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Abstract: Acute transmural ischaemia often shortens ventricular repolarization and increases repolarization dispersion, leading to life threatening ventricular arrhythmias in animal models and human subjects. Experimental studies and clinical observations have shown that acute subendocardial ischaemia rarely causes serious ventricular arrhythmia. We hypothesized that the different arrhythmia outcomes between transmural and subendocardial ischaemia are largely due to the homogenous prolongation in ventricular repolarization after acute subendocardial ischaemia.

Acute subendocardial ischaemia leads to homogenous prolongation in
ventricular repolarization

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Summary

Acute transmural ischaemia often shortens ventricular repolarization and increases repolarization dispersion, leading to life threatening ventricular arrhythmias in animal models and human subjects. Experimental studies and clinical observations have shown that acute subendocardial ischaemia rarely causes serious ventricular arrhythmia. We hypothesized that the different arrhythmia outcomes between transmural and subendocardial ischaemia are largely due to the homogenous prolongation in ventricular repolarization after acute subendocardial ischaemia.

Key words: subendocardial ischaemia; repolarization; ventricular tachycardia; electrophysiology.

Introduction

Subendocardial ischaemia is common in patients with coronary artery disease, often manifested by transient ST-T depression on body surface ECG. Previous studies have shown that a small proportion of patients who die suddenly of ventricular arrhythmias have S-T segment depression immediately prior to the death [1, 2]. Although ventricular premature beats and non-sustained ventricular tachycardia have been reported during subendocardial ischaemia attack (3, 4), the incidence of life-threatening ventricular arrhythmias is generally very low [5-7].

On the contrary, transmural ischaemia is associated with a high incidence of life-threatening ventricular arrhythmia. An increase in spatial dispersion of ventricular repolarization following acute transmural ischaemia is believed to be responsible for the pathogenesis of ventricular tachycardia and sudden cardiac death [8, 9]. It is unclear, however, if subendocardial ischaemia also increases the spatial dispersion of ventricular repolarization.

Pathogenesis of ventricular tachycardia during transmural ischaemia

A major anatomical substrate for ventricular tachycardia associated with coronary artery disease is a previous myocardial infarction resulting in significant left ventricular wall motion abnormalities (10). The extent of myocardial infarction and its position, especially whether the interventricular septum has been involved, appears to be the most important factor for developing malignant ventricular arrhythmias (11, 12). In animal models designed to reproduce arrhythmias in acute transmural ischaemia, ventricular tachyarrhythmias frequently occur spontaneously and can also be readily induced by

electrical stimulation (13, 14). The more ventricular tissue involved in the ischaemia, the higher the incidence of the ventricular arrhythmias (13). The incidence of the ischaemic ventricular arrhythmias is also related to the stress in the conscious animals (14), the mode of coronary artery occlusion (15) and the influence of the autonomic system (16).

Many studies have shown that the action potential duration and ventricular repolarization is shortened following transmural ischemia induced by total coronary artery occlusion [17, 18]. The shortening of ventricular repolarization is often associated with a significant increase in repolarization dispersion, which causes re-entry and development of ventricular arrhythmia [19, 20].

Electrophysiology during acute subendocardial ischaemia

Little is known about the changes in ventricular repolarization during acute subendocardial ischaemia. Subendocardial ischaemia only involves the innermost myocardium whereas the electrophysiological properties of the epicardium remained unchanged. Since repolarization normally proceeds in an epicardial-to-endocardial direction, delayed recovery in the subendocardial region due to ischaemia lengthens repolarization but does not reverse the direction of repolarization.

The low incidence of ventricular arrhythmia during acute subendocardial ischaemia indicates that subendocardial ischaemia plays a limited role in provoking ventricular arrhythmias or sudden cardiac death [5-7].

We hypothesized that subendocardial ischaemia leads to repolarization changes that are different from those caused by acute transmural ischaemia. Unlike transmural ischaemia where considerable changes in ventricular repolarization occurs in the central ischaemic

zone and the refractoriness in the non-ischaemic area remains unchanged, subendocardial ischaemia causes repolarization prolongation in all areas of endocardium and does not increase the spatial dispersion of ventricular repolarization. This homogenous lengthening in ventricular repolarization may be the main reason for the lower incidence of ventricular arrhythmia during subendocardial ischaemia.

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