EDITORIAL

Image fusion: the beauty of the truth from the inside and out

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Ischemic heart disease (IHD) is one of the leading causes for morbidity and mortality in the last decades, without a significant change in its rate over time. Coronary artery revascularization by percutaneous coronary intervention (PCI) is currently considered the gold standard procedure for the diagnosis of IHD and is a common method of definitive? treatment in selected patients. Therefore, the main question and dilemma in this devastating disease is whether ''to re-vascularize or not to re-vascularize?''. Moreover, if revascularization is considered, which vessel, or vessels should be treated. Numerous large scale randomized multi center studies aimed at investigating the management of IHD and the treatment strategy, whether with optimal medical therapy alone or together with interventional procedure, and the effect on patients' outcome.[1,2]

Currently however, there are no randomized clinical trials that convincingly demonstrated that PCI in stable IHD had significant effect on patients' survival or on the development rate of future acute myocardial infarction. This might be related to the fact that PCI is performed based on anatomical assessment alone and the hemodynamic significance of the coronary stenosis is not taken into consideration. Another explanation could be the presence of multi vessel disease while the treatment was performed to a non-hemodynamically significant vessel, or in cases of multiple stenoses in the same coronary artery where PCI was performed for the less significant stenosis.

The ability of coronary angiography to predict the functional significance of a coronary stenosis is limited. Some studies reported a mismatch of almost 50% between an anatomical narrowing (assessed visually) and its functional impact (as assess using fractional flow reserve (FFR) measurement).[3] Anatomical assessment of vessel narrowing may be inaccurate especially when evaluating coronary lesions of intermediate severity, or when the severity is ambiguous, such as in the setting of diffuse atherosclerotic disease and the absence of a normal segment for a reference. In addition, vessel foreshortening, angulation, severe calcification, eccentricity, vessel overlap and streaming of contrast-may all limit the anatomical assessment of coronary artery stenosis.

In addition to lumen size of the coronary artery, there are several factors that might have an impact on the hemodynamic significance of a lesion including low attenuation lesions, napkin ring morphology, positive remodeling and spotty calcifications which are all viewed by coronary computed tomography angiography (CTCA) but cannot be appreciated while performing invasive coronary angiography.[4] In fact, this same study showed that the presence of these features was associated with cardiac events even if the patients had non-obstructed coronary arteries. Therefore, the assessment of CAD severity and the decision for revascularization must take into account the evidence of reversible myocardial ischemia in addition to the anatomical criteria.[56] Furthermore, avoiding PCI of an anatomically intermediate but functionally non-significant stenoses was found to be at least as good as the performing of PCI in the short, long and very long terms.[7] Hence, the need for a method to assess the hemodynamic significance of the narrowed vessel either by perfusion defects with or without myocardial blood flow and flow reserve using nuclear cardiology techniques or FFR measurement during interventional coronary angiography ICA.

Both technologies for the assessment of functional significance of a lesion have their own pros and cons.

In our opinion the main limitation of FFR is its invasive nature, while MPI is a noninvasive method and might defer the need for an invasive procedure, it provides information not only about the hemodynamic significance of a coronary artery stenosis but also provides absolute quantification of the amount of ischemia, which has been shown to have a major role in the decision of revascularization.

In addition, an important condition for accurate FFR measurements is that microvascular resistance is reduced maximally and remains stable during the measurement.[8] In case of microvascular dysfunction, drug-induced coronary vasodilation is impaired, resulting in a blunted flow response and an elevated FFR. Furthermore, at the arterioles level, an impaired response to a dilator drug can lead to a falsely normal FFR value, and thus misguide the clinical decision. The higher prevalence of microvascular dysfunction in women may lead this population to be more vulnerable to this error.[9]

Other limitations of FFR include: The non-linear pressure-flow relationship during maximal vasodilation. This results in an increase of the microvascular resistance at low perfusion pressure and therefore FFR may be overestimated with the increase in stenosis severity.[10] Furthermore, in the presence of hemodynamic factors that increase extravascular compressive forces, such as tachycardia leading to a reduced diastolic duration, and an increased left ventricular end diastolic pressure, the hyperemic microvascular resistance may increase thus leading to a raise in the measured FFR.[10] FFR value is sensitive to the size of the perfusion territory, since this factor can influence the coronary flow rate and thus the pressure drop across the stenosis. FFR is also influenced by the minimal lumen diameter and lesion length. Finally, the procedure increases the duration of PCI.

