Scintigraphic perfusion defects due to right ventricular apical pacing: a pitfall in clinical cardiology

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Abstract
Right ventricular apical pacing (RVAP) with a left bundle branch block on the electrocardiogram may result in regional wall motion abnormalities and decreased left ventricular function (LVF). Furthermore, perfusion defects in dipyridamole technetium-99m-methoxisobutylisonitrile (^{99m}Tc-MIBI) myocardial perfusion imaging may occur despite a normal coronary angiogram. In a 68 years old patient, RVAP resulted in regional wall motion abnormalities, markedly decreased LVF and perfusion defects in dipyridamole ^{99m}Tc-MIBI myocardial perfusion imaging by single photon emission tomography (SPET). Coronary angiography excluded coronary heart disease. Reprogramming of the pacemaker resulted in physiologic activation of the ventricles. Echocardiography showed a normal LV systolic function. Repeated myocardial perfusion imaging was unremarkable. *In conclusion*, our case confirms that RVAP may lead to scintigraphic perfusion defects and wall motion abnormalities despite a normal coronary angiogram and thus may imitate ischemia-induced perfusion defects.

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Introduction

Right ventricular apical pacing (RVAP) is known to be associated with an asynchronous ventricular contraction due to an iatrogenic (extrinsic) left bundle brunch block (LBBB). Iatrogenic LBBB results in an impaired left ventricular (LV) performance with a decrease in stroke volume (SV) and an abnormal LV relaxation due to inter- and intraventricular dyssynchrony, which may lead to a more or less reversible myocardial dilatation and symptoms of congestive heart failure. Differences in myocardial blood-flow between areas of early and late activation due to RVAP have been shown [1]. We present a case of RVAP where perfusion defects in dipyridamole technetium-99m-methoxisobutylisonitrile (^{99m}Tc-MIBI) myocardial perfusion imaging had been interpreted as related to coronary artery disease. However, coronary angiography revealed normal coronary arteries.

Case report

A 68 years old male patient received a bioprosthetic valved conduit because of an aortic root aneurysm and severe aortic regurgitation. Three months later a two chambers pacemaker was implanted after a syncope due to a sick sinus syndrome. One year later, persistent atrial fibrillation was converted electrically. At admission for residential rehabilitation, transthoracic echocardiography (e-CG) (Toshiba Aplio™ CV 500, Medical Systems Europe) revealed a hypertrophic normal sized LV with an apical, distal anterior and septal wall akinesia. Left ventricular ejection fraction (EF) was severely reduced in e-CG, (29%), continuous wave Doppler and colour Doppler e-CG showed a regular function of the bioprosthesis. The surface electrocardiogram revealed atrial fibrillation with a heart rate of approximately 90min and a complete LBBB due to continuous right ventricular pacing (DDD mode). Laboratory tests were within normal range, N-terminal pro BNP (NT-proBNP) was increased (4001pg/mL; normal value <150). Dipyridamole ^{99m}Tc-MIBI myocardial perfusion imaging (performed with an Infinia dual-head nuclear imaging system, General Electric Healthcare, USA showed irreversible perfusion defects of the apex and the distal anterior, inferolateral and septal walls (Fig. 1). Despite his severe dyspnoea equivalent to New York Heart Association class III (NYHA III), coronary angiography was refused by the patient as he was free from angina. Early discharge and transfer to a department of pulmonology became necessary because of pneumonia. Before discharge,

the pacemaker mode was reprogrammed to VVI mode (ventricle paced, ventricle sensed and pacing inhibited if a beat is sensed) because of persistent atrial fibrillation.

