

Detection of Myocardial Injury During Radiofrequency Catheter Ablation by Measuring Serum Cardiac Troponin I Levels: Procedural Correlates

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OBJECTIVES In the present prospective controlled study, we measured blood levels of cardiac troponin I (cTnI) in patients undergoing radiofrequency (RF) catheter ablation (RFA), and we sought to investigate the degree of myocardial injury incurred by the application of RF energy and determine its procedural correlates.

BACKGROUND Measurement of serum creatine kinase (CK) levels after RFA may underestimate the degree of myocardial injury due to its thermal inactivation by RFA. Cardiac troponin I is a newer, more specific marker of myocardial injury, which may circumvent this limitation; its use in this setting has rarely been studied.

METHODS In 118 consecutive patients, 67 men and 51 women aged 38 ± 19 years undergoing RFA for a variety of arrhythmias, cTnI and creatine kinase isoenzyme (CK-MB) levels were measured before, immediately after and 4 to 24 h after RFA. Cardiac troponin I was also measured in 39 patients (control group) having only electrophysiologic studies (EPS) without RFA.

RESULTS All RFA procedures were uncomplicated, lasted 3.2 ± 2.0 h and included delivery of 16 ± 22 (median: 9) RF current applications. Baseline cTnI levels averaged 0.17 ± 0.18 ng/ml, rose to 0.88 ± 1.12 at the end of RFA and to 2.19 ± 2.46 at 4–24 h later. Creatine kinase isoenzyme was found to be elevated ($>6 \mu\text{g/l}$) in 32 patients (27%), while cTnI levels were increased (≥ 1 ng/ml) in 80 patients (68%) ($p = 0.0001$). Cardiac troponin I levels correlated with the number of RF lesions applied ($r = 0.53$, $p < 0.0001$), the site of RFA, being higher with ventricular $>$ atrial $>$ annular lesions ($p = 0.012$) and the approach to the mitral annulus (transaortic $>$ transseptal, $p = 0.004$). In a control group of 39 patients undergoing EPS, all but one patient had normal cTnI or CK-MB.

CONCLUSIONS The degree of myocardial injury incurred by RFA is far more accurately assessed by cTnI levels rather than by CK-MB measurements. Cardiac troponin I levels correlate with the number of RF lesions applied, the site of RFA and the approach to the mitral annulus. (J Am Coll Cardiol 1999;34:1099–105) © 1999 by the American College of Cardiology

The use of radiofrequency (RF) catheter ablation has become standard therapy for a variety of cardiac arrhythmias (1–9). The myocardial damage incurred by the thermal injury induced by RF current application has been considered small, due to the small size of the lesions that are produced and, in part, due to the low levels of serum creatine kinase (CK) measured in the postprocedural period. However, there are two caveats that are involved in this assumption. First, not uncommonly, an increased number of

RF lesions may be produced, especially in difficult or demanding cases or when multiple arrhythmia foci are targeted, leading to a large cumulative volume of myocardial injury. Second, thermal inactivation by RF ablation of CK could lead to underestimation of the actual degree of myocardial injury (10).

For a long time, CK isoenzyme (CK-MB) analysis had been the gold standard for diagnosis of myocardial injury. Recently, cardiac troponins (I or T) have been introduced (11–15). Troponin is the contractile regulatory protein complex of striated muscle. It consists of three components: troponin C (the calcium binding element), troponin I (the tropomyosin ATPase inhibitory element) and troponin T (the tropomyosin binding element). This complex serves to

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Abbreviations and Acronyms

AV	=	atrioventricular
CK	=	creatin kinase
CK-MB	=	creatin kinase MB isoenzyme
cTnI	=	cardiac troponin I
ECG	=	electrocardiogram
EPS	=	electrophysiology study or electrophysiologic studies
RF	=	radiofrequency

regulate the calcium-dependent interaction of myosin and actin, and it plays an integral role in muscle contraction. Troponin I exists in three distinct molecular forms found in fast-twitch skeletal muscle, slow-twitch skeletal muscle and heart, respectively. The cardiac isotype is specific for heart muscle injury detection. Recent clinical studies suggest an improved cardiac specificity for troponin I compared with CK-MB for detection of myocardial injury in the presence of skeletal muscle injury.

