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REVIEW

The current and future status of nuclear cardiology: a consensus report

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Cardiac imaging now provides a range of anatomical and functional information with some overlap in the ability of individual techniques to guide diagnosis and management. This report summarizes the conclusions of a panel of cardiac imagers who assembled to discuss the current state of the field. It focuses principally on options for nuclear cardiology, the choice between individual techniques, and areas where further advances would benefit patient management.

Keywords Nuclear cardiology • Myocardial perfusion scintigraphy • SPECT • PET

Introduction

Cardiac imaging now provides a range of anatomical and functional information with some overlap in the ability of individual techniques to guide diagnosis and management. In particular, technical advances make this an exciting time for nuclear cardiology. Developments in radiopharmaceuticals, hardware, and software have improved the diagnostic accuracy and risk assessment of patients with suspected cardiac disorders. However, there is overlap in the abilities of the several imaging techniques, which can make selection of the most appropriate technique difficult or idiosyncratic.

A group of experts therefore convened to discuss future directions in nuclear cardiology, radionuclide vs. other functional imaging, the impact of radiation on patient management, imaging in heart failure, and current educational needs. The aim was briefly to review these areas and to comment on current and future directions as an aid for professionals in the field and for companies with relevant supporting interests. This report therefore presents the consensus of a group with wide experience in cardiac imaging, and it was reviewed and approved by the nucleus of the working group on nuclear cardiology and cardiac computed tomography of the European Society of Cardiology.

Where is nuclear cardiology going?

There have been substantial recent developments in radiopharmaceuticals for both single photon emission computed tomography (SPECT) and positron emission tomography (PET), imaging devices, and computing hardware and software. When selecting an imaging agent for SPECT or PET, the resolution, quantification, cost, radiation burden, and clinical availability must all be considered. Some of the current or developing radiopharmaceuticals that were considered are ^{18}F-flurpiridaz (*Figure 1*), $^{13}NH_3$ (*Figure 2*), $H_2^{15}O$, ^{82}Rb, and ^{123}I-meta-iodo-benzylguanidine (mIBG). They all have strengths and weaknesses. For instance, the strengths of the PET perfusion tracers are image quality and ability to quantify perfusion, whereas their weaknesses are availability and cost. Advances in gamma cameras such as solid state detectors and more accurate reconstruction techniques have increased diagnostic accuracy and have the potential to reduce imaging duration, radiation exposure, and cost.[1–5]

Consensus points

(i) One imaging technique cannot answer all clinical questions and there are different ways of obtaining anatomical and functional information.
   (a) Each technique has its strengths and weaknesses and these should be considered by the cardiac imager before choosing an imaging strategy for an individual patient.
   (b) When a cardiac imager has experience of only a single technique, they should ensure that the imaging strategy is in the patient's best interest, including if necessary by discussion with the patient and referrer.

(ii) When using radionuclides to image myocardial viability and perfusion, the majority of the group agreed that they would use PET

