

Monitoring the Function of the Heart Using the Monophasic Action Potential - Investigation in the Langendorff Perfused Rabbit Heart

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Summary

In cardiac surgery, especially after cardiopulmonary bypass with cardioplegic arrest, alterations of myocardial function can often be found, although routine examinations such as the surface ECG do not overt significant changes. In our laboratory, we performed electrophysiological studies on the isolated rabbit heart, using specially designed electrodes to measure monophasic action potentials (MAP) in different areas and during different stages of cardiac function. Ten rabbit hearts were perfused in an isolated heart apparatus and monophasic action potentials were recorded from different parts of the heart. We used fractally coated electrodes (BIOTRONIK) which guarantee a safe detection of the MAP without artefacts. We examined the MAP in different states of cardiac function: Langendorff- and working-heart mode, during injection of cardioplegic solution and during reperfusion after cardioplegic arrest. Regarding the morphology, the atrial signal showed a steep depolarization, almost no plateau and an early repolarization. In opposition to this, the ventricular MAP showed a three times prolonged plateau. Infusion of cardioplegic solution led to a short, slight increase and afterwards to a rapid decrease in amplitude, MAPd25, MAPd50 and MAPd90. Reperfusion after cardioplegic arrest initially led to an increase in amplitude. After a short period, the amplitude decreases to nearly 30% below the values before infusion of cardioplegic solution. MAPd25, MAPd50 and MAPd90 were initially prolonged, but returned to normal levels after a short period of time. If using fractally coated electrodes, it is possible to record MAPs with reproducible results. Changes in myocardial function lead to a fast and localized change of the MAP's amplitude, plateau and duration. Although standard parameters like the surface ECG return to normal forms, regional alterations of myocardial function can be demonstrated by lasting alterations of the local MAP.

Key words

Monophasic action potential, Langendorff-model, cardioplegic arrest, cardiopulmonary bypass, isolated heart

Introduction

In 1997, more than 120,000 cardiac operations were performed in Germany. More than 90,000 of these operations were open heart procedures using the heart lung machine for extracorporeal circulation (ECC) [1]. The introduction of ECC by Gibbon [2] (1953) and Kirklin [3] (1955) enabled the surgeons to perform open heart surgery in the way we know it today. Although there are different techniques for the management during ECC, most surgeons prefer to use cardioplegic solutions, normally a cold saline solution containing potassium as the essential part, to achieve

cardiac arrest for a determined part of the operation. The cardiac arrest is strictly necessary for most open heart procedures and therefore, cardioplegia is unavoidable to protect the heart from ischemia. But, depending on the extent of cardioplegic arrest, alterations of myocardial function can be found. That happened even though the heart was protected as good as possible and no technical problems occurred. In many of these cases, standard examinations like surface ECG do not show any alterations and other tests like a continuously performed transesophageal echo are not