Cardiac troponin I (cTnI) has been shown to be more sensitive and specific than CK-MB and more specific than cardiac troponin T for the detection of minor myocardial injury (12-14). However, cardiac troponins have rarely been used to monitor myocardial injury after RF catheter ablation procedures and only in a small number of patients (16,17). The present prospective controlled study investigates in a large cohort of 118 consecutive patients whether measurement of serum levels of cTnI can detect myocardial injury incurred during RF ablation better than CK-MB and whether there are any procedural correlates with peak blood levels of cTnI.

METHODS

Patients. One hundred-eighteen consecutive patients undergoing RF ablation were included in the study over a span of 24 months. These were 67 men and 51 women, aged 38 ± 19 years (range 8-82) who underwent RF ablation of accessory (n = 48) or slow atrioventricular (AV) nodal (n = 34) pathways, atrial foci (n = 14), both slow pathway and atrial foci (n = 3), ventricular foci (n = 15) or the AV node (n = 4). All patients had symptomatic tachyarrhythmias and were diagnosed as having Wolff-Parkinson-White syndrome (n = 29) or preexcitation variant (n = 2), arrhythmias related to a concealed accessory pathway (n = 17), AV nodal reentrant tachycardia (n = 37), atrial tachycardia (n = 10) or flutter (n = 4), atrial fibrillation (n = 4), idiopathic ventricular tachycardia (n = 13) (right-sided in seven and left-sided in six) or ventricular tachycardia with underlying tetralogy of Fallot (n = 1) or right ventricular dysplasia (n = 1). Electrophysiologic testing and mapping were part of the ablation procedure and routinely preceded delivery of RF lesions.

In the study there were also 39 patients (control group) undergoing electrophysiologic studies (EPS) without RF

ablation consisting of 27 men and 12 women with a mean age of 47 ± 19 years. They underwent EPS for complaints of palpitations (n = 4), presyncope (n = 1) or syncope (n = 9) and for documented supraventricular (n = 7) or ventricular tachyarrhythmias (n = 17) or persistent sinus bradycardia (n = 1). All patients gave informed written consent for the procedures.

Electrophysiologic study. The diagnostic EPS was performed in the fasting state after all antiarrhythmic agents had been discontinued for a period of at least five drug elimination half-lives. For some patients in the control group, EPS was performed while the patients were receiving an antiarrhythmic drug (electropharmacologic testing). Routinely, three 6F quadripolar electrode catheters were introduced from the femoral vein(s) and positioned under fluoroscopy at the high right atrium, across the tricuspid valve for His bundle recording and at the right ventricular apex. In patients with known preexcitation or undiagnosed supraventricular tachycardia, a 6F steerable quadripolar catheter was placed in the coronary sinus from the right femoral vein. For patients undergoing electropharmacologic testing for ventricular tachycardia, one or two electrode catheters were inserted. Previously described standard recording methods, programmed stimulation techniques, protocols and definitions were used (1-3,6-9).

Ablation procedure. After the initial location of the arrhythmia focus had been determined during the EPS, a 7F steerable quadripolar deflectable-tip catheter with a 4-mm distal electrode and 2-5-2-mm interelectrode spacing (Cordis Webster, Baldwin Park, California) was used for precise mapping and subsequent ablation with delivery of RF current. Access to the left heart was obtained using the transeptal approach for ablation of left atrial foci, the transeptal or transaortic approach for ablation of left-sided accessory pathways (8,9) and the transaortic technique for ablation of left-sided ventricular tachycardia foci. Patients undergoing ablation of a left-sided arrhythmia focus received anticoagulation with heparin.

The RF current was generated at a frequency of 500 kHz by a conventional temperature-controlled electrosurgical unit (Osypka 300, Grenzach-Wyhlen, Germany) and was delivered between the distal electrode and a cutaneous indifferent dispersive pad positioned on the posterior thorax or left thigh. A preset target temperature of 70°C and a maximum power of 50 W was programmed. Once the target site was identified, 20 to 50 W of RF energy was delivered via the ablation catheter. If a temperature level of at least 48°C to 50°C was achieved and loss of preexcitation (in case of manifest accessory pathways) or termination of the tachycardia (in the case of concealed accessory pathways, atrial or ventricular tachycardias) or accelerated junctional rhythm (in the case of slow AV nodal pathway ablation) or complete heart block (in the case of AV node/His bundle ablation) occurred within 5 to 15 s, the RF application was continued for 30 s, otherwise it was stopped and attempts at

mapping and ablation continued. If impedance rose during ablation, RF application was interrupted, the catheter was removed and cleaned before reinsertion. One half hour to 1 h after ablation, programmed stimulation was performed to confirm the efficacy of ablation. After the procedure all patients were monitored for 24 to 48 h before discharge. During this period serial electrocardiograms (ECGs) were obtained to evaluate for recurring arrhythmia, and an echocardiogram was performed to evaluate for cardiac complications.

