



Planned use of GP IIb/IIIa inhibitors is safe and effective during implantation of the Absorb Bioresorbable Vascular Scaffold[☆]

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ABSTRACT

Bioresorbable Vascular Scaffolds (BVS) have the potential for adaptive vessel remodeling, restoration of vasomotion, and late luminal enlargement, thus allowing them to circumvent target lesion failures associated with bare metal stents (BMS) and drug-eluting stents (DES). However, recent data has shown a concerning increase in BVS-associated scaffold thrombosis (ScT) compared to DES. Upfront administration of GP IIb/IIIa inhibitors (GPIs) has shown to reduce early stent thrombosis (ST) compared to standard of care in BMS and DES. Since the use of GPIs was limited in BVS studies, the effect of GPIs on the rate of BVS-associated ScT is largely unknown. This is the first study investigating whether a planned use of GPIs during implantation of the Absorb BVS represents a safe and effective strategy in reducing ScT. In a retrospective chart review of 22 patients undergoing PCI with BVS implantation and planned GPI administration, no acute ScT, in-hospital MACE, or in-hospital major/minor bleeding events were observed. Bleeding reduction strategies such as shorter GPI infusion and radial access were implemented. This study provides valuable preliminary evidence on the benefit and safety in using planned GPI administration to reduce the incidence of ScT after implantation of BVS.

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1. Introduction

The introduction of the Bioresorbable Vascular Scaffold (BVS) is one of the most revolutionary and anticipated innovations in the field of percutaneous coronary intervention (PCI). The transient nature of the scaffolding allows for adaptive vessel remodeling [1], restoration of vasomotion [2], and late luminal enlargement [3], thereby potentially circumventing target lesion failures such as stent thrombosis (ST), restenosis, and neoatherosclerosis associated with bare metal (BMS) and drug-eluting (DES) stents [4–9]. However, recent trials [10,11], real-world data [12], and meta-analyses [13,14] have shown a concerning increase in scaffold thrombosis (ScT) rates associated with BVS. A potential explanation for the increase in ScT lies in the large strut thickness. The Absorb GT1 (Abbott Vascular, Santa Clara, CA), the first BVS available for clinical use, has a strut thickness of 157 μm compared to the first-generation Cypher (140 μm ; Cordis, Fremont, CA), Taxus Express (132 μm ; Boston Scientific, Natick, MA), and current-generation Xience V DES (81 μm ; Abbott Vascular, Santa Clara, CA). This results in a larger luminal protrusion and can therefore make the loss of laminar flow more frequent with BVS than with DES, thereby resulting in areas of oscillatory shear stress that could promote platelet activation [15,16],

especially when implanted in smaller reference vessel diameters (RVD < 2.25 mm) [17]. The majority of patients in BVS clinical trials received aspirin and an oral P2Y₁₂ inhibitor but no glycoprotein IIb/IIIa inhibitors (GPIs). Real-world studies and registries suggest that GPIs are only used in 6.5–29% of BVS implantations [12,18–20] and therefore the effect of GPIs on the rate of ScT is largely unknown. Case reports describing the occurrence of ScT showed successful restoration of flow with GPI administration [21,22], therefore the use of GPIs during and post-implantation could potentially help reduce ScT. This study investigates whether a judicious and planned use of GPIs during implantation of Absorb GT1 BVS represents a safe and effective strategy in reducing the incidence of ScT after BVS implantation.

