THE EFFECTS OF CLINICAL, LABORATORY, AND ANGIOGRAPHIC FACTORS ON STENT THROMBOSIS AND MAJOR ADVERSE CARDIAC EVENTS IN PACLITAXEL ELUTING STENTS

Kandemir Çağlayan Hasan,[1] Baytugan Zafer Nart[2]

[1] Department of Cardiology, Kocaeli Public Hospital, Kocaeli, Turkey
[2] Department of Cardiology, Gebze Fatih State Hospital, Kocaeli, Turkey

Abstract: **Background**: Drug-eluting stents (DES) have higher marked efficacy and lower revascularization requirements compared to bare metal stents (BMS). We aimed to determine the mid-term outcomes of patients implanted with a first-generation DES "paclitaxel-eluting stents" (PES).

Methods: Patients with at least 1 PES implanted in our cardiology clinic were received in the non-randomized group. Inclusion criteria were all patients undergoing percutaneous coronary intervention and PES implantation. The mean follow-up time was 35.14 + 13.4 months.

Results: A total of 302 patients (401 lesions and 337 PES) were enrolled in the study. The mean age was 61.86 + 10.27 years. Major adverse cardiac and cerebrovascular events (MACE) occurred at 17.9%, and the stent thrombosis rate was 4%. Independent predictors of stent thrombosis were serum creatinine levels [OR 1.59; 95% CI, 1.03-2.46, p = 0.03] and mean platelet volume [OR 1.59; 95% CI, 1.03–2.46, p = 0.03]. Also, poor functional capacity [OR 2.46: 95% CI, 1.42- 4.26, p < 0.001] and positive ischemia test [OR 3.43: 95% CI, (1.73-6.82), p < 0.001] were predictors of MACE's.

Conclusions: We have demonstrated that PES is safe and effective in the mid-term for use in coronary artery disease.

Keywords: Paclitaxel, restenosis, thrombosis, real-world.

INTRODUCTION

Stents are frequently applied by an interventional cardiologist and constitute more than 80% of all interventional procedures (1). Drug-eluting stents (DES) has reduced restenosis compared with bare metal stents (BMS) in different patients and lesion types (2, 3, 4). Although DES leads to a decrease in restenosis and repeats revascularization rates caused safety concerns such as higher stent thrombosis (ST) rates (2, 3). In the present work, we evaluated the frequency of Major adverse cardiac and cerebrovascular events (MACE) and ST with paclitaxel-eluting stents (PES). We planned a retrospective study to evaluate the effect of patients' clinical, angiographic, laboratory, and procedural variables on these parameters.

MATERIAL AND METHODS

Study population

A total of 302 patients who underwent PES in Kocaeli University Training and Research Hospital between April 2003 and July 2008 were analyzed retrospectively. Patients treated with at least 1 PES were included in the non-randomized group. Inclusion criteria were "all comers" for routine or emergency percutaneous coronary intervention and had native or graft vessel disease with > 18 years of age. The basic clinical and demographic features of the patients on admission are shown in Table 1. Patients who gave written informed consent to this work, without restriction on target vessel and a number of lesions, were included. Laboratory values, including complete blood counts and biochemical parameters (homocysteine, hs. CRP, fasting blood glucose, fibrinogen, fasting lipid panel, creatinine, and uric acid), were obtained from the hospital's electronic database system.

The procedures were applied following the current guidelines, and the stent placement strategy, pre-dilatation, post-dilatation, and use of Gp IIb-IIa were left to the operator's discretion. Dual antiaggregant therapy

(clopidogrel and acetylsalicylic acid) was started for all patients before the procedure. ST was defined with the Academic Research Consortium definitions (5) (Table 2).

ST segment elevation myocardial infarction (ST-MEI) was defined based on the ST-elevation in 2 or more contiguous leads ≥ 0.2 mV or new left bundle-branch block associated with new onset chest pain (6). Non-ST segment myocardial infarction (NSTEMI) was diagnosed according to the European Society of Cardiology criteria, as acute chest pain with the rise of cardiac markers without permanent ST-segment elevation (7). MACEs are defined as myocardial infarction (MI), stroke, heart failure, and/or death from cardiovascular disease (8). According to the Declaration of Helsinki, the present study was reviewed and approved by the local ethics committee.

Statistic

Data were analyzed in SPSS for Windows 17 statistical software program. Numerical variables were described as a mean ±standard deviation, and classified variables were expressed as a number and percentages. The patients were classified according to the development of thrombosis and MACE. Student t-test and Mann Whitney U test were used to compare continuous variables with normal and without normal distribution respectively. Classified variables were compared by Chi-square or Fisher's exact test. Parameters were analyzed with univariate and multivariate logistic regression analyses. Enter method was used in univariate analysis and parameters with p-values below 0.1 were included in the multivariable logistic regression model. The backward method used multivariate logistics regression analysis and p value < 0.05 was accepted as statistical significance. The appropriate cut-off values for the parameters found to be significantly different for the development of ST were determined by ROC curve analysis, which could be used to determine the event development. Kaplan Meier and long-rank analyses were used for the analysis of event-free survival.

