give sets of vertical long-axis, horizontal long-axis, and short-axis slices. Stress and rest slices are viewed side by side to facilitate comparison. A new design of cardiac gamma camera is now available, which uses cadmium zinc telluride (CZT) in columns of solid-state de- tectors, rather than the traditional single sodium iodide crystal. These cameras have far higher sensitivity and spatial resolution, offering the potential for substantially reduced acquisition times (2–5 min) and/or tracer dose reductions. Principles of stress testing for MPS The wide variety of stress modalities available to nuclear

cardiology is one of its major advantages. Exercise (or physiological) stress can be achieved with a treadmill or bicycle following a specified protocol, such as the Bruce protocol. This is the preferred method, mimicking ‘real world’ stress and providing valuable physiological data. The in- crease in myocardial oxygen demand provokes secondary coronary arteriolar dilatation. The radiopharmaceutical is injected at peak stress, and the patient maintains exercise for a further 1–2 min while it is being taken up by the myocardium. Patients unable to exercise can undergo pharmacological stress. Vasodilators such as dipyridamole, adenosine, or regadenoson can be injected or infused intravenously to induce maximal coronary ar- teriolar dilatation, provoking flow heterogeneity between coronary vascular beds. Dipyridamole and adenosine are contraindicated in patients with significant airways disease and those with unpaced second-or third-degree atrioventricular block because of their non- selective actions on adenosine receptors. However, regadenoson is a selective adenosine A2A receptor agonist which can safely be used in mild-moderate reversible airways disease. Vasodilator drugs can also be utilized to augment dynamic stress in patients unable to ex- ercise to target heart rate. In patients who are unable to exercise and in whom there is a contraindication to a vasodilator drug, ino- tropic stress with escalating doses of dobutamine (± atropine) can be employed. Some practical considerations for MPS The overall radiation exposure of a patient undergoing a stress-rest technetium study is 6–10 mSv, which is comparable to that of a diag- nostic coronary angiogram, but without the invasive and vascular complications. Much lower doses have been recorded with modern CZT cameras. Cost-effectiveness studies have been performed with SPECT in both Europe and the United States of America. In general, diag- nostic strategies that utilize MPS are more cost-effective than those that do not. This has helped to drive a significant increase in the number of SPECT procedures performed worldwide. Clinical value of MPS in the investigation of known or suspected coronary artery disease In a large meta-analysis of 33 studies the sensitivity and specificity of myocardial perfusion imaging were 87% and 73%, respectively. The Fig. 16.3.3.1 Myocardial perfusion imaging—an example of inducible hypoperfusion in the anterior wall and apex. Panels from left to right show representative vertical long axis (VLA), horizontal long axis (HLA), and mid short-axis (SAX) slices, with stress above rest. The white arrows show a perfusion defect on the stress slices which resolves at rest.

16.3.3 Cardiac investigations 3329 normalcy rate, which removes the referral bias of false-positive pa- tients being referred on for coronary angiography, was 91%. Similar results are available for vasodilator and dobutamine stress. More importantly, a wealth of prognostic data is available. The value of a normal SPECT study is beyond doubt, with a meta-analysis including just under 21 000 patients followed up for 2.3 years demonstrating a risk of cardiac death or nonfatal myocardial infarction of 0.7% per year. Follow-up studies extending up to 7 years have demonstrated similar low event rates. High-risk markers on SPECT have incremental prognostic value over electrocardiographic and clinical variables. They include multivessel disease patterns, a large burden of ischaemia (>10% of myocardium), transient ischaemic left ventricular dilatation, left ventricular ejection fraction (LVEF) less than 0.4 (see ‘Assessment of left ventricular volume and function’), and lung uptake (only with thallium-201). SPECT is also able to add prognostic data when risk scores such as the Duke treadmill score are applied to exercise ECG variables (Fig. 16.3.3.2), and can stratify risk in specific populations such as patients after myocardial infarction or with diabetes mellitus, women, and patients with an abnormal ECG (e.g. left bundle branch block). More recent data have emphasized the value of MPS even in pa- tients with proven coronary artery disease. In a large retrospective study from Cedars-Sinai Hospital (Los Angeles, California), patients

