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Prognosis and lipid profile improvement by a specialized outpatient clinic for acute coronary syndrome patients

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ABSTRACT

Background and aims: Prognosis variations in patients discharged after an acute coronary syndrome (ACS) according to the professionals involved has not been clearly outlined. The aim of our study was to assess the impact on a specific outpatient clinic (SOC).
Methods: We included all consecutive patients admitted for an ACS in a single center. We performed a propensity score matching with all patients discharged from hospital according to whether they were referred to the SOC or not.
Results: From the 1822 patients discharged, 260 couples of well-balanced ACS patients were obtained after propensity score matching. Median follow-up was 43.3 months and cardiovascular mortality rate was 10.4%, all-cause mortality was 13.9% and any MACE 38.2%. Patients attended the SOC had significantly lower rates at all three endpoints. Multivariate analysis results showed how the follow-up in the SOC was associated with significantly lower risk at all endpoints. SOC patients also had significantly lower rate at hospital readmissions and the multivariate analysis identified a negative association between the first cardiovascular readmission and SOC (sHR: 0.26 95%CI 0.18–0.367; $p < 0.01$). Mean LDLc levels at the time of ACS admission was 99.0 (36.7) mg/dl and no difference was observed in patients referred to SOC *vs.* non-referred. Patients followed at the SOC achieved significantly lower LDLc and higher percentage of LDLc <70 mg/dl (56.7% *vs.* 36.7%; $p < 0.01$). SOC follow-up was associated with 44% higher probability of final LDLc <70 mg/dl.
Conclusions: An SOC for ACS patients was independently associated with higher LDLc control and long-term survival.

1. Background

Patients with chronic coronary heart disease are an increasing population due to the large reductions of in-hospital mortality of patients admitted with acute coronary syndromes (ACS) [1,2]. Such advance invariably drives the fact that most patients admitted for an ACS would eventually be discharged and will attend outpatient clinics. Cardiology management of patients admitted for ACS has been associated with better in-hospital outcomes [3,4] and has been largely encouraged by many medical and scientific associations [5,6]. Nonetheless, the role of cardiology specific or specialized outpatient units on post-discharge prognosis variations has been less analyzed [7–10].

Risk factors control [11] and optimization of medical treatments [12,13] have been clearly associated with prognosis improvement although none of these two strategies is widely achieved. Many large clinical registries have highlighted the poor risk factor control in patients with chronic coronary heart disease [14–16] as well as the limitations of prescription of optimal medical treatments [12,13,17]. The aim of our study was to assess the impact of a specialized outpatient clinic (SOC) for patients discharged after an ACS compared to standard-of-care in follow-up prognosis and lipid control.

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2. Materials and methods

2.1. Study design

This is a retrospective study performed in a single center including all consecutive patients admitted with diagnosis of ACS over a time period of 60 months, resulting in a cohort of 1888 patients. The SOC was created for the clinical follow-up of high-risk ACS patients as well as patients with premature ACS, recurrent ACS, non-common causes of ACS, and complex percutaneous coronary intervention (PCI). Patients were referred after hospital discharge according to physicians' criteria. The protocol of SOC is based on a first visit at the outpatient clinic in the first 3 months after hospital discharge to assess risk factors control, medication adherence, and side effects, as well as assessment of symptoms or signs of heart failure or myocardial ischemia. A second visit is scheduled within 3 months if any complication is detected. All patients are scheduled for another visit at month 12 after hospital discharge where dual antiplatelet treatments are usually stopped and all medical treatments and risk factors are re-assessed. In the 12-month visit, patients who did not have any complications are referred to their primary care physicians, but those who had any complication remain in the SOC follow-up program. One physician is responsible for patients' management in the SOC in terms of drug prescription and visits schedule, and works closely with physicians involved in the pacemaker and devices outpatient clinic, as well as physicians responsible for the hospital division, for patients admitted at the cardiology unit.

Risk factors, clinical antecedents, treatments, complementary test and main diagnosis at discharge were collected from all patients by trained medical staff. Following current recommendations, optimal medical treatment (OMT) was codified when patients received these four treatments jointly: antiplatelets, statins, beta-blockers and an angiotensin-converter enzyme inhibitor or angiotensin-receptor blocker [12,18]. Patients were categorized according to their ischemic risk, assessed by the GRACE score, in low risk (<108), intermediate risk (109–140) and high-risk (>140) [19]. Premature ACS is defined when it occurred at age <45 in men or <55 in women [20]. Complex PCI was codified according to current recommendations when revascularization was performed in the three main vessels, used 3 or more stents, more than 60 mm of stents, bifurcations with 2 stents or included treatment of total coronary occlusions [21]. According to previous reports, ICR was defined when at least one of the main coronary arteries or secondary branch >1.5 mm, with significant lesions (>70%), were treated or successfully revascularized [22].