RESULTS

A total of 302 patients; 230 men (76.2%) and 72 women (23.8%), aged between 34-88 (61.86 ± 10.27 years) were analyzed. The average follow-up time was 35.14 + 13.4 months. The patients were categorized as silent ischemia, stable angina, unstable angina, NSTEMI, and STMEI according to their clinical status (Table 1).

Coronary angiographic findings

Stenting was applied to a total of 401 lesions, 337 of which were PES and 63 BMS. The average per-

Table 1. Basal demographic and clinical findings of study population

Variables	N	% or mean ± SD
Male gender	230	76.2
Weight (kg)		78 ± 11
Obesity^μ	69	22.8
Diabetes	116	38.4
Hypertension	209	69.3
Hyperlipidemia	270	89.4
Prior CABG	24	7.9
PVD	9	3
MI history	37	12.3
Family history	77	5.5
PCI history	29	12.9
Smoking^α	51	16.9
Atrial fibrillation	12	4
Clinical features		
Silent ischemia	50	16.6
Stable angina	45	14.9
Unstable angina	107	35.4
NSTEMI	32	10.6
STEMI	68	22.5

Abbreviations: CABG: coronary artery by-pass graft, kg: kilogram, STEMI: ST segment elevation myocardial infraction, MI: Myocardial infraction, NSTMEI: Non ST segment elevation myocardial infraction, μ: BMI > 30 kg/m², α: active smoking, PVD: peripheral vascular disease, PCI: Percutaneous coronary intervention.

Table 2. Stent thrombosis classification

Stent thrombosis in Academic Research Consortium definitions
According to time
·Acute   0-24 hours
·Subacute   24 hours- 30 day
·Late   30 day- 1 year
·Very late   > 1 year
Definite stent thrombosis
· Thrombus in stent or 5 mm distal-proximal segments in angiography
· Acute ischemic symptoms onset at rest
· New ischemic ECG changes supporting ischemic symptoms
· Typical elevation of cardiac biomarkers
· Non-occlusive, occlusive thrombus: Intracoronary thrombus
Probable stent thrombosis
· Unexplained death within the first 30 days after stent replacement
· Any MI with documented signs of ischemia, independent of time after stenting, without a obviously cause
Possible stent thrombosis
· Unexplained death from day 30 post stent implantation to end of study follow-up

Abbreviations: ECG: Electrocardiography, MI: myocardial infraction

Table 3. Main demographic, clinical, angiographic and laboratory feature in thrombosis groups

Variable	Thrombosis (-) N = 290	Thrombosis (+) N = 12	P	Variable	Thrombosis (-) N = 290	Thrombosis (+) N = 12	P
Demographic				*Angiographic*			
Age (mean)	61.97+10.22	59.42+11.62	0.40	Slow flow-No reflow	10 (%3.4)	2 (%16.7)	0.02
Male gender	219 (%75.5)	11 (%91.7)	0.30	Lesion type A	24 (%8.3)	0 (%0)	0.60
HT	200 (%69)	9 (%75)	0.76	type B	126 (%43.4)	5 (%41.7)	0.90
DM	111 (%38.3)	5 (%41.7)	1.0	type C	140 (%48.3)	7 (%58.3)	0.49
HL	259 (%89.3)	11 (%91.7)	1.0	TIMI 3 flow	258 (%89)	12 (%100)	0.62
Family history	74 (%25.5)	3 (%25)	1.0	LAD lesion	150 (%51.7)	5 (%41.7)	0.49
Cigarette[α]	48 (%16.6)	3 (%25)	0.43	Cx lesion	69 (%23.8)	5 (%41.7)	0.17
MI history	35 (%12.1)	2 (%16.7)	0.64	RCA lesion	71 (%24.5)	2 (%16.7)	0.73
PCI history	38 (%13.1)	1 (%8.3)	1.0	LMCA lesion	1 (%0.3)	0 (%0)	1.0
CABG history	23 (%7.9)	1 (%8.3)	1.0	Bifurcation	16 (%5.5)	0 (%0)	1.0
PVD history	7 (%2.4)	2 (%16.7)	0.04	Graft lesion	3 (%1)	0 (%0)	1.0
< 6 mount clopidogrel use	32 (11%)	4 (33.3%)	0.04	Stent restenosis	22 (%7.6)	1 (%8.3)	1.0
				Thrombus	5 (%1.7)	0 (%0)	1.0
				PSS length	21.50 + 7.08	19.25 + 6.62	0.27
				Total stent length	26.55 + 12.16	23.08 + 12.82	0.33
Clinical findings				*Laboratory Findings*			
Silent ischemia	50 (%17.2)	0 (%0)	0.22	FBG	102+56	105+45	0.31
Stable Angina	43 (%14.8)	2 (%16.7)	0.69	MPV	9.38 + 1.61	8.41 + 1.38	0.04
Stabil CAD	93 (%32.1)	2 (%16.7)	0.35	Homocysteine	15.99 + 8.21	19.86 + 10.73	0.26
Un-stable Angina	102 (%35.2)	5 (%41.7)	0.76	Creatinine	1.06 + 0.53	2.09 + 3.28	0.04
NSTEMI	30 (%10.3)	2 (%16.7)	0.37	Uric acid	5.65 + 1.63	6.77 + 2.32	0.08
STEMI	65 (%22.4)	3 (%25)	0.73	Total cholesterol	206.94 + 40.74	202.92 + 37.19	0.73
				HDL-C	41.07 + 10.3	36.75 + 8.02	0.15
				TC/HDL-C	5.25 + 1.48	5.81 + 1.83	0.21
				LDL-C	133.50 + 34.65	132.58 + 30.09	0.92
				Fibrinogen	4.46 + 1.53	4.80 + 2.25	0.71
				Hs-CRP	2.26 + 3.56	3.07 + 4.84	0.39

