

Electrical Cardioversion and Myocardial Injury: Evaluation by New Cardiac Injury Markers

Elizabete Silva dos Santos, Marcos Paulo Pereira, Luiz Minuzzo, Dalmo A. R. Moreira, Rui Ramos, Álvaro Avezum, Ari Timerman, Leopoldo Piegas
Instituto Dante Pazzanese de Cardiologia - São Paulo, SP - Brazil

OBJECTIVE

Evaluate, based on the evolution of new biochemical markers of cardiac damage, if electrical cardioversion (ECV) causes myocardial injury.

METHODS

Seventy-six patients (P) submitted to elective ECV for atrial fibrillation or atrial flutter were evaluated. Creatine phosphokinase (CPK), CK-MB activity, CK-MB mass, myoglobin and cardiac troponin I (cTnI) were measured before, and 6 and 24 hours after ECV.

RESULTS

ECV was successful in 58 P (76.3%). Cumulative energy (CE) was up to 350 joules (J) in 36 P, from 500 to 650 J in 20 P and from 900 to 960 J in 20 P; the mean energy delivered being 493 J (\pm 309). The levels of cTnI remained within normal limits in all 76 P. The increase of cumulative energy led to an elevation of CPK levels ($>$ p value = 0.007), CK-MB activity ($>$ p value = 0.002), CK-MB mass ($>$ p value = 0.03), and myoglobin ($>$ p value = 0.015). A positive correlation between the cumulative energy and CPK peaks was observed ($r = 0.660$; $p < 0.001$), CK-MB activity ($r = 0.429$; $p < 0.0001$), CK-MB mass ($r = 0.265$; $p = 0.02$), and myoglobin ($r = 0.684$; $p < 0.0001$), as well as between the number of shocks and the CPK peaks ($r = 0.770$; $p < 0.001$), CK-MB activity ($r = 0.642$; $p < 0.0001$), CK-MB mass ($r = 0.430$; $p < 0.0001$), and myoglobin ($r = 0.745$; $p < 0.0001$).

CONCLUSION

ECV does not cause myocardial injury detectable by cTnI measurement. Elevations of CPK, CK-MB activity, CK-MB mass and myoglobin result from skeletal muscle injury and are positively correlated with the CE delivered or with the number of shocks.

KEY WORDS

Cardioversion, myocardial injury, cardiac troponin I.

Even though electrical cardioversion (ECV) has been indicated for the treatment of tachyarrhythmia for over 30 years, it is still controversial whether this technique can cause myocardial injury¹. Evidence pointing to myocardial injury induced by this procedure is based on small studies that demonstrate moderate elevations of enzyme markers like creatine phosphokinase (CPK) and its isoenzyme CK-MB². Histological studies conducted later confirmed that these elevations may be secondary to the myocardial injury³⁻⁶. The injuries corresponded to localized necrosis and were observed only when high-energy shocks were applied after the delivery of repeated shocks⁷⁻¹⁰. A high-energy shock resulted in a higher number of injuries than several lower-energy shocks^{7,8}.

New markers of myocardial injury with a higher degree of cardiospecificity, such as troponins I and T, were developed recently. Troponins are proteins that regulate the actin-myosin interaction in the striated muscles, and a small percentage of troponins is free in the cytoplasm. Approximately 6% to 8% of troponin I and 2.8% to 4.1% of troponin T are found in the cytoplasm. The aminoacid sequence and molecular weight of both troponins differ, according to where they are found in the muscle. Cardiac troponin I (cTnI) has a unique aminoacid sequence, different from that of the skeletal troponin I, and it is not found in any human tissue other than the heart. Thus, no release of cTnI occurs in case of damage to skeletal muscle. Its measurement enables to discriminate between the myocardial or skeletal origin of muscle injuries¹¹, as well as the detection of even minimal injury observed in some clinical conditions or experimental situations¹²⁻¹⁴. Cell death and destruction of contractile apparatus induce a continuous release of cardiac troponin I for a period of seven to ten days¹⁵.

