ST-segment deviation behavior during acute myocardial ischemia in opposite ventricular regions: Observations in the intact and perfused heart

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BACKGROUND Acute myocardial ischemia in opposite regions may attenuate ST-segment changes, but whether this effect is expressed differently in extracardiac compared to direct intramyocardial recordings is not well known.

OBJECTIVE The purpose of this study was to characterize ST-segment changes induced by opposite ischemic regions in intact and isolated perfused pig hearts.

METHODS Left anterior descending (LAD) and right coronary arteries (RCA) were occluded in 7 closed chest pigs and in 5 isolated pig hearts. ST-segment changes were analyzed in 12-lead ECG and in local extracellular electrograms.

RESULTS Isolated LAD or RCA occlusion induced maximal ST-segment elevation in leads V_4 (0.84 ± 0.30 mV, $P = .003$) and III (0.16 ± 0.11 mV, $P = .04$), respectively. RCA occlusion also induced reciprocal ST-segment depression maximal in lead V_4 (−0.40 ± 0.16 mV, $P = .005$). Simultaneous LAD and RCA occlusion reduced ST-segment elevation by about 60% and blunted reciprocal ST-segment changes. Reperfusion of 1 of the 2 occluded arteries induced immediate regional reversion of ST-segment elevation with concurrent beat-to-beat re-elevation in the opposite ischemic region and reappearance of reciprocal ST-segment changes. In the isolated heart, single LAD or RCA ligature induced regional transmural ST-segment elevation that was maximal in endocardial electrograms with no appreciable reciprocal ST-segment depression. Simultaneous LAD and RCA ligature reduced ST-segment elevation by about 30% with no appreciable re-elevation after 1-vessel selective reperfusion.

CONCLUSION Acute myocardial ischemia in opposite ventricular regions attenuated ST-segment elevation and blunted reciprocal depression in conventional ECG leads but not in direct local myocardial electrograms.

KEYWORDS Myocardial ischemia; ST-segment cancellation; Double coronary occlusion; *In situ* heart; Isolated heart

ABBREVIATIONS ECG = electrocardiographic; **LAD** = left anterior descending; **LV** = left ventricle; **RCA** = right coronary artery

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Introduction

Simultaneous ischemia in opposite left ventricular (LV) regions may occur clinically, but the resultant electrocardiographic (ECG) changes have not been systematically studied and are not well understood.

Patients with significant multivessel coronary artery disease may present with ischemia in opposite LV regions during exercise, which may counterbalance ST-segment changes and result in falsely negative exercise ECG test.[1] In the literature, ST-segment changes have been described in patients with simultaneous occlusion of the left anterior descending (LAD) and right coronary arteries (RCA).[2–5] It also has been shown that in patients with a single distal occlusion of the LAD, elevation of the ST segment can be present in both inferior (II, III, aVF) and precordial leads (V_2–V_5) mimicking a pattern suggesting simultaneous LAD and RCA occlusion.[6,7]

Ischemic ST-segment shifts (both elevation and reciprocal depression) that are induced by simultaneous myocardial ischemia in opposite regions have not been systematically analyzed. Moreover, it is not known whether cancellation of ST-segment changes truly occurs in the local cardiac recordings or it is only detected by conventional ECG leads as a result of spatial summation of the injury currents of different direction generated by the opposite ischemic regions.

In this study, we performed single and combined occlusion of the LAD and RCA in *in situ* and isolated perfused pig heart in order to characterize the patterns of ST-segment

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cancellation induced by opposite ischemic regions and to determine whether this counteracting effect is detected differently in the intact and in the isolated perfused heart.

Methods

Study population

Twelve female domestic swine (Landrace–Large White cross) weighing 40 kg were sedated with azaperone (8 mg/kg intramuscular, Stressnil; Esteve Farma SA, Barcelona, Spain) and anesthetized with sodium thiopental (10 mg/kg intravenous, Pentothal; B. Braun Medical SA, Barcelona, Spain). They were intubated and mechanically ventilated with a mixture of oxygen and 2% isoflurane to maintain general anesthesia. Fentanyl (0.005 mg/kg intravenous, Fentanest; Kern Pharma SL, Barcelona, Spain) and atracurium besylate (1 mg/kg intravenous, Tracrium; GlaxoSmithKline SA, Madrid, Spain) were administered during the procedure for analgesia and muscular relaxation, respectively.