Abbreviations: ACS: Acute coronary syndrome, DM: diabetes mellitus, CABG: coronary artery by-pass graft, CAD: coronary artery disease, FBG: Fasting blood glucose, HL: Hyperlipidemia, HT: Hypertension, TC: Triglyceride, STEMI: ST segment elevation myocardial infraction, MI: Myocardial infraction, Non-STMEI: Non ST segment elevation myocardial infraction, α: active smoking, PVD: peripheral vascular disease, PCI: Percutaneous coronary intervention.

centage of stenosis intervention in coronary angiography was 87.53 ± 9.39 % (60%-100%). Single-vessel coronary artery disease was detected in 182 patients (60.3%), two vessel in 82 (26.8%), and three vessel in 39 patients (12.9%). While the average number of stents per procedure was 1.33 ± 0.53, a maximum of 4 stents were applied. The average total stent length was 26,41 ± 12,18 mm, the shortest size was 8 mm, and the longest was 68 mm.

Risk Factors Associated with Thrombosis

ST occurred in 12 patients (%4). Definite ST was detected in 8 and probable ST in 4 patients. While sub-acute thrombosis was being seen in 1, late 5, and very late in 6 patients, acute thrombosis was not detected. Platelet count and creatinine values were higher, and mean platelet volume was lower detected in the thrombosis group (Table 3). Risk factors predicting ST in the multivariate logistics regression analysis were found as serum creatinine levels (Table 4). The appropriate cut-off value for creatinine by ST was automatically determined as 1 mg/dl by ROC curve analysis (Figure 1). In the ST group, a history of peripheral vascular disease (PVD), slow-flow and no-reflow phenomenon, and P2Y12 receptor blockers use for less than six mounts was more frequently observed (Table 3).

Table 4. *Univariate and multivariate logistic regression analysis examining factors that may be associated with thrombosis and MACE*

Variable	Uni-variable OR (95%CI)	P	Multi-variable OR (95%CI)	P
Thrombosis				
PVD	8.08 (1.48-43.96)	**0.01**	1.20 (0.01-85.44)	0.93
< 6 ay clopidogrel use	4.03 (1.14-14.14)	**0.02**	2.04 (0.21-19.90)	0.53
Hematocrit	0.90 (0.81-1.01)	0.07	1.01 (0.83-1.20)	0.95
Platelet	1.00 (1.00-1.10)	0.07	1.01 (0.99-1.10)	0.57
MPV	0.61 (0.38-0.98)	**0.04**	0.83 (0.42-1.64)	0.60
Creatinine	**1.53 (1.06-2.21)**	**0.02**	**1.59 (1.03-2.46)**	**0.03**
Uric acid	1.37 (0.95-2.00)	0.09	1.28 (0.82-1.99)	0.26
Slow-flow + no-reflow	5.6 (1.08-28.98)	**0.04**	5.30 (0.35-78.84)	0.22
MACE				
Poor functional capacity	2.58 (1.55-4.28)	< 0.01	2.46 (1.42- 4.26)	**< 0.01**
< 6 mount clopidogrel use	2.28 (1.04-4.98)	**0.03**	2.67 (1.14-6.23)	**0.02**
Multi-vessel disease	2.10 (1.43-3.09)	< 0.01	1.81 (1.19 – 2.73)	**< 0.01**
Positive ischemia test	3.92 (2.05-7.47)	< 0.01	3.43 (1.73-6.82)	**< 0.01**
Creatinine	1.34 (0.95-1.88)	0.08	1,22 (0.81-1.83)	0.32
Hematocrit	0.92 (0.87-0.98)	< 0.01	1.01 (0.93-1.10)	0.82
Lesion type	1.62 (0.98-2.68)	0.05	1.39 (0.77-2.48)	0.26
Stent diameter	0.45 (0.18-1.10)	0.08	0.55 (0.19-1.54)	0.25

