Long-term outcomes after treatment of bare-metal stent restenosis with seal-wing or iopromide-coated paclitaxel-eluting balloon catheters.

Leos Pleva (leos.pleva@volny.cz)
University Hospital https://orcid.org/0000-0003-1484-6413
Pavel Kukla
Department of Cardiovasular Diseases, University Hospital Ostrava
Jana Zapletalova
Department of Medical Biophysics, Palacky University
Ota Hlinomaz
Department of Cardioagiology and ICRC, St. Anne´s University Hospital, Brno

Research article

Keywords: in-stent restenosis, paclitaxel-eluting balloon, seal-wing PEB

Posted Date: May 11th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-21176/v1

Abstract

Background:

The efficacy of paclitaxel-eluting balloon catheters (PEB) is affected by the method of binding paclitaxel to the balloon catheter surface.

The aim of this study was to compare the long-term efficacy of seal-wing and iopromide-coated PEB for bare-metal stent restenosis (BMS-ISR) treatment.

Methods:

We analyzed 3-year clinical follow-up data of 132 patients with BMS-ISR. 64 of them were treated with seal-wing PEB, the control group comprised 68 patients from the iopromide-coated PEB arm of the previous TIS clinical study.

Primary end-points included the occurrence of major adverse cardiac events (MACE; cardiovascular [CV] death, myocardial infarction [MI], or target vessel revascularization [TVR])

Results:

At 3 year clinical follow-up, the incidence of MACE was significantly higher in the seal-wing PEB than in the iopromide-coated PEB group (40.6 % vs. 19.1%; p=0.008); the same can be said about TVR (26.9% vs. 8.8%; p=0.011). Similarly, the event-free survival was significantly longer in the iopromide-coated PEB than in the seal-wing PEB group (p=0.021). No significant differences were found between the groups where CV mortality (4.7% vs. 5.9%; p=1.000), MI (6.3% vs. 4.4%; p=0.712), definite stent thrombosis (0% vs. 2.9%; p=0.497) or the second MACE (4.7% vs. 1.5%; p=0.354) are concerned.

***Conclusions*:**

Compared to iopromide-coated PEB, the use of seal-wing PEB for BMS-ISR treatment led to a significantly higher 3-year occurrence of MACE and TVR.

Trial registartion:

ClinicalTrials.gov; https://clinicaltrials.gov; NCT01735825 *(Registered 7 Nov 2012).*

Background

The method of binding paclitaxel to the balloon catheter surface represents the principal factor affecting the efficacy of paclitaxel-eluting balloon catheters (PEB). We previously demonstrated that in bare-metal stent restenosis (BMS-ISR) treatment, the use of iopromide-coated PEB resulted in significantly better 12-month angiographic and clinical outcomes in comparison with seal-wing PEB [1].

In our present study, we aimed to compare the long-term efficacy of BMS-ISR treatment using these PEBs with different methods of paclitaxel binding to their surface.

Methods

Patients and Study Design

The methods of our study have been previously described in detail [1, 2]. Briefly, two groups of patients were compared; the first (hereinafter treatment group) comprised consecutive adult patients (> 18 years of age) with BMS-ISR (≥ 50% diameter stenosis; DS) treated with seal-wing PEB (Protége) in the Cathlab of the University Hospital Ostrava over the period of three years (2013–2015). Patients with BMS-ISR who were treated using iopromide-coated PEB (Sequent Please) in the previous randomized part of the TIS study [2] formed the other group, hereinafter referred to as the control group. The principal exclusion criteria were as follows: concomitant diseases carrying expected survival of < 12 months or limiting the possibility of follow-up coronary angiography.

In this study, we extended the clinical follow-up to 3 years. Primary end-point included the inidence of major adverse cardiac events (MACE; cardiovascular [CV] death, myocardial infarction [MI], or target vessel revascularization [TVR]). In addition, the occurrence of stent thrombosis [ST] and the second MACE was also followed.

Interventions

The PCI was perormed on standard conditon [1, 2]. After appropriate lesion preparation, the PEB was inflated for 30 s at the recommended pressure. In the seal-wing PEB Protége (Blue Medical, Helmond, the Netherlands), paclitaxel (3 μg/mm^2) is firmly bound directly to the balloon catheter surface prior to folding (between the wings and the hydrophilic coating, which prevents releasing particles while bending the balloon or during its transition to the stenosis). In effect, only paclitaxel, not the coating, is released into the vessel wall [3, 4]. On the other hand, in the iopromide-coated PEB Sequent Please (B. Braun AG, Melsungen, Germany) paclitaxel (also 3 μg/mm^2) was bound via the hydrophilic contrast agent iopromide (Paccocath®), which increased its solubility and vascular wall penetration. The implantation of an additional bailout stent was allowed in case of edge dissection. The patients received aspirin 100 mg and clopidogrel 75 mg per day for 6 months.

