EDITORIAL

Apples and oranges in coronary artery disease diagnostics

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Related article
by Dębski et al.

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DOI: 10.33963/KP.a2023.0044

Received:
January 3, 2023

Accepted:
January 3, 2023

Early publication date:
February 15, 2023

Coronary artery disease (CAD) is the most common type of heart disease and causes morbidity and mortality globally despite advances in medical and procedural therapies [1]. The diagnostic pathway for stable CAD includes non-invasive tests before invasive testing to diagnose patients with stable chest pain and a low or intermediate probability of CAD. The current European Society of Cardiology (ESC) Guidelines for the diagnosis and management of chronic coronary artery syndromes recommend coronary computed tomography angiography (CTA) for patients with a low clinical likelihood of obstructive CAD and ischemia testing, preferably by imaging, in patients with a high likelihood of CAD [2]. Whereas CTA focuses only on anatomical information, the non-invasive imaging technique, computed tomography (CT) derived fractional flow reserve (CT-FFR), combines both anatomical and functional information based on standard CTA.

Risk stratification and diagnostics are conducted to confirm or rule out stable CAD. The vast majority of these patients do not have CAD. Even in patients with CAD, a large proportion does not need revascularization. Many patients undergoing invasive coronary angiography (ICA) after CTA have no indication for revascularization, meaning ICA could have been avoided. Both CTA and ICA involve the use of radiation and contrast media. Considering their possible detrimental effects on the skin, bone marrow, and kidney function, minimizing the utilization of radiation and contrast media would be beneficial to the patient [3, 4]. CT-FFR seems promising due to adding functional information to existing anatomic features without the need for additional scan time (radiation use) or contrast use [5]. Furthermore, selective ICA by means of visualizing the diseased vessel only might also reduce the need for radiation dose and contrast agent volume. A possible risk of this hybrid strategy can be found in missing significant coronary stenosis that requires revascularization.

In the current issue of *Kardiologia Polska* (*Kardiol Pol*, *Polish Heart Journal*), Dębski et al. [6] further refined this hybrid strategy by performing ICA only for the vessel that is significantly narrowed according to CT-FFR. The main objective was to assess the impact of a selective invasive approach (diseased-vessel-only) in patients undergoing ICA following coronary CTA and CT-FFR as compared to the standard of care (complete ICA). The study enrolled 100 consecutive patients who underwent ICA following CTA. ICA was performed if CTA findings suggested significant or borderline stenosis in an artery suitable for intervention in the presence of clinical symptoms suggestive of CAD or additional tests indicating cardiac ischemia. The diagnostic performance of CTA (including quantitative diameter stenosis analysis) and CT-FFR in the detection of significant CAD was assessed using ICA with quantitative coronary angiography (QCA) as reference. Diameter stenosis of at least 50% on CTA or ICA was defined as CAD. The authors observed an excellent diagnostic performance of CTA — sensitivity of 99%, specificity of 97%, positive predictive value (PPV) of 94%, and negative predictive value (NPV) of 100%. Beyond the diagnostic performance, a comparison of contrast agent and radiation use when performing the ICA strategy versus "diseased-vessel-only" ICA was made. Using CTA to guide ICA leads to a contrast volume reduction of 35% and estimated radiation dose

