タイトル	Same or different drug-eluting stent re-implantation for drug-eluting stent restenosis: An assessment including second-generation drug-eluting stents
別タイトル	薬剤溶出性ステント再狭窄に対する同一もしくは異なった薬剤溶出性ステント再留置: 第二世代薬剤溶出性ステントを含めた検討
作成者（著者）	矢部, 敬之
公開者	東邦大学
発行日	2017.03.28
掲載情報	東邦大学大学院医学研究科 博士論文. 47.
資料種別	学位論文
内容記述	主査 : 渡邉善則 / タイトル : Same or different drug-eluting stent re-implantation for drug-eluting stent restenosis: An assessment including second-generation drug-eluting stents / 著者 : Takayuki Yabe, Mikihito Toda, Rine Nakanishi, Daiga Saito, Ippei Watanabe, Ryo Okubo, Hideo Amano, Takanori Ikeda / 掲載誌 : Journal of Interventional Cardiology / 巻号・発行年等 : 29(3):311-8, 2016 / 本文ファイル: 査読後原稿 / This is the peer reviewed version of the following article:【Journal of Interventional Cardiology,29,311】, which has been published in final form at DOI: 【10.1111/joic.12299】. This article may be used for non-commercial purposes in accordance With Wiley Terms and Conditions for self-archiving.
著者版フラグ	ETD
報告番号	32661甲第817号
学位記番号	甲第548号
学位授与年月日	2017.03.28
学位授与機関	東邦大学
DOI	info:doi/10.1111/joic.12299
その他資源識別子	http://onlinelibrary.wiley.com/doi/10.1111/joic.12299/abstract
メタデータのＵＲＬ	https://mylibrary.toho-u.ac.jp/webopac/TD70687995

Same or different drug-eluting stent re-implantation for drug-eluting stent restenosis:

An assessment including second-generation drug-eluting stents

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This manuscript was supported in part by Grants-in-Aid (24591074 and 15K09103 to T.I.) for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

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Abstract

Objectives: We examined the long-term outcomes of implanting a different type of drug-eluting stent (DES), including second-generation DES, for treatment of DES-in stent restenosis (ISR).

Background: Treatment for DES-ISR has not been standardized.

Methods: The subjects were 80 patients with 89 lesions underwent DES implantation for DES-ISR. The patients were divided into the group of patients receiving the same DES for DES-ISR (Homo-stent: 24 patients, 25 lesions) and a different DES for DES-ISR (Hetero-stent: 56 patients, 64 lesions). The primary endpoint was survival free of major adverse cardiovascular events (MACE), including cardiac death, myocardial infarction, and target vessel revascularization. The secondary endpoint was late loss at 8-12 months follow-up. In the subgroup of patients who were treated with second-generation DES for DES-ISR, we also assessed the survival free of MACE.

Results: During a mean follow-up of 45.1 ± 21.2 months, 26 patients experienced MACE. There was no significant difference in the survival free of MACE (Log rank P=0.17). In the sub-analysis of second generation DES, MACE was significantly higher in the Homo-stent group compared to the Hetero-stent group (Log rank P=0.04). Late loss was significantly higher in the Homo-stent group than in the Hetero-stent group (0.86±1.03 vs. 0.38±0.74 mm, P=0.03). This trend was prominent in the first-generation DES group.

Conclusions: Although there was no significant difference in MACE between the Hetero-stent and the Homo-stent groups including both first and second-generation DES, the sub-analysis demonstrated different DES implantation for DES-ISR significantly improved the MACE rate among patients treated with second-generation DES.

Key Words: drug-eluting stent, in-stent restenosis, same drug-eluting stent, different drug-eluting stent,

