Editorial

Comparative accuracy of myocardial perfusion imaging: The final answer has yet to come

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In patients with suspected or known coronary artery disease (CAD) the presence of stress-induced myocardial ischemia is still considered an indication for invasive coronary angiography (ICA) and, if needed, coronary revascularization. This management is based on the "dogma" that in patients with CAD the presence and extent of inducible myocardial ischemia predicts adverse cardiovascular events, and that the reduction of ischemic burden would have a favourable impact on patients' outcome [1]. These considerations have been further reinforced by recent data demonstrating the extremely low diagnostic yield of ICA, with only about one third of the patients showing CAD amenable for revascularization [2], stressing on the need for a better selection of patients with suspected ischemic heart disease (IHD). Based on current ESC guidelines on stable angina, the majority of patients with symptoms suggestive of IHD should undergo a non-invasive evaluation of myocardial ischemic burden, followed by ICA only in the presence of "extensive" myocardial perfusion abnormalities. However, while the same guidelines report comparably excellent diagnostic performances of the different imaging modalities for the detection of CAD, more recent reports have contradicted those beliefs [3,4]. Most of the evidences in this field come from the results of meta-analyses including largely underpowered single-modality studies, with only few data coming from comparative multi-modality imaging trials. Moreover, the definition of test positivity varies greatly for the different imaging modalities, with no real diagnostic standard being available [6]. While fractional flow reserve (FFR) has been adopted as the reference standard for the presence and quantification of CAD hemodynamic relevance, it was originally validated against other non-invasive imaging modalities, posing the conditions for "circular reasoning". Finally, the most appropriate cut-off value of FFR that should be used is a matter of debate, with recent evidence demonstrating that much lower values that 0.75–0.80 would be needed to impact significantly patients' prognosis [5].

In this number of the Journal Yang K et al., report the results of a meta-analysis comparing the accuracies in unmasking CAD of two available stress imaging strategies, cardiac magnetic resonance (CMR) and nuclear cardiac imaging, with either single-photon emission computed-tomography (SPECT) and positron emission tomography (PET) [7]. In The major quality of the study derives from having tried to select only studies using FFR as gold-standard for the definition of test diagnostic accuracy. The study included 14, 13, and 5 studies using CMR, SPECT, and PET respectively, with patients' populations ranging from 19 to 293 subjects each, the greatest majority of which being single modality investigations. The main results of the meta-analysis were that the three modalities had comparable specificities (≥85%) for the detection of significant CAD, while showing significant different values of sensitivity. In particular, SPECT imaging had a significantly lower sensitivity (AUC 0.69) than the two competitors (AUC: 0.83 for PET and 0.88 for CMR), particularly in patients with multivessel CAD. Interestingly, the differences in terms of overall diagnostic accuracy were much lower, probably because of the generally low prevalence of CAD in the included studies that favoured specificity over sensitivity.

The authors should be commended for their effort in providing some additional comparative data on the diagnostic abilities of some of the most trusted cardiac imaging modalities for the diagnosis of inducible myocardial ischemia. However, several limitations of the analysis should also be acknowledged, possibly limiting the generalizability of the results. First and foremost, in most of the included studies, FFR was performed only in a limited proportion of patients, such as in those with intermediate CAD on visual analysis (i.e. 50–75% stenosis). However, it is now clear that such restrictive criterion for performing FFR could result in the misclassification of a variable proportion of coronary lesions. As a matter of fact, in the recent PACIFIC study, whose results were surprisingly not included in the present meta-analysis, and in which FFR was measured in each coronary vessel, PET had the highest

accuracy in unmasking significant CAD, while SPECT maintained an adequate diagnostic power because of superior specificity [4]. Moreover, the studies included in the meta-analysis were not homogeneous in terms of positivity criteria used for the definition of ischemia, since both the results of qualitative and quantitative analyses were included. In particular, in only two small SPECT studies (64 patients in total) quantitative myocardial perfusion analysis was performed, while this was more frequently done in case of CMR (273 patients), and was obviously the rule for PET (545 patients). This aspect poses relevant doubts on the comparability of the results, particularly in current days where quantitative myocardial perfusion analysis on novel SPECT devices can be performed almost routinely [8]. Moreover, no information regarding the possible impact of image quality on diagnostic accuracy was provided, an aspect of particular relevance since the recent EVINCI study has demonstrated that, when only good image quality studies are selected, the diagnostic accuracy of SPECT and PET are comparable, and are even slightly better than that of CMR [3]. Similarly, it is not reported whether the accuracy analyses were derived from center-based data or from independent core-lab evaluations, and whether the presence of myocardial ischemia was the only criteria used for the definition of significant CAD, two information that could have affected significantly the overall results. Finally, present analyses do not allow to obtain any information on the ability of cardiac imaging modalities to guide patients' management, ultimately impacting their prognosis, one of the most contended aspects in patients with stable CAD [9,10].

Present and previous data confirm that non-invasive cardiac imaging may still be valuable for the detection of significant CAD and possibly for the risk-stratification of patients. However, given the many confounding factors (i.e. pre-test probability of CAD, type of stressor, qualitative or quantitative analysis, image quality), no real ranking of the existent imaging modalities should be made. Moreover, since the ability to modify patients' prognosis rather than to predict the presence of CAD should be considered as the ultimate clinical gold-standard for the evaluation of cardiac imaging, only randomized comparative trials may allow to determine the real value of the existing strategies for the management of patients with IHD.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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