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Comparison of long-term outcomes in STEMI and NSTE-ACS after coronary stent placement: an analysis in a real world BMS and DES population

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ABSTRACT

Background/Objectives: The prognostic difference between STEMI and NSTE-ACS after coronary stent placement remains unclear. We aimed to compare the short- and long-term event rates in patients presenting with ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation acute coronary syndrome (NSTE-ACS) after percutaneous coronary intervention (PCI) with either bare-metal stents (BMS) or drug-eluting stents (DES).

Methods: Between 2000 and 2005 a total of 1749 STEMI and 1921 NSTE-ACS patients received either a BMS or DES in consecutive real world cohorts. Descriptive statistics and multivariate survival analyses were applied to compare the event rates in STEMI and NSTE-ACS during 4 years follow-up.

Results: NSTE-ACS patients had significantly higher clinical and angiographic risk profiles at baseline and were treated with less optimal medical therapy during follow-up. At 4 years follow-up, all-cause mortality was significantly higher in STEMI compared to NSTE-ACS after coronary stent placement (17.4% vs. 14.3%; HR 1.60, 95% CI 1.24–2.07). In a landmark analysis no difference was seen in all-cause mortality among STEMI en NSTE-ACS between 1 month and 4 years follow-up (HR 1.10, 95% CI 0.81–1.51). Cardiac death was more prevalent in STEMI patients, while the 4-year cumulative incidences of any myocardial infarction, any coronary revascularization, target lesion revascularization and definite stent thrombosis were similar in both ACS groups.

Conclusions: Patients presenting with STEMI have a worse long-term prognosis compared to NSTE-ACS after coronary stent placement, due to higher short-term death rates. However, after the first month STEMI and NSTE-ACS patients have a comparable long-term survival.

1. Introduction

Currently, no clear answer can be given to the prognostic difference between STEMI and NSTE-ACS after coronary stent placement. Previous studies used highly variable PCI rates with relatively low percentages of coronary stent placement [1–10]. The main focus in these studies was mortality and little attention has been given to other important end points, like myocardial infarction (MI), coronary revascularisation and stent thrombosis. Coronary angiography and subsequent revascularization are intended to prevent ischemic recurrences, death or other complications in the short and long-term. In STEMI and NSTE-ACS percutaneous coronary intervention (PCI) has superior benefits over a conservative strategy with an additional reduction of target vessel revascularization (TVR) when routine coronary stent implantation was performed [11–14]. In addition, significant reduction in mortality and myocardial infarction was reported in observational studies when drug-eluting stents (DES) were applied [15–17].

In order to compare the short- and long-term outcomes in STEMI and NSTE-ACS after coronary stent placement we used the data of the RESEARCH [18] (Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital) and T-SEARCH [19] (Taxus–Stent Evaluated At Rotterdam Cardiology Hospital) registry. We also used the data of a historical BMS registry [20] to investigate a potential impact of stent type. These registries of "all-comer" PCI patients may provide a good answer to the prognostic difference between STEMI and NSTE-ACS after DES or BMS placement.

2. Materials and methods

2.1. Patient population and study design

Between January 1, 2000 and December 31, 2005, a total of 7217 percutaneous coronary interventions were performed in our institution using either a BMS or DES. Procedures in which two different stent types were used were excluded. When restricting to primary

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cases presenting with an ACS, 3670 patients underwent PCI (Fig. 1). From January 2000 until April 16th 2002, percutaneous coronary interventions were performed using exclusively BMS. From April 16, 2002 until February 23, 2003, percutaneous coronary interventions were performed using sirolimus-eluting stents (Cypher®, Cordis Corp., Johnson & Johnson, Warren, NJ, USA), as part of the RESEARH registry [18], and from February 23, 2003 to December 31, 2005, percutaneous coronary interventions using exclusively paclitaxel-eluting stents (TAXUS™ Express2™ or Liberté™, Boston Scientific, Natick, MA, USA), as part of the T-SEARCH registry [19]. Of all DES implantations (n = 2248), 46.4% were presenting with a NSTE-ACS and 53.6% with a STEMI. Of all BMS implantations (n = 1422), 61.7% were presenting with a NSTE-ACS and 38.3% with a STEMI. In total 1749 STEMI patients were treated with a BMS (n = 545) or DES (n = 1204) and 1921 NSTE-ACS patients were treated with a BMS (n = 877) or DES (n = 1044). The study protocol was approved by the local ethics committee and performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients.