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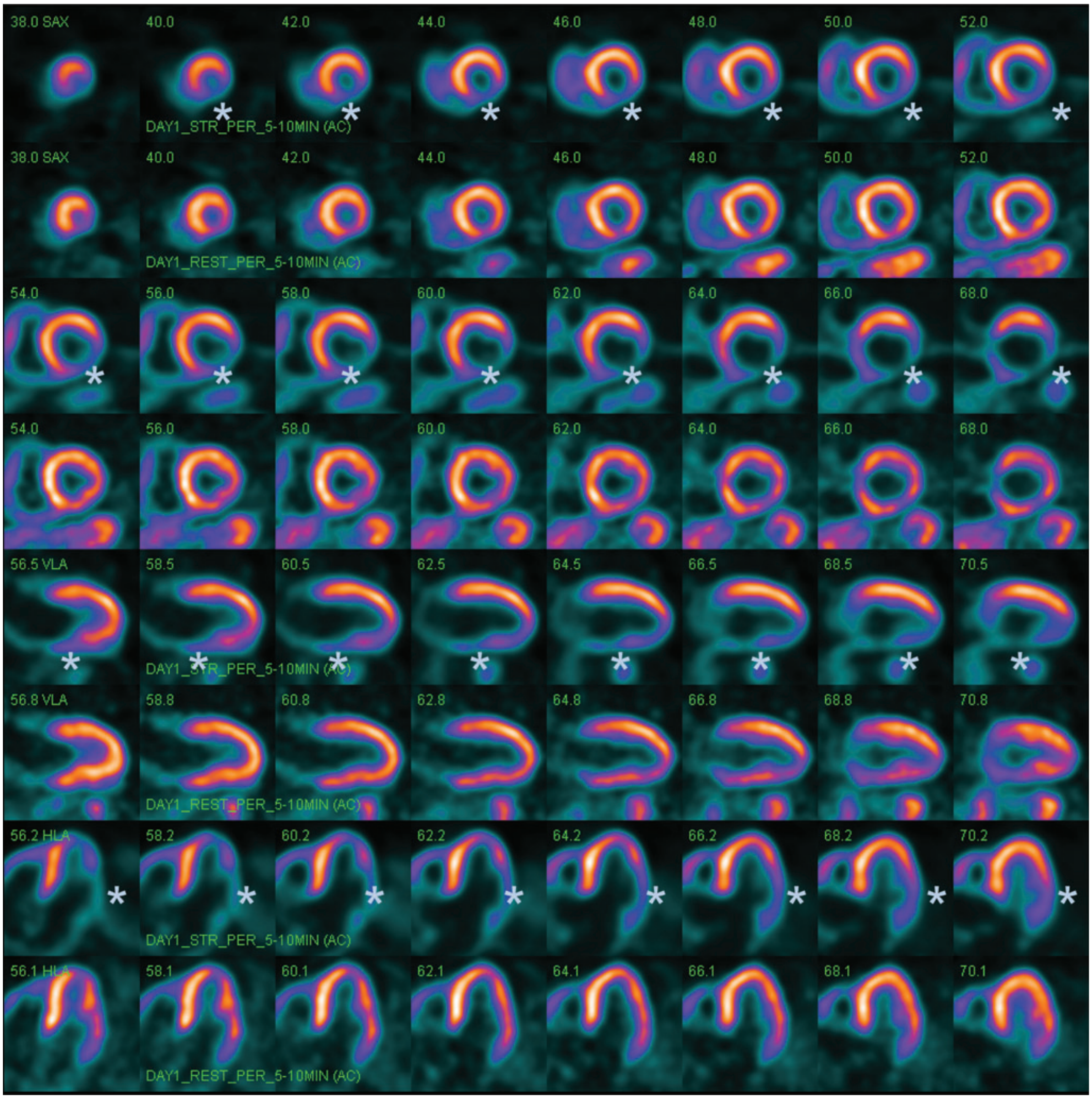

Figure 1: High quality MPS using ^{18}F-flurpiridaz PET. Stress images are in rows 1, 3, 5, 7 and rest in rows 2, 4, 6, 8, with short-axis rows 1–4, vertical long-axis rows 5–6 and horizontal long-axis rows 7–8. There is an inducible perfusion abnormality of the infero-lateral region (asterisks). Image courtesy of Dr J. Maddahi, UCLA.

in preference to SPECT, but barriers include the lack of access, cost, and availability of PET perfusion radiopharmaceuticals.

(iii) Capital costs will always restrain advances, and technology is often being developed ahead of a healthcare system's ability to pay for it.

(iv) Improved clinical outcome should always drive changes in practice, and future trials must be designed to answer clinically relevant questions.

Radionuclide vs. other functional imaging

Functional imaging can provide a deeper understanding of pathophysiology, make a more accurate diagnosis possible, assess prognosis, establish treatment strategies, and monitor a patient's response to treatment. For example, in ischaemic heart disease, functional imaging can detect inducible ischaemia and select patients who might benefit from revascularization in addition to medical therapy (*Figure 3*). It can assess risk before non-cardiac surgery; in heart failure, it can assist in the selection of patients for cardiac resynchronization therapy (CRT) with or without an implantable defibrillator (ICD; *Figure 4*).[8] When selecting an imaging technique, important considerations are accuracy, safety, and cost or cost effectiveness. Fusion imaging may become important by providing synergistic information that cannot be obtained from either anatomical or functional imaging alone.[9] It is essential that functional information is appreciated as adding value to anatomical information.

