


openheart Gold standard for diagnosing and treating chronic ischaemic coronary artery disease and the associated complications

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In this issue of *Open Heart*, an appealing manuscript titled ‘Dobutamine stress echocardiography (DSE) after positive CCTA: diagnostic performance using fractional flow reserve and instantaneous wave-free ratio as reference standards’ by Brătenu *et al*¹ was published.

DIAGNOSTIC ACCURACY OF INVASIVE AND NON-INVASIVE TESTING

The study by Brătenu *et al*¹ showed that the accuracy, sensitivity and specificity of dobutamine stress echocardiography (DSE) were 61%, 43% and 75% against fractional flow reserve (FFR) and 64%, 46% and 74% against instantaneous wave-free ratio (iFR) in 102 patients with positive coronary CT angiography (CCTA), with low to medium pretest probability (23±13). The diagnostic accuracy of DSE did not differ significantly between FFR and iFR as the reference (p=0.549).

One of the strengths of this study is the challenging question that the authors clearly outlined, giving some historical perspective: what are the gold standards for diagnosing coronary artery stenosis and their prognostic significance in ischaemic heart disease?

Stress echocardiography has long been a strong determinant of the significance of coronary artery stenosis and risk stratification for future events. However, it has some shortcomings, including its suboptimal acoustic window, the importance of matching cross-sectional planes prestressor and poststressor, and its operator dependence; it is also time-consuming in the era of fast food, like old grandma's chicken soup. All these led to the development of FFR by Dr Nico Pijls and others,² which was tested against stress echocardiography to determine the cut-off values. The intention was to have a one-stop shop in the cath lab rather than relying on stress

echocardiography. The industry jumped in with their interest, resulting in more support for randomised controlled trials (RCTs) for FFR (iFR, etc)³ than for stress echocardiography. Eleven trials, including some meta-analyses, demonstrated that FFR is more effective than angiography in guiding percutaneous coronary intervention (PCI). However, there are five trials, all RCTs, with negative results.⁴ It is worth noting that no individual RCT compares stress echocardiography with FFR or iFR in terms of decision-making. There is one retrospective non-randomised trial that has shown the superiority of stress echocardiography (using DSE segmental wall motion abnormality) over FFR in the risk stratification, regardless of whether PCI was performed or not.⁵

Nevertheless, in the latest ‘2024 European Society of Cardiology Guidelines for the management of chronic coronary syndromes’,³ FFR is determined to be of class 1, level of evidence A, while stress echo is of class 1, level of evidence B.⁶ Of particular note is the fact that reference 1173 in the guidelines concludes that stress echocardiography has no value post-PCI.⁷ This conclusion was false as only 0.59% (10 out of 1706) of patients underwent stress echocardiography. It is even more misleading as these numbers are not in the manuscript but was only discovered by someone curious enough to search for it in the supplement.

So can someone believe that stress echocardiography with left ventricular volumetry (power index), lung ultrasound (B-lines), heart rate reserve and the possible addition of coronary velocity flow reserve of the left anterior descending artery (the so-called ABCDE protocol) may be a better diagnostic and risk stratification tool for major adverse cardiovascular events and all-cause mortality than just

