Invasive coronary angiography (ICA) remains an essential component of the diagnostic workup of patients with suspected stable angina. The availability of ICA has increased significantly since it was first performed in the 1960s with remarkable improvements in efficiency and safety. The diagnosis of coronary artery obstruction is readily made anatomically, and its suitability for revascularization by percutaneous or surgical intervention can also be assessed. Therefore, ICA not only provides a diagnosis but it can also be a step towards treatment. Despite being unable to demonstrate athromata that does not encroach upon the arterial lumen, this invasive procedure is still a common standard for the diagnosis of coronary artery disease (CAD), particularly when assessing the efficacy of alternative diagnostic techniques.

Because treatment decisions partly depend upon the angiographic appearance of disease, ICA is often the initial diagnostic test in suitable patients with a high likelihood of obstructive disease causing their symptoms. However, this may not be appropriate in all cases for several reasons. One of the most important is the low power of the clinical history for predicting the likelihood of obstructive CAD, caused by the complex relation between symptoms, myocardial ischaemia, and coronary luminal narrowing. Classical angina, although highly specific, is reported by only a minority of patients with significant CAD, and atypical features are common. Thus, in stable symptomatic patients, routine ICA would result in an unacceptably high number of normal angiograms while denying ICA to patients with less convincing symptoms may lead to misdiagnosis with potentially fatal consequences. When patient selection relies entirely on the clinical history, ICA performs poorly. To refine patient selection, particularly in patients at an intermediate likelihood of CAD, some form of coronary functional testing is an important initial step, not least because true angina is a disturbance of coronary function rather than coronary anatomy. However, a preliminary exercise ECG still results in a low diagnostic yield for ICA because of its relatively poor sensitivity and specificity for predicting anatomical abnormalities. Recent work supports these earlier observations with a normal angiogram rate of nearly 40% even after an initial non-invasive test. Importantly though, patients with abnormal functional testing are more likely to have angiographically significant CAD than those without prior functional testing.

This brings us to the study of Buechel et al., in this issue of the Journal, who investigated myocardial perfusion scintigraphy (MPS) in a cohort of patients who underwent ICA for suspected CAD. Angiographically significant coronary artery stenosis (defined as ≥50% luminal diameter reduction) was found in just over half of patients. A similar low yield has been reported previously with just over 40% having obstructive CAD and, when the definition of angiographically significant CAD was narrowed to stenosis ≥70%, the proportion of abnormal angiograms fell to 38%. Another recent study reported a similarly low diagnostic yield with a high variation in the rate of normal angiograms (18–77%) across 17 hospitals in Ontario, Canada.

In the Buechel study, only 1773 of 7530 patients (24%) underwent functional assessment by MPS before ICA, which is similar to the use of functional imaging before elective ICA in another study that investigated the relationship between non-invasive imaging and downstream use of resources in 224 hospitals in the USA. The rate of non-invasive imaging varied significantly from 0.2 to 56% with a median of 20%. Of note, just over 80% of all imaging was MPS.

In the current study, the rate of abnormal angiograms was almost 30% higher in patients with abnormal MPS than in those who appeared to have undergone ICA without prior documentation of myocardial hypoperfusion or ischaemia. Abnormal MPS was also incrementally predictive of angiographic disease over and above symptoms and CAD risk factors. These results are consistent with previous studies, and they support the role of MPS as a gatekeeper to ICA. Abnormal MPS not only informs physicians about the presence of functionally significant CAD but also characterizes ischaemia by showing its location, extent, and depth. It is the best validated method of assessing ischaemic burden, which is a combination of the extent and depth of ischaemia and is expressed as percentage of the left ventricular myocardium. In turn, the ischaemic burden relates to the extent of coronary atherosclerosis and plaque burden, and it has independent prognostic value with a total ischaemic burden >10% identifying patients at high risk of cardiovascular death (>3% per year) and who may benefit most from revascularization. Hence, contemporary MPS provides a semi-quantitative assessment of coronary function, myocardial viability, and ventricular function that can rationalize the decision to proceed to ICA or...
otherwise. Moreover, highly abnormal scans alert physicians to the potential for extensive disease and can assist in triage of high-risk patients to early invasive investigation and potential revascularization.

There are two important results to note from this study. First, a lower than expected proportion of patients underwent non-invasive imaging before ICA. Numerous publications have shown that stress imaging, and in particular MPS, helps to reduce the number of unnecessary angiograms by discouraging further testing in patients with a normal scan. Normal MPS predicts a low rate of coronary events particularly in low-to-intermediate likelihood patients. On the other hand, abnormal MPS increases the probability of significant and potentially treatable coronary stenosis on angiography. Current guidelines and appropriateness criteria have been configured on the basis of this evidence, and non-invasive testing is rated as highly appropriate in the initial assessment of patients with suspected stable angina. Furthermore, the value of coronary function assessment has been confirmed from studies using fractional flow reserve (FFR). These have confirmed the poor relationship between coronary anatomy and function, and have provided strong evidence that intervention guided by coronary function improves clinical outcome and that revascularization of functionally insignificant lesions can be deferred without clinical or prognostic detriment.

Second, the rate of MPS did not change significantly with presenting likelihood of CAD. According to Bayes’ theorem, patients with an intermediate likelihood of disease benefit most from diagnostic testing and so greater use of MPS would be anticipated in these patients. This introduces another important finding: patients who underwent initial angiography had a slightly lower likelihood of CAD than those who had initial MPS. Patel et al. also found that non-invasive testing was performed before angiography more often in patients with a high than intermediate or low likelihoods. These observations suggest that other factors have a significant influence on decision-making. Indeed, Lin et al. indicated that the collective effect of physician- and hospital-related factors can be larger than patient characteristics and clinical history in predicting the strategy of investigation before percutaneous coronary intervention. The recent study of Safavi et al. suggests that more frequent non-invasive imaging might not translate into efficient use of resources if the findings are not heeded.

