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Bioresorbable scaffold implantation in patients with indication for oral anticoagulation: A propensity matched analysis

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ABSTRACT

Objectives: To examine ischemic and bleeding outcomes in patients on triple antithrombotic therapy (TAT) compared with dual antiplatelet therapy (DAPT) after the implantation of bioresorbable scaffolds (BRS).
Background: The optimal antithrombotic regimen in patients undergoing percutaneous coronary intervention that have an indication for oral anticoagulation is unclear, in particular among those undergoing BRS implantation.
Methods: Consecutive patients of a single-center, all-comers BRS registry were included. Patients were followed up after 30 days, 6 and 12 months, and thereafter yearly. Outcome parameters were target vessel failure (TVF), major adverse cardiac events (MACE) including target lesion revascularization (TLR), scaffold thrombosis (ST), death, myocardial infarction, and any bleeding as defined by BARC. Patients on TAT were matched to patients on DAPT.
Results: A total of 607 patients were included. Fifty-five patients receiving TAT were matched with 165 patients treated with DAPT. Acute coronary syndrome was an indication for coronary angiography in 50.9% vs 50.4% groups ($p = 0.97$). Major adverse cardiac events occurred in 16.4% of TAT patients vs. 8.9% DAPT patients ($p = 0.12$), TLR in 5.5% vs. 1.9% ($p = 0.17$), ST in 3.6% vs. 1.9% ($p = 0.46$), and TVF in 3.6 vs. 1.9% ($p = 0.46$). Patients died in 7.3% in the TAT group vs. 5.1% in the DAPT group ($p = 0.26$). No severe bleeding was recorded in either of the groups.
Conclusion: There was no difference in bleeding or ischemic events between the patients on TAT and those on DAPT after BRS implantation. The high rate of scaffold thrombosis in all of these patients, however, is not negligible.

1. Introduction

Patients undergoing percutaneous coronary intervention (PCI) with stent implantation require dual antiplatelet therapy (DAPT) consisting of aspirin and a $P2Y_{12}$ inhibitor [1]. This antithrombotic treatment is temporary and necessary to reduce ischemic events [2]. Approximately 5–10% of these patients are also on oral anticoagulation (OAC) for indications such as atrial fibrillation or a prosthetic valve [3].

It has been shown that DAPT after stenting reduces the incidence of stent thrombosis (ST) better than conventional anticoagulant therapy [4]. On the other hand, OAC therapy is superior to clopidogrel plus aspirin for prevention of vascular events in patients with atrial fibrillation at high risk of stroke [5]. Therefore, patients who undergo stent implantation and have an indication for OAC are treated with triple antithrombotic therapy (TAT) [1,6]. Multiple combinations are possible. TAT, however, has a higher bleeding risk [7], and ultimately hemorrhagic complications might offset all ischemic benefits [8]. To make the issue even more complex, potent $P2Y_{12}$ inhibitors (prasugrel and ticagrelor) have become the standard of care in patients with acute coronary syndrome, and new oral anticoagulants are now available. Of note, the current guideline on myocardial revascularization does not recommend the combination of a potent $P2Y_{12}$ inhibitors as part of triple therapy [1].

The bioresorbable scaffolds (BRS) have recently emerged as a potentially major breakthrough [9]. BRS offer a transient vessel support to resist acute recoil but are fully resorbed within approximately three years, thereby potentially overcoming long-term limitations of metallic drug-eluting stents. Patients treated with BRS who have an indication for OAC have not been well examined, as chronic treatment with anticoagulants has been an exclusion criterion for most BRS studies [10,11]. Recent investigations have shown that BRS implantation is associated with an increased risk of ST [12].

Abbreviations: BRS, bioresorbable scaffold; DAPT, dual antiplatelet therapy; MACE, major adverse cardiac event; ST, stent or scaffold thrombosis; TAT, triple antithrombotic therapy; TLF, target lesion failure; TLR, target lesion revascularization; TVF, target vessel failure; TVR, target vessel revascularization.

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Accordingly, we aimed to examine ischemic and bleeding outcomes in patients undergoing BRS implantation who were on TAT and compare results with those on DAPT.