Baseline, clinical and procedural patient characteristics were prospectively entered into a dedicated database. All procedures were performed according to standard clinical guidelines, and every patient was pre-treated with aspirin and ≥300 mg clopidogrel [21]. The post-PCI antiplatelet regimen consisted of ≥80 mg aspirin lifelong and ≥75 mg clopidogrel for at least 1 month if BMS were used, ≥3 months for patients with SES, and ≥6 months for patients with PES. Periprocedural glycoprotein IIb/IIIa antagonists were used at the discretion of the treating interventional cardiologist.

2.2. Definitions and clinical endpoints

NSTE-ACS and STEMI were defined according the ESC guidelines on myocardial revascularization [11]. Hypertension was defined as a blood pressure ≥140 mm Hg systolic and ≥90 mm Hg diastolic or based on the current use of antihypertensive treatment. Hypercholesterolemia was defined as a fasting total serum cholesterol level >5.5 mmol/L or the use of lipid lowering drugs at the time of the procedure [22]. Diabetes was defined as treatment with either an oral hypoglycaemic agent, insulin, or through diet. Procedural success was defined as the achievement of <50% diameter stenosis (visual assessment) and Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow in all lesions intended to treat. Cardiogenic shock was defined as systolic blood pressure persistently <90 mm Hg or the need for inotropic support or intra-aortic balloon pump implantation to maintain a systolic blood pressure >90 mm Hg with evidence of organ end failure and increased left ventricular filling pressures.

The primary endpoint was all-cause mortality at 4 years follow-up. Secondary endpoints were cardiac death, any myocardial infarction, any coronary revascularization, target lesion revascularization and definite stent thrombosis. The composite of patient-oriented endpoints was also considered as a separate secondary end point, defined as the occurrence of all-cause death, any myocardial infarction or any coronary revascularization at 4 years follow-up. Myocardial infarction was diagnosed by recurrent typical clinical symptoms, the development of ST-segment elevation or left bundle branch block on electrocardiography with a creatine kinase myocardial band rise of 3× the upper limit of normal and/or positive troponin levels in the laboratory values. Target lesion revascularization was defined as a repeat intervention (surgical or percutaneous) to treat a luminal stenosis within the stent or in the 5-mm distal or proximal segments adjacent to the stent [23]. Any coronary revascularization was defined as all surgical and percutaneous, target lesion, target vessel, and non–target vessel revascularizations after the index PCI. Definite stent thrombosis was defined as angiographically documented thrombosis with TIMI grade 0 or 1 flow or the presence of a flow limiting thrombus, accompanied by acute symptoms, irrespective of whether there has been an intervening re-intervention [24]. The timing of stent thrombosis was categorized as early (within 30 days after implantation), late (between 30 days and 1 year), or very-late (more than 1 year) [25].

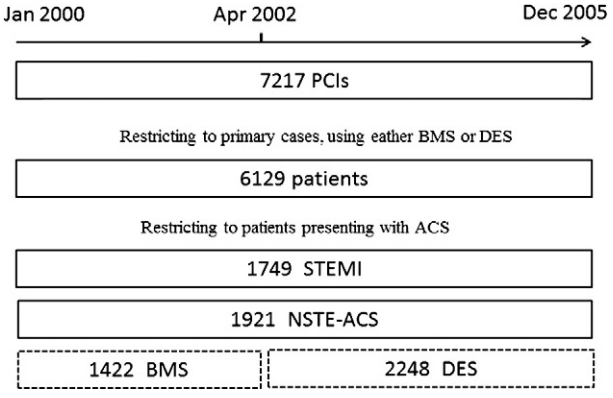

Fig. 1. Enrolment flowchart of the study population primary cases indicates the number of patients undergoing their first intervention in the study period (2000-2005). BMS were implanted between January 2000 and April 2002. Drug-eluting stents were used between April 2002 and December 2005. ACS = acute coronary syndrome, BMS = bare-metal stent(s), DES = drug-eluting stent(s), NSTE-ACS = non-ST-segment elevation acute coronary syndrome, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction.