A strategy that uses ICA as the initial diagnostic test can be effective but costly. An economic evaluation was not part of the current study, but the potential costs of the findings are worth considering. In line with previous reports, the recently published CECaT trial demonstrated that upfront ICA was the most expensive procedure of four diagnostic pathways that included MPS, CMR, and stress echocardiography in the assessment of patients with suspected angina after the exercise ECG. Moreover, 3 years after the initial assessment, the group randomized to MPS had the lowest mean cost of all strategies. In terms of cost-utility, all strategies had similar quality-adjusted survival rates, but MPS was the only strategy likely to be cost-effective compared with ICA alone. From an economic perspective, therefore, the CECaT trial supports an MPS-guided strategy in the diagnosis of patients with suspected CAD. Other comparative cost-effectiveness studies support MPS in preference to other forms of functional imaging, but it is becoming increasingly clear that large-scale economic evaluations are needed to establish the relative cost-effectiveness of functional and anatomical imaging-led strategies in the initial assessment of patients with suspected CAD.

The work of Buechel et al. is relevant to current European practice, and it adds new data confirming that reliance on ICA for the diagnosis of CAD is not in the best interests of all patients. It has shown that non-invasive imaging enhances the diagnostic performance of ICA by identifying patients who are more likely to have clinically relevant and potentially treatable lesions. It is widely accepted that revascularization decisions are best made with knowledge of both coronary anatomy and function and that functional imaging can be a reliable gatekeeper to invasive angiography, primarily from an estimate of ischaemic burden. However, the small number of patients undergoing functional imaging before angiography is at odds with current guidelines. It is therefore time to shift our attention from imaging efficacy to understanding the wider factors that influence decisions on diagnostic testing in patients with suspected CAD. These include not only local expertise and custom but also issues of inter-professional rivalry and reimbursement. We are all susceptible to self-interest, but our primary aim must be the best interests of our patients, and the application of the increasingly strong evidence that tests of coronary function and anatomy are equal partners that may both be required for optimal management.

Conflict of interest: None declared.

Funding
S.R.U. receives research funding from Spectrum Dynamics Medical Ltd, Israel, and share options from Rapidscan Pharma Solutions, Inc.

References
Simultaneous huge apical left ventricular diverticulum and a narrow annulus over the narrow neck

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Clinical message
A 5-year-old boy was referred to our institution for a cardiac murmur discovered at birth. The electrocardiogram revealed sinus rhythm, ST-segment depression with T inversion in leads V2–5. Two-dimensional echocardiography in apical four-chamber view showed a huge (38 × 23 mm) horseshoe-shaped apical left ventricular diverticulum with normal contractility. In addition, a narrow annulus (8 mm) was found over the narrow neck (Panel A, arrowhead, see Supplementary data online, Video S1). In diastole, blood flow entered towards the diverticulum from LV (Panel B, Supplementary data online, Video S2); while in systole, blood flow flowed out from the diverticulum (Panel C, arrowhead, Supplementary data online, Video S2). Acceleration through the narrow annulus with a peak velocity of 2.5 m/s was revealed by continuous Doppler spectrum (Panel D). Three-dimensional echocardiography facilitated clear visualization of the structure and characteristics of the annulus, and its area was ~1 cm² (Panel E, Supplementary data online, Video S3). These findings were confirmed by cardiac magnetic resonance (CMR) cine images [Panels F and G, arrowhead, in diastole (Panel F) and in systole (Panel G), Supplementary data online, Video S4]. It was apparent that the diverticulum had sufficient myocardial thickness and also contracted. Three-dimensional (3D) volume rendering post-processed images of the heart demonstrated a huge apical left ventricular diverticulum with a narrow annulus over the narrow neck (Panel H, arrowhead). The patient’s parents refused to undergo an operation and preferred conservative management, so medical follow-up was planned. Left ventricular diverticulum should be distinguished from LV aneurysm and pseudoaneurysm that are akinetic or dyskinetic outpouchings, and ventricular herniation.

Conflict of interest: None declared.

Panel A: Apical four-chamber view of two-dimensional echocardiography showing a huge apical left ventricular diverticulum, which communicated with the left ventricular through a narrow neck. In addition, there was a narrow annulus (arrowhead) over the narrow neck.

Panel B and C: Color Doppler echocardiography showed that blood flow was entering towards the diverticulum from left ventricle during diastole (Panel B) and was flowing out during systole (Panel C, arrowhead).

Panel D: High-speed blood flowing through the narrow annulus was showed by Continuous Doppler echocardiography.

Panel E: Three-dimensional echocardiography facilitated better border delineation of the annulus.

Panel F and G: Cine CMR, in diastole (Panel F) and in systole (Panel G), showing the diverticulum had sufficient myocardial thickness with normal contractility and a narrow annulus (arrowhead) over the narrow neck.

Panel H: 3D volume rendering post-processed images of the heart showed a huge apical left ventricular diverticulum with a narrow annulus (arrowhead) over the narrow neck. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; D, diverticulum.

Supplementary data are available at European Heart Journal – Cardiovascular Imaging online.

doi:10.1093/ehjci/jey079
Online publish-ahead-of-print 7 April 2015