

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 $\times$ 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 multi-channel 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% O₂ and 5% CO₂ using a clinical extracorporeal oxygenator (Palex SA, Barcelona, Spain), and the temperature was maintained around 37°C. 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 (pO₂ > 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

custom-made data analysis program. In each recording, we measured the magnitude of the ST-segment deviation at the J-point level.

Study protocol. Five animals were included in the series. All hearts underwent single occlusion of the LAD and RCA for 5 minutes spaced by 10 minutes of reperfusion. Thereafter, both coronary arteries were occluded simultaneously for 5 minutes, followed by sequential release of the LAD (2 cases) or the RCA (2 other hearts). Local electrograms were recorded at baseline and during each ischemia-reperfusion sequence. Hearts that presented with ventricular fibrillation during the coronary occlusion-reperfusion episodes were excluded from the study to avoid potential confounding effects of electrical defibrillation on the ST segment.

Data analysis

Data are given as mean $\pm$ SD. Statistical significance of the ST-segment changes from baseline to 5 minutes of coronary occlusion were assessed by either paired samples *t* test or 1-way repeated measures analysis of variance using PASW Statistics 18.0 software (SPSS Inc, Chicago, IL). *P* < .05 was considered significant.

Results

Intact heart

Seven pigs were included in the study. In 5 cases, the middle segments of the LAD and RCA were separately occluded for 5 minutes spaced by 10 minutes of reperfusion; thereafter the LAD and RCA were simultaneously reoccluded. As shown in Figure 1, mid-LAD occlusion induced ST-segment elevation in leads V₁–V₆ (maximal in lead V₄; $0.84 \pm$