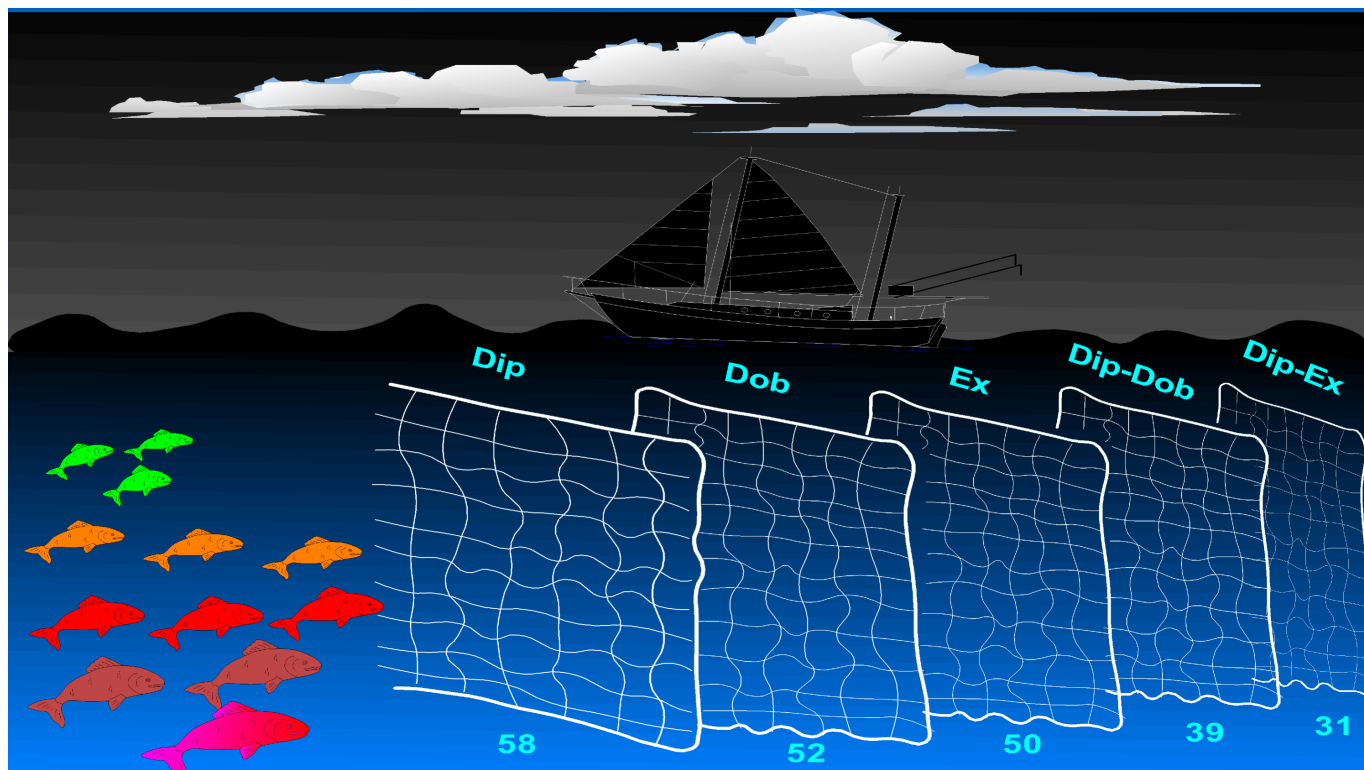


Figure 1 The fisherman approach. No CAD up to very severe CAD are presented as small fish (green) up to the biggest ones (purple), respectively. The nets with holes of different sizes, from the biggest up to the smallest, that is, dipyridamole (Dip), dobutamine (Dob), exercise (Ex), Dip–Dob and Dip–Ex, are presented. The ‘size of the holes’ for each stress was determined at the optimal cut-off between sensitivity and specificity where coronary angiography was used as the gold standard for each particular test in the same set of patients (204 tests in random order in 158 patients, 23 pre-PCI and post-PCI). It may be appreciated that the cut-off for Ex was exactly 50% stenosis (as postulated in animal experiments); for Dip, Dob, Dip–Dob and Dip–Ex, the cut-offs were 58%, 52%, 39% and 31%, respectively. Therefore, if the interest is just to catch a big fish, Dip will be used. CAD, coronary artery disease; PCI, percutaneous coronary intervention.

one number, that is, FFR or iFR? There is a lot of ongoing research on advanced stress echocardiography^{8 9} and adopting and implementing new findings into practice is not easy. Although it may sound too pessimistic, 1918 Nobel Prize winner Max Planck’s quote is still relevant: ‘The new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die and a new generation grows up that is familiar with it’.

