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Percutaneous coronary intervention reduces mortality in myocardial infarction patients with comorbidities: Implications for elderly patients with diabetes or kidney disease☆,☆☆

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ABSTRACT

Background: Percutaneous coronary intervention (PCI) reduces mortality in most myocardial infarction (MI) patients but the effect on elderly patients with comorbidities is unclear. Our aim was to analyse the effect of PCI on in-hospital mortality of MI patients, by age, sex, ST elevation on presentation, diabetes mellitus (DM) and chronic kidney disease (CKD).

Methods: Cohort study of 79,791 MI patients admitted at European hospitals during 2000–2014. The effect of PCI on in-hospital mortality was analysed by age group (18–74, ≥75 years), sex, presence of ST elevation, DM and CKD, using propensity score matching. The number needed to treat (NNT) to prevent a fatal event was calculated. Sensitivity analyses were conducted.

Results: PCI was associated with lower in-hospital mortality in ST and non-ST elevation MI (STEMI and NSTEMI) patients. The effect was stronger in men [Odds ratio (95% confidence interval) 0.30 (0.25–0.35)] than in women [0.46 (0.39–0.54)] aged ≥75 years, and in NSTEMI [0.22 (0.17–0.28)] than in STEMI patients [0.40 (0.31–0.5)] aged <75 years. PCI reduced in-hospital mortality risk in patients with and without DM or CKD (54–72% and 52–73% reduction in DM and CKD patients, respectively). NNT was lower in patients with than without CKD [≥75 years: STEMI = 6(5–8) vs 9(8–10); NSTEMI = 10(8–13) vs 16(14–20)]. Sensitivity analyses such as exclusion of hospital stays <2 days yielded similar results.

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Conclusions: PCI decreased in-hospital mortality in MI patients regardless of age, sex, and presence of ST elevation, DM and CKD. This supports the recommendation for PCI in elderly patients with DM or CKD.

1. Introduction

Current guidelines recommend percutaneous coronary intervention (PCI) for most patients with ST elevation acute myocardial infarction (STEMI) or with non ST elevation acute coronary syndrome (NSTEACS) [1–3]. In STEMI, PCI is advised in all patients in the first 12 h after symptom onset, the earlier the better [1,2]. In NSTEACS, the treatment strategy is to perform PCI during the first 72 h if patients have at least one intermediate risk criterion such as diabetes mellitus (DM), chronic kidney disease (CKD), or reduced left ventricular ejection fraction, among others [3].

The recommendation stands for elderly patients (aged 75 years and older), as it has been shown that STEMI and NSTEACS patients have reasonable outcomes when treated invasively [4–7]. In elderly acute coronary syndrome (ACS) patients, individual circumstances including life expectancy, quality of life, and comorbidities should also be taken into account [2,6,8–11]. While comorbidities are one of the decisional factors that determine an invasive strategy in elderly ACS patients, there is no specific advice concerning elderly patients with comorbidities in current guidelines.

Two of the most common comorbidities in elderly ACS patients are DM and CKD, each one affecting 20–30% of this population [12]. Management of STEMI patients with DM should be the same as for individuals without DM [2]. In NSTEACS patients with DM, an invasive strategy is recommended over non-invasive management [3]. Advisement on managing CKD is only available for NSTEACS patients, in which coronary angiography and revascularization, if needed, are recommended after assessment of benefits, risks, and the severity of renal dysfunction [3,13]. There are no studies comparing survival outcomes after revascularization in elderly ACS patients with and without DM and only one small study has analysed revascularization and mortality in association with renal function in elderly NSTEACS patients [14].

The goal of this study was to provide robust data on the effect of PCI on in-hospital mortality risk in patients with myocardial infarction (MI) with and without ST elevation, by age group, sex, and presence of DM or CKD.

2. Methods

2.1. Data source

The EUROTRACS (EUROpean Treatment & Reduction of Acute Coronary Syndromes cost analysis) database contains data on 94,474 ACS patients admitted in European hospitals during 2000–2014. The EUROTRACS database includes 3 European registries of ACS patients (EURHOBOP [15] – EURopean Hospital Benchmarking by Outcomes in ACS Processes-, Euro Heart Survey I [16] and Euro Heart Survey II [17]), and 6 national/regional registries (Greek HELIOS [18] –Hellenic Infarction Observation Study- MI registry; regional health information system from Lazio [19], Italy; Spanish MASCARA [20] – Manejo del Síndrome Coronario Agudo. Registro Actualizado- ACS registry; MONICA/KORA [21] MI registry from Augsburg, Germany; REGICOR [22] – REgistre GIroní del COR- MI registry from Girona, Spain; and the Italian MCH-ESREFO [23] registry). Main characteristics of the registries are described in Suppl. Table 1. The EUROTRACS Study was approved by the Hospital del Mar review committee.