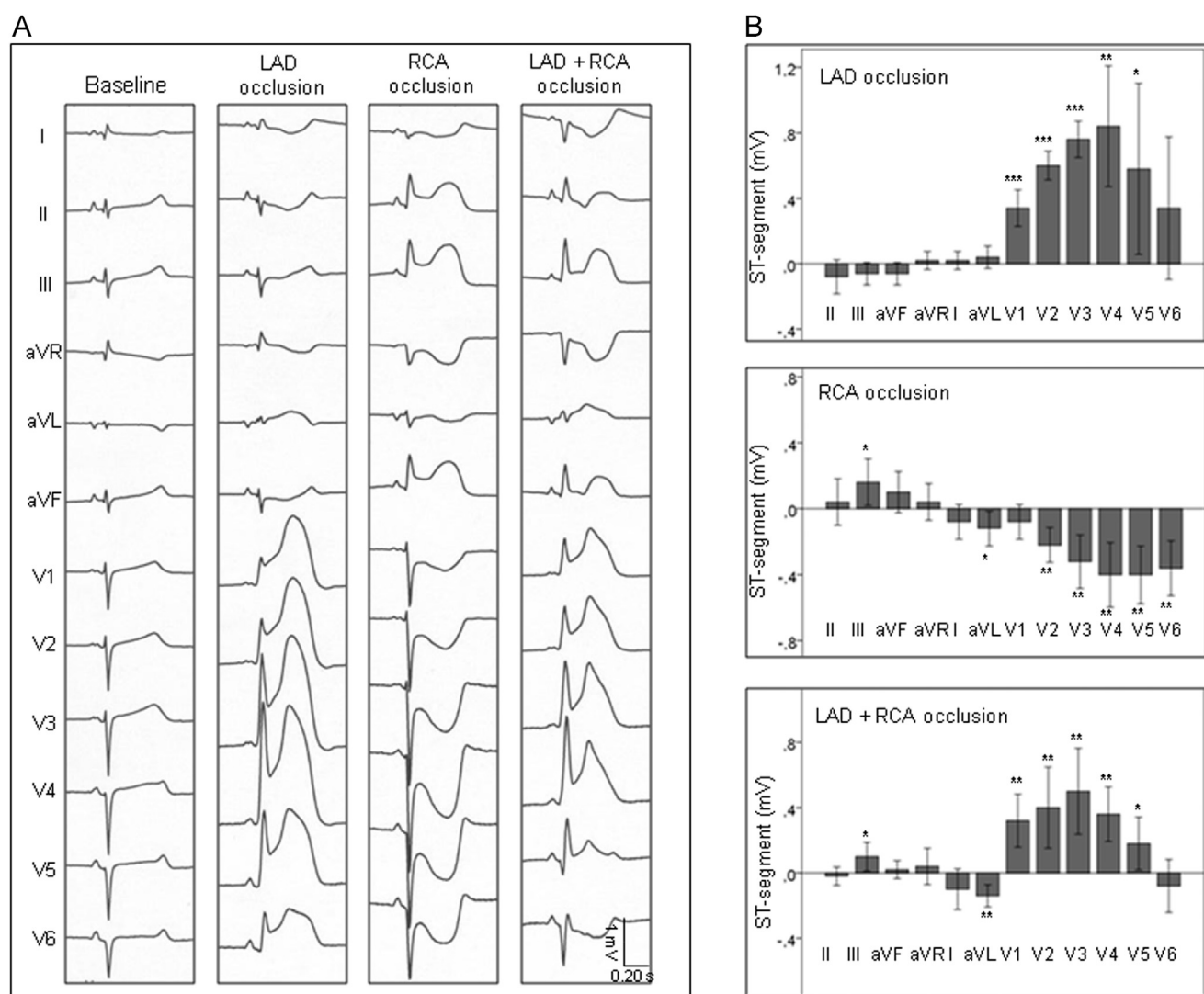


Figure 1 ST-segment changes induced by single and combined occlusion of the left anterior descending (LAD) and right coronary arteries (RCA) in anesthetized pigs. **A:** Twelve-lead ECG recorded in a pig at baseline and after 5 minutes of single and combined LAD and RCA ligation, all spaced by 10 minutes of reperfusion recovery. **B:** ST-segment displacement (mean $\pm$ SD [bars]) in the 12-lead ECG in 5 pigs submitted to single and combined LAD and RCA occlusion separated by 10 minutes of reperfusion recovery. Double coronary occlusion attenuated ST-segment elevation and blunted reciprocal ST-segment changes. Asterisks indicate level of statistical significance (**P* < .05; ***P* < .01; ****P* < .001).

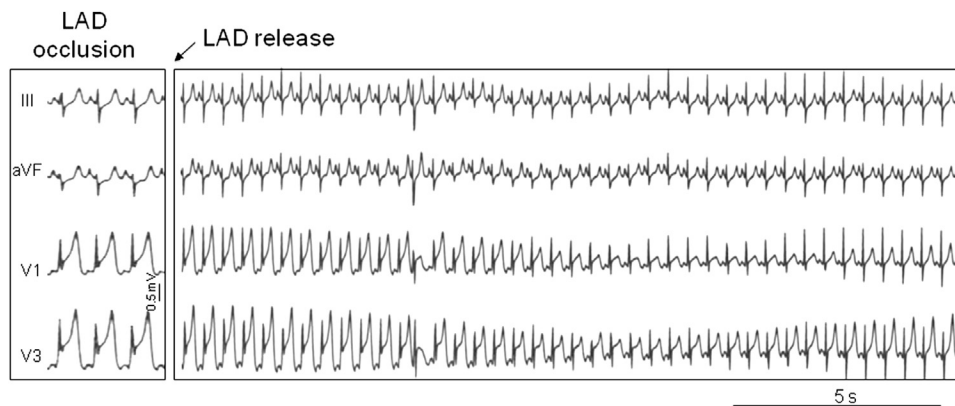


Figure 2 Effects of coronary reperfusion on ischemic ECG changes induced by 5 minutes of left anterior descending artery (LAD) occlusion in an anesthetized pig. ECG leads III, aVF, V₁, and V₃ are shown at 5 minutes of LAD occlusion (**left**) and continuously after release of the LAD (**right**). Coronary reperfusion induced rapid normalization of ST-segment elevation with transient appearance of peaked T waves. Time scale is indicated in seconds.

0.30 mV, $P = .003$) and slight nonsignificant reciprocal ST-segment depression in leads II, III, and aVF. Occlusion of the mid-RCA elicited ST-segment elevation in leads II, III, and aVF (maximal in lead III: 0.16 ± 0.11 mV, $P = .04$) and reciprocal ST-segment depression in leads I, aVL, and V₁–V₆ (maximal in lead V₄: -0.40 ± 0.16 mV, $P = .005$). Coronary reperfusion after a single 5-minute coronary ligature elicited fast normalization of ST-segment elevation and transient appearance of peaked T waves (illustrative example shown in [Figure 2](#)). Simultaneous LAD and RCA occlusion was followed by a reduction of approximately 60% in the magnitude of ST-segment elevation attained during the previous single-vessel occlusion. Moreover, double coronary occlusion abolished the reciprocal ST-segment depression that was recorded in leads II, III, and

aVF or in leads V₁–V₅ during separate LAD and RCA occlusion, respectively. Of note, leads I, aVL, and V₆ continued to show reciprocal ST-segment depression (maximal in lead aVL: -0.14 ± 0.05 mV, $P = .005$). A typical example of single and combined LAD and RCA occlusion is shown in [Figure 1A](#). Of interest in the LAD occlusion is, in addition to the ST-segment changes, the development of R waves in the precordial leads suggestive of delay in conduction to the epicardial layer. These R waves persisted in case of simultaneous LAD and RCA occlusion. Selective release of either of the 2 occluded coronary arteries induced immediate regional reversion of the ST-segment elevation associated with concurrent beat-to-beat re-elevation of the ST segment in the opposite ischemic region and reappearance of reciprocal ST-segment changes. The magnitude of

