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'ICD in Primary Prevention: Potential Role of Sympathetic Nerve Imaging'

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Abstract: Patients with chronic heart failure (CHF) and left ventricular ejection fraction (LVEF) ≤ 35% are at increased risk for sudden cardiac death (SCD). These patients are likely to receive an implantable cardioverter defibrillator (ICD), effective in reducing the occurrence of SCD in primary prevention. The decision to use an ICD in CHF, according to the current guidelines, is based on New York Heart Association classification (NYHA) of II or III and a LVEF ≤ 35%, but reduced LVEF is a nonspecific predictor of potentially fatal arrhythmic events. Many studies have shown that a (123)I-metaiodobenzylguanidine ((123)I-MIBG) scintigraphy, which identifies sympathetic nervous system dysfunction, is useful for determining the prognosis in CHF patients. This case report describes the potential role of (123)I-MIBG into the decision-making process for ICD placement, improving the accuracy in the selection of patients most likely to benefit from an ICD implantation.

Keywords: Primary prevention ICD; congestive heart failure; MIBG myocardial scintigraphy.

CASE REPORT

T.A., 68-year-old man, mild smoker, suffering from dyslipidemia, had a myocardial infarction on May 2012 treated with a percutaneous coronary intervention (PTCA) + bare metal stenting (BMS) on interventricular coronary artery. He was then referred to our department in order to receive a cardiologic rehabilitation and optimize his medical treatment. His transthoracic echocardiogram showed a dilated left ventricle with diffused hypokinesia (LVEF 25%), a moderate mitral regurgitation, and a moderate to severe pulmononary pulmonary hypertension (53 mmHg), with a NYHA functional class of II-III. In order to identify sympathetic nervous system dysfunction of this patient, a ^{123}I-Iobenguane SPECT and a myocardial perfusion SPECT with 99m-Tc tetrofosmin (Fig. **1**) were performed above one month after coronary revascularization. [1-3] I-Iobenguane scintigraphy demonstrated an early heart to mediastinum ratio (H/M) of 1.18, a late H/M of 1.15 with a washout rate (WR) of 2.5% (Fig. **2**). These results identified a denervated patient at high risk for ventricular arrhythmias and sudden cardiac death. The patient was revaluated, according to the current guidelines, three months after PTCA intervention by a transthoracic echocardiogram: his LVEF was not improved (LVEF 28%), his NYHA class was worst (III-IV) and he was treated with high doses of diuretics. Eventually, after having optimized his medical therapy, the patient underwent an ICD implantation on primary prevention. At the follow up visit the device had not delivered any therapy; patient's NYHA functional class did not modified and there were signs of fluid overload, neurohormonal activation (plasma brain natriuretic peptide, BNP = 901 pg/ml) and a significant renal impairment (creatinine 1.92 mg/dl, eGFR 34 ml/min/-1,73mq). His medical therapy was reassessed and the patient was strictly controlled by our nurse counselling, reaching better haemodynamic conditions and saving from frequent hospital readmissions.

DISCUSSION

ICD placement should be considered in CHF patients when guidelines' criteria are satisfied: NYHA functional class of II or III, LVEF less than or equal to 35% and at least 3 months after a cardiac revascularization or 40 days after an acute myocardial infarction, optimal medical treatment and reasonable expectation of survival for more than one year [1-2]. The prognostic value of NYHA functional class and LVEF in identifying patients at high risk for adverse outcomes is well established, whereas their association with cardiac events such as SCD is not well defined [3]. In this situation the majority of patients who die suddenly are not eligible for ICD placement under the current guidelines, whereas a lot of ICD implanted patients' never require ICD therapy during their lives [4].

Cardiac imaging with Iobenguane Scintigraphy (IS) might play an important role in improving the selection of patients who most benefit from an ICD. IS, in fact, can detect impaired global left ventricle sympathetic innervation and regional myocardial sympathetic heterogeneity, which are highly arrhytmogenic [5].