2.2. Design and study population

This was a cohort study of patients from the EUROTRACS database designed as a matched analysis by a propensity score (PS) for PCI use. Patients were followed during their hospital stay for the occurrence of all-cause mortality. We included all EUROTRACS component registries with information on diagnosis and on the required covariates, and selected patients aged ≥18 years with a diagnosis of MI. As shown in Suppl. Fig. 1 79,791 MI patients were included.

2.3. Study variables

The primary outcome of the study was in-hospital mortality and the exposure of interest was use of PCI during hospitalization, independently of the type (primary, rescue, elective, other) and the time since onset of symptoms. Other variables of interest included age, sex, initial presence of ST elevation, DM, and CKD. Age was categorized in 2 groups: 18–74 and ≥75 years. Presence of DM was based on previous history, and CKD was based on previous history and on the estimated glomerular filtration rate (eGFR). The eGFR was calculated with admission creatinine using the 4-component Modification of Diet in Renal Disease equation [24]. CKD was assumed if previous history or if the eGFR was <60 mL/min/1.73 m^2.

2.4. Potential confounders of PCI use

To select potential confounders of PCI use to construct the PS, we explored the association of pre-PCI variables with PCI use and with the outcome (in-hospital mortality). We selected all available pre-PCI variables associated with PCI use and in-hospital mortality once variables with excessive missing values were excluded from statistical analysis. Ten variables were selected: age, sex, hypertension, DM, CKD, previous history of MI, admission Killip class, initial presence of ST elevation, year of treatment (categorized in 3 groups: 2000–2004, 2005–2009 and 2010–2014), and hospital characteristics such as university hospital, on-site catheterization laboratory and coronary surgery.

2.5. Statistical analysis

Variables with >50% of missing values in the EUROTRACS database and/or 100% missing in any of the component registries were excluded from the analysis. The remaining variables had <4% of missing data in the EUROTRACS database. Missing data was completed with 20 multiple imputations by chained equations [25]. Analyses were carried out in the 20 multiple imputed datasets and then estimates were combined.

Demographic and clinical data were summarized by the mean and standard deviation (SD) or by frequencies for continuous (normally distributed) or categorical variables, respectively. Means and frequencies were compared between groups using ANOVA or chi-squared tests, respectively.

Four separate analyses were undertaken to examine the in-hospital mortality risk of patients who received PCI compared to those who did not: by age group and sex; by age group and ST elevation; by age group, ST elevation, and DM; and by age group, ST elevation, and CKD.

The PS was computed as the predicted values of PCI use from a logistic regression model taking the selected potential confounders as the predictor variables. The variables used to stratify risk (age, sex, ST elevation, DM, and CKD, depending on the analysis) were not included in the PS used in the specific stratified analysis. Every patient receiving PCI was matched with one patient who did not receive PCI, according to their PS values within a caliper of 0.2 of the logit-transformed PS SD [26]. Balance of covariates was assessed by computing the standardized differences between patients who did or did not receive PCI [27].

In-hospital mortality and its 95% confidence interval (CI) were calculated for each group under analysis. The odds ratio (OR) of in-hospital mortality and its 95% CI for patients receiving PCI compared to the rest were calculated using conditional logistic regression. These models were adjusted for the variables not sufficiently balanced after PS matching (standardized difference > 10%). In-hospital mortality estimates and ORs between groups were compared using the chi-square test and z-scores, respectively, and adjusted for multiple comparisons with the Bonferroni correction.

The number needed to treat (NNT) to prevent one in-hospital death was calculated as the inverse of the absolute risk reduction as follows: $1/(M_{nonPCI} - M_{PCI})$, where M_{nonPCI} and M_{PCI} are the average in-hospital mortality rates predicted by a non-conditional logistic model as if all individuals received PCI and as if none of them received PCI, respectively. Matched pairs were introduced in the non-conditional model as a random effects factor.

Several sensitivity analyses were carried out. First, patients who stayed <2 days at the hospital were excluded. Second, stratification was used instead of matching. OR of in-hospital mortality for patients receiving PCI compared to the rest were obtained by PS tertile, age group (18–59, 60–69, 70–79, and >79 years), and sex/ST elevation using mixed effects logistic regression. PS models included the same variables as the PS of the main analysis except for age. Models for in-hospital mortality included PCI use, the specific PS (logit-transformed), age, thrombolysis, coronary artery bypass grafting (CABG), and maximum Killip class during hospitalization as fixed effects, and country as a random effect. Finally, analyses were undertaken using non-conditional instead of conditional