Abbreviations: MPV: Mean platelet volume, PVD: peripheral vascular disease.
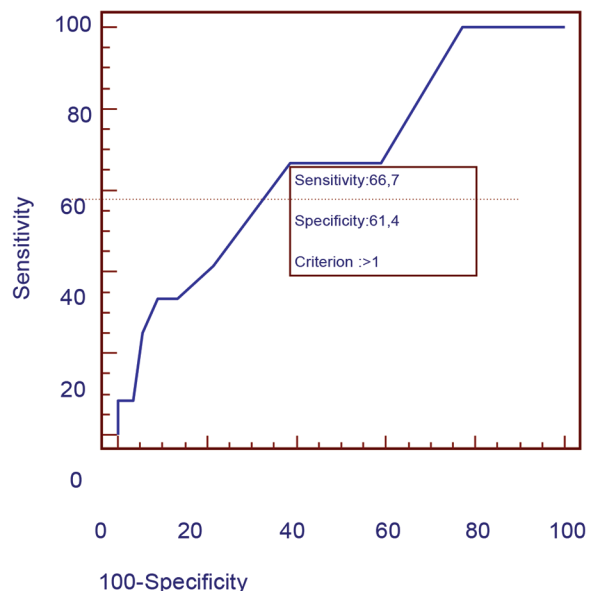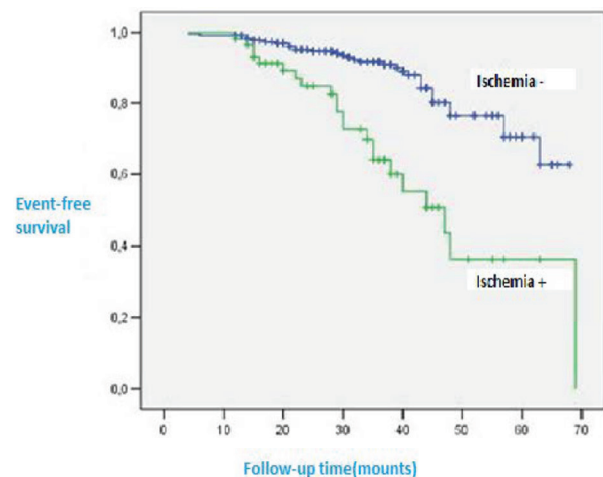

Area	0,670
Standard error	0,0872
95% CI	0,614 - 0,723
z statistic	1,949
p	0,05

Figure 1. *ROC curve analysis for creatinine in predicting stent thrombosis*

	Chi-Square	df	Sig.
Log Rank (Mantel- Cox)	23,180	1	,000

Figure 2. *Kaplan-Meier curve in patients with and without positive ischemia test during follow-up*

Major adverse cardiovascular events (MACE)

The frequency of MACE was observed in 54 patients (% 17.8). 16 deaths, 4 strokes, 18 myocardial infarctions, and 16 hospitalizations for heart failure were

Table 5. Clinical, laboratory and angiographic variables in patients grouped by MACE development

Variable	MACE (-) n = 248	MACE (+) n = 54	p
Single vessel disease	162 (%65.3)	20 (%37)	< 0.01
Multiple vessel disease	86 (%34.7)	34 (%63.0)	< 0.01
Hemoglobin	13,96 + 1,71	13,21 + 1,90	< 0.01
Hematocrit	40,59 + 4,76	38,60 + 5,67	< 0.01
Creatinine	1,05 + 0,45	1,33 + 1,71	0.02
Stent restenosis	15 (%6)	8 (%14.8)	0.04
NYHA I	189 (%76.2)	29 (%53.7)	< 0.01
NYHA III	4 (%1.6)	5 (%9.3)	0.01
< 6 month clopidogrel use	25 (%10.1)	11 (%20.4)	0.03
Positive ischemia test	37 (%14.9)	22 (%40.7)	< 0.01

observed during this follow-up period. Hemoglobin and hematocrit values were lower in the MACE group, while creatinine values were higher (table-5). Patients with a positive ischemia test had significantly lower event-free survival and a higher risk of MACE (Figure 2). Risk factors predicting MACE in the multivariate logistics regression analysis were poor functional capacity, use of P2Y12 receptor blockers for less than six months, positive ischemia test at follow-up, and multi-vessel disease (Table 4).

