



MIBG and imaging of cardiac adrenergic system: From heart failure to ventricular arrhythmias and atrial fibrillation, through cardiac asynchrony. What else?

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The role of the autonomic nervous system in the pathogenesis of ventricular arrhythmias and sudden cardiac death is well documented.¹⁻³

Since the first report on the imaging of cardiac neuronal damage by 123I-mIBG late in the 80', the evaluation of the integrity of the cardiac autonomic nervous system and its relation with myocardial perfusion and function has been documented in a wide clinical scenarios.

In early canine experimental studies, it was documented that myocardial ischemia induces an area of neuronal damage larger than the ischemic or necrotic area.⁴⁻⁷ This viable, denervated, myocardium is affected by a sympathetic denervation supersensitivity that makes the myocardium prone to ventricular fibrillation during the infusion of norepinephrine compared with the control group.⁴

In a small clinical study in patients with recent myocardial infarction, Stanton et al documented that 10 (83%) of the 12 postinfarction patients with ventricular arrhythmias had areas of 123I-mIBG/thallium-201 mismatch, but only 2 (29%) of the 7 patients without ventricular arrhythmias demonstrated 123I-mIBG /thallium-201 mismatch.⁸

Areas of mismatch were also documented in patients with idiopathic dilated cardiomyopathy, and the H/M was inversely correlated with left ventricular ejection fraction⁹; in a more recent study, Marini et al. concluded that perfusion defects seem to differently affect 123I-mIBG retention in heart failure caused by ischemic heart disease or dilated cardiomyopathy.¹⁰

Several studies have demonstrated the usefulness of 123I-mIBGs to identify patients with a deregulated autonomic nervous system and a mismatch with regional perfusion that may predispose to cardiac electrical instability and, finally, to a high risk of malignant arrhythmias,¹¹⁻¹³ mainly in patients with ischemic heart disease.

In the field of congestive heart failure, several single center experiences or retrospective studies initially suggested the prognostic value of cardiac 123I-mIBG imaging. The multicenter ADMIRE-HF study, the larger study so far, prospectively enrolled 964 patients with left ventricular dysfunction and heart failure and documented the higher event rate, sudden arrhythmic death, or death due to worsening heart failure, in patients with a H/M ratio < 1.6.¹⁴

Available studies, reviews and meta-analysis, thus strongly indicate that 123I-mIBGs imaging has the capability to identify patients at high risk of MACE (death, malignant ventricular arrhythmias) or worsening heart failure and those with a more favorable prognosis, due to the very high negative predictive value, and with a prognostic impact that is incremental over clinical information alone (e.g., left ventricular ejection fraction and BNP).

Moreover, Boogers et al¹⁵ documented in 116 patients with ICD implanted for primary or secondary prevention, that 123I-mIBG SPECT defect score (with a

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summed score greater than 26) was an independent predictor of appropriated ICD therapy.

The prognostic values of late H/M and wash-out rate were also documented in patients with heart failure and preserved left ventricular ejection fraction (HFpEF).¹⁶ Last but not least myocardial sympathetic denervation, evaluated by 123I-mIBG imaging, matched with the perfusion pattern and was also linked to regional asynchrony, in particular with the most dyssynchronous walls.^{17,18}

In this issue of the journal, Sazanova et al¹⁹ used adrenergic imaging to predict outcome in 82 patients with atrial fibrillation (AF) undergoing catheter ablation procedure; they concluded that 123I-mIBG imaging data (H/M and WO) performed before ablation were independently associated, at multivariable analysis, to AF relapse at follow-up, with an AUC at ROC analysis of 0.79 and 0.71, respectively.

This is a relatively new field of investigation for 123I-mIBG imaging. The correlation between cardiac autonomic nervous system and AF occurrence and maintenance has been documented by several authors.²⁰⁻²³ In patients with AF, 123I-mIBG imaging has been classically performed to predict hard events: myocardial infarction and heart failure.²⁰⁻²⁴

Recently, several authors investigated the possible link between 123I-mIBG imaging performed before ablation and the outcome, with discordant results.²²⁻²⁴

Discrepancies between the manuscript by Sazanova et al and other studies have been discussed in depth and mainly ascribed to the possible presence of patients with latent HFpEF (thus prone to sympathetic system derangement) or to differences in imaging modalities (e.g., different collimator use, with different values for H/M and wash-out rate).

Recently, solid-state CZT SPECT was used in a preliminary study to assess the adrenergic innervation of the left atrium that actually is the target of ablation procedure.²⁵

CONCLUSION

Since its first use late in the 80', a lot of studies documented that 123I-mIBG and Imaging of Cardiac Adrenergic System progressively extended and demonstrated its value in a wide clinical scenario: from heart failure and myocardial infarction, including cardiac asynchrony, to ventricular arrhythmias and sudden death prediction to atrial fibrillation. Furthermore, myocardial innervation can only be assessed by nuclear techniques.

From the analysis of available literature, major limitations can still be identified in a widespread utilization of the techniques to have a potential impact on the clinical decision making: a real standardization of

the cut-off used for prognostication, either H/M, Wash-out or summed scores, in different settings, and according to the different acquisition modalities, and a more diffuse utilization of solid-state cameras. Larger multicenter studies in the different clinical scenario are needed.

After that, what else? Hopefully, perhaps, to convince cardiologist.

Conflict of interest

None declared

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