Cardiac Troponin T and Cardiac Enzymes After External Transthoracic Cardioversion of Ventricular Arrhythmias in Patients With Coronary Artery Disease*

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Background: Serum levels of cardiac troponins after external cardioversion (ECV) for atrial fibrillation and atrial flutter are widely investigated, and no increases in cardiac troponin T (cTnT) levels have been reported. However, the effect of ECV on cardiac enzyme release may depend on the type of arrhythmias. Furthermore, ventricular tachycardia (VT) or ventricular fibrillation (VF) could cause release of cardiac enzymes after ECV due to underlying myocardial ischemia, myocardial dysfunction, or more pronounced hemodynamic deterioration during arrhythmia.

Aim: The purpose of this study was to determine whether direct current (DC) shock may increase cardiac enzyme levels in patients with coronary artery disease undergoing ECV for VT or VF, so that diagnosis of acute myocardial infarction, which initially presents with VT or VF, can be excluded.

Method and results: We obtained measurement of cTnT, total creatine kinase (CK), and CK MB isoenzyme (CK-MB) activity before and after ECV in 27 patients (mean ± SD age, 62 ± 13 years) with induced VT or VF (22 patients) who required ECV during provocative electrophysiologic testing and who underwent ECV due to VT (5 patients) in the cardiology department. Blood samples were drawn before, and 4 h, 8 h, and 24 h after ECV. The total energy used was 630 ± 375 J (range, 200 to 1,280 J). CK levels rose to the upper limit of reference range in seven patients (26%), and CK-MB activity was higher than the normal reference range in five patients (19%) after ECV. In contrast, cTnT concentrations remained within the normal range (< 0.1 μg/L) in all patients. Peak CK and CK-MB activity levels strongly correlated with the total energy delivered.

Conclusion: Elevation of cTnT level after an urgent DC shock strongly indicates the diagnosis of acute myocardial infarction presented with life-threatening arrhythmias, rather than myocardial damage caused by ECV.

Key words: acute myocardial infarction; external cardioversion; troponin T; ventricular arrhythmias

Abbreviations: CK = creatine kinase; CK-MB = creatine kinase MB isoenzyme; cTnT = cardiac troponin T; DC = direct current; ECV = external transthoracic cardioversion; VF = ventricular fibrillation; VT = ventricular tachycardia

External transthoracic cardioversion (ECV) is performed in cases of life-threatening ventricular arrhythmias in the emergency department. Differentiating between primary and secondary (caused by acute myocardial infarction) ventricular arrhythmias has significant therapeutic and prognostic implications. If the arrhythmias are triggered by acute myocardial infarction, then the risk of arrhythmic death after discharge is only slightly greater than that of patients with uncomplicated acute myocardial infarction. However, if the arrhythmias are triggered by a factor other than acute myocardial infarction, an electrophysiologic study may be necessary due to the increased risk of further malignant cardiac
arrhythmias,\textsuperscript{2} and treatment may take the form of an antiarrhythmic drug therapy or an implantable cardioverter-defibrillator.

During recent years, assays for highly cardiospecific biological markers, such as troponins T and I, have been developed with high sensitivity, specificity, and positive predictive value for myocardial cell necrosis.\textsuperscript{3} No, or only minor, increases in cardiac troponin I levels\textsuperscript{4,5} and no increases in cardiac troponin T (cTnT) levels after ECV for atrial fibrillation and atrial flutter have been reported.\textsuperscript{6–8} However, it has been reported that cTnT levels are increased in patients successfully resuscitated from out-of-hospital cardiac arrest.\textsuperscript{9} Chest compression and/or ECV or arrhythmia-induced myocardial ischemia may account for the elevation of cardiac enzymes. Furthermore, it has been shown that mechanical cardioversion of postischemic ventricular fibrillation contributes to myocardial damage and increase of cTnT in isolated rat heart.\textsuperscript{10}

However, there are no data on effect of ECV for ventricular tachycardia (VT) and ventricular fibrillation (VF) on cardiac troponins in patients with coronary artery disease to facilitate the diagnosis of acute myocardial infarction in patients after emergency cardioversion. Development of myocardial injury after ECV may depend on the type of arrhythmias such as supraventricular tachycardia or VT. The latter one could cause release of cardiac enzymes after ECV due to underlying myocardial ischemia, myocardial dysfunction, and more pronounced hemodynamic deterioration during arrhythmia. Therefore, this study aims to determine whether direct current (DC) shock may cause a rise in cardiac enzyme levels in patients with coronary artery disease undergoing ECV for VT or VF, so that diagnosis of acute myocardial infarction, which initially presents with VT or VF, can be excluded.