Blood sample collection and cTnI, CK and CK-MB assay. Blood samples were obtained from venous sheaths and introduced into tube collectors containing no preservatives. Within 1 h they were centrifuged for 15 min at 3,000 rpm and the supernatant serum was removed and kept at -20°C until the assay was performed.

Serum or plasma cTnI levels were determined by the Stratus Cardiac Troponin I assay (Dade International Inc., Miami, Florida), an automated, two-site immunoassay that uses two monoclonal antibodies that are specific for the cardiac isotype of troponin I. The lower detection limit of the assay is 0.1 ng/ml. In our laboratory, normal values for cTnI are <1.0 ng/ml for healthy subjects. Serum CK and CK-MB activity levels were measured by routine laboratory assays, which have an upper reference limit of 230 mU/ml for CK activity and 6 $\mu\text{g/l}$ for CK-MB activity.

From each patient undergoing RF ablation, four blood samples were taken for cTnI, CK and CK-MB measurements. Initially, blood samples were obtained immediately after insertion of the venous sheaths and before introduction of the electrode catheters (baseline measurements). Subsequently, blood samples were taken upon completion of the RF ablation procedure (post-procedural measurements). A third sample was obtained 4 h after the end of the procedure. A fourth sample was taken 12 h later and, only if these measurements were higher compared with the third sample; an extra sample was obtained at 24 h. Blood sampling was based on previously reported patterns of troponin kinetics (15). Due to a delay in the release of cTnI from injured myocardial cells, most values are not usually much elevated in samples obtained immediately after the procedures, but abnormal values are detected at 4 h after the procedure, while 97% of them can be detected by 12 h (15).

Serum cTnI, CK and CK-MB levels were also determined in 39 patients (control group) undergoing EPS without RF ablation. In this group of patients, blood samples were similarly obtained at baseline and upon completion of the EPS, and at 4 h and 12 h later.

Patient follow-up and statistics. Periprocedurally, patients received antithrombotic therapy with aspirin and/or ticlopidine (18). After discharge from the hospital, patients were followed up at our arrhythmia clinic or by their referring cardiologists every three to six months for the first year and annually thereafter.

All values are expressed as mean \pm SD; the median and

Table 1. Clinical and Procedural Characteristics of 118 Patients Undergoing Radiofrequency Catheter Ablation

Age (yr)	38 \pm 19
Men/Women	67/51
Ablation target	
Accessory pathway	48
Slow pathway	34
Atrial focus	14
Slow pathway + atrial focus	3
Ventricular focus	15
AV node/His bundle	4
Number of RF lesions	16 \pm 22 (median: 9)
Procedure duration (h)	3.2 \pm 2.0

AV = atrioventricular; RF = radiofrequency.

range of values are also provided for data with nonnormal distribution. For quantitative data, statistical comparisons were performed using analysis of variance with Fisher's PLSD post-hoc correction and paired or unpaired *t* tests as appropriate for normal distributions, and the Mann-Whitney, Wilcoxon signed rank, Friedman or Kruskal-Wallis tests for nonnormal distributions. For qualitative data, the chi-square test or the *z*-statistic were used. Correlations between procedural variables and serum cTnI levels were performed using linear and multiple regression analysis and Spearman's rank correlation (Statview 4.01 program, SAS Institute Inc., Cary, North Carolina). A *p* value of <0.05 was considered significant.