2. Methods

2.1. Study design and population

All consecutive patients of a single-center, all-comers BRS registry at the Medizinische Klinik I, University of Giessen, Giessen, Germany, were included in this study. Patients were enrolled irrespective of their clinical presentation. Exclusion criteria were age < 18 years and lesions that appeared unsuitable for BRS implantation. All patients gave written informed consent. If patients were not competent to give consent, it was obtained from their legal guardians. The investigation conforms to the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of the University of Giessen (AZ 264/12).

2.2. Percutaneous coronary intervention

PCI was performed in accordance with standard clinical practice using the radial approach, if technically feasible, or the femoral approach. Unfractionated heparin (70 U/kg body weight) was administered immediately prior to the procedure. Lesion preparation was initiated with intracoronary application of nitroglycerine. Deployment of the novolimus-eluting BRS (DESolve, Elixir Medical Corporation, Sunnyvale, California, USA) was accomplished using slow balloon inflation: 1 atm over 10 s, 2 atm over 10 s, then 2 s per atm. Deployment of everolimus-eluting BRS (Absorb BVS, Abbott Vascular, Santa Clara, CA, USA) was performed with an initial pressure of 2 atm and increasing pressure in increments of 2 atm every 5 s until fully deployed. The recommended pressure was not exceeded, and maximum pressure was maintained for 20–30 s. The use of a debulking device or intravascular imaging modalities was left to the operator's discretion.

Patients received a loading dose of aspirin 250–500 mg before PCI, unless the patients were already on chronic aspirin therapy, and thereafter 100 mg oral daily. A loading dose of clopidogrel (600 mg), prasugrel (60 mg), or ticagrelor (180 mg) was followed by a maintenance dose of clopidogrel (75 mg/day), prasugrel (10 mg/day), or ticagrelor (90 mg twice/day). The duration of DAPT and TAT was left to the operator's discretion.

2.3. Follow-up

Patients who had been successfully treated qualified for the entry in the study. They were followed up via telephone according to a standardized interview after 30 days and 6 and 12 months, and thereafter yearly. Major adverse cardiac events (MACE) included death, any myocardial infarction, emergency coronary artery bypass surgery, and ischemia-driven percutaneous or surgical target lesion revascularization (TLR). Target vessel failure (TVF) was defined as death from myocardial infarction, re-occlusion of the target vessel, and revascularization of the target vessel (TVR). Target lesion failure (TLF) comprised the combination of target vessel myocardial infarction, death from known cardiac cause, TLR, and any unexplained death within the first 30 days (probable scaffold thrombosis). The Academic Research Consortium (ARC) criteria were applied for the definition of scaffold thrombosis [13]. The standardized bleeding definitions of the Bleeding Academic Research Consortium (BARC) were used to characterize bleeding events [14].

2.4. Statistical analysis

Given the differences in baseline characteristics in eligible patients in the registry treated with either DAPT or TAT, propensity-score matching was used to identify a cohort with similar characteristics. Matching was performed with the following parameters: age (≥65 years or <65 years), multi-vessel disease, left ventricular ejection fraction (≥40% or <65%), scaffold length (equality accepted ± 5 mm), and clinical presentation (ACS or stable angina). Patients treated with TAT were matched in a 1:3 ratio to the DAPT patients. Categorical variables are given as absolute values and percentages. Continuous variables are expressed as means and standard deviations. Chi-square and Fisher's exact test were used for comparison of categorical variables, and Student's *t*-test or the Wilcoxon rank-sum test was applied for continuous variables. *p* values < 0.05 were considered statistically significant. Kaplan–Meier methods were used to derive the event rates at follow-up and to plot time-to-event curves. Statistical difference between the survival curves was assessed by a log-rank test. Statistical analysis was performed using IBM SPSS Statistics (SPSS Statistics 23.0.0.2, IBM Deutschland GmbH, Ehningen, Germany).