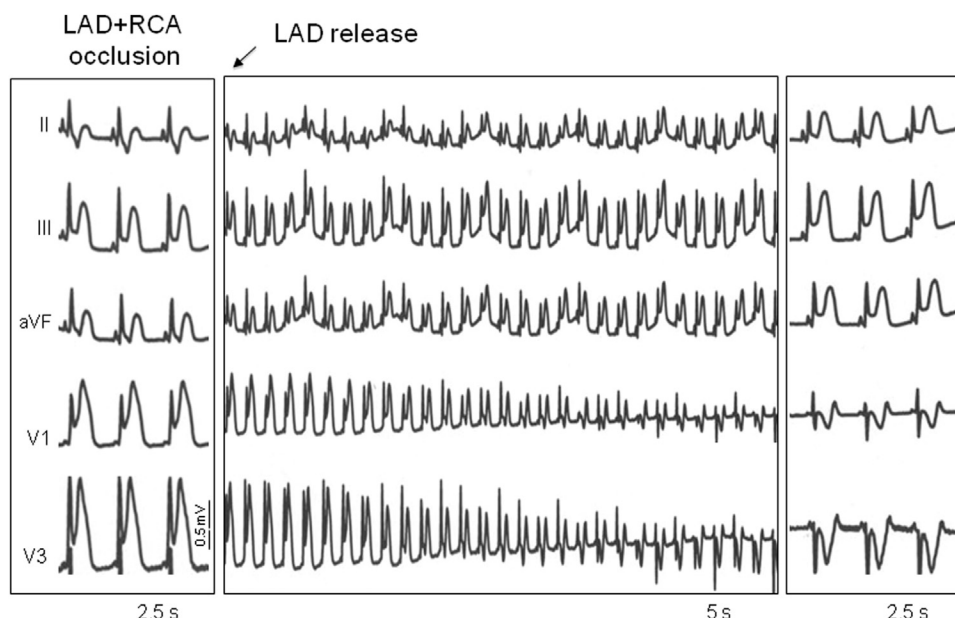


Figure 3 Effects of selective coronary reperfusion on ischemic ECG changes induced by 5 minutes of double left anterior descending (LAD) and right coronary arteries (RCA) occlusion in an anesthetized pig. ECG leads II, III, aVF, V₁, and V₃ are shown at 5 minutes of double LAD and RCA occlusion (**left**) and during release of the LAD while the RCA remained occluded (**middle, right**). Release of the LAD induced fast normalization of ST-segment elevation in leads V₁ and V₃ leading to reciprocal ST-segment inversion associated with concurrent beat-to-beat ST-segment re-elevation in leads II, III, and aVF. Time scale is indicated in seconds.