RESULTS

Procedural data. One hundred eighteen patients undergoing RF ablation and 39 control patients having EPS alone were included in the study. All procedures were successfully completed without any complications. The total duration of the procedure of RF ablation in the 118 patients averaged 3.2 ± 2.0 h (Table 1), while the mean duration of the EPS in the 39 control patients was 2.3 ± 0.4 h ($p = 0.006$). Three to four catheters were used in the control group (except in 10 patients having repeat EPS where one or two catheters were often used) and four to five catheters were used in the ablation group. In the ablation group, the mean number of RF lesions was 16 ± 22 (median: 9); 60 patients had <10 lesions, whereas 58 patients had ≥ 10 lesions. A relatively high number of RF applications was required in 1/4 of patients in this series. These were patients with multiple ($n = 7$), uncommon ($n = 2$) or right free wall ($n = 7$) accessory pathways; multiple tachycardias ($n = 5$); atrial flutter ($n = 7$) or macroreentry ventricular tachycardia ($n = 3$).

Radiofrequency lesions were produced in the atrial myocardium or atrial aspect of the annuli in 90 patients and in the ventricular myocardium or ventricular aspect of the annuli in 28 patients. More specifically, atrial wall lesions were created in 17 patients, AV (annular) lesions in 86 patients and ventricular wall lesions in 15 patients. Left-

Table 2. Cardiac Troponin I, CK and CK-MB levels in 118 Patients Undergoing RF Ablation and in 39 Patients (Controls) Undergoing Electrophysiologic Studies

	Patients n = 118	Controls n = 39	p Value
Baseline cTnI	0.17 ± 0.18 ng/ml (median: 0.1; range: 0.1-0.9)	0.16 ± 0.12 ng/ml (median: 0.1; range: 0.1-0.6)	NS
Postprocedural cTnI	0.88 ± 1.12 ng/ml (median: 0.4; range: 0.1-5.3)	0.24 ± 0.24 ng/ml (median: 0.1; range: 0.1-0.9)	0.001
cTnI at 4-24 h	2.19 ± 2.46 ng/ml (median: 1.5; range: 0.1-15)	0.43 ± 0.31 ng/ml (median: 0.4; range: 0.1-1.0)	0.001
Peak cTnI	2.25 ± 2.47 ng/ml (median: 1.5; range: 0.1-15)	0.43 ± 0.31 ng/ml (median: 0.4; range: 0.1-1.0)	0.001
cTnI ≥ 1 ng/ml	68%*	2.6%	0.0001
Peak CK	267 ± 678 mU/ml** (median: 130; range: 36-6,509)	104 ± 85 mU/ml (median: 72; range: 29-405)	NS
Peak CK-MB	4.9 ± 5.8 µg/l (median: 3.1; range: 0.1-39.8)	0.7 ± 1.2 µg/l (median: 0.1; range: 0.1-5.2)	0.001
CK-MB > 6 µg/l	27%*	0%	0.001

*p < 0.0001; **includes a peak CK level of 6,509 mU/ml in one patient who received 7 DC cardioversions during the ablation procedure for recurring atrial fibrillation.
CK = creatine kinase; CK-MB = creatine kinase isoenzyme; cTnI = cardiac troponin I; RF = radiofrequency.

sided accessory pathways (n = 27) and one slow pathway were ablated, either on the atrial aspect of the mitral annulus accessed via transseptal catheterization in 15 patients or on the ventricular aspect of the annulus via a transaortic approach in 13 patients. All right-sided accessory pathways in 21 patients were ablated on the atrial aspect of the tricuspid annulus.

Cardiac troponin I, CK and CK-MB levels in the ablation group. In the ablation group of the 118 patients during baseline measurements, the mean cTnI levels were 0.17 ± 0.18 ng/ml, CK levels were 83 ± 69 mU/ml and CK-MB levels were 0.6 ± 1.0 µg/l (Table 2, Fig. 1). At the

end of the RF ablation procedure, cTnI levels rose to 0.88 ± 1.12 ng/ml, representing a significant increase when compared with baseline (p < 0.0001), CK levels rose to 123 ± 130 mU/ml (p = NS) and CK-MB levels rose to 2.6 ± 3.4 µg/l (p < 0.001). At 4 to 24 h after the end of the ablation procedure, cTnI levels rose to 2.19 ± 2.46 ng/ml (p < 0.0001), CK activity rose to 267 ± 678 mU/ml (p = 0.001) and CK-MB rose to 4.9 ± 5.8 µg/l (p < 0.001). Peak cTnI levels were 2.25 ± 2.47 ng/ml and most were measured at the 4-h sampling.