managed conservatively had higher event rates than those managed with revascularization if they had inducible hypoperfusion that was more extensive than 10% of the left ven- tricular myocardium (see Fig. 16.3.3.3). The COURAGE trial failed to show any prognostic benefit of percutaneous coronary intervention (PCI) plus optimal medical therapy (OMT) over OMT alone. However, a nuclear substudy suggested that PCI was better at reducing inducible hypoperfusion than OMT alone, and that event rates were lower for patients with greater decreases in inducible hypoperfusion. Further research is ongoing to identify if MPS could be used to identify a subgroup of patients in whom, despite OMT, the prognosis could be improved by PCI. Nuclear techniques are well suited to the identification of myo- cardial viability, which predicts functional recovery (identified by echocardiography) in approximately 80% of dysfunctional seg- ments after revascularization. Comparative studies with low-dose dobutamine echocardiography (see Chapter 16.3.2), positron emis- sion tomography (PET), and cardiovascular magnetic resonance (CMR) have been performed. Each test is broadly similar in its ability to predict functional recovery. SPECT has also been used to assess success of revascularization procedures. In the acute setting, resting SPECT may be performed in patients attending the emergency department with chest pain and a non- diagnostic initial ECG. A normal perfusion scan is associated with a low risk of future events, lower likelihood of requiring cardiac cath- eterization, and lower costs owing to the shorter hospital stay and fewer subsequent investigations. Nonperfusion uses of SPECT techniques Myocardial perfusion imaging for the investigation of suspected or known coronary disease is by far the most commonly performed nuclear cardiology investigation. However, scintigraphic imaging using other radiopharmaceuticals is increasingly performed to answer specific physiological questions in several other cardiac diseases. It has been recognized for almost 40 years that some patients with cardiac amyloidosis exhibit myocardial uptake of phosphate bone tracers. More recently, it has become apparent that this phenom- enon tends to be limited to those with transthyretin-type (ATTR) cardiac amyloidosis, as opposed to those with the light-chain-type (AL). Cardiac planar and SPECT imaging using bone tracers such as technetium-99m-3,3-diphosphono-1,2-propanodicarboxylic acid (DPD—Europe) or technetium-99m-pyrophosphate (PYP—USA) can therefore be used to confirm a diagnosis of ATTR-amyloid with very high positive predictive value, thereby obviating the need for cardiac biopsy. Iodine-131-meta-iodobenzylguanidine (mIBG) is a false- transmitter analogue of norepinephrine and can be used to image the state of cardiac sympathetic innervation, which can become abnormal in patients with heart failure. Reduced cardiac uptake and increased washout of mIBG is associated with increased mor- tality, heart failure progression, and re-admission, independent of 0 1 2 3 4 5 6 7 8 9 low intermediate high risk normal mild-abnormal

> “ mild abnormal Result of exercise ECG (Duke treadmill score) SPECT result hard events/year (%) Fig. 16.3.3.2 Incremental value of myocardial perfusion imaging over exercise ECG: hard event rates per year as a function of exercise SPECT in patients initially stratified by low, intermediate, and high Duke treadmill scores. Fig. 16.3.3.3 Annualized cardiac death rate according to ischaemic burden and treatment strategy. Increasing ischaemia appears to be better treated with revascularization in this retrospective study. From Hachamovitch, R. et al. (2003). Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior

coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation, 107, 2900–7.

section 16 Cardiovascular disorders 3330 left ventricular (LV) ejection fraction and brain natriuretic peptide (BNP) level. There is interest in using mIBG scintigraphy to stratify the risk of sudden arrhythmic death to help gauge the likely benefit of an implantable cardioverter-defibrillator (ICD). The increasing use of implantable cardiac devices (pacemakers, ICDs, prosthetic valves) has led to a rise in the number of pa- tients presenting with suspected device-related infection. Echo imaging, even transoesophageally, is not always diagnostic, and scintigraphic imaging using the patient's own labelled white cells may have a role. This technique is less sensitive but more specific than fluorine-18-fluorodeoxyglucose (FDG), and can be particu- larly useful within three months of valve replacement when false- positive FDG scans are common due to noninfective post-surgical inflammation. Assessment of left ventricular volumes and function using nuclear techniques Nuclear cardiology techniques have been used for the noninvasive assessment of left ventricular function since the early 1970s. Three radionuclide techniques are available for assessing left ventricular function: first-pass radionuclide ventriculography, equilibrium radionuclide ventriculography, and gated myocardial perfusion SPECT. The first is rarely performed nowadays and will not be con- sidered further. Equilibrium radionuclide ventriculography This investigation, also affectionately (but inaccurately) known as multigated acquisition (MUGA), is performed following label- ling of red blood cells with technetium-99m-pertechnetate. This is usually performed in vivo following a preceding injection of stan- nous pyrophosphate. For a simple assessment of LVEF, gated planar imaging of the blood pool is performed in a LAO 45° projection to optimize separation of the left and right ventricular cavities. This method is independent of left ventricular geometry, and hence very accurate and reproducible. The wide availability of echo (with its lack of radiation exposure) has led to a substantial decrease in the number of equilibrium radionuclide ventriculography studies performed. However, the radionuclide method can still be valuable when a quick and repro- ducible assessment of LVEF is required, for example in the moni- toring of patients undergoing chemotherapy with anthracyclines or trastuzumab. ECG-gated myocardial perfusion SPECT SPECT acquisition during MPS can be gated at no extra incon- venience, cost, or risk to the patient. Tomographic slices are re- constructed for each of 8 or 16 frames and can be played as a cine for visual assessment. Left ventricular volumes and LVEF can be derived following endomyocardial border definition. Gated SPECT (Fig. 16.3.3.4) can be very useful in identifying at- tenuation artefacts (which appear as fixed perfusion defects but demonstrate normal wall motion). Indices of left ventricular func- tion (ejection fraction and end-systolic volume) provide inde- pendent prognostic information and are powerful predictors of cardiac death. Importantly, changes in regional and global func- tion from post-stress to rest imaging can help unmask multivessel ischaemia which has been underestimated by the visible regional perfusion defects. Positron emission tomography PET scanners employ coincidence detection of 511-keV photons travelling 180° apart following annihilation of a positron with an electron. Cardiac PET studies are no longer confined to research centres, mainly due to the rapid increase in availability of combined PET/CT scanners driven by developments in oncological practice. Myocardial perfusion can be assessed with nitrogen-13-ammonia (requiring an on-site cyclotron) or rubidium-82 (from a generator), but is best done with oxygen-15-water (though this tracer requires a cyclotron and does not permit myocardial imaging). Myocardial viability in terms