DISCUSSION

Stent application is widely used over the world, and it seems that new treatment methods will not replace this application in the near future. We determined the rates of ST and MACE after PSS was applied in our clinic. Accordingly in a mean follow-up of about three years, ST was found to be 4% and MACE 17.9%. In the DESIRE registry study (6), which had a similar protocol to our study, the long-term development of MACE was evaluated in 2084 patients. In this study, in which the follow-up period was around 31 months, the MACE was 8.5%, target lesion revascularization (TLR) was 3.3%, and ST was detected at a rate of 1.6%. Also, diabetes mellitus (DM), presentation with acute MI, calcific lesion, graft disease, and post-procedure residual stenosis were found as MACE-related risk factors. Compared to our study, the development of MACE occurred at a lower rate in this study, and this difference may be due to the difference in stent types, follow-up time, and new P2Y12 receptor blockers usage times. In the REAL registry study, in the DES-administered group (patients while PSS was used in 36.71% of them), TLR was 7.3% at the end of two years. In the REAL registry, DM, renal failure, and reference vessel diameter indicated an increased risk of TLR (9, 10). Comparing the use of on-label and off-label PSS in the ARRIVE 1 study, MACE rates were 5.8% in the TLR on-label group and 9.4% in the off-label group at the end of two years (11). In SIRTAX (VERY LATE) trial, MACE was attenuated at 1 year at 11%, at 5 years at 20.8 %, and 32.5 % at 10 years, respectively (12). The risks of MACE were similar between sirolimus-eluting stent (SES) and PES groups. In this study, they showed the risks of TLR and ST significantly reduced 5 years after stent implantation. Galløe et al demonstrated that on years follow-up MACE occurred at 33.1%, ST at 13.3% in the PES group (13). There was a statistically non-significant trend toward increased rates of MACE and ST in PES than in SES. In the study of Räber et al, which compared the first-generation DES, they found more frequency of MACE rate in the PES group in the first year after the stent was implanted, but this adverse outcome decreased in the subsequent years (14).

In a recent study by Simsek et al, SES and PES decreased the frequency of MACE compared to the BMS, but no significant difference was found in all-cause mortality/MI at 6-year follow-up. Also in this study, very late ST was more common in first-generation DES patients than BMS (15). Park et al. showed that in patients with left main coronary artery lesions, there was no significant difference in clinical outcomes at 10-year follow-up between those treated with SES and PES groups (16). Also, ISAR-DESIRE 3 trial found that within 10 years, PES stents significantly reduced target vessel revascularization compared with a plain balloon (17). Thuijs et al reported that at a 10-year follow-up period, no significant difference existed in all-cause death between coronary artery bypass grafting compared to percutaneous coronary intervention (PCI) using PES in patients with three-vessel and left main coronary artery disease (18).

In our study, poor functional capacity, positive follow-up ischemia test, multivessel coronary artery

disease, and P2Y12 receptor blockers use for less than six months were found to be associated with the development of MACE**.** The increase in revascularization rates in these patients contributes to the frequency of MACE. Multivessel disease and poor functional capacity are the most commonly used factors in prognosis assessment in daily practice.

The important risk factor of ST is the discontinuation of antiplatelet therapy in the early period. Autopsy studies indicated delayed healing of thrombosed DES specimens, degeneration of the metal alloy, poor endothelialization, stent malposition, and vessel remodeling as possible factors leading to late /very late ST (19).

In our group, ST was 4%, and it was found to be higher compared to the previous studies. However, the development of defined ST occurred at 2.6% and can be considered similar. In the ESFORA study, definite ST was reported in 2% of 23500 patients after 3 years (20). In this study, subacute and late ST predictors as DM, chronic kidney disease, myocardial infarction, and left anterior descending artery (LAD) lesion. In the ARRIVE 1 registry study, definite and probable ST was 2.2% in patients who underwent PSS at the end of two years (11). In the PREMIER registry study, the discontinuation of clopidogrel after one month was associated with increased mortality (21). In the BASKET-LATE study, clopidogrel was discontinued after six months, and thereafter, a higher rate of death and MI was found in the DES group than BMS group (22). In another real-world study, the TYCOON registry study, the use of clopidogrel for 12 months and 24 months were compared, and less ST was found in 24 months (23). In a single-center study by Slottow et al., it was shown that clopidogrel use was less in the group with ST (24). In parallel, Spertus et al. reported that thienopyridine discontinuation 30 days after DES treatment were more likely to die during the next 11 months (7.5% versus 0.7%) (18).In the AUTAX study in which 441 PSS implanted patients were followed for 2 years, rates of ST were < 1 % (25). This trial showed multiple PSS implantation was safe for patients with multivessel coronary artery disease, with a low incidence of ST rate. Also in SIRTAX (VERY LATE) study, the risk of late ST decreases annually over an extended period at a ten-year follow-up. (12). In the DESET trial, independent clinical correlates of late ST were younger age, current smoking, multivessel disease, longer stented length, overlapping stents, vein graft lesions, and LAD lesions (26). Bundhun et al. observed 16.724 patients, and there was no difference between SES and PES for ST. They noted both SES and PES are expected to be equally effective (27). In addition, very late ST (> 10 years) has been found in the literature in patients treated with PES (28).