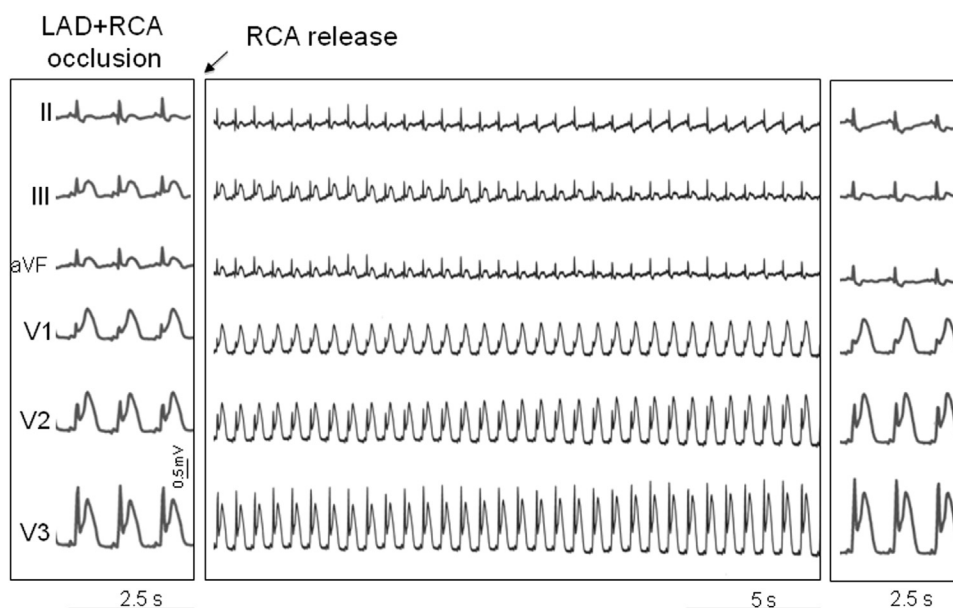


Figure 4 Effects of selective coronary reperfusion on the ischemic ECG changes induced by 5 minutes of double left anterior descending (LAD) and right coronary arteries (RCA) occlusion in an anesthetized pig. ECG leads II, III, aVF, and V₁–V₃ are shown at 5 minutes of double LAD and RCA occlusion (**left**) and during release of the RCA while the LAD remained occluded (**middle, right**). Release of the RCA induced fast normalization of ST-segment elevation in leads II and III with concurrent beat-to-beat ST-segment re-elevation in leads V₁–V₃. Time scale is indicated in seconds.

ST-segment re-elevation measured within the 30 seconds after reperfusion was approximately 50%. Two examples of the ST-segment behavior after selective release of the LAD or RCA in pigs with double occlusion are shown in [Figures 3](#) and [4](#), respectively. In 2 of 7 pigs, we performed double LAD and RCA occlusion as the first intervention thereby not preceded by previous ischemia. In these cases, the trend of ST-segment changes induced by reperfusion of 1 of the 2 occluded vessels was comparable to that observed in the 5 pigs with previous ischemic episodes.

Isolated Langendorff perfused heart

Five complete isolated heart experiments were included in the analysis. In all hearts, the middle segments of the LAD and RCA were separately occluded for 5 minutes spaced by 10 minutes of reperfusion. Thereafter, a combined reocclusion of both vessels was performed.

As shown in [Figure 5](#), mid-LAD occlusion induced significant ST-segment elevation in the epicardial, midmyocardial, and endocardial extracellular electrograms of the anterior LV region (maximal in endocardium: 3.0 ± 1.1 mV, $P = .003$) but failed to induce reciprocal ST-segment depression in lateral or posterior LV regions. Likewise, RCA occlusion induced transmural ST-segment elevation in the posterior LV region (maximal in endocardium: 3.0 ± 1.6 mV, $P = .03$) with no reciprocal ST-segment depression in the anterior or lateral areas. Simultaneous ligation of the LAD and RCA led to transmural elevation of the ST segment, maximal in the mid-myocardium of the anterior (2.3 ± 0.8 mV, $P = .002$) and posterior (2.1 ± 0.7 mV, $P = .003$) LV regions, respectively. The magnitude of ST-segment elevation was approximately 30% lower than that elicited by each previous single-vessel ligation. A typical

example of single and combined LAD and RCA occlusion is shown in [Figure 5A](#). Selective release of 1 of the 2 occluded vessels did not induce appreciable re-elevation of the ST segment in the local recordings of the opposite ischemic zone. Moreover, no reciprocal ST-segment changes were observed during combined LAD and RCA ligation.

Discussion

ST-segment cancellation

Combined anterior and inferior regional ischemia was induced in the *in situ* and the isolated perfused pig hearts by occluding simultaneously the LAD and RCA. In comparison with a single myocardial ischemic location, simultaneous ischemia at these 2 opposite areas attenuated by approximately 60% the magnitude of ST-segment elevation in the ECG leads overlying the ischemic area and blunted the reciprocal ST-segment depression that was previously induced by a single LAD or RCA occlusion.

Two potential mechanisms may explain the attenuation of ST-segment changes during double coronary occlusion: (1) ischemic preconditioning elicited by the preceding single coronary occlusions^{8,9} or (2) true cancellation of the ST-segment potential secondary to the opposite location of the 2 ischemic regions. Our data support the concept that ST-segment cancellation rather than preconditioning was the prevailing mechanism. Indeed, selective reopening of 1 of the 2 simultaneously occluded coronary arteries was immediately followed by reversion of ST-segment elevation in the reperfused region and, at the same time, by concurrent beat-to-beat ST-segment re-elevation in leads overlying the opposite ischemic region. Moreover, a similar ST-segment behavior was observed in the 2 pigs submitted to double

