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Etiological diagnoses of out-of-hospital cardiac arrest survivors admitted to the intensive care unit: Insights from a French registry☆

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ABSTRACT

Background: Respective proportions of final etiologies are disparate in cohorts of cardiac arrest patients, depending on examined population and diagnostic algorithms. In particular, prevalence and characteristics of sudden unexplained death syndrome (SUDS) are debated. We aimed at describing etiologies in a large cohort of aborted out-of-hospital cardiac arrest (OHCA) patients, in order to assess prevalence and outcome of SUDS.

Patients and methods: We analyzed data from our prospective registry of successfully resuscitated OHCA patients admitted to a cardiac arrest centre between January 2002 and December 2014. The in-ICU diagnostic strategy included early coronary angiogram, brain and chest CT scan. This was completed by an extensive diagnostic strategy, encompassing biological and toxicological tests, repeated electrocardiograms and echocardiography, MRI and pharmacologic tests. Two independent investigators reviewed each final diagnosis. Baseline characteristics were compared between subgroups of patients. Three-month mortality was compared between subgroups using univariate Kaplan-Meier curves.

Results: Over the study period, 1657 patients were admitted to our unit after an aborted OHCA. The event was attributed to a non-cardiac and a cardiac cause in 478 (32.0%) and 978 (65.5%) patients, respectively. The main cause of cardiac related OHCA was ischemic heart disease (76.7%) while primary electrical diseases accounted for only 2.5%. Sudden unexplained deaths (SUDS) were observed in 37 (2.5%) patients.

Conclusion: We observed that ischemic heart disease was by far the most common cause of cardiac arrest, while primary electrical diseases were much less frequent. SUDS accounted for a very small proportion of patients who suffered an aborted OHCA.

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Introduction

Out-of-hospital cardiac arrest (OHCA) remains a leading cause of death in industrialized countries, with an incidence of more than 359,000 new cases per year in the United States [1] and nearly 40,000 in France [2]. Besides the activation of the "chain of survival", identifying and treating the cause is currently a major issue, involving hospital and prehospital teams, as underlined in recent guidelines from the International Liaison Committee On Resuscitation (ILCOR) [3].

Among the causes of aborted OHCA, many high quality studies have reported a high prevalence of coronary artery disease (CAD) [4,5], but there is a lack of knowledge regarding the other causes. An undetermined proportion of events are the consequence of a

non-ischemic cardiac disease, which can be structural or primary electrical diseases (such as a channelopathies). The real proportion of patients with these etiologies is difficult to assess, as most published studies included selected populations such as survivors in whom diagnosis was already made as part of a previous family investigation [6,7]. On the whole, respective proportions of final etiologies are disparate in cohorts of cardiac arrest patients, depending on examined population and diagnostic algorithms. In particular, prevalence and characteristics of sudden unexplained death syndrome (SUDS) and idiopathic ventricular fibrillation (IVF) are debated. In these patients in whom no diagnosis was possible despite extensive exploration, the management strategy of both patients and relatives is not well clarified. To date, knowledge about these SUDS patients regarding their characteristics and outcome is considered to be insufficient for many experts [8].

We aimed at describing etiologies in a large cohort of aborted out-of-hospital cardiac arrest (OHCA) patients, in order to better characterize SUDS victims.

Patients and methods

Study setting and population

Pre-hospital management

We have previously described pre-hospital management of OHCA patients in the geographic area of south Great Paris, France [9]. Briefly, out-of-hospital resuscitation is delivered by an emergency team, which includes at least one physician trained in emergency medicine according to standard procedure based on the ILCOR recommendations [10]. Patients in whom return of spontaneous circulation (ROSC) is achieved are then referred to our academic tertiary hospital.