The new generation P2Y12 inhibitors (ticagrelor and prasugrel) were not used in our study population which may have affected the incidence of ST and MACEs. In this study, in accordance with the guidelines (29), the mean recommended duration of P2Y12 receptor blockers was approximately 12 months, but the use of P2Y12 inhibitors for less than 6 months increased the incidence of thrombosis**.** We found that the most important parameter for ST is serum creatinine levels. In addition, a history of PVD, slow-flow or no-reflow phenomenon development, higher mean platelet count, and lower mean platelet volume were found associated with thrombosis.

Limitation of the study

When compared to similar studies, there was no relationship between classical thrombosis risk factors and ST because our population was not randomized. Also, our study was single-center, and the number of total patients was low. The absence of a control group also caused us problems in determining the benefit experienced by the patients who underwent PSS. The fact that the follow-up periods of the patients were not fixed, prevented us from reflecting on the events that may develop in the future of the study. In addition, the actual frequency may be higher in patients who cannot be contacted, since the development of adverse cardiac events cannot be learned. Also, intravascular ultrasound imaging was not performed after stent replacement, so stent malposition or incomplete stent dehiscence could not be evaluated. Furthermore, the effect of 63 BMS applications on study end-points is not clearly unexplained.

CONCLUSION

Patients who underwent PSS in our clinic have similar procedural success and complication rates in the early and long-term when compared to other publications. According to our findings, silent ischemia, angina, and positive ischemia test are associated with poor prognosis. Therefore, ischemia examination can be considered in all patients with or without symptoms in the determination of prognosis. Our study also confirms safetyand efficacy of the PES-treated patients as in other studies.

Abbreviations

BMS - Bare metal stents
DES - Drug-eluting stents
LAD - Left anterior descending artery
MACE - Major adverse cardiac and cerebrovascular events

MI - Myocardial infraction

NSTEMI - Non-ST segment myocardial infraction

PES - Paclitaxel-eluting stents

PVD - Peripheral vascular disease

SES - Sirolimus eluting stent

ST- Stent thrombosis

STMEI - ST-segment elevation myocardial infraction

TLR - Target lesion revascularization

Licensing

Sažetak

EFEKTI KLINIČKIH, LABORATORIJSKIH I ANGIOGRAFSKIH FAKTORA NA TROMBOZU STENTA I NEŽELJENI KARDIOVASKULARNI DOGAĐAJI U STENTOVIMA OBLOŽENIM PAKLITAKSELOM

Kandemir Čağlayan Hasan,[1] Baytugan Zafer Nart[2]

[1] Department of Cardiology, Kocaeli Public Hospital, Kocaeli, Turkey
[2] Department of Cardiology, Gebze Fatih State Hospital, Kocaeli, Turkey

Uvod: „Drug-eluting stents" (DES) su efikasniji i i imaju smanjenju naknadnu potrebu za ponovnom revaskularizacijom u poređenju sa metalnim stentom. Cilj nam je bio da utvrdimo srednjoročne ishode pacijenata sa implantiranim DES-om prve generacije „stentovi obloženi paklitakselom (PES)".

Metode: Pacijenti sa najmanje 1 PES implantiranim u našoj kardiološkoj klinici su primljeni u nerandomizovanu grupu. Kriterijumi za uključivanje bili su svi pacijenti koji su podvrgnuti perkutanoj koronarnoj intervenciji i implantaciji PES-a. Prosečno vreme praćenja bilo je 35,14 + 13,4 meseca.

Rezultati: Ukupno 302 pacijenta (401 lezija i 337 PES) su bila uključena u studiju. Prosečna starost je bila 61,86 + 10,27 godina. Veliki neželjeni srčani i cerebrovaskularni događaji (MACE) javili su se u 17,9%, a stopa tromboze stenta bila je 4%. Nezavisni prediktori tromboze stenta bili su nivoi serumskog kreatinina [OR 1,59; 95% CI, 1,03-2,46, p = 0,03] i srednja zapremina trombocita [OR 1,59; 95% CI, 1,03–2,46, p = 0,03]. Takođe, slab funkcionalni kapacitet [OR 2,46: 95% CI, 1,42-4,26, p < 0,001] i pozitivan ishemijski test [OR 3,43: 95% CI, (1,73-6,82), p < 0,001] bili su prediktori MACE-a.