Abbreviations

DES Drug-eluting stent

ISR In-stent restenosis

MACE Major adverse cardiac events

Introduction

For a decade, drug-eluting stents (DESs) have been widely used and have more reduced the incidence of in-stent restenosis (ISR) as the Achilles' heel of percutaneous coronary intervention (PCI), compared to bare-metal stents (BMSs), which resulted in further expanding the indications for PCI.[1-3] However, target lesion revascularization (TLR) after DES implantation can still be needed in patients at high risk, such as those with complex lesions.[4] Several previous studies reported that ISR occurred in approximately 15-20% of patients with expansion of the PCI for a complex lesion or patients at high-risk with diabetes.[4,5] The outcomes of PCI for DES-ISR were poor, even when compared to PCI for BMS-ISR.[6-9] Revascularization using a drug-coated balloon (DCB) has recently been allowed and may be a potential alternative to re-implantation of a DES for DES-ISR. In recent randomized clinical trials, however, the DCB did not show a significant benefit in terms of treatment for DES-ISR compared to DES.[10,11] Similarly, few studies have examined the efficacy of revascularization using the same DES as previously placed or a different DES; they did not show a significant difference in terms of treatment for DES-ISR with short-term follow-up.[12-14] In this regard, the treatment for DES-ISR has not been standardized. The second-generation DES has recently used for de-novo lesions and showed excellent clinical outcomes.[15] However, the treatment effect using the second-generation DES between the same and different DESs for DES-ISR has not been examined.

The objective of the present study was to compare long-term incidence of major adverse cardiovascular events (MACEs) between treatment with the same and with different types of DESs including the second-generation DES among patients who had DES-ISR.

Methods

Patient Population

Between January 2006 and May 2013, we retrospectively identified 89 consecutive DES-ISR lesions among 80 patients who underwent DES re-implantation at our institution. All patients were treated with DES implantation for the DES restenosis for recurrent symptoms or the presence of ischemia. Restenosis was defined as >50% diameter stenosis by quantitative coronary angiography within the stent segment, including the 5-mm margins proximal and distal to the stent edge. Patients with stent thrombosis were excluded from the current study. The patterns of restenosis were categorized into four groups according to the classifications described previously by Mehran et al.[16] The patients were divided into a group of 24 patients (25 lesions) receiving the same DES as that initially implanted (Homo-stent group) and a group of 56 patients (64 lesions) receiving a different DES (Hetero-stent group). This protocol was approved by the ethics committee of our hospital.

PCI strategy and antiplatelet therapy

Invasive coronary angiography was performed in accordance with the American College of Cardiology/American Heart Association Guidelines for Coronary Angiography.[17] All patients had continued to take 100 mg of aspirin and 75 mg of clopidogrel or 200 mg of ticlopidine until the follow-up coronary angiography. In the catheterization laboratory, intravenous unfractionated heparin (100 U/kg) was administered for anticoagulation during the procedure; it was given as a loading dose followed by additional boluses to maintain the activated clotting time between 250 and 300 seconds. During the period from January 2006 to February 2010, re-implantation of first-generation DESs, including a sirolimus-eluting stent (SES) (Cypher; Cordis/Johnson & Johnson, Warren, NJ, USA) and a paclitaxel-eluting stent (PES) (Taxus; Boston Scientific, Natick, MA, USA), was performed. Re-implantation using second-generation DESs, including a zotarolimus-eluting stent (E-ZES) (Endeavor; Medtronic, Santa Rosa, CA , USA), an everolimus-eluting stent (EES) (Xience V, Xience Prime, Xience Xpedition; Abbott Vascular, Santa Clara, CA, USA or PROMUS, PROMUS element; Boston Scientific), a biolimus-eluting stent (BES) (Nobori; Terumo, Tokyo, Japan), and a zotarolimus-eluting stent (R-ZES) (Resolute Integrity; Medtronic), was performed during the period from March 2010 to May 2013. The Homo-stent group was defined as the same stent's drug coating type which was used to the first one (e.g. SES for SES ISR, or EES for EES ISR). DES with different polymer or platform with the same drug coating was categorized into the Homo-stent group. The Hetero-stent group was defined as switching the generation of the

stent or the stent's drug coating (e.g. EES for SES ISR, or R-ZES for EES ISR). DES with different drugs coating but within the same family (limus) was considered as the Hetero-stent group. The choices of DESs and the treatment strategy were taken by the operators. All patients after PCI received lifelong 100-mg aspirin and 75-mg clopidogrel or 200-mg ticlopidine for at least 12 months.

Quantitative coronary angiography (QCA) analysis

Coronary angiograms were analyzed using the CCIP310 system (Gadelius Medical Co, Tokyo, Japan). Diastolic frames were taken at the angle that showed the least shrinkage of the lesions; the same angle was used before and after treatment for recording the image. Reference vessel diameter (RVD), minimal lumen diameter (MLD), and percentage of diameter stenosis (%DS) were measured at baseline, post-procedure, and at follow-up. In-stent late loss was defined as post-procedure MLD minus MLD at follow-up. Angiographic restenosis was defined as %DS >50 by QCA within the target lesion including the 5-mm margins proximal and distal to the stent edge at follow-up.