Diagnostic strategy

In all aborted OHCA patients without any obvious cause, the initial diagnostic strategy that we routinely use includes immediate coronary angiography and/or brain and chest CT-scans, according to prodromes, as previously described [11,12]. After this early imaging procedure, patients are then admitted to the intensive care unit (ICU). In patients without identified diagnosis despite the first-line imaging strategy, the following explorations are performed when appropriate, according to previously published guidelines [13]:

- careful examination of past medical and familial history
- repeated electrocardiograms,
- transthoracic and/or transoesophageal echocardiography,
- cardiac magnetic resonance imagery,
- toxicological screening,

Intracardiac electrophysiologic testing, Holter monitor, provocative tests with methyl-ergometrine and ajmaline are performed in young patients discharged alive from ICU without any identified diagnosis according to the situation. These explorations are performed in the cardiology ward after ICU discharge and decided by the physician in charge.

Patients selection

We retrospectively reviewed charts of all consecutive patients admitted alive in our hospital between January 2002 and December 2014. We included all consecutive OHCA patients who were admitted alive to ICU and who were investigated according to the diagnostic strategy described above. We excluded in-hospital cardiac arrest patients, those who presented major hemodynamic instability precluding the physician in charge to do any complementary exploration and those who received early withdrawal of care related to chronic underlying comorbidities.

Data analysis and classification

All data were prospectively collected according the Utstein style [10], including age and gender, location of cardiac arrest and initial rhythm, time from collapse to cardio-pulmonary resuscitation (CPR) ("no-flow") and from CPR to ROSC ("low-flow"), presence of a witness on scene and bystander CPR. Cardiovascular risk factors (hypertension, diabetes mellitus, dyslipidemia and current smoking) and sudden death family history were collected as well. Inhospital variables (post-resuscitation shock, therapeutic hypothermia, coronary angiography and percutaneous coronary intervention) were collected too.

The terms "aborted cardiac arrest", "unexplained sudden cardiac death" and "idiopathic ventricular fibrillation" are used as previously defined by the 2015 Task Force for the Management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology [8]. Briefly, "aborted cardiac arrest" refers to unexpected circulatory arrest, occurring within 1 h of onset of acute symptoms, which is reversed by successful resuscitation manoeuvres". "Unexplained sudden cardiac death" refers to sudden death without an apparent cause and in which an autopsy has not been performed while "idiopathic ventricular fibrillation" refers to a specific case where clinical investigations are negative in a patient surviving an episode of ventricular fibrillation. Analyzing information obtained during the diagnosis process, investigators attributed a final etiology to each OHCA in the following classification:

- the etiology was considered being non-cardiac when the cause was a neurological disease (stroke, intracranial bleed, seizure, as previously described [14]), an acute respiratory failure (acute pneumonia, pulmonary embolism, . . .) or was related to various other conditions (i.e., hemorrhagic shock, anaphylactic shock, intoxication and aortic dissection);
- the etiology was considered being cardiac when the cause was primarily due to any heart disease [15,16]. Within this group of cardiac causes, we classified the patients into 4 different groups according to the following etiologies: coronary artery disease (acute coronary syndrome, chronic myocardial ischemia and coronary spasms), structural non-ischemic heart disease (dilated, hypertrophic, restrictive, congenital, valvular heart diseases, right-ventricle arythmogenic dysplasia), primary electrical diseases (all arhythmogenic heart diseases without any structural abnormality that could be evidenced) and miscellaneous causes (toxic, pacemaker dysfunction, metabolic or ionic major disturbances)
- all other events were considered being unsolved at time of the analysis, corresponding to the group of sudden unexplained death syndrome (SUDS). Within this SUDS subgroup, patients who suffered from a cardiac arrest related to an initial shockable rhythm were considered under the approved denomination of idiopathic ventricular fibrillation (IVF) [13].

Two investigators (OP and GG) independently reviewed all charts. Each discordant conclusion on diagnosis was resolved by consensus with the intervention of a third senior expert investigator (AC) (rate of discordance <1%).

In order to investigate both short- and long-term outcome in these patients, we chose survival from hospital discharge and at day-90 as our main outcomes, as previously recommended. Three-months mortality was collected as previously described [17].