Clinical Research

Regular Drug-Eluting Stent vs Dedicated Coronary Bifurcation BiOSS Expert Stent: Multicenter Open-Label Randomized Controlled POLBOS I Trial

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ABSTRACT

Background: Results of regular drug-eluting stents (rDESs) in bifurcation treatment are not optimal. The aim of the Polish Bifurcation Optimal Stenting I (POLBOS I) trial was to compare bifurcation treatment with any rDES vs the dedicated bifurcation paclitaxel-eluting stent BiOSS Expert (Balton, Poland). The second aim was to study the effect of final kissing balloon (FKB) inflation on clinical outcomes.

Methods: Between October 2010 and January 2013 patients with stable coronary artery disease or non-ST-elevation acute coronary syndrome were assigned 1:1 to 1 of 2 treatment strategies: BiOSS Expert stent or rDES implantation. Coronary angiography was performed at 12 months. The primary end point was a composite of

RÉSUMÉ

Introduction : Les résultats sur les endoprothèses médicamenteuses habituelles (EMh) dans le traitement des bifurcations ne sont pas optimaux. Le but de l’essai POLBOS I (Polish Bifurcation Optimal Stenting I) était de comparer le traitement des bifurcations au moyen de toute EMh vs à l’endoprothèse spécialisée à éluition de paclitaxel de BiOSS Expert (Balton, Pologne). Le second but était d’étudier l’effet du « final kissing balloon » sur les résultats cliniques.

Méthodes : Entre octobre 2010 et janvier 2013, les patients souffrant de coronaropathie stable ou de syndrome coronarien aigu sans sus-décalage du segment ST étaient répartis selon un rapport 1:1 à 1 des 2 stratégies de traitement : l’implantation de l’endoprothèse BiOSS

Bifurcation lesions pose a therapeutic challenge during percutaneous coronary intervention (PCI). Their presence is associated with higher rates of periprocedural complications as well as in-stent restenosis and stent thrombosis.¹ The use of dedicated bifurcation stents (DBSs) is 1 of the proposed potential solutions to improve short-term as well as long-term outcomes. However, there is a paucity of randomized trials with DBSs.²

The aim of the Polish Bifurcation Optimal Stenting I (POLBOS I) trial was to compare coronary bifurcation treatment with any regular drug-eluting stent (rDES) vs stenting of bifurcation lesions with the dedicated bifurcation paclitaxel-eluting stent BiOSS Expert (Balton, Poland). The second aim was to study the effect of final kissing balloon (FKB) inflation on clinical outcomes.

Methods

Study population and study design

The POLBOS I study was an open-label randomized controlled trial conducted between October 2010 and January
Results : Le BiOSS Expert était implanté chez 120 patients (49.4 %). Dans le rDES group, 38,2% recevaient paclitaxel-eluting stents. Il y avait 3 stent implantation failures entre les 2 groupes (2 dans le rDES group and 1 dans le BiOSS Expert group). Side branch treatment with an rDES was required in 10% of cases in both groups. At 12 months, the incidence of cumulative major adverse cardiovascular events (MACE) was comparable between the 2 groups; however, the TLR rate was higher in the BiOSS Expert group. A more aggressive protocol yielded better angiographic and clinical outcomes.

Conclusions : MACE rates were comparable between the 2 groups; however, the TLR rate was higher in the BiOSS Expert group. A more aggressive protocol yielded better angiographic and clinical outcomes.
Figure 1. Polish Bifurcation Optimal Stenting I (POLBOS I) study flow chart. DES, drug-eluting stent; FKB, final kissing balloon; FU, follow-up, ITT, intention to treat.

Figure 2. (A, B) BiOSS Expert stent crimped on Bottle balloon with visible difference in diameters of proximal and distal parts. The proximal part of the stent has a larger diameter in relation to the distal part. The stent is available in the following nominal parameters: proximal diameter, 3.25-4.5 mm; distal diameter, 2.5-3.75 mm; and length, 15, 18, and 23 mm. (C) BiOSS Expert stent has a unique delivery system with 3 markers (proximal, middle, and distal), which ensures exact stent placement at the point of the bifurcation.
discretion, whereas in the rDES group it was performed according to the result of the second randomization.

A stent in the SB was implanted only if there was proximal residual stenosis >70% after balloon dilation, significant flow impairment after MV-MB stenting, a flow-limiting dissection, or a combination of these factors.

