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Title: Coronary angioplasty is associated with a better neurological outcome in the era of modern management of out-of-hospital cardiac arrest.

Short title: Angioplasty and neurologic outcome of cardiac arrest.

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Dear editor,

The prognosis of out-of-hospital cardiac arrest (OHCA) is still poor. Because of its neuro-protective benefits, mild therapeutic hypothermia (MTH) is recommended for comatose adult patients with return of spontaneous circulation (ROSC) after OHCA [1,2]. However, in the era of modern management of OHCA, including MTH, prognostic factors of neurologic outcome for those patients are still unclear.

METHODS: We performed a single-center retrospective review of all the patients admitted to our Intensive Cardiac Care Unit (ICCU) for a non-traumatic OHCA after successful resuscitation, from January 2008 to December 2011. Patients were excluded when OHCA was due to obvious non-cardiac cause and when MTH was not induced, regardless of the reason, such as response to verbal commands after ROSC. Coronary angiography was performed on all patients, except in the case of obvious non-coronary cause (e.g.: known non-ischemic cardiopathy). MTH was initiated as soon as possible, without deferring any required treatments.

The primary outcome was a favorable neurological outcome in living patients at hospital discharge, defined as a Pittsburgh cerebral performance category score (CPC) of 1 or 2 (respectively good recovery or moderate disability). Poor outcomes were category 3, 4 and 5 (respectively severe disability, vegetative state or death) [3,4].

Univariate analysis was performed using the Pearson-Khi square test to identify the risk elements associated with survival. Prognostic factors that were found to be associated with a p value ≤ 0.20 in the univariate analysis were eligible to be tested in the multivariate model. Multiple imputation was performed to take missing data into account [5]. Logistic regression was performed using a stepwise procedure. The final model included only covariates associated with a p value ≤ 0.05 . Odds ratios (OR) and their confidence interval (95% CI) were presented. All calculations were performed using SAS 9.1 (SAS Institute, Cary, NC) and R (<http://R-project.org>) software.

RESULTS: Seventy patients who had been admitted for a resuscitated OHCA and treated by MTH in our ICCU constituted our study group (Table 1). The mean age was 59 ± 7 years and the men-to-women ratio was 7:1. The OHCA was witnessed in 62 patients (88%), with a bystander cardiopulmonary resuscitation (CPR) in 35 (50%). “No-flow” mean-delay was 4.2 ± 5 minutes (median: 2) and “low-flow” was 22.6 ± 16 (median: 15). The initial rhythm was shockable in 56 patients (80%). The number of electric shocks was 3.5 ± 3 and 3.5 ± 5 mg epinephrine was administered. The electrocardiogram (ECG) performed at the waning of the resuscitation was normal in 17 patients (24%). Biomarkers on admission were: arterial pH: 7.28 ± 0.1 , lactate: 3.7 ± 2 mmol/L, creatinine: 112 ± 41 μ mol/L.

Table 1: Baseline characteristics of patients, according to the outcome.

	Good outcome n=35	Poor outcome n=35	p value
<i>Characteristics and medical history</i>			
Male gender	31 (89)	29 (82)	0.73
Age	55.6 ±12	63.1 ± 15	0.018
Diabete mellitus	3 (8)	6 (17)	0.47
Current smoker	13 (37)	12 (34)	0.80
Hyperlipidemia	17 (49)	19 (54)	0.63
Hypertension	8 (23)	19 (54)	0.013
Known cardiopathy	17(49)	24 (69)	0.08
<i>Cardiac arrest history</i>			
Chest pain as 1 st symptom	15 (43)	12 (34)	0.62
Location : public place	15 (43)	14 (40)	0.23
Time of occurrence (8am-8pm)	28 (80)	21 (60)	0.12
Witnessed arrest	35 (100)	27 (77)	0.003
Bystander CPR	21 (60)	14 (40)	0.47
No-flow mean delay (min)	2.5 ± 3	6 ± 8	0.017
Low-flow mean delay (min)	17 ±13	30 ±18	0.007
Time between collapse and ROSC	20 ±16	37 ±16	0.005
VF/VT as initial rhythm	29 (83)	27 (77)	0.55
<i>Initial treatment</i>			
Number of electric shocks	3.4 ± 1	4.4 ± 3	0.68
Dose of epinephrine (mg)	2.6 ± 2	4.9 ± 7	0.012
Antiarrhythmic drugs	15 (43)	9 (25)	0.62
Attempted PCI	21 (60)	7 (20)	0.002
Successful PCI	20 (57)	5 (14)	0.006
<i>ECG Patterns</i>			
ST-segment elevation	14(40)	12 (34)	0.8
Unspecific ST or T patterns	9 (26)	11 (31)	0.8
Unknown Left Bundle Branch Block	4 (11)	3 (9)	0.7
Normal ECG	8 (22)	9 (25)	0.7
<i>Blood biomarkers on admission</i>			
Arterial pH	7.30 ±0.1	7.27 ±0.1	0.09
Lactate (mmol/L)	2.7 ±2	4.7 ±4	0.006
Potassium (mmol/L)	4.0 ±1	3.9 ±1	0.42
I Troponin (ng/mL)	8.2 ±25	6.1 ±19	0.92
Creatinine (µmol/L)	103 ±39	121 ±41	0.013
Glucose (mmol/L)	12 ±6	15 ± 6	0.61

