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Review

The effects of ventricular asynchrony on myocardial perfusion

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Abstract

Asynchronous depolarization and contraction sequence, secondary to intraventricular conduction defects or to permanent right ventricular apical pacing, is associated with adverse effects that may be clinically evident in the failing heart. Experimental and clinical studies have suggested that asynchronous ventricular contraction deteriorates left ventricular performance and induces unfavourable left ventricular remodelling. Although such contraction does not appear to affect resting coronary artery blood flow, it increases endomyocardial pressure during diastole and decreases regional myocardial perfusion in the interventricular septum. The magnitude of these effects may correlate with the duration of the asynchrony. Despite these detrimental effects, there is no evidence that ventricular asynchrony reduces collateral myocardial blood flow, myocardial oxygen consumption or cardiac efficiency, neither in patients with normal coronary arteries, nor in patients with coronary artery disease. Furthermore, in patients with acute ischaemic syndromes, ventricular asynchrony exerts a neutral effect on the ischaemic myocardium.

Cardiac resynchronization therapy improves left ventricular systolic and diastolic function without an increase in myocardial oxygen consumption or energy cost. This therapy may decrease the inhomogeneity in regional oxidative metabolism, myocardial perfusion and cardiac efficiency. Further experimental and clinical studies are needed on this area.

Keywords: Asynchrony; Myocardial perfusion; Coronary blood flow; Cardiac efficiency

1. Introduction

The role the specialized His-Purkinje system is to conduct the electrical impulse in the myocardium of the two ventricles much faster than the ventricular myocytes. As a result, all parts of the ventricular myocardium contract almost simultaneously, producing an efficient mechanical systole. Asynchronous contraction ensues when ventricular excitation is eccentric, i.e. it begins at a ventricular myocardial site distant from the normal conduction system and is conducted to the ventricles, at least in part, through the ventricular myocardium and not through the His-Purkinje system. This induces temporal delays in the contraction and relaxation of various parts of the ventricular myocardium, resulting in a less effective systolic and diastolic ventricular function. Ventricular pacing and intraventricular conduction defects are the two conditions, commonly encountered in clinical practice, in which the sequence of ventricular excitation and contraction is chronically altered.

The effects of asynchronous contraction on ventricular performance were first studied by Wiggers [1]. Since then, experimental studies have revealed unfavourable effects of asynchronous ventricular depolarization on ventricular performance, both in normal hearts and in experimentally induced heart failure [2–4]. A variety of abnormalities have been reported, such as decreased cardiac output, slowed relaxation rates and reduced peak filling velocities [2–4]. The detrimental effects of ventricular asynchrony caused by right ventricular apical pacing have been confirmed by several human studies [5–7]. These effects are prominent in patients

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with depressed baseline left ventricular function, and consist of deterioration in systolic and diastolic function indices, exercise capacity, quality of life and prognosis [5–7]. Similarly, human studies have examined the association between left bundle branch block-induced ventricular asynchrony and cardiac disease [8–14]. Although earlier reports [10,11] have suggested that acquired left bundle branch block in asymptomatic individuals without other risk factors is a benign condition, this notion was subsequently challenged by newer findings [12,13]. In the Framingham Study, patients with left bundle branch block were more likely to have or subsequently present with advanced cardiovascular abnormalities than patients with right bundle branch block [12]. This study demonstrated that the 10-year cardiovascular mortality after the onset of left bundle branch block was approximately 50% [12]. In patients with chronic coronary artery disease in the CASS registry [13], left bundle branch block was a strong predictor of mortality, independently of the severity of heart failure, extent of coronary artery disease, or other important variables. In the DAVID trial, [14] patients with depressed left ventricular function, indications for defibrillator therapy, but without indications for pacemaker therapy were implanted with a device with dual-chamber, rate-responsive pacing capability. Patients were randomly assigned to have the device programmed to low-rate ventricular backup pacing (essentially no pacing was used) or to dual-chamber rate-responsive pacing at 70 beats per min. There was a trend towards lower hospitalisation and lower mortality rates in patients programmed to back-up pacing, while the combined end-point reached statistical significance, in favour of back-up pacing.

