International Journal of Cardiology 176 (2014) 885–890

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Impact of previous coronary artery bypass surgery on clinical outcome after percutaneous interventions with second generation drug-eluting stents in TWENTE trial and Non-Enrolled TWENTE registry

Hanim Sen [a], Ming Kai Lam [a], Kenneth Tandjung [a], Marije M. Löwik [a], K. Gert van Houwelingen [a], Martin G. Stoel [a], Hans W. Louwerenburg [a], Frits H.A.F. de Man [a], Gerard C.M. Linssen [b], Jan G. Grandjean [c], Carine J.M. Doggen [d], Clemens von Birgelen [a,d,*]

[a] Department of Cardiology, Thoraxcentrum Twente, Medisch Spectrum Twente, Enschede, The Netherlands
[b] Department of Cardiology, Ziekenhuisgroep Twente, Almelo and Hengelo, The Netherlands
[c] Department of Cardiothoracic Surgery, Thoraxcentrum Twente, Medisch Spectrum Twente, Enschede, The Netherlands
[d] Health Technology and Services Research, MIRA — Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

ARTICLE INFO

Article history:
Received 3 March 2014
Received in revised form 6 June 2014
Accepted 5 August 2014
Available online 13 August 2014

Keywords:
Drug-eluting stent
Percutaneous coronary intervention
Previous coronary artery bypass grafting
TWENTE trial
Non-enrolled TWENTE registry

ABSTRACT

Background: Patients with previous coronary artery bypass grafting (CABG) who underwent percutaneous coronary intervention (PCI) have an increased repeat revascularization rate, but data on contemporary second-generation drug-eluting stents (DES) are scarce.
Methods: We evaluated 1-year clinical outcome following secondary revascularization by PCI in patients of the TWENTE trial and non-enrolled TWENTE registry, and compared patients with previous CABG versus patients without previous CABG.
Results: Of all 1709 consecutive patients, 202 (11.8%) had previously undergone CABG (on average 11.2 ± 8.5 years ago). CABG patients were older (68.5 ± 9.4 years vs. 64.1 ± 10.7 years, $P < 0.001$) and more often had diabetes (28.7% vs. 20.9%, $P = 0.01$) and previous PCI (40.1% vs. 19.8%, $P < 0.001$) compared to patients without previous CABG. Nevertheless, a higher target vessel revascularization (TVR) rate following PCI in the CABG patients (9.4% vs. 2.3%, $P < 0.001$) was the only significant difference in clinical outcome at 1-year follow-up (available for 99.6%). Among CABG patients, the TVR rate was significantly higher in patients treated for graft lesions ($n = 65$; 95.4% in vein grafts) than in patients treated for native coronary lesions only ($n = 137$) (18.5% vs. 5.1%, $P = 0.002$). Among 1638 patients with PCI of native coronary lesions only, there was only a non-significant difference in TVR between patients with previous CABG versus patients without previous CABG (5.1% vs. 2.3%, $P = 0.08$).
Conclusions: Patients with previous CABG showed a favorable safety profile after PCI with second-generation DES. Nevertheless, their TVR rate was still much higher, driven by more repeat revascularizations after PCI of degenerated vein grafts. In native coronary lesions, there was no such difference.

1. Introduction

In patients with previous coronary artery bypass graft surgery (CABG), progression of atherosclerosis and degeneration of bypass grafts may lead to secondary revascularizations — in the majority of patients by means of percutaneous coronary intervention (PCI) [1,2]. So far, most PCI studies with comprehensive assessment of patients with a history of CABG were performed in the era of bare metal and early generation drug-eluting stents (DES) [3–5], while only limited data are available from second-generation DES.

Second-generation DES with more bio-compatible coatings have been shown to be safe and efficacious in several randomized clinical trials with limited exclusion criteria. An example of such a trial is the randomized TWENTE trial, which studied a broad population of patients undergoing PCI with second-generation DES [6]. In parallel with the randomized TWENTE trial, we performed a registry which assessed patients who also underwent PCI with second-generation DES and were eligible for enrollment in the randomized trial but were not enrolled for various reasons [7]. The pooled population of the randomized trial and the non-enrolled registry represent a consecutive series of patients with stable angina or non-ST-elevation myocardial infarction

Abbreviations: DES, drug-eluting stent; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; TVR, target vessel revascularization; Non-ST-ACS, non-ST-elevation acute coronary syndromes; CABG, coronary artery bypass grafting.

