Understanding ST depression in the stress-test ECG

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ABSTRACT

Objective: The electrocardiogram (ECG) obtained during stress testing often shows a typical pattern of primary ST depression. A similar pattern can occur in unstable angina. Current textbooks consider ST depression as a direct result of partial occlusion of a coronary artery. However, animal models could not reproduce this phenomenon. An alternative explanation for ST depression specific to stress testing involves global subendocardial ischemia. In this study, we evaluated both explanations with a realistic mathematical model of the human heart.

Methods: The ECG was simulated with an anisotropic reaction-diffusion model of the human heart and an inhomogeneous boundary-element model of the human torso.

Results: Limited subendocardial ischemic zones caused small ST depression in ECG leads not overlying the ischemic region. An ischemic zone of 50% transmural extent covering the entire left ventricular subendocardium caused an ST-depression pattern similar to that observed during stress test.

Conclusion: In contrast to regional subendocardial ischemia, global subendocardial ischemia can explain ST depression in our model. *(Anadolu Kardiyol Derg 2007: 7 Suppl 1; 145-7)*

Key words: ischemia, ST deviation, non-ST-elevation myocardial infarction, computer model, stress test

Introduction

The ECG obtained during stress testing often shows a typical pattern of ST depression. A similar pattern can occur spontaneously in patients with unstable angina (1). The current textbook explanation of ST depression involves regional subendocardial ischemia as a direct result of partial occlusion of one or more coronary arteries. This would imply that ST-segment changes depend on the affected artery or arteries (2). However, in contrast to ST elevation, ST-depression patterns appear to be independent of the affected arteries (1, 3). Moreover, animal models could not reproduce ST depression at a resting heart rate (4–6). Recent theoretical work has shown that the classical relation between regional subendocardial ischemia and epicardial ST depression relies on an isotropic mathematical model of the myocardium (7, 8). Isotropic models were previously used because of practical limitations. In a more realistic anisotropic computer model of the human heart, ST depression could only be obtained with subendocardial ischemic zones that covered more than half of the left ventricle (8). In this study, we investigated whether such a realistic model can reproduce the pattern of ST depression that is typical for the stress test.

Methods

The ECG was simulated with a reaction-diffusion model of the human heart incorporating anisotropic myocardium with transmurally rotating fiber orientation at 0.25-mm resolution, and an inhomogeneous boundary-element torso model. Details of this model have been published previously (9). Ionic currents in the propagation model were computed with the Ten Tusscher–Noble–Noble–Panfilov (TNNP) model of the human ventricular myocyte (10). Ischemia was represented by setting the extracellular potassium concentration to 10 mM (normal value 5 mM).

Our model is based on the bi-domain model of the myocardium. It represents the myocytes and gap junctions as a continuum called the "intracellular domain," and the interstitium and microvasculature as another continuum, called the "extracellular domain." Both domains have anisotropic conductivity. The model accounts for both these anisotropies when it computes propagating action potentials, but it cannot deal with extracellular anisotropy (Re) when computing the ECG. To compensate, we used a reduced intracellular anisotropy (Ri) for ECG computation. Thus, the ratio of intracellular to extracellular anisotropy (R) was realistic. This ratio is much more important for ST-segment changes than the individual anisotropy ratios of the two domains (8). Normal values are Ri=10 and Re=2.5, so R=Ri /Re=4 (11). Bound to using Re=1, we set Ri=4 for ECG computation.

Results

An ischemic zone of 50% transmural extent covering the entire left ventricular subendocardium caused an ST-depression pattern similar to that observed during stress test. This was

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verified for intracellular to extracellular anisotropy ratios R=1 and R=4 (Fig. 1). This increase in anisotropy ratio slightly increased T-wave amplitude in the precordial leads, but did not significantly affect the ST segment. Compared to a simulated normal ECG, the QRS complex was only slightly affected: R peak amplitudes were reduced by 20% in leads II, III and AVF.

In contrast to a global subendocardial ischemia, regional subendocardial ischemia induced ST-segment changes that depended strongly on the anisotropy ratio of the myocardium. Figure 2 shows ST changes due to an ischemic zone with 5 cm diameter and 50% transmural extent in the lateral wall of the left ventricle. The ECGs were simulated with isotropic tissue (R=1) and anisotropic tissue (R=4). Lead V6, which overlies the ischemic zone, is shown in panel A. Panel b shows the ST deviation in all precordial leads. ST depression in the leads overlying the ischemic zone was only obtained with isotropic tissue. With a more realistic anisotropy ratio of 4 the maximum ST depression shifted to lead V3.

Despite the smaller affected muscle mass, regional ischemia led to more prominent QRS changes than global subendocardial ischemia. Especially the end of the QRS complex was affected. As a result of regional ischemia, the QRS complex became narrower in lead III.

Discussion

We have shown that regional subendocardial ischemia leads to an ST-deviation pattern that strongly depends on the anisotropy of the tissue. When a realistic anisotropy ratio was used, ST depression was not centered over the ischemic region. Global subendocardial ischemia led to considerable ST depression in all standard leads, with little dependence on anisotropy.

