IMPORTANCE OF PLAQUE MODIFICATION BEFORE CORONARY ARTERY STENTING

Andrejs Erglis,[1,2] Inga Narbute,[1,2] Karlis Strenge,[1] Sanda Jegere[1,2]

[1]Latvian Centre of Cardiology, Pauls Stradins Clinical University Hospital, Riga, Latvia
[2]Latvian Institute of Cardiology, University of Latvia, Riga, Latvia

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ABSTRACT

Lately, the importance of plaque modification prior to stent implantation, particularly the use of cutting and scoring balloons, has been a subject of debate. Pre-treatment or plaque modification before stent implantation is an important step to achieve the best possible result and ensure long term safety and efficacy of percutaneous coronary intervention (PCI). The rationale behind plaque modification is that it may minimise arterial injury and subsequent neointimal proliferation and/or restenosis. Artery scoring before stent implantation gives almost perfect stent apposition with reduced inflation pressure and minimised plaque shifting, it also prevents balloon slippage, alters calcification, increases artery compliance and enhances stent deliverability. Appropriate use of scoring balloons for plaque modification with subsequent stent implantation significantly increases acute and post-procedural results of angioplasty. With bioabsorbable stents and bioresorbable vascular scaffolds, plaque modification will be an essential tool to perform complete 'vessel repair procedures'.

Keywords: Angioplasty, cutting balloon, stent.

INTRODUCTION

Understanding the pathophysiology of atherosclerosis and emerging technological innovations in past decades has greatly advanced the treatment possibilities for coronary artery disease patients. Number of coronary angioplasties with stent implantation has grown substantially. Advances in this technique have expanded the indications for the procedure, dramatically improved safety, and reduced the rate of restenosis.[1-4] Nevertheless, stent-related failure leading to repeated revascularisation and life threatening adverse events is the major limitation of long term success of percutaneous coronary interventions (PCI).[5]

The main pitfall of plain old balloon angioplasty (POBA) was acute vessel occlusion due to recoil or dissection following balloon inflation and high rates of restenosis.[6,7] Introduction of bare metal coronary stents (BMS) dramatically reduced POBA-related issues and prevented negative remodeling of arteries.[8,9] However, BMS efficacy was sabotaged by significant proliferative artery response leading to neointimal hyperplasia-driven restenosis.[10] The era of drug-eluting stents (DES) designed to deliver antiproliferative agents preventing neointimal growth began with promising results regarding reduction of in-stent restenosis.[11] Enthusiasm with growing rate of DES implanted over years worldwide was casted away by concerns of DES-related risk of late and very late stent thrombosis owing to delayed endothelialisation and need for long-term dual antiplatelet therapy.[12,13]

Pretreatment of Plaque

To achieve the best possible result and ensure long-term safety and effectiveness of PCI there are three important steps to consider (Figure 1):

- pre-treatment or plaque modification before stent implantation;
- stent implantation;

- post-treatment to achieve full stent expansion and complete stent apposition.

Lately, the importance of pre-treatment and plaque modification prior to stent implantation, particularly the use of cutting and scoring balloons, has been a subject of debate. The rationale behind plaque modification is that it may minimise arterial injury and subsequent neointimal proliferation and/or restenosis. With regular balloon inflation the entire balloon surface contacts the vessel wall disrupting endothelium, non-uniformly compressing plaque and causing arterial wall damage. Scoring balloon produced injury is strictly localised to the scoring sites sparing most of endothelium, compressing plaque, and reducing trauma to the media layer.[14] Artery scoring before stent implantation gives almost perfect stent apposition with reduced inflation pressure even if very long stents are deployed. In bifurcation treatment it minimises plaque shifting between main branch and side branch, thus helping to avoid side branch stenting. Complex coronary lesion interventions in case of aorto-ostial, small vessel and calcified lesions, can benefit from pre-treatment with scoring devices to minimise balloon slippage, alter calcification, increase artery compliance and enhance stent deliverability. With bioabsorbable stents and bioresorbable vascular scaffolds it will be an essential tool to perform complete 'vessel repair procedures'.

CUTTING BALLOON

Cutting balloon (CB) features several atherotomes (microsurgical blades) depending on balloon diameter. The atherotomes are mounted longitudinally on the outer surface of a balloon and, during expansion, deliver longitudinal incisions in the plaque. The atherotomes deliver a controlled fault line during dilatation to ensure that the crack propagation ensues in an orderly fashion.[15] Cutting balloon (CB) increases vessel lumen diameter in a more controlled fashion and lower balloon inflation pressure is needed thus decreasing the risk of a neoproliferative response and restenosis (Figure 2).