Follow-Up

After the first year, patients were followed up every 12 months (+/-2 months) through an office visit or at least a phone call with the aim to assess very long-term outcomes, as per study protocol. At 3 years (+/-0.5 year), the final clinical follow-up was performed, which included a full clinical evaluation and recording of all MACE.

The adjudication of events was blinded and performed by an independent investigator. Any death that was not clearly due to non-cardiac causes was considered cardiac related. The third universal definition

of myocardial infarction by the European Society of Cardiology [5] was used as a definition of MI; stent thrombosis was defined according to the Academic Research Consortium criteria [6].

Statistical Analysis

Continuous variables were tested for normality using the Shapiro-Wilk test. Depending on the results of that test, the values were either tested using the independent-sample Student's t-test and are presented as mean and standard deviation (SD) where the distribution was normal, or tested using Mann-Whitney/Wilcoxon U test and presented as median and 25%-75% interquartile range where the distribution was not normal. Categorical variables are presented as counts and percentages and were compared using the χ^2 or Fisher's exact test as appropriate. A P value of < 0.05 was considered significant. Kaplan-Meier analysis with Log-rank test was used to analyze time-to-event data. Cox proportional hazard regression was performed to evaluate hazard ratio with or without adjustment for significantly different baseline variables. All statistical analyses were performed using IBM SPSS Statistics version 22.

Results

The course of the study is shown in the CONSORT flow diagram (Figure 1). We analyzed 3-year clinical follow-up data of 132 patients with BMS-ISR. 64 of them were treated with seal-wing PEB and the control group comprised 68 patients from the iopromide-coated PEB arm of the previous TIS clinical study. Table 1 presents the baseline demographic, clinical, angiographic, and ISR characteristics of both groups.

At the 3-year follow-up, clinical data of all patients were collected. The mean time to the 3-year follow-up was 1170 days (±176; median 1260) in the seal-wing PEB and 1210 days (±167; median 1270) in the iopromide-coated PEB group (p=0.089).

Table 2 shows the MACE incidence within 12 months from the intervention, between months 13-36, and over the entire follow-up period. At the 3-year clinical follow-up, the seal-wing PEB was associated with significantly higher incidence of MACE (p=0.008) and TVR (p=0.011) compared to the iopromide-coated PEB. However, no significant differences were found between the groups regarding CV mortality (p=1.000), MI (p=0.712), definite ST (p=0.497) or the second MACE (p=0.354). The greatest difference in the incidences of MACE and TVR between the groups was observed in the first year of the follow-up (p=0.003 and 0.009, respectively).

Figures 2 and 3 present estimates of event-free survival (EFS). EFS (time-to-MACE and time-to-TVR) was significantly longer in the iopromide-coated PEB compared to the seal-wing PEB group (p=0.021 and 0.006, respectively).

Cox proportional hazards regression analysis revealed significantly higher risk of MACE (including TVR) in the seal-wing PEB group, even after the adjustment for significantly different baseline variables (e.g. postdilatation) [Table 3].

Discussion

In clinical practice, paclitaxel is used in DEB as an effective antiproliferative agent. The drug is highly lipophilic, with rapid penetration into the tissue. The method of paclitaxel binding to the balloon catheter surface is probably the single most significant factor influencing the PEB efficacy. Originally, as described by Scheller et al., paclitaxel was bound via a hydrophilic contrast agent iopromide increasing its solubility and vascular wall penetration [7]. It has been established that 3 μg/mm^2 is the optimum drug concentration [7], which is the case also in both compared PEBs.

Multiple studies with follow-up times of 9 to 12 months demonstrated the efficacy of iopromide-coated PEB treatment for BMS-ISR in comparison with POBA or paclitaxel-eluting stents (PES); however, the comparison of PEB with the 2nd generation DES with everolimus (everolimus-eluting stents; EES) still remains unclear. Moreover, the long-term results of these studies are now also available.

In the long-term follow-up (5.4+/-1.2 years) of Paccocath I and II studies, the PEB group confirmed the sustained significant reduction of MACE (p = 0.009) compared to POBA, which was largely driven by the TVR incidence reduction from 38.9–9.3% (p = 0.004) [8, 9].

In the PEPCAD II study, despite the trends toward reduced 12-month incidences of binary restenosis (p = 0.06) and MACE (p = 0.08) [10], at 3-year follow-up, the differences in incidences of MACE (p = 0.14) and TVR (p = 0.10) between PEB and PES groups did not reach statistical significance [11].

Contrary to different 12-month angiographic results between the TIS and RIBS V studies comparing the PEB and EES [2, 12] in the long-term clinical follow-up, the only significant difference was a lower incidence of target lesion revascularisation in the EES group of the RIBS V study (p = 0.04). The overall incidence of 3-year MACE did not differ between the groups in both studies (p = 0.230 and p = 0.64, respectively) [13, 14].