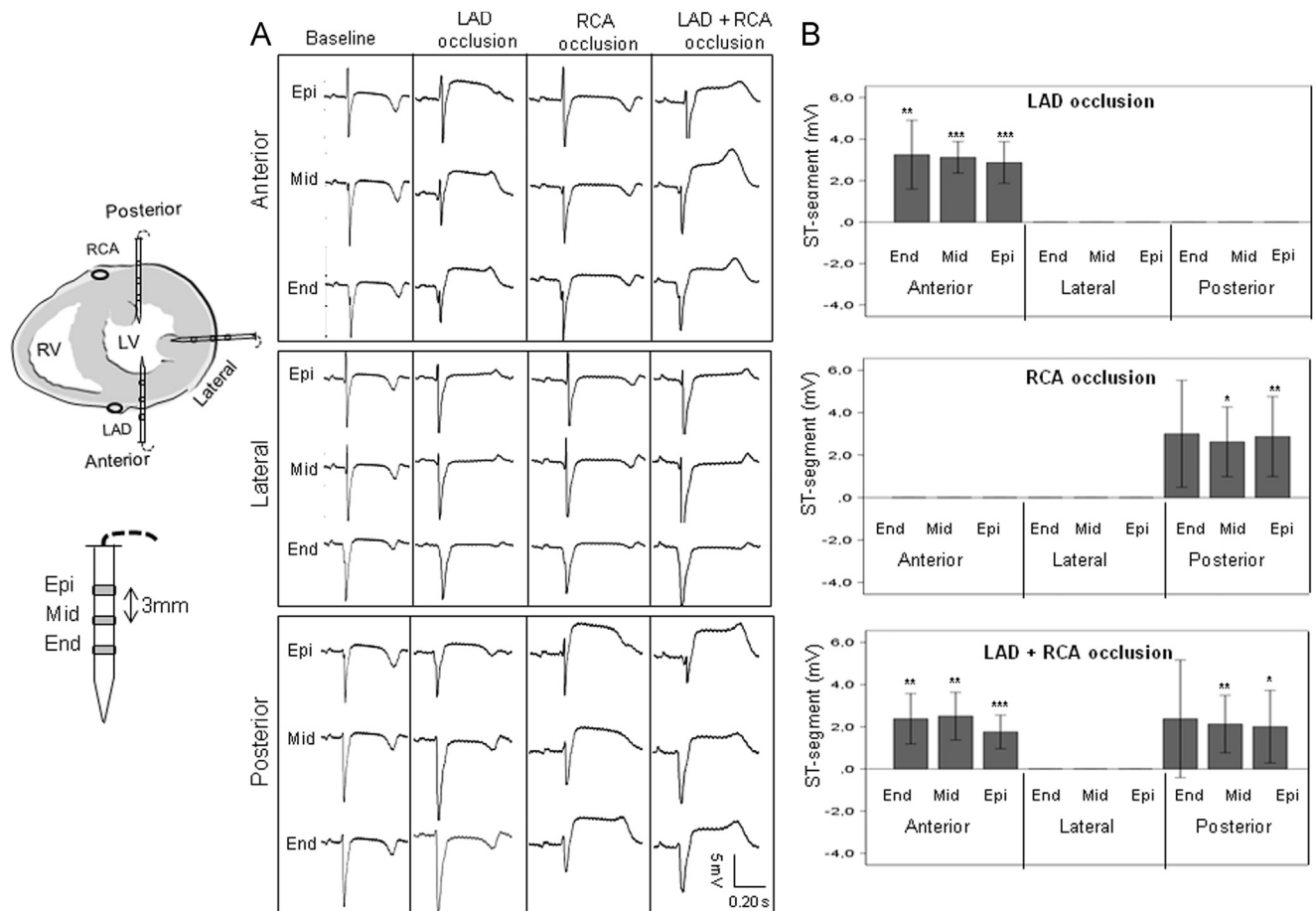


Figure 5 ST-segment changes in local extracellular electrograms induced by single and combined ligation of the left anterior descending (LAD) and right coronary arteries (RCA) in isolated Langendorff perfused pig heart. **A:** Epicardial (Epi), midmyocardial (Mid), and endocardial (End) electrograms recorded with needle electrodes inserted in the anterior, lateral, and posterior left ventricular wall at baseline and 5 minutes after single and combined LAD and RCA ligation in an isolated pig heart. **B:** ST-segment displacement (mean $\pm$ SD values [bars]) in local electrograms recorded in the anterior, lateral, and posterior ventricular regions in 5 isolated perfused pig hearts submitted to single and combined LAD and RCA occlusion separated by 10 minutes of reperfusion recovery. Coronary occlusion induced transmural regional ST-segment elevation without appreciable reciprocal ST-segment changes. Double coronary occlusion slightly attenuated ST-segment elevation. Asterisks indicate level of statistical significance (* P < .05; ** P < .01; *** P < .001).

