Nuclear cardiology and CVD in the developing world: Are we applying our scarce resources appropriately? Why is our mortality rate so high?

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While mortality rates from cardiovascular diseases have progressively decreased in developed nations, this has not been observed to the same extent in the developing world. Nuclear Cardiology utilization remains low or non-existent for most of those living in the low-to-middle-income countries. How much of the decline in mortality observed in the developed world has to do with advanced cardiac imaging? Are we applying our scarce resources appropriately for myocardial perfusion imaging? Are myocardial revascularizations being guided by appropriate use criteria? Is more imaging necessary to reduce the mortality rates further in the developing world?

Key Words: Myocardial perfusion imaging • SPECT • cost-effectiveness • coronary artery disease

INTRODUCTION

Over the past several years, the United Nations has been calling attention to the dramatic and increasing burden of non-communicable diseases in developing nations, especially the high mortality rates due to cardiovascular diseases (CVD).[1] Changes in lifestyle, lack of exercise, inappropriate nutrition habits, and obesity are contributing to an increase in type 2 diabetes mellitus prevalence and consequently**SON coronary artery disease (CAD) and ischemic heart disease (IHD).[2] While mortality rates have progressively decreased over the past 4 decades in the developed world, mostly in North America and Western Europe, the same phenomenon is not observed in many of the low- and middle-income countries.[3]

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HOW MUCH OF THE REDUCTION IN MORTALITY OBSERVED IN DEVELOPED NATIONS HAS TO DO WITH THE USE OF TECHNOLOGY AND ADVANCED CARDIAC IMAGING?

This is a difficult question, and certainly we do not have data for a definitive and precise answer. Nevertheless, we can safely say that an effective way to reduce CVD mortality is to promote primary prevention, identifying and controlling modifiable risk factor, and to initiate secondary prevention when individuals at a higher risk with established CVD are identified. This in itself carries a very intimate relationship with cardiovascular imaging. In fact, recently randomized published data demonstrated that identification of individuals with CAD, using computed coronary tomography angiography (CCTA), increased the number of patients undergoing secondary prevention and importantly, resulted in better patient outcome, including mortality reduction, compared to patients randomized to standard of care (SCOT-HEART study).[4]

In contrast, the true benefit of invasive procedures and costly myocardial revascularization using stents or open heart surgery for stable patients remains a topic of

major controversy and uncertainty, with solid literature pointing exactly to the absence of benefits (COURAGE and BARI 2D trials, just to mention a few). The nuclear cardiology literature, over the past 4 decades, have clearly demonstrated solid evidence that the vast majority of patients with a normal myocardial perfusion and preserved left ventricular function are at a low risk and do not benefit from myocardial revascularization in most instances. In addition, studies such as the EMPIRE by Underwood R et al and the END study by Shaw L et al have demonstrated that myocardial perfusion imaging (MPI) can be used as a gatekeeper to prevent patients from undergoing unnecessary invasive procedures and revascularizations, implicating in costs reduction. This certainly is particularly important for developing nations. In addition, there is a vast literature demonstrating that an abnormal MPI identifies a group of patients with increased mortality, being worse in more severe and extensive perfusion deficits. Identifying a patient with IHD by MPI should lead, at least, to initiation of aggressive secondary prevention using guideline-directed optimal medical treatment (OMT) as a way to reduce mortality.

A topic that remains controversial is if ischemia is solely a marker of mortality that would deserve OMT but cannot be modified by myocardial revascularization or if revascularization can indeed reduce mortality beyond MT alone, as suggested in a large observational study by Hachamovitch et al.[5] If so, to what degree of ischemia and to what extent can mortality be reduced? This has been the main subject of a large ongoing randomized trial called the ISCHEMIA trial, which is randomizing patients internationally, with moderate or severe ischemia, to OMT or OMT + revascularization.[6] A mean follow-up of 3 years on a few thousands of patients should shine a light on this very important subject. So, going back to our original question of how much of the reduction in mortality observed in developed nations has to do with the use of technology and advanced cardiac imaging, we can say that most likely a combination of prevention and the use of technology, including imaging, to guide treatment is being responsible for the benefits observed in developed countries, and should be applied to developing nations following, as much as possible, the principles of evidence-based medicine and appropriate use criteria (AUC).