Creatine kinase MB isoenzyme was found elevated (>6 µg/l) only in 32 patients (27%), whereas cTnI levels were increased (≥1.0 ng/ml) in 80 patients (68%) (p = 0.0001) (Table 2). Patients with normal cTnI had fewer RF lesions, fewer ventricular lesions and shorter procedures.

Cardiac troponin I, CK and CK-MB levels in the control group. In the control group of 39 patients undergoing EPS without RF ablation, the baseline cTnI levels averaged 0.16 ± 0.12 ng/ml, CK averaged 84 ± 78 mU/ml and CK-MB averaged 0.24 ± 0.41 µg/l. At the end of EPS, cTnI was 0.24 ± 0.24 ng/ml (p = NS), CK was 86 ± 77 mU/ml (p = NS) and CK-MB was 0.36 ± 0.57 µg/l (p = NS). Within 4 to 24 h after the EPS, peak cTnI levels were 0.43 ± 0.31 ng/ml (p = 0.001), peak CK levels were 104 ± 85 mU/ml (p = NS) and peak CK-MB levels were 0.71 ± 1.16 µg/l (p = 0.028). In the control group at all stages before or after the EPS, all but one patient had normal serum levels of either cTnI, CK or CK-MB; in one patient a borderline cTnI level of 1 ng/ml was measured after the procedure.

Procedural correlates, postprocedural data and patient follow-up. There was a correlation of maximal (peak) cTnI levels with the number of RF lesions applied (r =

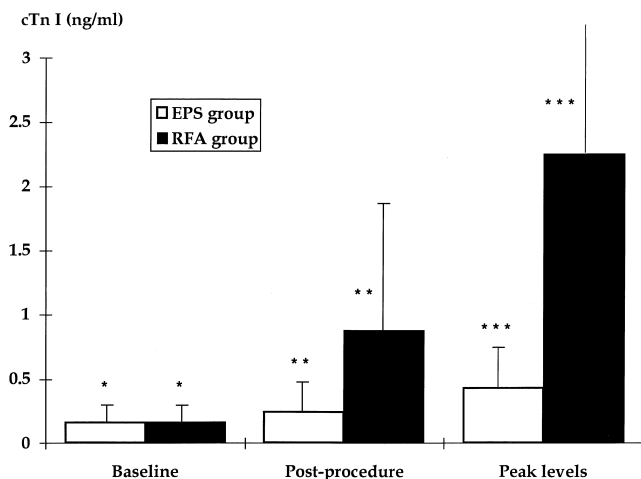


Figure 1. Baseline, post-procedural and late (4-24 h) serum cTnI levels in 118 patients undergoing RFA and in 39 control patients having EPS alone. cTnI = cardiac troponin I; EPS = electrophysiologic studies; RFA = radiofrequency ablation. *p = NS; **p = 0.001; *** p < 0.001.

Table 3. Procedural Factors Associated With Higher Cardiac Troponin I Levels After RF Ablation

Procedural Factor	Cardiac Troponin I Levels (ng/ml)
Number of RF lesions (r = 0.53, p < 0.0001)	
≥10 lesions (n = 58)	3.26 ± 2.88
<10 lesions (n = 60)	1.27 ± 1.43
p Value	0.0001
Site of RF ablation*	
Ventricular (n = 15) > atrial (n = 17) > annular (n = 86)	3.56 ± 2.90 > 2.36 ± 2.29 > 2.00 ± 2.37
p Value	0.012
Approach to mitral annulus**	
Transaortic (n = 13) > transseptal (n = 15)	4.04 ± 3.85 > 1.46 ± 2.54
p Value	0.004
Duration of RF ablation (r = 0.50, p < 0.0001)	

*Number of RF lesions: 15 ± 10 (ventricular) versus 24 ± 36 (atrial) versus 16 ± 21 (annular) (p = NS); **number of RF lesions: 20 ± 26 (transaortic) versus 13 ± 11 (transseptal) (p = NS). NS = nonsignificant; RF = radiofrequency.