Many other PEBs with different coating are currently used in clinical practice, including the DIOR II (shellac-coated; Eurocor, Bonn, Germany), the IN.PACT Falcon (urea-coated; Medtronic, Minneapolis, USA), the Pantera Lux (butyryl-tri-hexyl citrate [BTHC]-coated; Biotronik, Berlin, Germany), etc. Nevertheless, among several registries, the most favourable results were achieved with the use of iopromide-coated PEB.

In a subanalysis of the SCAAR registry, iopromide-coated PEB (paclitaxel 3 μg/mm2) was used for treating ISR lesions. Compared to uncoated PEB (paclitaxel 2 μg/mm2), iopromide-coated PEB was associated with a lower risk of binary restenosis (adjusted HR: 0.48; 95%CI: 0.23–0.98 [15].

Benezet et al. found that patients with BMS or DES-ISR treated with iopromide-coated PEB displayed a significantly lower TLR rate at 36 months (p = 0.03) compared to shellac-coated PEB [16].

In contrast, in the Düsseldorf DCB registry, patients treated for ISR with BTHC-coated PEB had significantly longer event-free survival rates (p = 0.405) than those treated with the iopromide-coated PEB

[17].

In a non-randomised study, Nijhoff et al. compared the efficacy of urea-coated and shellac-coated PEB in patients with BMS or DES-ISR. The urea-coated PEB group showed significantly lower 6-month LLL (p = 0.014), a higher FFR value distally (p = 0.029), and a reduced volume percentage of neointimal hyperplasia (p = 0.006). The incidence of repeated binary restenosis was not significantly different between groups (p = 0.16) and a trend was observed towards lower TLR (p = 0.057) in the urea-coated PEB group [18].

Our results confirm that iopromide coating influenced the efficacy of PEB in ISR treatment. We previously demonstrated that patients with BMS-ISR showed significantly higher 12-month LLL ($p < 0.0001$), incidence of repeated binary restenosis ($p = 0.012$), 12-month MACE ($p = 0.003$) and TVR ($p = 0.009$) rates following treatment with seal-wing PEB compared to iopromide-coated PEB [1].

The difference in the overall MACE incidence was predominantly caused by the significantly higher incidence of TVR in the seal-wing PEB group due to a higher rate of repeated binary restenosis. No significant differences were found between the groups where CV mortality, MI, definite ST or the second MACE are concerned. These differences in the clinical outcomes (MACE and TVR) occurred mainly during the first year, however they also persisted after 3 years of follow-up.The use of the seal-wing PEB for BMS-ISR treatment was associated with a significantly higher risk of MACE (including TVR), even after the adjustment for significantly different baseline variables.

Limitations

Our study has several limitations. In particular, it was a non-randomized study comparing patients who underwent one type of treatment (seal-wing PEB) with patients from the control arm of the previous TIS study.

Nevertheless, the baseline parameters of both patient cohorts did not differ with respect to main baseline parameters and hence, it is unlikely that the selection bias would have played a major role. Similarly, the further clinical follow-up and medical therapy, including duration of dual antiplatelet treatment, were also the same.

Conclusions

Treatment of BMS-ISR using seal-wing PEB led to a significantly higher 3-year TVR and overall MACE incidences compared to iopromide-coated PEB.

Abbreviations

BMS-ISR - bare-metal stent restenosis

CV - cardiovascular

DES-ISR - drug-eluting stent restenosis

EES - everolimus-eluting stent

EFS -.event-free survival

FFR - fractional flow reserve

ISR - in-stent restenosis

MACE - major adverse cardiac events

MI - myocardial infarction

PCI - percutaneous coronary intervetnion

PEB - paclitaxel-eluting balloon catheters

POBA - plane old balloon angioplasty

SD - standard deviation

ST - stent thrombosis

TLR- target lesion revascularization

TVR - target vessel revascularization

Declaration Section

Ethics approval and consent to participate

The study protocol complied with the Declaration of Helsinki and was approved by the Ethics Committee of University Hospital Ostrava, Czech Republic.

The study was registered at ClinicalTrials.gov (NCT01735825) on the7th November 2012.

Written informed consent was obtained from each patient before enrollment in the study.

Consent for publication

Written informed consent for publication was obtained from each patient before enrollment in the study.

Availability of data and materials

The data sets supporting the results of this article are available in the LabArchives repository [http://dx.doi.org/10.25833/2pxh-1q10].

Competing interests

The authors declare that they have no competing interests.

Funding

This article was supported by Ministry of Health, Czech Republic - conceptual development of research organizations - FNOs/2015.

Authors' contributions

LP: study design; PK, OH: literature search; LP, PK: data collection; LP, PK, OH: data analysis; JZ: statistical analysis; LP, OH: data interpretation; All authors: manuscript revision. All authors read and approved the final manuscript.