of metabolic integrity is assessed with fluorine-18- fluorodeoxyglucose (FDG), which has become widely commercially available with the growth of oncological PET. FDG-PET is increas- ingly used to image intracardiac infection and inflammation as it is avidly taken up by metabolically active white cells. For this in- dication, careful patient preparation is essential to suppress myo- cardial FDG uptake using a carbohydrate-restricted diet followed by fasting. FDG-PET has a high sensitivity for identifying cardiac device-related infection, though white cell scintigraphy is more reli- able within three months of valve surgery. Its role in cardiac sarcoid- osis is also well-established, especially for disease monitoring. Sodium fluoride-18 (NaF) PET is an interesting research tool for imaging microcalcification in coronary atheromatous plaques, which may identify those most likely to become unstable causing an acute coronary syndrome. Fig. 16.3.3.4 Gated SPECT to assess left ventricular systolic function at rest in a patient with an extensive anteroapical and septal infarct and poor left ventricular systolic function. Left column: end-diastolic frame showing (from top to bottom) apical, mid, and basal short-axis slices, horizontal, and vertical long-axis slices. Right column: end-systolic frame showing corresponding slices. Right column: calculated volumes and ejection fraction (middle panel), with time-volume curve (bottom panel).

16.3.3 Cardiac investigations 3331 Comparison of nuclear techniques with other imaging modalities For physiological assessment of known or suspected coronary artery disease, the alternatives to SPECT and PET are exercise electrocar- diography, stress (exercise or dobutamine) echocardiography, and stress CMR (with vasodilator stress for perfusion or dobutamine for wall motion). The exercise ECG is inferior, mainly due to its depend- ence on exercise ability and the poor sensitivity and specificity of ECG changes. Stress echocardiography is a good alternative technique, with a slightly lower sensitivity but higher specificity in comparative studies. It is physician-intensive and operator-dependent, but har- monic imaging and microbubble contrast agents have greatly im- proved image quality. An important advantage over the radionuclide techniques is the avoidance of ionizing radiation, which makes it particularly attractive for younger patients. Cardiac MRI can assess regional and global left ventricular sys- tolic function during a dobutamine infusion, similar to stress echo- cardiography. Alternatively, gadolinium can be used as a first-pass myocardial perfusion tracer during vasodilator stress, with late-enhancement used to identify infarction. A large multicentre com- parative study has suggested that CMR is an equivalent alternative to SPECT. In practice, the different modalities should be regarded as largely interchangeable, with local clinical expertise being more important than any marginal differences in technical performance between them. Functional imaging, however performed, is recommended in the latest National Institute for Health and Care Excellence (NICE) guidelines for the assessment of patients with chest pain of recent onset. Cardiac MRI Introduction Cardiovascular MRI (CMR) has undergone significant advancement in terms of imaging capabilities, ease of use, and speed of acquisition over the past 20 years. A study of cardiovascular anatomy, left and right ventricular function, and viability/fibrosis (late gadolinium en- hancement) with a modern CMR scanner can be performed in less than 30 min by an experienced operator. These improvements have led to the widespread adoption of CMR in clinical practice. How CMR works MRI is typically based on the magnetic properties of the hydrogen nucleus, though other nuclei can also be used. Hydrogen nuclei (protons), which are abundant in the human body, behave like small spinning magnets that have an alignment (magnetic moment) par- allel to the direction of the external magnetic field and a rotation (precession) frequency proportional to the strength of the field. Radio waves in the form of a radiofrequency pulse transmitted into the patient cause the alignment of the protons to change, that is, the magnetic moments in that region are flipped out at

an angle (flip angle) to the magnetic field (excitation). When this radiofrequency pulse is turned off, the protons in the patient's body return to their neutral position (relaxation), emitting their own weak radio-wave signals, which are detected by receiver coils and used to produce an image. The contrast between tissues (e.g. heart muscle and fat) depends on the tissue density of hydrogen atoms (proton density), and on two distinct MR relaxation processes that affect the net magnetization: the longitudinal relaxation time (T1), and transverse re- laxation time (T2). The differences in these parameters in distinct tissues are used to generate contrast in MR images. Image contrast can also be modified by modulating the way the radiofrequency pulses are played out (the MR sequence): for example, in so-called T1-weighted images, myocardial tissue is dark whereas fat is bright. On the other hand, T2-weighted images highlight unbound water in the myocardium and are used to demonstrate myocardial oedema due to inflammation or acute ischaemia. CMR requires advanced technology, including a high-field super- conducting magnet which produces a homogeneous and stable magnetic field (1.5 or 3.0 Tesla), gradient coils within the bore of the magnet which generate the gradient fields, a radiofrequency amplifier to excite the spins with radiofrequency pulses, and a radiofrequency antenna (coil), which receives the radio signals coming from the patient. A computer and specific software are also needed to control the scanner and generate (reconstruct) the im- ages. To prevent artefacts from cardiac motion, most CMR images are generated with ultrafast sequences gated to the R wave of the ECG. Respiratory motion, which is another factor that can pro- duce artefacts, is eliminated by acquiring most CMR images in end- expiratory breath-hold. When acquisition is long and cannot be completed within one breath-hold, special free-breathing sequences that track the diaphragm's position (navigators) are used. CMR safety MRI scan subjects and operators are not exposed to ionizing radi- ation and there are no proven detrimental biological side effects of MRI, if safety guidelines are followed. Ferromagnetic objects can be attracted by the scanner, becoming projectiles that could lead to significant patient or operator injury and also damage the scanner. The presence of certain medical implants and devices (e.g. most pacemakers and defibrillators, cochlear implants, cerebrovascular clips) is a contraindication for routine MR scanning, but nearly all prosthetic cardiac valves, coronary and vascular stents, and ortho- paedic implants are safe in a 3-T (or less) MR environment. MRI conditional pacemakers and defibrillators (generator and leads) are now available. Whenever there is uncertainty regarding a particular device or implant, the CMR operator should consult a more detailed source of information, such as reference manuals, dedicated websites (e.g. http://www.mrisafety.com), or the manufacturer's product information. Claustrophobia may be a problem for a few patients, and mild sedation usually helps to overcome this. Gadolinium contrast agents are safe for most patients (safer than iodine-based contrast), but gadolinium-containing contrast agents have been linked with the development of a rare systemic disorder called nephrogenic systemic fibrosis. The patients at risk for developing this disease are those with acute kidney injury or chronic kidney disease (glomerular filtration rate <30 ml/min/1.73 m2), or acute renal dysfunction of any severity due to the hepatorenal syndrome, or in the perioperative liver trans- plantation period. To date, there is no evidence that other patient groups are at risk. The risk of nephrogenic systemic fibrosis also de- pends on the nature of the gadolinium-containing agent employed, and most MR centres now use gadolinium agents that are tightly