Of particular note is that not all stressors are equal in terms of their existence in real life (exercise, mental and cold stress, hyperventilation, shovelling snow, etc), including the so-called pharmacological stressors, which are more suitable in imaging (but patients do not inject dobutamine, atropine, adenosine, etc, in everyday life). They act on different demand–supply scales and may be allies. A metaphor using the fisherman approach is depicted in [figure 1](#).^{10 11}

COMPLICATIONS OF TESTING IN THE REAL WORLD

Another strength of this study is its detailed reporting of the complications and side effects associated with both invasive and non-invasive testing during the typical work-up of an average patient with chronic coronary

syndrome. It is well recognised that diagnostic tests described in scientific literature often demonstrate lower accuracy and safety when applied in real-world settings that involve actual patients, physicians and challenges. This applies to both non-invasive and invasive testing.

In the case of dobutamine stress testing, the results in one patient were uninterpretable due to poor image quality at rest, while another test was terminated prematurely due to supraventricular tachycardia. Additionally, two patients experienced myocardial infarction during the test. One patient suffered brainstem cerebral infarction during invasive coronary angiography with pressure measurements. Another patient developed a transient third-degree atrioventricular block during infusion of adenosine.

On average, patients received a median radiation dose of 5 millisieverts (mSv) from coronary angiography with PCI, 4 mSv from CCTA and 2 mSv from diagnostic coronary angiography with intracoronary pressure measurement alone. While these doses are low compared with the reference values, the cumulative dose for the 104 patients enrolled in the study exceeded 10 mSv, equivalent to 500 chest X-rays, with associated long-term cancer risk of around one extra cancer in 1000 exposed patients. The

risk of cancer is higher in organs receiving the highest doses during cardiology examinations, such as the lungs, red bone marrow and female breasts. Additionally, there is a risk of acute anaphylaxis and subacute nephrotoxicity from the iodinated contrast material used in both diagnostic and interventional radiology.

Recently, and particularly in the era of climate-conscious healthcare, the environmental impact of cardiology imaging has also gained attention. The full suite of invasive and non-invasive testing generates at least 300 kg of carbon dioxide emissions. Although freedom does not have a price, it is just very small part of the carbon dioxide produced by wars and its consequences. However, everybody has to clean in front of their house. The direct economic cost of these procedures is substantial, the complication rate of invasive and non-invasive procedures exceeds 1%, radiation burden and the associated long-term cancer risk are not negligible, and subacute nephrotoxicity induced by iodinated contrast remains a potential risk.¹²

CONCLUSION

The abovementioned factors must be carefully considered when pursuing extensive non-invasive and invasive testing, particularly considering the extra stenotic factors contributing to coronary risk and the blind spots of anatomical or functional assessments based only on regional wall motion. The substantial value of simultaneously searching for pulmonary congestion (B-lines), global systolic function (volumetric calculations for power index), coronary microcirculatory dysfunction and cardiac autonomic dysfunction, among others, could not be overemphasised. The extra information that cardiac imaging provides should also be weighed against the robust risk stratification capability of a simple stress ECG. This test offers an integrated risk assessment based on symptoms, blood pressure response, chronotropic incompetence, arrhythmias and ST-segment changes.

Recognising that these costs, risks and environmental impacts stem from diagnostic investigations, not from calculating therapeutic interventions, is essential. Therefore, reassessing current strategies that incorporate broader considerations, such as non-cardiological risks (including cancer), economic costs, environmental impact and real-world complications, may lead us to adopt a 'Choosing-Wisely' approach to managing coronary patients. The risk to benefit ratio of current testing strategies may shift when evaluating intermediate-risk populations, where diagnostic performance is often suboptimal, and when factoring in both acute and long-term risks. In this regard, an optimal testing strategy for coronary artery disease that minimises costs and risks while maximising benefits remains a significant challenge.

A final note: The results of the study may be interpreted as real-world findings. They also come from the most experienced radiologists, stress echocardiographers and invasive cardiologists and a substudy of the more significant projects from Norway. Norway has one of the best health systems

available to citizens, which very well contributed to the country's ranking as the seventh happiest country in the world.

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