SHOULD WE BE USING MORE TECHNOLOGY AND ADVANCED CARDIAC IMAGING IN DEVELOPING NATIONS AS A WAY TO REDUCE THE RATES OF CVD MORTALITY?

Trying to reduce mortality rates is particularly challenging considering the social structure and lack of appropriate financial resources in most of the developing world. The appropriate use of technology such as nuclear cardiology can be helpful to diagnose, stratify risk, and to guide cost-effective management, which are important for patients in any country but particularly relevant to those developing nations which are financially challenged, and where cost control is imperative. Nevertheless, imaging has to be used judiciously based on established recommendations from scientific societies applying AUC as a guide, which has been abundantly published in the field of cardiology. While nuclear cardiology is widely used in developed countries, unfortunately its utilization in the developing world is quite heterogeneous or just non-existent (Figure 1).[7] Many of these countries coincide with the countries demonstrating higher mortality rates from IHD.[1] The use of technology, or the lack of it, relates to several factors ranging from financial capacity and political willingness to invest, to the level of information on the value of a given technology to help deliver cost-effective care. At the same time, on a given environment, where the use of non-invasive imaging is modest or non-existent, many patients might go directly to the invasive catheterization laboratory, leading to revascularization, despite the lack of benefit shown in the literature for most stable patients.[8] Any procedures, invasive or non-invasive, should be applied and guided by scientific evidence and AUC whenever available.

In this issue of the *J Nucl Cardiol*, Santos et al[9] raise the important topic of AUC for MPI in a government hospital in Brazil, a developing country in Latin America. The appropriate use of nuclear cardiology should be scientifically based. Its utilization should be reserved if the information provided will impact patient management. Using the technology and resources on a patient who do not require is beyond inappropriate, in scientific terms, but it is also unfair, in social terms, because it may also limit the possibility of another needy patient to have access to the test, a test which could potentially help to guide an invasive or medical, potentially life-saving, treatment. A more cost-effective use of financial resources could mean for example more patients undergoing primary and secondary prevention, well proven to reduce mortality which is so needed in developing nations.

The study by Santos et al[9] was conducted in a tertiary care facility in Brazil. They describe that 12% of the MPIs where considered ‘‘inappropriate’’, or, using the new terminology adopted in 2013 it would be called rarely appropriately. The ‘‘inappropriate’’ use of MPI certainly needs to be controlled to prevent the unnecessary expenses as recommended by these authors. It is indeed unfortunate that inappropriate tests are ordered, even in academic institutions, while many patients with

