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IMAGE

How to explore coronary artery disease?

Comment explorons-nous la cardiopathie ischémique?

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Background

Cardiovascular disease is the leading cause of mortality worldwide, and subsequent management of coronary artery disease (CAD) presents a major challenge to our healthcare system. Cardiovascular imaging plays a major role in CAD management, and recent technological advances have led to a multimodality approach. Cardiovascular medicine now benefits from a myriad of diagnostic methods to guide clinical decision-making and interventions, but from a medical point of view, it is important to propose a patient-centred strategy. In this setting, an update on the advantages and disadvantages of each cardiovascular imaging technique is of interest, to define the best strategies for our healthcare system.

Gold standard and new paradigm

Current evaluation of CAD is based on Bayes' theorem. The 2013 European Society of Cardiology guidelines on stable CAD emphasized the use of the pretest probability (PTP) of disease, and physicians should begin their evaluation

Abbreviations: CAD, coronary artery disease; CMR, cardiovascular magnetic resonance; CTA, coronary computed tomography angiogram; FFR, fractional flow reserve; PET, positron emission tomography; PTP, pretest probability; SPECT, single-photon emission computed tomography.

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Table 1 Clinical pretest probabilities in patients with stable chest pain symptoms [1].

	Pretest probability (%)					
	Typical angina		Atypical angina		Non-anginal pain	
Age (years)	Men	Women	Men	Women	Men	Women
30–39	59	28	29	10	18	5
40–49	69	37	38	14	25	8
50–59	77	47	49	20	34	12
60–69	84	58	59	28	44	17
70–79	89	68	69	37	54	24

using a pretest likelihood of disease (Table 1). When the PTP value is between 15% and 85%, a stress test assessing myocardial ischaemia should be performed at first intention, followed by invasive coronary angiography according to ischaemic burden and efficacy of optimal medical treatment. Guidelines provide a Class I recommendation for the use of ischaemia imaging before invasive angiography in symptomatic patients with a PTP of 15–85% [1]. Invasive coronary angiography with fractional flow reserve (FFR) is used as a new gold standard to diagnose CAD as a consequence of functionally significant stenoses [2].

All functional tests (stress echocardiography, single-photon emission computed tomography [SPECT], cardiovascular magnetic resonance [CMR] imaging and positron emission tomography [PET]) now have the same level of recommendation (Class IA). Stress echocardiography, SPECT, CMR and PET all yielded a high sensitivity for the diagnosis of CAD (defined as a stenosis $\geq 50\%$ documented by invasive coronary angiography or an FFR value < 0.80) [1]. Stress echocardiography and SPECT are widely available, and have been extensively validated; PET achieved the highest diagnostic performance; and CMR may provide an alternative without ionizing radiation, and with a diagnostic accuracy similar to that of PET [3–5]. Physicians should choose either one or other methodology, taking into account the local expertise and infrastructure and the patient's characteristics. This choice and its implementation also depend on the patient's preferences, relevant contraindications for each test and the ALARA (As Low As Reasonably Achievable) principle. Exercise stress testing is recommended rather than pharmacological testing whenever possible (recommendation class IC), which directs towards the preferential use of stress echocardiography or SPECT. Indeed, the physiological nature of exercise stress testing increases the imaging performance. However, submaximal exercise decreases the sensitivity for the detection of ischaemia and prevents accurate assessment of the extent of ischaemia, and it is important to achieve $\geq 85\%$ of the maximum heart rate. Consequently, alternatives to exercise stress testing are still used, such as dobutamine or persantine. Interestingly, the improvement in scanning technology has led to improved spatial and temporal resolutions with lower radiation doses, and thus the wide use of coronary computed tomography angiograms (CTAs) as a new interesting tool for cardiologists. Studies have established that CTAs have excellent sensitivity (95–99%) and high specificity (64–83%) for the detection of coronary stenoses $\geq 50\%$ [1]. CTAs are excellent tools for ruling out CAD in low-risk patients. However, large randomized clinical trials such as PROMISE [6] and SCOT-HeART at 5 years [7] have raised the question of redefining the role of CTAs in our strategies. Accordingly, the National Institute for Health and Care Excellence in the UK is now suggesting that a CTA is the most appropriate test in patients with stable chest pain [8]. Further studies are required, however, before achieving a paradigm shift. The main limitation of a CTA is its interpretation in elderly patients presenting with major coronary calcifications. Fig. 1 shows the different algorithms.