Two years later, the patient was readmitted for cardiac rehabilitation because of symptomatic heart failure NYHA II. Two months before, coronary angiography had revealed normal coronary arteries. The electrocardiogram showed atrial fibrillation with a heart rate of 55min, left axis deviation, and narrow QRS complexes. Transthoracic e-CG revealed a concentric LV hypertrophy, a normal sized LV with normal systolic function and no segmental wall motion abnormalities. Elevated NT-proBNP (1943pg/mL), an E/E´ratio of 18 in pulsed wave Doppler e-CG (E indicates the peak early diastolic mitral inflow velocity, E´ indicates the tissue Doppler-derived peak early diastolic E´ mitral annulus velocity, E/E´ reflects left atrial pressure) and a high end-diastolic pressure of 23mmHg during left ventriculography were noticed which confirmed the presence of diastolic heart failure. Since the previously reduced left ventricular ejection improved from 29% to 60%, dipyridamole ^{99m}Tc-MIBI myocardial perfusion imaging was repeated. In contrast to the previous examination no perfusion defects could be documented (Fig. 2). We therefore hypothesized that the initial perfusion defects were induced by RVAP. Changing the pacemaker mode to VVI resulted in a physiologic conduction and activation of the ventricles, without inducing further atrial fibrillation due to the DDD mode of the pacemaker.

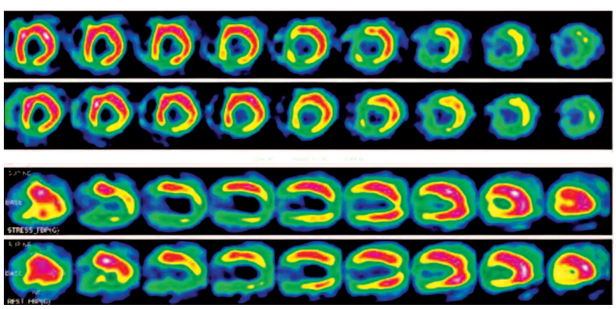

Figure 1. Dipyridamole ^{99m}Tc-MIBI myocardial perfusion imaging during RVAP. Horizontal short-axis and long-axis slices (upper row stress and lower row 24h post stress). Irreversible apical and inferoposterolateral defects, during RVAP.

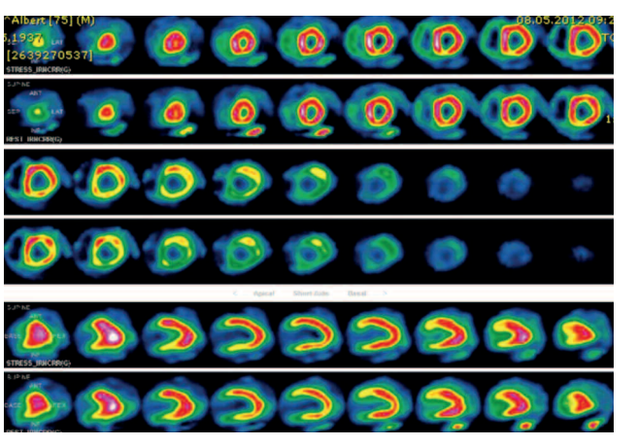

Figure 2. Dipyridamole ^{99m}Tc-MIBI myocardial perfusion imaging after reprogramming of the pacemaker without any electrical stimulation of the myocardium and a surface electrocardiogram with narrow QRS complexes. Horizontal short-axis and long-axis slices (upper and middle row stress and lower row 24h post stress). No perfusion defect could be documented.