### Materials and Methods

A total of 27 patients (mean ± SD age, 62 ± 13 years) with induced VT or VF who required ECV during provocative electrophysiologic testing, and who had undergone ECV due to VT in the cardiology department, were enrolled into the study. All the patients had coronary artery disease documented by coronary angiography. Patients were excluded if they had had a myocardial infarction, unstable angina pectoris, a coronary intervention (coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, stent placement), or if they had received an IM injection in the preceding month. Also excluded were patients with renal failure or skeletal muscle disease.

ECV was performed using ordinary synchronous defibrillator (model 4310A; Hewlett-Packard; Andover, MA) with handheld electrode paddles placed in the apex anterior configuration. Routinely, the initial energy used was 200 J; 360 J of delivered energy was used for subsequent cardioversion or defibrillation attempts when multiple shocks were required for termination of arrhythmia. Blood samples were obtained at baseline and after the ECV at 4 h, 8 h, and 24 h, and were analyzed for cTnT and activity of creatine kinase (CK) and CK MB isoenzyme (CK-MB). cTnT was determined with enzyme-linked immunosorbent assay method, based on a streptavidin technique (Boehringer Mannheim; Mannheim, Germany) on a microprocessor-controlled photometer (ES 300; Boehringer Mannheim). The upper reference limit was 0.1 μL. In the same serum samples, the activity of CK was measured colorimetrically at 25° (NAC, Modular Autoanalyser; Roche Diagnostic; Mannheim, Germany), and the reference range was 16 to 190 U/L. CK-MB was assessed by an immunoinhibition assay with reagents from the Roche Diagnostic Modular Autoanalyser (reference range < 24 U/L).

#### Statistical Analysis

Data are expressed as mean ± SD. Comparisons between the ECV subgroups with and without an increase in enzyme activity were made by the independent-samples t test. When data were nonparametrically distributed, the Wilcoxon test was applied. A p value of < 0.05 was considered to be significant.

### Results

The clinical characteristics of the patients studied are shown in Table I. Twenty-two VT or VF episodes that required DC shock were induced during the procedure. While 13 patients had hemodynamically intolerated VT (8 patients) or VF (5 patients), 9 patients had sustained VT with resistance of pacing therapy. In five patients, ECV was indicated due to drug-resistant VT all through the hospitalization period. All arrhythmias were successfully converted to sinus rhythm. The total energy used was 630 ± 375 J (range, 200 to 1,280 J). The maximum number of shocks delivered was four. The duration of sustained arrhythmias before ECV averaged 165 s (range, 14 to 1,806 s), and the cycle length of the induced VT averaged 254 ms (range, 190 to 480 ms).

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<th>Table 1—Patient Characteristics (n = 27)*</th>
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<td>Age, yr</td>
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<td>Left ventricular ejection fraction, %</td>
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<td>Arrhythmias during EPS, No.</td>
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<td>Intolerated VT</td>
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*Data are presented as mean ± SD. No. (range), or mean ± SD (range) unless otherwise indicated. EPS = electrophysiologic study; intolerated = hemodynamically unstable; tolerated = hemodynamically stable.
The baseline activity of CK ranged from 19 to 380 U/L (mean, 95 U/L). Before the ECV, the total CK was already elevated in two patients (253 U/L and 380 U/L, respectively); in both patients, these high CK levels were the result of preceding physical activity. Baseline activity of the CK-MB isoenzyme was below the upper limit of the normal range (< 24 U/L) in all the patients. cTnT measurements before cardioversion were negative (under the discriminator value of 0.1 μL) for all the patients. After ECV, CK level rose to upper limit of reference range in seven patients (26%), which is the peak level at 24 h. CK still remained high in two patients after ECV, even though it much higher in the first place (Fig 1). Peak CK levels strongly correlated with the total energy delivered \((r = 0.67, p < 0.001)\). CK-MB activity was higher than normal reference range in five patients (19%) after defibrillation (Fig 1). Peak CK-MB activity levels also correlated with the total energy delivered \((r = 0.58, p < 0.001)\). In contrast, cTnT concentrations remained within the normal range (< 0.1 μL) in all the patients. A comparison of patients with elevated total CK or CK-MB activity and patients without elevation in total CK or CK-MB activity showed no differences in age (61 years vs 64 years), mean left ventricular ejection fraction (36% vs 39%), tachycardia cycle length (242 ms vs 264 ms), or duration of arrhythmia (187 ± 20 s vs 161 ± 122 s, respectively). However, there was a significant difference between those who did not have an elevation in CK activity and those who did with respect to the total cumulative energy delivered (420 ± 525 J vs 840 ± 685 J, respectively; \(p < 0.001\)).