Progress made to address weaknesses

The limits and weaknesses of techniques are constantly being redefined. For example, administration of specific contrast agent over the course of stress echocardiography with suboptimal echogenicity improves endocardial visualization at rest, and so during stress, leading to greater accuracy in the assessment of CAD [9]. New SPECT cadmium-zinc-telluride cameras are significantly reducing imaging time and patient dosimetry, while providing higher-quality images [10]. Rubidium-82 PET myocardial perfusion imaging is being used more widely because of its superior diagnostic accuracy and availability without the need for an onsite cyclotron. CMR is a multiparametric imaging modality that yields high spatial resolution images that can be acquired in any plane for the assessment of global and regional cardiac function, myocardial perfusion and viability and tissue characterization, all within a single study protocol and without exposure to ionizing radiation. Stress perfusion CMR requires the induction of hyperaemia using a vasodilator, such as adenosine or dipyridamole, before the use of a gadolinium-based contrast agent for the assessment of myocardial perfusion. Large prospective randomized trials have demonstrated the relevance of perfusion CMR [11]. This powerful technique has several limitations, the main one being its limited availability. Other limitations include:

- the requirement for patients to hold their breath and remain still for prolonged periods during imaging;
- no exercise stress testing in routine practice with current device;
- specific training of physicians and technicians;
- high costs with long scan times;
- contraindications, such as claustrophobia, devices incompatible or severe renal dysfunction against injection of gadolinium-based contrast agent;
- the presence of dark rim artefacts during stress;
- severe arrhythmia decreasing CMR performance.

