The Evaluation of Myocardial Lesions after Radiofrequency Ablation Using Electrophysiological and Biochemical Markers

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Summary

To evaluate the clinical significance of mechanical and thermal injury of radiofrequency ablation (RFA) on the myocardium, we focused on factors determining the extent of myocardial necrosis, and estimated safe parameters to minimize the negative influence of the technique in adult and pediatric patients. Our study group consisted of 87 patients (mean age 24.0 ± 13.2 years) with arrhythmias and no other cardiac pathology; they were analyzed before and after RFA of the arrhythmogenic zone. 37 patients were children ranging from 3 to 18 years (mean age 12.3 ± 4.2 years). All patients underwent full clinical evaluation including body surface mapping (BSM). The results revealed a good correlation between the pathological value of biochemical markers of myocardial damage (troponin I or troponin T) the number of RFA applications, total duration of the procedure, and size of the application area. The relative concentrations of troponin I and troponin T after RFA, with respect to measurements before RFA, and the ratio of creatine phosphokinase MB (CPK-MB) to creatine phosphokinase (CPK) are important in determining the extent of injury. The same result applies to the BSM. In the pediatric subgroup (excluding patients with Wolff-Parkinson-White syndrome) there was a correlation between BSM parameters and the CPK-MB/CPK ratio. RFA causes subendocardial injury of the myocardium with subsequent changes of the biochemical markers and BSM parameters. The relative changes of biochemical and non-invasive electrophysiological markers compared to baseline levels are important in determining the extent of injury. The most sensitive markers are troponins I and T, then myoglobin. The levels of traditional CPK-MB and parameters of BSM show less significance because of a low specificity. Nevertheless, CPK-MB and BSM parameters correlate highly in children and could be used in a clinical practice as less expensive (CPK-MB) and easily reproducible (BSM) methods. Parameters of RFA such as number of RFA applications, total duration of the procedure, and size of the application zone should be selected in a way to minimize the myocardial injury. They should not exceed threshold values, especially in pediatric patients.

Key Words

Radiofrequency ablation, myocardial lesion, electrophysiological and biochemical markers, body surface mapping

Introduction

Radiofrequency ablation (RFA) is one of the most effective methods for treatment of symptomatic tachyarrhythmia. We performed this procedure in 750 patients with different types of rhythm disturbances. Experimental studies [1-2] showed that this technique made it possible to achieve optimal balance between patient safety and effectiveness of the procedure, adequately localize the application area, and reduce myocardial damage by lowering the transmitted energy. Typically, 200 mm^3 of tissue were damaged using a 7F catheter with a 4 mm tip. In several studies [3-5] the size of endomyocardial damage following RFA was evaluated with biochemical markers, both traditional – creatine phosphokinase (CPK) and fraction creatine phosphokinase MB (CPK-MB) – and recently introduced myoglobin and troponins I and T, due to their high cardioselective specificity. To evaluate the clinical significance of myocardial mechanical and thermal injury following RFA, we focused on factors determining the extent of myocardial necrosis and

established safe parameters for minimization of the negative influence of RFA in adult and pediatric patients.

Methods

From 750 patients undergoing RFA, a study group of 87 patients (mean age 24.0 ± 13.2 years) was selected who had arrhythmia and no other cardiac pathology before and after RFA. 37 patients were children from 3 to 18 years (mean age 12.3 ± 4.2 years). 54 from 87 patients were presented with the Wolff-Parkinson-White (WPW) syndrome, ten patients with concealed accessory pathway, four with so-called "slow Kent", 12 patients with atrioventricular (AV) nodal reentry tachycardia, and five with ventricular arrhythmia. All patients underwent full clinical evaluation including body surface mapping (BSM) performed using Cardiag system (ZPA Chakovice, Czech; EKVA, Czech) capable of recording 12 traditional leads simultaneously, Frank orthogonal leads X, Y, Z, and 80 chest unipolar leads. Electrodes were placed between the 1^{st} and 6^{th} intercostal space on the chest surface. Data could be analyzed as instantaneous isopotential maps, as isointegral maps and as departure index (DI) maps. Isointegral maps were calculated for two time intervals of the cardiac cycle: ST-T (stimulus-T) and QRST. DI in every lead was calculated according to the formula:

DI = (individual value – reference value) / standard deviation of the reference,

where individual value was ST-T or QRST integral in a given lead, and reference values and standard deviation of the reference were calculated from isointegral maps of a group of 40 healthy young adult men. An absolute value of DI greater than 2 was considered significant. Based on the departure maps designed for ST-T and QRST intervals it was possible to estimate changes of ventricular repolarization, the largest negative ($DI^{negative}$) and the largest positive ($DI^{positive}$) deviations from the reference value, as well as their localization on the chest wall and approximate extent compared to the total chest wall surface.