LAD and RCA occlusion as the first intervention and therefore free of ischemic preconditioning.

The mechanism of ST-segment cancellation induced by ischemia in opposite regions has not been directly elucidated but can be inferred from the solid angle theory.¹⁰ Indeed, the ST-segment potential (ϵ_{ST}) recorded by an exploring electrode is $\epsilon_{ST} = \Omega/4\pi(V_{mI} - V_{mN})K$, where Ω is the solid angle formed by lines from the recording electrode to every point along the ischemic boundary; V_{mI} and V_{mN} are the transmembrane potential at ischemic and normal regions, respectively; and K is a constant that corrects for differences in intracellular and extracellular conductivity and occupancy of heart muscle by interstitial tissue and space. The transmembrane potential differences existing between normal and ischemic (depolarized) myocardial cells drive local injury currents that flow across the ischemic border zone and are responsible for the elevation of the ST segment in local extracellular electrograms.^{11,12} When 2 ischemic myocardial areas are located in opposite sites, their corresponding solid angles are of opposite magnitude, and the resultant ST-segment magnitude may approach zero.^{10,13} In our study, the

degree of ST-segment cancellation induced by ischemia in opposite regions was of greater magnitude in precordial ECG leads than in local epicardial and intramural electrograms recorded in the ischemic regions. Hypothetically, this may indicate that the solid angle subtended at the precordium is more influenced by the summed solid angles generated at the boundaries of 2 ischemic regions than the solid angle subtended at sites in direct contact with ischemic myocardium.

An additional feature differentiating precordial and local electrograms was the lack of appreciable reciprocal ST-segment depression in the latter recordings. According to the mathematical predictions of the solid angle theory derived from epicardial and precordial recordings in anesthetized pigs with acute myocardial ischemia,¹⁴ a precordial electrode moving at a distance from the ischemic border zone will detect negative values and hence ST-segment depression. In contrast, an epicardial electrode closer to the heart will not detect negative values beyond the border zone.¹⁴ The injury currents cannot propagate at a distance of the ischemic zone because of their short space constant, and only sites close to

the border zone might disclose reciprocal ST-segment depression.¹¹ Moreover, a possible volume conductor effect on the reciprocal ST-segment changes in the isolated empty heart was excluded in a previous study in which we recorded simultaneously the conventional ECG leads and local intramural electrograms in anesthetized open chest pigs.¹⁵ In that study, acute occlusion of the RCA with a catheter balloon did not induce reciprocal ST-segment changes in local electrograms of the normal left anterior wall, but they were present in the precordial ECG leads projecting this particular normal region.¹⁵ Therefore, the reciprocal ST-segment depression observed in the 12-lead ECG likely is related to the conventional ECG lead system design and not the result of an active flow of injury currents propagating toward the distant normal myocardium.

During LAD occlusion, endocardial ST-segment elevation was greater than midmyocardial, and this was greater than epicardial. Whether this endo–epicardial gradient should lead to ST-segment depression rather than elevation in the overlying precordial surface ECG leads was elucidated in a previous study in anesthetized pigs in which a similar endo–epicardial gradient was always projected as ST-segment elevation in the simultaneously recorded precordial ECG leads.¹⁶

Clinical implications

Compelling evidence supporting extrapolation of the present findings to clinical electrocardiology is founded on the resemblance of the cellular electrophysiologic derangements induced by acute myocardial ischemia and the ECG patterns elicited by coronary occlusion at different locations in pigs^{12,15} and humans.^{12,17–19}

The ECG pattern induced by simultaneous LAD and RCA occlusion in our study (ST-segment elevation in leads III, aVF, aVR, V₁–V₅, and ST-segment depression in leads I, aVL, and V₆) was comparable to that described in patients with a similar double LAD and RCA occlusion.^{2–5} Likewise, ECG recordings in a clinical case report support the concept that ST-segment cancellation also occurs in humans with double coronary occlusion.⁵ In this particular patient,⁵ successful lysis of the thrombus in the LAD, while RCA occlusion persisted, allowed re-elevation of the ST segment in inferior leads (II, III, aVF) and appearance of reciprocal ST-segment depression in leads V₂–V₅ thus mimicking the ST-segment response elicited by selective reopening of 1 of the 2 occluded vessels in our pigs.