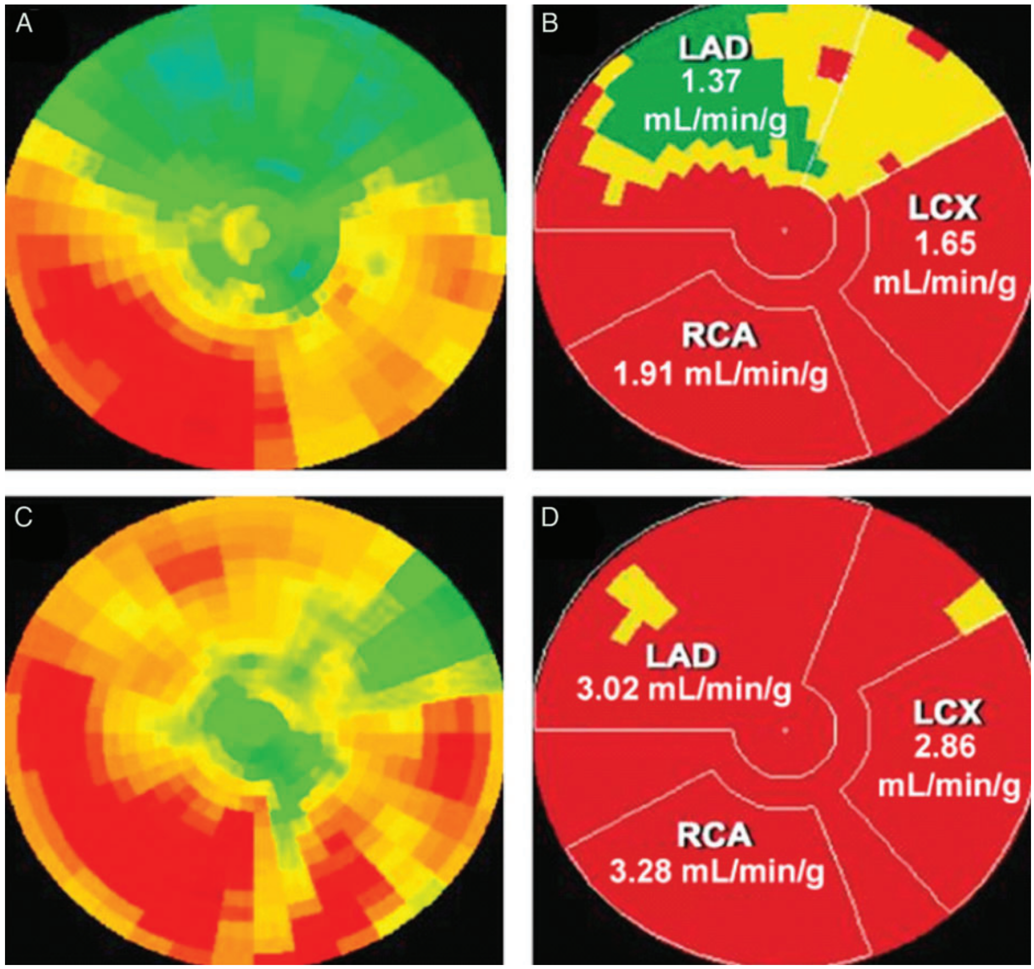

Figure 2: Polar plots from MPS using technetium-99m SPECT (left) and nitrogen-13 ammonia PET (right) before (top) and 1 year after aggressive lipid-lowering therapy (bottom). The stress SPECT images show moderately reduced perfusion in the anterior and mid reduction infero-laterally and these areas improve after lipid lowering. However, the quantitative PET images show abnormal stress perfusion (<2 mL/g/min) in all three coronary territories and all areas improve after lipid lowering. The case illustrates the benefit of quantifying myocardial perfusion. From ref.[6]

Consensus points

(i) While the development of new techniques is encouraging, they must provide incremental information alongside existing techniques or they must provide equivalent information at reduced cost or risk.

(ii) Information on real-world effectiveness and cost effectiveness are essential before new technology is adopted. Studies in single expert centres are indicative of the value of a new technique, but multicentre studies in a range of patients must be performed before widespread adoption of a technique.

