Global subendocardial ischemia can explain ST depression in chronic angina

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Introduction

The ECG obtained during stress testing often shows a typical pattern of ST depression. A similar pattern can occur spontaneously in angina patients. The mechanism underlying this ECG type is still unclear.

Transmural ischemia causes ST elevation on the epicardium. For partial-thickness ischemia, the situation is less clear.

ST depression In the past, ST depression was explained with solid angle theory, which assumes an *isotropic* myocardium:

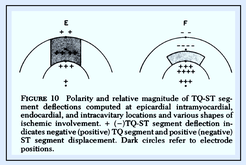
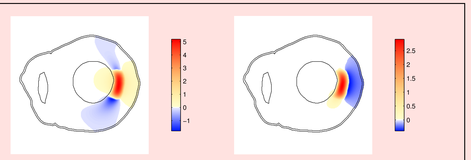


FIGURE 10 Polarity and relative magnitude of TQ-ST segment deflections computed at epicardial intramyocardial, endocardial, and intracavitary locations and various shapes of ischemic involvement. + (−)TQ-ST segment deflection indicates negative (positive) TQ segment and positive (negative) ST segment displacement. Dark circles refer to electrode positions.

(figure from R. P. Holland et al, *J. Clin. Invest.*, 1977 [1])

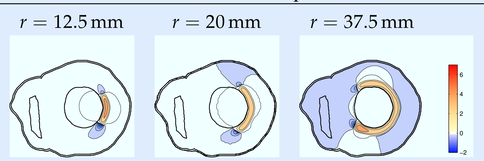
ST elevation However, myocardium is strongly *anisotropic*. Conductivity is higher along than across fibers, and more so inside than outside the cells. Recent computer simulations which account for this unequal anisotropy predicted local epicardial ST elevation and remote depression [2, 4]:



ST deviations in the extracellular domain, shown in a transverse section of the heart. Potential differences are shown as pseudocolors, the scale is in mV. Left: realistic unequal anisotropy. Right: isotropic. In the anisotropic case, ST elevation is found on the epicardium. In the isotropic case, ST depression is seen.

(figure from Potse et al., *Heart Rhythm* 2007 [4])

ST depression again But when the ischemic zone is very extended, ST depression is found even with an anisotropic model



Extracellular potentials in a transmural slice of the heart, resulting from 3 different ischemic regions with a transmural extent of 30 % and radius varying from 12.5 to 37.5 mm.

Hypothesis

The purpose of this study was to investigate what ischemic geometry may, in an anisotropic heart model, underly the most common presentation of primary ST depression: the "stress-test ECG." This pattern appears to be unrelated to the occlusion site [3]. In addition, we know that an extended ischemic zone is necessary to obtain primary ST depression (see Introduction). Therefore we hypothesized that the ischemia would have to cover the entire subendocardium.

Methods

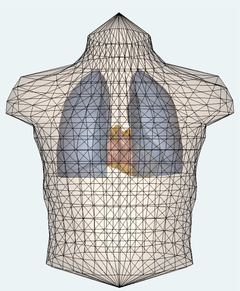
A computer model of the human heart was used to compute propagating membrane potentials throughout a heart with an ischemic zone. This reaction-diffusion model, based on the TNNP model for the human ventricular myocyte [7], had a resolution of 0.25 mm, a realistic cardiac anatomy, and anisotropic ventricles with transmural fiber rotation.

The heart model, here embedded in a thin layer of fluid (pink). The right circumflex artery is shown for orientation.

Ischemia was modeled by setting the extracellular K^+ concentration to an elevated value. As in our previous work, diffusion of K^+ was assumed to obtain a realistic representation of the ischemic boundary [4, 5].

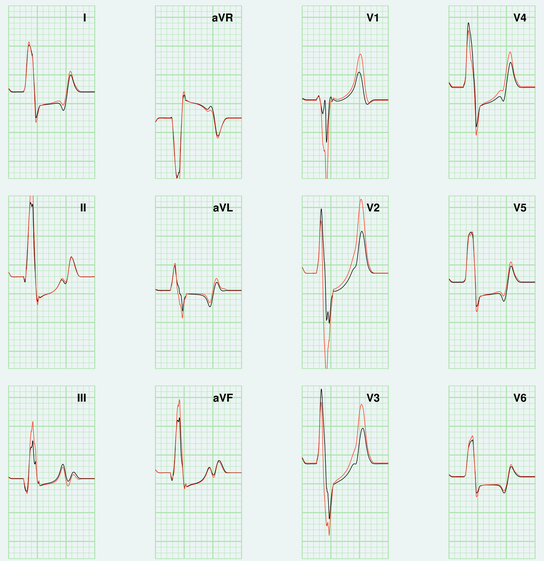
From the simulated membrane potentials, the ECG was computed using a torso model including lungs, ventricular blood masses, and a skeletal muscle layer.

The torso model, including high-conductivity intracavitary blood, low-conductivity lungs, and a skeletal muscle layer (not shown).



Results

Global subendocardial ischemia causes a typical stress-test ECG, with several millimeters ST depression in most leads. The maximum ST depression is found in lead V5.



Simulated ECG corresponding to global subendocardial ischemia. Black: isotropic heart; Red: anisotropic heart.

It has been shown previously that anisotropy has a major effect on the sign of ST deviation in the ECG in case of local subendocardial ischemia [2, 6]. In contrast, it has little influence on the ECG changes due to global subendocardial ischemia.

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Discussion

Current theory predicts that local subendocardial ischemia results in ST elevation on the overlying epicardium. Subendocardial ischemia can only cause primary ST depression when it is very extensive. We have investigated what would result if the subendocardial ischemia extends to the entire ventricular subendocardium. This turns out to reproduce the typical "stress-test ECG" with ST depression in all precordial leads, and deepest in lead V5.

Another situation in which primary depression may occur is multivessel disease or partial occlusion of the left main stem. Such occlusions could result in ischemic areas that are sufficiently extended to cause ST depression.

In contrast to ST elevation, primary ST depression is not clearly linked to an affected territory [3]. However, previous modeling studies have shown that, if local subendocardial ischemia exists, the resulting ECG pattern would be predictive of the affected region [2]. We assumed therefore that ST depression is caused by global, rather than local subendocardial ischemia. This study shows that this may indeed explain the typical ECG that is often obtained during stress testing. Previous authors have attributed this pattern to more severe ischemia in the apex of the heart. The pattern due to global subendocardial ischemia may imitate that of an apical subendocardial ischemia, because contributions from other than apical regions cancel. Due to its location opposite the atrioventricular valves, the apical component remains. This explains why the ST-depression vector points in the direction of the left precordial leads.

References

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