2. Methods

This is a retrospective, single-arm, single-center chart review study approved by the Institutional Review Board of CarolinaEast Medical Center. The need for written informed consent for this retrospective analysis of clinically acquired data was waived. Patients were enrolled from December 2016 to February 2017 at the CarolinaEast Medical Center. Eligible subjects were men and women >18 years of age presenting with stable ischemic heart disease (SIHD), non-ST elevation acute coronary syndrome (NSTEMI-ACS), or ST elevation myocardial infarction (STEMI) who underwent PCI by the principal investigators and received the Absorb GT1 BVS and a GPI. GPIs were started at the beginning of each case. Tirofiban was administered as a high dose bolus of 25 $\mu\text{g/kg}$

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followed by an infusion of 0.15 µg/kg/min. For patients with renal insufficiency (creatinine clearance ≤60 mL/min), the infusion was adjusted to 0.075 µg/kg/min. Abciximab was administered as a bolus of 0.25 mg/kg followed by an infusion of 0.125 µg/kg/min. Infusion length was left to the discretion of the operator. Balloon predilatation and postdilatation was performed in all patients. A loading dose of clopidogrel (600 mg) or ticagrelor (180 mg) was administered immediately after BVS implantation for patients not already on a P2Y12 inhibitor.

The site coordinator conducted a retrospective chart review of existing electronic medical record to collect demographic, procedural, and BVS-related data, as well as in-hospital clinical outcomes. Chronic renal insufficiency was defined as serum creatinine >2.5 mg/dL or on hemodialysis. In-hospital major/minor bleeding was defined as a hemoglobin drop of >3 g/dL. The definitions of definite or probable acute ST was outlined by the Academic Research Consortium criteria and used for ScT. MACE was defined as in-hospital cardiac death/all myocardial infarction/target vessel revascularization. In-hospital vascular access site complication (VASC) was defined as any of the following: access site hematoma, arteriovenous fistula, peripheral ischemia, peripheral nerve injury, pseudoaneurysm, or retroperitoneal hemorrhage (definition outlined by the Standardized Definitions for Cardiovascular and Stroke End Point Events in Clinical Trials [23]).

3. Results

A total of 27 Absorb GT1 BVS were implanted in 22 patients who underwent PCI between December 2016 and February 2017 by the principal investigators and received upfront GPI. Tirofiban was administered in all but one patient, who received abciximab.

Patient characteristics and risk factors at baseline are shown in Table 1. All patients were under 85 years of age, with the average patient age being 60, and males comprising 68% of patients. The prevalence of chronic renal insufficiency and diabetes was 23% and 14%, respectively. 45% of patients presented with SIHD, 36% with unstable angina or non-ST elevation myocardial infarction, and 18% with STEMI. Left ventricular ejection fraction was measured in 18 (82%) patients; only 1 patient had ejection fraction <30%.

Procedural characteristics and outcomes are shown in Table 2. 73% of patients underwent radial artery access, while the remainder underwent femoral artery access. One patient had initial access through the radial artery for diagnostics and subsequently underwent femoral artery access for PCI. All but one (95%) patient received bivalirudin; the other patient received unfractionated heparin according to standard

Table 1
Patient characteristics.

	Overall population (n = 22)
Patient characteristics	
Age, years	
<85	22 (100%)
>85	0
Gender	
Male	15 (68%)
Female	7 (32%)
Chronic renal insufficiency	5 (23%)
Diabetes	3 (14%)
LV ejection fraction	
>30%	17 (77%)
<30%	1 (5%)
Not-assessed	4 (18%)
Clinical presentation	
SIHD	10 (45%)
UA/NSTEMI	8 (36%)
STEMI	4 (18%)

Values are n (%).

LV, left ventricular; NSTEMI, non-ST elevation myocardial infarction; SIHD, stable ischemic heart disease; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

Table 2
Procedural characteristics and outcomes.

	Overall population (n = 22)
Procedural characteristics	
Access site	
Radial	16 (73%)
Femoral	7 (32%)
Anticoagulant	
Heparin	1 (5%)
Bivalirudin	21 (95%)
Antiplatelet	
Aspirin	21 (95%)
Clopidogrel or ticagrelor	21 (95%)
Outcomes	
Major/minor bleeding	0
Vascular access site complication	1 (5%)
MACE	0
Acute scaffold thrombosis	0

Values are n (%).

MACE, major adverse cardiac event.

treatment. The average bivalirudin dose was 68 mg, and 9 patients were given a heparin dose ranging from 1500 to 5000 U.