0.53, p < 0.0001) and a longer RFA procedure correlated with higher cTnI levels (r = 0.50, p < 0.0001). Patients having ≥10 radiofrequency lesions (n = 58) had higher cTnI levels (3.26 ± 2.88 ng/ml) compared with those (n = 60) having fewer lesions (1.27 ± 1.43 ng/ml) (p = 0.0001) (Table 3, Fig. 2). Patients (n = 32) having only one to three RF lesions had relatively low peak cTnI levels (1.08 ± 1.13 ng/ml) but 50% of them had abnormal cTnI values, whereas only one of these patients (3.1%) had an abnormal

CK-MB level (p < 0.001). Maximal cTnI levels also correlated with the site of RF ablation, being higher for ventricular versus atrial versus annular sites of RF lesions (p = 0.012). Also, cTnI levels were dependent on the type of approach to the mitral annulus, being higher for the transaortic approach versus the transseptal approach (p = 0.004), and this result was not due to any significant difference in the number of RF lesions applied with each approach (20 ± 22 vs. 13 ± 11, p = NS).

Echocardiograms obtained after the procedure failed to detect any intracardiac thrombi, wall motion abnormalities or valvular problems. Apart from repolarization abnormalities consistent with the cardiac memory phenomenon in patients with manifest preexcitation, there were no ECG abnormalities suggestive of ischemia after the procedures. No patient in the RF ablation group or in the control group suffered any coronary ischemic events during hospitalization or during follow-up after discharge.

DISCUSSION

Cardiac troponin I levels and RF ablation procedures.

This study demonstrates that serum levels of cTnI are more sensitive than CK-MB levels in detecting myocardial injury incurred during RF ablation procedures. In our cohort of 118 consecutive patients undergoing RF ablation for a variety of cardiac arrhythmias, only 32 (27%) had elevation of CK-MB despite a significant number of RF lesions. These results are consistent with previous reports of RF ablation quantitating myocardial necrosis produced during these procedures by determining CK and CK-MB, which have failed to detect a significant injury in most patients (1-9). Creatine kinase inactivation by RF ablation has been proposed as a cause of underestimation of the total myocardial injury incurred (10).

Cardiac troponin I is a more sensitive and specific marker of myocardial injury. However, it has rarely been used

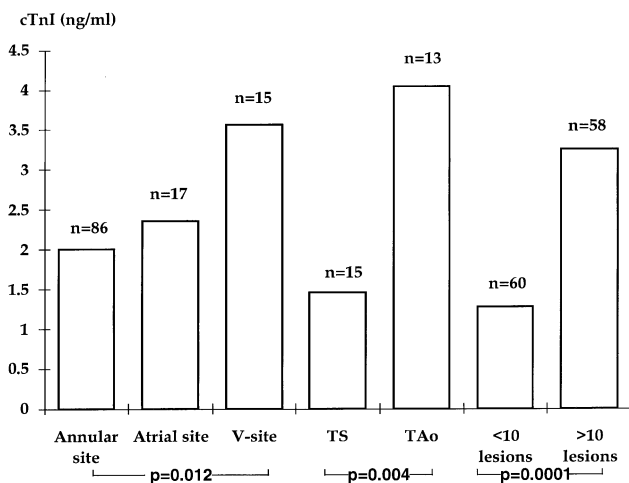


Figure 2. Procedural factors affecting peak cTnI levels during RF ablation include site of RF ablation and number of RF lesions produced. Highest cTnI levels are measured during ablation of ventricular myocardium (V-site), intermediate levels during ablation of atrial myocardium (Atrial site) and lowest levels during ablation at annular sites. With a TS approach to the mitral annulus, where lesions are applied to the atrial aspect, cTnI levels are lower compared with a TAO approach with lesions mainly applied at the ventricular aspect. When more than 10 RF lesions are produced, cTnI levels are significantly higher than with fewer lesions. cTnI = cardiac troponin I; RF = radiofrequency; TAO = transaortic; TS = transseptal.

previously to monitor myocardial injury during RF ablation. Our results show that, overall, 68% of patients undergoing RF ablation have abnormal cTnI levels, a significantly higher percentage representing a 2.5-fold increase, compared with those detected by CK-MB. This is consistent with the results of two recent studies, one utilizing cardiac troponin T measurements in a smaller patient group of 28 patients undergoing RF ablation, where 93% of patients had abnormal cardiac troponin T levels compared with only 36% having abnormal CK-MB levels (16) and the other study using cTnI in 51 patients having RF ablation, where 92% of patients had an abnormal cTnI level versus 63% of patients having elevated CK-MB levels (17). Cardiac troponin I has been considered more specific than cardiac troponin T, since cTnI is never present in skeletal muscle and is not affected by renal insufficiency (14). Another major advantage of cTnI relates to its normal levels (in contrast to a moderate increase in CK-MB) reported during electrical cardioversion, indicating the absence of detectable myocardial lesion even for high energy cardioversion (19). Determining cTnI rather than CK-MB in such a setting helps detect true myocardial injury. This was the case with one patient in our ablation group who required multiple cardioversions for recurring atrial fibrillation (Table 2). Furthermore, all but one patient in the control group had normal cTnI levels, despite some who were cardioverted for arrhythmia termination.

