Passive transmission of ischemic ST segment changes in low electrical resistance myocardial infarct scar in the pig

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Abstract

Objectives: To analyze the passive electrical properties of a healed infarction and assess their role on transmission of contiguous ischemic ST segment potential changes. Methods: We measured tissue resistivity ($\Omega$cm) at 1 kHz and the epicardial ST segment during 1 h of proximal reocclusion of the left anterior descending (LAD) coronary artery in 12 anesthetized pigs with one-month-old transmural infarction elicited by LAD ligation below the first branch. The impedance spectrum (1 to 1000 kHz) of normal and infarcted myocardium was measured in seven other pigs with similar infarctions. Electrical transmission of current pulses (30 $\mu$A) in infarcted tissue and in test solutions was also investigated. Results: The infarct scar has a lower than normal resistivity (110±30 $\Omega$cm vs. 235±60 $\Omega$cm, $p<0.0001$) and, unlike the normal myocardium, resistivity and phase angle of the scar did not change at increasing current frequencies, reflecting no capacitative response. LAD reocclusion induced a resistivity rise (510±135 $\Omega$cm, $p<0.01$) and a ST segment elevation (0.6±0.7 to 9.5±5.1 mV, $p=0.002$) in the ischemic peri-infarction zone, whereas the infarcted area showed ST segment elevation (0.5±0.5 to 3.8±2.6 mV, $p=0.03$) with no resistivity changes. Potential decay of both ST segment and current pulses in the scar and in 0.9% NaCl solution was less than 1 mV/mm. Transmural deposition of connective tissue was seen in the center of the infarction. Conclusions: A one-month-old transmural infarction is a low resistance, noncapacitative medium that allows a good transmission of current pulses and of ST segment potential changes generated by contiguous peri-infarction ischemia.

Keywords: Electrophysiology; Connective tissue; ECG; Infarction; Ischemia; Necrosis

1. Introduction

Myocardial ischemia depresses active electrical cell membrane properties and this generates regional potential differences between normal and ischemic compartments [1,2]. As a result of these potential gradients, intra- and extracellular injury currents flow between normal and ischemic myocardial areas during the cardiac cycle [1,2]. During the early repolarization period, an extracellular current flowing from ischemic to normal areas is responsible for the ST segment elevation in electrodes overlaying the acute ischemic region [1−3] whereas, at the same time, electrodes brought in contact with normal bordering myocardium show isoelectric ST segment potential or reciprocal downward ST segment deviation. Although ST segment elevation is a characteristic feature of ischemia, a similar electrocardiographic pattern can be observed when the exploring electrode is brought in contact with a contiguous region of healed myocardial infarction. Indeed, in a model of ischemia superimposed at the borders of a healed myocardial infarction, we [4] have recorded ST segment elevation in electrodes overlaying the contiguous necrotic scar, despite there being no ischemia of viable tissue in this particular region. We hypothesized that ST segment potential changes were passively transmitted from the peri-infarction zone towards the necrotic scar, but the passive electrical properties of the infarct scar were not

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investigated in this model. Theoretically, to allow propagation of injury currents, the infarcted tissue should possess low resistance properties. Data on tissue electrical resistance in areas of chronic infarction have been only reported in sheep [5] and showed values lower than in normal myocardium. However, the electrical properties of the scar during superimposed peri-infarction ischemia are not known and have not been correlated with ST segment potential transmission in the infarct scar.

Therefore, this study aimed to delineate the passive electrical properties of a healed myocardial infarction devoid of viable tissue and to correlate these properties with the ST segment potential changes transmitted into the infarct scar during acute peri-infarction ischemia.

