

Comment on Myocardial Perfusion Study in Obese Patients without Known Cardiac Ischemia

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"All human knowledge is fallible and therefore uncertain.

It follows that we must distinguish sharply between truth and certainty... This is the task of scientific activity. Hence, we can say: our aim as scientists is objective truth; more truth, more interesting truth, more intelligible truth. We cannot reasonably aim at certainty."

Karl Popper

We congratulate Dippe et al.¹ for their work that addressed the role of myocardial scintigraphy in the diagnosis of myocardial ischemia in obese patients.¹ Despite limitations, body mass index (BMI) has been the most used anthropometric tool for assessing nutritional status in adults.² Epidemiologic studies have identified high BMI as a risk factor for an expanding set of chronic diseases, including cardiovascular disease and diabetes mellitus. The Global Burden of Disease (GBD) Obesity Collaborators found that excess body weight accounted for about 4 million deaths in 2015. Nearly 70% of these deaths were due to cardiovascular disease, and more than 60% of them occurred among obese persons (BMI \geq 30 Kg/m²).³ The use of a database of consecutive patients provides a sample of obese patients from the real-world scenario and portrays the current clinical practice in which the cardiologist faces major diagnostic challenges in obese patients. All diagnostic methods have significant challenges in obese patients such as the limitation of the acoustic window in the echocardiogram, higher incidence of photon attenuation on computed tomography and myocardial scintigraphy and bore size limitations to cardiac resonance imaging. Radiation-sparing techniques are more difficult to use in heavier patients.⁴ The finding that clinical data such

as the presence of diabetes mellitus, older age and typical symptoms of angina highlights the need of careful clinical evaluation in order to adequate request ischemic screening tests in patients with suspected coronary artery disease, especially in the obese. Another important finding of their study was the absence of association between obesity alone, especially in the group with BMI greater than 40, with the presence of ischemia. A technical aspect that was not clear in the article and whether the authors used the prone acquisition when there was doubt about the presence of breast attenuation and also the technique used to quantify the visual or automatic ischemia.

In an editorial about this article, Hueb⁵ points out the multiple mechanisms involved in the pathophysiology of myocardial ischemia, including the microvascular mechanisms that determine ischemia in patients with epicardial coronary arteries without obstruction. Functional methods are important in the identification of microvascular ischemic abnormalities, which have diagnostic and prognostic value, especially in diabetic patients and in patients with multiple risk factors. Functional imaging is superior to anatomic imaging in patients with microvascular disease because of their focus on different levels of the ischemic cascade including wall motion abnormalities (echocardiography and stress cardiac magnetic resonance), relative perfusion abnormalities (stress cardiac magnetic resonance and single-photon emission computed tomography), and changes in physiological absolute regional myocardial perfusion (PET).⁶ The creation of the patient-centered imaging culture that prioritizes patient safety and effectiveness requires the understanding of the better diagnostic techniques for every clinical need.⁷

Karl Popper stated that science is composed of transient truths. The role of scientists is to prove the falsifiability of their findings and others in the search of a more intelligible true. In the absence of contrary evidence, current evidence points that invasive treatment in patients with myocardial ischemia area greater than 10% is associated with better prognosis in comparison with medical management alone. The results of the ISCHEMIA study to be published in the near future should provide additional new scientific evidence regarding whether an invasive management strategy improves clinical outcomes when added to optimal medical therapy in patients moderate or severe ischemia.⁸

Keywords

Coronary Artery Disease; Myocardial Perfusion Imaging; Obesity/mortality; Myocardial Ischemia; Diabetes Mellitus.

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Reply

Regarding our manuscript,¹ we would like to make some comments about the letter sent to the editor by Universidade Federal Fluminense (UFF) and about the short editorial written by Dr. Whady Hueb.²

Although body mass index (BMI) correlates with the percentage of body fat in most individuals, the limitations of this index is widely known.³⁻⁵ On the other hand, major cohort, prospective and observational studies, such as the Framingham study⁶ and the Nurse's Health Study,⁷ used BMI as a diagnostic parameter for obesity, demonstrating a nearly linear relationship between BMI and coronary artery disease (CAD) from a value equal to or greater than 25 kg/m².

The World Health Organization (WHO) uses BMI for the diagnosis and classification of obesity.⁸ In our study,¹ which evaluated 5,526 obese patients undergoing myocardial perfusion scintigraphy, one of the largest samples ever published in the world literature, 29.7% of the individuals had BMI equal to or greater than 35 kg/m².

Regarding the questioning of the UFF colleagues, we pointed out that the limitations of the manuscript include that our patients were not submitted to attenuation correction techniques routinely.

Before we make any specific comments on the short editorial, we would like to emphasize our deep admiration for Dr. Whady Hueb, a Brazilian scientist of great importance for the world cardiology, who we highly appreciate and respect. We would also like to emphasize, with no reservations, his contribution to the international literature with the MASS study,⁹ quoted and admired all over the world. Today, among other things, the MASS study allows us to work together on the ISCHEMIA study,¹⁰ on which both Dr. Whady Hueb's and our group worked hard for a successful completion.

Regarding the minieditorial on our study, we would first like to make some comments about the tests recommended and the perfusional abnormality rate we found.

Note that our registry in Curitiba, which is certainly one of the largest nuclear cardiology registries in the world,

includes patients referred to our diagnostic center, about whom we have no control over which are the tests to be recommended, as this is the responsibility of the referring clinician. (I do not understand this)

Besides that, we cannot infer that the tests have been inappropriately recommended based on 77% of normal scintigraphies. We are sure that this data should not be used as a criticism of our study, since in many clinical situations this is exactly the information sought by the clinician requesting a provocative ischemia test, that is, the absence of ischemia can avoid unnecessary anatomical evaluations, such as cineangiography, for example.

It is true that many of these patients with suspected CAD could have their disease ruled out by coronary angiography. Unfortunately, this practice is still limited in our country, because of the restrictions imposed by health insurance plans or unavailability in the public health system (SUS). We believe that this would be an excellent way to "rule out" CAD, avoiding additional tests, including myocardial perfusion scintigraphy itself.

Although our perfusion abnormality rate (23%) was considered low by Dr. Whady Hueb, it is nearly three times greater than that found in reference laboratories in the United States, as found by the Cedars Sinai Hospital registry, which revealed about 8.7% of perfusion abnormalities.¹¹ Similarly, the randomized study PROMISE¹² found a perfusion abnormality rate close to 10% in symptomatic patients.

In our sample, 31% of the patients were known diabetics, and this certainly differentiates our group from other studies, and helps us understand our high abnormality rate.

Another excerpt of the short editorial reads: *based on this data, by applying a "creative statistics", they found a 245% risk increase for typical angina.*

Note that nowhere in the manuscript we mentioned that a perfusional abnormality would increase the risk of typical angina. We have published that the patients who reported typical angina before the test, compared to asymptomatic patients (reference) had 245% higher chances of having

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abnormal myocardial perfusion (odds ratio of 2.45 [1.82-3.31], see page 125 of the manuscript, table 4).¹ There is no “creative statistics” at all. This conclusion was reached after multivariate logistic regression analysis. It is pure statistics.

Finally, we would like to thank UFF for the letter sent to the editor of *Arquivos Brasileiros de Cardiologia* and to

Dr. Whady Hueb for his short editorial. The productive discussion and scientific production certainly help to add further value to our admired Brazilian cardiology.

Tufi Dippe Junior
João Vicente Vítola

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