Current international guidelines for the investigation of patients with suspected coronary artery disease

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Patients suspected of having coronary artery disease (CAD) who present with new onset chest pain can be investigated by numerous diagnostic modalities. National and international guidelines have been drawn up to assist cardiologists in selecting the most appropriate investigation(s). Here, we summarize and compare three current guidelines and discuss the differences between them.

The UK National Institute for Health and Care Excellence (NICE) published its guidelines in 2010.1 The guidelines recommend that patients are categorized into ‘low’ or ‘high’ risk of CAD groups, depending on whether they have a cardiovascular risk factor (diabetes, smoking, and hyperlipidaemia). Patients are assigned a pre-test probability (PTP) score of having CAD based on risk category, age, gender, and typicality of chest pain. The guidance then suggests that patients with a PTP of <10% should not be investigated further. Patients with a PTP of 10–29% are recommended to undergo computed tomography (CT) calcium scoring. If the calcium score is above zero, it is recommended to proceed to a CT coronary angiogram (CTCA). If there is extensive calcification (calcium score of >400), a functional imaging test or invasive coronary angiography (ICA) is recommended. Patients with an intermediate PTP of 30–60% are recommended to have a functional imaging test; i.e. myocardial perfusion scintigraphy (MPS), stress echocardiography, or stress cardiac magnetic resonance imaging. Patients with a high PTP of 61–90% are recommended to undergo ICA, and patients with a PTP of >90% are assumed to have CAD without requiring further testing to make the diagnosis. The assessment of prognosis and management of patients diagnosed as having stable angina is covered in a separate guideline, which emphasizes the importance of secondary prevention and optimal medical therapy.2 According to this guideline, revascularization should be considered in all patients with confirmed significant CAD, particularly if they have ongoing symptoms on optimal medical therapy, on the basis of an informed discussion about the potential additional benefit.2

The European Society of Cardiology (ESC) published its most recent guidelines in 2013.3 Similar to NICE, the ESC guidelines incorporate a PTP model, including age, gender, and typicality of chest pain, but not cardiovascular risk factors. In the ESC guidelines, left ventricular ejection fraction (LVEF) serves as an additional parameter to guide the choice of investigation (Table 1). Based on their PTP, patients are divided into low, intermediate, and high likelihood of CAD. Patients with a low PTP of <15% are recommended to be investigated for other causes of chest pain. Patients with an intermediate PTP of 15–85% are further subdivided, based on LVEF and PTP. Patients with a PTP of 15–65% and LVEF ≥50% are recommended to have a functional imaging test and if not available an exercise electrocardiogram (ECG). Patients with a low-to-intermediate PTP of 15–50% and LVEF ≥50% can undergo CTCA as an alternative to functional tests. The ESC guidelines emphasize that the calcium score alone is not sufficient to rule out CAD. Patients with a PTP of 66–85% or LVEF <50% without typical chest pain are recommended to undergo functional imaging testing, whereas those with typical chest pain and LVEF <50% are recommended to undergo ICA. The management of patients with CAD confirmed on investigation(s) or those with a high PTP of >85%, who are assumed to have CAD, is dependent on an annual risk of mortality. This risk is calculated based on clinical assessment, LVEF, and anatomical and/or functional imaging test results. Patients are divided into low-, intermediate-, and high-event risk groups with annual mortality <1, ≥1 but <3, or ≥3%, respectively. According to the guidelines, low-event risk patients should be trialled on optimal medical therapy and further intensive medical therapy prior to ICA. Intermediate-event risk patients are trialled on optimal medical therapy with a low threshold to perform ICA. For high-event risk patients, referral for ICA with fractional flow reserve is recommended.

The American Societies of Cardiology (ASC) published their most recent guidelines in 2012.4 In these, the patient’s ability to exercise, interpretability of resting ECG, and contraindication to stress testing dictate the choice of investigation. Importantly, while the
ASC guidelines include the PTP model, they do not propose cut-off values to differentiate between mild, intermediate, and high likelihood of CAD. Patients able to exercise with interpretable resting ECGs and low or intermediate likelihood of CAD are recommended to have exercise ECG. Patients able to exercise with uninterpretable ECG or those with intermediate-to-high likelihood of CAD are recommended to have a functional imaging test. Patients with low-to-intermediate PTP, who are unable to exercise, or those with a contraindication to stress testing may also undergo CTCA as an alternative to stress testing. Patients diagnosed with CAD, after investigation, are initially treated medically unless findings are suggestive of high-risk CAD or patients remain symptomatic despite optimal medical therapy, in which case ICA is recommended.

Discussion

There are important similarities and differences between the three guidelines. NICE and ESC have incorporated the Duke Clinical Score and a modified Diamond–Forrester Method PTP model, respectively, to select the appropriate investigation, whereas the ASC acknowledged the PTP models, but recommended the use of clinical judgment to define the likelihood of CAD.\(^5\,^6\) The PTP scores have consistently been shown to overestimate the likelihood of CAD, for example in the international registry, CONFIRM, in 14 048 patients who underwent CCTA.\(^7\) In an attempt to reduce this overestimation, the ESC guidelines use the modified Diamond–Forrester Method which adjusts the likelihood of CAD for a more contemporary European patient population.\(^4\) This is important in view of the lower prevalence of CAD, especially in primary care populations.