In the second half of the 90's, studies about electrical cardioversion aiming to assess cardiac injury markers with a higher degree of cardiospecificity were first published¹⁶⁻¹⁸. Some of them described slight elevations of troponin, both cTnI¹⁷ and troponin T¹⁸, after repeated cardioversions in patients who had undergone electrophysiological study.

The purpose of this study was to evaluate whether elective external ECV causes myocardial injury, based on the evolution of these biochemical markers of cardiac injury.

METHODS

Consecutive patients referred to elective ECV for atrial fibrillation or atrial flutter, from July 2001 to August 2003, were considered eligible for inclusion in the study. Patients with acute coronary syndrome or who had undergone myocardial revascularization (surgical or percutaneous) in the previous month, had muscle disease or history of muscle injury in the last thirty days were excluded. Seventy-six patients were enrolled in the study, and after informed

consent was obtained, baseline characteristics such as past history, current medications, vital signs, weight and height were documented (Tab 1). All patients were appropriately anticoagulated (international normalized ratio [INR] above 2) and maintained anticoagulated for at least forty days after the procedure.

The study protocol was approved by the Institutional Research Ethics Committee.

Table 1 – Baseline characteristics

Age (mean age ± SD)	58 ± 11
Male	51 (67.1%)
Underlying disease	
• Coronary artery disease	8 (10.5%)
• Valve disease	28 (36.8%)
• Cardiomyopathy	21 (27.6%)
• Others	13 (17.1%)
Current medication	
• Digitalis	29 (38.2%)
• Amiodarone	56 (73.7%)
• Beta-blockers	19 (25%)
• Calcium channel blockers	4 (5.3%)
Pre-ECV echocardiogram	42 (55.3%)
Type of arrhythmia	
• atrial fibrillation	58 (76.3%)
• atrial flutter	18 (23.7%)
Weight (mean in kg ± SD)	78 (± 19)
Height (mean in cm ± SD)	167 (± 10)
Body surface	1.89 (± 0.26)
Systolic blood pressure (mm Hg)	139 (± 20)
Diastolic blood pressure (mm Hg)	88 (± 15)
INR (mean ± SD)	3.45 ± 3.67
<i>SD – standard deviation; kg = kilogram; cm = centimeters; mmHg = millimeters of mercury; INR = international normalized ratio</i>	

Patients were informed about the technique used in the procedure and submitted to general anesthesia with intravenous Thionembutal (3 to 5 mg/kg). A 12-lead electrocardiogram was obtained immediately before and after cardioversion.

Cardioversions were performed using a direct-current, monophasic cardioverter and rectangular pads of 8 cm long in its longer axis coated with conductive gel. One pad was placed on the right second intercostal space and the other at the level of left hemiclavicular line on the sixth intercostal space. Shocks synchronized to the R-wave peak were delivered, the energy ranging from 50 to 360 joules (J), starting at 50 J for the atrial flutter and followed by 100, 200, 300 J or a second energy discharge of 300 J, and starting at 100 J for the atrial fibrillation, followed by 200, 300 or 360 J. The interval between shocks was the shortest possible, bearing always in mind the need to keep approximately 10-kg weight over the pads, as well as not to withdraw them too fast after each shock delivered to prevent energy dispersion. The population studied was divided into

three groups, according to the cumulative energy (CE) delivered. Group A = CE up to 350 J (36 patients); Group B = CE from 500 to 650 J (20 patients); Group C = CE from 900 to 960 J (20 patients). The results among the three groups were compared, as well as the evolution of each group over time.

All patients were kept under observation in the emergency unit for six hours after the procedure.

Venipuncture was performed in one of the upper extremities for blood sampling and measurement of serum potassium and INR value. As serum potassium and INR levels were found to be adequate for cardioversion, the decision was taken to perform the procedure. The patients thus underwent blood sampling before and at 6 and 24 hours after cardioversion, for CPK, CK-MB activity, cTnI, CK-MB mass and myoglobin measurements.