Study definitions and follow-up

Clinical follow-up was performed by office visit or telephone contact at 12 and 24 months after the procedure. Angiographic follow-up was suggested for patients at 8-12

months post-procedure. Angiographic restenosis, target lesion revascularization (TLR), target vessel revascularization (TVR), myocardial infarction (MI), cardiac death, major adverse cardiac events (MACE) including cardiac death, non-fatal MI, or TVR, and stent thrombosis were analyzed. The primary endpoint of this study was survival free of MACE during follow-up period. TLR was defined as any repeat percutaneous intervention or surgical bypass for stenosis >50% within the stent or within the 5-mm proximal or distal to the stent edge. TVR was defined as revascularization of the target vessel. MI was defined as >2 times the upper limit of normal of creatine kinase-MB fraction and new ST-segment elevations or new Q-waves on the electrocardiogram. Stent thrombosis was defined according to the Academic Research Consortium classification.[18]

Statistical analysis

Statistical analysis was performed using SPSS version 20 for Windows (SPSS, Inc., Chicago, IL, USA). Continuous variables were compared between the Homo-stent and Hetero-stent groups using paired Student's *t*-tests and are presented as means ± SD. Categorical variables were compared between the two groups using the χ^2-test or Fisher's exact test as appropriate. Baseline clinical characteristics, lesion characteristics, procedural characteristics, QCA data, and clinical events at one and two years were compared between the same and different DES groups. MACE was analyzed using multivariable Cox

proportional hazard model adjusted for age, gender, second-generation DES-ISR, Hetero-stent group, implanted stent diameter and implanted stent length before re-PCI. Cumulative MACE-free survival during the chronic phase was determined using the Kaplan-Meier method, and survival curves were compared by the log-rank test. In addition, we analyzed the MACE-free survival in the subgroup of patients who were treated with only second-generation DES for DES-ISR [same second-generation DES group (12 patients, 12 lesions) versus different second-generation DES group (36 patients, 40 lesions)]. A P value of <0.05 was considered significant.

Results

The patient baseline clinical characteristics are shown in **Table 1**. There were no significant differences in coronary risk factors between the Homo-stent and Hetero-stent groups. Overall, 32.5% of patients had a prior MI. Laboratory data and medication did not differ between the two groups.

Table 2 shows lesion characteristics before PCI for DES-ISR. There was no significant difference in first-generation DES restenosis between the two groups (P=0.053). Implanted stent diameter before re-PCI was significantly larger in the Hetero-stent group than in the Homo-stent group (2.76 ± 0.28 vs. 2.96 ± 0.38 mm, P=0.022). There was no significant difference in the ISR pattern between the two groups (P=0.320).

Procedure characteristics are shown in **Table 3**. Intravascular ultrasound (IVUS) was used in 82.0% of all lesions, and there was no significant difference in IVUS use between the two groups. The rate of sirolimus-eluting stent implantation was significantly higher in the Homo-stent group than in the Hetero-stent group, with 44.0% in the Homo-stent group and 14.1% in the Hetero-stent group, respectively (P=0.002). There were no significant differences in stent diameter, stent length, and the rate of post dilatation.

QCA data are listed in **Table 4**. Angiographic follow-up was available in 18 lesions (72.0%) in the Homo-stent group and 53 lesions (82.8%) in the Hetero-stent group (P=0.846). There were no significant differences in RVD, MLD, and %DS at pre-procedure and post-procedure between the two groups. The rate of restenosis at follow-up was 27.7% and 13.2% in the Homo-stent and Hetero-stent groups, respectively (P=0.154).

Figure 1 summarizes late loss at follow-up. Late loss in overall was significantly higher in the Homo-stent group than in the Hetero-stent group (0.86 ± 1.03 vs. 0.38 ± 0.74 mm, P=0.036). This trend was more evident in the first-generation group (0.99 ± 0.79 vs. 0.42 ± 0.73 mm, P=0.040). In the second-generation DES group, late loss after treatment of DES-ISR using the Homo-stent was higher compared to the Hetero-stent, but not statistically different (0.65 ± 1.37 vs. 0.35 ± 0.75 mm, P=0.452).