In patients with NSTE-ACS, a loading dose of clopidogrel (600 mg) was given, as well as a loading dose of acetylsalicylic acid (300 mg) if needed. All patients undergoing planned procedures received acetylsalicylic acid (75 mg/24 h) and clopidogrel (75 mg/24 h) 72 hours before PCI. Procedures were performed in a standard way using radial or femoral access with 6F or 7F guiding catheters. After insertion of the arterial sheath, all patients received unfractionated heparin (100 IU/kg). Additional boluses were given to maintain an activated clotting time >250 seconds. Dual-antiplatelet therapy (acetylsalicylic acid 75 mg daily and clopidogrel 75 mg daily) was prescribed for 12 months.

All patients had troponin I (TnI), creatine kinase (CK), and CK-MB levels assayed before the procedure, as well as 6 and 24 hours afterward. Periprocedural MI (type 4a) was assessed according to the third universal definition (the elevation of TnI values at least 5 times greater than the 99th percentile of the upper reference limit in patients with normal baseline values or a rise in TnI values of at least 20% if the baseline values were elevated and were stable or falling).7

Follow-up

Clinical follow-up was performed with office visits or by telephone at 1 and 12 months after intervention. Adverse events were monitored throughout the study period. Follow-up coronary angiography was performed at 12 months unless clinically indicated earlier.

End points

The primary end point was the cumulative rate of major adverse cardiovascular events (MACE) consisting of cardiac death, MI, and repeated target lesion revascularization (TLR). Secondary end points included cardiac death, all-cause death, MI, TLR, target vessel revascularization (TVR), stent thrombosis, late lumen loss (LLL), device success, and angiographic success. Cardiac death included death resulting from an acute MI, sudden cardiac death, death resulting from heart failure, and death from cardiac procedures. All deaths were deemed cardiac related unless proved otherwise. MI was defined according to the third universal definition. Clinically driven TLR was defined as reintervention of the target lesion because of the presence of a symptomatic stenosis ≥50% diameter during follow-up. Angiographically driven TLR was defined as reintervention caused by angiographic detection of significant restenosis (≥70%) in a patient who is clinically asymptomatic. TVR was defined as any revascularization of any segment of the index coronary artery. LLL was calculated based on quantitative coronary angiographic analysis (QCA) results and was defined as the postprocedural minimal luminal diameter minus the minimal luminal diameter (in millimeters) at the 12-month follow-up. Device success was defined as successful deployment of the intended stent in the target site without a system failure. Angiographic success was defined as MB diameter stenosis <20% and SB ostial stenosis <70% without significant dissection and flow impairment at the end of the procedure.

Angiographic analysis

Two orthogonal projections were chosen to visualize the treated bifurcation. All recordings were obtained after intracoronary administration of nitroglycerin (200 μg). QCA analysis was performed using the Medis QCA, version 5.0 (software for single vessel) by 2 researchers independently (JB and DV). Catheter calibration was performed in all cases. MV (the artery before SB takeoff), MB (artery beyond the ostium of SB), and SB (the smaller vessel at the point of vessel divergence) were analyzed separately according to the European Bifurcation Club Consensus.8 Lesion length, reference vessel diameter, minimal lumen diameter (MLD), percent diameter stenosis, acute lumen gain and LLL were calculated as described previously.

Statistical analysis

The mean incidence of MACE rates with currently available stents at 1 year is 15%-20%.6 With a test hypothesis of 50% relative reduction, a sample size of 120 patients per group was needed to achieve 80% statistical power with an alpha of 0.05 and assuming a dropout rate of 5%.

Continuous variables were presented as mean ± standard deviation. Categorical data were presented as numbers (%). Continuous variables were compared using an unpaired 2-sided Student t test, and categorical data used the χ² test or Fisher exact test, as appropriate. If distribution was not normal (verified with the Shapiro–Wilk test), Wilcoxon signed-rank tests and Mann-Whitney U tests were used. The interobserver agreement was tested using Pearson’s coefficient of correlation. P values of <0.05 were considered statistically significant. Statistical analyses were performed using SPSS, version 13.0, for Windows (SPSS, Chicago, IL).