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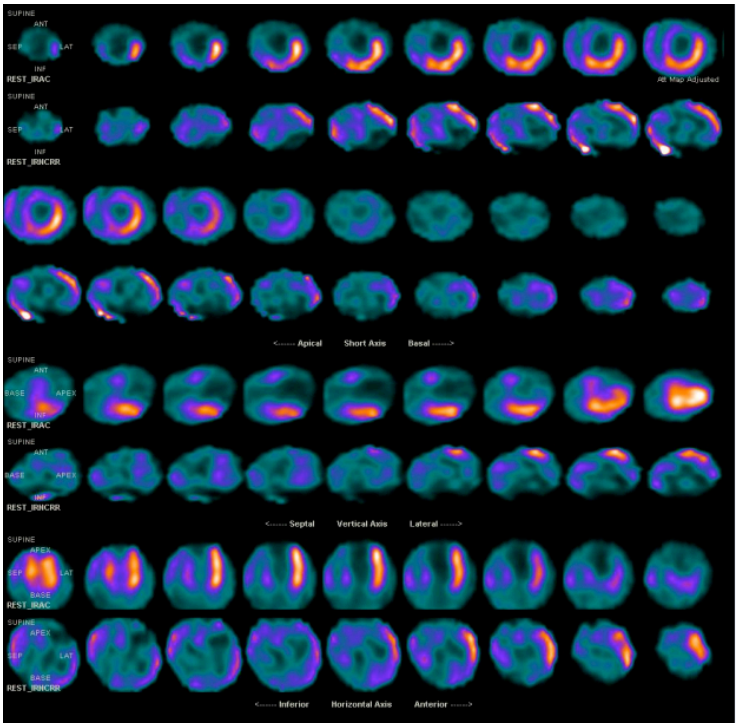
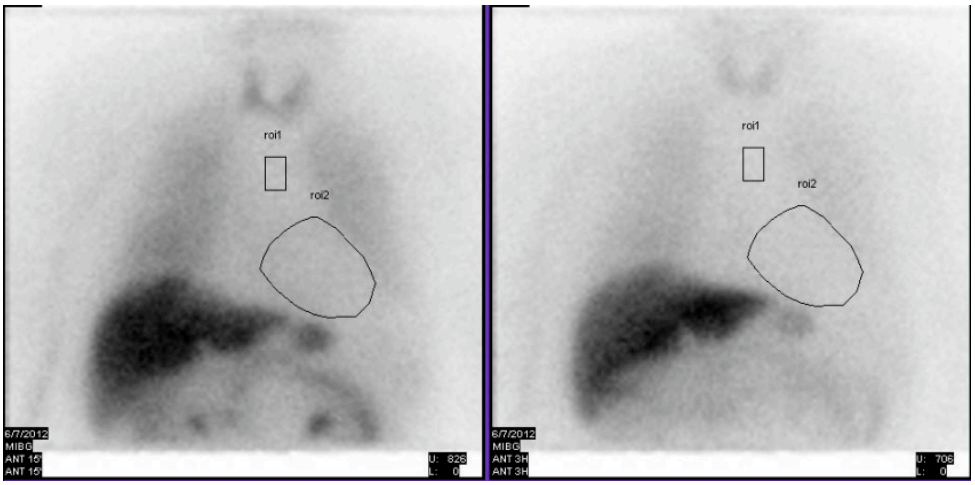


Fig. (1). Comparison of Iobenguane (lower series) and rest perfusion 99m-Tc tetrofosmin (upper series) SPECT images. Images clearly demonstrated an absent myocardial perfusion in antero-septal, apex, anterior wall of left ventricle. The SPECT images obtained with Iobenguane are usually worse in term of anatomical definition.



Early **Late**

Fig. (2). Anterior planar images of the thorax obtained early (15-min) and late (4-hour) after Iobenguane injection. The heart to mediastinum rate was 1.18 (early) and 1.15 (late). The ROIs depicted the areas of interest for the Iobenguane uptake and compared the mediastinum area with the heart.

Several studies have demonstrated the association between impaired (123)I-MIBG values and arrhythmic events, SCD and appropriate ICD discharges [6-8]. Furthermore in the prospective study of Nagahara *et al.* [7], the occurrence of ICD shocks due to fatal arrhythmias are correlated with cardiac MIBG activity, LVEF and BNP level; whereas Arora *et al.* [8] have shown that appropriate ICD discharges occur when both MIBG and heart rate variability are highly depressed. In other recent studies the only independent predictors of mortality have been the heart to mediastinum ratio (H/M) and the LVEF, considering especially an H/M ratio < 1.60 to be a significant predictor of major arrhythmic events. HF patients with reduced late H/M or increased (123)I-MIBG washout rate have a worse prognosis and an increased incidence of SCD as compared with patients with normal (123)I-MIBG uptake and washout parameters [9-10].

ADMIRE-HF study has recently provided further validations on the prognostic value of H/M on (123)I-MIBG scintigraphy in predicting potentially fatal outcomes in patients with CHF [11] and in better stratifying HF population. It has demonstrated a clear association between severity of myocardial sympathetic neuronal dysfunction, risk for subsequent cardiac death and CHF progression (increasing of NYHA functional class). Moreover, the

multivariable analysis has produced a model contributing to the risk stratification of HF patients, using 4 independent variables: late H/M, LVEF, NYHA functional class and plasma BNP.

In our patient the low H/M score obtained with IS has indicated a patient with an effective CHF progression and has predicted the following need of an ICD implantation. The correct timing for Iobenguane scintigraphy after coronary revascularization should be evaluated, considering that a partial re-innervation has been demonstrated in myocardial segments 3-4 months after revascularization (if coronary restenosis does not occur) [12], and further studies are needed to establish the potential role of IS into the decision-making process for ICD placement in primary prevention.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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Declared none.

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