Electrophysiological studies (EPS) and RFA were performed according to the standard protocol by using the Cardiolab (Prucker Engineering, Houston, TX, USA) and the Atakr generator (Medtronic, USA) with a 500 kHz ablation frequency. We used RF catheters of 4F (Biotronik, Germany) and 6-7F (Medtronic) in size, with a temperature control of the catheter tip. No early or late complications nor mortality were observed. We used the transaortale (retrograde) approach for all left-sided arrhythmogenic substrate ablation except for one case with transseptale approach. We considered the following parameters for RFA:

N_{RFA}: number of applications;
$time_{RFA}$: total duration of the procedure (s);
$zone_{RFA}$: size of application area (mm).

Prior to EPS, blood samples for biochemical analysis were drawn after introduction of the catheter in order to exclude changes due to mechanical injury. Blood tests were repeated immediately after the last RFA application, and every 4 hours for the next 24 - 48 hours after RFA. Myocardial damage was studied using CPK, CPK-MB, myoglobin, troponin T and troponin I as markers.

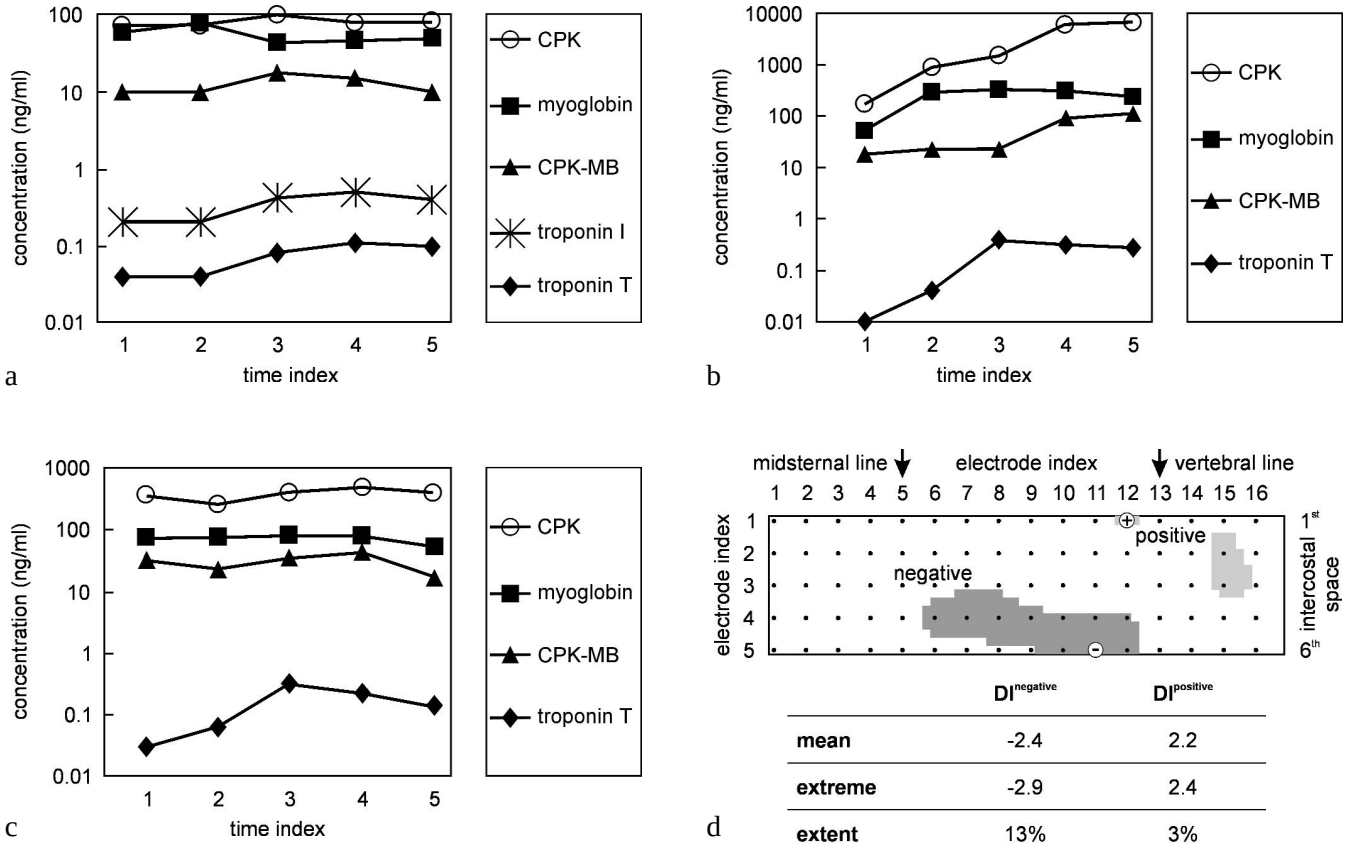
Concentrations of CPK < 190 and CPK-MB < 19.4 ng/ml, myoglobin < 76 ng/ml, troponin T < 0.1 ng/ml and troponin I < 1 ng/ml were considered normal. The ratio of maximal concentrations after RFA to initial pre-EPS concentrations ($X_0 = X_{ma} / X_{init}$), and the maximum CPK-MB/CPK ratio were calculated (normally < 10 %). During corelation analysis according to Pearson, a value < 0.05 was considered significant.