Stent thrombosis and early revascularization <3 months after PCI were not observed in this study. Although the incidences of TLR and MACEs were higher in the Homo-stent

group than in the Hetero-stent group, statistically differences were not found (TLR one year: 20.0% vs. 7.8%, P=0.101; two years: 20.0% vs. 9.3%, P=0.171; MACEs one year: 29.1% vs. 14.2%, P=0.118; two years 37.5% vs. 17.8%, P=0.059). By contrast, the incidence of TVR was significantly higher in the Homo-stent group than in the Hetero-stent group (one year: 28.0% vs. 9.3%, P=0.025; two years: 32.0% vs. 10.9%, P=0.017).

In multivariable Cox proportional hazard model after adjusting for age, gender, second-generation DES-ISR, Hetero-stent group and lesion characteristics including implanted stent diameter and implanted stent length before re-PCI, implanted stent diameter (HR 0.76, 95% CI 0.21-2.68, P=0.68) and implanted stent length (HR 0.96, 95% CI 0.89-1.03, P=0.32) were not significant predictors of MACE.

The Kaplan-Meier curves for freedom from MACEs in the Homo-stent and Hetero-stent groups. During a mean follow-up of 45.1 ± 21.2 months, there was no significant difference in MACE-free survival between the two groups (log-rank P=0.165). However, in the sub-analysis of second-generation DES implantation (Homo-stent group 12 patients, Hetero stent group 36 patients) for DES-ISR, MACE rate was significantly higher in the Homo second-generation DES implantation group than in the Hetero second-generation DES group (log rank P=0.036) (**Figure 2**).

Discussion

The present study compared the efficacy of the same type of DES versus a different type of DES for the treatment of DES-ISR during long-term follow-up of over 5 years. The primary finding of this study was that, during a mean follow-up of 45.1 ± 21.2 months, the MACE rate after treatment of DES-ISR using different DES implantation showed lower, but not statistically different compared to that after implantation of the same DES. Of interest, however, in a sub-analysis of patients who underwent PCI with second-generation DES for DES-ISR, the MACE rate was significantly lower in the different second-generation DES group than in the same second-generation DES group.

Given the poor outcome of DES-ISR, DES-ISR has been considered to be a complex lesion. The mechanisms of DES-ISR involve mechanical factors such as under- or overexpansion of the DES, stent fracture, non-uniform strut distribution, or stent malapposition, as well as drug-specific factors such as non-uniform drug deposition, polymer disruption due to stent delivery, or drug resistance.[13,19-22] The rationale for implantation of a different DES for DES-ISR is based on the different mechanisms of action of their active pharmacologic agents. The drug-specific factors may inhibit greater formation of intimal hyperplasia in stents using different DESs when compared to that using the same DESs. Taking into account these contributing factors, several investigations have examined the treatment of DES-ISR using different types of DES re-implantation, but failed to show a significant improvement compared to the same type of DES.[12-14,23] A limited paper reported

by Mishkel et al.[24] demonstrated treatment with a different DES for DES-ISR tended to result in better 12-month outcomes than with the same DES, though it was not statistically significant. Most of those studies were conducted to investigate a cohort treated in the first-generation DES era. Alfonso et al. [25] reported the RIBS III (Restenosis Intra-Stent: Balloon Angioplasty Versus Drug-Eluting Stent) prospective multicenter study. This trial allocated 363 patients with DES-ISR to either the different DES implantation (n=274) or alternative therapeutic modalities (balloon angioplasty, bare-metal stent implantation, or same DES implantation) (n=89), and second- generation DES were used in 33% of patients treated for DES-ISR. MLD at follow-up was larger (1.86 ± 0.7 mm vs. 1.40 ± 0.8mm, P=0.003) and recurrent restenosis rate was lower (22% vs. 40%, P=0.008) in the different DES group. Moreover, the use of a different DES provided better angiographic results than the use of the same DES when the analysis was restricted to patients treated with second-generation DES.[25]