CPK measurements were determined by the automated kinetic enzymatic method using a Hitachi 912[®] analyzer manufactured by Roche Diagnostics, and CK-MB activity was determined by the kinetic enzyme immunoassay method using the same device. The reference value for CPK is up to 80 U/L; and for CK-MB activity values up to 10 U/L were considered. CK-MB mass, myoglobin and cTnI were measured using the automated chemiluminescence method with IMMULITE[®] analyzer manufactured by DPC MedLab. Reference values are up to 70 ng/mL for myoglobin, up to 4.5 ng/mL for CK-MB mass, and up to 1.0 ng/mL for cTnI. The intra-assay coefficient of variation for CPK and CK-MB activity measurements is lower than 2.5%, and for the measurements using the chemiluminescence method the values do not exceed 6%.

Means and standard deviations were calculated to describe continuous variables. Analysis of variance with repeated measurements, followed by multiple comparisons of means, was performed to determine the evolution of each marker over time in the different groups of cumulative energy (SAS Software). The relationship between cumulative energy and each marker was estimated by Person's correlation, and the relationship

between the number of shocks and each marker was estimated by Spearman's correlation.

RESULTS

Of the 76 patients studied, 58 had atrial fibrillation (76.3%) and 18 had atrial flutter (23.7%). Fifty-one patients (67.1%) were male, mean age of 58 years (± 11). The underlying disease was cardiomyopathy in 21 patients (27.6%), valve disease in 28 (36.6%) and coronary artery disease in 8 (10.5%) (Tab. 1). In 67 patients (88.1%) the duration of arrhythmia exceeded six months.

A maximum of five shocks was determined for each patient, mean of 2.68 shocks (± 1.1). The mean shock energy delivered was 493 J (± 309). Fifty-eight patients (76.3%) were successfully cardioverted, with no complications related to the procedure and no ST-segment or T-wave changes (dynamics) on electrocardiogram after ECV. All patients were discharged six hours after ECV and asked to return 24 hours later for blood sampling.

There was no significant difference regarding marker levels before ECV in the different groups of cumulative energy. Only one trend for higher CPK values was detected before ECV in group C as compared to group A ($p = 0.053$) or B ($p = 0.05$). The same occurred with myoglobin between groups A and C ($p = 0.058$) (tab. 2).

The measurements of the biochemical markers at the three times (before, and at 6 and 24 hours after the procedure) were performed for cTnI in 73 patients (96%), CPK in 69 (90.8%), CK-MB activity in 72 (94.7%), CK-MB mass and myoglobin in 70 (92.1%).

Cardiac troponin I remained undetectable (< 0.5 ng/mL) in 74 patients (97.4%) at all times. One patient in Group B showed values of 0.5 ng/mL and 0.52 ng/mL, respectively, at 6 and 24 hours after cardioversion. Another one in Group C showed value of 0.64 ng/mL

Table 2 – Means levels of the markers in the groups of cumulative energy (CE) with their respective standard deviations (SD)