Clopidogrel or ticagrelor were administered in 95% of patients, and aspirin was administered in 95% of patients. There were no occurrences of in-hospital major/minor bleeding, acute ScT, or in-hospital MACE. VASC occurred in 1 patient in the form of a hematoma which resolved prior to discharge.

Scaffold characteristics are shown in Table 3. A total of 27 Absorb GT1 BVS were placed. Three different BVS diameters were used: size 2.5 mm (15%), size 3.0 mm (48%), and 3.5 mm (37%). All target lesions were predilated and postdilated with non-compliant balloons, with the majority of lesions predilated to 16 atm (ranged 8–18 atm) and postdilated to 18 atm (ranged 12–20 atm). None of the BVS were placed in either bifurcations or ostial sites. IVUS was used in 1 case and atherectomy was used in 2 cases. In one of these two cases both IVUS and atherectomy were used.

4. Discussion

This is the first study investigating the impact of routine, upfront use of GPIs during implantation of the Absorb GT1 BVS. Overall, no in-hospital thrombotic/ischemic events or major/minor bleeding events were observed except for one case of hematoma, suggesting that the

Table 3
Scaffold characteristics.

	Overall population (n = 27)
Scaffold characteristics	
Scaffold diameter, mm	
2.5	4 (15%)
3.0	13 (48%)
3.5	10 (37%)
Predilatation	27 (100%)
Predilatation balloon inflation pressure, atm	
8	2 (7%)
10	2 (7%)
12	6 (22%)
16	16 (59%)
18	1 (4%)
Postdilatation	27 (100%)
Postdilatation balloon inflation pressure, atm	
12	1 (4%)
16	9 (33%)
18	13 (48%)
20	4 (15%)
Bifurcation stent placement	0
Ostial stent placement	0
Use of atherectomy during procedure	2 (7%)
Use of IVUS during procedure	1 (4%)

Values are n (%).

IVUS, intravascular ultrasound.

use of GPIs during BVS implantation may be an effective and safe strategy in reducing BVS-associated ScT.

Data from the ABSORB II [11,24] and ABSORB III [17] trials revealed a definite/probable scaffold thrombosis (ScT) rate of 0.9–3.0% in the BVS group compared to 0–0.7% in the DES group, and such increases in ScT risk continue to be reflected in meta-analyses [13,14,25] and registry studies [12]. More specifically, acute (0–1 day) ScT rates of 0.2–0.3%, subacute (2–30 days) ScT rates of 0.3–0.9%, and very late (>365 days) ScT rates of 2% are observed in the BVS group. Acute and subacute (0–30 days) ScT rates were 3.3% vs. 1.5% in lesions with reference vessel diameter (RVD) <2.25 mm compared to those with RVD ≥2.25 mm [17]. Although our study was not powered to detect such low-frequency events, it does show that in a small sample size of patients treated with GPI during BVS implantation, there were no occurrences of acute ScT or MACE. The small molecule GPI, tirofiban, was used in all but one patient. Upfront administration of tirofiban before PCI has been shown to significantly reduce early (0–30 days) and acute thrombosis compared to heparin with dual antiplatelet therapy (aspirin and 600 mg clopidogrel) in BMS and DES [26]. Therefore, upfront administration of a GPI during BVS implantation may help prevent early ScT as supported by our study. This has been previously proposed by Fernandez-Rodriguez et al., who successfully treated a BVS-associated acute ScT using abciximab and thrombectomy in a STEMI patient who was given clopidogrel before and prasugrel after the procedure [21]. Oral P2Y₁₂ inhibitors, including ticagrelor and prasugrel, have been shown to exhibit a delayed onset of action of platelet aggregation inhibition in ACS patients [27–29], particularly in the STEMI population that has reduced gut absorption [30,31]. GPIs, on the other hand, rapidly reach optimal levels of platelet aggregation inhibition [32,33] and have the additional ability to dissolve existing thrombus [22,34,35]. Therefore, GPIs could be useful in reducing periprocedural thrombotic complications such as acute ScT in high-risk patients who are inadequately pre-treated, which has a class I recommendation from the 2014 AHA/ACC NSTEMI-ACS guidelines but has yet to gain universal acceptance. It is of interest to note that in a multicenter study of 1305 BVS patients examining predictors of BVS-associated ScT, the univariate hazard ratio for the use of GPIs was 0.68 (95% CI: 0.24–1.94; $p = 0.471$), suggesting a trend towards lower ScT rates with GPI use [20].