In the current study, MLD at follow-up was 2.40 ± 0.82 mm and restenosis rate was 13.2% in the different DES group. These results were consistent with the aforementioned RIBS III study. Furthermore, the unique of the current study is the second-generation DES was used in 60% of our population. In the sub-analysis of patients who underwent revascularization for DES-ISR by second-generation DESs, the MACE rate was significantly higher in the same DES group than in the different DES group. This might be explained by

differences in the tissular response to the different DES. Second-generation DESs have become standard to be used for coronary revascularization because they show greater inhibition of intimal hyperplasia and decreased late loss compared to first-generation DESs for de-novo or ISR lesions.[15,26] Kim et al.[27] reported that the percentage of uncovered struts and malapposed struts was significantly less in second-generation DESs than in first-generation DESs on optical coherence tomography. In the recent large network meta-analysis of 51 trials including 52,158 randomized patients, second-generation DESs have substantially better long-term safety and efficacy outcomes than first-generation DESs.[28] This mechanisms may be related to enhanced endothelialization of second-generation DES compared to first-generation DES, with greater strut coverage, less inflammation and chronic hypersensitivity reactions, and less fibrin deposition.[29] The findings of these studies support the concept that the second-generation DESs may also inhibit late loss and improve clinical outcomes after DES implantation compared to the first-generation DES. Some evidence in support of this hypothesis was observed. In the current study, IVUS was used in 82.0% of all lesions. We found that late loss was 2-fold higher in the Homo-stent group than in the Hetero-stent group. Moreover, the second-generation DES implantation for DES-ISR tended to more favorable inhibition of late loss than the first-generation DES implantation (0.65 ± 1.37 vs. 0.99 ± 0.79 mm, P=0.512 for the Homo-stent group: 0.35 ± 0.75 vs. 0.42 ± 0.73 mm, p=0.893 for the Hetero-stent group). The similar finding was reported by Yamashita et al. [26]

They revealed the treatment with a second-generation DES for DES-ISR reduces late lumen loss and have favorable outcomes compared with a first-generation DES.[26] In this regard, the present findings suggest that selection of stent types or generations might improve outcomes in individual patients who develop DES-ISR, and the different second-generation DES implantation for DES-ISR may have the potential benefit of providing an alternative mechanism for the inhibition of intimal hyperplasia.

Limitations

This study has the limitations inherent to the analysis of retrospective, nonrandomized, and single-center data. We must also acknowledge the small sample size. This is considered to be one of the factors that there was no significant difference in late loss of the second-generation DES implantation between the Homo and the Hetero-stent groups. Another limitation is that the choice of the DES implanted was at the operator's discretion. However, there were no significant differences in clinical characteristics, quantitative coronary angiographic data before and after the procedure, procedural characteristics, or IVUS use between the Homo and Hetero-stent groups, which may be potential factors affecting future events. Implanted stent diameter before re-PCI was significantly larger in the Hetero-stent group than the Homo-stent group (2.96 ± 0.38 mm vs. 2.76 ± 0.28 mm, P=0.022). However, after adjusting for multiple factors, implanted stent diameter was not a significant predictor.

Further large, randomized, prospective studies comparing effectiveness between homo and hetero stent groups for patients with DES-ISR are needed.

Conclusions

In the present study, there was no significant difference in the MACE rate between the same and different types of DES implantation for DES-ISR during long-term follow-up, whereas the use of a different type of DES improved the MACE rate more than the use of the same type of DES in patients who were treated with second-generation DESs.

Disclosure

All authors have no conflict of interest.

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Figure legends

Figure 1. Late loss at 8-12 months angiographic follow-up between the Homo-stent and Hetero-stent groups in overall (Homo-stent group: 18 lesions, Hetero-stent group: 53 lesions), first-generation DES (Homo-stent group: 11 lesions, Hetero-stent group: 22 lesions), and second-generation DES (Homo-stent group: 7 lesions, Hetero-stent group: 31 lesions) for DES-ISR.

Abbreviations: DES- drug-eluting stent, ISR- in-stent restenosis

Figure 2. Kaplan-Meier curves for MACE Free survival (cardiac death, non-fatal MI, TVR) in the Homo-stent (n=12) and Hetero-stent (n=36) groups among patients with second-generation DES for DES-ISR.

Abbreviations: MACE- major adverse cardiovascular events, MI- myocardial infarction, TVR- target vessel revisualization, DES- drug-eluting stent, ISR- in-stent restenosis