Patients with acute myocardial infarction caused by single occlusion of the distal LAD may also present with an ECG pattern of combined ST-segment elevation in inferior leads and in anterior leads.⁶ In these patients, elevation of the ST segment in inferior leads was thought to occur whenever the basal anterior LV wall was spared and the apical portion of the LV inferior wall was affected because the occluded LAD wrapped around the apex supplying this region.⁷ The differentiation between patients with single occlusion of the distal LAD and those with double LAD and RCA occlusion is of

clinical relevance because the latter group of patients had a worse prognosis. Although these patients may share a comparable ST-segment elevation pattern involving the precordial and inferior leads, we observed that double LAD and RCA occlusion elicited ST-segment depression in leads I and aVL in our pigs and also in clinical case reports of combined LAD and RCA occlusion.^{2–5} Important to make the distinction is the absence of ST-segment depression in leads I and aVL in patients with a single distal LAD occlusion.^{6,20}

Patients with multivessel coronary atherosclerotic disease can develop simultaneous ischemia at various myocardial regions under conditions of low cardiac output or increased myocardial oxygen demands; therefore, the resultant ischemic ST-segment changes could be cancelled. During exercise testing, this may lead to a falsely negative ECG response in patients with multivessel disease.¹

Study limitations

The patterns of ST-segment cancellation described in this study are valid for models of acute transmural myocardial ischemia and therefore might not apply when the combined ischemia in opposite regions is limited to the subendocardial layers. Although it is conceivable that combined subendocardial ischemia in opposite regions would also result into cancellation of ST-segment depression, this assumption has not yet been verified in experimental models of ongoing stable subendocardial ischemia.

During RCA occlusion, the magnitude of reciprocal ST depression in the precordial leads was greater than that of ST elevation in the inferior leads. This finding is in contrast with current clinical practice and likely could be explained by the fact that the pig heart is in close contact with the chest wall, and therefore the cardiac electrical potentials might be preferentially projected on the precordial than inferior ECG leads.

The time course of ischemic ST-segment changes in the *in situ* heart evolve more rapidly than in the isolated unloaded heart; therefore, the duration of ischemia in both models might not be fully comparable. However, after 5 minutes of coronary occlusion, the magnitude of ST-segment elevation in the local electrograms was remarkable (about 3 times greater than that recorded in the ECG leads), and this permitted assessment of ST-segment behavior after selective release of 1 occluded vessel in the isolated heart.

Conclusion

Simultaneous acute myocardial ischemia in opposite ventricular regions exerted a noticeable cancellation of both ST-segment elevation and reciprocal ST segment depression in the conventional 12-lead ECG. In contrast, this phenomenon was nearly absent in local transmural electrograms recorded directly in ischemic myocardial regions.