Incidence of post-discharge events is performed by a well-established protocol that achieves very low percentage of lost-to-follow-up [23]. Two staff members review clinical records and, in absence of hospital contact, the electronic medical history is consulted. All physicians in the medical area use a unified electronic resource that collects every contact with the system, either with medical or nurse visits. In case of lack of electronic medical reports, one nurse has been trained for phone contacts aimed to assess all endpoints through follow-up. All medical interventions of patients related to our hospital performed in primary care are made by a single informatics system. Similarly, all emergency calls, visits to the emergency room of the hospital or hospital readmissions are registered in a single informatics application. The vital status was assured by phone calls in absence of medical reports. Cardiovascular mortality is attributed to fatalities directly related to cardiovascular events, such as ACS, heart failure hospitalization or sudden death; non-cardiovascular mortality is coded when another concurrent process is the main cause of fatality, mainly infections, cancer or accidents.

For the antecedent of previous coronary heart disease, patients needed to have a clinical diagnosis of myocardial infarction, stable or unstable angina or angina-driven coronary revascularization. Glomerular filtration rate was estimated from serum creatinine values with the Modification of Diet in Renal Disease Study equation. Previous heart failure was codified if patients had at least one hospitalization with such main diagnosis at discharge-medical report, as well as those with typical signs and symptoms of heart failure who had a compatible imagine diagnosis (X-ray or echocardiogram). The ethics committee of the hospital approved the study protocol and informed consent. Overall estimation of comorbidities was assessed by the Charlson index, adapted for patients with coronary heart disease [24].

Main endpoints for the follow-up were cardiovascular mortality, all-cause mortality and time to first major cardiovascular event (MACE) that included hospitalization for ACS, heart failure, stroke or major bleeding, un-planned revascularization or sudden death. Time to first readmission for cardiovascular cause was also analyzed and we performed an economic estimation on cost savings matching our data on readmissions with the official reports of our institution, to obtain an estimated cost of each patient's resource costs. Lipid control was assessed at the target of low-density lipoprotein cholesterol (LDLc) < 70 mg/dl[25].

2.2. Statistical analysis

Data were processed with IBM SPSS 22.0 and STATA 14.2 statistic packages for MAC. Quantitative variables are presented as mean (SD) and differences were assessed by *t*-Student and Chi-square tests. Qualitative variables are presented as percentages and differences were analyzed by ANOVA test. An analysis of interactions and colinearity between main clinical variables was performed and results were taken under consideration in further analysis. Statistical difference was accepted at $p < 0.05$.

In order to minimize the fact that SOC follow-up was not assigned in a randomization fashion, we obtained a subset of paired patients by propensity score matching. This methodology has been largely described [26] and it equates group characteristics using defined variables to analyze the effect of a single variable or treatment. We applied a greedy 1:1 matching algorithm without replacement and defined optimal matching as a standard deviation of 0.2. We firstly performed a binary logistic regression where the dependent variable was SOC and explanatory variables were age, gender, hypertension, diabetes, dyslipidemia, previous coronary heart disease, heart failure or stroke, GRACE score, revascularization, OMT and Charlson index. Results were used to decide the covariates in the propensity score matching that provided a sample of 260 pairs of patients with the same probability of being assigned to SOC. Predictive capacity of the model used to generate the propensity score was 0.72 (95% CI 0.68–0.75; $p < 0.01$) with a good fit (Hosmer-Lemeshow $p = 0.72$).

Cox regression models were performed for the assessment of major endpoints through follow-up, once proportional risk test were verified. Models was adjusted by all variables that obtained *p* values < 0.1 in the univariate analysis or could have plausible clinical implication; results are presented as hazard ratio (HR) and 95% confidence intervals (95% CI). The model's discriminative accuracy was assessed by the Harrell's C-statistic, while its calibration was tested by the Gronnesby and Borgan test. First cardiovascular hospital admission and LDLc control could be affected by patients' death and, therefore, the usual techniques for time-to-event analysis would provide biased or un-interpretable results due to the presence of competing risks. With the aim of avoiding such effects, we applied the model introduced by Fine and Gray [27] to test the competing events and results of the multivariate analysis as sub-