Acknowledgement

This article was supported by Ministry of Health, Czech Republic - conceptual development of research organizations - FNOs/2015.

CONSORT guidelines statement

We hereby declare that our study adheres to CONSORT guidelines and include a completed CONSORT checklist as an additional file.

References

1. Pleva L, Kukla P, Zapletalova J, Hlinomaz O. Efficacy of a seal-wing paclitaxel-eluting balloon catheters in the treatment of bare metal stent restenosis. BMC Cardiovasc Disord 2017;17:168 DOI 10.1186/s12872-017-0602-6.
2. Pleva L, Kukla P, Kusnierova P, Zapletalova J, Hlinomaz O. Comparison of the Efficacy of Paclitaxel-Eluting Balloon Catheters and Everolimus-Eluting Stents in the Treatment of Coronary In-Stent Restenosis. The Treatment of In-Stent Restenosis Study. Circ Cardiovasc Interv 2016; 9: e003316. DOI: 10.1161/CIRCINTERVENTIONS.115.003316.
3. Vaquerizo B, Aizpurua DA, Cuscullida JC, Peñaranda AS. Update on drug-eluting balloons for percutaneous coronary interventions. EMJ Int Cardiol. 2013;1:80-90.
4. van Driel A, Ijsselmuiden S, Polad J, Scholte M, Vries A, Weevers A. Interim results of a new paclitaxel-coated DEB in real-world PCI indications. [Abstract]. In: Abstracts of EuroPCR 2016, Paris, France, Euro 16A-POS0885. http://www.pcronline.com/eurointervention/AbstractsEuroPCR2016_issue/abstracts-europcr-2016/. Accessed on December 28, 2019.

5. Thygesen K, Albert JS, Jafe AS, Simoons ML, Chaitman BR, White HD. Third universal definition of myocardial infarction. EHJ 2012;33:2551-2567.
6. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, et al. Clinical end points in coronary stent trials. A case for standardized definitions. Circulation 2007;115:2344-2351.
7. Scheller B, Speck U, Abramjuk C, Bernhardt U, Böhm M, Nickenig G. Paclitaxel balloon coating, a novel method for prevention and therapy of restenosis. Circulation 2004;110:810-814.
8. Scheller B, Hehrlein C, Bocksch W, Rutsch W, Haghi D, Dietz U, et al. Treatment of coronary in-stent restenosis with a paclitaxel-coated ballon catheter. NEJM 2006;355:2113-24.
9. Scheller B, Clever YP, Kelsch B, Hehrlein C, Bocksch W, Rutsch W, et al. Long-Term Follow-Up After Treatment of Coronary In-Stent Restenosis With a Paclitaxel-Coated Balloon Catheter. J Am Coll Cardiol Intv 2012;5:323-30.
10. Unverdorben M, Vallbracht C, Cremers B, Heuer H, Hengstenberg C, Maikowski C, et al. Paclitaxel-coated balloon catheter versus paclitaxel-coated stent for the treatment of coronary in-stent restenosis. Circulation 2009;119:2986-94.
11. Unverdorben M, Vallbracht C, Cremers B, Heuer H, Hengstenberg C, Maikowski C, et al. Paclitaxel-coated balloon catheter versus paclitaxel-coated stent for the treatment of coronary in-stent restenosis: the three-year results of the PEPCAD II ISR study. EuroInterv 2015;11:926-34.
12. Alfonso F, Pérez-Vizcayno MJ, Cárdenas A, del Blanco BG, Seidelberger B, Iñiguez A, et al. A randomized comparison of drug-eluting balloon versus everolimus-eluting stent in patients with bare-metal stent in-stent restenosis. JACC 2014;63:1378-86.
13. Pleva L, Kukla P, Zapletalova J, Hlinomaz O. Long-term outcomes after treatment of bare-metal stent restenosis with paclitaxel-coated balloon catheters or everolimus-eluting stents: 3-year follow-up of the TIS clinical study. Catheter Cardiovasc Interv 2018;00:1-9.
14. Alfonso F, Pérez-Vizcayno MJ, del Blanco BG, Otaegui I, Masotti M, Zueco J, et al. Long-Term Results of Everolimus-Eluting Stents Versus Drug-Eluting Balloons in Patients With Bare-Metal In-Stent Restenosis 3-Year Follow-Up of the RIBS V Clinical Trial. J Am Coll Cardiol Intv 2016;9:1246-55.
15. Bondesson P, Lagerqvist B, James SK, Olivecrona GK, Venetsanos D, Harnek J. Comparison of two drug-eluting balloons: a report from the SCAAR registry. EuroInterv. 2012;8:444-449.
16. Benezet J, Agarrado A, Gutiérrez-Barrios A, Ruiz-Fernandez D, del Río A, Cañadas D. Comparison of two different drug-coated balloons for the treatment ofin-stent restenosis: A long-term single-centre experience. Cardiovasc Revasc Med 2016;17:176–180.
17. Assadi-Schmidt A, Mohring A, Liebsch E, Dannenberg L, Achilles A, Pöhl M et al. SeQuent Please vs. Pantera Lux drug coated balloon angioplasty in real life: Results from the Düsseldorf DCB registry. Int J Cardiol 2017;(15)231:68-72. doi:10.1016/j.ijcard.2016.12.022.
18. Nijhoff F, Stella PR, Troost MS, Belkacemi A, Nathoe HM, Voskuil M, et al. Comparative assessment of the antirestenotic efficacy of two paclitaxel drug-eluting balloons with different coatings in the treatment of in-stent restenosis. Clin Res Cardiol 2015;11p. DOI 10.1007/s00392-015-0934-0.