A further difference between the guidelines is the role of the exercise ECG. The ASC guideline recommends exercise ECG for patients with a low and intermediate likelihood of CAD. The ESC recommends exercise ECG in the same subgroup of patients, but only if there is limited local availability for functional imaging tests. NICE went further and recommended that the exercise ECG should no longer be used in the diagnosis of CAD. The rationale for NICE and ESC to move away from recommending the exercise ECG is its lower sensitivity and specificity, compared with imaging tests, that leads to a higher rate of second-line investigations, particularly ICA and thus higher follow on costs despite the lower upfront cost of the test.\(^8\)

Importantly, all three guidelines have introduced cardiac CT for the first time. The recommendation was limited to patients with low PTP in NICE and as an alternative to functional testing in patients with low and intermediate PTP in both ESC and ASC guidelines. The inclusion of cardiac CT in the guidelines reflects its emerging role as a highly effective rule out test, with an excellent negative predictive value (NPV).\(^9\) However, the evidence for cardiac CT is still unfolding with major trials such as PROMISE,\(^10\) which randomized 10 000 to CTCA or functional imaging tests, to report by the end of 2014. The use of CT calcium scoring in the NICE guidelines is motivated by its low cost and lower radiation exposure, combined with an excellent NPV, equivalent to the NPV of CTCA, in populations with low PTP, which was recently demonstrated in the CONFIRM registry.\(^11\) The ESC, however, stated that the zero calcium score

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<tr>
<th>Table 1</th>
<th>Summary of NICE, ESC, and ASC guidelines</th>
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<tr>
<td><strong>NICE</strong></td>
<td><strong>ESC</strong></td>
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<tr>
<td><strong>CAD likelihood score</strong></td>
<td>Yes</td>
</tr>
<tr>
<td>Low CAD likelihood</td>
<td>10–29%</td>
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<tr>
<td></td>
<td>• Calcium score ± CTCA</td>
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<tr>
<td>Intermediate CAD likelihood</td>
<td>30–60%</td>
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<tr>
<td></td>
<td>• Non-invasive functional imaging (MPS, SE, or CMR)</td>
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<td></td>
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<tr>
<td>High CAD likelihood</td>
<td>&gt;85%</td>
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<td></td>
<td>• Low risk (mortality &lt; 1%/year)—trial OMT</td>
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<tr>
<td></td>
<td>• Intermediate risk (mortality ≥ 1% and &lt; 3%)—OMT ± ICA</td>
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CAD, coronary artery disease; CTCA, CT coronary angiography; SE, stress echocardiography; MPS, myocardial perfusion scintigraphy; CMR, cardiac magnetic resonance; ICA, invasive coronary angiogram; OMT, optimal medical therapy; LMS, left main stem; CP, chest pain.

*Any patient with prior sudden death or serious ventricular arrhythmia or prior stent in unprotected LMS.
was not sufficiently accurate to rule out CAD. As the radiation dose for CTCA on modern CT scanners continues to drop, it is often only marginally higher than for the calcium score, which may well be reflected in future guidelines.

Finally, NICE attempted to limit the use of ICA, by limiting it to patients with a high PTP. However, this has been undermined by the mounting evidence that PTP models overestimate the incidence of CAD. The ESC guidelines on the other hand recommend ICA for those with a positive functional imaging test and a high-event risk or those who fail medical therapy in the lower event risk groups, whereas the ASC guidelines recommend ICA for patients who have failed medical therapy. The trend in all three guidelines is to try to limit the use of diagnostic ICA. This is important as a recent large American registry demonstrated that only 37.6% of patients undergoing diagnostic ICA had obstructive CAD.

In summary, all three guidelines are based on a similar framework that takes into account the PTP and the diagnostic accuracy of the tests in the different PTP groups. The PTP models, including the modified Diamond–Forrester used by the ESC, were derived from patient populations in tertiary settings with a high prevalence of CAD that overestimate the prevalence of CAD in primary care populations. In addition, there is an European trend to move towards more functional imaging tests such as PROMISE and EVINCI. The guidelines do not specify preferred functional imaging tests within population subsets, due to the lack of large comparative studies. The USA has traditionally used functional imaging tests, predominately MPS, much more widely, with huge cost implications and increased radiation burden to the population from multiple testing. Hence, the ASC guidelines appear to be curbing the use of MPS by substituting it with exercise ECG. Studies comparing the outcomes of cardiac CT and functional imaging tests such as PROMISE and EVINCI will help clarify the optimal diagnostic test and will help refine future guidelines. For now the differences between the guidelines outlined above give cardiologists a degree of clinical freedom to choose the diagnostic tests based on local availability, local expertise, and local prevalence of CAD.

References