Discussion

Right ventricular apical pacing is known to be associated with an asynchronous ventricular contraction due to an iatrogenic (extrinsic) LBBB resulting in an electrical asynchrony which is reflected by a prolonged QRS duration. The electrical activation starts in the apex and propagates through the myocardium, rather than through the Hiss-Purkinje conduction system, with the earliest mechanically activated parts in the septum and the latest activation at the inferoposterior base of the LV [1]. Iatrogenic LBBB results in an impaired left ventricular performance with a decrease in stroke volume and an abnormal left ventricular relaxation [2, 3]. Furthermore, significant inter- and intraventricular dyssynchrony may occur which is associated with LV dysfunction [4-6]. Recent studies have also demonstrated that asynchronous myocardial contraction may lead to a more or less reversible myocardial dilatation and symptoms of congestive heart failure [1, 7, 8]. Both the abnormal electrical and mechanical activation pattern of the ventricles can result in abnormalities of cardiac metabolism and perfusion, of remodeling and of mechanical function. Regional changes of mechanical load, as in long-term asynchronous electrical activation, lead to asymmetrical changes of LV wall mass. Early activated regions have a lower preload due to rapid early systolic shortening leading to a pre-stretch of the late activated areas. This results in thinning of the myocardial wall of early as compared to late activated regions [9]. The precise time course of the development of LV dysfunction, heart failure, and LV dyssynchrony after RVAP is still unclear. In a study by Delgado et al (2009) 36% of 25 patients developed significant LV dyssynchrony during RVAP, as assessed by two-dimensional e-CG speckle-tracking strain imaging [10]. In addition, significantly reduced LV ejection fraction was observed as well as an impaired LV longitudinal shortening and reduced LV twist. Whether this acutely induced LV dyssynchrony is responsible for the further development of heart failure after long-term RVAP requires further studies. As demonstrated by Tse et al (2002) in patients with normal coronary arteries RVAP can induce regional myocardial blood flow, perfusion and wall motion abnormalities near the site of electrical stimulation, which became even more pronounced with an increased duration of RVAP [11]. After long-term RVAP these pathologies may be present in up to 65% of the patients and are mainly located near the pacing site [12, 13]. Moreover, altered regional adrenergic innervation presenting as myocardial perfusion defects during iodobenzylguanidine (^{123}I-MIBG) scintigraphy has been shown [14, 15]. These regional disturbances affect mainly the inferior, apical and posterior wall, all of which are activated early after right apical stimulation [15]. However, as the global ^{123}I-MIBG uptake in the study by Marketou et al (2002) did not change significantly, it seems to be a functional alteration of sympathetic activity [13]. A decrease in segmental contractility in early activated regions may result in a compensatory increase in norepinephrine uptake by the nerve terminals resulting in ^{123}I-MIBG uptake defects [13, 14]. Furthermore, other researchers re-

ported that iatrogenic LBBB was associated with a 65% increase in cardiac norepinephrine spillover, an index of efferent cardiac sympathetic nerve activity [16]. Right VAP and the consecutively decreased LV contraction with a reduction in firing rate of ventricular mechanoreceptors seem to lead to withdrawal of vagal tone and increased cardiac sympathetic activity.

Although there are electrocardiographic similarities in the surface electrocardiogram in intrinsic and iatrogenic LBBB due to RVAP, intrinsic LBBB perfusion defects are rather confined to the septum. The earliest activated regions are the basal segments and the latest activated areas are the posterior and inferior lateral segments. Delayed and asynchronous activation of the left side of the septum may be responsible for false positive septal defects associated with LBBB in stress radionuclide myocardial perfusion imaging. In LBBB, septal contraction occurs at the end of systole. Delayed ventricular relaxation and the contraction of the septum in systole could restrict myocardial perfusion in early diastole [17, 18].

As with LBBB, adenosine or dipyridamole radionuclide myocardial perfusion imaging is recommended by the TASC Force of the European Society of Cardiology for the diagnosis of suspected coronary artery disease in patients with a paced ventricular rhythm [19]. In a study of 14 patients with permanent right ventricular pacemakers and normal coronary angiograms, 50% had false positive perfusion defects during dipyridamole stress radionuclide myocardial perfusion imaging [13]. This finding can be explained by a lower flow reserve in the coronary artery as well as an impairment of microvascular flow which both induce perfusion defects of the regional myocardium. Furthermore, reduced septal myocardial blood flow is a rate-dependent phenomenon. Other researchers had found in dogs that septal hypoperfusion was due to compression of septal branches arising from the posterior descending coronary artery, rather than from the left anterior descending (LAD) coronary artery during rapid pacing [20]. Marketou et al could not find deteriorations in LV perfusion after a pacing period of three months [14]. However, there is evidence that long-term permanent RVAP may lead to scintigraphic perfusion defects [12]. This implies the development of histological alterations of myocardial tissue and in particular of the microvascular blood flow over time. In contrast, Ten Cate et al (2009) showed that RVAP resulted in myocardial perfusion defects in ^{99m}Tc-MIBI SPET perfusion imaging at rest [21]. Despite the same amount of tracer activity in the myocardium during atrial pacing and RVAP, perfusion defects became significantly more extensive during RVAP. The area and severity of these defects correlated with the altered wall motion.

In conclusion, our case confirms that RVAP may lead to scintigraphic perfusion defects and wall motion abnormalities despite a normal coronary angiogram and thus may imitate ischemia-induced perfusion defects.

The authors declare that they have no conflicts of interest.

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