Editorials

Cardiac marker elevation after cardioversion: sorting out chicken and egg

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In the early 1960s external direct current electrical reversion of tachyarrhythmias was introduced \[1\]. The American Heart Association has since identified early electrical cardioversion as the critical component in the survival of patients suffering cardiac arrest from ventricular tachycardia or fibrillation. In part due to enhanced training and availability of this therapy, the number of patients presenting to hospitals as survivors of an out-of-hospital arrest has increased. For example, in U.S. cities with aggressive pre-hospital training such as Miami and Seattle the number of survivors of pre-hospital arrest increased from 10–14% in the early 1970s to over 30% by the late 1980s, with survival to hospitalization as high as 88% for the subgroup with documented sustained VT \[2,3\]. On evaluation in the inpatient setting, a substantial proportion of patients surviving pre-hospital resuscitative efforts have elevation of total creatine kinase and its MB isoenzyme, creatine kinase-MB \[4–6\]. Defining the aetiology of the increased creatine kinase for such a patient is of paramount importance as the presence or absence of myocardial infarction plays a central role in directing further evaluation as well as both short- and long-term therapy. Clinicians need to consider three primary possible aetiologies for an elevated cardiac marker in the situation described above: (1) The elevated marker reflects an acute myocardial infarction as the cause of the arrhythmia. (2) The arrhythmia resulted in sufficient imbalance in myocardial oxygen supply and demand to result in acute myocardial infarction. (3) Electrical cardioversion or other resuscitative efforts caused myocardial damage. Discriminating between these three possibilities may present a substantial challenge and thus eliminating even one alternative is advantageous.

Direct current transthoracic cardioversion for tachyarrhythmias under elective circumstances is associated with elevation of total creatine kinase in approximately 50% of cases \[7–10\]. Though not universal \[9\], most reported series have documented an association between the degree of creatine kinase elevation and the total number of shocks as well as the total energy delivered \[9–13\]. Similar observations have also been made with CKMB among patients undergoing elective cardioversion \[7,9–11,13,14\]. This positive correlation between the energy delivered and the rise in total creatine kinase and CKMB have raised concern that direct current transthoracic cardioversion may cause measurable myocardial damage \[11,12\]. Indeed, a number of studies have shown morphological and functional derangement of the myocardium following electrical shocks in animal models \[7,15,16\]. These studies include direct histological evidence of myocardial damage as well as abnormal technetium pyrophosphate scintigrams \[7,14,15,17\]. Alternatively, injury to the skeletal muscle of the chest wall has been considered as the source of serum ‘cardiac’ marker elevation. Histopathological examination has revealed pectoralis muscle damage among patients previously cardioverted \[18\]. Similar to that from studies of cardiac muscle, technetium pyrophosphate uptake in skeletal muscle after direct current transthoracic cardioversion has been demonstrated in both animal and human series \[14,17\]. Regardless of cause, elevation of total creatine kinase and CKMB may confound the evaluation of a possible myocardial infarction.

Fortunately, the availability of the cardiac specific troponins T (cTnT) and I (cTnI) has enabled researchers to discriminate more effectively between the contribution of skeletal vs myocardial muscle damage. By virtue of their absence in the circulation of healthy individuals and their high concentration in cardiac myocytes, the cardiac isoforms of these two troponin regulatory complex components are highly sensitive and specific markers of myocardial damage. Lund and colleagues conducted a large study using prospective serial determinations of CKMB mass, and cardiac troponins in the setting of elective direct current transthoracic cardioversion for atrial tachyarrhythmias \[19\]. Among 72 elective cardioversions using a maximum cumulative total of 1280 J of energy, they found no elevation of cTnT, and only a mild rise in cTnI for two patients (within the
of variation for the cTnI assay utilized and ≤0.6 ng . ml⁻¹ at peak). Their experience is consistent with previously reported studies which in aggregate with Lund’s study have shown no elevation of cTnT among 293 patients undergoing elective direct current transthoracic cardioversion[13,19–24]. Several investigators have measured cTnI after elective direct current transthoracic cardioversion and detected rare mild elevation of cTnI using the Dade Stratus assay[9,10]. Allan and colleagues[10] found cTnI elevations in 3/38 patients (peak values: 0.8, 1.2 and 1.5 ng . ml⁻¹), while Bonnefoy et al.[9] detected mild cTnI elevation in 4/28 patients studied (peak values: 0.6, 0.6, 0.6 and 0.9 ng . ml⁻¹). Such mild increases in cTnI with the Stratus assay have been associated with adverse outcomes in unstable angina and are believed to reflect minimal myocardial damage or microinfarction[25]. Thus, it remains plausible, on the basis of histopathological data, and the observed mild increases in cTnI, that minor myocardial injury may occur during elective direct current transthoracic cardioversion, dependent on the number and timing of external shocks delivered[12,15]. However, these minor elevations are unlikely to confound the diagnosis of clinically significant myocardial infarction and therefore substantial elevation of either of the cardiac troponins (e.g. >1.5 ng . ml⁻¹ for cTnI) in the setting of elective direct current transthoracic cardioversion suggests causes unrelated to electrical cardioversion.