Table 1. Baseline clinical characteristics

	Homo-stent group	Hetero-stent group	P value
Number of patients	24	56	
Age (years)	69.87 ± 9.78	69.28 ± 8.29	0.784
Male	21 (87.5%)	51 (91.0%)	0.626
BMI (kg/m^2)	23.59 ± 2.64	25.16 ± 4.03	0.084
Hypertension	16 (66.6%)	38 (67.8%)	0.917
Dyslipidemia	15 (62.5%)	35 (62.5%)	0.911
Diabetes mellitus	12 (50.0%)	25 (44.6%)	0.660
History of smoking	16 (66.6%)	42 (75.0%)	0.444
Hemodialysis	4 (16.6%)	11 (19.6%)	0.755
Prior myocardial infarction	10 (41.6%)	16 (28.5%)	0.298
Prior CABG	1 (4.1%)	5 (8.9%)	0.436
LVEF (%) of echocardiography	64.52 ± 13.02	61.94 ± 12.53	0.406
Laboratory data			
eGFR (ml/min/1.73m^2)	53.00 ± 26.67	45.65 ± 27.53	0.418
HbA1c (%)	5.99 ± 1.13	5.95 ± 0.94	0.881
Triglyceride (mg/dL)	131.41 ± 80.38	123.21 ± 46.72	0.568
HDL cholesterol (mg/dL)	43.25 ± 12.09	49.28 ± 13.52	0.063
LDL cholesterol (mg/dL)	113.87 ± 43.03	101.48 ± 25.78	0.115
LDL/HDL ratio	2.85 ± 1.38	2.30 ± 1.09	0.059
BNP (pg/mL)	334.23 ± 896.97	190.08 ± 415.68	0.336
Medication (%)			
Aspirin	24 (100%)	58 (100%)	-
Clopidogrel	22 (91.6%)	51 (91.0%)	0.934
Ticlopidine	1 (4.1%)	2 (3.5%)	0.823
ACE-I/ARB	21 (87.5%)	43 (76.7%)	0.272
Insulin	2 (8.3%)	7 (12.5%)	0.589
Statin	13 (54.1%)	38 (67.8%)	0.243

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BNP, brain natriuretic peptide; DAPT, dual antiplatelet therapy; ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

Table 2. Lesion characteristics

	Homo-stent group	Hetero-stent group	P value
Number of lesions	25	64	
1st generation DES restenosis	13 (52.0%)	47 (73.4%)	0.053
2nd generation DES restenosis	12 (48.0%)	17 (26.6%)	-
Implanted stent diameter (mm)	2.76 ± 0.28	2.96 ± 0.38	0.022
Implanted stent length (mm)	23.39 ± 4.69	20.81 ± 5.98	0.065
Target arteries			0.605
Right coronary artery	12 (48.0%)	28 (43.7%)	
Left anterior descending	11 (44.0%)	25 (39.0%)	
Left circumflex	1 (4.0%)	8 (12.5%)	
Left main trunk	1 (4.0%)	3 (4.6%)	
ISR pattern[a]			0.320
I	17 (68.0%)	50 (78.1%)	
II•III•IV	8 (32.0%)	14 (21.9%)	
Extent of CAD			0.093
1 vessel disease	11 (44.0%)	14 (21.9%)	
2 vessel disease	7 (28.0%)	20 (31.2%)	
3 vessel disease	7 (28.0%)	30 (46.9%)	
Coronary calcification	7 (28.0%)	23 (35.9%)	0.477
Chronic total occlusion	2 (8.0%)	3 (4.6%)	0.302

Abbreviations: DES, drug-eluting stent; CAD, coronary artery disease.

[a]According to the classification of Mehran et al. [16].