Tables

Table 1. Baseline parameters

	seal-wing PEB	iopromide-coated PEB	*p*
Demographic parameters			
Patients/ ISR lesions, n	64/69	68/74	
Male/female	49(76.56%)/ 15(23.44%)	43(63.24%)/ 25(36.74%)	0.288[c]
Age, years	65.25 ± 11.01[a]	65.6 ±10.9[a]	1.000[d]
Body mass index, kg/m^2	28.38± 4.93[a]/21.19[b]	28.7± 4.0[a]/19.23[b]	1.000[e]
Ejection fraction, %	52.31± 10.01[a]/55.00[b]	49.74± 11.95[a]/50.0[b]	0.732[e]
Diabetes mellitus	18 (28.12%)	17 (25.00%)	1.000[c]
Renal insufficiency	2 (3.12%)	2 (2.94%)	1.000[f]
CABG	6 (9.38%)	3 (4.41%)	1.000[f]
Ever smoked	31 (48.44%)	31 (45.59%)	1.000[f]
Previous MI	31 (48.44%)	43 (63.24%)	0.117[c]
2VD/3VD	43 (67.19%)	38 (55.88%)	1.000[c]
Multi ISR	5 (7.81%)	4 (5.88%)	1.000[f]
Baseline PCI			
ACSy (STEMI/NSTEMI)	37 (57.81%)	45 (66.18%)	0.966[c]
stable AP	27 (42.19%)	23 (33.82%)	
Type of lesion			
B2/C	47 (68.12%)	51 (68.92%)	1.000[c]
Lesion localization			
LAD/RD	34 (49.28%)	35 (47.30%)	1.000[f]
RCx/OM	15 (21.74%)	16 (21.62%)	
RCA	18 (26.09%)	22 (29.73%)	
SVG	2 (2.9%)	1 (1.35%)	
Diameter of the previous stent, mm	3.09± 0.48[a]/3.00[b]	3.18±0.43[a]/3.0[b]	0.390[e]
Length of the previous stent, mm	25.67± 15.48[a]/20.00[b]	22.65±11.70[a]/19.0[b]	0.720[e]
In-stent restenosis			
ACSy, STEMI/NSTEMI	19 (29.69%)	24 (35.29%)	1.000[f]
Stable AP	42 (65.62%)	41 (60.29%)	
Other, silent ischemia	4 (6.25%)	3 (4.41%)	
Time to ISR, months	12.49± 11.06[a]/7.00[b]	12.10± 8.47[a]/9.0[b]	1.000[e]
Type of ISR			
I (focal; all)	25 (36.23%)	30 (40.54%)	1.000[f]
II (diffuse)	33 (47.83%)	34 (45.95%)	

III (proliferative)	6 (8.7%)	5 (6.76%)	
IV (occlusion)	5 (7.25%)	5 (6.76%)	
Periprocedural parameters			
Cutting predilatation	20 (28.99%)	16 (21.62%)	0.933[c]
ISR; PEB/EES diameter, mm	3.27± 0.47[a]/3.17[b]	3.32± 0.39[a]/3.5[b]	1.000[e]
ISR; PEB/EES length, mm	23.19± 12.98[a]/20.00[b]	22.53± 8.13[a]/20.0[b]	1.000[e]
Postdilatation, atm	13.48± 2.34[a]/12.00[b]	14.84± 2.77[a]/16.0[b]	**0.009**[e]
Second stent implantation	8 (11.59%)	11 (14.86%)	1.000[c]
Crossover to DES	2 (2.9%)	2 (2.7%)	1.000[c]

Qualitative data are given as n (%); quantitative data as [a] mean (± standard deviation) and [b] median;

[c] chi-square test; [d] Student T-test; [e] Mann–Whitney U test; [f] Fisher's exact test.