The Cutting Balloon Global Randomised Trial was one of the first large multicentre studies to evaluate the effectiveness of cutting balloon angioplasty in the setting of simple coronary lesions.[16] Only de novo type A or B1 lesions in native coronary arteries, up to 20 mm in length and 2.0 – 4.0 mm in diameter, were eligible. A total of 1,238 patients were enrolled in the study and randomly assigned to treatment with a single cutting balloon inflation (n=617), with

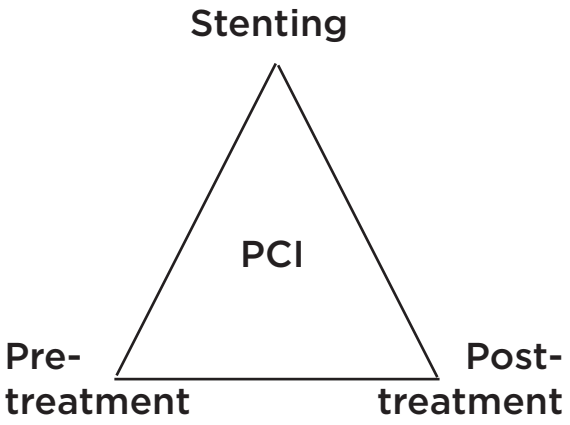

Figure 1. 'Trinity of PCI.

a balloon–artery ratio of 1.1:1 or POBA (n=621). The surgical dilatation using cutting balloon showed no reduction of binary angiographic restenosis rate at 6 months (31.4% for CB and 30.4% for percutaneous transluminal coronary angioplasty (PTCA); p = 0.75). The secondary endpoints of target lesion revascularisation (TLR) and major adverse cardiac events (MACE) after 9 months were also not statistically significantly, although freedom from target vessel revascularisation (TVR) was slightly higher in the CB arm (88.5% vs 84.6%, log-rank p=0.04). The trial showed that CB angioplasty alone was equivalent in safety and efficacy endpoints to POBA, but did not prove superiority. From perspective of plaque modification prior to stent implantation the results of this trial have no considerable value since no stenting was done after treatment with balloon.

Small vessel disease is of particular interest since the advantage of stenting with BMS over balloon angioplasty is moderate and only provisional stenting may be recommended to avoid repeated revascularisations and MACE.[17] The treatment with DES, compared to the BMS, is associated with a significant reduction of angiographic and clinical events.[18,19] However, the small coronary vessel remains an independent predictor of angiographic restenosis even in the DES era and possibly technically challenging due to stent deliverability issues. In a retrospective study of Iijima et al.[20] a total of 327 lesions of small coronaries (less than 2.5 mm in diameter) were treated either by CB (n=87), POBA (n=130) or BMS implantation (n=110). At angiographic follow-up, CB angioplasty resulted in less restenosis comparing to the plain balloon or stenting subgroups (31%, 46.5% and 43.9% respectively; p=0.048). MACE (death, myocardial

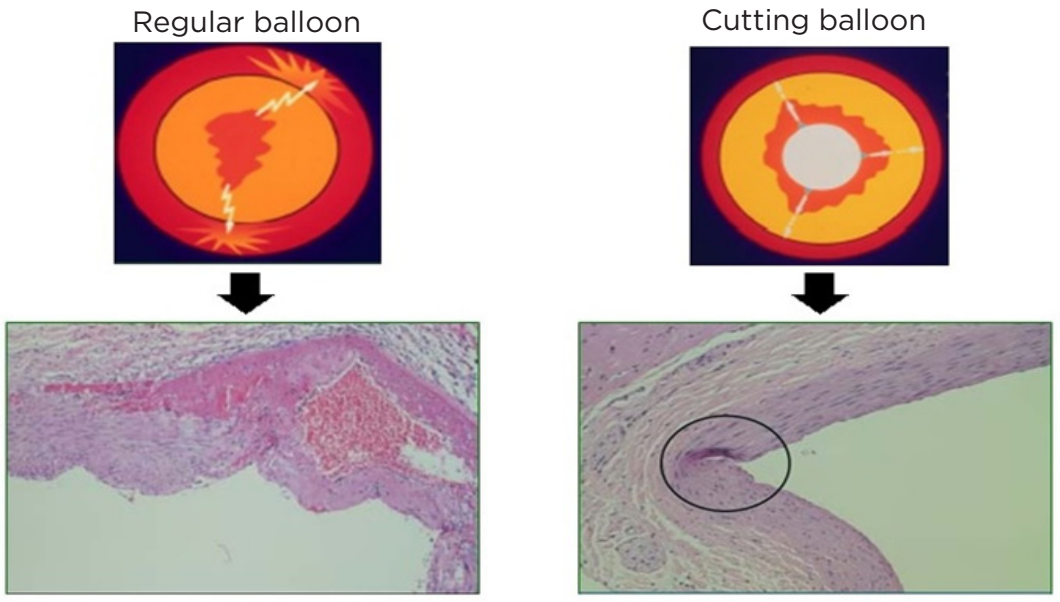

Figure 2. Regular balloon and cutting balloon: mechanisms of action.