The study protocol was approved by the ethics and animal welfare committee of our institution, according to the regulations for treatment of animals established by the *Guide for the Care and Use of Laboratory Animals* published by the U.S. National Institutes of Health (NIH Publication No. 85-23, revised 1996).

Experimental series

In situ heart

Seven pigs were included in the series. All animals were free of significant atherosclerotic coronary artery disease as determined by coronary angiography.

Coronary artery occlusion. Acute transmural myocardial ischemia was induced by percutaneous coronary catheter balloon occlusion. Both femoral arteries were catheterized, and two 7Fr introducers were used to insert 6Fr guide catheters (Merit Medical Europe, Maastricht, The Netherlands). Under fluoroscopic control, the catheters were advanced to the ostium of the left and right coronary arteries. Then, 2 coronary catheters with a 3-mm × 15-mm balloon (Maverick, Boston, MA) were positioned at the mid-segment of the LAD, distal to the first septal and first diagonal branch, and mid-segment of the RCA. The position of the catheter balloon was verified by coronary angiography. Sodium heparin (70 IU/kg, bolus injection) was given to prevent thrombus formation during the procedure. Coronary occlusion was induced by transient (5-minute) inflation of the balloon at 12 atm.

Conventional 12-lead ECG. The 12-lead ECG was continuously recorded and stored on a hard disk of a multichannel recording system (Prucka Engineering Inc, Houston, TX). Because of species anatomy, the precordial leads were placed 1 intercostal space above that used in current clinical ECG. In each ECG recording, we measured the magnitude of the ST-segment deviation at the J-point level.

Study protocol. Five of the 7 pigs underwent single occlusion of the LAD and RCA for 5 minutes spaced by 10 minutes of coronary reperfusion. Thereafter, both coronary arteries were occluded simultaneously for 5 minutes, followed by selective release of the LAD or the RCA. In the remaining 2 pigs of this series of 7, a double LAD and RCA was performed as the first intervention to assess whether the trend of ST-segment changes during selective reperfusion were comparable in pigs with and those without previous ischemia. The ECG was recorded at baseline and continuously during each ischemia–reperfusion cycle. Pigs that presented with ventricular fibrillation were excluded from the study to avoid potential confounding effects of electrical defibrillation on the ST segment.

Isolated Langendorff perfused heart

This model was used to assess whether the ST-segment changes induced by opposite ischemia were detected differently in the peripheral ECG and in direct local intramural electrograms. A mid-sternotomy was performed to expose the heart. After administration of intravenous sodium heparin (70 IU/kg, bolus injection), 1000 mL of blood was collected. Then, the heart was removed and rapidly immersed in cold Tyrode's solution. The aorta was cannulated and connected to a Langendorff perfusion setup filled with the extracted blood. The circulating blood was oxygenated by a mixture of 95% O_2 and 5% CO_2 using a clinical extracorporeal oxygenator (Palex SA, Barcelona, Spain), and the temperature was maintained around 37ºC. Likewise, the perfusion flow was maintained at a mean pressure of about 70 mm Hg. Samples of the perfusate were extracted to keep blood gases and pH at normal values ($pO_2 > 90\%$, pH $\approx$ 7.45). A direct current electrical shock of 15 J was applied to defibrillate the heart.

Coronary artery occlusion. The LAD was dissected at its middle segment after the origin of the first diagonal branch and looped with a Prolene 3/0 snare. The RCA was also dissected at its middle segment, and a Prolene snare was placed around it. The 2 ends of the suture were threaded through a smooth plastic tube, and the artery was acutely occluded by sliding the tubing over the suture and clamping it with a small hemostat clamp. Reperfusion was accomplished by releasing the ligature.

Transmural local electrograms. Transmural needle electrodes containing 3 electrodes spaced 3 mm apart were inserted in the wall of the left ventricle in a row extending from the anterior to the posterior region, spaced about 2–3 cm. The reference electrode was placed in the aortic root. Signals were recorded using a BioSemi Mark-V acquisition system (Amsterdam, The Netherlands). A waiting period of 60 minutes was followed to allow recovery of the injury caused during insertion of the electrodes. Local electrograms that did not recover were excluded from the study. Offline analysis of all recorded electrograms was done using a