Bleeding remains a concern with the use of GPIs [36]. In this study, no major or minor bleedings were observed. One patient experienced a VASC in the form of a hematoma which resolved prior to discharge. Radial artery access and short (<8 h) GPI infusions were implemented in the majority of patients to minimize bleeding risk. Therefore, the judicious use of GPIs in combination with bleeding reduction strategies represents a contemporary way to maintain the ischemic benefit while reducing the bleeding risk of GPIs [37,38].

The main factor underlying BVS-associated ScT has been attributed to implantation in coronary artery lesions with a RVD <2.5 mm as well as a lack of proper implantation technique, such as intravascular imaging, systematic aggressive lesion preparation with predilatation, and mandatory high-pressure postdilatation [20,39]. High-pressure postdilatation, with the goal to achieve 1:1 BVS:vessel ratio and to minimize scaffold malapposition, was implemented rarely in the Absorb II trial [11] and occasionally in the ABSORB III trial [17], and has been shown to reduce BVS-associated ScT rates [12,20]. Therefore, pre- and postdilatation steps were carried out in all patients of this study, and could contribute to the absence of ScT events observed. Other limitations of this study include its retrospective nature, sample size, lack of control arm, and lack of long-term follow-up. A larger prospective study with an appropriate comparator arm, randomization, and 30-day follow-up is warranted to assess the true impact of GPI use during BVS implantation. A further attempt to maintain an optimal and consistent implantation technique by using intravascular imaging in all patients would further reduce confounding factor.

Currently, the European use of the Absorb BVS has been restricted to centers participating in formal registries in light of the increased ScT

rates. In the United States, operators remain free to use the Absorb BVS as long as proper implantation techniques are in place and implantation in small-diameter vessels is avoided. The risk of ScT, however, may remain despite strict adherence to proper implantation techniques (reported by the AIDA trial investigators at EuroPCR 2017) and therefore this publication provides valuable preliminary evidence on the benefit and safety of using planned GPI administration to mitigate BVS-associated ScT.