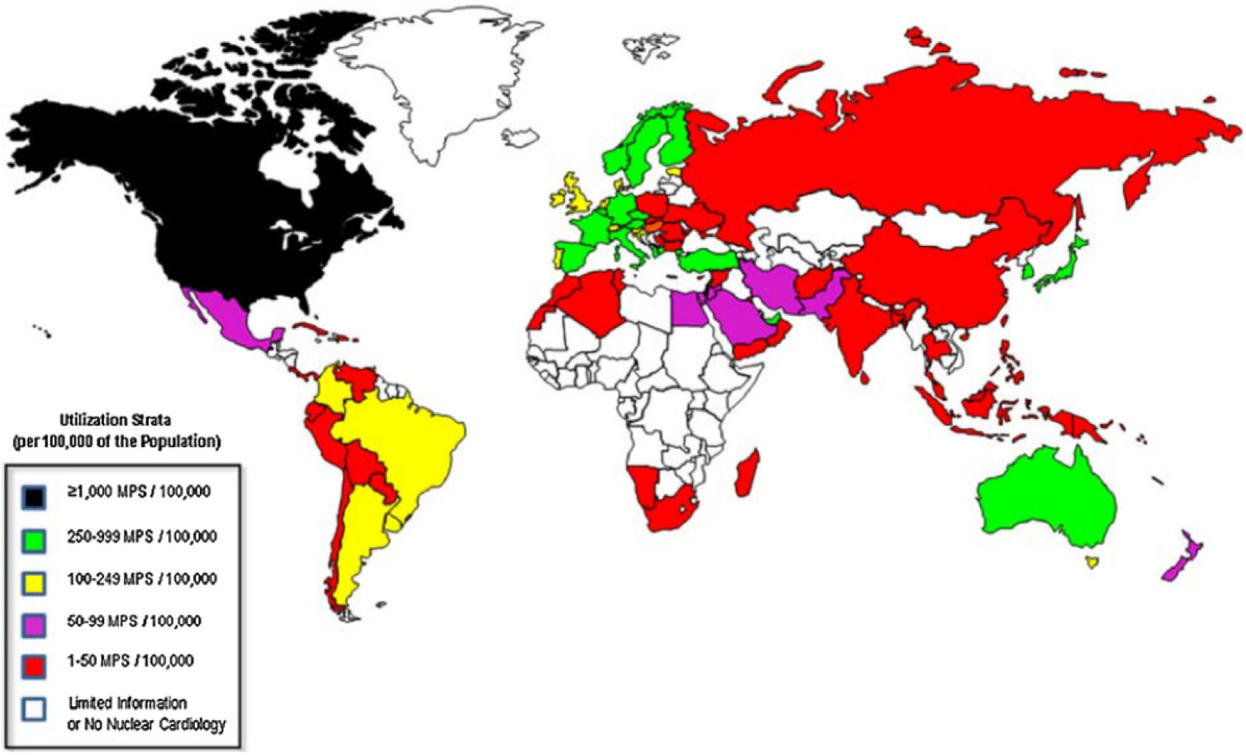

Figure 1. Estimates of worldwide utilization (per 100,000 of the population) of nuclear cardiology procedures. Reproduced with permission[7].

appropriate indications may never have their tests ordered. The judgment of appropriateness in this study was from the point of view of the physician seeing the patient in the nuclear laboratory and not from the perspective of a physician seeing the patient at the cardiology clinic and deciding what strategy to follow. Therefore, one important question that could be raised would be how many patients, in that same institution, were in fact going straight to invasive coronary angiography and perhaps revascularization without an ''appropriate'' evaluation of ischemic burden by MPI? Is AUC being applied in the decision making of revascularization? Could nuclear imaging be used to save resources, helping to promote cost-effective care to government institutions in Brazil? This information is not available in the study of Santos et al, going beyond the scope of that study, but there are data from other government administered centers in Brazil pointing to the fact that patients frequently undergo revascularization without prior functional assessment.[8] Looking at the private sector, in the same country, where resources are not so scarce as in a government hospitals in Brazil, we observe examples where the use of nuclear cardiology can be significant in terms of volume and has been growing in many large center. To illustrate this, we show the utilization rates of nuclear cardiology

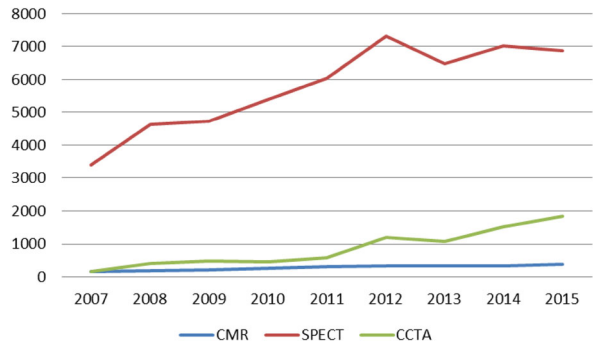

Figure 2. Number of studies performed per year in 2 referral centers (Quanta and DAPI) in Curitiba, Brazil. Population of 1.7 million inhabitants *Source*: Quanta Registry, Vitola JV, Cerci R, Zapparoli M. *SPECT*, single photon emission computed tomography; *CCTA*, computed coronary tomography angiography; *CMR*, cardiac magnetic resonance.