While it is reasonable to postulate that the cardiac troponins may perform as effectively in the setting of emergency cardioversion for ventricular arrhythmias, one must be cautious about such an extrapolation on the basis of Lund’s data. With respect to the ventricular origin of the arrhythmia, data from the electrophysiology laboratory show that only mild elevations of cardiac specific markers occur during external cardioversion for ventricular tachycardia or fibrillation under such controlled circumstances[8,20]. However, the clinical situation during pre-hospital resuscitation attempts is far more complex. Substantial skeletal muscle trauma, prolonged arrhythmia, hypoxaemia, and chest compressions confound the interpretation of cardiac markers[27]. In at least one study of patients suffering out-of-hospital arrest, elevation of CKMB, which is not unexpectedly occurred more frequently than in series involving elective cardioversion, correlated with both the number of chest compressions as well as total energy applied among patients without known coronary artery disease[27]. Although, the myocardial specificity of the cardiac troponins is maintained in the setting of massive musculoskeletal trauma, the combined effects of prolonged cardiopulmonary resuscitation and repeated transthoracic shocks over a short period of time on the release of cardiac troponins have not been completely defined. Two published reports evaluating cardiac troponins after pre-hospital resuscitative efforts have shown elevation of cTnT among 80–85% patients without evidence of acute myocardial infarction by ECG criteria, or in some cases thallium scintigraphy or autopsy[5,6]. Further research evaluating the interactions between components of pre-hospital resuscitation and elevation of cardiac specific troponins may be helpful in clarifying the prognostic and treatment implications of such marker abnormailities. At the present time, it seems reasonable to expect that direct current transthoracic cardioversion for supraventricular tachyarrhythmias causes either no elevation of troponin levels or only a slight increase, and that more substantial increases are indicative of myocardial damage unrelated to the external shock. Clinicians should be cautious about extrapolating beyond the above statement to patients resuscitated from out of hospital arrests until more information is available.

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References

Sex differences in outcome following community-based cardiopulmonary arrest

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Today sudden death still represents a frequently observed event and a significant number of deaths are from cardiac causes. Among these latter, ischaemic cardiopathy is without any doubt the main, if not the unique, event responsible. Sudden death may also be the result of other cardiac non-ischaemic pathologies or of non-cardiac diseases\[1,2\]. Leach et al\[3\], examining a series of 333 out-of-hospital deaths found, at autopsy, that two-thirds of them were attributable to other cardiac non-ischaemic or non-cardiac diseases. Male gender usually predominates in those cases affected by ischaemic heart disease.

Sudden death due to ischaemic heart disease may be subdivided into two further groups: one in which an acute pathological lesion (acute thrombosis or acute infarction) could be considered the cause of death, and the other in which no acute thrombosis can be observed and the cause of death is presumed to be chronic coronary artery disease.

With regard to the clinical presentation of the fatal event, very frequently a ventricular fibrillation, or a so-called shockable rhythm may be observed, but in several other instances, complete asystole is present, unresponsive to any electrical treatment. Finally, the symptomatology preceding sudden death might be important and last for hours or days, while in other cases it could be non-existent, the fatal event being the first pathological manifestation in the patient.

In the many attempts to analyse gender as an independent factor in the determination of sudden death, the quantity of variables rendered reaching conclusions difficult. Kurkcyian et al\[4\], for instance, on examining a series of 593 patients with
Is the exercise test of use in post-menopausal women with unstable coronary artery disease?

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The correct answer cannot be a simple ‘yes’ or ‘no’. The answer is a complex one. A first observation is that the exercise test has a very low predictive value for the presence of coronary artery disease in men as well as women in populations with a low incidence of coronary artery disease, for instance in pre-menopausal women or in men less than 40 years old[1]. Although the prevalence of coronary artery disease in women is lower than that in men, particularly in the pre-menopausal years, the prevalence of ST depression is higher in women younger than 45 years. This high prevalence of false-positive findings on exercise testing has been attributed to the presence of a higher oestrogen level. There is indeed good evidence that oestrogen may be a vasoconstrictor to coronary arterioles. It has a chemical structure similar to that of digitalis, which also has been demonstrated to be a vasoconstrictor. Men receiving large doses of oestrogen may have increased degrees of ST depression. This is, moreover, well known that because women have a lower prevalence of coronary artery disease than men, there are likely to be a higher number of false-positive tests with, as a consequence, a higher number of coronary angiograms performed in women for the diagnosis of coronary artery disease after a positive exercise test.

This bias in many studies will reduce the specificity, thus supporting the concept that false-positive tests in women. The true cause of the increased false-positive rate of exercise tests in women is nevertheless still being debated. In patients with a well documented history of coronary artery disease, as in patients after myocardial infarction or with angina pectoris, stable or unstable, ST segment depressions during exercise test or Holter monitoring are highly predictive of myocardial ischaemia[2]. Several authors have found that women with coronary artery disease have a frequency of myocardial ischaemia similar to that of men.

A second point is that women with coronary artery disease are more likely to have atypical symptoms, including the absence of chest pain at exercise; pain in other locations, such as the jaw, arms, shoulder, back, and epigastrium; and angina-equivalents, such as dyspnoea, palpitations, and pre-syncope. A safe and accurate approach for the detection of coronary artery disease in women must be guided by clinical likelihood based on patient age, chest-pain quality, and risk factors, mainly diabetes and post-menopausal status without hormone replacement therapy. Although computerized exercise ST-segment analysis and a multivariable approach for the interpretation of exercise tests were used, several authors have demonstrated that stress echocardiography is more sensitive than exercise score, and more sensitive and specific than ST-segment analysis for the diagnosis of coronary artery disease in women[3].

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