Lack of Peri-Procedural Myocardial Necrosis Reduction from Abciximab in Patients on Dual Antiplatelet Therapy Revascularized with Rotational Atherectomy

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Abstract

Rotational atherectomy allows plaque remodeling in severely calcified lesions and, prior to the adoption of clopidogrel as standard therapy, small trials showed that abciximab reduces transient hypoperfusion associated with the procedure. However, no studies have evaluated it among patients receiving dual antiplatelet therapy. This study aimed to evaluate whether abciximab reduces procedure-related myocardial injury in a non-selected population of patients receiving dual antiplatelet therapy. The study comprised a retrospective review of a non-selected cohort of 139 consecutive procedures of rotational atherectomy performed in patients pre-treated with dual antiplatelet therapy. Abciximab was administered in 48 (34.5%) patients, whereas 91 (65.5%) did not receive it. The only difference between groups was a higher rate of diabetes mellitus in the abciximab group (89% vs. 51%, \(p=0.001\)). The rate of procedural complications was 10.5% for patients with abciximab vs. 6.2% for patients without (\(p=0.537\)). After 24 hours, the peak of biomarkers of myocardial damage (CKmb and TnT) did not differ, and the rate of procedure-related myocardial injury was 23.9% with abciximab and 20.7% without (\(p=0.664\)). In a restricted analysis to diabetic patients (n=84), the rate of myocardial injury was 27.5% with abciximab vs. 18.6% without, \(p=0.435\). After adjusting by clinical and procedural parameters in a logistic regression model, abciximab use did not confer any significant reduction on procedure-related myocardial injury. In conclusion, in a non-selected cohort of patients receiving dual antiplatelet therapy, the administration of abciximab in the setting of rotational atherectomy did not reduce the incidence of procedure related myocardial injury.

Keywords: Abciximab; Antiplatelet therapy; Rotational atherectomy; Coronary

Introduction

Coronary calcium is commonly found, being present in 50% to 80% of individuals and increasing with age [1-3]. In the setting of percutaneous coronary interventions (PCI), the presence of severely calcified lesions difficult the dilatation and may result in stent under expansion; therefore, severely calcified lesions are associated with a greater complication rate and worse long-term results [4-6]. To deal with this limitation, rotational atherectomy (RA) allows plaque remodeling and facilitates stent implantation with a higher success and lower complication rates [7,8].

In this context, the use of abciximab during RA has been shown to reduce procedural morbidity as well as the incidence, extent and severity of transient hypoperfusion [9,10]. However, this evidence is supported by small trials performed prior to the adoption of clopidogrel as the standard therapy in patients undergoing PCI [11,12]. Therefore, the role of abciximab in the current scenario of rotational atherectomy in patients receiving dual antiplatelet therapy has not been assessed.

This study was conducted to evaluate whether abciximab is associated with a reduction in procedure-related myocardial injury, in a consecutive series of patients pretreated with clopidogrel who underwent RA and stent implantation in severely calcified lesions.

Methods

Study population

The study population comprised a retrospective review of all consecutive procedures of RA performed in the cardiology department of a university centre, in a time period of 36 months. RA was chosen as the treatment option by the interventionist, after confirming the presence of severely calcified lesions and prior to any lesion dilatation attempt. Severely calcified lesion was defined according to the SYNTAX classification [13], as the presence of persistent multiple opacifications of the vascular wall visible in more than one projection and completely surrounding the vessel of the area of the lesion. All the patients received treatment with 150-300 mg/day of acetyl salicylic acid and clopidogrel (300 mg as loading dose and 75 mg/day as maintenance dose), at least 24 hours before the procedure according to guidelines [14,15].

Rotational atherectomy procedure

A 0.09-inch guide wire was used directly or after exchange using a coaxial microcatheter or balloon. RA was carried out using the Rotablator® device (Boston Scientific-Scimed Corp, Natick, MA) at a rotation speed of 140,000-180,000 rpm, with the intention of using just one burr, in relation of less than 0.7 to the artery. Only when a first burr advance did not allow a correct balloon dilatation, a second burr was used. The advances were short (a maximum of 10 seconds), and saline was infused with heparin, nitroglycerin, and verapamil

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during the atherectomy. All the patients received at least one stent after balloon pre-dilatation. DES was used in all cases, except those that showed contraindications for prolonged double antiplatelet therapy. The stent was post dilated when residual stenosis was greater than 20%. Unfractionated heparin (70-100 U/kg) was administered to all the patients and abciximab was applied as a coadjuvant medication at the operator's discretion. When abciximab was required, at operator discretion based on clinical evidence, immediately before the procedure of RA patients received abciximab (0.25 mg/kg of body weight bolus, followed by a 10 µg/kg per minute infusion for 12 hours), plus unfractionated heparin, 70 U/kg.

After the procedure, dual antiplatelet therapy with aspirin (100-300 mg/day) and clopidogrel (75 mg/day) was prescribed for at least 12 months in the case of patients treated with DES, and for at least one month in patients treated with conventional stents.

Angiographic success was defined as a <30% diameter obstruction at the end of the procedure.

Myocardial necrosis and procedural complications

Procedural complication was defined as the occurrence of death, perforation, acute vessel closure, slow reflow (>5 beats to refill the vessel) or significant (>2 mm) branch loss. The presence of myocardial damage was monitored after the procedure, at 8, 12, and 24 hours. Blood samples were processed and the markers of myonecrosis measured were TroponinT (TnT, Roche Diagnostics. Germany), Creatine Kinase (CK) and the MB-fraction (CK-MB). Procedure-related myocardial injury was defined, as recently proposed: “the increase five times upper the normal limits [16], what result in a concentration higher than 0.5 ng/mL”.