(iii) With regard to the selection of techniques, the decision often relies upon local experience and education is required for a fully informed decision.

(iv) Each functional imaging technique has strengths and limitations. The advantage of myocardial perfusion scintigraphy (MPS) using SPECT and PET is the use of tracers that behave like microspheres with initial or longer term distribution according to their delivery to the myocardium.

(a) This allows injection of the tracer to be decoupled from imaging, which simplifies the procedure.

(b) With SPECT more than with PET, artefact can mimic perfusion abnormalities and reduce specificity, especially in inexperienced hands.

(v) Micro-bubble contrast agents for perfusion echocardiography are true blood pool agents, but the contrast between areas of different perfusion is low and the technique is not widely used.

(vi) Contrast agents for magnetic resonance imaging (MRI) and CT perfusion imaging behave neither as microspheres nor as blood pool agents and they require rapid first-pass imaging.

(a) Artefacts in perfusion MRI can be confused with true perfusion abnormalities, and there are safety concerns in patients with impaired renal function.[10,11]

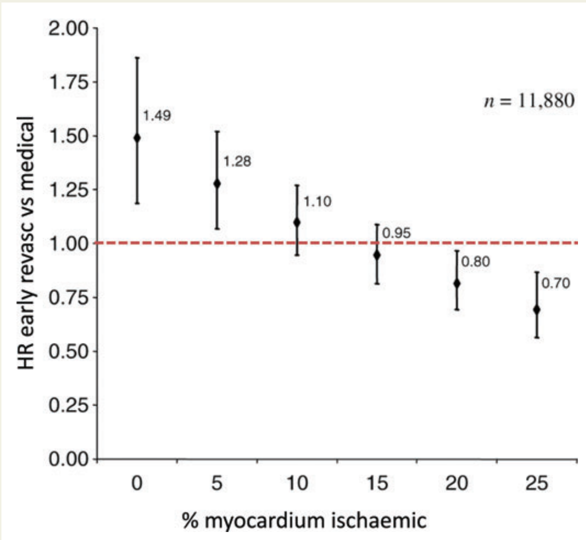

Figure 3: Hazard ratio associated with early revascularization compared with medical therapy according to myocardial ischaemic burden in patients without large prior infarction (<10% myocardial scar). A total of 13 555 patients were followed for a mean of 8.7 years. From ref.[7]

(b) CT perfusion imaging has similar associated concerns, although this is a technique in its infancy.[10]

(c) If microsphere agents were to be developed for MRI and CT, the balance could change in favour of these techniques because of their higher resolution.

(vii) The clinical scenario is most often the deciding factor between anatomical and functional imaging. Anatomy is most helpful to exclude disease in asymptomatic or low likelihood patients, whereas function is most helpful in symptomatic patients.

(viii) The skill of the imaging team often has the largest impact on the value of a technique, rather than the technology itself.

Does radiation matter?

The potential for harm from radiation-based techniques such as nuclear cardiology and CT is open to debate, particularly as echocardiography and MRI have been developed to provide similar information. It has sometimes been difficult to keep a sense of proportion and to balance risk and benefit for the patient. In fact, it has been difficult to demonstrate the harm that low doses of radiation might provide to our patients and the current state of radiation biology knowledge includes the hypotheses that low doses of radiation may be harmless or even beneficial to health. Nonetheless, the consensus is that low doses of radiation might be harmful and that we should reduce patient exposure when possible.

^{99m}Tc-labelled radiopharmaceuticals provide a lower radiation burden than ^{201}Tl.[9] Other radiation-reducing mechanisms, including high-sensitivity solid state cameras, can be used to decrease radiation burden or imaging time or a combination of the two.[2] Improved methods of image acquisition and reconstruction such as resolution recovery algorithms can be used to similar effect.[3–5] PET perfusion tracers reduce radiation burden because of their short half-lives, but cost and complexity generally limit their use.[12] Generator-produced ^{82}Rb is a simpler option and the promise of an ^{18}F-labelled tracer may bring PET perfusion imaging into the main stream.