Group CE	Time	cTnI (ng/mL)	CPK mean (\pm SD)	CK-MB activity mean (\pm SD)	CK-MB mass mean (\pm SD)	Myoglobin mean (\pm SD)
A	Before	<0.5	42.91 (\pm 18.68)	5.17 (\pm 2.29)	3.24 (\pm 3.4)	31.59 (\pm 17.88)
	6 hrs	<0.5	74.42 (\pm 66.98)	6.53 (\pm 2.62)	2.97 (\pm 1.9)	97.61 (\pm 131.41)
	24 hrs	<0.5	153.94 (\pm 176.68)	7.20 (\pm 3.54)	3 (\pm 1.9)	58.90 (\pm 61.81)
B	Before	<0.5	40.65 (\pm 16.05)	5.25 (\pm 2.17)	2.8 (\pm 2.4)	31.21 (\pm 19.97)
	6 hrs	*0.5	508.20 (\pm 527.85)	14.30 (\pm 16.13)	7.3 (\pm 12.89)	623.94 (\pm 204.20)
	24 hrs	*0.52	989.39 (\pm 626.58)	24.39 (\pm 29.43)	9.6 (\pm 17.8)	217.45 (\pm 154.99)
C	Before	*0.6	58.35 (\pm 45.94)	5.85 (\pm 2.96)	3.3 (\pm 3.9)	59 (\pm 88.07)
	6 hrs	*0.64	531.65 (\pm 557.18)	11.35 (\pm 6.17)	5.5 (\pm 5.02)	589.05 (\pm 285.22)
	24 hrs	<0.5	1,494.24 (\pm 924.50)	30.76 (\pm 22.83)	11.4 (\pm 11.4)	336.88 (\pm 282.40)

The absolute values correspond to detectable values of two patients separately: one in Group B and the other in Group C

6 hours after the procedure, but undetectable after 24 hours (fig. 1a).

Six hours after cardioversion, a significant increase in CPK level was observed between groups A and B (mean value in group B > A; $p < 0.001$) and between groups A and C (mean value in group C > A; $p < 0.0001$). A significant increase was also observed after 24 hours between the three groups of cumulative energy (mean value in group B > A [$p < 0.0001$], mean value in group C > A [$p < 0.0001$], mean value in group C > B [$p = 0.007$]). The analysis of each cumulative energy group over time demonstrated that there was a significant increase in CPK at 6 and 24 hours after the procedure in groups B ($p < 0.0001$) e C ($p < 0.0001$) (fig. 1b); which did not occur in group A (lowest p value = 0.2). An important correlation was found between CPK peak and the cumulative energy delivered ($r =$

0.660; $p < 0.001$) or the number of shocks ($r = 0.770$; $p < 0.001$).

A significant increase in CK-MB activity six and 24 hours after cardioversion was observed between groups A and B (mean value in group B > A; $p = 0.002$) and 24 hours after cardioversion between groups A and C (mean value in group C > A; $p < 0.0001$). The analysis of the evolution of each cumulative energy group over time showed that patients in groups B and C had a rather significant increase as compared to the precardioversion levels ($p < 0.0001$), which was not observed in group A (lowest p value = 0.3) (fig. 1c). A positive correlation was found between CK-MB activity peak and the cumulative energy delivered ($r = 0.429$; $p < 0.0001$) or the number of shocks ($r = 0.642$; $p < 0.0001$).

Among the markers that changed after cardioversion, CK-MB mass had lower expressivity, with increase

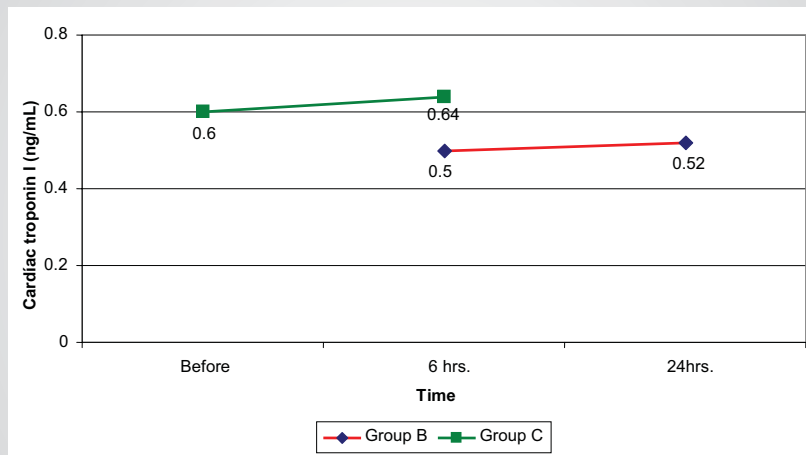


Fig. 1a – Graphic showing the detectable values of Cardiac troponin I in two patients, one from Group B obtained six and 24 hours after ECV and the other from Group C obtained before and six hours after ECV. Seventy-four patients had undetectable cTnI at all times. Normal value for cTnI up to 1 ng/mL; values < 0,5 ng/mL are not detectable