 bound to a cyclic chelate, for which the incidence of nephrogenic systemic fibrosis is near zero. However, it seems prudent to avoid use of gadolinium-based contrast media in high-risk patients unless the diagnostic information is essential and not available with non- contrast-enhanced CMR or other imaging modalities. Whether im- mediate post-

imaging haemodialysis protects against nephrogenic systemic fibrosis is not known.
Applications of CMR Normal and pathological anatomy Historically, the first widespread application of CMR was the three- dimensional analysis of cardiovascular anatomy. By providing ex- cellent soft tissue contrast, cardiovascular anatomy can be assessed in virtually any imaging plane (coronal, transverse, sagittal), or indi- vidualized double-angulated planes. The latter is particularly valu- able in complex congenital heart disease. Myocardial function and mass CMR is the accepted gold standard for quantification of left and right ventricular function. Using steady-state free precession tech- niques that provide excellent delineation of the blood-myocardium interface, long-axis, and short-axis cine views (Fig. 16.3.3.5) can be obtained during all phases of the cardiac cycle (cine-CMR). Planimetry of each short-axis slice and summation of slice vol- umes allow precise determination of systolic and diastolic left and right ventricular volumes, stroke volumes, and ejection fraction with high reproducibility. Ventricular mass can also be determined by multiplication of the myocardial volume by its specific weight of 1.05 g/cm3. The excellent interstudy reproducibility of volume and mass measurements by CMR has allowed reductions of sample sizes of 80–97% to achieve the same statistical power for demonstrating a given change in left ventricular volumes, ejection fraction, or cardiac mass. Analysis of regional myocardial function is feasible both at rest and during pharmacological stress, typically using dobutamine. Dobutamine stress CMR has high sensitivity and specificity for detecting ischaemic heart disease and is particularly useful in pa- tients with difficult acoustic windows. Blood flow Phase contrast mapping of velocities through planes transecting blood flow in the main pulmonary artery and the ascending aorta can provide accurate measurements of cardiac output, shunt flow, aortic or pulmonary regurgitation and, indirectly, of mitral and tricuspid regurgitation. For stenotic jets, the peak velocity can be measured on through-plane velocity-encoded images. Peak pres- sure gradients can be estimated according to the modified Bernoulli equation. Valve morphology can be assessed with the use of steady- state free precession (SSFP) cine images and valve area can be as- sessed with accuracy by direct planimetry using cross-sectional cine images, although valve structure is generally better assessed by echocardiography. Bicuspid aortic valves or fused valve leaflets can be readily identified. CMR is an excellent technique for the quan- titative assessment of regurgitation. If a single valve is affected, the regurgitant volume can be measured from the difference in left and right ventricular stroke volumes. If both the mitral and tricuspid valves are affected, the regurgitant volumes can be calculated by sub- tracting the flow in main pulmonary artery and the ascending aorta, measured by CMR velocity mapping, from the left and right stroke volumes (measured by the volumetric method), respectively. This technique compares favourably with measurements from catheter- ization and Doppler echocardiography techniques. For pulmonary and aortic regurgitation, direct measurement of regurgitant volume is also possible using CMR velocity mapping. These CMR tech- niques have high interstudy reproducibility and can be used for the longitudinal follow-up of patients with valve disease over time. Apart from the evaluation of patients with valve pathologies, flow imaging by CMR is regularly used in assessing patients with congenital heart disease. By measuring flow in the ascending aorta and main pulmonary artery with velocity-encoding CMR, the pulmonary-to-systemic flow ratio (Qp/Qs) can be determined. These CMR measurements show excellent correlation with calculations obtained from oximetry during haemodynamic catheterization. Fig. 16.3.3.5 End-diastolic still images from multiple contiguous short-axis SSFP cines that encompass the left ventricle, from base to apex. Note the position of the short-axis (SA) slices marked on the still frames of end-diastolic horizontal long axis (HLA) cine image and the excellent delineation of the myocardium from the blood and the surrounding tissue.