2.3. Follow-up

The municipal civil registries were contacted yearly until October 2007 to document the survival data of all treated patients from each cohort. Causes of death were obtained from the Central Bureau of Statistics, The Hague, The Netherlands. Causes of death were classified according to the International Classification of Diseases and Related Health Problems (ICD-10) [26]. For the present analysis, death from ischemic heart disease (I-20, I-25), sudden cardiac death (I-46), sudden death undefined (R-96) or death from heart failure (I-50) were considered to be cardiac. All living patients received a questionnaire, consisting of queries regarding repeat hospital stay and major adverse cardiac events. In case of a suspected event, the medical records and coronary angiographies from our hospital or the referring institution were systematically reviewed by 2 independent experienced interventional cardiologists. Follow-up status was complete for 97.5% of the STEMI patients and 99.2% of the NSTE-ACS patients.

2.4. Statistical analysis

Continuous variables are presented as mean ± standard deviation and categorical variables are expressed as percentages. Comparisons among the baseline and procedural characteristics in NSTE-ACS and STEMI were performed using Pearson's Chi-Square test for categorical variables and independent-samples *T*-test for continuous variables. The Kaplan–Meier method was used to study the cumulative incidence of events over time, whereas log rank tests were applied to evaluate differences between the NSTE-ACS and STEMI group. Patients lost to follow-up were considered at risk until the date of last contact, at which point they were censored. Subsequently, we repeated this analysis for the patients who survived the first month in a landmark analysis. Cox proportional-hazards regression analyses were applied to evaluate the relationship between PCI indication (STEMI versus NSTE-ACS) and the incidence of our primary and secondary outcomes. Baseline clinical and procedural characteristics listed in Table 1 were considered potential confounders. The number of co-variables in the final model was limited to a maximum of 1 clinically relevant confounder per 10 events for each specific endpoint. Final results are presented as hazard ratios with 95% confidence intervals. These analyses were also applied as a landmark analysis of data from 30 days to 4 years follow-up. To evaluate a possible heterogeneity in treatment effects an interaction term between PCI indication and stent type was included in our model with the use of Cox regressions. Cox proportional-hazards regression analyses were also applied to evaluate the relationship between stent type (BMS versus DES) and the incidence of our primary and secondary outcomes. Pearson's Chi-Square tests were used to compare the hierarchical patient counts of our patient-oriented composite in STEMI and NSTE-ACS patients. All statistical tests were two-tailed, and a p-value <0.05 was considered statistically significant. All statistical analyses were performed with SPSS for Windows version 17.0 (SPSS, Inc., Chicago, Illinois).

3. Results

3.1. Population and treatment characteristics

A total of 1749 STEMI patients and 1921 NSTE-ACS patients were treated with either a BMS or DES between January 1, 2000 and December 31, 2005. The mean age of the study population was 61.4 years and 73.4% were male. Baseline clinical and procedural characteristics are presented in Table 1. NSTE-ACS patients were older and cardiovascular risk factors like diabetes (DM), hypertension and hypercholesterolemia were more prevalent in this patient group. Previous PCI, CABG and MI were also more prevalent in NSTE-ACS patients compared to STEMI patients. Coronary angiography of NSTE-ACS patients showed more multivessel disease and a higher lesion complexity. NSTE-ACS patients were treated with more stents and larger stent diameters.

Medical therapy during follow-up was available for 73% of the study population and is presented in Table 2. NSTE-ACS patients used significantly less ace-inhibitors/angiotensin II antagonist, beta-blockers and statins during follow-up. Aspirin, oral nitrates and calcium channel blockers were used more frequently in NSTE-ACS patients during follow-up. Clopidogrel was used for a longer time period after the index PCI in STEMI patients compared to NSTE-ACS patients, because STEMI patients were more often treated in a DES cohort.

3.2. Long-term outcomes

Survival data were available for 98% of the patients and median follow-up was 3.7 years. Cumulative survival curves of all-cause