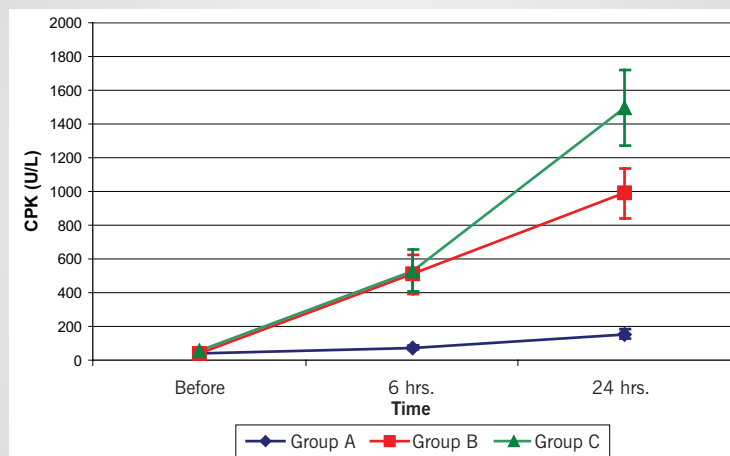


Fig. 1b - Graphic showing mean levels of CPK before and after ECV

between groups A and B, mean value of $B > A$ at six hours ($p = 0.03$) and 24 hours ($p = 0.02$) and between groups A and C at 24 hours, with mean value of $C > A$ ($p = 0.01$). The evolution of each cumulative energy group over time showed significant increase in CK-MB mass for patients in group B, between precardiaversion times and at 6 or 24 hours postcardioversion ($p = 0.001$) and between six and 24 hours ($p = 0.02$). The same occurred in group C ($p < 0.0001$) (fig 1d). A less expressive yet still significant correlation was found between CK-MB mass peak and cumulative energy delivered ($r = 0.265$; $p = 0.02$) or number of shocks ($r = 0.430$; $p < 0.0001$).

Similarly to CPK, myoglobin showed rather elevated peak values after cardioversion. Six hours postcardioversion, there was a relevant increase in myoglobin upon an increase in cumulative energy ($p < 0.0001$), and peak values were observed in all groups at this time. Twenty-four hours after the procedure, myoglobin levels remained

elevated with the increase in cumulative energy ($p < 0.001$ between groups A and B or C [mean value of B or $C > A$]; $p = 0.015$ between groups B and C [mean value of $C > B$]) (fig.1e). An important correlation was found between myoglobin peak and the cumulative energy delivered ($r = 0.684$; $p < 0.0001$) or number of shocks ($r = 0.745$; $p < 0.0001$).

Analyzing the correlation of all markers with body surface, a correlation of the latter was observed with CPK peaks ($r = 0.261$; $p = 0.024$) and myoglobin ($r = 0.300$; $p = 0.009$).

DISCUSSION

This study shows that, based on cTnI measurement, a highly specific marker of myocardial injury, no myocardial injury is detected after ECV, even when elevated cumulative energy is used.