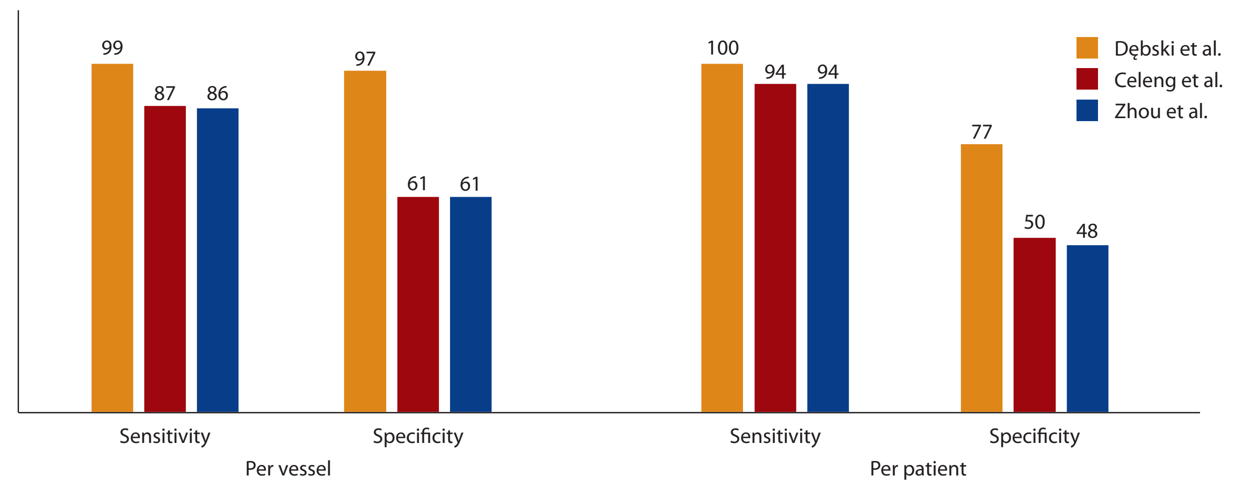

Figure 1. Sensitivity and specificity of computed tomography angiography for the detection of coronary artery disease (CAD). CAD is defined by angiographic stenosis >50%. Coronary computed tomographic angiography performance presented by Dębski et al. [6] is represented in orange. For the comparison, the results of the meta-analyses by Celeng et al. [7] and Zhou et al. [8] are displayed in red and blue. Data are given as percentages

reduction of 42%. Both can be further reduced when using CT-FFR — to 57% and 69%, respectively.

The results of the study by Dębski et al. [6] seem very promising, especially given the increasing numbers of patients undergoing CTA. However, the results should be interpreted with caution. First of all, in the discussion, the authors mention that the reported diagnostic values for both CTA and CT-FFR are similar to those found in previous studies. In fact, these are remarkably higher, particularly for CTA and especially since a threshold of 50% diameter reduction was used (Figure 1) [7, 8]. A possible explanation can be found in the selection criteria for the study. Only those patients who underwent ICA after a significant or borderline stenosis was identified on CTA were included, causing significant selection bias.

Secondly, for intermediate coronary stenoses (50%–90% diameter reduction), the correlation between anatomical stenosis severity and hemodynamic significance is not straightforward [9]. This is regardless of operator experience or the accuracy of stenosis severity assessment. A 50% diameter reduction can lead to impaired coronary blood flow while a stenosis of 80% might have no relevant impact. Especially with a threshold of 50% diameter stenosis used as a revascularization indication, there exists a significant risk of overtreatment. This is associated with worse long-term clinical outcomes. Therefore, the current guidelines recommend functional assessment of intermediary lesions to assess the revascularization indication [10].

The current standard for functional assessment is invasive fractional flow reserve (FFR), the ratio of blood pressure distal to a stenosis divided by the proximal pressure [2]. Imaging-based techniques that derive functional information from images, such as CT-FFR, are calibrated and verified against invasive FFR. However, in the study by Dębski et al. [6] a functional assessment was compared to an anatomical reference as revascularization indication was assessed with QCA. This is like comparing apples and oranges — they are not comparable. However, the authors are not alone in making this skewed comparison. When indicated, functional measurements such as FFR are only used in fewer than 20% of situations, and many studies assessing the diagnostic value of CT-FFR have compared this to QCA, or even visual estimates [11, 12]. The authors conclude that omitting those vessels that had <50% diameter stenosis on CTA and negative FFR-CT on ICA will not lead to missed diagnoses. This is difficult to assess based on those data alone as this study only included patients who underwent both CTA and ICA without functional measurements. Moreover, the future position of revascularization in the management of stable CAD is uncertain. Previous studies such as the ISCHEMIA [13] and ORBITA trial [14] showed that the actual benefit of revascularization in stable CAD might be smaller than previously thought.

To conclude: the future position of revascularization in stable CAD remains uncertain although the current guidelines still recommend revascularization of ischemia-inducing lesions. With the development of noninvasive assessments such as CT-FFR, functional assessments might finally make their way from the guidelines into routine clinical care.

Article information

Conflict of interest: None declared.

Funding: None.

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