Update review

ST segment mapping and infarct size

Michiel J. Janse*

Department of Clinical and Experimental Cardiology and The Interuniversity Cardiology Institute, Amsterdam, The Netherlands

Keywords: Antiarrhythmic agents; Autonomic nervous system; ECG; Infarction; Ischemia

1. Introduction

Following the pioneering studies of Julian [1] and Lown and coworkers [2], demonstrating that ventricular fibrillation is common in patients with acute ischaemia, with and without infarction, and that it can be treated, coronary care units were installed in many medical centres, and attempts were made to hospitalise patients with acute ischaemic attacks as early as possible. As Professor Shillingford writes in this issue [3], the introduction of the coronary care unit offered the possibility to study patients who developed a myocardial infarction in a variety of ways. Pelides et al. [4] reported on nine patients ‘who had sustained an acute myocardial infarction within 72 hours’ in whom the administration of the beta-adrenergic blocker practolol reduced precordial ST segment elevation, which was interpreted as a reduction in the extent and severity of ischaemia.

The background for this 1972 study formed experimental studies by Maroko et al. in 1971 [5]. In this paper, it was stated: ‘Of greatest interest, from the clinical point of view, is the finding that the severity and extent of myocardial ischemic injury resulting from coronary occlusion could be radically altered not only by pretreatment of the animal but also by an appropriate intervention as late as 3 hours after the coronary occlusion’ [5]. In that study, propranolol administered 3 h after coronary artery occlusion reduced average ST elevation from 7.6 to 4.9 mV.

In the 1970s, a great many experimental studies were performed with the aim of reducing infarct size by a variety of means ranging from beta-blockers, nitroglycerin, mannitol, glucose-insulin-potassium infusion, hyaluronidase, hydrocortison and cobra venom (see [6,7]). In most of these studies ischaemic damage was determined by summation of ST segment elevation recorded at a number of epicardial sites. The precise mechanism of ST segment changes were unknown at that time, but Holland and Brooks in several papers emphasised that ST segment changes are influenced by both spatial and non-spatial factors [8–10]. Important spatial factors included the position of the recording electrode with respect to the ischaemic tissue boundaries and the size of the ischaemic zone; non-spatial factors are the differences in transmembrane voltage between ischaemic and non-ischaemic myocardium, which could be altered, for example, by changes in plasma concentration of K⁺. An increase in the size of the ischaemic area may increase the magnitude of ST segment elevation, but an increase in the differences in transmembrane voltage across the ischaemic boundary may do the same, without any change in the size of the ischaemic zone. They demonstrated that an increase in the ischaemic area does increase ST elevation recorded from the precordium, but may result in a decrease in ST segment elevation in epicardial recordings. An important message from their studies was that ‘an ultimate decrease in the magnitude of the TQ–ST segment deflection will not necessarily indicate a decrease in the extent of ischaemic injury’ [8].

When Schaper and co-workers developed accurate methods to determine infarct size [11,12], they demonstrated that infarct size, expressed as the percentage of the perfusion area, was not significantly altered by beta-adrenergic blockade [13]. It is the purpose of this update to briefly describe the changes in transmembrane potential and in cell-to-cell electrical coupling that occur after coronary artery occlusion, and how they alter the TQ- and ST-segments of extracellular waveforms.

2. Changes in intra- and extracellular potentials during acute ischaemia

Early studies on the effects of myocardial injury on local extracellular electrograms already indicated that elevation of the ST segment, as recorded with condensor-coupled
amplifiers (AC-recordings) could be due both to diastolic TQ-segment depression and true, systolic ST elevation [14]. Samson and Scher in 1960 [15] were the first to provide evidence that TQ-segment depression was caused by loss of resting membrane potential in the ischaemic zone. Later studies established the relationship between intra- and extracellular potentials more clearly [16].

Fig. 1 shows simultaneously recorded transmembrane potentials and local unipolar DC extracellular electrograms from an isolated Langendorff-perfused porcine heart, before and after occlusion of the left anterior descending coronary artery. The first change following arrest of coronary flow is a decrease in resting membrane potential, which is reflected in the direct current electrogram by a negative displacement of the TQ-segment (the direct current recordings were made with non-polarizable cotton wick electrodes and with DC coupled amplifiers; the horizontal line through the extracellular electrogram was obtained by moving the extracellular recording probe to the aortic root, where the ‘indifferent’ electrode was located; it serves as ‘zero’ potential). Between 2 and 4 min following onset of ischaemia, resting membrane potential further decreases to −75 mV, with a concomitant increase in TQ depression to −11 mV. Action potential upstroke becomes slow and slurred. After 5 min, the action potential was reduced to a very small amplitude response, and in the electrogram, true ST-segment elevation has now become apparent. Fig. 2 shows in a diagrammatic fashion the mechanism of TQ depression and ST elevation, using superimposed intra- and extracellular potentials from another experiment before (stippled tracings) and after 4 min (A) and 5 min (B) after coronary occlusion (solid tracings). In (A) the intracellular potential during diastole (indicated by the vertical stippled line) in the ischaemic zone is more positive than that in the non-ischaemic zone. Consequently, an intracellular current flows from ischaemic towards non-ischaemic cells, the so-called diastolic current of injury. This current crosses the cell