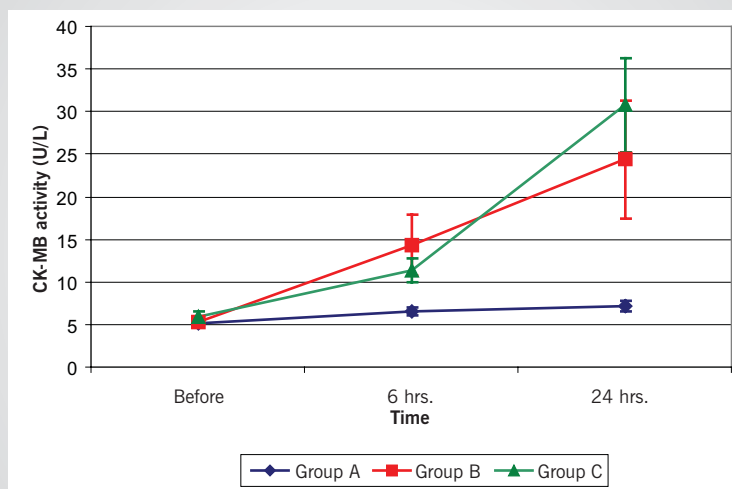


Fig. 1c - Graphic showing mean levels of CK-MB activity before and after ECV

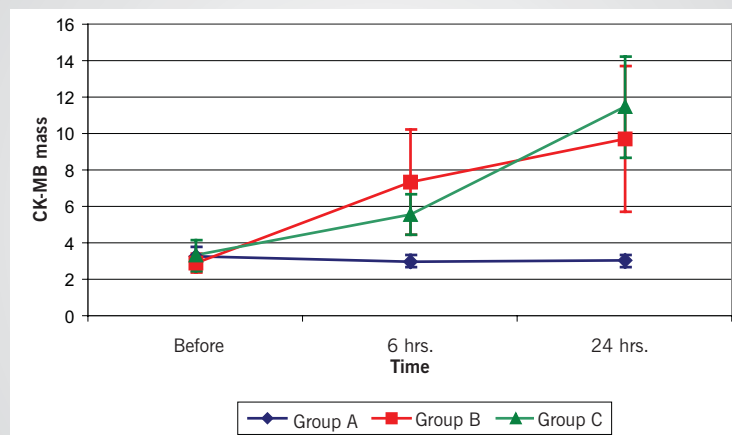


Fig. 1d - Graphic showing mean levels of CK-MB mass before and after ECV

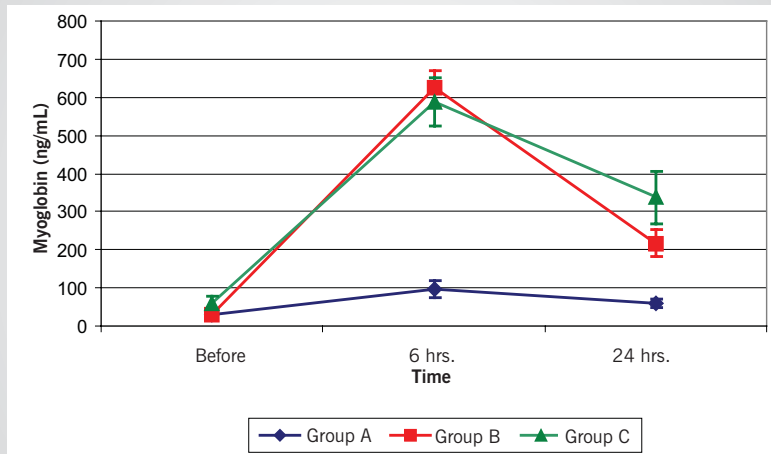


Fig. 1e - Graphic showing mean levels of myoglobin before and after ECV

In previous studies, CPK and CK-MB elevations were found in a large proportion of patients after external ECV, ranging from 9.3% to 50%¹⁹. Due to the lack of biological specificity of these markers, no conclusion could be reached about what may have caused the release of these enzymes. Based on results from experimental studies conducted during the 70's, the hypothesis of a cardiac origin for the elevation of these markers was supported because of the localized necrosis observed after repeated high-energy shocks. The delivery of direct-current shocks may cause reversible damages to subcellular structures involved in the oxidative phosphorylation and trigger a release of striated muscle proteins, such as CPK, CK-MB and myoglobin^{20,21}. These markers, however, fail to reveal minor myocardial injuries, especially when a skeletal muscle injury takes place simultaneously^{20, 22}.