2. Methods

2.1. Experimental preparation

Twenty six three-month-old pigs (25–30 kg) of either sex that had been premedicated with azaperone (4 mg/kg, i.m.) underwent general anesthesia with sodium thiopental (30 mg/kg, i.v.). Pulmonary ventilation was maintained with a pressure respirator (Trans-PAC 5K257) at a 41% oxygen concentration. The thorax was opened through a sterile left lateral thoracotomy at the level of the fifth intercostal space and the corresponding rib was removed. The pericardium was incised and the left anterior descending (LAD) coronary artery was dissected and was permanently ligated below the first diagonal branch using a Prolene 5/0 snare [2]. The chest was immediately closed in layers and pleural air was aspirated. Cardiac rhythm was monitored with standard ECG leads I, II and III during the ensuing 2 h, to allow reversion of ischemic malignant ventricular arrhythmias by external electric DC counter-shock of 200 Joules. Immediately after LAD occlusion, we administered a prophylactic dose of lidocaine (100 mg, i.m.). The animals were allowed to recover and received analgesics (magnesium metamizol, 2 g i.m.), and anti-infectives (sodium benzylpenicillin, 5,000,000 IU, i.m.).

One month after the first coronary ligation, 19 pigs (73%) survived. All survivors received a dose of azaperone (4 mg/kg, i.m.) and were anesthetized with metomidate (4 mg/kg, i.v.) followed by alpha-chloralose (100 mg/kg, i.v.). The thorax was opened through a mid sternotomy under mechanical ventilation and the pericardium was gently detached. The LAD was dissected 2 to 3 cm above the primary ligation and a Prolene 5/0 snare was placed around the vessel for further coronary reocclusion. Aortic blood pressure was measured with an intraarterial femoral cannula. At regular intervals, blood gases were analyzed and were kept within normal limits. This investigation conforms with the Guide for the Care and use of Laboratory Animals published by the US National Institutes of Health (NIH Publication No. 85-23, revised 1985) and the study was approved by the Committee on ethics of our institution.

2.2. Myocardial impedance

2.2.1. Theoretical background

Measurement of the whole tissue electrical impedance is an overall estimation of the passive electrical properties of the myocardium, which includes the intra- and extracellular resistance and the membrane capacitance [6]. Impedance (Z) is defined as the voltage (V) measured in a particular region divided by the sinusoidal current (I) of a given frequency (f) applied through this region (Z=VI). Since biological tissues are not purely resistive, there will be a time delay (Δt) between the voltage and current waves that can be measured as a phase angle shift (θ=360°Δt/f). Therefore, myocardial impedance is better characterized by measuring its two components: tissue resistivity (ρ) and phase angle (θ). Tissue resistivity was calculated from the relation R=ρk, where R is the in phase component of V with respect to I, and k is the cell constant of the electrode determined by measuring the electrical resistance of a 0.9% NaCl solution at 25°C, which has a resistivity of 70 Ωcm.

2.2.2. Tissue resistivity at 1 kHz

Tissue impedance was measured using a four-electrode probe [7] because, with this electrode arrangement, the measurements are not distorted by the presence of the electrode–tissue interface impedance [8,9]. The impedance probe consisted of a linear array of four platinum electrodes (length=3.5 mm, diameter=0.2 mm) placed at an interelectrode distance of 2.5 mm, which were isolated to the tip with a teflon layer, to reduce the possible interference of the thin layer of epicardial inflammatory reaction [9]. However, the reduced electrode–tissue contact area of the isolated electrodes increased electrode capacitance and this caused a phase angle shift that hampered the accurate measurement of absolute phase angle values.

An alternating current (10 μA, 1100 Hz) was applied through the outer pair of platinum electrodes and the in phase component of V across the inner pair of electrodes was recorded, to obtain the resistivity values using a high input impedance lock-in amplifier (Princeton Applied Research model 5110). Changes in tissue resistivity were measured simultaneously by inserting one probe electrode at the center of the infarction zone and a second electrode in the bordering noninfarcted myocardium that became ischemic after the second LAD ligation. The latter electrode was always sutured perpendicular to the LAD, to avoid the influence of tissue anisotropy on the impedance measurements [10]. However, the interelectrode distance is larger than the myocardial fiber dimensions and is expected to average the effects of fiber orientation [5]. The appropriate location of the two electrode probes was verified at the end of the study. The acute ischemic
peri-infarction region was identified as a nonstained region after a left intra-atrial injection of 10 ml of 25\% fluorescein [11], whereas the infarcted region was recognized by its thinning and fibrotic consistency.

