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EDITORIAL COMMENTARY

Cardiac sympathetic imaging with mIBG: a tool for better assessment of the diabetic heart

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Diabetes is a major risk factor for heart disease and is becoming a global health-care problem. Cardiovascular complications including coronary artery disease, are the most common causes of mortality and morbidity in patients with type 2 diabetes. In addition, associated cardiac autonomic neuropathy is one of the most common complications and has been associated with increased risk of mortality and major cardiovascular events [1].

Cardiac sympathetic imaging with ^{123}I-mIBG is increasingly used for prognostic assessment in heart failure [2]. Recent prospective data coming from the ADMIRE-HF study indicate that cardiac sympathetic imaging provides additional incremental prognostic value over LVEF and BNP measurements [3], and that cardiac sympathetic imaging is helpful in defining risk of cardiac events. In the present era of cost containment and escalating health-care costs, such ability to better assess the population at risk is becoming crucial. On the other hand, while cardiac sympathetic imaging is becoming clinically applied, it is important to know how concomitant disease conditions such as diabetes may influence cardiac sympathetic imaging and ^{123}I-mIBG neuronal uptake in patients with heart failure.

In this issue of the EJNMMI, Scholte et al. [4] examine the relationship between cardiac autonomic neuropathy, as determined using heart rate variability measurements and cardiac ^{123}I-mIBG imaging parameters, in diabetic patients without symptoms of coronary disease. The use of cardiac sympathetic imaging to risk-stratify this patient population is justified by the poor long-term prognosis of asymptomatic diabetic patients with cardiac autonomic neuropathy. The authors performed a head-to-head comparison between ^{123}I-mIBG scintigraphy and heart rate variability measurements, and showed that ^{123}I-mIBG scintigraphy identifies significantly more patients with cardiac autonomic neuropathy than identified by heart rate variability measurements. These findings suggest that ^{123}I-mIBG myocardial scintigraphy may have a role in the early detection of cardiac autonomic neuropathy.

It is important to note that the definition of cardiac autonomic neuropathy is most appropriately based upon measurements related to autonomic function, such as heart rate variability, while ^{123}I-mIBG imaging provides insight into the norepinephrine reuptake cycle at presynaptic sympathetic nerve terminals, but cannot in itself establish a diagnosis of autonomic neuropathy. However, the study by Scholte et al. showed that cardiac ^{123}I-mIBG myocardial scintigraphy is able to detect cardiac autonomic neuropathy before physiological evidence becomes apparent, and may become an important imaging technique for the early detection of such neuropathy. Such early detection may be important for risk stratification and modification in diabetic patients, which at the end should facilitate better outcomes.

The present study included diabetic patients only, and therefore was limited by the lack of a control group to help define thresholds for normal values of ^{123}I-mIBG parameters. However, the authors took advantage of the fact that the cardiac clinical risk stratification for their outpatient diabetic patients at their institution includes ^{123}I-mIBG myocardial scintigraphy and heart rate variability measurements to assess cardiac autonomic neuropathy, and therefore they were able to analyse this patient population

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to evaluate the prevalence of this neuropathy in patients with type 2 diabetes and without symptoms of coronary artery disease providing a direct comparison between heart rate variability measurements and ^{123}I-mIBG myocardial scintigraphy. From 155 patients who were referred for risk stratification including adenosine stress SPECT myocardial perfusion imaging to assess myocardial ischaemia, ^{123}I-mIBG myocardial scintigraphy and heart rate variability measurements, a cohort of 88 patients with normal SPECT perfusion studies were finally selected. The mean duration of diabetes in these patients was nearly 10 years and most of them were on oral antidiabetic therapy. In 28 patients complications of diabetes were seen including peripheral neuropathy and/or peripheral vascular disease.

In such a patient cohort, the selected threshold value of 1.80 in heart to mediastinum ratio may seem high in comparison to the values used in large multicentre trials to assess prognosis in heart failure. Similarly, the washout rate cut-off of 25% seems low in comparison with values found in heart failure patients, and may not apply to other patient populations. It would be interesting to see if the analysis of the study data in terms of heart to mediastinum and washout ranges rather than using the box plots with definite cut-off values would have rendered additional information. Although most reported threshold values of normal healthy volunteers are based on small populations, previous work exploring the relationship between ^{123}I-mIBG uptake and age in European subjects has rendered similar normal values in healthy individuals of similar age to those in the cohort studied by Scholte et al. Estorch et al. [5] reported heart to mediastinum ratio values for patients aged between 40 and 60 years of 1.83±0.28, which is in line with the threshold value selected in the present study. Furthermore, despite the fact that the total defect cut-off score of >13 is not based upon specific data, it was converted to percentage of the total denervated myocardium and used to identify abnormal patients. In the study by Scholte et al., the percentage of denervated myocardium was calculated as in a study by Kasama et al. [6], correcting for the four-point scoring system used, resulting in a total defect score of >13 being considered abnormal. Detailed analysis of the data, including all ^{123}I-mIBG parameters, clearly showed that more diabetic patients exhibit abnormalities in ^{123}I-mIBG imaging than by heart rate variability measurements.

It would also be interesting to see how diabetic patients with and without ^{123}I-mIBG abnormalities differ, principally in relation to glycaemic control, since this is strongly related to the process of left ventricular adrenergic denervation [7].

The present study by Scholte et al. adds to the knowledge about the potential applications of cardiac sympathetic imaging in various patient populations. The ADMIRE-HF study demonstrated the capacity of quantitation of sympathetic innervation of the myocardium, measured by the heart to mediastinum ratio on ^{123}I-mIBG scintigraphy, to predict the likelihood of significant cardiac events in subjects with heart failure and significant left ventricular dysfunction. ^{123}I-mIBG scan findings could also be helpful in patients who meet criteria for implantation of an automatic cardioverter-defibrillator but are ambivalent about this procedure and require further convincing information. The present study showed that abnormalities in cardiac sympathetic innervation, as seen with cardiac ^{123}I-mIBG imaging, occur prior to ECG parameter changes of cardiac autonomic dysfunction. In all these patients, cardiac sympathetic imaging with ^{123}I-mIBG may provide an additional means of assessing overall risk of events to guide clinical decisions.

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