Zaključak: Pokazali smo da je PES bezbedan i efikasan u srednjoročnom periodu za primenu u koronarnoj arterijskoj bolesti.

Ključne reči: paklitaksel, restenoza, tromboza, stvarni svet.

REFERENCES

1. Ahadi F, Azadi M, Biglari M, Bodaghi M, Khaleghian A. Evaluation of coronary stents: A review of types, materials, processing techniques, design, and problems. Heliyon. 2023; 9(2): e13575. doi: 10.1016/j.heliyon.2023.e13575.

2. Chhabra L, Zain MA, Siddiqui WJ. Coronary Stents. 2023 Jan 28. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.

3. Kuramitsu S, Sonoda S, Ando K, Otake H, Natsuaki M, Anai R, et al. Drug-eluting stent thrombosis: current and future perspectives. Cardiovasc Interv Ther. 2021; 36(2): 158-68. doi: 10.1007/s12928-021-00754-x.

4. Condello F, Spaccarotella C, Sorrentino S, Indolfi C, Stefanini GG, Polimeni A. Stent thrombosis and restenosis with contemporary drug-eluting stents: predictors and current evidence. J Clin Med. 2023; 12(3): 1238. doi: 10.3390/jcm12031238.

5. Laskey WK, Yancy CW, Maisel WH. Thrombosis in coronary drug-eluting stents: report from the meeting of the Circulatory System Medical Devices Advisory Panel of the Food and Drug Administration Center for Devices and Radiologic Health, December 7–8, 2006. Circulation. 2007; 115: 2352–7. doi: 10.1161/CIRCULATIONAHA.107.688416.

6. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018; 39(2): 119-77. doi: 10.1093/eurheartj/ehx393.

7. Collet J.-P., Thiele H. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation and coexistent atrial fibrillation-Dual versus triple antithrombotic therapy. Eur. Heart J.Eur Heart J. 2021; 42(20): 2020-1. doi: 10.1093/eurheartj/ehaa909.

8. Bosco E, Hsueh L, McConeghy KW, Gravenstein S, Saade E. Major adverse cardiovascular event definitions used

in observational analysis of administrative databases: a systematic review. BMC Med Res Methodol. 2021; 21(1): 241. doi: 10.1186/s12874-021-01440-5.

9. Sousa A, Costa R, Moreira AC, Cano M, Maldonado G, Costa RA, et al. Long-term clinical outcomes of the drug-eluting stents in the real world (DESIRE) Registry. J Interven Cardiol. 2008; 21(4): 307–14.doi: 10.1111/j.1540-8183.2008.00379.x.

10. Marzocchi A, Saia F, Piovaccari G, Manari A, Aurier E, Benassi A, et al. Long-term safety and efficacy of drug-eluting stents two-year results of the REAL (REgistro AngiopLastiche dell'Emilia Romagna) Multicenter Registry. Circulation. 2007; 115(25): 3181-8. doi: 10.1161/CIRCULATIONAHA.106.667592.

11. Lasala JM, Cox DA, Dobies D,Muhlestein JB, Katopodis JN, Revtyak G,et al. Usage patterns and 2-year outcomes with the TAXUS Express Stent: Results of the US ARRIVE 1 Registry. Catheter Cardiovasc Interv. 2008; 72(4): 433–45.doi: 10.1002/ccd.21618.

12. Yamaji K, Räber L, Zanchin T, Spitzer E, Zanchin C, Pilgrim T, et al. Ten-year clinical outcomes of first-generation drug-eluting stents: the Sirolimus-Eluting vs. Paclitaxel-Eluting Stents for Coronary Revascularization (SIRTAX) VERY LATE trial. Eur Heart J. 2016; 37(45): 3386-95. doi: 10.1093/eurheartj/ehw343.

13. Galløe AM, Kelbæk H, Thuesen L, Hansen HS, Ravkilde J, Hansen PR, et al. 10-year clinical outcome after randomization to treatment by sirolimus- or paclitaxel-eluting coronary ctents. J Am Coll Cardiol. 2017; 69(6): 616-24. doi: 10.1016/j.jacc.2016.11.055.

14. Räber L, Wohlwend L, Wigger M,Togni M, Wandel S, Wenaweser P, et al. Five-year clinical and angiographic outcomes of a randomized comparison of sirolimus-eluting and paclitaxel-eluting stents: results of the Sirolimus-Eluting Versus Paclitaxel-Eluting Stents for Coronary Revascularization LATE trial. Circulation. 2011; 123(24): 2819-28. doi: 10.1161/CIRCULATIONAHA.110.004762.