* Corresponding author at: Department of Cardiology, Thoraxcentrum Twente, Medisch Spectrum Twente, Haaksbergerstraat 55, 7513 ER Enschede, The Netherlands. Tel.: +31 53 4872108; fax: +31 53 4872107.
E-mail address: c.vonbirgelen@mst.nl (C. von Birgelen).

http://dx.doi.org/10.1016/j.ijcard.2014.08.036
0167-5273/

(MI) who underwent a PCI at Thoraxcentrum Twente during a period of 26 months. A total of 11% of patients of the TWENTE trial and 17% of the non-enrolled TWENTE registry had a history of CABG.

In the present study, we analyzed the pooled population of the TWENTE trial and non-enrolled TWENTE registry to assess the impact of previous CABG on individual clinical endpoints following PCI with second-generation DES. In addition, we investigated the potential impact of lesion location (i.e. in bypass graft versus native coronary artery) on clinical outcome.

2. Methods

2.1. Study design and patient population

We performed a pooled analysis of the prospective TWENTE trial and TWENTE non-enrolled registry. We analyzed 1709 consecutive patients, undergoing PCI with second-generation DES for stable angina or non-ST-elevation acute coronary syndromes (Non-ST-ACS) at Thoraxcentrum Twente in Enschede, The Netherlands. Patients were treated between June 2008 and August 2010. To compare baseline characteristics and clinical outcome between patients with previous CABG versus patients without previous CABG, the patient population was sub-divided, based on history of CABG. Details of the randomized TWENTE trial have previously been reported [6]. In brief, TWENTE (ClinicalTrials.gov NCT01066650) is a randomized, prospective, controlled, patient-blinded DES trial, comparing Resolute ZES and Xience V EES stents after 1:1 randomization in 1391 patients. Patients with stable angina or non-ST-ACS were eligible, and few exclusion criteria were applied [6]. The non-enrolled TWENTE registry has also been reported in detail; it included 318 eligible patients who were not enrolled during the course of the randomized TWENTE trial [7].

2.2. Intervention, medication, electrocardiography, and laboratory testing

Five experienced interventional cardiologists, of whom each had individual experience of at least 4000 PCI procedures as a first operator, performed all PCI procedures by the use of standard techniques. Pharmacological therapy before, during, and after PCI as well as systematic laboratory testing and ECG assessment have previously been described and did not differ between the TWENTE trial and TWENTE non-enrolled registry [6]. Angiographic analyses were performed offline at Thoraxcentrum Twente.

2.3. Definitions of clinical endpoints

Definitions of clinical endpoints have been fully described in the main report on the randomized TWENTE trial [6]. In general, the definitions of the Academic Research Consortium (ARC) were applied [8,9]. Cardiac death was defined as any death due to proximate cardiac cause, unwitnessed death and death of unknown cause, and all procedure-related deaths, including those related to concomitant treatment.

Myocardial infarction (MI) was defined by any creatine kinase concentration of more than twice the upper limit of normal with elevated confirmatory cardiac biomarkers [9]. Further classification and location of MI have been previously described [6]. Target vessel-related MI was related to the target vessel or could not be related to another vessel. Target vessel and target lesion revascularization (TVR and TLR) were defined as any repeat coronary revascularization of the target vessel or target lesion by re-PCI or surgery. Stent thrombosis was defined according to ARC [8].

2.4. Data acquisition and follow-up

In-hospital adverse events were recorded prior to discharge. One-year follow-up data after PCI of all patients were obtained at visits in outpatient clinics or, if not feasible, by telephone follow-up or questionnaire. For any event trigger, all clinical information available from the referring cardiologist, general practitioner, and hospital involved was gathered. The adjudication of adverse clinical events was performed by an independent CRO (Cardialysis, Rotterdam, The Netherlands).