Procedural correlates. A correlation between cTnI levels and the number of RF current applications has been recently reported (17) and is also confirmed by our study. Patients having more than 10 RF current applications had much higher cTnI levels. However, the relatively weak overall correlation ($r = 0.53$) may be related to the fact that not all RF applications resulted in effective lesion formation, either due to unstable catheter position or our practice of interrupting RF application within 5 to 15 s if it was unsuccessful or if a minimum temperature of 48°C to 50°C could not be achieved within this time frame. Due to a lack of consistent logging of peak temperature during the procedures, a correlation of greater cTnI levels with higher achieved temperature cannot be established with accuracy.

Another important correlation detected in this study was between the peak cTnI levels and the site of RF ablation. To our knowledge, this study is the first one to show a correlation between the degree of myocardial injury incurred during RF ablation as reflected by cTnI levels and the specific site of RF ablation, as well as the approach to the mitral annulus. Lesions created in the ventricular myocardium, albeit numerically fewer, apparently entailed more extensive myocardial injury as reflected by the higher cTnI levels when compared with those measured during RF application in the atrial myocardium or in the annuli (Table 3, Fig. 2). Annular lesions produced the lowest increase in cTnI levels. However, at least for the lesions applied to the mitral annulus, this increase was dependent on the approach

to the annulus, with significantly higher levels observed during the transaortic approach, where ventricular lesions were produced most often, compared with the transeptal technique where lesions were applied to the atrial aspect of the annulus. It is important to note that this result could not be ascribed to a significantly greater number of RF lesions applied with the transeptal approach ($p = \text{NS}$, Table 3).

Also, of 32 patients having only one to three RF lesions (mostly at annular sites, $n = 27$) and relatively low peak cTnI levels (1.08 ± 1.13 ng/ml), 50% had abnormal cTnI values, whereas only one of these patients (3.1%) had an abnormal CK-MB level ($p < 0.001$). This demonstrates the very high sensitivity of cTnI in detecting minor myocardial injury.

Study limitations. This study dealt with a rather heterogeneous population in terms of different underlying arrhythmia substrate and, therefore, different approaches to catheter ablation. However, this fact has allowed for a better understanding of the variable degree of myocardial injury incurred with RF ablation applied at different sites. Another limitation of this study was the lack of consistent logging of peak temperature during the procedures and, thus, an association of higher cTnI levels with greater temperature measurements could not be established.

Clinical implications. This study offers new insight into the assessment of myocardial injury incurred during RF ablation. Monitoring of myocardial tissue damage, even of a minor degree, is more accurate with the use of cTnI, which is a more sensitive and specific marker than CK-MB. Our study also determined the procedural correlates that characterize such myocardial injury, demonstrating its dependence on the number of lesions applied and the site of RF ablation. More extensive tissue damage is produced during ablation of ventricular myocardium, rather than during ablation performed at atrial or annular sites, the latter producing the lowest increase in cTnI levels. Thus, the results of this study raise important issues concerning efficacy and safety and preferable target sites of RF ablation. It suggests that to minimize the extent of myocardial injury, the operator, apart from striving to be successful with as few RF applications as possible, should also aim to deliver them at the annular or atrial side, if possible. This may be particularly important in younger patients (20), in light of previous studies indicating possible developmental effects in younger hearts (21). Finally, although it became apparent that myocardial injury produced by RF ablation can be detected more accurately with the cTnI rather than CK-MB assay, its prognostic significance remains to be explored in future studies.

