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Procedural and clinical outcomes after use of the glycoprotein IIb/IIIa inhibitor abciximab for saphenous vein graft interventions

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ABSTRACT

Background: Percutaneous coronary intervention (PCI) of saphenous vein grafts (SVG) poses a high-risk for distal coronary thromboembolic events. Glycoprotein IIb/IIIa inhibitors are frequently used in hope of reducing the impact of this, although the safety and efficacy of these drugs to improve outcomes in this setting are understudied.
Methods: Patients were included if they had prior coronary artery bypass surgery and subsequently underwent PCI of ≥1 SVG graft at a Dutch academic center between 1997 and 2008. These patients were matched 1:1 based on peri-procedural use of abciximab using a propensity-score matching algorithm based on 17 variables. Conditional logistic regression and Cox regression stratified on matched pairs were performed to evaluate the association between abciximab use and MACCE (the composite measure of mortality, myocardial infarction, stroke and repeat revascularization) at 30 days and up to 1 year.
Results: The composite of 30-day MACCE occurred in 18 patients (15.3%) in the abciximab group and 16 patients (13.6%) in the propensity matched control group (OR: 1.13, 95% CI: 0.57–2.21, $p = 0.73$). At 1-year follow-up, MACCE rates were also similar (32.5% vs. 33.9%, HR: 0.97, 95% CI: 0.59–1.59). Major bleeding (BARC types 3a–c) was higher in the abciximab group (11.9% vs. 4.2%, OR: 2.80, 95% CI: 1.01–7.77). Ischemic outcomes did not differ among patients with acute coronary syndromes.
Conclusion: The use of intravenous abciximab was not associated with improved clinical outcomes up to 1-year among patients undergoing SVG PCI, but was related to more bleeding.

1. Introduction

Although coronary artery bypass grafting (CABG) surgery is an effective treatment for patients with multi-vessel disease, long-term efficacy is limited by graft failure and progression of native coronary artery disease [1,2]. Significant stenosis or occlusion of saphenous vein grafts (SVG) occurs in about half of all patients at 10 years post-surgery frequently requires repeat interventions [3,4]. As SVG grafts are generally very large compared with native coronary arteries and lack side branches, stenosis or occlusion results in large plaque burden and thrombus formation throughout the graft, making subsequent percutaneous coronary intervention (PCI) not only more difficult, but also subject to a greater potential for peri-procedural myocardial infarction due to showering of atheromatous and thrombotic debris in the distal coronary bed [5,6]. In theory, a number of adjunctive therapies have potential to lower the risk of these peri-procedural complications and include the use of embolic protection devices, thrombus aspiration catheters and glycoprotein IIb/IIIa inhibitors. Of these only embolic protection devices have been shown to reduce these procedure-related complications.

While the clinical utility of glycoprotein IIb/IIIa inhibitors during PCI is established among patients undergoing PCI of native coronary arteries, its efficacy/effectiveness in patients undergoing SVG interventions remains unknown. Accordingly, we performed a retrospective analysis to evaluate the effectiveness of abciximab in improving clinical outcomes of patients undergoing PCI of at least one SVG lesion.

2. Methods

2.1. Study population and data collection

We studied data on consecutive patients who underwent PCI for ≥1 SVG lesion at the Academic Medical Center–University of Amsterdam, a tertiary referral center in the Netherlands, between January 1st 1997 and December 31st 2008. Intravenous abciximab (Reopro®, Janssen Biologics, Leiden, the Netherlands) was administered in the catheterization laboratory to patients who underwent PCI. Patients were treated with unfractionated heparin (5000 IU) or low-molecular weight heparin, aspirin and, approved since 2004, also clopidogrel before PCI.

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Table 1
Baseline and angiographic characteristics before and after propensity score matching.

	Unadjusted			After PS matching		
	Abciximab ($n = 133$)	No abciximab ($n = 230$)	Stand diff	Abciximab ($n = 118$)	No abciximab ($n = 118$)	Stand diff
Demographics						
Age, yrs	70 ± 10	69 ± 9	9.5	69 ± 9	70 ± 8	3.7
Male	90.2	79.6	35.8	89.0	88.1	2.8
BMI	26.7 ± 4.0	26.9 ± 4.1	4.6	26.7 ± 3.2	26.5 ± 3.2	6.3
ACS	46.6	31.3	31.6	43.2	41.5	3.4
Yrs since CABG	13 ± 5	11 ± 6	24.8	13 ± 5	13 ± 6	3.2
CV history						
Diabetes	29.3	26.1	7.1	28.0	28.0	0.0
Hypertension	37.6	43.5	12.1	38.1	39.0	1.7
eGFR	82 ± 27	82 ± 26	0.9	83.8	82.1	6.3
PAD	24.8	18.1	19.6	23.6	21.8	5.4
Prior stroke/TIA	27.7	23.3	14.0	25.8	25.7	0.3
Prior MI	70.7	60.9	21.5	71.2	69.5	3.7
LVEF ≤ 30%	20.3	11.7	21.2	16.9	15.3	4.2
Angiographic						
Ostial lesion	16.5	15.7	2.4	16.1	15.3	2.3
Stenosis grade	93.7 ± 8.3	93.5 ± 8.4	3.4	93.7 ± 6.0	93.5 ± 6.2	3.4
Lesion length	17.5 ± 8.5	16.9 ± 10.6	3.4	17.5 ± 8.5	16.9 ± 10.6	3.4
ASP/EPD	33.1	32.2	1.8	33.1	32.2	1.8
IABP/Impella	8.3	3.0	18.9	5.1	5.1	0.0