16.3.3 Cardiac investigations 3333 Myocardial viability The assessment of myocardial viability using gadolinium-based contrast agents (late gadolinium enhancement (LGE) technique) has revolutionized the use of CMR in cardiology. Gadolinium che- lates are extracellular tracers that cannot cross cell membranes. In normal myocardium the myocytes are densely packed, and the extracellular space and vascular volume represents less than 15% of the myocardial volume; hence after injection of gadolinium there are only few gadolinium molecules in a myocardial sample volume. By contrast, when the membranes of myocytes rupture, gadolinium molecules can penetrate into the myocytes and stay there, even late after gadolinium injection, such that in scar tissue the interstitial space is expanded and increased gadolinium concentration is found (Fig. 16.3.3.6). In practice, on inversion-recovery T1-weighted sequences obtained 5–10 min after gadolinium administration, nonviable myocardium (scarred or irreversibly injured) shows high signal intensity, whereas normal and viable (stunned, hibernating) myocardium shows low signal intensity. Myocardial infarction (acute or chronic) has a characteristic LGE pattern due to the wavefront of myocardial necrosis that always involves the subendocardium at the core of the infarct (Fig. 16.3.3.7). The LGE technique has undergone extensive histo- pathological validation. The superb spatial resolution of LGE-CMR allows the detection of even small subendocardial infarcts that might otherwise be missed by lower spatial resolution techniques such as SPECT. Several studies have demonstrated an inverse re- lationship between the transmural extent of myocardial infarction and segmental functional recovery after revascularization. In prac- tice, segments which show more than 50% scarring are considered nonviable, whereas segments with only subendocardial enhance- ment (<50%) have a high likelihood of functional recovery. CMR can also assess myocardial viability using a low-dose dobutamine protocol in a way analogous to echocardiography, but in practice, this is rarely required. Several CMR techniques, including LGE, can also identify areas of microvascular obstruction (no-reflow phenomenon) after revascularization in patients with acute myo- cardial infarction. LGE-CMR in nonischaemic cardiomyopathies Specific patterns of regional fibrosis and scarring have also been described for many nonischaemic cardiomyopathic processes (Fig. 16.3.3.8). For example, the majority of patients with hypertrophic cardiomyopathy show patchy fibrosis in the hypertrophied septum involving left/right ventricular junctions, whereas about a third of patients with dilated cardiomyopathy show a midwall band of septal fibrosis. Furthermore, most patients with myocarditis have subepicardial LGE in the lateral left ventricular wall. Several other patterns of LGE exist for other rarer cardiomyopathies such as cardiac amyloidosis or sarcoidosis. The LGE technique is a major part of nearly every scanning protocol and provides valuable diag- nostic and pathophysiological insights in both ischaemic and nonischaemic cardiomyopathies. normal myocytes acute cell injury myocardial scar Gadolinium collagen matrix Fig. 16.3.3.6 Mechanism for late gadolinium enhancement (LGE) in acute and chronic myocardial damage. (a) Densely packed myocytes with intact cell membrane—gadolinium chelates only in the vessels and extracellular space. (b) Acute myocardial damage with ruptured cell membranes of myocytes—intracellular accumulation of gadolinium chelates. (c) Chronic myocardial damage with loss of myocytes and replacement by scar tissue—mostly collagen fibres that are filled with gadolinium chelates.
Fig. 16.3.3.7 Short-axis LGE image at the midventricular level in a patient with near transmural anteroseptal myocardial infarction (white arrows). Fig. 16.3.3.8 Short-axis LGE image at the midventricular level in a patient with hypertrophic cardiomyopathy. Note the patchy LGE due to fibrosis in the hypertrophied septum (white arrows), including both left- right ventricular junctions.

section 16 Cardiovascular disorders 3334 Myocardial perfusion Regional myocardial perfusion can be measured during the first pass of a gadolinium-based contrast agent. Using sequential multislice fast gradient-echo CMR, passage of the contrast agent through the heart chambers and the myocardial tissue can be followed. From a series of such images, regional time–signal intensity curves can be derived. Pharmacological vasodilatation (with adenosine, dipyrid- amole, or regadenoson) induces a three-to fivefold increase of blood flow in myocardial areas subtended by normal coronary arteries, whereas no (or only minimal) change is found in areas subtended by stenotic coronary arteries. Contrast arrival in these areas is delayed, hence they appear hypointense (dark) compared to adjacent normal myocardium (Fig. 16.3.3.9). Many clinical trials have assessed the feasibility, safety, and diag- nostic accuracy of stress perfusion CMR. A meta-analysis showed that first-pass perfusion CMR under vasodilator stress has excel- lent sensitivity (89%) and very good specificity (76%) to diagnose coronary artery disease, with quantitative coronary angiography (≥50% diameter stenosis) as the gold standard. The CE-MARC study compared the diagnostic accuracy of stress perfusion CMR with SPECT and showed that both techniques have similar speci- ficity, but CMR is more sensitive to detect ischaemia compared to scintigraphy. It should be noted that CMR perfusion techniques have higher spatial resolution than nuclear techniques (by at least an order of magnitude) and can be used to study the transmural aspect of myocardial perfusion. Noninvasive magnetic resonance perfusion imaging can guide patient management with stable cor- onary disease as safely as the currently used invasive coronary angi- ography supported by fractional flow reserve in a population at high risk for cardiovascular events. Myocardial oedema Various technical improvements have enabled the wide clinical use of T2-weighted CMR for the qualitative or semi-quantitative detec- tion of myocardial oedema and inflammation, primarily in acute coronary syndromes and myocarditis. Despite these improvements, a few well-recognized limitations of conventional T2-weighted tech- niques remain, including the need for a ‘normal’ reference region of interest in either remote myocardium or skeletal muscle. This can lead to false-negative results when these reference areas are also af- fected in systemic processes. Quantitative parametric T1 and T2 mapping techniques have been developed to overcome these limi- tations. Myocardial haemorrhage in patients with acute myocardial infarction can also be assessed using T2-weighted or T2*- CMR. Coronary arteries CMR of the coronary arteries remains a technical challenge because of their small size (up to 4 mm) and continuous, complex movement. Fast, flow-sensitive gradient-echo sequences allow imaging of prox- imal coronary arteries using breath-hold or navigator techniques, with a maximum in-plane resolution of about 700 μm2. However, the sensitivity for coronary stenosis is only 60–90% because of the inferior spatial resolution compared to CT or invasive coronary angiography. Further developments (parallel acquisition, gradient performance, intravascular contrast agents, higher-field magnets) might in the future allow the development of high-resolution MR coronary angiography with CT-like quality. At present, MR cor- onary angiography can be used for diagnosis of anomalous coronary arteries or coronary aneurysms. Iron overload The most common cause of iron overload cardiomyopathy is re- peated blood transfusions in patients with transfusion-dependent anaemias (e.g. β-thalassaemia major) and in primary hemochroma- tosis. The cardiomyopathy is reversible if chelation is commenced early, but diagnosis is often delayed because of the late onset of symptoms and patients often die from heart failure. T2* MRI allows the accurate quantification of cardiac and liver iron levels. This al- lows identification of patients who are at risk of developing heart failure (i.e. those with myocardial T2* <10 ms), allowing more ag-gressive iron chelation therapy to be administered. T1 and T2 parametric mapping T1 and T2 mapping refers to parametric maps that are generated from a series of images acquired with