infarction, and target lesion revascularisation) rates at follow-up were significantly lower in the CB angioplasty compared to other groups (CB, 20.3%; POBA, 37.3%; stent, 33.3%; p=0.036).

Efficacy of plaque modification prior to bare stent implantation was shown in Restenosis Reduction by Cutting Balloon Evaluation III (REDUCE III) Japanese prospective, randomised multicentre trial.[21] The hypothesis was that cutting balloon angioplasty (CBA) prior to bare-metal stent (BMS) implantation would assist in achieving full stent expansion with safety and improve accommodation of reactive intimal hyperplasia, thereby producing a favourable long-term outcome. The study enrolled 521 patients who were randomised to CBA before BMS (CBA-BMS; n=260) and to balloon-angioplasty (BA) before BMS (BA-BMS; n=261). The primary endpoint was angiographic restenosis (≥50% diameter stenosis at follow-up by quantitative coronary angiography (QCA)) and subsequent target lesion revascularisation (TLR) at 7 month follow-up. Intravascular ultrasound (IVUS) guided procedures were performed in 279 (54%) patients. Although balloon size prior to stenting was similar between the two groups, the inflated pressure was significantly lower with CBA than BA. Post procedural % diameter stenosis (%DS) was less in CBA-BMS than BA-BMS (14.0±5.9% vs 16.3±6.8%, p<0.01). %DS-follow-up was subsequently less in CBA-BMS than BA-BMS (32.4±15.1% vs 35.4±15.3%, p<0.05) associated with lower rates of restenosis in CBA-BMS than BA-BMS (11.8% vs 19.6%, p<0.05) and less TLR in CBA-BMS than BA-BMS (9.6% vs 15.3%, p<0.05). Patients were divided into four groups based on the device used before stenting and IVUS use (IVUS-CBA-BMS: 137 patients; Angio-CBA-BMS: 123; IVUS-BA-BMS: 142; and Angio-BA-BMS: 119). At follow-up, IVUS-CBA-BMS had a significantly lower restenosis rate (6.6%) than Angio-CBA-BMS (17.9%), IVUS-BA-BMS (19.8%) and Angio-BA-BMS (18.2%, p<0.05). In addition, multivariate analyses indicated that the use of BA (but not of CBA) was an independent predictor for stent restenosis at follow-up. The results of this study strongly suggested that use of appropriate plaque modification and IVUS guidance during intervention significantly increases acute and post-procedural result of angioplasty.

The restenosis rates obtained with IVUS guidance and use of CBA in REDUCE III study were comparable to those achieved with DES.[21] To examine whether IVUS-guided CBA with BMS could convey similar restenosis rates to DES, a quantitative coronary angiography-matched comparison was done between an IVUS-guided CBA-BMS strategy of

REDUCE III study and DES strategy of the Rapamycin-Eluting Stent Evaluation At Rotterdam Cardiology Hospital (RESEARCH) study patient populations. QCA-matched comparison resulted in 120-paired lesions. While acute gain was significantly greater in IVUS-CBA-BMS than DES (1.65±0.41 mm vs. 1.28±0.57 mm, p=0.001), late loss, not surprisingly, was significantly less with DES than with IVUS-CBA-BMS (0.03±0.42 mm vs. 0.80±0.47 mm, p=0.001). However, no difference was found in restenosis rates (IVUS-CBA-BMS: 6.6% vs. DES: 5.0%, p=0.582) and TVR (6.6% and 6.6%, respectively).[22]

Percutaneous coronary interventions (PCI) with DES implantation are used to treat high risk lesions and clinical conditions including bifurcation lesions, long lesions, calcified lesions, left main disease, diabetes, and multivessel disease. The risk of suboptimal stent deployment: stent underexpansion, incomplete stent apposition and incomplete lesion coverage increases are strong IVUS predictors of stent restenosis and stent thrombosis.[23,24] For such interventions, IVUS guidance is required and plaque modification prior to DES implantation has a pivotal role. Different pre dilatation strategies have yet to be established in the DES population.