Results

Baseline clinical characteristics

Between October 2010 and January 2013, a total of 243 patients were enrolled and randomly assigned to either the BiOSS Expert group (n = 120) or the rDES group (n = 123). Among patients from the rDES group, 61 were randomized to FKB and 62 to no FKB (Fig. 1). The mean age in the BiOSS Expert Group was 65.9 ± 10.5 years, and in the rDES group the mean age was 66.2 ± 9.3 years (P = 0.9). Baseline clinical characteristics were well matched between the 2 groups; however, in the BiOSS Expert group more patients presented with NSTE-ACS (9.2% vs 5.7%; P = 0.02), diabetes (37.5% vs 25.2%; P = 0.04), and peripheral artery disease (9.2% vs 5.7%; P = 0.02) (Supplemental Table S1).

Angiographic and procedural characteristics

In both groups, lesions were more frequently located in the left anterior descending (LAD) artery (BiOSS Expert vs rDES: 52.5% vs 69.9%; P = 0.35) than in the LMS coronary artery (22.5 vs 14.6; P = 0.07), the left circumflex artery (17.5% vs 13.0%; P = 0.18), and the right coronary artery (7.5% vs 2.4%; P < 0.01) (Fig. 3A). In the rDES group, the EES (41.5%) was used most frequently, followed by the PES
More details including the list of implanted stents are presented in Figure 3B. No difference between the 2 groups was observed regarding the distribution of true (Medina 1.1, 1.0, 0.1, 1.1) and nontrue bifurcations (76.6% vs 75.6%) (Supplementary Table S2).

The main procedural variables are presented in Supplementary Table S3. The device success rate in the BiOSS Expert group was 99.1% (n = 119 of 120), and in the rDES group it was 98.4% (n = 121 of 123). Mean BiOSS Expert stent nominal parameters were as follows: proximal diameter, 3.67 ± 0.34 mm; distal diameter, 2.98 ± 0.33 mm; and length, 17.44 ± 2.47 mm, whereas the mean maximal implantation pressure was 15.4 ± 3.3 atm. In the rDES group, stent nominal parameters were as follows: diameter, 3.24 ± 0.47; length, 20.7 ± 6.78 mm; and mean maximal implantation pressure, 18.1 ± 2.1 atm. Procedural characteristics in the 2 groups were similar except for rates of FKB and POT, which were higher in the rDES group—20.8% vs 49.6% (P < 0.01) and 37.5% vs 69.1% (P < 0.01), respectively. In both groups, the MV was predilated in two thirds of cases. The SB required additional balloon dilation in more than half of lesions in both groups (BiOSS, 55% vs rDES, 64.2%; P = not significant [NS]), and implantation of an rDES in the SB was required in 13 cases in each group (BiOSS Expert, 10.8% vs rDES, 10.6%, P = NS).

Clinical outcomes

There was 1 periprocedural MI in the BiOSS Expert group and 2 in the rDES group (resulting from transient SB occlusion). Additionally, there were 7 cases of an in-hospital increase of TnI level (maximum, 1.5 ng/mL) in the BiOSS Expert group and 5 cases in the rDES group. These increases were asymptomatic, without electrocardiographic changes and did not require repeated coronary angiography.

Clinical follow-up at 12 months was available in all patients (Table 1). The cumulative incidence of MACE was similar in the BiOSS Expert and rDES groups—13.3% vs 12.2% (P = 0.7), respectively. There were 2 non–cardiac-related deaths (ileus and abdominal aortic aneurysm rupture) in the BiOSS Expert group and 1 non–cardiac–related death (gastrointestinal bleeding) in the rDES group. In the BiOSS Expert group, 1 MI 6 days postoperatively was associated with subacute stent thrombosis (most probably caused by stent underexpansion), and in the rDES group there were 2 MIs (both associated with significant restenosis). The TLR rate was significantly higher.
in the BiOSS Expert group compared with the rDES group—11.5% vs 7.3% \( (P = 0.02) \). When considering only clinically driven TLR, there were 7 cases in the BiOSS Expert group and 4 cases in the rDES group (5.8% vs 3.2%; \( P = NS \)). All cases of TLR were treated by PCI (15 with plain old balloon angioplasties and 8 with another rDES).

**Clinical outcomes—subgroup analysis**

In further analysis, when comparing the BiOSS Expert group to only the PES subgroup of the rDES group, the rate of TLR in both groups was comparable (11.5% vs 10.6%; \( P = NS \)). In patients undergoing LMS bifurcation lesion treatment, the BiOSS Expert was superior to the rDES (TLR, 7.4% vs 11.1%; \( P = 0.04 \)) (Supplementary Table S4).