Results

Although biochemical changes and ECG changes were present in all patients following RFA, in some cases they remained within normal limits. One should be aware, however, that the kinetics of these biochemical markers showed peak levels earlier than expected and were comparable to those usually found in myocardial infarction. The concentration of the troponins was highest in the 8 - 12 hour interval following RFA. Extracardiac events could also influence some biochemical parameters such as CPK and myoglobin, due to their low myocardial specificity.

We found ECG signs of transient T-wave changes in corresponding leads appearing immediately after the procedure, and decreasing at different periods after intervention. However, the magnitude of ECG changes in patients with similar arrhythmia was different.

Figures 1a and 1b show changes in the CPK, CPK-MB, myoglobin, troponin T and troponin I in adult



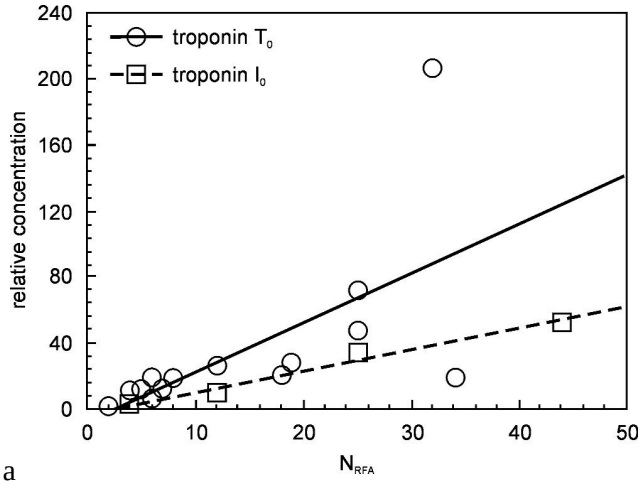
	$DI^{negative}$	$DI^{positive}$
mean	-2.4	2.2
extreme	-2.9	2.4
extent	13%	3%

Figures 1a - 1c. Profiles of CPK, myoglobin, CPK-MB, troponin I and troponin T in three different patients after successful RFA. Time index 1: after catheter introduction and before electrophysiological study; time index 2: after RFA; time index 3: 4 hours after RFA; time index 4: 8 hours after RFA; time index = 5: 12 hours after RFA. Figure 1a refers to a 52-years-old patient suffering from AV nodal tachycardia, Figure 1b to a 50-years-old with a concealed WPW syndrome, and Figure 1c to a 6-years-old with AV nodal tachycardia. Figure 1d is related to the same patient from Figure 1c, showing the scheme of the thoracic surface cut along the right-axillary line. The sign "•" indicates 80 different lead locations, the sign "+" ("-") indicates the maximum value of $DI^{positive}$ ($DI^{negative}$), the shadowed areas indicate the zones with $DI^{positive} > 2$ ($DI^{negative} < -2$) during the QRST time interval. Mean values, maximum values, and the extent of the chest surface, all with $|DI| > 2$, are presented in the corresponding table.

patients during 24 hours after successful RFA with a minimal number of applications (N = 4 and N = 3, respectively). Concentrations of troponin I and troponin T changed mostly after the RFA. In both cases, the tachycardia was of an AV nodal origin, but in the second case the patient had a skin burn. Such cases where an extracardial phenomenon resulted in a modification of biochemical parameters (here CPK, myoglobin) were excluded from the analysis. Figures 1c and 1d show changed levels of the same markers and DI map from the time-aver aged BSM signals over the QRST interval in a child (experiencing tachycardia) after successful RFA of the AV node.

As seen in Figure 2, the analysis of our study group revealed good correlation between the pathological value of the biochemical markers troponin I_0 or troponin T_0, N_{RFA}, and $time_{RFA}$. Obviously, an increasing number and duration of RFA applications induced more pronounced relative changes in troponin concentrations, whereas correlation with $zone_{RFA}$ was not as evident. In general, we found that the relative changes of biochemical markers compared to baseline levels ($X_0 = X_{max} / X_{init}$), in contrast to absolute values, are important in determining the extent of injury.