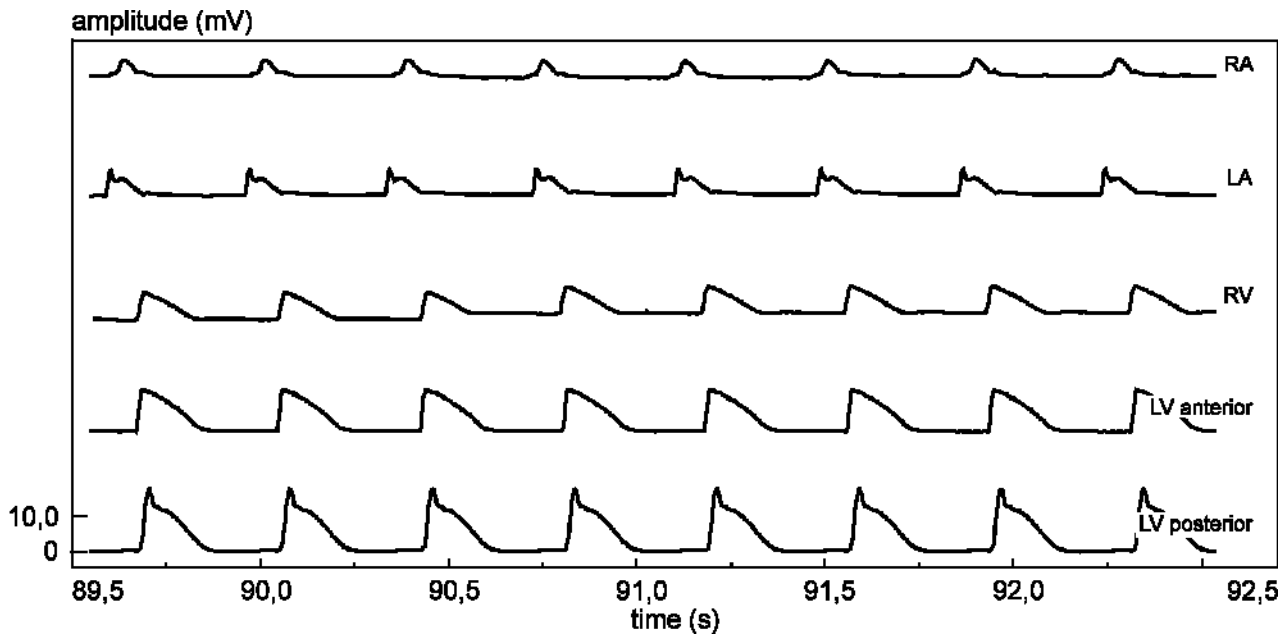


Figure 1. MAP-morphology in the Langendorff model.

always available. These techniques are very much dependent on the examiner, so that it is not always easy to receive objective judgements. But, in contrast to this, the clinician sees an impairment in cardiac function and sometimes, inotropic drugs are necessary to maintain or restore myocardial function.

The question evolves, whether there is an ischemic effect on the myocytes, although the myocardium is supposedly well protected. The objective is to find a parameter which is sensitive enough to identify the alterations of cellular activity.

In our laboratory, we are able to simulate parts of an open heart procedure using the isolated rabbit heart in a Langendorff-model. In order to detect changes in myocyte function, the monophasic action potential (MAP) seems to be a suitable parameter, because of its already known changes due to myocardial alterations such as ischemia, rhythm disturbances and different loading conditions [4-6].

Our hypothesis is, that changes of the postcardioplegic MAP are due to global ischemia.

Methods

The Langendorff-heart-model (Hugo Sachs) allows examinations on the isolated rabbit heart. On the one

hand, it is possible to perfuse the heart with nutrition solution and without stress; on the other hand, a working-heart mode can also be performed. Through an extra line, drugs or cardioplegic solution can be infused. We examined the hearts of ten female, white New Zealand rabbits with a mean body weight of 3.5 kg, mean heart weight was $10 \text{ g} \pm 1 \text{ g}$. The animals received premedication with Ketamine subcutaneously, then an ear vein was punctured and Ketamine and Disoprivane were given intravenously. Heartbeat and breathing were continuously controlled.

The heart was explanted using a combined transversal abdominal and parasternal approach. The pericardium was opened and after cutting the big vessels, the heart was immediately brought into the Langendorff-model, where perfusion with the nutrition solution started. Mean time between explantation and perfusion was 30 ± 5 seconds.

During the first ten minutes of perfusion, a surface ECG was attached to the heart, and the electrodes were placed to measure the MAPs. We used fractally Iridium-coated electrodes (BIOTRONIK), which were located in the left and right atrium, the right ventricle and on the anterior and the posterior wall of the left ventricle. Ten minutes after start of perfusion, the first MAPs were recorded as a baseline for com-

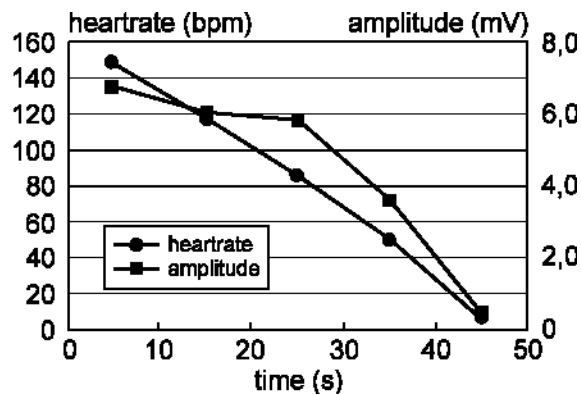


Figure 2a. Changes of heartrate and MAP-amplitude during injection of cardioplegia.

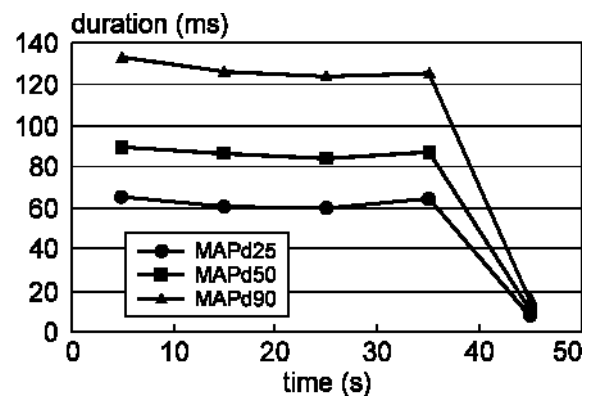


Figure 2b. Changes of MAP during injection of cardioplegia.

paring to the following measurements. Then, cold crystalloid cardioplegia (Custodiol) was infused, an amount of 22 ± 2 ml was needed to achieve cardiac arrest. During this time, MAPs were recorded continuously. After ten minutes of cardioplegic arrest, the heart was reperfused, the MAPs were recorded again during the re-appearance of cardiac activity and again ten minutes later.