Table 2. Incidence of MACE within 12 months, 1 to 3 years and for the entire follow-up period

	Seal-wing PEB	Iopromide PEB	
	n (%)	n (%)	p[a]
patients, n	64	68	
0-12 month			
MACE all	17 (26.9%)	7 (10.3%)	**0.003**
CV death	0 (0%)	1 (1.5%)	1.000
MI	4 (6.3%)	1 (1.5%)	0.468
TVR	13 (20.6%)	5 (7.4%)	**0.009**
Definite ST	0 (0%)	1 (1.4 %)	1
1-3 years			
MACE all	9 (14.1%)	6 (8.8%)	0.343
CV death	3 (4.7%)	3 (4.4%)	1.000
MI	0 (0%)	2 (2.9%)	0.497
TVR	4 (6.3%)	1 (1.5%)	0.198
Definite ST	0 (0%)	1 (1.5%)	1.000
2nd MACE/TVR	3 (4.7%)	1 (1.5%)	0.354
non CV death	6 (9.4%)	2 (2.9%)	0.156
all cause of death	9 (14.1%)	5 (7.4%)	0.264
0-3 years			
MACE all	26 (40.6%)	13 (19.1%)	**0.008**
CV death	3 (4.7%)	4 (5.9%)	1.000
MI	4 (6.3%)	3 (4.4%)	0.712
TVR	17 (26.9%)	6 (8.8%)	**0.011**
Definite ST	0 (0%)	2 (2.9%)	0.497
2nd MACE/TVR	3 (4.7%)	1 (1.5%)	0.354
non CV death	6 (9.4%)	2 (2.9%)	0.156
all cause of death	9 (14.1%)	6 (8.8%)	0.416
Event-free survivals	43 (67.2%)	57 (83.2%)	**0.026**

[a] Fisher's exact test

Table 3. Cox regression analysis

Event	Predictor	Unadjusted estimates				Adjusted estimates			
		Sig.	HR	95% CI for HR		Sig.	HR	95% CI for HR	
				Lower	Upper			Lower	Upper
MACE	Group (1= Seal-wing PEB)	**0.025**	**2.265**	1.111	4.619	**0.026**	**2.325**	1.107	4.881
CV death	Group (1= Seal-wing PEB)	0.981	0.982	0.215	4.477	0.848	0.856	0.174	4.209
Acute MI	Group (1= Seal-wing PEB)	0.367	2.184	0.400	11.93	0.287	2.648	0.441	15.894
TVR	Group (1= Seal-wing PEB)	**0.010**	**3.162**	1.320	7.573	**0.009**	**3.387**	1.363	8.420
All course of death	Group (1= Seal-wing PEB)	0.198	1.987	0.698	5.653	0.202	2.034	0.683	6.059
Definite ST	Group (1= Seal-wing PEB)	0.475	0.016	0	1383	-	-	-	-
2nd MACE	Group (1= Seal-wing PEB)	0.164	5.078	0.514	50.16	0.204	4.5781	0.439	47.84