2.2.3. Tissue impedance spectroscopy

A fundamental difference between normal and infarcted tissue is that the former contains viable cells. Since the presence of cell membranes confers specific tissue capacitative properties [12], the normal myocardium and the necrotic tissue would have distinct capacitative characteristics. Therefore, to better delineate the intrinsic electrical properties of normal and infarcted tissues, we measured their impedance spectra at frequencies ranging from 1 to 1000 kHz under baseline conditions. This frequency range was chosen because measurement errors may occur both below 1 kHz, due to electrode impedance, and above 1000 kHz, due to cable effects. Measurements were made with four-electrode probes constructed from platinum electrodes (length=3.5 mm, diameter=0.4 mm) spaced 2.5 mm but that were not isolated to the tip to reduce electrode impedance. A Hewlett-Packard 4192A impedance analyzer with a front-end amplifier [13] adapted for this study (to obtain a common-mode rejection ratio of 72 dB at 1 MHz) was placed close to the heart and was connected to the platinum electrodes with cables of 15 cm length. Data acquisition and management was done using customized software. To correct the loading-dependent errors, we did a three-reference calibration procedure [14] by measuring the impedance spectrum (1 to 1000 kHz) of three NaCl solutions of different concentrations. The three NaCl concentrations were adjusted to give resistivities similar to the maximum, minimum and intermediate values found in each explored myocardial tissue. Calibration measurements were made with the same electrode probe used in the in vivo study in order to reduce errors caused by electrodes, cables and by the amplifier response.

2.3. Epicardial ST segment potential

Extracellular direct-current epicardial electrograms were recorded with a multichannel differential amplifier system. Samples of 2 s duration were digitized at a frequency of 500 Hz and stored in a computer. Selected analog signals were continuously recorded with a seven-channel Elema ink jet polygraph. The electrodes were made of polyethylene tubes of 0.5 mm diameter containing a cotton thread imbibed with isotonic saline solution. Connection of the wick electrode to the amplifiers was done through a Ag/AgCl interface. Twelve cotton electrodes were sutured to a rubber membrane at interelectrode distances of 5 mm, forming a linear array. The electrode membrane was sutured parallel to the LAD and covered an area extending from the center of the necrotic scar towards the acute ischemic peri-infarction zone and normal myocardium (Fig. 1). A 0-mV potential reference was given by a cotton wick electrode placed at the mediastinal fat. The ST segment was measured as total TQ+ST segment displacement because this corresponds to the ST segment recorded by conventional ECG [4].

2.4. Arrhythmia analysis

Episodes of ventricular tachycardia (sequence of three or more consecutive ventricular premature beats) and ventricular fibrillation occurring during the 60 min of the second coronary occlusion were analyzed by continuous monitoring of conventional ECG (leads I, II and III) on a seven-channel Elema ink jet polygraph. Ventricular fibrillation was treated with internal DC countershocks of 15 to 20 Joules. During application of the DC current, the tissue impedance recording system was transiently disconnected.

2.5. Electrical transmission in healed infarction

Electrical transmission through the necrotic scar was estimated in vivo and in vitro by measuring the voltage decay of current pulses applied in the infarction area.
2.5.1. In situ measurements

Current pulses of 30 µA amplitude and 25 ms duration were delivered at a frequency of 10 Hz using a GRASS S88 stimulator (Grass Medical Instruments, Quincy, MA, USA) that was modified to act as a current generator with a 1 MΩ source resistance. Pulses were applied between a pair of platinum electrodes (length=3.5 mm, diameter=0.4 mm) inserted transmurally in the infarcted tissue. As illustrated in Fig. 1, these two current electrodes (I⁺ and I⁻) were inserted at two opposite sites within the infarcted region, separated by a distance of 32.5 mm. The resulting potential difference was measured between a fixed reference electrode (V⁻) located next to the current reference electrode (I) and an exploring electrode (V⁺) that was moved at 2.5 mm intervals from the active current electrode (I') towards the reference potential electrode using a millimetric scale. In each case, 11 sites were sampled. The recorded potential pulses were amplified with an AC-coupled instrumentation amplifier [15] and were visualized on a digital oscilloscope (Kenwood CS 8010). The signals were digitized at 10,000 samples per second and were stored in a computer. Pulse amplitude was plotted against distance and the slope of the regression line that best fits the data was considered to represent the magnitude of voltage attenuation.

