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Clinical evaluation of unselected cardiac arrest survivors in a tertiary center over a 1-year period (the LAZARUZ study)☆,☆☆

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Abstract

Objectives: When the cause of an aborted cardiac arrest is unclear the initiation of therapy, counseling and family screening is challenging.

Methods: We included 43 unselected, prospectively identified cardiac arrest survivors with or without a diagnosis. Family history for cardiac disease and supplemental electrocardiograms were evaluated for additional diagnostic information.

Results: 43 cardiac arrest survivors were included, 34 (79%) were male and the average age was 48 years (range 23–64, SD 13.0). The most common etiologies identified in cardiac arrest survivors were ischemic heart disease (33%), cardiomyopathies (14%), miscellaneous (e.g. drug induced arrhythmias, coronary spasms) (12%) and channelopathies (5%). Family history of cardiac disease – even inheritable conditions – was not indicative of etiology in cardiac arrest survivors. Supplemental ECGs were abnormal in 10 of 43 patients; in the majority of these patients (7) no conclusive diagnosis was reached.

Conclusions: In this study 16/43 (37%) of unselected, prospectively included cardiac arrest survivors remained without a diagnosis despite exhaustive investigations. We may extract additional diagnostic information from simple maneuvers during the recording of the electrocardiogram. We suggest that these ECG derived clues be investigated in future studies including genetic test results and data from relatives.

Keywords: Cardiac arrest survivor; Family history; Sudden cardiac death; Non-invasive electrophysiology

Introduction

Prevention of recurrences and evaluation of risk in relatives possibly affected by an inheritable cardiac disease challenge physicians caring for cardiac arrest survivors. Optimally, provided a specific etiology is identified, disease specific therapy can be prescribed. For instance, beta-adrenergic receptor blocking agents or sympathectomy in patients with malignant arrhythmias that are sensitive to sympathetic stimuli, avoidance of certain medications or life-style modifications in patients with altered cardiac repolarization can be recommended. In addition, a specific diagnosis in the proband allows for a focused evaluation of family members. In families with sudden cardiac death a specific diagnosis is not achieved in approx. 60% of cases in spite of extensive evaluation of the index case [1–10]. The results are somewhat better in cardiac arrest survivors (in the CASPAR registry this number was around 40%) [11]. For this reason, we initiated a prospective registry on cardiac arrest survivors (the LAZARUZ project) and in this paper we present our data including a focused family history and specific supplemental electrocardiograms (ECGs) as additional parameters to cardiac arrest survivors.

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Methods

Cardiac arrest survivors aged 18–64 years admitted to Department of Cardiology at the Copenhagen University Hospital/Rigshospitalet during the period July 15th 2014–August 31st 2015 were invited to participate in the study. Inclusion was performed prospectively. We collected their history and test results from the clinical chart. In addition, a thorough review of the family history was obtained and supplementary ECGs were performed.

Clinical data

A family history was considered positive for sudden cardiac death if a 1st or 2nd relative had died suddenly and non-violently and unexpectedly before the age of 65 years. The family history was considered positive for ischemic heart disease (IHD) if IHD had occurred among 1st or 2nd degree relatives. Also, known inheritable cardiac conditions were noted.

The work-up included the following tests

Transthoracic echocardiograms (TTE)

Echocardiograms were performed according to the recommendations from the Danish Society for Cardiology (http://www.cardio.dk/rapporter/holdningspapir-menu). The first full echocardiography after the acute phase was noted in order to prevent potential myocardial stunning after cardiac arrest. A cardiologist reviewed all scans.

Coronary angiogram, coronary CT-scan and stress test

A coronary angiogram was considered positive if one or more stenoses with over 50% vessel lumen occlusion were found. CT-angiography was considered positive if the left main artery had a stenosis > 50% and/or a > 70% stenosis in the other large coronary arteries. Exercise stress test was performed using Bruce protocol on a bicycle and was terminated at maximum exertion, if the patient developed ≥ 1 mV ST-elevations or ventricular arrhythmia (> three premature ventricular beats). Non-ascending ST depressions > 0.1 mV combined with angina pectoris were considered significant.

Cardiac magnetic resonance imaging (CMR)

CMR scans were done on a 1.5 or 3 Tesla scanner (Siemens, Germany) with chest surface coils and 32-channel back. The cardiac volumes were obtained by steady-state free precession cine images with retrospective electrocardiographic gating as a short axis stack and as transversal stack covering the heart. (No interpolated gaps, slice thickness 8 mm). Late gadolinium enhancement was obtained by T1-weighted gradient echo images as a short-axis stack approximately 10–20 min. After administration of an intravenous bolus of gadolinium (0.10 mmol/kg bodyweight), (Gadovist, Bayer Schering, Germany). Inversion time was continuously determined to null the signal from the normal myocardium. T1-weighted images were obtained with prospective electrocardiographic triggering. T2-weighted images were performed at the discretion of the performing physician when there was a suspicion of inflammatory disease. Images were analyzed with the use of CVI42 (Circle Cardiovascular Imaging Inc., Canada). Late gadolinium enhancement (LGE) images were visually assessed. Two independent investigators reviewed CMR scans.

Invasive electrophysiology studies

The electrophysiological (EP) studies were individually evaluated and set against the suspected electrical finding. A monomorphic sustained ventricular arrhythmia was always considered a positive finding.

Endomyocardial biopsies

The endomyocardial biopsies were immunohistochemically stained for myocarditis (Dallas criteria), amyloid (Prussian blue and Congo red stains) and fibrosis (Masson trichrome) followed by evaluation by a cardiac pathologist.

Late potentials (LP)

Late potentials were derived from a signal-averaged electrocardiogram, using 300 beats on average (GE Medical Systems, MAC 5500 HD). A noise level < 0.3 μV (standard deviation) was obtained. LP were considered positive if > 1 of the following criteria were met: filtered QRS duration > 114 ms, terminal QRS root means square (RMS) voltage < 20 μV or low amplitude (< 40 μV) signal (LAS duration > 38 ms.

Pharmacological provocation

Pharmacological provocation was performed by infusion of either flecainide or isoprenaline. Flecainide in doses up to maximally 2 mg/kg was infused during continuous ECG monitoring and considered positive if a terminal R wave and a ≥ 2 mm ST-segment elevation occurred in ≥ 1 of leads V1–V3. Isoprenaline test was performed under continuous ECG recording with infusion of 0.02 μg/kg/min isoprenaline and increasing to 0.1 μg/kg/min for 10 min.

Supplementary ECG recordings

Patients rested in bed for 5 min before the recording of the first ECG, subsequently an ECG was recorded using upwards displacement of the V1–2 leads to intercostal areas 2 and 3. Subsequently, each patient was instructed to stand and ECGs were recorded every minute while the patient remained standing for 5 min. The corrected QT interval (QTc) was calculated using the Bazett's formula (maximal QT duration in lead V2 or V5 divided by the square-root of the RR-interval). Precordial leads were used as brisk standing inevitable induced noise on the ECGs that interfered with the determination of QTc duration in limb leads.

As the QTc interval may be difficult to measure [13], two investigators (JT and PM who previously published data with low intra- and interobserver variation on the QTc duration in a prospective patient cohort) analyzed the ECGs independently and blinded from the clinical data [12,13].

The supplementary ECGs did not form part of the regular workup of the cardiac arrest survivors (described in the methods' section). Also, two investigators (blinded to the