The use of a functional non-invasive test as an initial step in the investigation of patients with intermediate to high pretest probability for the presence of CAD is a class I indication as per the recent guidelines.[11,12] Hence, Single Photon Emission Computer Tomography (SPECT) Myocardial Perfusion Imaging (MPI) has been suggested as a gatekeeper for invasive coronary angiography.[13]

As such, the majority of the patients, especially when treatment is ischemia driven, will be referred to a functional test. MPI is a well-established procedure and serves as the standard practice in nuclear cardiology for the assessment of ischemia. This modality is advancing continuously, and recently it includes the measurement of myocardial blood flow and flow reserve both using SPECT and PET MPI technologies, adding to the sensitivity and specificity of these studies.

The use of artificial intelligence (AI) in the field of nuclear cardiology is very well recognized[14,15] and has been in use for decades. AI was found to be of value in all steps of the study the acquisition parameters and localizing the heart, through the image processing and enhancement and interpretation. Then, followed by the application of machine learning, providing automated quantitative analysis of the MPI using the raw data, reconstructs tomographic slices to generate 3-dimensional trans-axial slices. Studies are then introduced to pre-trained algorithms that compare these data to existing data of normal individuals with the same gender and age. The output of such a process will be a comprehensive map with the extent, severity and location of the ischemic tissue or scar if present.

In the past, there have been several attempts to use software based integration of SPECT images and ICA for matching myocardial territories and corresponding coronary arteries, however it was not clinically implemented since the invasive part of it does not allow pre interventional analysis.[16,17]

In this issue of the Journal of Nuclear Cardiology®,[18] Xu et al nicely demonstrated the use of hybrid imaging relying on both functional non-invasive and anatomical invasive technologies to better diagnose and manage CAD.

The authors used advanced imaging processing software using two different data sets from two different technologies fused together to come up with a multimodality image which in turn enables a patient tailored approach or even a vessel tailored approach.

The use of a volume rendering technique to facilitate a three-dimensional display is of great importance because it allows the most accurate evaluation of the different myocardial territories and the corresponding coronary artery or branches. When co registration of the two sets of data is done correctly one can overcome the erroneous PCI to a non-hemodynamically significant coronary artery. This process is challenging and requires a special software for the fusion purposes of the two data sets of a study with gated nature and another static image, this needs special software for co registration in suitable time points.

The results of this combination is not surprising and is very logical. When observing an ischemic myocardial territory, the observer might be misled by the ''normal'' anatomical rout of coronary arteries especially when multi vessel disease is present and the ''side by side'' technique is used. However, in the fused images, even when normal anatomical variation or multi vessel disease is present the observer is able to visualize the actual coronary artery superimposed over the ischemic territory. This in deed increases the accuracy of interpretation, reporting, and therefore, results in better management and better patient outcome.

While we are used in our daily routine to the mental integration of different sets of data while interpreting ''the side by side'' methods used to assess IHD, fusion of coronary angiography data and MPI not only bypasses the mental integration of functional and anatomical images but also enables a comprehensive interpretation and showed significant prognostic benefits according to the authors.

Beyond the benefits of image fusion, the results of this study might also be related to the frequent variations of the coronary arteries patterns, including dominance, course of arteries or branches, the supply of the inferior wall and the presence of a Ramus intermedius.

The inferior wall might have several variations according to dominance. LAD might be long (wrap-around LAD) and wraps around the apex. In a case when Ramus intermedius is present it can take the rout of a Diagonal branch or a Marginal, and therefore ischemia in anterolateral or inferior wall might be confused with a stenosis in a Marginal that could possibly not be of hemodynamic significance. And again, image fusion can overcome these obstacles.

This work emphasizes the importance of a functional test prior to interventional procedure whether diagnostic or PCI to guide treatment. It is more precise, it prevents unnecessary interventions with all its related consequences, such as the need for otherwise non indicated use of dual anti platelet therapy and the potential complications of an invasive procedure.

The future holds promise for the development of newer software and hardware that will provide us with more accurate tools for better diagnostic accuracy and prognostication, better patient centered approach and management.

Disclosures

Samia Massalha and Zohar Keidar have no relevant financial or non-financial interests to disclose.

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