2.5.2. In vitro measurements

After completion of the in vivo study, the heart was removed and a transmural strip of the necrotic scar, approximately 35 mm long and 17 mm wide, was placed into a bath chamber (40×35×15 mm). The thickness of the necrotic scar varied between 3 and 4 mm. Current pulses like those used in the in vivo preparation were applied between two intramural platinum electrodes (length=3.5 mm, diameter=0.4 mm) inserted at opposite ends of the preparation (Fig. 1). As in the in vivo study, the potential generated by the stimulating electrodes was measured by moving the exploring electrode at 2.5 mm intervals using a micromanipulator. Voltage attenuation was also calculated as the slope of the regression line that best fits pulse amplitude data plotted against distance. Seven sites were explored on each tissue sample. The aim of the in vitro studies was to validate the measurements obtained in vivo. Specifically, we focused on the possibility that electrodes inserted in the thinner infarcted region might be in close proximity with the intracardiac blood and that this influenced measurements of both resistivity and electrical pulse transmission. Therefore, we measured (a) the resistivity of the scar and blood separately using the four-electrode probe and (b) the voltage attenuation in explanted infarct scar covered with nonoxygenated blood at 37°C, in explanted infarct scar alone kept at room temperature, and in nonoxygenated blood alone at 37°C. The amount of blood used for the measurements was equivalent to that needed to fill the bath chamber.

To have comparative reference data, we also measured voltage decay in low resistance 0.9% NaCl solution and in high resistance 300 mmol/l sucrose solution at 37°C.

Since explantation of the infarct scar may alter its passive electrical properties, we assessed the biophysical stability of the in vitro preparation in two cases by continuously measuring tissue resistivity with the same implanted electrodes at room temperature for 80 min, beginning immediately after explantation. Likewise, the in vitro resistivity measurements were done using the same four-electrode probe that was employed in vivo and its cell constant was calculated by measuring the resistance of 0.9% NaCl solution at 37°C in a volume equivalent to that of the bath chamber.

2.6. Histological examination

Samples of the infarct tissue were embedded in paraffin and stained with Masson’s trichrome [16] and hematoxylin–eosin. Histologic examination was performed using conventional light microscopy.

2.7. Protocol and study population

In 12 pigs (group 1), we recorded tissue electrical resistivity at 1 kHz, ST segment potential, conventional ECG, and blood pressure at baseline and every minute during 1 h of LAD reocclusion. In the remaining seven pigs (group 2), the baseline impedance spectrum and pulse voltage decay was measured in normal and necrotic myocardium in vivo. In five of these seven hearts, the same variables were measured in explanted infarcted tissue, and anatomical analysis was undertaken at the end of the protocol.

2.8. Data analysis

Changes in tissue resistivity and ST segment potential induced by 1 h of LAD reocclusion in the acute ischemic peri-infarction area and in the infarct scar were compared, and differences between these two regions were assessed by repeated measures analysis of variance (ANOVA) using commercially available software (SYSTAT Inc.). Results are expressed as mean±1 standard deviation and as significance tests for linear, quadratic and cubic contrasts, the level was set to p<0.05. The assumption of normality for ANOVA residuals was graphically verified using normal probability plots. The regression line of pulse amplitude against distance was accepted if the correlation coefficient r>0.90. Differences between in vivo ST segment and pulse current slopes were assessed by paired Student’s t-test, whereas the slopes measured in vitro were evaluated by ANOVA and Tukey tests.
3. Results

Pigs submitted to 1 h of coronary reocclusion showed a significant decrease in aortic blood pressure (from $111\pm14$ to $98\pm14$ mmHg, $p=0.002$) and a tendency to have an increase in heart rate, but the latter was not statistically significant ($124\pm33$ vs. $132\pm26$ bpm).