Statistical analysis

The continuous variables were expressed as mean ± SD. When non-normal distribution was observed, continuous variables were expressed as median and interquartile range (IQR). The categorical variables were expressed as number and percentages. Comparisons between continuous variables were conducted using t-test (or Mann-Whitney when normal distribution was not assumed). Categorical variables were compared with chi-square (or F-Fisher exact test when normal distribution was not assumed). The statistical analysis was carried out using the SPSS 15.0 software (SPSS-IBM inc., Chicago, IL).

Results

Study population and characteristics

Among the 4832 procedures of PCI performed in the 36 months study period, a total of 139 (2.9%) were RA and represent the study population. Abciximab was used in 48 (34.5%) patients, as co-adjuvant therapy to the RA, and represent the abciximab group. All of 139 patients were on dual antiplatelet therapy at the time of the RA. The indication for the procedure was stable coronary disease in 43 (31%) and acute coronary syndrome in 96 (69%). The main demographic data are shown in Table 1. The mean age was 72 ± 8 years-old, 100 (72%) were men and 84 (60.5%) were patients with diabetes. No statistically significant differences were found between both groups, except for a higher prevalence of diabetes mellitus in the group of patients who received abciximab (50.6% vs 89.4%, p=0.001). The procedure characteristics are shown in Table 2, and no differences were found between patients who received abciximab and those who did not.
The incidence of procedure-related myocardial injury in diabetics was 27.5% in those who received abciximab vs. 18.6% in those who did not receive the drug \((p=0.435)\).

A subanalysis restricted to diabetic patients was also performed. The incidence of procedure-related myocardial injury in diabetics was 27.5% in those who received abciximab vs. 18.6% in those who did not receive the drug \((p=0.435)\).

In a logistic regression analysis including age, gender, hypertension, diabetes, dyslipidemia, abciximab use, stent length, renal dysfunction, burr diameter and unstable condition, only the stent length was predictor of peri-procedural MI (OR 1.026, CI 1.006-1.047; \(p<0.011\)). After adjusting for the aforementioned clinical and procedural parameters, the use of abciximab did not show to reduce periprocedural myocardial injury. In a logistic regression analysis including age, gender, hypertension, diabetes, dyslipidemia, abciximab use, stent length, renal dysfunction, burr diameter and unstable condition, only the stent length was predictor of peri-procedural MI (OR 1.026, CI 1.006-1.047; \(p<0.011\)). After adjusting for the aforementioned clinical and procedural parameters, the use of abciximab did not show to reduce periprocedural myocardial injury.

Discussion

The main finding of this observational study is that the use of abciximab in the setting of RA did not reduce the procedure-related myocardial injury when patients were receiving dual antiplatelet therapy. Previous published studies showed that rotablation induces platelet activation, thus leading to platelet aggregation [18]. Small randomized trials found the benefit of abciximab during rotational atherectomy in reducing procedural morbidity, CK-MB elevation, as well as the incidence, extent and severity of transient hyperperfusion, as assessed by single-photon emission computed tomography [9,10]. Nonetheless, this evidence is prior to the generalization of clopidogrel as coadjuvant therapy. In our study, the administration of intravenous abciximab in patients pretreated with clopidogrel showed no benefit in terms of procedure-related myocardial injury in a population of complex patients/complex lesions. There was no reduction in the peak of biomarkers, which seems to be even higher in those receiving abciximab. This could be attributed to the higher number of diabetics patients in the group who received abciximab. However, in the subgroup of diabetics, this difference was still remarkable. The rate of procedural success and complications was otherwise similar in both groups.

The role of abciximab after clopidogrel pretreatment in patients undergoing PCI has been in discussion with controversial results in different trials [19,20]. Specially striking is the fact that, in patients with diabetes the protective effect of abciximab was absent, and even a higher level of myocardial damage markers was observed. This result is probably explained, in part, by the administration of abciximab in more severe patients due to the non randomized nature of the study, although no benefit was observed in patients with diabetes in previously released clinical trials on non-STEMI patients such as ISAR-REACT 2 [20]. Nonetheless, to the best of our knowledge, this is the first study addressing the effect of abciximab in patients treated with rotablation and dual antiplatelet pretreatment. No other studies exist for comparing the findings of the presented study. Some limitations are recognized, as the non-randomized and single center nature. The non-randomized and retrospective methodology of our study, the number of patients included, as well as the use of abciximab according to operator selection limits the conclusions to be drawn. However, this study provides new findings and improves the knowledge according with the current standard therapy that incorporates dual antiplatelet therapy in all patients. In whole, further confirmatory studies including large populations should be addressed in order to confirm these findings.

Conclusion

In conclusion, this study showed that, in a cohort of patients on dual antiplatelet therapy who underwent coronary percutaneous atherectomy in reducing procedural morbidity, CK-MB elevation, as well as the incidence, extent and severity of transient hyperperfusion, as assessed by single-photon emission computed tomography [9,10].

Nonetheless, this evidence is prior to the generalization of clopidogrel as coadjuvant therapy. In our study, the administration of intravenous abciximab in patients pretreated with clopidogrel showed no benefit in terms of procedure-related myocardial injury in a population of complex patients/complex lesions. There was no reduction in the peak of biomarkers, which seems to be even higher in those receiving abciximab. This could be attributed to the higher number of diabetics patients in the group who received abciximab. However, in the subgroup of diabetics, this difference was still remarkable. The rate of procedural success and complications was otherwise similar in both groups.

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revascularization with rotablation and stent implantation, the administration of abciximab was not associated with a benefit in terms of procedure-related myocardial injury reduction. This is the first study addressing the issue of IIb/IIIa inhibitors as ancillary medication in rotation since the generalization of clopidogrel pretreatment.

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References