different T1 or T2 weighting so that each pixel can be assigned a T1 or T2 value. These maps are usually displayed using colour or thresholded scales to enable quantitative visual interpretation. Each tissue type exhibits a char- acteristic range of normal T1 and T2 relaxation times at a particular field strength, deviation from which may be indicative of disease. Myocardial T1-mapping methods are used for native (i.e. without the use of gadolinium-based contrast agents) and also for post- contrast T1 measurements. In combination with haematocrit, these T1 measurements enable the quantification of extracellular volume fraction (ECV). Elevated native T1 times and ECV in the myocardium have been reported in several commonly encountered cardiac conditions including myocardial infarction, myocarditis, hypertrophic and Fig. 16.3.3.9 Example of a stress perfusion scan. Short-axis stress perfusion at the midventricular level showing an extensive perfusion defect (black arrows) in the anterior wall, septum, and the inferior wall. The lateral wall (white arrow) has relatively normal perfusion.

16.3.3 Cardiac investigations 3335 dilated cardiomyopathy, cardiac amyloidosis (Fig. 16.3.3.10), car- diac involvement in systemic diseases, and diffuse fibrosis in patients with aortic stenosis. Native myocardial T1 values may be lowered by water–protein interactions, fat or iron content, and thus can also serve as a diagnostic tool in characterizing Anderson–Fabry disease, fat in cardiac masses, and myocardial siderosis. Native T1 mapping is particularly useful in the differential diagnosis of patients with acute chest pain including acute coronary syndromes, myocarditis, and takotsubo cardiomyopathy. T2 mapping can detect oedematous myocardial territories in a variety of cardiac pathologies, including acute myocardial infarc- tion, myocarditis, takotsubo cardiomyopathy, and heart transplant rejection. Patients with poor renal function (or on dialysis), where gadolinium-based contrast agents are relatively contraindicated, may benefit from using native T1 mapping instead of LGE imaging. CMR and prognosis The evolving prognostic evidence base of CMR is rapidly expanding for both ischaemic and nonischaemic cardiomyopathies. The com- pletion of ongoing multicentre trials and registries (e.g. HCMR study) is expected to provide more outcome and cost-effectiveness data, which will further strengthen the clinical role of CMR. Cardiac CT Multidetector computed tomography can be used to produce high- quality anatomical images in a variety of cardiac pathologies (e.g. complex congenital heart disease). However, its most widespread use is in the noninvasive anatomical assessment of the coronary ar- teries. The entire coronary tree is imaged during a single breath-hold over a few cardiac cycles (or even a single cycle if the scanner has sufficient detectors). A stack of transaxial slices is acquired, covering the thorax be- tween the carina and the diaphragmatic border of the heart. This is achieved over a few cardiac cycles, depending on the number of detectors. Coronary calcification is assessed from a noncontrasted scan. For angiographic imaging (to assess for luminal stenoses), an intravenous power injection of an iodinated X-ray contrast agent is given, typically 40–80 ml at 4–6 ml/s, followed by a saline flush. Following a breath-hold, the scan is triggered once the left side of the circulation is sufficiently opacified. The timing can be judged either by using an initial test bolus, or by a bolus tracking method where a test slice is monitored until the Hounsfield value in the ascending or descending aorta exceeds a certain threshold. ECG gating is required to image the coronary arteries free of motion. Prospective gating is now the preferred method, with the Fig. 16.3.3.10 Cardiac magnetic resonance (CMR) end-diastolic frame from cine (left panel), ShMOLLI noncontrast T1 map (middle panel), and late gadolinium enhancement (LGE) images (right panel) in normal volunteer, aortic stenosis patient, and cardiac amyloid patient. Note the markedly elevated myocardial T1 time in the cardiac amyloid patient (1170 ms, into the red range of the colour scale) compared to the normal control (955 ms) and the patient with aortic stenosis

and left ventricular hypertrophy (998 ms). ED, end-diastolic. Reprinted from the Journal of the American College of Cardiology, Vol 6, Issue 4, Karamitsos TD, et al., Noncontrast T1 mapping for the diagnosis of cardiac amyloidosis, pp. 488–97, Copyright (2013) with permission from Elsevier.