3. Results

3.1. Patient characteristics

A total of 607 patients were enrolled in the BRS registry. After propensity-score matching, 55 patients treated with TAT were compared with 165 patients treated with DAPT. Patients were treated between December 2012 and July 2015. Patients in the TAT group were aged 67.7 ± 8.2 years and in the DAPT group 66.0 ± 9.1 years (Table 1). The two groups did not differ significantly with respect to age, sex, and cardiovascular risk profile. Approximately one third had diabetes mellitus (34.5% vs. 35.4%, $p = 0.90$) that was not treated with insulin in most of the cases (22.2% vs. 38.0%, $p = 0.16$). Significantly more patients with chronic kidney disease were found in the TAT group (23.6% vs. 12.0%, $p < 0.04$); however, patients with TAT were on dialysis no more frequently than patients in the DAPT group (1.8% vs. 0.6%, $p = 0.43$).

Table 1
Baseline characteristics.

	TAT ($n = 55$)	DAPT ($n = 165$)	*p*
Age (years)	67.6 ± 8.2	66.0 ± 9.1	0.09
Male sex (%)	83.6	75.9	0.23
Body mass index (kg/m^2)	28.4 ± 4.6	28.3 ± 4.6	0.89
Hypertension (%)	90.9	88.6	0.64
Hyperlipoproteinemia (%)	67.3	67.1	0.98
Diabetes (%)	34.5	35.4	0.90
IDDM (%)	22.2	38.0	0.16
Current smoker (%)	21.8	31.0	0.19
Family history (%)	27.3	29.7	0.73
Chronic kidney disease (%)	23.6	12.0	0.04*
Dialysis (%)	1.8	0.6	0.43
History of POAD (%)	7.3	8.9	0.72
Prior percutaneous intervention (%)	45.5	45.2	0.97
Prior myocardial infarction (%)	20.0	27.8	0.25
Prior coronary artery bypass graft (%)	14.5	8.2	0.18
Prior stroke/transient ischemic attack (%)	5.0	7.0	0.70
History of chronic obstructive pulmonary disease (%)	14.5	10.8	0.45
Atrial fibrillation (%)	87.3	0	<0.001*
CHA_2DS_2-VASc score	3.5 ± 1.1	3.5 ± 1.2	0.91
HAS-BLED score	1.8 ± 0.5	1.8 ± 0.5	0.89
Left ventricular ejection fraction (%)	54.3 ± 10.1	55.5 ± 11.3	0.41
Clinical indication			
Stable angina (%)	45.6	45.6	0.98
ST-elevation myocardial infarction (%)	12.7	19.0	0.29
Non-ST-elevation myocardial infarction (%)	18.2	20.9	0.67
Unstable angina (%)	20.0	10.8	0.08
Number of diseased vessels			0.94
1 (%)	16.4	17.1	
2 (%)	43.6	41.1	
3 (%)	40.0	41.8	

Abbreviations: TAT, triple antithrombotic therapy; DAPT, dual antiplatelet therapy; IDDM, insulin dependent diabetes mellitus; POAD, peripheral occlusive arterial disease.
* Significant difference between DAPT und TAT groups.

3.2. Indications for anticoagulation therapy

The indication for OAC in the TAT group was in 87.3% atrial fibrillation, 3.6% apex aneurysm, 3.6% pulmonary embolism/venous thrombosis, 1.3% antiphospholipid syndrome, and 4.2% other reasons. The estimated risk of stroke as assessed by the CHA_2DS_2-VASc-score [15] was the same for the two groups (3.45 ± 1.12 vs. 3.47 ± 1.22, $p = 0.91$) and bleeding risk as estimated by the HAS-BLED-score was also not different (1.78 ± 0.53 vs. 1.78 ± 0.53, $p = 0.89$).

3.3. Coronary lesions

Approximately half of the patients presented with acute coronary syndrome as an indication for coronary angiography (50.9% in TAT group vs 50.4% in DAPT group, $p = 0.97$). Single-vessel disease was present in only 16.4% in the TAT group vs. 17.1% in the DAPT group. The predominant lesion site was the LAD in 40.0% vs. 43.7% (Table 2). Lesions were of de novo-type in the majority (89.1% vs. 91.8%, $p = 0.55$). The treated segments typically did not include bifurcations (0% vs. 3.8%, $p = 0.14$). Lesions were classified using the criteria advocated by the American College of Cardiology/American Heart Association [16] and tended to be more complex in the TAT group (Table 2).

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