Qualitative data are expressed as counts and percentages.

CPR: Cardio-Pulmonary Resuscitation; ROSC: Return Of Spontaneous Circulation; VF: Ventricular Fibrillation/ VT: Ventricular tachycardia; PCI: Percutaneous Coronary Intervention.

The neurological outcome on hospital discharge was favorable (“good outcome” group) for 35 (50%) patients (CPC 1: 26 patients; CPC 2: 9 patients). The “poor-outcome” group included 35 (50%) patients (CPC 3: 1 patient, CPC 5: 34 patients).

All pre-hospital delays (no- and low-flows) were shorter in the "good outcome" group. Regardless of the outcome, post resuscitation ECG in the global population showed ST-segment changes in 75% of patients, including a ST-segment elevation in 26 patients (37%). The predictive positive and negative values of the latter associated with an acute coronary syndrome (ACS) were 96% and 41% respectively, whereas sensitivity and specificity were 49% and 95% respectively.

Final diagnosis of OHCA etiology was coronary artery disease for 53 patients (75%), including 37 (52%) of ACS, with similar prevalence in both groups (60% in the “good outcome” group vs 46%; $p=0.3$). The remaining causes of OHCA were other cardiomyopathies in 12 patients (17%) (dilated in 5, hypertrophic in 1, valvulopathy in 5, and channelopathy in 1 patient). No etiology was found in 5 patients (7%).

Multivariate analysis identified 4 independent factors which are significantly associated with neurological prognosis: a witnessed OHCA (100% in the “good outcome” group vs 77%, OR=0.18 [0.05-0.80]), an attempted PCI (68 vs 27%, OR=0.11 [0.02-0.51]), a ROSC delay ≥ 25 min (23 vs 66% OR=6.05 [1.58-23.23] and a creatinine blood level ≥ 104 $\mu\text{mol/L}$ at hospital admission (31 vs 68% OR=4.62 [1.23-17.39]).

DISCUSSION

In this population, the survival rate was 51% and a good neurological outcome was found in 50% of the patients on hospital discharge, in accordance with literature [6]. This confirms the favorable impact of short delays and the presence of a witness in OHCA. Given the crucial importance of the time from collapse to CPR, efforts should be made to promote the culture of resuscitation not only among health professionals, but also among the general population [7].

Otherwise, more than 80% of resuscitated patients underwent coronary angiography, in agreement with the fact that approximately 80% of sudden cardiac deaths are attributed to CAD [8]. Overall, it remains difficult to identify which patients will benefit from early angiography and/or PCI after OHCA, as usual assessment criterion (chest pain and ST elevation) may be poor predictors of ACS in OHCA patients. Indeed, ST-segment elevation has poor accuracy in the setting of post resuscitation [9]: reported sensitivity and specificity of ST-elevation to detect the presence of an underlying acute coronary lesion are 50% and 88%, respectively [10]. This led to the recommendations that emergent coronary angiography may be reasonable in all OHCA patients, regardless of the initial post-ROSC ECG [2]. Furthermore, only PCI and MTH showed in the last decade a positive influence on long term prognosis following OHCA [11,12].

Finally, none of our patients cumulating the four independent prognostic factors of good neurologic outcome (witnessed OHCA, ROSC<25min, admission creatinine <104 μ mol/l and PCI) had a poor neurological outcome, even though the small number of patients and the selected population of the study preclude the development of prediction models.

There are several obvious limitations in this study: this is a single-center, retrospective and observational study, thus subject to confounders and selection bias.

CONCLUSION

Half of the patients hospitalized in our ICCU had a good neurological outcome after a resuscitated OHCA and treatment with MTH. Multivariate analysis showed 4 predictive independent factors of a good neurological outcome: a witnessed OHCA, ROSC<25min, admission creatinine <104 μ mol/l and a coronary angioplasty. These findings confirm the importance of public awareness for resuscitation care, and the importance of using emergency coronary angiography, in order to improve the neurological outcome.

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