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References

1. Madias JE, Khan M, Manyam B. The role of "ischemic ST-segment counterpoise" in rendering the response of exercise electrocardiogram falsely negative. *Clin Cardiol* 1997;20:489–492.
2. Hosokawa S, Hiasa Y, Miyamoto H, Suzuki N, Takahashi T, Kishi K, Tanimoto M, Ohtani R. Acute myocardial infarction showing total occlusion of right coronary artery and thrombus formation of left anterior descending artery. *Jpn Heart J* 2001;42:365–369.
3. Sia SK, Huang CN, Ueng KC, Wu YL, Chan KC. Double vessel acute myocardial infarction showing simultaneous total occlusion of left anterior descending artery and right coronary artery. *Circ J* 2008;72:1034–1036.
4. Araszkievicz A, Olasinska-Wisniewska A, Skorupski W, Lesiak M, Mularek-Kubzdela T, Grajek S. Simultaneous occlusion of 2 coronary arteries—a rare cause of cardiogenic shock. *Am J Emerg Med* 2009;1175.e5–175.e7.
5. Gan F, Hu D, Dai T. Acute multivessel coronary occlusion: a case report. *BMC Res Notes* 2012;5:523–527.
6. Sadanandan S, Hochman JS, Kolodziej A, Criger DA, Ross A, Selvester R, Wagner GS. Clinical and angiographic characteristics of patients with combined anterior and inferior ST-segment elevation on the initial electrocardiogram during acute myocardial infarction. *Am Heart J* 2003;146:653–661.
7. Sapin PM, Musselman DR, Dehmer GJ, Cascio WE. Implications of inferior ST-segment elevation accompanying anterior wall acute myocardial infarction for the angiographic morphology of the left anterior descending coronary artery morphology and site of occlusion. *Am J Cardiol* 1992;69:860–865.
8. Deutsch E, Berger M, Kussmaul WG, Hirshfeld JW Jr, Herrmann HC, Laskey WK. Adaptation to ischemia during percutaneous transluminal coronary angioplasty: clinical, hemodynamic, and metabolic features. *Circulation* 1990;82:2044–2051.
9. Cinca J, Worner F, Carreno A, Coronel R, Soldevilla A, Perez-Villa F, Janse MJ, Soler-Soler J. T-Q S-T segment mapping and hyperemia in reperfused pig heart with ischemic preconditioning. *Am J Physiol* 1992;263:H1732–H1738.
10. Holland RP, Brooks H. TQ-ST segment mapping: critical review and analysis of current concepts. *Am J Cardiol* 1977;40:110–129.
11. Janse MJ, Cinca J, Moréna H, Fiolet JW, Kléber AG, de Vries GP, Becker AE, Durrer D. The "border zone" in myocardial ischemia: an electrophysiological, metabolic, and histochemical correlation the pig heart. *Circ Res* 1979;44:576–588.
12. Cinca J, Janse MJ, Moréna H, Candell J, Valle V, Durrer D. Mechanism and time course of the early electrical changes during acute coronary artery occlusion: an attempt to correlate the early ECG changes in man to the cellular electrophysiology in the pig. *Chest* 1980;77:499–505.
13. Fozzard HA, DasGupta DS. ST-segment potentials and mapping: theory and experiments. *Circulation* 1976;54:533–537.
14. Holland RP, Brooks H, Lidl B. Spatial and nonspatial influences on TQ-ST segment deflection of ischemia: theoretical and experimental analysis in the pig. *J Clin Invest* 1977;60:197–214.
15. Noriega FJ, Jorge E, Arzamendi D, Cinca J. Mechanism and diagnostic potential of reciprocal ECG changes induced by acute coronary artery occlusion in pigs. *Heart Rhythm* 2013;10:883–890.
16. Cinca J, Figueras J, Bardají A, Rius J. Retraso del ECG convencional en reflejar las alteraciones eléctricas del área isquémica en el cerdo. *Rev Esp Cardiol* 1986;39:47–52.
17. Camara EJ, Chandra N, Ouyang P, Gottlieb SH, Shapiro EP. Reciprocal ST change in acute myocardial infarction: assessment by electrocardiography and echocardiography. *J Am Coll Cardiol* 1983;2:251–257.
18. Rude RE, Croft CH, Willerson JT. "Reciprocal" anterior ST depression early in the course of transmural inferior myocardial infarction: an ECG finding of uncertain clinical significance. *Int J Cardiol* 1983;4:80–85.
19. Becker RC, Alpert JS. Electrocardiographic ST segment depression in coronary heart disease. *Am Heart J* 1988;115:862–868.
20. Engelen DJ, Gorgels AP, Cheriex EC, De Muinck ED, Ophuis AJ, Dassen WR, Vainer J, Van Ommen VG, Wellens HJ. Value of the electrocardiogram in localizing the occlusion site in the left anterior descending coronary artery in acute anterior myocardial infarction. *J Am Coll Cardiol* 1999;34:389–395.

CLINICAL PERSPECTIVES

Using an experimental model close to human cardiac electrophysiology, we disclosed the cancelling effect elicited by extensive myocardial ischemia on ECG ST-segment patterns. Compared with 1-site ischemia induced by single LAD or RCA occlusion, extensive ischemia induced by simultaneous LAD and RCA occlusion depicted less ST-segment elevation and absence of reciprocal ST-segment changes. Thus, the ECG patterns currently used to identify the occluded coronary artery will not be fully applicable if ischemia developed simultaneously in 2 opposite myocardial regions.

In clinical practice, ischemia in opposite myocardial regions may develop in patients with multivessel coronary atherosclerotic disease during increased myocardial oxygen demands (ie, exercise testing) or in those presenting with simultaneous occlusion of 2 coronary vessels, but the resultant ECG patterns have not been well characterized. Our observations may help improve the ECG diagnosis of transmural myocardial ischemia in opposite cardiac regions in patients with acute coronary syndromes. However, in patients with diffuse ischemia limited to the subendocardial regions, the cancelling effect on ECG changes would need to be confirmed using purposely designed models of stable acute subendocardial ischemia.

Our findings in the isolated heart further indicated that the cancelling effect on ST-segment behavior is more apparent in peripheral ECG leads than in local extracellular electrograms.