Although a considerable amount of research has been devoted to the study of the haemodynamic consequences of asynchronous ventricular contraction, little is known on its effects on coronary blood flow, myocardial perfusion and cardiac energetics. Newer techniques and technology, such as intracoronary Doppler catheters and guide-wires, digital subtraction angiography, thermodilution techniques, and positron emission tomography, permit the study of the coronary circulation and cardiac energetics under a variety of physiologic conditions.

In this paper, we review the current knowledge on the effects of ventricular asynchrony on coronary haemodynamics, myocardial perfusion and cardiac energetics.

2. Ventricular asynchrony and myocardial perfusion

Long-term asynchronous ventricular contraction may produce changes in the myocardial architecture. Adomian and Beazell [15] studied the effects of asynchrony on ventricular remodelling on a cellular level in dogs; complete atrioventricular block was produced and right ventricular apical pacing was performed for 3 months. With the use of light microscopy, they [15] demonstrated marked myofibrillar disarray in both ventricles. These changes may produce alterations in regional myocardial fiber strain, work load and wall tension [16], leading to a redistribution of oxygen demand and blood flow [17].

These data are of particular importance in humans. Patients with left bundle branch block display a high incidence of thallium-201 perfusion defects in the interventricular septum and in the anterior left ventricular wall, in the absence of coronary artery disease [18]. Right ventricular apical pacing has a similar effect [19–21] and the magnitude of these perfusion defects may correlate with the duration of pacing [20]. The responsible mechanisms are not fully understood. In a study in dogs, Ono et al. [22] evaluated the effects of apical pacing-induced left bundle branch block on myocardial perfusion and glucose uptake, using thallium-201 and F-18-labeled 2-fluoro-2-deoxy-D-glucose, respectively. They [22] found that during ventricular pacing, the uptake of both substances was decreased in the interventricular septum, compared to the free wall (Fig. 1). Furthermore, regional myocardial flow (measured by radioactive-labelled microspheres) was lower in the interventricular septum than in the left ventricular free wall and systolic thickening of the interventricular septum was reduced. Diastolic endomyocardial pressure was higher during ventricular than during atrial pacing (Fig. 2), whereas aortic pressure, left anterior descending blood flow velocity and lactic acid concentration did not change. These findings suggest that thallium-201 defects during ventricular pacing are not secondary to myocardial ischaemia. In another study in dogs, chronic left bundle branch block (induced by radiofrequency ablation) resulted in a decreased left ventricular ejection fraction and in an increased left ventricular cavity size [23]. Myocardial blood flow (measured with fluorescent microspheres) and systolic circumferential shortening decreased in the septum and increased in the lateral wall, indicating that ventricular asynchrony induces ventricular remodelling and deterioration in left ventricular systolic function, in otherwise normal

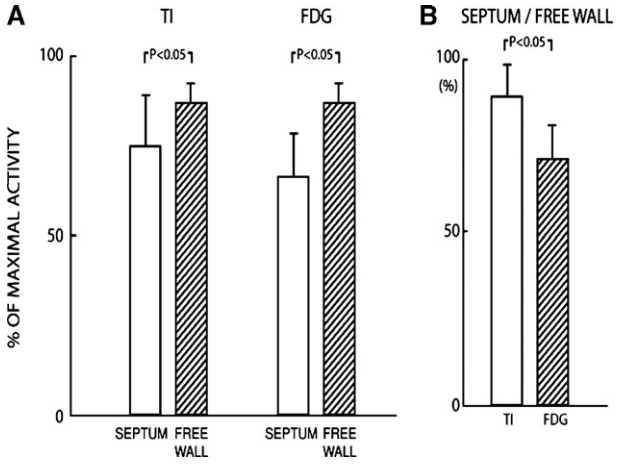

Fig. 1. Bar graphs showing (panel A) relative myocardial uptake of Thallium-201 (Tl) and 18F-labeled 2-fluoro-2-deoxy-D-glucose (FDG) calculated from tissue counting and (panel B) ratios of septal to free wall activity for Tl-201 and FDG. Tl-201 and FDG were injected in dogs during electrical left bundle branch block induced by right ventricular pacing. (From reference [22], with permission).