![Figure 1. Time course of changes in plasma levels of CK and CK-MB activities in 27 patients who underwent ECV for VT or VF.](http://journal.publications.chestnet.org/pdffaccess.ashx?url=/data/journals/chest/21985/)


**Discussion**

The major finding of this study is that cTnT plasma levels do not rise after ECV for defibrillation of hemodynamically tolerated or intolerated ventricular arrhythmias as well as VF, indicating that significant cell injury with release of myocardial protein is unlikely to occur with cumulative energies up to 1,360 J.

Increases in levels of CK\(^{11}\) and CK-MB\(^{12}\) after elective ECV in a comparable percentage of patients (ranging from 9.3 to 50\%) have previously been reported. In our study, 26\% of the patients had elevated CK levels and 19\% of patients had elevated CK-MB activity levels above the reference range. However, consistency of cTnT levels after ECV indicate that the elevation of CK and CK-MB activity probably resulted from injury of skeletal muscle during the DC shock rather than from a myocardial injury. It has been shown that the largest CK-MB proportion of 10.4\% was found in the intercostal musculature.\(^{5}\) Thus, a damage to the intercostal muscle group, which is in the pathway of the trans-thoracic defibrillating current, could account for the magnitude of MB isoenzyme release noted in the present study. Therefore, total CK and CK-MB activity has the potential to produce false-positive results in defibrillated patients.

O’Neil et al\(^{13}\) investigated the plasma total CK and CK-MB activity after DC shock for ventricular arrhythmias induced during electrophysiologic testing. Despite the fact that they studied the same group of patients as we did, they reported 50\% elevation rate of CK and CK-MB activity after ECV. The reason for this discrepancy could simply be that the cumulative energy amount they used was much higher than ours. Both these studies suggest a strong positive correlation between enzyme release and cumulative energy delivered, which is in agreement with other studies.\(^{12}\) However, they could not precisely identify the source of this enzyme release, because specific myocardial protein, such as cardiac troponin, was not evaluated.

We examined the cTnT to overcome the problem of insufficient specificity of CK-MB and to reveal myocardial cell injury reliably after ECV. cTnT is the tropomyosin-binding protein of the troponin regulatory complex located on the thin filament of the contractile apparatus. It is largely compartmentalized in the contractile apparatus and has to be dissociated in a time-consuming process from the troponin complex of the thin filament before it can gain access to the serum. The persistent elevation of cTnT in blood (10 to 14 h), notwithstanding a rather short serum half-life (2 h), due to long-lasting release and the enormous increase of its serum concentra-

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myocardial infarction. Such investigations as coronary angiography and electrophysiological stimulation may be appropriate.2

In a previous study, Gnubb et al9 reported that clinically significant levels of cTnT and CK-MB were determined in the serum of patients who had been successfully resuscitated from out-of-hospital cardiac arrest, having no other objective evidence of myocardial infarction at that time. Our study suggests that the observed increase in enzyme levels in the study by Gnubb et al9 is not likely to have been due to electrical injury. We think either mechanical cardiac trauma during cardiopulmonary resuscitation or prolonged global hypoxia is the cause of the observed increase in enzyme levels. Our results also suggest that the presence of coronary artery disease does not cause increase in cardiac enzyme levels after ECV.

One study has shown minimal elevation of cTnT in 3 of the 38 patients after cardioversion, suggesting minor myocardial injury.5 Two of the three patients had impaired left ventricular function on echocardiography. In our study, although mean ejection fraction of the patients was lower (38%), no one had elevated values of the cTnT. To the best of our knowledge, this is the first study into how patients with low ejection fraction respond to defibrillation with regard to the cTnT. Based on our study results, diagnostic electrophysiologic studies themselves do not seem to cause an elevation in the cTnT level.

**CONCLUSION**

These results lead us to conclude that DC cardioversion or defibrillation, even in patients with hemodynamically intolerated VT or VF, does not cause an increase in cTnT levels, and that the source of elevated CK and CK-MB activity in some patients must be only skeletal. Elevation of cTnT level after an urgent DC shock strongly indicates the diagnosis of acute myocardial infarction presenting with life-threatening arrhythmias, and it may be very useful particularly when ECG changes are nonspecific or nondiagnostic.

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