All data were recorded using an amplifier, an A/D-converter and a computer system with two special programs (Biocord, Bioview, BIOTRONIK). Biocord was used to store the MAP data on the computer. This stored data was automatically analyzed by using the program Bioview. Points of interest for evaluation were the changes of amplitude, MAPd25, MAPd50 and MAPd90 and morphological changes of the MAP.

Results

The fractally coated electrodes enabled us to record the MAPs precisely. First of all in the Langendorff-model, we saw morphological differences depending on the examined area. The atrial MAP was significantly shorter with a triangular shape in contrast to the ventricular MAP, that was longer and showed a clearly recognizable plateau (Figure 1).

Injecting cardioplegic solution, we recognized an immediate decrease in amplitude, the MAP duration remained stable for nearly half a minute (Figure 2a, Figure 2b), followed by a sudden decline before cardioplegic arrest (Figure 2a, Figure 2b). During this process, the morphology changed from the above described ventricular MAP to a more triangular shape with a slower upstroke velocity and a decreasing

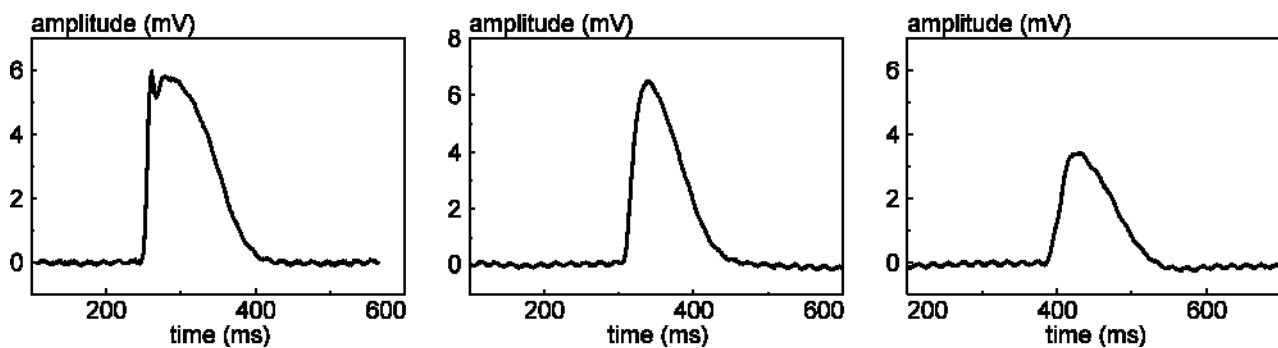


Figure 3. Morphological changes during injection of cardioplegic solution.

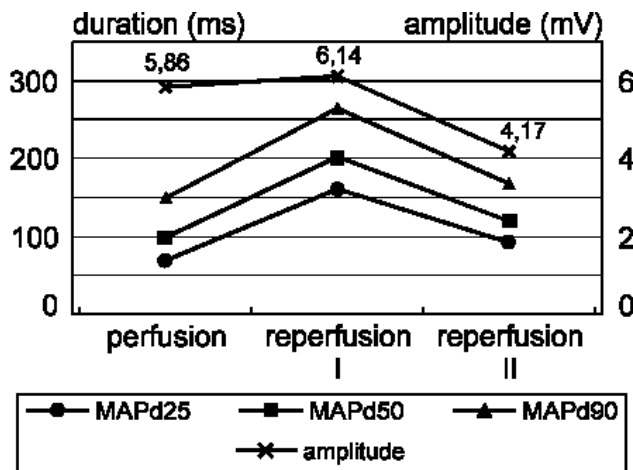


Figure 4. MAP parameters before and after cardioplegia.

amplitude (Figure 3). But the length of the MAP was stable up to 35 seconds after cardioplegia had infused. Then, the duration of the MAP strongly decreased (Figure 2a). Starting reperfusion after cardioplegic arrest, the first changes were prolonged MAPs with high amplitudes, nearly 10% higher compared to the amplitude in the beginning of the attempt (Figure 4). But after a short period of time, the relations changed with a normalization of the MAP duration and a decrease of the amplitude to values about 30% below the reference.

