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# Acute Haemodynamic and Echocardiographic Effects of Multiple Configurations of Left Ventricular Pacing Sites in Acute Myocardial Infarction: Experimental Study

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Background	Left ventricular (LV) pacing is unsuccessful in a significant number of patients, mainly due to sub-optimal LV pacing location. Nevertheless, data about the impact of different pacing sites on LV function in ischaemic myocardium are scarce. The purpose of this study was to investigate the effect of combinations of alternative LV pacing sites on LV mechanics after experimental acute anterior myocardial infarction (AMI), in order to define the optimal configuration.
Methods	Atrioventricular epicardial pacing at alternative pacing sites was performed in 16 healthy pigs simulta- neously, after experimental AMI. Standard right ventricular (RV) apical pacing was combined with: i) LV apex lateral wall; ii) LV basal posterior wall; iii) LV basal anterior wall, and; iv) LV basal anterior wall + LV basal posterior wall. Moreover the pacing configurations of; v) LV basal posterior wall + LV apex lateral wall; vi) LV basal posterior wall + LV basal anterior wall, and; vii) LV basal anterior wall + LV apex lateral wall; vi) LV basal posterior wall + LV basal anterior wall, and; vii) LV basal anterior wall + LV apex lateral wall were also investigated. Haemodynamic parameters, together with classic and novel echocardiographic indices were used, to evaluate the effect of each pacing combination. A speckle tracking technique using EchoPAC software was used.
Results	After AMI, the pacing combination of LV apex lateral wall and LV basal posterior wall had the most favourable effect on LV function, leading to similar haemodynamic and torsional effects with sinus rhythm (all variables p>0.05).
Conclusions	In pig hearts after AMI, the combination of pacing LV apex lateral wall and LV basal posterior wall managed to maintain the LV function at a level comparable to the sinus rhythm.
Keywords	Pacing • Torsion • Acute myocardial infarction • Cardiac mechanics

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### Introduction

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More than a half a century has passed since Furman and Schwedel published their work on endocardial lead placement for cardiac pacing in humans [1]. Since then, the apex of the right ventricle (RV) remains the standard of choice regarding the site of lead placement due to the accessibility, feasibility, and the safety it provides.

However, in the last decade there is growing evidence which demonstrates that pacing the apex of the RV has unfavourable effects, influencing morbidity and mortality [2–5]. These findings are consistent with Wigger's observations, who, in 1925, reported about the adverse left ventricular (LV) haemodynamic effects that occurred, secondary to RV apical pacing [6]. These harmful effects are produced, mostly due to the alteration of the normal conduction pathway. The electrical stimulation bypasses the atrioventricular node and the highly specialised His-Purkinje system, and is spread slowly through the common myocardium, causing abnormal ventricular contraction and reducing pump function.

Obviously, it is time to seek alternative pacing sites to minimise the adverse clinical outcomes of RV apex stimulation. Investigation in this area is also extensive due to the introduction of cardiac resynchronisation therapy (CRT), and the fact that almost one-thirds of patients receiving this therapy do not respond to treatment [7,8].

A number of studies have been published about alternative pacing sites, mostly in patients with heart failure [9–11]. However, data about the impact of different pacing sites on LV function in myocardium under ischaemia is scarce. Moreover, the evaluation of cardiac mechanics in this condition, with novel techniques such as two-dimensional speckle tracking echocardiography (STE), are limited. The STE allows detailed evaluation of LV mechanics, including LV mechanical dyssynchrony, LV strain, and LV torsion, and provides important additional information for the selection of the optimal pacing site [12,13]. Data based on STE comparing the effects of different LV pacing and sites on the LV mechanics, LV strain, and LV torsion — are still limited [14,15].

The purpose of this study was to assess the acute haemodynamic and echocardiographic response to different pacing configurations after experimental acute myocardial infarction (AMI). The ultimate goal was to determine the optimal combination of pacing sites that preserve LV function under ischaemic conditions.

### **Methods**

The protocol complied with the "Principles for the Care of Experimental Animals" and the "Guidelines for the Care and Use of Experimental Animals" issued by the US National Academy of Sciences and National Institute of Health (version 85-23, revision 1996), and was approved by the Scientific Committee of our Hospital.

#### **Surgical Preparation**

Sixteen healthy pigs, weighing  $40\pm5$  kg, were pre-medicated with intramuscular administration of ketamine potassium 5 mg/kg, and midazolam 5 mg/kg. Anaesthesia was induced with thiopental sodium 5 mg/kg intravenously (IV), and the animals were then intubated and ventilated by mechanical ventilation (Sulla 808 V, Drager Medizintechnik GmbH, Germany). Throughout the experiment anaesthesia was maintained with IV propofol 0.1-0.2 mg/kg, and analgesia was maintained with the administration of opioid-fentanyl. Lead II of the standard electrocardiogram (ECG), haemoglobin oxygen saturation, and the animal's temperature with a rectal thermometer were monitored constantly by a multichannel device (Dynamap Plus Vital Signs Monitor, Criticon, Tampa, FL, USA).

A 6F sheath was inserted into the right internal jugular vein for the delivery of drugs and fluids. A suprapubic urinary catheter was inserted to measure urine output, and fluid loss was compensated by continuous infusion of saline into the right jugular vein. Moreover, left external carotid artery was cannulated and a 6F pigtail catheter was placed into the LV cavity and used for the measurement of LV pressure and peak rate of LV pressure increase (dP/ $dt_{max}$ ). To avoid endovascular thrombus formation, a 5000 IU heparin bolus was administered. Loading conditions were kept constant during the different manoeuvres.

We used the same surgical procedure that we have developed in our previous experiments [15,16]. Briefly, a regular median sternotomy was performed after thymoma resection, and a longitudinal pericardiotomy was performed. The left anterior descending (LAD) coronary artery was surgically exposed, and two 3-0 Prolene sutures (Ethicon, Johnson & Johnson Co., European Logistics Centre, Sint-Stevens-Woluwe, Belgium) were placed after the origin of the first diagonal branch of the LAD, to be used for future ligation. Before ligation, left coronary artery entrapment was confirmed by upward traction. The apex of the LV was observed for evidence of myocardial blanching indicating interruption to coronary flow, confirming epicardial ischaemia (Figure 1, Figure 2). Moreover, ECG from limb leads also confirmed the experimental AMI (Figure 3).

#### Pacing

Temporary myocardial pacing leads (Medtronic, type 6500, Minneapolis, MN, USA) were attached to the surface of the right atrium, to the epicardium of the RV apex, and in different positions of the epicardium of the LV. These different positions of the LV were the basal posterior wall, the basal anterior wall, and the apex lateral wall (Figure 1, Figure 2). All pacing positions were kept outside the infarcted zone.

The pacing leads were connected to an external pacemaker (Medtronic Model 5388 dual chamber temporary pacemaker, Minneapolis, MN, USA). Pacing was unipolar with an indifferent electrode positioned in between the intercostal muscles. The AV delays were short enough to produce an activation wave originating from the ventricular pacing lead,

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