Consensus points

(i) The harmful effect of acute exposure to high doses of radiation is undoubted, but there is less evidence to support a harmful effect of chronic exposure to low doses such as those used in medical imaging. Nonetheless, the group agreed that while there may be a harmful effect, radiation exposure should be minimized when possible, provided that it is not at the expense of diagnostic accuracy.

(ii) Patients should be informed about the potential risks and benefits of any procedure in gaining their consent. This information should be personalized and the risk will differ significantly between, for instance, a young woman without known heart disease and an elderly patient with heart failure. In the latter case, radiation exposure is unlikely to be a relevant factor.

(iii) When radiation is discussed with a patient, there is a sliding scale of risk with <2 mSv often considered very low. There are no grounds to support this threshold except that it approximates to our annual background exposure and so has a 'level of comfort'. If life on earth has evolved in an environment with this exposure, it would be surprising to find large effects at this level.

(iv) Where guidelines provide a range, the actual dose used should be chosen from a personalized assessment of risk and benefit. There are some studies of the effect of dose on imaging outcome, but more studies would be helpful to cover all circumstances.

What are the imaging needs in heart failure?

It is important to consider the pathogenesis of heart failure and the clinical questions associated with each stage of the syndrome. MPS using SPECT and PET remains strong in the diagnosis of underlying ischaemic heart disease and the assessment of myocardial function, viability, ischaemia, and hibernation. More recent data demonstrating the ability of mIBG scintigraphy to assess the risk of cardiac death, arrhythmia, and disease progression have still to find widespread clinical application (*Figure 5*),[8,13–17] mainly because of the value of cheaper techniques such as measuring left ventricular ejection fraction and brain natiuretic peptide. The possibility that the detection of mechanical dyssynchrony by imaging might identify patients who will benefit from resynchronization pacing is an area of research interest.[11]

Consensus points

(i) The assessment of left ventricular dyssynchrony and the imaging of myocardial sympathetic innervation have the potential to refine patient management but, without studies of clinical outcome, they may not be used more widely.

(ii) Although a sizable minority of patients with guideline-indicated CRT do not respond to the intervention, it has not yet been demonstrated that selection for CRT based on the measurement of dyssynchrony can be more specific.