3.1. Myocardial impedance

3.1.1. Tissue resistivity

Resistivity of one-month-old myocardial infarction at 1 kHz was significantly lower than that of normal myocardium ($110\pm30$ vs. $235\pm60$ $\Omega cm$, $p<0.0001$) in the 19 pigs included in this study. Fig. 2 shows that, 1 h after proximal reocclusion of the LAD, the 12 pigs of group 1 showed a marked increase in tissue resistivity in the acute ischemic region (from $265\pm74$ to $510\pm135$ $\Omega cm$, $p<0.01$), whereas this variable remained virtually unchanged in the center of the necrotic scar ($113\pm40$ vs. $116\pm42$ $\Omega cm$). Individual analysis of the resistivity changes revealed an initial slow rise of 49% from baseline during the first 25 to 30 min, followed by a faster rise leading to a 121% increase after 60 min of coronary occlusion.

Application of DC countershocks to treat episodes of ventricular fibrillation did not shift the values of tissue resistivity significantly.

In vitro measurements of the resistivity of the infarct scar and of blood at room temperature showed lower values in the scar than in blood ($166\pm26$ vs. $218\pm38$ $\Omega cm$, $p<0.01$). The stability of the electrical properties of the explanted strips of infarct scar was assessed in two cases over an 80 min period. In these two pigs, resistivity values of the explanted scar remained unchanged during the study period ($233$ and $226$ $\Omega cm$, respectively). By contrast, strips of explanted nonperfused normal myocardium from the same two animals showed a progressive resistivity rise, leading to maximal values of 926 and 850 $\Omega cm$, respectively.

3.1.2. Tissue impedance spectroscopy

Data from the seven pigs of group 2 indicate that normal myocardium and healed infarcted tissue can be differentiated by their distinct impedance spectrum. Fig. 3 shows that, as the current frequency increases, the resistivity of the normal myocardium decreases progressively (from $254\pm86$ to $176\pm25$ $\Omega cm$ at 1000 kHz, $p<0.01$), whereas resistivity of the infarct scar remained unchanged throughout the frequency spectrum ($122\pm21$ vs. $123\pm22$ $\Omega cm$). Likewise, the phase angle of normal myocardium decreased progressively, from $-1.0\pm1.4^\circ$ at 1 kHz to a transient minimum value of $-11.5\pm5.6^\circ$ at 250 kHz, whereas the phase angle of the infarcted tissue did not change significantly ($-3.45\pm5.6$ vs. $-2.15\pm1.7^\circ$). The slight negative phase angle shift seen at low frequencies is due to electrode impedance effects.

3.2. Epicardial ST segment potential

Coronary occlusion above the primary LAD ligature induced significant ST segment elevation in electrodes located in the peri-infarction area (from $0.6\pm0.7$ to $9.5\pm5.1$ mV at 5 min of ischemia, $p=0.002$) and also significant ST segment elevation in the center of the necrotic scar (from $0.5\pm0.5$ to $3.8\pm2.6$ mV, $p=0.03$). The remote normal myocardium showed normal ST segment potential or specular ST segment depression. As illustrated in Fig. 4, the time course of the ST segment changes in the ischemic peri-infarction area paralleled those recorded in the necrotic scar, although the magnitude was higher in the acute ischemic peri-infarction region than at the center of the scar (ANOVA: $p=0.03$). The ST segment potential decreased as the epicardial electrode moved from the periphery towards the center of the necrotic region (Fig. 5A). Decay of the ST segment potential shift in the infarction region was $-0.12\pm0.08$ mV/mm (Fig. 5B).

3.3. Electrical transmission in healed infarction

In vivo measurements of pulse amplitude attenuation in the infarcted myocardium performed in five pigs of group 2 indicated a decay of $-0.07\pm0.05$ mV/mm. This voltage decay was comparable to the ST segment potential attenuation measured in the same anatomical region (illustrated in Fig. 5B).

In vitro measurements of the voltage decay in the necrotic scar, blood and in a 0.9% NaCl solution were performed in five pigs of group 2 (Fig. 6). A voltage attenuation of $-0.55\pm1.1$ mV/mm was observed in the scar exposed to the air; a decay of $-0.37\pm0.09$ mV/mm in the scar covered by nonoxygenated blood; an attenuation of $-0.18\pm0.04$ mV/mm in 0.9% NaCl solution and a
decay of $-0.58 \pm 0.09 \text{ mV/mm}$ in nonoxygenated blood alone. By contrast, voltage attenuation in a highly resistive solution containing 300 mmol/l of sucrose was markedly higher ($-111 \pm 74 \text{ mV/mm}$, $p < 0.001$).