section 16 Cardiovascular disorders 3336 patient being imaged (and irradiated) for only a brief period of the cardiac cycle, typically at 75% of the R-R interval. This usually repre- sents end-diastole, when the coronary arteries (particularly the right coronary) are at their stillest. Retrospective gating offers imaging throughout the cardiac cycle, which can be valuable when heart-rate control is poor or information about cardiac function is required. However, radiation exposure is relatively high, and the prospective method is routinely preferred. High-quality angiographic images also depend on the patient having a relatively slow heart rate (<65 and preferably <60 bpm), which is achieved by giving a β-blocker, either orally or intraven- ously. Many centres also give sublingual glyceryl trinitrate prior to the study to achieve coronary vasodilatation. Once the scan has been acquired and reconstructed, it must be carefully examined. The thin transaxial slices must be reviewed, and several tools are available to help reorientate the images to display the coronary arteries and other cardiac structures. Some of the technical limitations of cardiac CT are shown in Box 16.3.3.1. Clinical uses of cardiac CT CT coronary calcium scoring The ability of CT to detect and quantify calcified structures is un- rivalled by other imaging techniques. Pathological studies indicate that coronary calcification is an integral part of the atherosclerotic process, and unique to it (with the possible exception of patients with renal failure). Specifically, the square root of the extent of calci- fication is directly proportional to the square root of the overall ex- tent of atheromatous plaque. On a noncontrast-enhanced CT scan, the Agatston score is used to quantify the total amount of coronary calcium, and assesses the area and density of plaques in all arteries. The coronary calcium score is a good measure of the overall coronary atheroma burden and predicts the likelihood of luminal coronary stenoses, as well as the risk of cardiac events over at least 10 years of follow-up. In particular, a score of zero predicts an ex- tremely low risk. Stand-alone coronary calcium scoring may be valuable in the risk stratification of asymptomatic patients or those with atypical chest pain. However, its value in patients with possible angina is less Box 16.3.3.1 Limitations of coronary CT • Radiation exposure, which is highly dependent on the scanner being used and the mode of gating: calcium scoring alone delivers approxi- mately 1 mSv. Angiography with retrospective gating on a 64-slice scanner could deliver as much as 15 mSv, while prospective gating may routinely deliver less than 1 mSv. • Iodinated X-ray contrast required. This can problematic for patients with renal dysfunction or hypersensitivity. • β-blockade required to achieve low heart rate (preferably <60 bpm) to minimize motion artefacts in angiography. • Calcium and stents can cause blooming and beam-hardening arte- facts, obscuring the lumen. Fig. 16.3.3.11 CT coronary angiography of the left anterior descending coronary artery. Note how the heavy calcification makes it difficult to exclude or confirm significant luminal stenosis at several locations. Image courtesy of Dr N. Sabharwal, Oxford Heart Centre.

16.3.3 Cardiac investigations 3337 straightforward: a few patients with no coronary calcification will nevertheless have a significant coronary stenosis due to soft plaque. Moreover, the location of calcification is a poor guide to the exact location of luminal stenoses, which are typically caused by non- calcified soft plaques. Therefore, in patients with possible angina, most authorities would regard coronary calcium scoring as comple- mentary to angiography rather than an alternative. CT coronary angiography Multidetector CT is unique among the noninvasive imaging modalities in providing anatomical (rather than physiological) information about the coronary arteries. Invasive

coronary angi- ography remains the gold standard as CT does not yet approach its spatial or temporal resolution. However, CT is extremely reliable for the exclusion of coronary stenoses, with a negative predictive value that approaches 99% in the literature. Positive predictive values are less robust, largely due to artefacts, particu- larly in relation to calcified plaques (Fig. 16.3.3.11). These ob- servations make CT coronary angiography (CTCA) particularly suitable for the diagnostic investigation of patients with low to intermediate probability of obstructive coronary disease (Fig. 16.3.3.12). As well as its role in patients with stable chest pain, cardiac CT is increasingly used in low-risk patients admitted with acute chest pain, where it is cost-effective compared with alternative strategies. CT can also be useful in certain groups of patients with estab- lished coronary disease. It offers a very straightforward way of as- sessing graft patency after coronary artery bypass surgery and can also be valuable in the exclusion of stent obstruction (though arte- fact can make this difficult for smaller stents). Two large randomized studies (SCOT-HEART and PROMISE) have compared CTCA with more traditional functional assessment in the investigation of patients with suspected coronary disease. In the short-term, the two investigational approaches are equivalent in terms of patient events and symptom outcomes. However, CTCA leads to higher rates of coronary angiography and revascularization, with higher usage of preventative medication such as aspirin and statins. Whether the resultant increase in expense will be justified by better long-term outcomes remains to be seen. Other uses of cardiac CT Although CT coronary angiography is essentially an anatomical imaging technique, it can be used to provide physiological informa- tion in patients with coronary disease. Using sophisticated compu- tational fluid dynamics, a virtual fractional flow reserve (FFR) can be calculated throughout the coronary tree, analogous to the FFR that can be obtained with a pressure wire during invasive coronary angiography. This can be particularly valuable in the assessment of moderate coronary stenosis, although further large-scale clinical val- idation is necessary to fully establish this technique. An alternative Fig. 16.3.3.12 CT coronary angiography showing a critical soft plaque stenosis in the left anterior descending coronary artery also involving the first diagonal. No coronary calcification is present. Image courtesy of Dr N. Sabharwal, Oxford Heart Centre.