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REFERENCES

1. Jackman WM, Wang X, Friday KJ, et al. Catheter ablation of accessory atrioventricular pathways (Wolff-Parkinson-White syndrome) by radiofrequency current. *N Engl J Med* 1991;324:1605-11.
2. Calkins H, Langberg JL, Sousa J, et al. Radiofrequency catheter ablation of accessory AV connections in 250 patients. *Circulation* 1992;85:1337-46.
3. Kay GN, Epstein AE, Dailey SM, Plumb VJ. Role of radiofrequency ablation in the management of supraventricular arrhythmias: experience in 760 consecutive patients. *J Cardiovasc Electrophysiol* 1993;4:371-89.
4. Manolis AS, Wang PJ, Estes NAM III. Radiofrequency catheter ablation for cardiac tachyarrhythmias. *Ann Intern Med* 1994;121:452-61.
5. Scheinman MM. NASPE survey on catheter ablation. *PACE* 1995;18:1474-8.
6. Manolis AS, Wang PJ, Estes NAM III. Radiofrequency ablation of slow pathway in patients with atrioventricular nodal reentrant tachycardia: do arrhythmia recurrences correlate with persistent slow pathway conduction or site of successful ablation? *Circulation* 1994;90:2815-9.
7. Lesh MD, Van Hare GF, Schamp DJ, et al. Curative percutaneous catheter ablation using radiofrequency energy for accessory pathways in all locations: results in 100 consecutive patients. *J Am Coll Cardiol* 1992;19:1303-9.
8. Manolis AS, Wang PJ, Estes NAM III. Radiofrequency ablation of left-sided accessory pathways: transaortic versus transseptal approach. *Am Heart J* 1994;128:896-902.
9. Manolis AS, Wang PJ, Estes NAM III. Radiofrequency ablation of atrial insertion of left-sided accessory pathways guided by the "W sign." *J Cardiovasc Electrophysiol* 1995;6:1068-76.
10. Haines DE, Whayne JG, Walker J, Nath S, Bruns DE. The effect of radiofrequency catheter ablation on myocardial creatine kinase activity. *J Cardiovasc Electrophysiol* 1995;6:79-88.
11. Antman EM, Tanasigevic MJ, Thompson B, et al. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute syndromes. *N Engl J Med* 1996;335:1242-9.
12. Hamm CW, Goldmann BU, Heeschen C, Kreymann G, Berger J, Meinertz T. Emergency room triage of patients with acute chest pain by means of rapid testing for cardiac troponin T or troponin I. *N Engl J Med* 1997;337:1648-53.
13. Adams JE III, Bodor GS, Davila-Roman VG, et al. Cardiac troponin I: a marker with high specificity for cardiac injury. *Circulation* 1993;88:101-6.
14. Brown CS, Bertolet BD. Cardiac troponin: see ya later CK! *Chest* 1997;111:2-4.
15. Luescher MS, Thygesen K, Ravkilde J, Heickendorff L, for the TRIM Study Group. Applicability of cardiac troponin T and I for early risk stratification in unstable coronary artery disease. *Circulation* 1997;96:2578-85.
16. Katriotis D, Hossein-Nia M, Anastasakis A, et al. Use of troponin-T concentration and kinase isoforms for quantitation of myocardial injury induced by radiofrequency catheter ablation. *Eur Heart J* 1997;18:1007-13.
17. Madrid AH, Del Rey JM, Rubi J, et al. Biochemical markers and cardiac troponin I release after radiofrequency catheter ablation: approach to size of necrosis. *Am Heart J* 1998;136:948-55.
18. Manolis AS, Vassilikos V, Maounis T, et al. Pretreatment with aspirin and ticlopidine confers lower thrombogenic potential of radiofrequency catheter ablation. *Am J Cardiol* 1997;79:494-7.
19. Bonnefoy E, Chevalier P, Kirkorian G, Guidolet J, Marchand A, Touboul P. Cardiac troponin I does not increase after cardioversion. *Chest* 1997;111:15-18.
20. Manolis AS, Vassilikos V, Maounis T, Chiladakis J, Cokkinos DV. Radiofrequency catheter ablation in older children and adolescents by an adult electrophysiology team. *J Interv Cardiac Electrophysiol* 1999;3:79-86.
21. Saul JP, Hulse E, Papagiannis J, Van Praagh R, Walsh EP. Late enlargement of radiofrequency lesions in infant lambs. Implications for ablation procedures in small children. *Circulation* 1994;90:492-9.