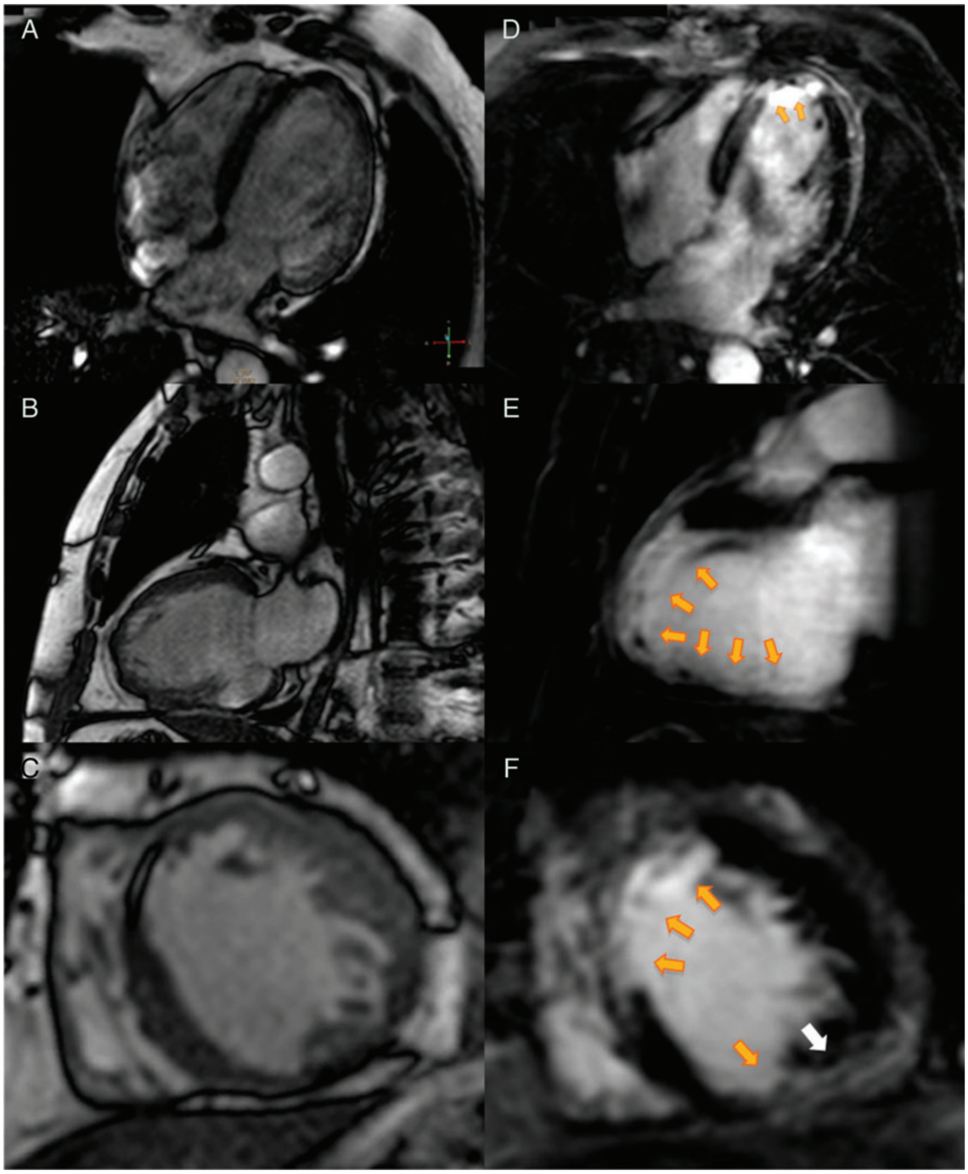

Figure 4: Assessment of myocardial scarring in ischaemic heart disease with impaired left ventricular function being assessed before resynchronization pacing. (*A–C*) Cine cardiovascular magnetic resonance (CMR) showing severe LV dysfunction, with akinesis and thinning of the antero-septal and infero-lateral regions. (*D–F*) Delayed contrast enhancement CMR showing transmural scarring in the same areas (orange arrows) and partial thickness scarring in the basal inferior wall (white arrow). The absence of scar in the lateral wall suggests that effective pacing is possible at this site. (Adapted from: Advanced approaches in Echocardiography. Series Editor, Catherine Otto, Elsevier 2011, Chapter 12, pp. 199–246).

(iii) Similarly, mIBG imaging to predict the need for ICD is promising, but randomized trials to assess clinical outcome would be required before the technique could be incorporated in guidelines.

What are the educational needs in cardiac imaging?

Cardiac imaging is now in effect a subspecialty, to some extent separating those who request the techniques from those who deliver them.[12] This applies whether the provider of imaging is a cardiologist, a nuclear physician, or a radiologist. Sub-specialization within medicine is not accepted in some countries, but this is the direction of travel. Education is important for referrers and providers to ensure that the most appropriate test is requested, and that it is performed in an optimal fashion. Subspecialty training is available at a local, national, and international level in Europe and in other continents, but the quality of nuclear cardiology practice is variable and has disadvantaged the subspecialty. A widely accepted subspecialty qualification in nuclear cardiology and in the other imaging