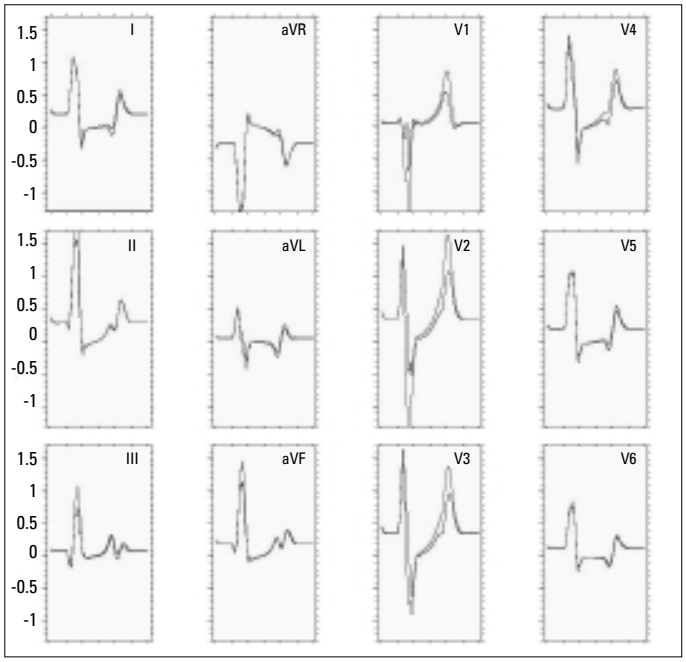

Figure 1. Simulated ECG with an ischemic zone of 50% transmural extent covering the entire LV subendocardium. Black traces: isotropic myocardium (R=1). Grey traces (red online): anisotropic myocardium (R=4). Anisotropy has little influence on the ECG in this global subendocardial ischemia.

ECG- electrocardiogram

Classically, primary ST depression has been considered to be a direct result of subendocardial ischemia due to partial occlusion of one or more coronary arteries. Previous modeling studies have shown that if regional subendocardial ischemia is present, it can be localized on the body surface (2). Our simulations of regional subendocardial ischemia confirm this result. If the myocardium was isotropic (R=1), the ST depression was maximal in the leads overlying the ischemic region. With a more realistic anisotropy ratio R=4 the pattern still depended on the location of the ischemia, but the maximum ST depression occurred adjacent to the ischemic region.

Thus, modeling studies suggest that if partial occlusion leads to regional subendocardial ischemia, the occlusion can be localized by the ECG. However, in contrast to ST elevation, primary ST depression during stress testing and in unstable angina usually occurs in a typical pattern that does not depend on the affected artery or arteries (1, 3). Moreover, partial occlusion of a coronary artery in animal models did not lead to ST depression (4–6). We hypothesized therefore that the "stress-test ECG" is not caused by regional ischemia, and is not a direct result of partial occlusion. During stress testing, reduced diastolic coronary filling time and elevated left ventricular end-diastolic pressure can reduce perfusion in the subendocardium, leading to a global subendocardial ischemia (12). Our present results suggest that global subendocardial ischemia can explain the stress-test ECG. This ST depression would not depend on the territory of the affected artery.

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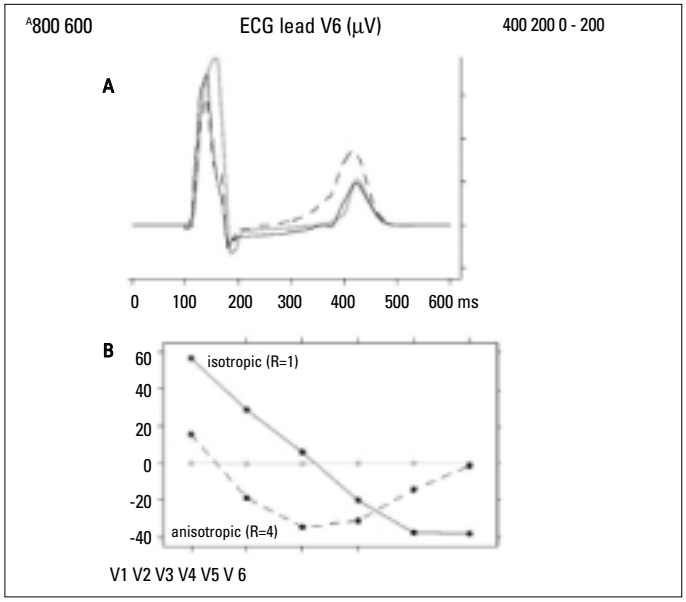

Figure 2. Effect of regional ischemia. Panel A: ECG lead V6 without ischemia (grey line), with regional subendocardial ischemia and isotropic tissue (solid black line), and regional subendocardial ischemia with anisotropic tissue (dashed line). Panel B: ST-segment changes in all precordial leads, for isotropic (solid line) and anisotropic tissues (dashed line)

ECG- electrocardiogram

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