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Clinical paper

Gender differences in early invasive strategy after cardiac arrest: Insights from the PROCAT registry☆

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ABSTRACT

Aim: Early invasive strategy, including percutaneous coronary intervention (PCI), may improve survival in out-of-hospital-cardiac-arrest (OHCA) due to coronary artery disease but selection of suitable patients is challenging. Differences and results across gender remain unknown. We aimed to assess the relationship between gender and the use of an early invasive strategy after OHCA, and the relationship with outcome according to gender.

Methods: All patients admitted after OHCA were prospectively included (2000–2013). Using a gender-independent algorithm for its indication, we assessed the association between the use of an early invasive strategy and the outcome at hospital discharge (using the Cerebral Performance Category scale), according to gender.

Results: 1817 patients were included (520 women, 29%). Women were older (62.8 vs 59.1 years, P < 0.0001). They had less shockable rhythm (42% vs 61%, P < 0.001). After multivariate logistic regression, female gender was negatively associated with early coronary angiogram (OR = 0.57, 95%CI 0.41–0.79, P = 0.001). Results after propensity-score matching were consistent (P = 0.02). Among 1157 patients who underwent coronary angiogram, rates of PCI did not differ between men and women (adjusted OR = 1.26, 95%CI 0.87–1.82, P = 0.23). Early invasive strategy was associated with favorable outcome in multivariate logistic regression (OR = 1.43, 95%IC 1.02–2.0, P = 0.04) with no interaction between gender and PCI (P for interaction = 0.11). Association between PCI and outcome was consistent across genders.

Conclusions: After OHCA, women are less likely to undergo early invasive strategy. However, rates of PCI after coronary angiogram do not differ across gender, and the association between PCI and outcome is similar across gender.

Introduction

Out-of-hospital cardiac arrest (OHCA) is a major public health concern, with 200,000–300,000 cases reported annually in the United States,[1,2] or in Europe.[3] Survival rates remain low,[4] but recent data suggest that outcome improved.[5] This improvement is mainly attributable to higher prehospital survival rates,[6] but might be also due to post-resuscitation care. Thus, early invasive strategy (coronary angiogram (CAG) and percutaneous coronary intervention (PCI)) is associated with an improvement in both short and long-term outcomes in OHCA patients.[7,8]

Abbreviations: AED, automated external defibrillator; BLS, basic life support; CAG, coronary angiogram; CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; CT, computerized tomography; CVRF, cardioascular risk factor; ICU, intensive care unit; OHCA, out of hospital cardiac arrest; PCI, percutaneous coronary intervention; PROCAT, Parisian Registry out-of-hospital cardiac arrest; ROSC, return of spontaneous circulation.

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Selection of the best candidates for an early invasive strategy is still debated. By analogy with acute coronary syndromes, gender could influence the management of these patients and particularly the decision for CAG. Important differences have been reported between men and women in management of myocardial infarction.[9,10] Accordingly, an enhanced survival benefit from restoring myocardial perfusion for women compared with men during primary angioplasty has been reported.[11] In the field of OHCA, several gender specificities have been identified,[12–16] but to the best of our knowledge, no data regarding gender differences in the coronary management of survivors of OHCA are available, and studies leading to current guidelines mainly included men.[7,8] The need for specific gender-studies has been recently emphasized.[17] Highlighting gender differences in coronary management of OHCA could lead to specific recommendations for women, and therapeutic strategies could differ according to gender.

We used the large prospective PROCAT (Parisian Registry out-of-hospital cardiac arrest) registry in order to assess the relationship between an early invasive strategy and outcome according to gender in patients admitted after OHCA

Methods

Study setting

In Paris (France), management of OHCA involves mobile emergency units and fire departments.[18] They cover a population of approximately 6.6 million during the day and 2.5 million at night. Upon witnessed call and in suspected cases of OHCA, the closest emergency unit is dispatched on the scene. Out-of-hospital resuscitation is delivered by an emergency team, which includes at least one trained physician in emergency medicine according to the international guidelines.[19] Patients in whom return of spontaneous circulation (ROSC) is achieved are then referred to a tertiary "cardiac arrest center" with an intensive care unit (ICU) and coronary intervention facilities available 24 h a day, 7 days a week. Patients without an obvious extra-cardiac cause are entered into an immediate diagnostic algorithm.