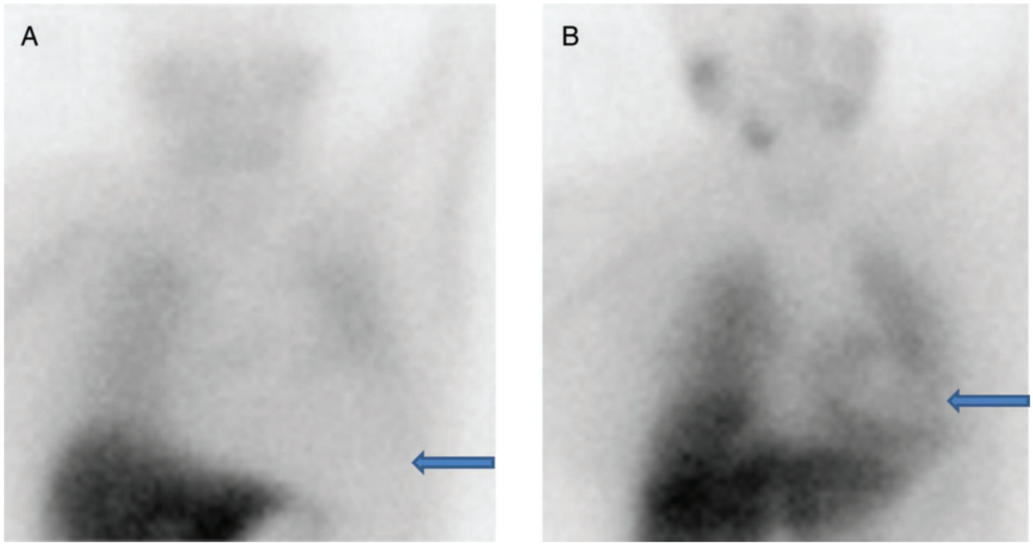

Figure 5: Cardiac mIBG scintigraphy. These are anterior planar images 4 h after the injection of mIBG in two patients with heart failure. (*A*) There is absent uptake within the myocardium (arrow) with a heart to mediastinal ratio of 1.08. (*B*) There is a regional defect of mIBG uptake in the anterior myocardium corresponding with previous infarction (arrow), but myocardial uptake is otherwise preserved with heart-to-mediastinal ratio 1.73. The ADMIRE-HF study used a threshold of 1.6 to separate high- (<1.6) and low-risk groups (>1.6).

techniques would be of great benefit to the profession and to our patients.

Consensus points

(i) A subspecialist in cardiac imaging will have knowledge of all imaging techniques and expertise in more than one.
(ii) Education in cardiac imaging must involve multiple specialties, including cardiology, nuclear medicine, radiology, and medical physics.[13,14]
(iii) Imaging education should be focused on solving clinical problems and benefitting patients.
(iv) Education is most appropriately provided at the local level, but regional, national, and international initiatives are helpful to standardize practice.
(v) There is a need for societies and meetings related to individual techniques as well as of associations directed at clinical problems. Collaboration is more productive than competition between specialities and techniques.
(vi) The interests of patients, clinicians, imagers, and industry can potentially conflict. It is the mark of a mature professional to work with all relevant partners in the best interests of the patient.

Conclusions

A complete assessment of many cardiac disorders, particularly CAD, requires both anatomical and functional information. This can be obtained in a variety of ways and the common imaging techniques overlap in their capabilities, particularly for the assessment of myocardial viability, function, and coronary anatomy. NICE guidance in the UK on the assessment of patients newly presenting with possible angina states that the accuracy and cost of the techniques are similar, and that choice between them can be based on local availability and expertise.[18] While their accuracy might be similar in ideal hands, it is not known if the newer perfusion techniques perform as well in the real world and there have been no robust comparative studies of cost effectiveness. Each of the techniques is supported by appropriateness criteria that overlap in the common ground of patients with an intermediate likelihood of coronary artery disease (CAD).

One important difference between echocardiography, nuclear cardiology, cardiovascular MRI, and CT is that they have been developed in the hands of different specialists, such as cardiology, nuclear medicine, or radiology. Professional and financial considerations mean that a technique is more likely to be used if it is in the hands of the referring physician. Thus, in some cases, the choice is made in the best interests of the doctor rather than the patient. There are considerable differences between countries in this regard. The interests of the imaging industry have also in some cases influenced the development of techniques. Such a situation should not prevail.

The group agreed that a balanced use of cardiac imaging will best be achieved by education of users and providers of imaging services, and that this should be independent as far as possible of the background training of the specialist, be it cardiology, nuclear medicine, or radiology. The group was also optimistic that increasing collaboration between specialists and subspecialists would allow the best interests of the patient to prevail and the impressive developments in all areas of cardiac imaging in recent years to be translated into better outcomes for patients.

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Corrigendum

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Corrigendum to: 'Age-related risk of major adverse cardiac eventrisk and coronary artery disease extent and severity by coronary CT angiography: results from 15 187 patients from the International Multisite CONFIRM Study' [*Eur Heart J Cardiovasc Imaging* 2014;**15**:586–594, doi: 10.1093/ehjci/jet132].

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