### 3.4. Arrhythmia analysis

During the 2 h following the first coronary occlusion, seven out of the 26 pigs presented with ventricular fibrillation. In four cases, the arrhythmia was successfully terminated by external DC shocks, whereas in the three other cases, the electrical defibrillation was followed by irreversible atrio-ventricular conduction block.

During the second intervention, seven out of the 12 pigs of group 1 developed ventricular fibrillation during 1 h of LAD coronary reocclusion. These animals presented a total number of 17 episodes of fibrillation, which were successfully terminated by a single internal DC countershock in nine instances. The remaining eight episodes required two to three DC shocks. In no instances had animals to be excluded because of irreversible ventricular fibrillation. The hemodynamic conditions remained stable after electrical defibrillation. During the reocclusion period, all pigs developed episodes of ventricular tachycardia. This arrhythmia occurred in 184 instances, which were grouped into two phases with a peak activity at about 4 and 30 min, respectively. Twelve out of the 17 episodes of ventricular fibrillation occurred during the second arrhythmia phase, whereas the remaining five episodes appeared during the first arrhythmia phase.

### 3.5. Post-mortem examination

One month after permanent coronary occlusion, all of the pigs developed a transmural healed myocardial infarction (Fig. 7) with sharply demarcated margins. The infarcted tissue was composed of fibroblasts, collagen fibers and a few capillary vessels. In the center of the scar,
we observed necrotic myocardial cells that were heterogeneously distributed. A thin layer of surviving fibers was observed in the subendocardium, forming a rather homogeneous band of approximately 0.20 to 0.30 mm in width. Surviving bands of about 0.03 mm were also present in the epicardium, but, in this region, they were irregularly distributed. Surviving myocardial cells at the edges of the infarction displayed slight-to-moderate signs of hypertrophy, but degenerative changes such as pyknosis or steatosis were not observed.

4. Discussion

4.1. Electrical impedance of healed myocardial infarction

This study shows that areas of healed myocardial infarction can be differentiated from normal myocardium by their low electrical resistivity and negligible capacitative response. In accordance with the study by Fallert et al. [5] in sheep, the present study in swine shows an approximately 50% lower impedance in healed infarcted tissue than in normal myocardial regions. Our analysis of impedance spectroscopy from 1 to 1000 kHz further revealed that the normal myocardium and the infarct have a different impedance spectrum: the normal myocardium shows a negative shift in resistivity and phase angle at increasing frequencies, whereas the infarcted tissue depicts negligible frequency-related changes. The absence of a frequency-dependent response suggests that the infarct scar is a noncapacitative medium. This is based on the fact that a frequency response in biological media occurs if cell membranes with preserved capacitative properties are present [17]. Surviving cells in the infarcted tissue are scarce and this circumstance is therefore consistent with the lack of capacitative response in healed infarction.

The mechanism by which a healed infarction possesses
low resistance properties is not well known, although it seems reasonable to link this electrical characteristic to the extracellular matrix of the infarct scar. The extracellular matrix, which increases during infarct healing [5, 18, 19], may afford a high ionic diffusibility and, hence, a low tissue electrical resistivity, due to its particular biochemical composition. Indeed, the extracellular matrix contains fibrous proteins (collagen, elastin and fibronectin, among others) immersed in an amorphous substance composed of water and electrically charged glycoproteins (proteoglycans) [19, 20]. This aqueous phase permits diffusion of nutrients, metabolites and hormones between the blood and tissue cells [20]. The moment at which resistivity of the infarcted tissue falls to lower than normal values has not yet been determined. In the study by Fallert et al. [5], this resistivity drop occurred between the first 4 h of ischemia and one week after infarction, but intermediate time frames were not explored.

Our study rules out the possibility that the low infarct resistivity was in fact a measuring error caused by a closer...
proximity of the impedance electrodes to the intracavitary blood in the thinned infarcted regions. Indeed, in vitro data indicate that the infarct scar continues to have lower resistivity than blood alone.