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References

- [1] Gogas BD, Serruys PW, Diletti R, Farooq V, Brugaletta S, Radu MD, et al. Vascular response of the segments adjacent to the proximal and distal edges of the ABSORB everolimus-eluting bioresorbable vascular scaffold: 6-month and 1-year follow-up assessment: a virtual histology intravascular ultrasound study from the first-in-man ABSORB cohort B trial. *JACC Cardiovasc Interv* 2012;5:656–65.
- [2] Brugaletta S, Heo JH, Garcia-Garcia HM, Farooq V, van Geuns RJ, de Bruyne B, et al. Endothelial-dependent vasomotion in a coronary segment treated by ABSORB everolimus-eluting bioresorbable vascular scaffold system is related to plaque composition at the time of bioresorption of the polymer: indirect finding of vascular reparative therapy? *Eur Heart J* 2012;33:1325–33.
- [3] Simsek C, Karanasos A, Magro M, Garcia-Garcia HM, Onuma Y, Regar E, et al. Long-term invasive follow-up of the everolimus-eluting bioresorbable vascular scaffold: five-year results of multiple invasive imaging modalities. *EuroIntervention* 2016;11:996–1003.
- [4] Natsuaki M, Morimoto T, Furukawa Y, Nakagawa Y, Kadota K, Yamaji K, et al. Late adverse events after implantation of sirolimus-eluting stent and bare-metal stent: long-term (5–7 years) follow-up of the Coronary Revascularization Demonstrating Outcome study-Kyoto registry Cohort-2. *Circ Cardiovasc Interv* 2014;7:168–79.
- [5] Camenzind E, Wijns W, Mauri L, Kurowski V, Parikh K, Gao R, et al. Stent thrombosis and major clinical events at 3 years after zotarolimus-eluting or sirolimus-eluting coronary stent implantation: a randomised, multicentre, open-label, controlled trial. *Lancet* 2012;380:1396–405.
- [6] Iijima R, Araki T, Nagashima Y, Yamazaki K, Utsunomiya M, Hori M, et al. Incidence and predictors of the late catch-up phenomenon after drug-eluting stent implantation. *Int J Cardiol* 2013;168:2588–92.
- [7] Gada H, Kirtane AJ, Newman W, Sanz M, Hermiller JB, Mahaffey KW, et al. 5-year results of a randomized comparison of XIENCE V everolimus-eluting and TAXUS paclitaxel-eluting stents: final results from the SPIRIT III trial (clinical evaluation of the XIENCE V everolimus eluting coronary stent system in the treatment of patients with de novo native coronary artery lesions). *JACC Cardiovasc Interv* 2013;6:1263–6.
- [8] Smits PC, Vlachojannis GJ, McFadden EP, Royakkers KJ, Wassing J, Joesoef KS, et al. Final 5-year follow-up of a randomized controlled trial of everolimus- and paclitaxel-eluting stents for coronary revascularization in daily practice: the COMPARE Trial (A Trial of Everolimus-Eluting Stents and Paclitaxel Stents for Coronary Revascularization in Daily Practice). *JACC Cardiovasc Interv* 2015;8:1157–65.
- [9] Taniwaki M, Stefanini GG, Silber S, Richardt G, Vranckx P, Serruys PW, et al. 4-year clinical outcomes and predictors of repeat revascularization in patients treated with new-generation drug-eluting stents: a report from the RESOLUTE All-Comers trial (A Randomized Comparison of a Zotarolimus-Eluting Stent With an Everolimus-Eluting Stent for Percutaneous Coronary Intervention). *J Am Coll Cardiol* 2014;63:1617–25.
- [10] Brugaletta S, Gori T, Low AF, Tousek P, Pinar E, Gomez-Lara J, et al. Absorb bioresorbable vascular scaffold versus everolimus-eluting metallic stent in ST-segment elevation myocardial infarction: 1-year results of a propensity score matching comparison: the BVS-EXAMINATION Study (bioresorbable vascular scaffold—a clinical evaluation of everolimus eluting coronary stents in the treatment of patients with ST-segment elevation myocardial infarction). *JACC Cardiovasc Interv* 2015;8:189–97.
- [11] Serruys PW, Chevalier B, Sotomi Y, Cequier A, Carrie D, Piek JJ, et al. Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II): a 3 year, randomised, controlled, single-blind, multicentre clinical trial. *Lancet* 2016;388:2479–91.
- [12] Imori Y, D'Ascenzo F, Gori T, Munzel T, Fabrizio U, Campo G, et al. Impact of postdilatation on performance of bioresorbable vascular scaffolds in patients with acute coronary syndrome compared with everolimus-eluting stents: a propensity score-matched analysis from a multicenter “real-world” registry. *Cardiol J* 2016;23:374–83.
- [13] Cassese S, Byrne RA, Ndrepepa G, Kufner S, Wiebe J, Repp J, et al. Everolimus-eluting bioresorbable vascular scaffolds versus everolimus-eluting metallic stents: a meta-analysis of randomised controlled trials. *Lancet* 2016;387:537–44.
- [14] Lipinski MJ, Escarcega RO, Baker NC, Benn HA, Gaglia Jr MA, Torguson R, et al. Scaffold thrombosis after percutaneous coronary intervention with ABSORB bioresorbable vascular scaffold: a systematic review and meta-analysis. *JACC Cardiovasc Interv* 2016;9:12–24.
- [15] Kawamoto H, Panoulas VF, Sato K, Miyazaki T, Naganuma T, Sticchi A, et al. Impact of strut width in periprocedural myocardial infarction: a propensity-matched