Currently there are many publications [6-8] on the so-called "cardiac memory" effect after successful RFA in



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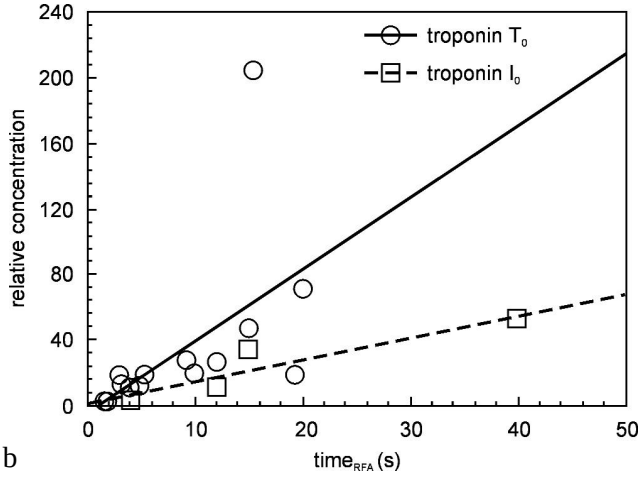

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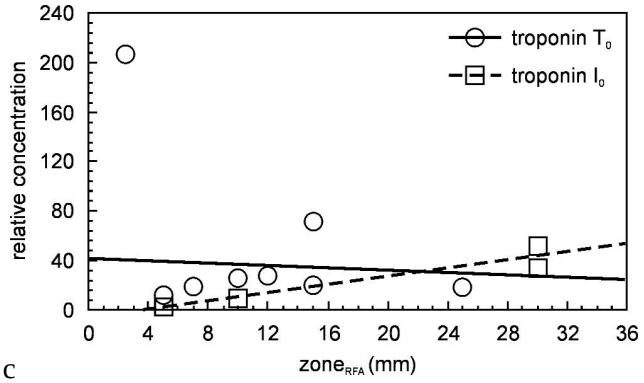

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Figure 2. Linear regression between relative concentration of troponin T_0 and troponin I_0 and the number of RFA applications (N_{RFA}, Fig 2a), total duration of the procedure (time $_{RFA}$, Fig 2b), and the size of the application area (zone $_{RFA}$, Fig. 1c).

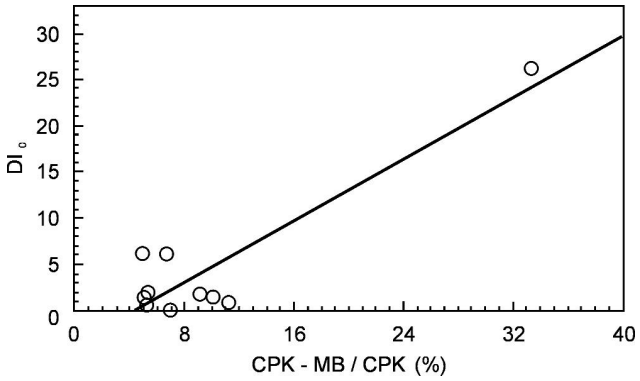

Figure 3. Linear regression between the relative changes of the mean negative value of departure index on the chest, DI_0, and the maximal value of CPK-MB / CPK (in %) after RFA. These data come from the pediatric subgroup, except for patients with WPW syndrome.
DI_0 = ($DI^{negative}$ after RFA)/($DI^{negative}$ before EPS).

patients manifesting WPW syndrome and persistence of anomalous ventricular repolarization. To exclude the influence of these factors, we analyzed data in the pediatric subgroup, except for those patients manifesting WPW syndrome. The Pearson correlation coefficient reached the value of 0.9, i.e. large modifications in BSM were associated with maximal relative concentrations CPK-MB/CPK. Thus, using DI maps from BSM, measured during the QRST interval, it is possible to evaluate abnormalities of de- and re-polarization

Discussion

RFA causes subendocardial injury of the myocardium with subsequent changes in the biochemical markers and BSM parameters. The relative changes of the biochemical and non-invasive electrophysiological markers compared with the baseline levels are important in determining the extent of injury. The same result applies to BSM maps. The most sensitive markers are troponins I and T, then myoglobin. CPK-MB and BSM parameters exhibit a high correlation in children and could be used in a clinical practice as less expensive (CPK-MB) and easily reproducible (BSM) methods.

Conclusion

Thanks to the known peak levels of CPK, CPK-MB, myoglobin and troponin T and I concentrations in patients with myocardial infarction, we were able to

assess the influence of each RFA parameter, as to determine safety limits. RFA parameters such as number of applications, total duration of the procedure, and the size of the application zone should be selected in a way to minimize the myocardial injury. They should not exceed threshold values, especially in pediatric patients.

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