4.2. Electrical transmission in healed myocardial infarction

In accordance with the low resistance properties of the infarct scar, this study demonstrates that the necrotic tissue is able to afford a good transmission of current pulses and of ST segment potential changes elicited by ischemia of contiguous peri-infarction myocardium. Voltage attenuation of current pulses across a transmural healed infarction is as low as that yielded by a high conductive 0.9% NaCl solution, and both were comparable to the ST segment potential decay measured in the infarct scar. Therefore, present data support the concept that a healed myocardial infarction is a highly conductive medium that is able to allow passive transmission of extracellular injury currents responsible for ST segment shift, the main sources of which are localized in the ischemic–normal border zone [2]. For this passive transmission, the necrotic scar would act as an expansion of the extracellular space without the need for any intracellular current pathway. Since injury currents may induce across a transmural healed infarction is as low as that yielded by a high conductive 0.9% NaCl solution, and both were comparable to the ST segment potential decay measured in the infarct scar. Therefore, present data support the concept that a healed myocardial infarction is a highly conductive medium that is able to allow passive transmission of extracellular injury currents responsible for ST segment shift, the main sources of which are localized in the ischemic–normal border zone [2]. For this passive transmission, the necrotic scar would act as an expansion of the extracellular space without the need for any intracellular current pathway. Since injury currents may induce effects on the necrotic scar thus intervening in arrhythmogenesis. The possibility also, speculatively, remains of conduction of local currents generated by activation of neighboring excitable myocardium through the fibrous matrix.

Because the infarct scar lacks capacitative cell membrane properties, the shape of the transmitted current pulses in the infarcted tissue was not distorted. By contrast, electrotonic conduction through unexcitable gaps in Purkinje fibers causes a deformation of action potential upstroke (foot-potential) [22,23].

4.3. Electrical resistivity in acute ischemic peri-infarction myocardium

Our data demonstrate that the advent of an ischemic episode at the borders of a healed infarction induces a marked resistivity rise in the ischemic peri-infarction zone, without altering the low resistivity values in the contiguous healed infarction. Therefore, hearts suffering an acute reinfarction are exposed to marked inhomogeneities in electrical impedance between normal, infarcted and acute ischemic myocardium.

A rise in tissue resistivity after coronary occlusion has been reported in several species [5,7,24–28] and reflects the increase in extra- and intracellular electrical resistance that leads to cell-to-cell electrical uncoupling [24]. Cellular uncoupling is a consequence of the increase in gap junctional resistance caused by accumulation of intracellular Ca$^{2+}$ [27], reduction of adenosine triphosphate content [29] and accumulation of amphipathic lipid metabolites [30] in the ischemic myocardium, among other things. The major determinants of myocardial impedance in the intact heart are intracellular and extracellular resistance, gap junction conductance and membrane capacitance [6,31,32]. The rise in tissue resistivity at 1 kHz follows a two-phase pattern [7]. The initial slowly rising phase lasts for about 15 min and has been related to a rise in extracellular resistance [24] that is secondary to the collapse of the extracellular compartment caused by cessation of coronary perfusion and by osmotic cell swelling [33]. The second resistivity rise is apparent after 30 min of ischemia and has been attributed to increases in both intra- and extracellular resistance leading to cell-to-cell electrical uncoupling.

4.4. Clinical implications

Studies in patients with autopsy-proven myocardial infarction [34] confirm that, like pigs with a one-month-old coronary ligation, old coronary occlusion elicits transmural infarcts with collagen deposition and with an irregular band of surviving cells in the subendocardial and subepicardial myocardium. Based on this anatomical resemblance, healed transmural myocardial infarcts in humans may also have a low electrical resistivity and this may permit transmission of local currents involved in the genesis of local ST segment potential changes and arrhythmias. Reelevation of ST segment in infarct-related ECG leads is currently considered indicative of either left ventricular dysfunction [35–37] or ischemia of residual viable myocardium [38,39]. However, the low resistance of the infarct scar seen in this study strengthens a previous observation from our laboratory showing that reelevation of ST segment in the infarcted region may simply indicate passive ST segment potential transmission from the ischemic peri-infarction zone [4]. The distinct impedance spectrum of normal and infarcted myocardium may settle the basis for the development of new technologies that are able to detect areas of healed infarction in patients, either using intracavitary probes or using noninvasive tomographic systems.

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