- comparison between bioresorbable scaffolds and the first-generation sirolimus-eluting stent. *JACC Cardiovasc Interv* 2015;8:900–9.
- [16] Kollandaivelu K, Swaminathan R, Gibson WJ, Kolachalama VB, Nguyen-Ehrenreich KL, Giddings VL, et al. Stent thrombogenicity early in high-risk interventional settings is driven by stent design and deployment and protected by polymer-drug coatings. *Circulation* 2011;123:1400–9.
 - [17] Ellis SG, Kereiakes DJ, Metzger DC, Caputo RP, Rizik DG, Teirstein PS, et al. Everolimus-eluting bioresorbable scaffolds for coronary artery disease. *N Engl J Med* 2015;373:1905–15.
 - [18] Cortese B, Buccheri D, Stefanini GG, Mehran R. The contemporary pulse of bioresorbable-scaffold thrombosis among expert operators. *J Am Coll Cardiol* 2016;67:2905–6.
 - [19] Saad M, Abidin A, Thiele H, Desch S, Ibrahim P, Wikstrom G, et al. Bioresorbable vascular scaffolds in a real-world patient population—results from a mid-term angiographic follow-up. *J Interv Cardiol* 2016;29:341–7.
 - [20] Puricel S, Cuculi F, Weissner M, Schmermund A, Jamshidi P, Nyffenegger T, et al. Bioresorbable coronary scaffold thrombosis: multicenter comprehensive analysis of clinical presentation, mechanisms, and predictors. *J Am Coll Cardiol* 2016;67:921–31.
 - [21] Fernandez-Rodriguez D, Brugaletta S, Otsuki S, Sabate M. Acute Absorb bioresorbable vascular scaffold thrombosis in ST-segment elevation myocardial infarction: to stent or not to stent? *EuroIntervention* 2014;10:600 [discussion].
 - [22] Timmers L, Stella PR, Agostoni P. Very late bioresorbable vascular scaffold thrombosis following discontinuation of antiplatelet therapy. *Eur Heart J* 2015;36:393.
 - [23] Hicks KA, Hung HMJ, Mahaffey KW, Mehran R, Nissen SE, Stockbridge NL, et al. Standardized definitions for cardiovascular and stroke end point events in clinical trials. Draft definitions for CDISC; 2014. p. 1–33.
 - [24] Serruys PW, Chevalier B, Dudek D, Cequier A, Carrie D, Iniguez A, et al. A bioresorbable everolimus-eluting scaffold versus a metallic everolimus-eluting stent for ischaemic heart disease caused by de-novo native coronary artery lesions (ABSORB II): an interim 1-year analysis of clinical and procedural secondary outcomes from a randomised controlled trial. *Lancet* 2015;385:43–54.
 - [25] Stone GW, Gao R, Kimura T, Kereiakes DJ, Ellis SG, Onuma Y, et al. 1-year outcomes with the Absorb bioresorbable scaffold in patients with coronary artery disease: a patient-level, pooled meta-analysis. *Lancet* 2016;387:1277–89.
 - [26] Heestermaas AA, Van Werkum JW, Hamm C, Dill T, Gosselink AT, De Boer MJ, et al. Marked reduction of early stent thrombosis with pre-hospital initiation of high-dose Tirofiban in ST-segment elevation myocardial infarction. *J Thromb Haemost* 2009;7:1612–8.
 - [27] Alexopoulos D, Xanthopoulos I, Gkizas V, Kassimis G, Theodoropoulos KC, Makris G, et al. Randomized assessment of ticagrelor versus prasugrel antiplatelet effects in patients with ST-segment-elevation myocardial infarction. *Circ Cardiovasc Interv* 2012;5:797–804.