In our study, 57 patients (75%) displayed CPK levels above normal limits in at least one of the times after cardioversion. Thirty-nine patients (51.3%) had elevation of CK-MB activity, whereas no abnormal values of this marker were observed in patients with normal levels of CPK. The percentage of CK-MB mass above normal levels was lower (32 patients [42.1%]). Similarly to CPK, myoglobin values rose to values above the reference limits for many patients.

The analysis of variance with repeated measurements and multiple comparisons of means showed a proportional increase over time in all markers, culminating with the peak of CPK at 24 hours and myoglobin at the 6 hours. An important correlation was found between the peak of each marker and the cumulative energy delivered or the number of shocks, and these correlations were more significant for CPK and myoglobin.

A large number of patients who undergo ECV have CPK, CK-MB activity, CK-MB mass, and myoglobin

elevation, and the skeletal muscle injury in the chest wall is thought to cause the release of these enzymes. This fact has already been demonstrated in histopathological studies and radionuclide imaging^{20,23}. The release of these cardiac markers is directly related to the cumulative energy delivered or to the number of shocks.

The comparison of both safety and efficacy of electrical cardioversion using monophasic versus biphasic shocks for atrial fibrillation showed that biphasic shock is superior²⁴⁻²⁶ and that it may cause less damage to the myocardium and skeletal muscle, possibly because of the lower energy delivered²⁴.

The most relevant information derived from our study is the lack of cTnI elevation after elective electrical cardioversion using a monophasic cardioverter, even with high-energy shocks.

Although a highly specific biochemical marker of myocardial injury was used in this study²⁷, in thesis, we could argue that the possibility exists that the myocardial injury caused by ECV is not detected by cTnI measurement. This hypothesis would gain credence if myocardial necrosis were detected in ECV by more specific complementary techniques, such as the one determined by histopathological studies or nuclear magnetic resonance^{28, 29}.