Figures

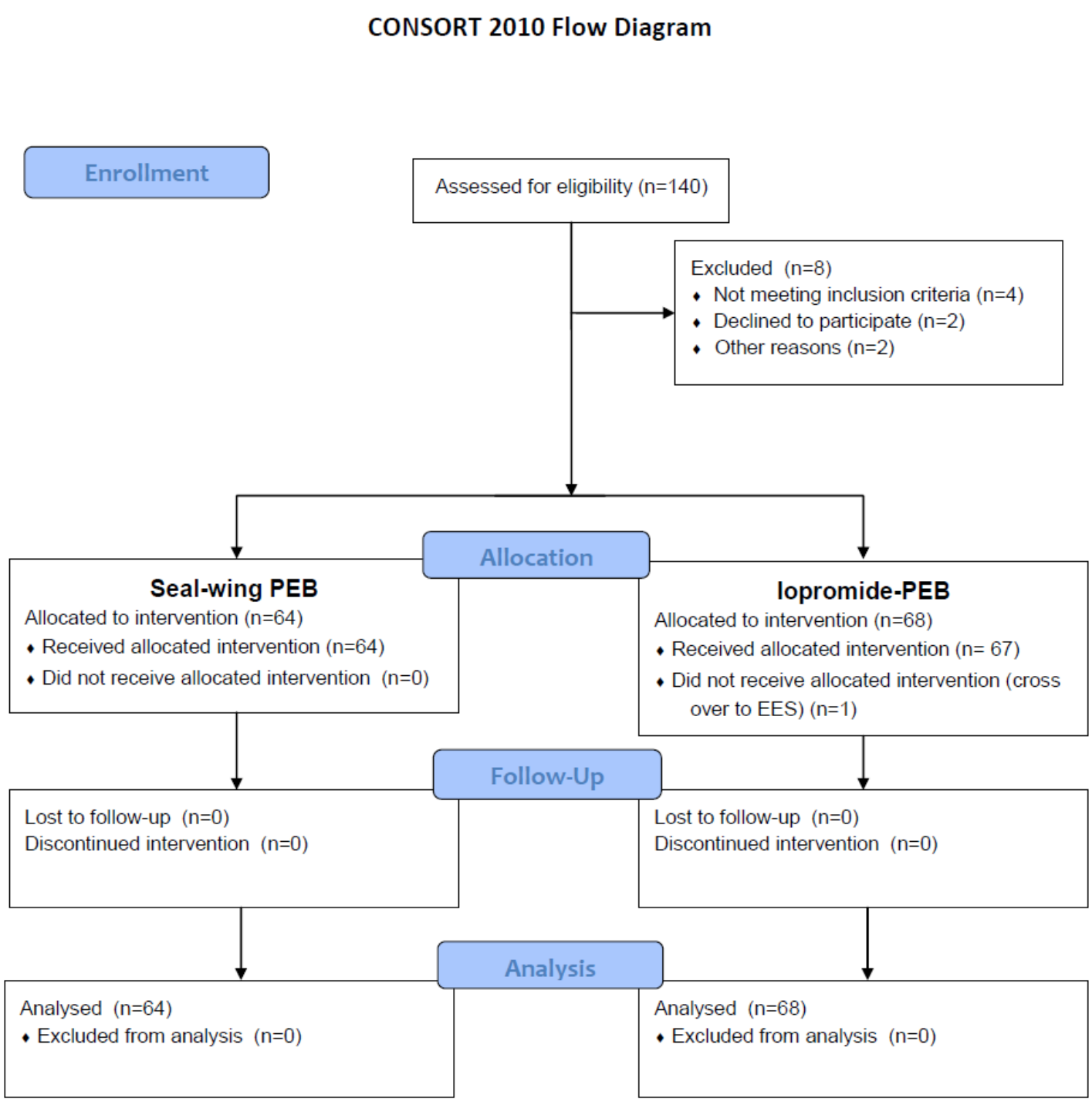

Figure 1

the CONSORT flow diagram

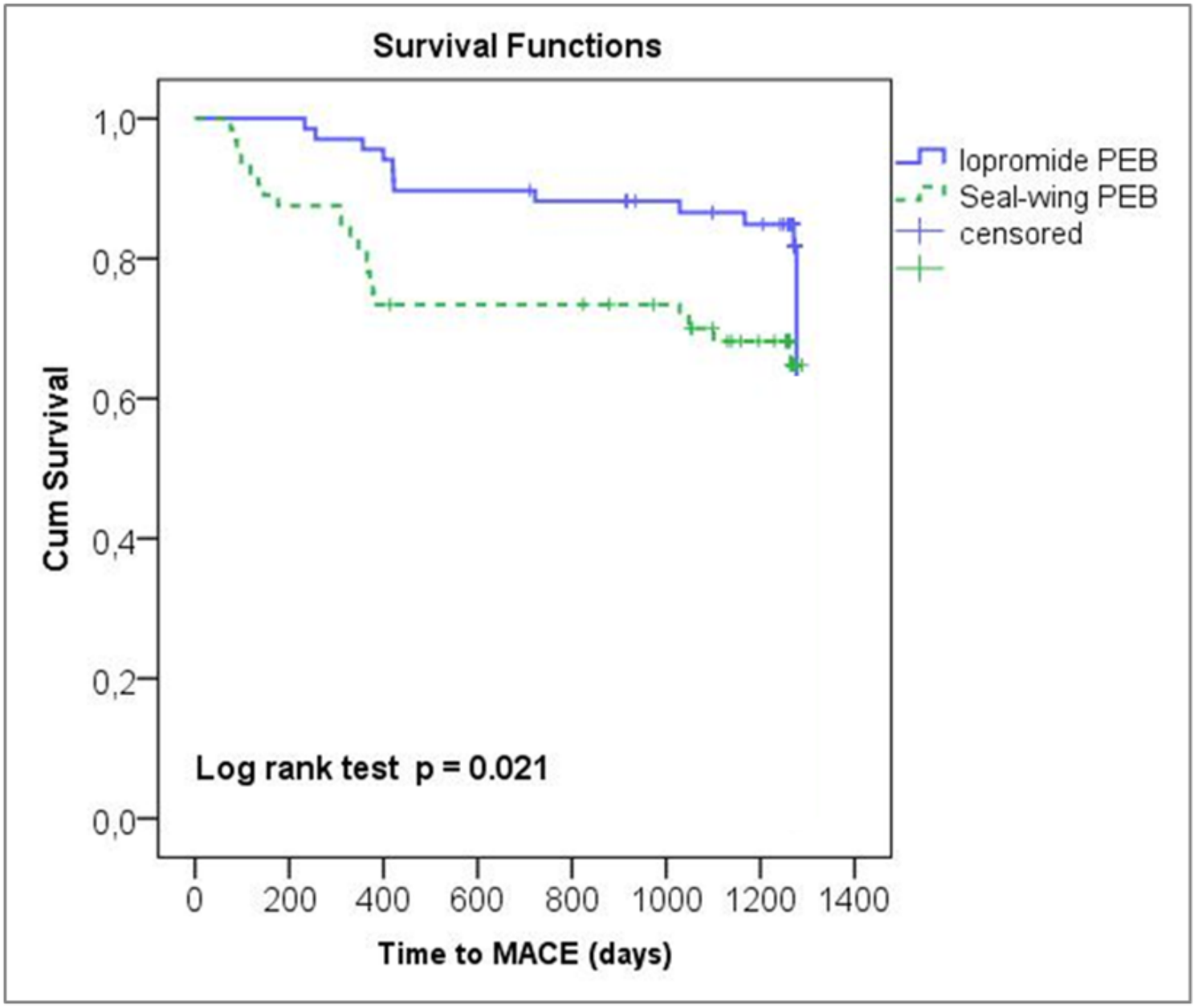

Figure 2

Event-free survival_time-to MACE