![Fig. 1. Transmembrane potentials (top traces) and local direct current (DC) extracellular electrograms (lower traces) of the left ventricle of an isolated, perfused pig heart before (control), and 2.5, 4 and 5 min after occlusion of the left anterior descending coronary artery. (Reproduced with permission from Ref. [22].)
Inhibition of ST segment elevation by $\beta$-blockade

The basis for changes in the ST-segment in AC recordings are the differences in transmembrane potentials of ischaemic and non-ischaemic cells during both diastole and systole. The magnitude of ST-segment elevation is, on the one hand, determined by the magnitude of these potential differences, and, on the other hand, by the intercellular resistance of ischaemic and normal cells. Normally, the gap junctions provide low-resistance connections between cardiac cells, permitting intercellular current flow. However, during ischaemia coupling resistance of ischaemic cells increases after a certain time, so that current flow between ischaemic and normal myocardium becomes hampered [17,18]. In isolated, arterially perfused rabbit papillary muscles, intercellular resistance rises explosively 15 to 20 min after the onset of ischaemia. This cellular uncoupling marks the beginning of irreversible injury, or, in other words, the transition from ischaemia to infarction. The moment of uncoupling can be delayed by ischaemic preconditioning, and the major factor causing uncoupling is an abrupt rise in intracellular calcium concentration [18–20]. In contrast to normal hearts, preconditioning in failing hearts advances the moment of uncoupling [21]. Extrapolation of these experimental findings to the human heart with thrombotic occlusion of a major coronary artery is hazardous, but it may be expected that the moment of cellular uncoupling will vary among patients depending on the following questions. How abrupt is the occlusion? Was the final prolonged ischaemic episode preceded by one or more brief ischaemic periods followed by reperfusion (preconditioning)? Was left ventricular function normal or depressed prior to ischaemia? Was there still collateral flow to the ischaemic zone? All these questions, to which the answer is usually unknown, might influence the moment of uncoupling. It is, however, beyond doubt that with time coupling resistance will increase, and because this will result in a decrease in current flow between ischaemic and non-ischaemic regions of the heart, it will decrease the magnitude of ST-segment elevation. Indeed, detailed isopotential maps during diastole and systole in isolated, Langendorff-perfused pig hearts with regional ischaemia showed a marked reduction in the magnitude of TQ-depression and ST-elevation after 1 h, as compared to 15 min after onset of ischaemia [16].

3. Concluding remarks

Because the spatial factors influencing the magnitude of ST-segment deflections have been analysed in detail by Holland and Brooks [8–10], I have limited this brief update to a discussion of non-spatial factors: differences between transmembrane potentials during diastole and systole between ischaemic and non-ischaemic cells, and intercellular coupling resistance. Although the moment of

![Fig. 2. Mechanism of TQ- and ST-segment changes. Transmembrane- and extracellular potentials of normal myocardium (dashed lines) are superimposed over potentials (recorded after 4 and 5 min of coronary artery occlusion (solid lines) at the left in panels (A) and (B). In the diagrams the local current circuits during diastole and systole are depicted (during the moment in the cardiac cycle indicated by a vertical dashed line through the redrawn potentials). Intra- and extracellular potentials are given in mV. I=ischae mic area, N=normal myocardium, each represented as one cell. In (C), extracellular potentials are shown, recorded from the ischaemic zone after 5 min of ischaemia with both alternating (AC) and direct current (DC) amplifiers. (Reproduced with permission from Ref. [22].)](image)
electrical uncoupling in patients who develop an acute myocardial infarction is not known, and may depend on many factors, it is clear that the time following onset of ischaemia is an important determinant of the magnitude of ST-segment changes. With time, these changes will decrease, without indicating a reduction of severity and extent of ischaemia. On the contrary, a decrease in ST-segment elevation may well be associated with the onset of irreversible injury. This is not to say that beta-adrenergic blockade may not reduce infarct size, as suggested by Pelides et al. [4]. In dogs, infarct size, assessed by visual inspection of ‘the macroscopically identifiable anatomic damage’, was reduced by propranolol [23]. This effect was thought to be largely due to the reduction in overall myocardial oxygen consumption, caused by the reduction in heart rate, systemic blood pressure and cardiac contractility. In the Göteborg Metropolit Trial, enzymatically estimated infarct size (lactate dehydrogenase, transaminases) was significantly reduced in patients receiving the drug compared with patients on placebo [24].

In retrospect, one may conclude that papers such as that of Pelides et al. [4] have served as important stimuli for further research, elucidating pathophysiological mechanisms involved in the transition from ischaemia to infarction. It has now become clear that ‘ST-segment mapping’ is an unreliable method to determine severity and extent of ischaemia. In a review article from 1987 [25], entitled ‘Infarct size — can it be measured or modified in humans?’ only precordial QRS mapping, but not ST segment mapping is briefly mentioned. Nowadays, biochemical methods (creatine kinase MB, troponine), echocardiography (wall motion score) or scintigraphy are used to estimate infarct size.

References