procedures at two referral centers for non-invasive cardiac imaging in a city of 1.7 million inhabitants in Latin America (Curitiba, Brazil), demonstrating progressively the increasing utilization between 2007 and 2015, even compared to other diagnostic modalities such as CMR and CCTA (Figure 2). It seems that in this scenario, nuclear cardiology is being widely used to diagnose, stratify risk, and to provide guidance on cost-

Table 1. Gender differences in 41,671 patients undergoing SPECT MPI in a referral center in Brazil Adapted from Vitola[10]

Variable	Women $n = 18,628$	Men $n = 23,043$	*P* value
Age	64 ± 39	62 ± 42	<.0001
BMI, kg/m^2	27.5 ± 5.2	28.0 ± 4.4	<.0001
DM	4188 (22,5%)	5281 (22,9%)	.74
Known CAD	3891 (20,9 %)	8187 (35,5 %)	<.001
Pharm stress	6770 (36,3%)	5580 (24,2%)	<.001
Abnormal SPECT	5027 (27,0 %)	8040 (34,9%)	<.001
SSS > 13	918 (4,9 %)	2529 (11,0 %)	<.001

Data presented as means (SD), percentage or absolute number
BMI, body mass index; *CAD*, coronary artery disease; *DM*, diabetes mellitus; *Pharm stress*, pharmacological stress required; *SPECT*, single photon emission computed tomography; *SSS*, summed stress score

effective management, which are important for patients in any country but particularly relevant to those developing nations which are financially challenged and cost control is imperative. Not to speak of, the urgent need to fight increased CVD mortality as previously described. What is also interesting to observe in Figure 2 is that the introduction of CCTA has not affected significantly the utilization of nuclear cardiology in this part of the world, pointing to the fact that these techniques are more often complimentary than competitive. Demographic data of the patients seen for SPECT MPI in these laboratories are shown in Table 1. These are basically Brazilian patients aged in mid-60s, 22% diabetics, resulting in an abnormal MPI rate which is quite high at 27% for women and 35% for men, suggesting, overall, a group of patients that would benefit from this technology.[10] It is observed that up to 11% of these patients had summed stress perfusion score >13, which was considered severe, implying a higher risk group of patients for mortality. Interestingly, epidemiological data recently published from this region in Brazil demonstrate a significant progressive decline of mortality due to IHD, interpreted by local authorities as a consequence of progressive improvement in the access of this population to diagnostic tools and treatment.[11] These authors point that the reduction in mortality observed is not seen to the same extent in other regions of the same country, and correlate this finding with lifestyle, habits, and access of the population to medical care. This interesting finding in Brazil is corroborated by other authors on a Lancet paper correlating reduction in mortality and access to basic health care, technology, and treatment.[12] This seems a good demonstration of the benefits of prevention coupled with increasing use of technology to guide management, which most likely can still be significantly improved, especially where the resources are more scarce such as the case of government led institutions in a country like Brazil.

In conclusion, the AUC, classifying procedures as appropriate, maybe appropriate, or rarely appropriate, was certainly a major step forward, to be applied for both developed and developing nations. Nevertheless, the major difference is that in general, nuclear cardiology is extensively used in developed nations, in a scenario where mortality is decreasing and perhaps not used enough in many developing nations where mortality is not decreasing enough! It is disappointing that in many places where the use of nuclear cardiology is low, you may find high rates of invasive coronary angiography, as a way to investigate CAD. This frequently leads to myocardial revascularization of questionable benefit to the patient. In this scenario, at least AUC for revascularization should be applied, but this is not frequently the case. Could some of these scarce financial resources be used to promote primary and secondary prevention and to invest in non-invasive imaging, helping ''appropriately'' to select patients who would benefit from invasive procedures, using it as a gatekeeper for unnecessary revascularizations? Most likely so!

Disclosure

There is no financial conflict of interest with this topic beyond the fact that this author works in the field of nuclear cardiology.

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