 approach is to perform first-pass CT myocardial perfusion imaging during vasodilator stress. However, this requires a second injection of iodinated contrast and image acquisition following the initial CT coronary angiogram, and is not widely performed in clinical practice. For routine CT coronary angiography, prospective gating is now- adays preferred over retrospective gating because of the signifi- cant reduction in radiation exposure. However, when retrospective gating is performed for technical or clinical reasons, it is possible to reconstruct sets of slices throughout the cardiac cycle (typically 10). This makes it possible to quantify left ventricular function (or even right ventricular function if an appropriate contrast infusion protocol is used) using automated software. Cardiac CT offers an excellent anatomical assessment of the heart from a single standardized image acquisition. It can therefore be of great value in complex congenital heart disease, particularly when the exact anatomy is unclear or echocardiography and cardiac MRI have proven inconclusive. Contrast injection and imaging protocols can be modified according to the information required. Cardiovascular CT has become an essential ‘one stop shop’ in the investigation of patients with severe aortic stenosis who are being con- sidered for transcatheter aortic valve implantation. From a single injec- tion of contrast it is possible to assess the dimensions and shape of the aortic annulus, the optimal imaging angle for valve deployment in the catheterization laboratory, the heights of the coronary ostia above the an- nulus, the presence of important coronary disease, the state of the aorta throughout its length, the suitability of the iliac and femoral arteries for a transfemoral approach, and the presence of comorbidity (e.g. unex-

pected malignancy) that might influence decision-making. Acknowledgements The authors of the CMR section acknowledge support from the National Institute for Health Research Oxford Biomedical Research Centre Programme. Professor Stefan Neubauer also acknowledges support from the Oxford British Heart Foundation Centre of Research Excellence. FURTHER READING Nuclear imaging Anagnostopoulos D, et al. (2012). Myocardial perfusion scintig- raphy: technical innovations and evolving clinical applications. Heart, 98, 353–9. Berman DS, et al. (2006). Roles of nuclear cardiology, cardiac com- puted tomography, and cardiac magnetic resonance: noninvasive risk stratification and a conceptual framework for the selection of noninvasive imaging tests in patients with known or suspected coronary artery disease. J Nuclear Med, 47, 1107–18. Cardiac Radionuclide Imaging Writing Group (2009). ACCF/ASNC/ ACR/AHA/ASE/SCCT/SCMR/SNM 2009 appropriate use criteria for cardiac radionuclide imaging: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the American Society of Nuclear Cardiology, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the Society of Cardiovascular Computed Tomography, the Society for Cardiovascular Magnetic Resonance, and the Society of Nuclear Medicine. Circulation, 119, e561–87. Dilsizian V, Narula J (2013). Atlas of nuclear cardiology, 4th edition. Springer, New York. Dorbala S, et al. (2019). ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/ SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis: part 2 of 2—diagnostic criteria and ap- propriate utilization. J Nucl Cardiol, doi: 10.1007/s12350-019-01761-5. Sabharwal NK (2017). State of the art in nuclear cardiology. Heart, 103, 790–9. Sabharwal NK, Arumugam P, Kelion A (2017). Oxford handbook of nuclear cardiology. Oxford University Press, Oxford. Zaret B, Beller GA (2010). Clinical nuclear cardiology: state of the art and future directions, 4th edition. Mosby, London. Computed tomography Chahal H, et al. (2016). Cardiac CT: present and future applications. Heart, 102, 1840–50. Taylor AJ, et al. (2010). ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/ SCAI/SCMR 2010 Appropriate use criteria for cardiac computed tomography. J Cardiovasc Comput Tomogr, 4, 407, e1–407. Williams MC, et al. (2011). Cardiac and coronary CT comprehen- sive imaging approach in the assessment of coronary heart disease. Heart, 97, 1198–205. MRI American College of Cardiology Foundation Task Force on Expert Consensus Documents, Hundley WG, et al. (2010). ACCF/ACR/ AHA/NASCI/SCMR 2010 expert consensus document on cardio- vascular magnetic resonance: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents. J Am Coll Cardiol, 55, 2614–62. Bluemke DA, et al. (2008). Noninvasive coronary artery imaging: mag- netic resonance angiography and multidetector computed tomog- raphy angiography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention of the Council on Cardiovascular Radiology and Intervention, and the Councils on Clinical Cardiology and Cardiovascular Disease in the Young. Circulation, 118, 586–606. Eitel I, Friedrich MG (2011). T2-weighted cardiovascular magnetic resonance in acute cardiac disease. J Cardiovasc Magn Reson, 13, 13. Greenwood JP, et al. (2012). Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. Lancet, 379, 453–60. Haaf P, et al. (2016). Cardiac T1 mapping and extracellular volume (ECV) in clinical practice: a comprehensive review. J Cardiovasc Magn Reson, 18, 89. Jaarsma C, et al. (2012). Diagnostic performance of noninvasive myo- cardial perfusion imaging using single-photon emission, computed tomography, cardiac magnetic resonance, and positron emission tomography imaging for the detection of obstructive coronary ar- tery disease. J Am Coll Cardiol, 59, 1719–28. Karamitsos TD, et al. (2009). The role of cardiovascular magnetic res- onance imaging in heart failure. J Am Coll Cardiol, 54, 1407–24. Kim RJ, et al. (2000). The use of contrast-enhanced magnetic reson- ance imaging to identify reversible myocardial dysfunction. N Engl J Med, 343,

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