**Quantitative coronary angiography analysis**

Angiographic follow-up at 12 months was performed in 220 patients (90.5%), 109 of whom (90.8%) were randomized to the BiOSS Expert group, and 111 (90.2%) were randomized to the rDES group. Angiographic data are presented in Supplementary Table S5. The 2 groups were well matched in baseline QCA characteristics. The immediate angiographic success rate in both groups was 100%. QCA revealed that BiOSS Expert stent implantation as well as rDES implantation caused a significant increase of percent diameter stenosis in MV and MB. However, this procedure did not affect the alpha angle between the MV and SB. When comparing LLL values, there were significant differences in the MV (BiOSS Expert vs rDES, 0.35 vs 0.25 mm; \( P < 0.05 \)) and in the MB (0.43 vs 0.30 mm; \( P < 0.05 \)) but not in the SB (Supplementary Table S6). The smallest LLL value was observed in the EES subgroup, and the largest was seen in the PES subgroup (Fig. 4). LLL values were greater in non-LMS bifurcation lesions in all subgroups. Among 2118 segments, the interobserver agreement was high \( (r = 0.87; 95\% \text{ confidence interval, 0.85-0.91; } P < 0.05) \).

**FKB vs no FKB—subgroup analysis**

Subgroup analysis regarding FKB vs no FKB revealed that in both groups (BiOSS Expert group and rDES group), FKB was related to a higher rate of SB stenting, longer fluoroscopy time, and greater likelihood of the treated lesions being located in the LMS coronary artery. However, in the FKB subgroups, there was a significantly lower rate of restenosis in the BiOSS Expert group (8.1% vs 13.2%; \( P < 0.05 \)) as well as in the rDES group (4.9% vs 9.5%; \( P < 0.05 \)) \( (P_{\text{interaction}} = 0.179) \). In the rDES group, the rate of restenosis in the FKB + POT subgroup was even lower (1 of 42 [2.4%] cases). The same association was observed in the BiOSS Expert group (Supplementary Table S7). Additionally, there was a trend for lower LLL in both the BiOSS Expert group and the rDES group when POT was applied.

**Discussion**

To our knowledge, this is the first study to compare, in a randomized design, the performance of a single DBS with rDES. The main findings of this study are as follows: (1) the cumulative MACE rate at 12 months was comparable between the BiOSS Expert and rDES groups, (2) the TLR rate was significantly higher in the BiOSS Expert group compared with the rDES group, (3) FKB (especially with POT) during stent implantation yielded better angiographic and clinical outcomes, (4) the rate of TLR in the PES subgroup was comparable to that of the BiOSS Expert group, and (5) the BiOSS Expert provided a single stent bifurcation treatment option with a high rate of implantation success.

The cumulative MACE rates in the 2 groups were similar during follow-up. There were 2 deaths (1.6%) of unknown cause in the rDES group; therefore, they were treated as cardiac-related deaths (both cases without FKB and possible late stent thrombosis). The TLR rate was higher in the BiOSS Expert group than in the rDES group. The TLR rates in both groups were comparable to those in other studies (6.6%-12%). Interestingly, when taking into account the eluted drug, the EES subgroup of the rDES group was characterized by the lowest TLR rate, a finding consistent with previous studies showing that “limus”-eluting stents are better than paclitaxel-eluting ones. However, in contrast to most registries, we achieved a very high rate of angiographic follow-up that is known to increase the rate of TLR. The rates of clinically driven TLR in our study were markedly lower in the BiOSS Expert group and in the rDES groups and did not differ significantly. This is comparable to the best results of rDES in coronary bifurcation treatment.

The LLL results with the BiOSS Expert compare favourably with the results of previous studies with PESs. LLL with the BiOSS Expert was 0.43 mm in the MB and 0.35 mm in the MV, whereas the LLL with the PESs, LucChopin2 stent and the TAXUS LIBERTE (Boston Scientific) was 0.46-0.59 mm and 0.34 mm, respectively. Moreover, in our study, LLL was lower than in the original BiOSS Expert Registry (LLL MV, 0.56 mm; LLL MB, 0.26 mm). This may be associated with an early phase of the learning curve and treatment of longer lesions in the previous work, with the subsequent need to implant additional stents. The current results are similar to those recently reported by our group on LMS coronary artery treatment. A lower LLL in the LMS subgroup suggests that this stent might be better suited for bifurcations with a greater difference in diameters between the MV and MB, such as the LMS coronary artery/LAD artery/left circumflex artery.
complex. This hypothesis is also supported by the rate of TLR in the LMS subgroup (BiOSS Expert vs rDES, 7.4% vs 11.1%; trend in favour of the BiOSS Expert); however, these observations require further confirmation from adequately powered randomized trials.