 - [28] Bonello L, Laine M, Camoin-Jau L, Noiro F, Guieu R, Dignat-George F, et al. Onset of optimal P2Y₁₂-ADP receptor blockade after ticagrelor and prasugrel intake in Non-ST elevation acute coronary syndrome. *Thromb Haemost* 2015;114:702–7.
 - [29] Parodi G, Valenti R, Bellandi B, Migliorini A, Marcucci R, Comito V, et al. Comparison of prasugrel and ticagrelor loading doses in ST-segment elevation myocardial infarction patients: RAPID (Rapid Activity of Platelet Inhibitor Drugs) primary PCI study. *J Am Coll Cardiol* 2013;61:1601–6.
 - [30] Heestermaas AA, van Werkum JW, Taubert D, Seusing TH, von Beckerath N, Hackeng CM, et al. Impaired bioavailability of clopidogrel in patients with a ST-segment elevation myocardial infarction. *Thromb Res* 2008;122:776–81.
 - [31] Bonello L, Berbis J, Laine M, Amero S, Bessereau J, Jacquin L, et al. Biological efficacy of a 600 mg loading dose of clopidogrel in ST-elevation myocardial infarction. *Thromb Haemost* 2012;108:101–6.
 - [32] Danzi GB, Capuano C, Sesana M, Mauri L, Sozzi FB. Variability in extent of platelet function inhibition after administration of optimal dose of glycoprotein IIb/IIIa receptor blockers in patients undergoing a high-risk percutaneous coronary intervention. *Am J Cardiol* 2006;97:489–93.
 - [33] Mardikar HM, Hiremath MS, Moliterno DJ, Mathew R, Arora R, Deo D, et al. Optimal platelet inhibition in patients undergoing PCI: data from the Multicenter Registry of High-Risk Percutaneous Coronary Intervention and Adequate Platelet Inhibition (MR PCI) study. *Am Heart J* 2007;154:344.e1–5.
 - [34] Goto S, Tamura N, Ishida H. Ability of anti-glycoprotein IIb/IIIa agents to dissolve platelet thrombi formed on a collagen surface under blood flow conditions. *J Am Coll Cardiol* 2004;44:316–23.
 - [35] Moser M, Bertram U, Peter K, Bode C, Ruef J. Abciximab, eptifibatide, and tirofiban exhibit dose-dependent potencies to dissolve platelet aggregates. *J Cardiovasc Pharmacol* 2003;41:586–92.
 - [36] Safley DM, Venkitachalam L, Kennedy KF, Cohen DJ. Impact of glycoprotein IIb/IIIa inhibition in contemporary percutaneous coronary intervention for acute coronary syndromes: insights from the National Cardiovascular Data Registry. *JACC Cardiovasc Interv* 2015;8:1574–82.
 - [37] Fung AY, Saw J, Starovoytov A, Densen C, Jokhi P, Walsh SJ, et al. Abbreviated infusion of eptifibatide after successful coronary intervention. The BRIEF-PCI (Brief Infusion of Eptifibatide Following Percutaneous Coronary Intervention) randomized trial. *J Am Coll Cardiol* 2009;53:837–45.
 - [38] Gurm HS, Hosman C, Bates ER, Share D, Hansen BB, Blue Cross Blue Shield of Michigan Cardiovascular C. Comparative effectiveness and safety of a catheterization laboratory-only eptifibatide dosing strategy in patients undergoing percutaneous coronary intervention. *Circ Cardiovasc Interv* 2015;8:e001880.
 - [39] Biscaglia S, Ugo F, Ielasi A, Secco GG, Durante A, D'Ascenzo F, et al. Bioresorbable scaffold vs. second generation drug eluting stent in long coronary lesions requiring overlap: a propensity-matched comparison (the UNDERDOGS study). *Int J Cardiol* 2016;208:40–5.