Summarizing, we can describe a stable change of the MAP after cardioplegic arrest with lower amplitudes, lower upstroke velocity and nearly unchanged duration. These alterations did not normalize during the remaining time of the experiment (up to 30 minutes after reperfusion) (Figure 5).

Conclusions

The MAP is a sensitive parameter which allows the examination of local electrical myocardial function. Depending on the localization of the electrodes, different morphologies of the MAP can be seen. On the other hand, the detection of localized myocardial alterations indicates changes in the electrical state of the heart, although, global parameters, like ECG, seem not to be influenced.

The use of cardioplegic solution to achieve cardiac arrest leads to typical changes which seem to be an

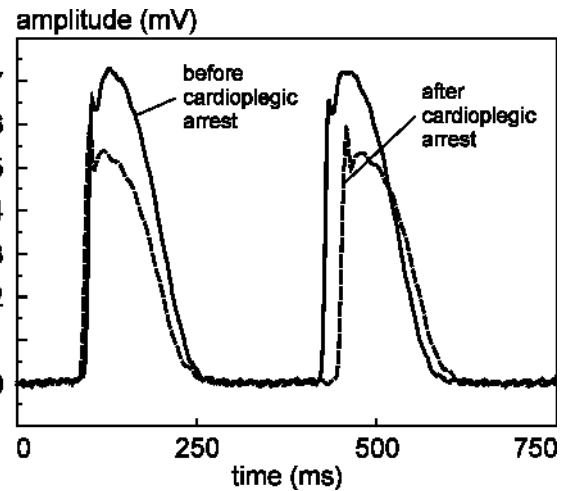


Figure 5. MAP before and after cardioplegic arrest.

equivalent to a reduced cardiac function. Directly after reperfusion, we saw a slightly prolonged MAP with an increased amplitude, changes that were also described by Dilly and his group in 1988 after regional ischemia in pigs [7]. Moments later, we recorded a reduction in amplitude and a lower upstroke velocity, the MAP duration was reduced. These changes were stable during the remaining time of the experiment.

Comparing our results with literature, we recognize that the changes were often described in the context of regional ischaemic alterations [8][9]. However, we did not induce ischaemia. We used a technique that protects the human heart from ischaemia during cardiac operations. The rabbit hearts were protected accordingly, and after ten minutes of cardiac arrest, we found no alterations in cardiac function, the surface ECG was normal and there was no global reduction in myocardial contractility. The MAP proved, though, that in opposition to this, there was a negative influence on cellular activity, that can be described as an ischaemic alteration.

We conclude, that in spite of myocardial protection, ischaemic alterations occur in hearts after cardioplegic arrest. The MAP seems to be a sensitive and reliable parameter for detection of these changes. Clinical studies need to be performed to observe, whether the MAP is useful for the improvement of myocardial protection in cardiac surgery or for the early detection of ischaemic events.

References

- [1] Kalmar P, Irrgang A. Cardiac surgery in Germany during 1997, *Thorac Cardiovasc Surg.* 1998; 46: 307-310.
- [2] Gibbon JH Jr. Application of a mechanical heart and lung apparatus to cardiac surgery. *Minn Med.* 1954; 37: 171.
- [3] Kirklin JW, DuShane JW, Patrick RT, et al. Intracardiac surgery with the aid of a mechanical pump-oxygenator system (Gibbon-type): Report of Eight Cases. *Mayo Clin Proc.* 1955; 30: 201.
- [4] Taggart P. Some effects of ischemia and changes in ventricular loading on repolarisation. In: Franz MR, Schmitt C, Zrenner B: *Monophasic Action Potentials*; Springer Verlag Berlin, 1997: 201-211.
- [5] Dilly SG, Lab MJ. Changes in monophasic action potential duration during the first hour of regional myocardial ischemia in the anaesthetised pig; *Cardiovasc Res.* 1987; 21 (12): 908-915.
- [6] Franz MR. Bridging the gap between basic and clinical electrophysiology: what can be learned from monophasic action potential recordings? *J Cardiovasc Electrophysiol.* 1994; 5 (8): 699-710.
- [7] Dilly SG, Lab MJ. Electrophysiological alternans and restitution during acute regional ischemia in myocardium of anaesthetised pig. *J Physiol.* 1998; 402: 315-333.
- [8] John RM, Taggart PI, Sutton PM, Ell PJ, Swanton H. The interrelation between the monophasic action potential duration, cycle length and ischemia in the human left ventricle. *Eur Heart J.* 1992; 13 (3): 310-315.
- [9] Franz MR: Monophasic action potential recordings: What are they, how can they be recorded, what is their use? In: Franz MR, Schmitt C, Zrenner B: *Monophasic Action Potentials*; Springer Verlag Berlin, 1997: 22-39.