ANGIOSCULPT

AngioSculpt scoring balloon featuring new flexible nitinol helical scoring elements, was evaluated in IVUS guided study conducted by de Ribamar Costa et al.[25] 224 consecutive patients with 299 *de novo* lesions treated with one DES in a non-randomised fashion were assigned to direct stenting without pre-dilatation (n=145); conventional semi-compliant balloon (n=117) or pre-dilatation with AngioSculpt scoring balloon (n=37). The primary goal was to assess stent expansion defined as the ratio of IVUS-measured minimum stent diameter (MSD) and area (MSA) to the predicted stent diameter (PSD) and area (PSA). Patients pre-treated with AngioSculpt had significantly better stent expansion, reaching 88%±18% of the predicted final stent area (p<0.001). No significant difference was found between patients pre-treated with the conventional semi-compliant balloon and those with direct stent deployment (76%±13% vs 76%±10%, p=0.8). Only 0.6% of direct-stent patients and 5% stents placed after conventional pre-dilatation achieved PSD as opposed to 18.9% of stents pre-treated with ASC (p<0.001). The MSA/PSA and MSD/PSD ratios were larger with ASC pre-dilatation; and a greater percentage of stents had a final MSA >5.0 mm^2. The main conclusion of this study is that DES are commonly underexpanded and fail to achieve even minimum standards of stent expansion that may lead to DES related adverse events. Notably, conventional balloon pre-dilatation does not improve the final stent expansion compared to direct stenting.[25]

PLAQUE MODIFICATION FOR TREATMENT OF BIFURCATION LESIONS

The issue of restenosis in complex anatomies such as bifurcated coronary lesions remains unclear. In our opinion, plaque debulking with directional coronary atherectomy or modification with a scoring device before stent deployment could minimise arterial injury and subsequent neointimal proliferation, and could prevent restenosis formation. We believe that plaque modification with a scoring device or directional coronary atherectomy before stenting minimises plaque shifting between the main branch and side branch and thus could help to avoid sidebranch stenting as well as giving better stent apposition with reduced inflation pressure, even if very long stents are deployed.

Tsuchikane et al.[26] reported registry data of 99 patients with bifurcation lesions, who received directional coronary atherectomy before stenting. Simple stenting was achieved in 97 patients. The 9 month binary restenosis rates in the main branch and side branch were 1.1 and 3.4%, respectively. TLR was performed only in two patients.

We performed a single-centre substudy (Nordic I, II + Riga bifurcation registry) with the purpose of demonstrating the safety and efficacy of plaque modification with a scoring device prior to main-vessel stenting and/or side-branch treatment in

MACE	CB (n=209)	Non-CB (n=347)	p value
Death, n (%)	7 (3.3)	10 (2.9)	0.802
MI, n (%)	7 (3.3)	9 (2.6)	0.609
Non-Q-wave MI, n (%)	6 (12.0)	4 (8.0)	0.518
ST, n (%)	5 (2.4)	10 (2.6)	0.999
TLR, n (%)	11 (5.3)	38 (11.0)	0.021
TVR, n (%)	17 (8.1)	48 (13.8)	0.056

Table 1. Nordic I, II + Riga bifurcation registry cutting balloon substudy: 8 months outcomes.

bifurcation lesions.[27] We compared CB (n=209) versus non-cutting balloon (n=347) interventions in bifurcation lesions. Primary end points were cardiac death, myocardial infarction, stent thrombosis, TLR and TVR after 8 months. Our results showed (Table 1) that TLR was lower in the CB group (5.3%; n=11) compared with the non-cutting balloon group (11.0%; n=38; p=0.021).

These results are very promising and we believe that plaque debulking before stenting, especially in complex bifurcated lesions, can avoid the need for complex stenting and may provide a good long-term outcome in patients within the first year.[26,27]

CONCLUSION

Plaque modification prior to stent implantation using cutting and scoring balloons is an essential tool to achieve the best possible result and ensure long-term safety and efficacy of PCI.

Appropriate of use-scoring balloons for plaque modification with subsequent stent implantation significantly increases acute and post-procedural results of angioplasty. IVUS guidance for intervention with lesion pre-treatment and BMS implantation can significantly lower rates of restenosis and TLV achieving results comparable to those with DES. Lesion modification with scoring balloon prior to DES implantation facilitates stent expansion that may provide better long term vessel patency and eliminate late DES related adverse events. In bifurcation lesion intervention, prior plaque debulking can avoid the need for complex stenting and may provide a good long-term outcome. With bioabsorbable stents and bioresorbable vascular scaffolds plaque modification will be an essential tool to perform complete 'vessel repair procedures'.

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