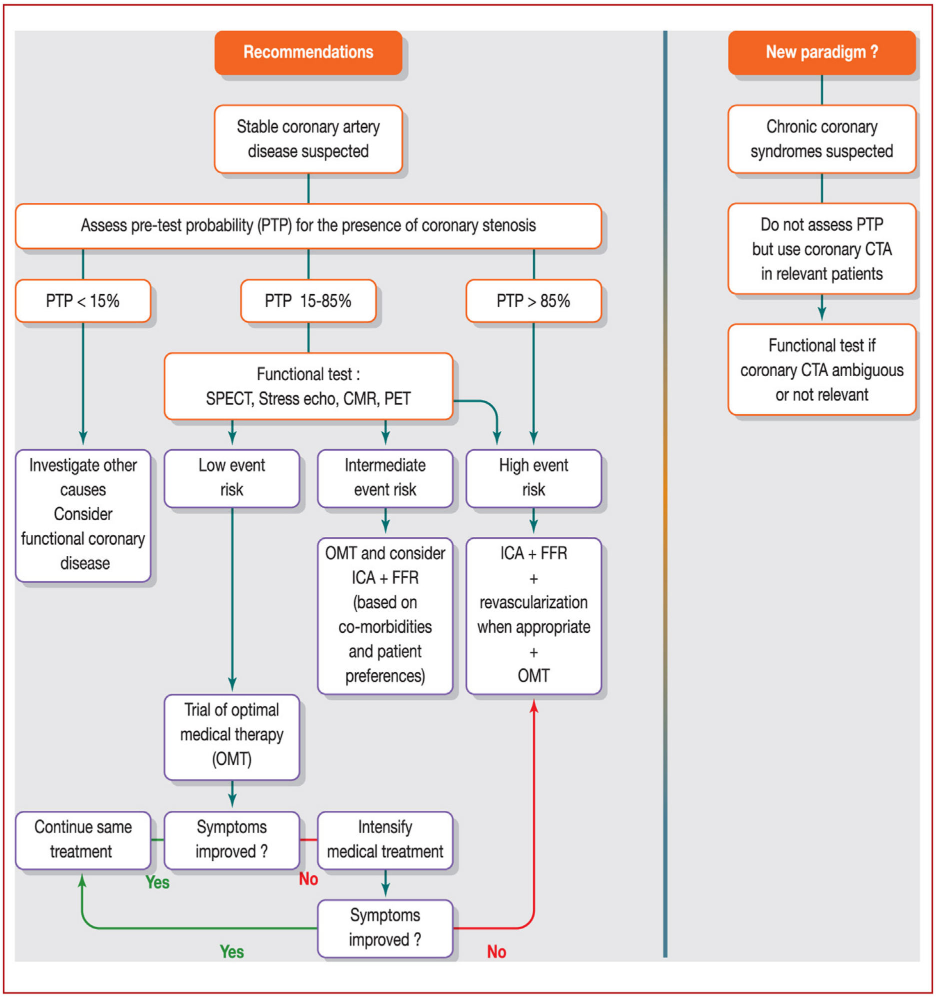

Figure 1. Algorithm for exploration of coronary artery disease. CMR: cardiovascular magnetic resonance; CTA: coronary computed tomography angiogram; echo: echocardiography; FFR: fractional flow reserve; ICA: invasive coronary angiography; OMT: optimal medical treatment; PET: positron emission tomography; PTP: pretest probability; SPECT: single-photon emission computed tomography.

Although 1.5 T is the standard field strength used in clinical CMR, imaging at the higher field strength of 3.0 T offers increased signal-to-noise and contrast-to-noise ratios, thereby providing improved spatial and temporal enhancements. However, the 3.0 T field strength involves greater field inhomogeneity, susceptibility artefacts and higher local energy deposition. Typical CMR perfusion imaging is currently performed using three short-axis slices of the left ventricle, and conventional stress perfusion CMR does not truly calculate the global ischaemic burden. Three-dimensional whole-heart perfusion imaging has been developed to achieve full coverage of the left ventricle used to calculate the global ischaemic burden [12]. A limitation of conventional CTA is its poor specificity regarding the haemodynamic significance of a given stenosis. This limitation is significant in light of emerging evidence for the relevance of invasive haemodynamic variables. CT perfusion and CT-FFR improve the performance of CT and could allow functional evaluation of a stenosis. Currently, clinical trial data with CT-FFR and CT perfusion are insufficient to make a recommendation for use in clinical practice [13]. Moreover, only one company offers CT-FFR analysis software approved for clinical use, which probably limits its use.

New technology

The use of non-invasive cardiovascular imaging to assess patients with CAD has benefited from new technologies in multiple ways, allowing improved or novel means of evaluating ischaemia. For stress echocardiography, specific contrast agent and semiautomatic methods less dependent upon operator expertise are being developed, whereas CT improvement is facilitated by spectral analysis [14]. By exploiting stress T1 mapping, CMR holds promise for the detection of ischaemia without the need for gadolinium [15]. Hybrid PET-CMR is emerging as a promising combination of the strengths of each imaging modality.

Technological advances to answer a clinical question

Technological progress is even more relevant when it turns out to be useful to address a lack of efficiency in the practitioner's daily practice. Strong evidence is now available that non-invasive imaging testing for obstructive CAD is more cost-effective when applied to patients with an intermediate likelihood of CAD. However, multiple recent studies have concluded that the Diamond and Forrester model leads to a significant overestimation of the PTP of obstructive CAD. In this setting, the use of calcium scoring to better evaluate PTP is interesting. During the past decade, the development of new tools to identify vulnerable atherosclerotic plaques has mobilized considerable energy, but no non-invasive methodology has emerged in clinical routine practice. Molecular imaging has the greatest potential for plaque detection through novel radiopharmaceuticals currently undergoing clinical translation. Although each imaging technique provides a method for the assessment of coronary reserve, ischaemia caused by coronary microvascular dysfunction remains a diagnostic challenge in general cardiology practice. Invasive methods such as FFR and the index of microcirculatory resistance can assess the severity of epicardial CAD and coronary microvascular dysfunction, respectively, but remain invasive methodologies. Interesting, new methods using CMR stress T1-mapping appear promising [15].

The future

It is difficult to decipher what the future of CAD imaging may be. However, it is likely that such a future will involve an evolution of imaging use in care, teaching and research, with continued appraisal of the added value of each imaging methodology within a patient-centred strategy, with more collaborations between academic and corporate partners, the establishment of bridges between disciplines [16] and the development of big data analysis and artificial intelligence [17].

Conclusions

Cardiovascular imaging benefits hugely from technological innovation. Simultaneously, the fundamental pathophysiological principles of ischaemia remain at the centre of CAD management strategies. Cardiologists must be aware of the strengths and weaknesses of each imaging methodology in order to follow a relevant patient-centred strategy.

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Disclosure of interest

The authors declare that they have no competing interest.

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