Table 3. Procedural characteristics

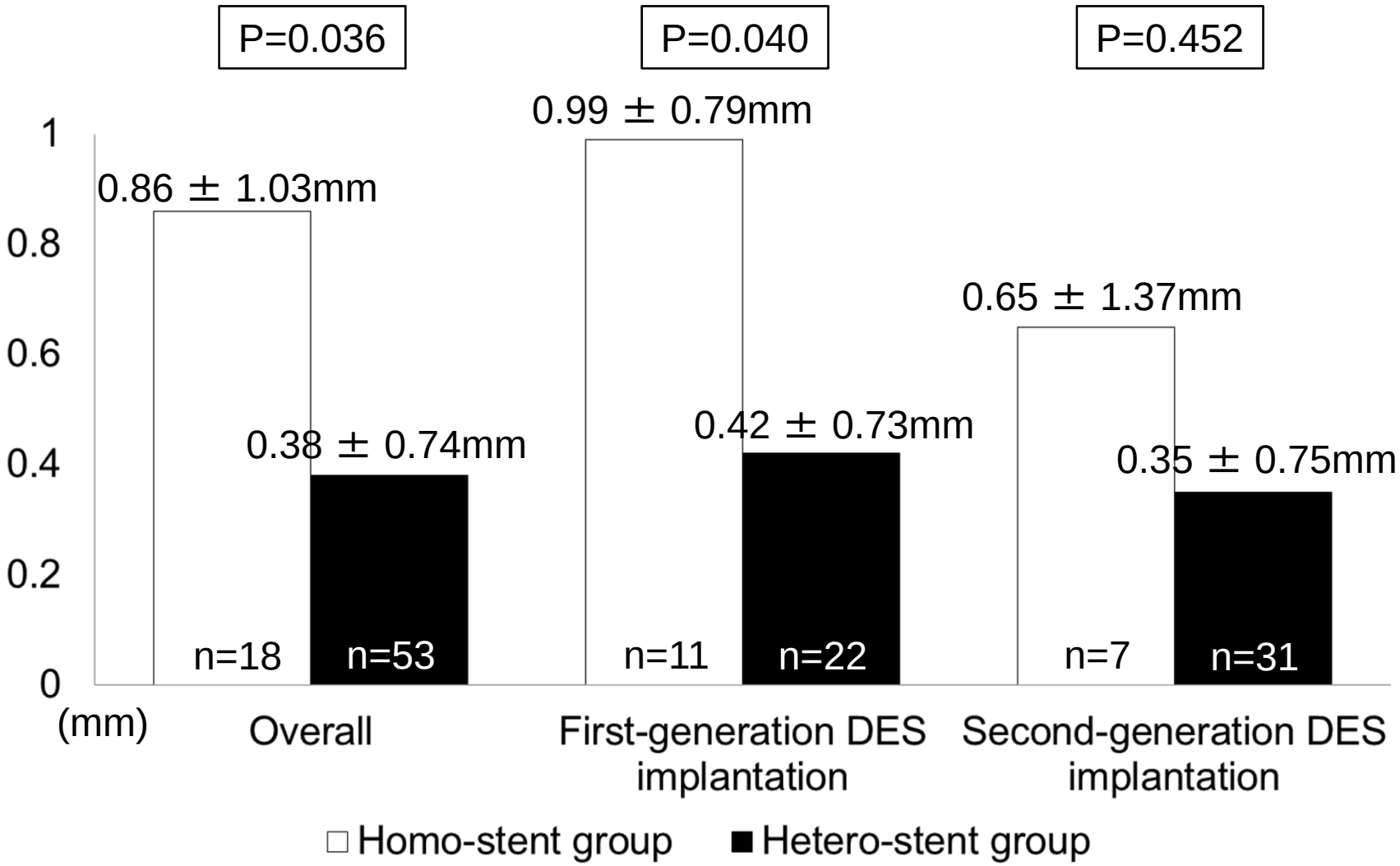
	Homo-stent group	Hetero-stent group	P value
Number of lesions	25	64	
IVUS use	22 (88.0%)	51 (79.6%)	0.359
Treatment of DES restenosis			
SES implantation	11 (44.0%)	9 (14.1%)	0.002
PES implantation	2 (8.0%)	15 (23.4%)	0.096
EES implantation	12 (48.0%)	28 (43.8%)	0.717
ZES implantation	0 (0%)	5 (7.8%)	0.150
BES implantation	0 (0%)	7 (10.9%)	0.085
2^{nd} generation DES implantation	12 (48.0%)	40 (62.5%)	0.212
Stent diameter (mm)	2.85 ± 0.36	2.98 ± 0.37	0.121
Stent length (mm)	18.92 ± 6.19	18.12 ± 6.72	0.610
Post dilatation	20 (80.0%)	57 (89.0%)	0.261