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REFERENCES

1. Neumayr G, Hagn C, Gänzer H et al. Plasma levels of troponin T after electrical cardioversion of atrial fibrillation and flutter. *The American Journal of Cardiology* 1997; 80: 1367-9.
2. Beck CS, Pritchard VM, Feil HS. Ventricular fibrillation of long duration abolished by electric shock. *JAMA* 1947; 135: 985-90.
3. Warner ED, Dahl C, Ewy GA. Myocardial injury from transthoracic defibrillator countershock. *Arch Pathol* 1975; 99: 55-60.
4. Trouton TG, Allen JD, Adgey AA. Oxidative metabolism and myocardial blood flow change after transthoracic DC countershocks in dogs. *Eur Heart J* 1992; 13: 1431-40.
5. Reiffel YA, McCarthy DM, Leahey EB. Does DC conversion affect isoenzyme recognition of myocardial infarction? *Am Heart J* 1979; 97: 269-75.
6. Stabilini R, Agostini A, Berli GC et al. Serum myoglobin, total CK, and MB CK isoenzyme after DC cardioversion and during the early phase of acute myocardial infarction. *Acta Cardiol* 1980; 5: 373-80.
7. Eshani A, Gordon AE, Sobel BE. Effects of electrical countershock on serum creatine phosphokinase (total CPK) isoenzyme activity. *Am J Cardiol* 1976; 37: 12-8.
8. Dahl CF, Ewy GA, Warner ED. Myocardial necrosis from direct current countershock: effect of paddle size and time interval between discharges. *Circulation* 1974; 50: 956-61.
9. Dalzell GWN, Cunningham SR, Anderson J et al. Electrode pad size, transthoracic impedance and success of external ventricular defibrillation. *Am J Cardiol* 1989; 64: 741-4.
10. Moak JP. Acute nonpharmacologic treatment of tachyarrhythmias and bradyarrhythmias in pediatric arrhythmias. In Gillette PC, Garson A, (ed.) *Electrophysiology and pacing*. Philadelphia: WB Saunders, 1990: 516-28.
11. Morrow DA, Antman EM. Cardiac marker elevation after cardioversion: sorting out chicken and egg. *Eur Heart J* 2000; 21: 171-3.
12. Del Rey JM, Madrid AH, Rubí J et al. Cardiac troponin I and minor cardiac damage: biochemical markers in a clinical model of myocardial lesions. *Clin Chem* 1998; 44: 2270-6.
13. Madrid AH, Sánchez JMR, Rebollo JMG et al. Correlación anatomopatológica y bioquímica de las lesiones producidas por la radiofrecuencia con catéteres estándar e irrigados de 4mm. *Rev Esp Cardiol* 2000; 53: 1347-55.
14. Madrid AH, Del Rey JM, Rubí 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.
15. Bonnefoy E, Chevalier P, Kirkorian G et al. Cardiac troponin I does not increase after cardioversion. *Chest* 1997; 111(1): 15-18.
16. Greaves K, Crake T. Cardiac troponin T does not increase after electrical cardioversion for atrial fibrillation or atrial flutter. *Heart* 1998; 80: 226-8.
17. Lund M, French JK, Johnson RN, Williams BF, White HD. Serum troponins T and I after elective cardioversion. *Eur Heart J* 2000; 21: 245-52.
18. Runsio M, Kallner A, Kallner G, Rsenqvist M, Bergfeldt L. Myocardial injury after electrical therapy for cardiac arrhythmias assessed by troponin T release. *Am J Cardiol* 1997; 79: 1241-5.
19. Georges J, Spentchian M, Caubel C et al. Time course of troponin I, myoglobin, and cardiac enzyme release after electrical cardioversion. *Am J Cardiol* 1996; 78: 825-7.
20. Sánchez JMR, Madrid AH, Rebollo JMG et al. Cardioversión eléctrica externa y sistemas de cardioversión interna: evaluación prospectiva y comparativa del daño celular con troponina I. *Rev Esp Cardiol* 2002; 55(3): 227-34.
21. Trouton T, Allen I, Adgey A. Oxidative metabolism and myocardial blood flow changes after transthoracic DC countershocks in dogs. *Eur Heart J* 1992; 13: 1431-40.
22. Zabel M, Kaster W, Hohnloser H. Usefulness of CK-MB and troponin T determinations in patients with acute myocardial infarction complicated by ventricular fibrillation. *Clin Cardiol* 1991; 16: 23-5.
23. Corbitt JD Jr, Sybers J, Levin JM. Muscle changes of the anterior chest wall secondary to electrical countershock. *Am J Clin Pathol* 1969; 51: 107-12.
24. Kosior D, Chwyczko T, Stawicki S et al. Myoglobin and troponin I as markers of myocardial damage during cardioversion of atrial fibrillation. *Pol Arch Med Wewn* 2003; 110(2): 827-36.
25. Carunchio A, Burattini M, Coletta C et al. Electrical cardioversion for atrial fibrillation: advantages of the transthoracic biphasic method. *Ital Heart J Suppl* 2002; 3(6): 638-45.
26. Kosior DA, Opolski G, Tadeusiak W et al. Serum troponin I and myoglobin after monophasic versus biphasic transthoracic shocks for cardioversion of persistent atrial fibrillation. *Pacing Clin Electrophysiol* 2005; 28(Suppl 1): S128-32.
27. Adams 3D JE, Boder GS, Davila-Roman VG et al. Cardiac troponin I. A marker with high specificity for cardiac injury. *Circulation* 1993; 88(1): 101-6.
28. Pinto IM, Da Luz PL, Magalhães HM et al. Consensos sobre métodos em cardiologia. *Arq Bras Cardiol* 1995; 65: 446-68.
29. Shan K, Constantine G, Sivananthan M, Flamm SD. Role of Cardiac Magnetic Resonance Imaging in the Assessment of Myocardial Viability. *Circulation* 2004; 109: 1328-34.