Data are presented as number and percentage or mean and standard deviation. Abbreviations: PS = propensity score, BMI = body mass index, ACS = acute coronary syndrome, IABP = intra-aortic balloon pump, GFR = glomerular filtration rate, PAD = peripheral arterial disease, TIA = transient ischemic attack, MI = myocardial infarction, LVEF = left ventricular ejection fraction, ASP/EPD = aspiration catheter and/or embolic protection device.

The choice of procedural strategies, i.e. the use of catheters, guidewires, stents and other equipment, abciximab and embolic protection devices, was left to the discretion of the operator. Information on all-cause mortality was synchronized with electronic records from the national population registry. Additional follow-up information for non-fatal cardiac events was obtained at 1 year after the initial event by written questionnaire sent to all patients. When major cardiac and cerebrovascular events were reported, follow-up data were completed using hospital and outpatient charts. Peri-procedural bleeding data were obtained by collecting blood sample scores, transfusion count and bleeding related information from electronic medical records.

2.2. Outcomes of interest and definitions

The primary outcome of interest was a composite of all-cause mortality, stroke, myocardial infarction or repeat revascularization (MACCE) at 30-day and 1-year follow-up. Secondary outcomes were mortality at 1-year follow-up and the individual components of the composite endpoint at 30 days. Additionally, we also compared procedural outcomes, including major bleeding events during hospitalization. Death, defined as all cause mortality, was determined using hospital records and the Dutch population registry. For procedural MI in stable and unstable angina, creatine kinase-MB (CKMB) had to be greater than 3 times the upper reference limit of normal. In patients with acute ST-segment elevation MI (STEMI) or non-STEMI, re-infarction was defined by a re-elevation of at least 20% of the previously stable or decreasing CKMB values. Repeat revascularization was defined as any re-PCI or CABG during the follow-up period. Major bleeding (types 3a–c) was defined according to the BARC definitions [7].

2.3. Statistical analysis

Given that the use of abciximab was not random, we performed propensity score matching among patients who underwent SVG PCI to reduce the effects of treatment selection bias. The propensity score (or the probability for assignment to abciximab) was constructed using multivariable logistic regression from available demographics, clinical, angiographic and procedural characteristics (see Table 1). Patients who underwent SVG PCI with administration of abciximab in the catheterization laboratory were matched in a 1 to 1 ratio with patients who underwent SVG PCI without abciximab. A nearest neighbor-matching algorithm without replacement on the logit of the propensity score using a caliper width equal to 0.25 standard deviations of the logit of the propensity score was used. After propensity score matching we tested whether the balance on the covariates was achieved using standardized differences and assessment of global balance using Hansen and Bowers's overall balance test ($p = 1.00$) [8]. Comparisons for peri-procedural outcomes were performed using McNemar's test for binomial outcomes or paired T-test for continuous variables. Comparisons for 30-day clinical outcomes were performed using conditional logistic regression analyses accounting for the matched nature of the propensity score matched sample. The Kaplan–Meier method was used to create event curves for the composite primary endpoint as well as for all-cause mortality and Cox proportional hazard regression analyses stratified on matched pairs were used to examine differences in these outcomes up to 1 year after PCI. Lastly we explored association of abciximab use on outcomes among patients with stable angina or ACS, and among those who underwent PCI with or without the use of embolic protection devices (EPD) or aspiration catheters (AC). Statistical analyses were performed with IBM SPSS Statistics

Table 2
Procedural characteristics and peri-procedural outcomes.

	Abciximab ($n = 118$)	No abciximab ($n = 118$)	*p*-Value
Procedural characteristics			
Clopidogrel (pre-loading)	45.5 (60)	54.5 (72)	0.12
Low molecular weight heparin use	25.4 (30)	16.1 (19)	0.08
Stent use			0.73
Balloon angioplasty	19.5 (23)	24.6 (29)	
Bare metal stent	68.6 (81)	66.9 (79)	
Covered stent	6.8 (8)	3.4 (4)	
EPC stent	0.8 (1)	0.8 (1)	
Drug-eluting stents	4.2 (5)	4.2 (5)	
Total stent length	22.6 ± 12.0	21.8 ± 12.5	0.69
Number of stents used	1.1 ± 0.4	1.1 ± 0.3	0.41
Stent diameter	3.9 ± 0.5	3.8 ± 0.7	0.68
Peri-procedural outcomes			
Residual stenosis ≤20%	91.5 (108)	89.8 (106)	0.65
Post TIMI 3 flow	85.6 (101)	87.3 (103)	0.70
Acute occlusion	0.0 (0)	1.7 (2)	0.50
Major bleeding	11.9 (14)	4.2 (5)	0.031