2.5. Statistical analysis

Data analysis was performed with the Statistical Package for Social Sciences (SPSS; version 17, SPSS Inc., Chicago, IL). Data were reported as frequencies and percentages for dichotomous and categorical variables and as mean ± standard deviation for continuous variables. The chi-square test and the Fisher's exact test were used to compare frequencies as appropriate. The Student's *t*-test was used to compare normally distributed continuous variables. The Kaplan–Meier method was used to calculate the time to clinical endpoints and the Log-rank test was used to compare between-group differences. A two-sided P value < 0.05 was considered statistically significant.

3. Results

3.1. Characteristics of patients, lesion, and PCI procedures

Of all 1709 patients, 202 (11.8%) had a history of CABG (Table 1). These patients were older (68.5 ± 9.4 vs. 64.1 ± 10.7 years), more often males (79.7% vs. 71.1%), and suffered more often from diabetes (28.7% vs. 20.9%), chronic renal failure (6.4% vs. 3.1%), and heart failure (6.9% vs. 3.2%) than patients without a history of CABG. In addition, patients with previous CABG had more often a history of MI (40.6% vs. 33.5%) and PCI (40.1% vs. 19.8%). Despite the – on average – higher cardiovascular risk profile, patients with previous CABG were more often treated for stable angina, rather than for acute coronary syndromes (55.0% vs. 47.4%; Table 1). At discharge, patients with previous CABG did not differ from patients without previous CABG in use of statins (90% vs. 86%, P = 0.18), ACE inhibitors (31% vs. 29%, P =0.42), beta blockers (82% vs. 82%, P = 0.85), acetylsalicylic acid (99% vs. 99%, P = 0.76), and thienopyridine (99% vs. 99.5%, P = 0.13) (Table 1).

Patients with previous CABG versus patients without history of previous CABG differed in several lesion characteristics and procedural details (Table 1), including more index PCI for in-stent restenosis (11.4% vs. 5.9%) and type C lesions (62.4% vs. 48.7%) — a difference that was mainly related to bypass graft lesions. Patients with previous CABG less often underwent PCI of lesions in left anterior descending coronary arteries (17.3% vs. 55.4%).

Of the 202 patients with previous CABG, 65 (32.2%) patients were treated for at least one lesion in a bypass graft, of which 62 (95.4%) were located in saphenous vein grafts and 3 (4.6%) in arterial grafts. PCI was performed on average 11.2 ± 8.5 years after CABG. Time between CABG and PCI differed significantly between patients treated for bypass lesions versus native coronary lesions only (9.6 ± 8.6 vs. 14.3 ± 7.5 months, P < 0.001). Fig. 1 shows the distribution of patients in time intervals from CABG to index PCI for 65 patients with PCI in graft lesions versus 132 patients with PCI in native coronary lesions only.

3.2. Clinical outcome

One-year follow-up was available in 1703 (99.6%) patients. Table 2 shows the clinical outcome of patients with previous CABG versus patients without previous CABG. The only difference was a higher TVR rate in patients with previous CABG (9.4% vs. 2.3%, P < 0.001) (Fig. 2A) and explains the significantly higher rate of dual anti-platelet therapy continuation beyond 12 months (12.7% vs. 4.5%, P < 0.001) in these patients.

Table 3 presents the outcome of the 202 patients with previous CABG; it shows that *the TVR rate was much higher in 65 patients who were treated for bypass graft lesions* than in the 137 patients who were treated for native coronary lesions only (18.5% vs. 5.1%, p = 0.002) (Fig. 2B).

As shown in Table 4, among 1638 patients who underwent PCI for the treatment of native coronary lesions only (irrespective of a history of CABG), there was a non-significant difference in TVR between patients with previous CABG versus patients without previous CABG (5.1% vs. 2.3%, P = 0.08).

4. Discussion

4.1. Major findings

In this pooled analysis of 1709 consecutive patients of the prospective TWENTE trial and the TWENTE non-enrolled registry, patients with previous CABG had a 4-fold higher 1-year risk of TVR after PCI than patients without previous CABG. Differences in the incidence of cardiac death, target vessel-related MI, and stent thrombosis showed the same trend, but were non-significant. Within patients who underwent PCI for native coronary lesions only, there also appeared to