Diagnostic algorithm

Our local algorithm guiding the early imaging strategy has been previously published.[20] It includes CAG, brain and chest Computerized Tomography (CT)-scan. After admission of a patient after resuscitated OHCA, our diagnostic algorithm is based on medical history and clinical symptoms preceding the arrest, and does not depend from the gender:

- If neurological or respiratory symptoms are reported before OHCA: CT-scan is performed first. If CT-scan is unconclusive, CAG is realized then, before admission to ICU.
- In case of cardiovascular symptoms (such as chest pain) or lack of symptoms, CAG is performed first. If CAG is normal or no coronary lesion can be considered responsible for OHCA, a CT-scan is then realized immediately before the patient is transported to the ICU.

Early invasive strategy was defined as coronary angiography, followed by PCI if a coronary lesion is deemed to be the cause of OHCA, in the very first hours following hospital admission, before ICU admission. After the procedure, patients are admitted to the ICU for supportive treatment, which includes therapeutic hypothermia initiated in the ICU (no protocol change during the study). For patients who did not undergo early PCI, the cause of OHCA is evaluated during hospitalization, through multimodal tools (using every clinical, biological, or imaging tests available). Finally, the cause of OHCA is assumed ischemic if the CAG finds an acute coronary occlusion, or if multimodal evaluation and medical consensus across physicians is consistent with an ischemic cause.

The local ethic committee approved the registry and database and its use for clinical research.

Study population

Patients' data were prospectively entered in an ongoing electronic registry database (PROCAT registry) that was created in 2000, and was previously described.[20–22] From January 2000 to December 2013, all consecutive cases of patients, >18 years old, admitted in our closed 24-bed medical ICU of the Cochin Hospital (Paris, France) for OHCA with ROSC, were included in the present analysis. OHCA data were collected according to Utstein recommendations[23] and included age (according to its median), gender, cardiovascular risk factors CVRF (such as hypertension, diabetes mellitus, dyslipidemia, and current smoking), location of cardiac arrest, and initial cardiac rhythm. The time from collapse to basic life support and from basic life support to ROSC, as well as initial administrated epinephrine (mg) were collected. Post-OHCA shock was defined as the need for continuous norepinephrine or epinephrine infusion to maintain mean arterial pressure above 60 mmHg for more than 6 h following restoration of spontaneous circulation (ROSC), despite adequate fluid loading.

Endpoints

The main endpoint was cerebral performance categories scale (CPC) at hospital discharge.[24] Favorable outcome included patients with a good cerebral performance (CPC 1) or a moderate cerebral disability (CPC 2). Unfavorable outcome was defined by a severe cerebral disability (CPC 3), a coma or a vegetative state (CPC 4), or death (CPC 5). The CPC level was prospectively assessed. We also performed sensitivity analysis using survival at discharge as outcome, to stress consistency of our results (ESM 1).

Statistical analysis

This report was prepared in compliance with the STROBE checklist for observational studies.[25] Continuous variables were presented as median and interquartile range, and discrete variables were presented as percentages. We checked the linearity of quantitative variables using fractional polynomial regression. In the absence of linearity, continuous variables were dichotomized according to their median. Missing data account for less than 10% (except regarding CVRF, 12%) and were handled using case-complete analysis (sensitivity analysis using multiple imputations were performed). Regarding main factors (early invasive strategy, PCI, gender, survival, CPC at discharge), there were no missing data. Considering the study period spanned 13 years, we dichotomized the study period (before or after 2007), to assess period effect. Comparisons between groups were made with χ^2 or Fisher's exact tests for discrete variables, and with t-tests for continuous variables.

In the first part, to assess the association between gender and early invasive strategy, factors associated with the use of an early invasive strategy, including gender, were identified using univariate analysis. Multivariate logistic regression analysis was then performed, including factors with $P < 0.15$ in the univariate analysis. Additionally, we performed a sensitivity analysis with propensity score analysis. Baseline characteristics independently associated with gender were identified using a multivariate logistic regression analysis. A propensity score (probability from 0 to 1 of being a man, given baseline characteristics) was established including characteristics with $P < 0.15$. We assessed association between gender and the use of an early invasive strategy through 2 methods: condi-