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ORIGINAL ARTICLE

Iodine-123-metaiodobenzylguanidine scintigraphy in risk stratification of sudden death in heart failure☆

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Abstract Metaiodobenzylguanidine (MIBG) is a false neurotransmitter noradrenaline analogue that is taken up by the 'uptake 1' transporter mechanism in the cell membrane of presynaptic adrenergic neurons and accumulates in catecholamine storage vesicles. Since it is practically unmetabolized, it can be labeled with a radioisotope (iodine-123) in scintigraphic exams to noninvasively assess the functional status of the sympathetic innervation of organs with a significant adrenergic component, including the heart. Studies of its application in nuclear cardiology appear to confirm its value in the assessment of conditions such as coronary artery disease, heart failure, arrhythmias and sudden death.

Heart failure is a global problem, with an estimated prevalence of 2% in developed countries. Sudden cardiac death is the main cause of its high mortality. The autonomic nervous system dysfunction, including sympathetic hyperactivity, that accompanies chronic heart failure is associated with progressive myocardial remodeling, declining left ventricular function and worsening symptoms, and contributes to the development of ventricular arrhythmias and sudden death.

Since ^{123}I-MIBG cardiac scintigraphy can detect changes in the cardiac adrenergic system, there is considerable interest in its role in obtaining diagnostic and prognostic information in patients with heart failure.

In this article we present a literature review on the use of ^{123}I-MIBG scintigraphy for risk stratification of sudden death in patients with heart failure.

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PALAVRAS-CHAVE
Cintigrafia com iodo-123-metaiodobenzilguanidina;
Insuficiência cardíaca;
Morte súbita cardíaca;
Arritmias cardíacas;
Sistema nervoso simpático

Utilização da cintigrafia com iodo-123-metaiodobenzilguanidina na estratificação do risco de morte súbita na insuficiência cardíaca

Resumo A metaiodobenzilguanidina (MIBG) é um falso neurotransmissor análogo da noradrenalina, captada essencialmente por um mecanismo de transporte de tipo 1 na membrana celular dos neurónios adrenérgicos pré-sinápticos, acumulando-se em grânulos de armazenamento de catecolaminas. Como praticamente não é metabolizada, a sua marcação com um radioisótopo (iodo-123) permite, através de imagens cintigráficas, avaliar de forma não invasiva o *status* funcional da inervação simpática de órgãos com importante componente adrenérgico, incluindo o coração. A sua aplicabilidade em cardiologia nuclear tem vindo a ser estudada e parece revelar importância na avaliação de patologias como a doença arterial coronária, insuficiência cardíaca, arritmias e morte súbita.

A insuficiência cardíaca é um problema à escala global, com uma prevalência estimada nos países desenvolvidos de 2%. Apresenta uma mortalidade elevada, sendo a morte súbita cardíaca a principal causa. A disfunção do sistema nervoso autónomo, nomeadamente a hiperatividade simpática, que acompanha a insuficiência cardíaca crónica, relaciona-se com a remodelação progressiva do miocárdio, o declínio da função ventricular esquerda e o agravamento dos sintomas, participando no desenvolvimento de arritmias ventriculares e morte súbita.

Dado que a cintigrafia cardíaca com ^{123}I-MIBG permite a identificação de alterações do sistema adrenérgico cardíaco, questiona-se o seu papel na obtenção de informação diagnóstica e prognóstica em doentes com insuficiência cardíaca.

Pelo interesse e a atualidade do assunto, pareceu-nos oportuno rever os dados publicados sobre a utilização da cintigrafia com ^{123}I-MIBG na estratificação do risco de morte súbita em pacientes com insuficiência cardíaca.

List of abbreviations

ANS	autonomic nervous system
BNP	brain natriuretic peptide
ICD	implantable cardioverter-defibrillator
LVEF	left ventricular ejection fraction
H/M	heart/mediastinum ratio
MIBG	metaiodobenzylguanidine
NA	noradrenaline
NYHA	New York Heart Association
PNS	parasympathetic nervous system
SCD	sudden cardiac death
SNS	sympathetic nervous system
SPECT	single-photon emission computed tomography
VF	ventricular fibrillation
VT	ventricular tachycardia
WR	washout rate

Introduction

Heart failure (HF) has an estimated global prevalence of 2–3%.[1] In Portugal, its overall prevalence is 4.3%, increasing with age (estimated at 16.14% in those aged over 80).[2] Despite advances in treatment, the number of patients with HF continues to rise in developed countries with ageing populations.

Systolic HF develops following myocardial damage; it is accompanied by a decline in cardiac function, which activates compensatory mechanisms designed to preserve cardiac homeostasis that initially maintain heart rate, blood pressure and cardiac output, keeping the patient asymptomatic.[3,4] The most important elements involved are the renin–angiotensin–aldosterone axis, the sympathetic nervous system (SNS) and cytokines, chronic activation of which lead to changes in cardiac structure and performance as the disease progresses,[4] including hypertrophy and myocyte apoptosis, fibroblastic proliferation and interstitial collagen accumulation. The result is myocardial remodeling and contractile dysfunction and hence reduced left ventricular ejection fraction (LVEF),[3] as well as increased susceptibility to arrhythmias and sudden cardiac death (SCD).[5] In diastolic HF, by contrast, LVEF is preserved.[1,3,6]

SCD is one of the main causes of mortality in HF[7] (30–50%[8]), mainly due to ventricular tachycardia (VT), ventricular fibrillation (VF) and bradycardia. The autonomic nervous system (ANS) plays a central role in these arrhythmias[9,10]; the electrophysiological and potentially arrhythmogenic effects of catecholamines have been shown to be one of the main causes of VT and SCD in patients with autonomic dysfunction and sympathetic hyperactivity.[11]

The pro-arrhythmic effects of HF, which are related to changes in intracellular calcium concentrations and ANS tone, predispose to tachyarrhythmias and bradyarrhythmias that can result in cardiac arrest and SCD.[12] The most common electrical activation sequence is VT degenerating into VF; this is most often seen in dilated cardiomyopathy and ventricular dysfunction with reduced LVEF.[13]