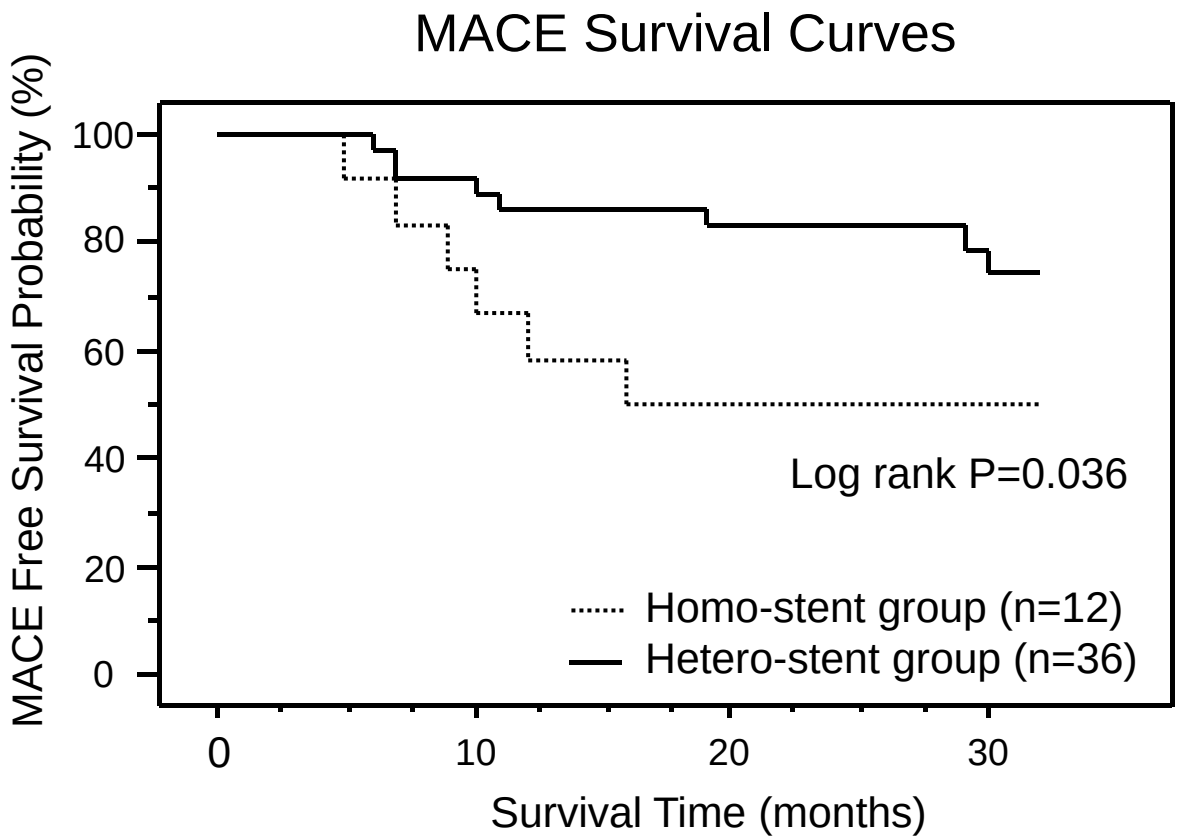
Abbreviations: IVUS, intravascular ultrasound; SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; EES, everolimus-eluting stent; ZES, zotarolimus-eluting stent; BES, biolimus-eluting stent.

Table 4. Quantitative coronary angiographic data

	Homo-stent group	Hetero-stent group	P value
【Pre procedure】			
Number of lesions	25	64	
RVD (mm)	2.73 ± 0.57	2.87 ± 0.50	0.280
MLD (mm)	0.72 ± 0.42	0.77 ± 0.41	0.577
DS (%)	74.16 ± 13.16	73.03 ± 13.27	0.719
Lesion length (mm)	15.07 ± 6.53	15.27 ± 6.53	0.897
【Post procedure】			
Number of lesions	25	64	
RVD (mm)	2.82 ± 0.55	2.89 ± 0.47	0.564
MLD (mm)	2.69 ± 0.57	2.80 ± 0.50	0.348
DS (%)	4.00 ± 11.13	2.81 ± 11.32	0.656
【Follow-up at 8 months】			
Number of lesions	18	53	
MLD (mm)	2.08 ± 0.95	2.40 ± 0.82	0.180
DS (%)	29.33 ± 30.93	19.56 ± 26.44	0.199
Restenosis	5 (27.7%)	7 (13.2%)	0.154

Abbreviations: RVD, reference vessel diameter; MLD, minimal lumen diameter; DS, diameter stenosis.


P=0.036
P=0.040
P=0.452
1
0.8
0.6
0.4
0.2
0
(mm)
0.86 ± 1.03mm
0.38 ± 0.74mm
0.99 ± 0.79mm
0.42 ± 0.73mm
0.65 ± 1.37mm
0.35 ± 0.75mm
n=18
n=53
n=11
n=22
n=7
n=31
Overall
First-generation DES implantation
Second-generation DES implantation
□ Homo-stent group
■ Hetero-stent group



Number at risk

Homo-stent	12	8	6	1
Hetero-stent	36	32	29	17