The rates of stent deployment in the SB were low in both the BiOSS Expert group (10.8%) and the rDES group (10.6%) despite the fact that >75% of patients in our study had true bifurcations. This is in contrast to previous studies of other DBSs in which stents were implanted in the SB in 20%-50% of cases.\(^{10,12,18}\) In addition, there were no real difficulties with rewiring the SB, also suggesting that the BiOSS Expert is well suited to the provisional T-stenting strategy.\(^{4}\) The device success rate of the BiOSS Expert was comparable to that of rDESs and to the implantation success rates of other DBSs (89.3%-98%),\(^{11,12,18}\) as well as to PCI with LMS coronary artery bifurcations (98%).\(^{10}\)

The higher rate of POT observed in the rDES group could be caused by the fact that rDES nominal parameters were chosen according to MB size, and then MV postdilation was performed using recommendations of the European Bifurcation Club.\(^{19}\) The stepped design of the BiOSS Expert stent delivery balloon was to theoretically ensure a POT-like effect, thus allowing operators to frequently omit this part of the procedure. However, we found that similar to the rDES group, POT in the BIOSS group was also associated with a lower rate of restenosis (Supplementary Table S7).

The subgroup analysis regarding FKB vs no FKB, revealing a significantly lower rate of restenosis in the FKB subgroups of both the BiOSS Expert group and the rDES group, is in agreement with the results of the Nordic-Baltic Bifurcation Study III (NORDIC-3), in which FKB reduced angiographic SB restenosis, especially in patients with true bifurcation lesions.\(^{21}\)

Although the clinical results obtained with the BiOSS Expert are satisfactory, the BiOSS Expert concept remains under development. A version of the BiOSS Expert eluting sirolimus (BiOSS Expert LIM) is already approved for use in Europe. A more potent drug may provide even better results.\(^{21}\) Indeed, preliminary results with the BiOSS Expert LIM stent as well as studies using other platforms have suggested that sirolimus-eluting stents may be more effective than paclitaxel-eluting ones.\(^{22,23}\) Moreover, BiOSS Expert stents are made of stainless steel and therefore have relatively thick struts (naked, 120 \(\mu\)m), which might predispose to excessive neointimal proliferation. The use of a cobalt-chromium alloy allows for thinner stent struts (60-90 \(\mu\)m), which may result in lower LLL. The Intracoronary Stenting and Angiographic Results: Strut Thickness Effect on Restenosis Outcome (ISAR-STEREO) trial demonstrated that a thin strut stent had a lower rate of restenosis than did a thick strut stent of similar design.\(^{24}\) Similar results were found in several other trials.\(^{25-28}\) Therefore, the next generation of the BiOSS Expert stent will be on a cobalt-chromium platform.

**Study limitations**

Although the sample size was relatively small, it is in line with similar studies found in the literature, was based on predefined statistical considerations, and primarily affects the robustness of observations of subgroup analyses. Furthermore, although a 100% angiographic follow-up rate was not achieved, the follow-up rate of >90% is in line with similar studies. The use of multiple stent types and drugs in the control group is also a limitation, although this aspect of the design was intended to replicate real-world clinical practice. The predictable randomization scheme may have potentially biased the decisions of investigators to randomize patients with certain angiographic characteristics. Potentially this could have contributed to the uneven vessel distribution between groups. Finally, the differences in FKB strategies between the 2 study groups (randomization in the rDES group and operator choice in the BIOSS group) may also have influenced the results.

**Conclusions**

The success rate of implantation of the BiOSS Expert stent is high. The cumulative rate of MACE is comparable between the BiOSS Expert and rDES groups. The TLR rate achieved with the BiOSS Expert was inferior to that obtained with “limus”-eluting stents but appeared to be comparable to that achieved with PESs. The use of FKB and POT during stent implantation results in more favourable angiographic and clinical outcomes. The POLBOS I trial sets an important benchmark for future studies with new generations of BIOSS stents eluting “limus” drugs and using newer stent materials.

**Disclosures**

R.J.G. is a medical consultant for Balton Company. The other authors have no conflicts of interest to disclose.

**References**


**Supplementary Material**

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at http://dx.doi.org/10.1016/j.cjca.2014.12.024.