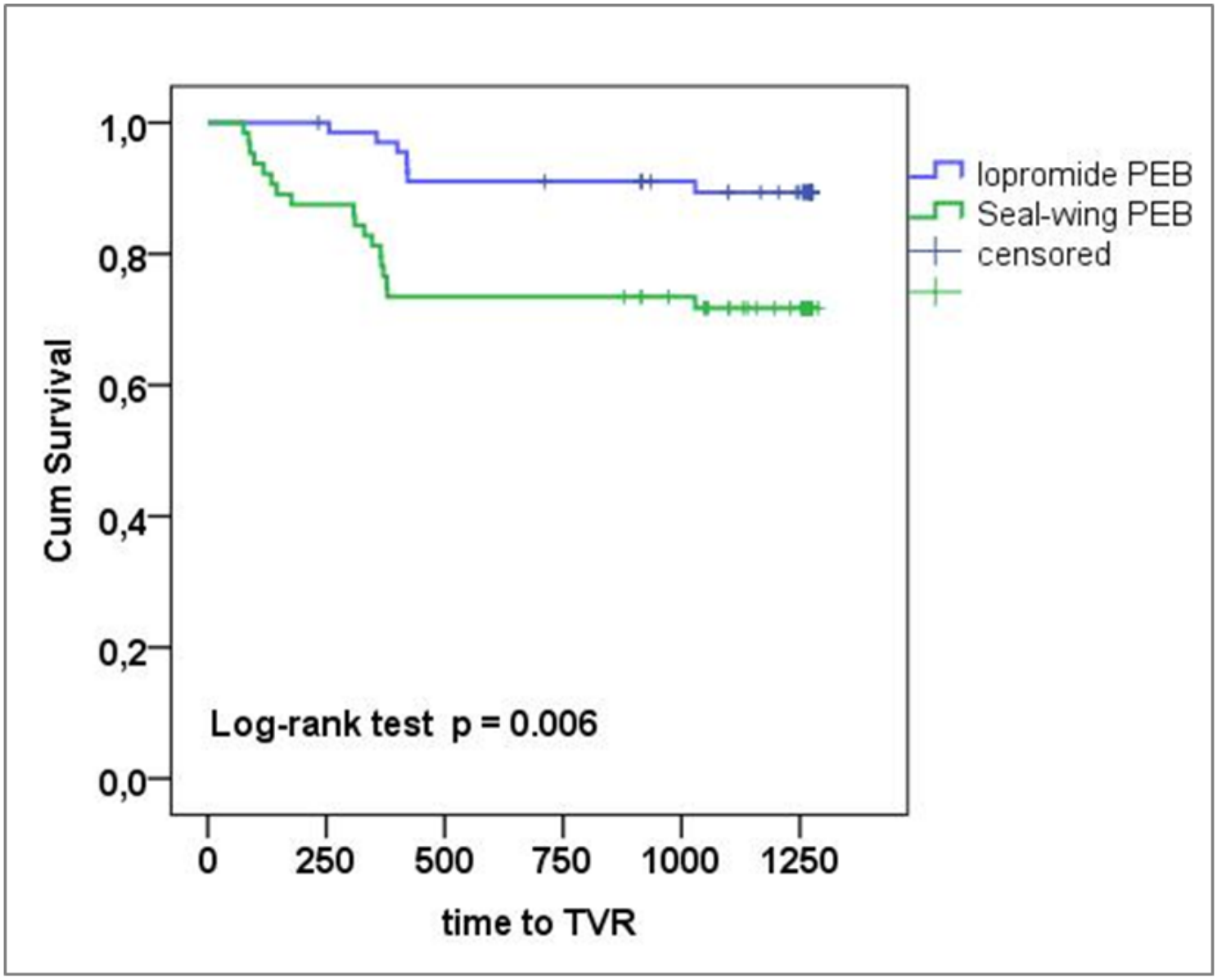

Figure 3

Event-free survival_time-to TVR

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CONSORT2010Checklist.docx