15. Simsek C, Magro M, Boersma E, Onuma Y, Nauta ST, Gaspersz MP,et al. The unrestricted use of sirolimus- and paclitaxel-eluting stents results in better clinical outcomes during 6-year follow-up than bare-metal stents: an analysis of the RESEARCH (Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital) and T-SEARCH (Taxus-Stent Evaluated At Rotterdam Cardiology Hospital) registries. JACC Cardiovasc Interv. 2010;3 (10): 1051-8. doi: 10.1016/j.jcin.2010.08.003.

16. Park H, Kang DY, Kim SO, Lee J, Kim JH, Hyun J et al. Ten-year outcomes of early generation sirolimus- versus paclitaxel-eluting stents in patients with left main coronary artery disease. Catheter Cardiovasc Interv. 2021; 98(5): E705-14. doi: 10.1002/ccd.29930.

17. Giacoppo D, Alvarez-Covarrubias HA, Koch T, Cassese S, Xhepa E, Kessler T, et al. Coronary artery restenosis treatment with plain balloon, drug-coated balloon, or drug-eluting stent: 10-year outcomes of the ISAR-DESIRE 3 trial. Eur Heart J. 2023; 44(15): 1343-57. doi: 10.1093/eurheartj/ehad026.

18. Thuijs DJFM, Kappetein AP, Serruys PW, Mohr FW, Morice MC, Mack MJ, et al. Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. Lancet. 2019; 394(10206): 1325-34. doi: 10.1016/S0140-6736(19)31997-X.

19. S. Cook, E. Ladich, G. Nakazawa, Eshtehardi P, Neidhart M, Vogel R, et al. Correlation of intravascular ultrasound findings with histopathological analysis of thrombus aspirates in patients with very late drug-eluting stent thrombosis. Circulation. 2009; 120(5): 391-9. doi: 10.1161/CIRCULATIONAHA.109.854398.

20. De la Torre-Herna´ndez JM, Alfonso F, Herna´ndez F, Elizaga J, Sanmartin M, Pinar E,et al. Drug-eluting stent thrombosis: Results from the multicenter Spanish Registry ESTROFA. J Am Coll Cardiol. 2008; 51(10): 986–90.doi: 10.1016/j.jacc.2007.10.057.

21. Spertus JA, Kettelkamp R, Vance C, Decker C, Jones PG, Rumsfeld JS, et al. Prevalence, predictors, and outcomes of premature discontinuation of thienopyridine therapy after drug-eluting stent placement: Results from the PREMIER Registry. Circulation. 2006; 113(24): 2803-09. doi: 10.1161/CIRCULATIONAHA.106.618066.

22. Pfisterer M, Brunner-La Rocca HP, Rickenbacher P, Hunziker P, Mueller C, et al. Late clinical events after clopidogrel discontinuation may limit the benefit of drug-eluting stents: An observational study of drug-eluting versus bare-metal stents. J Am Coll Cardiol. 2006; 48(12): 2584–91. doi: 10.1016/j.jacc.2006.10.026.

23. Tanzilli G, Greco C, Pelliccia F, Pasceri V, Barillà F, Paravati V, et al. Effectiveness of two-year clopidogrel + aspirin in abolishing the risk of very late thrombosis after drug-eluting stent implantation (from the TYCOON [two-year ClOpidOgrel need] study). Am J Cardiol. 2009; 104(10) :1357-61. doi: 10.1016/j.amjcard.2009.07.002.

24. Slottow TLP, Steinberg DH, Roy PK, Buch AN, Okabe T, Xue Z,et al. Observations and outcomes of definite and probable drug-eluting stent thrombosis seen at a single hospital in a four-year period. Am J Cardiol. 2008; 102(3): 298–03. doi: 10.1016/j.amjcard.2008.03.055.

25. Gyöngyösi M, Christ G, Lang I, Kreiner G, Sochor H, Probst P, et al. AUTAX Investigators. 2-year results of the AUTAX (Austrian Multivessel TAXUS-Stent) registry beyond the SYNTAX (synergy between percutaneous coronary intervention with TAXUS and cardiac surgery) study JACC Cardiovasc Interv. 2009; 2(8):7 18-27.doi: 10.1016/j.jcin.2009.05.019.

26. Waksman R, Kirtane AJ, Torguson R, Cohen DJ, Ryan T, Räber L, et al. Correlates and outcomes of late and very late drug-eluting stent thrombosis: results from DESERT (International Drug-Eluting Stent Event Registry of Thrombosis). JACC Cardiovasc Interv. 2014; 7(10): 1093-102. doi: 10.1016/j.jcin.2014.04.017.

27. Bundhun PK, Wu ZJ, Chen MH. Is there any significant difference in stent thrombosis between sirolimus and paclitaxel eluting stents?: A systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore). 2016;95(5):e2651. doi: 10.1097/MD.0000000000002651.

28. Sleiman E, Tabet R, Karam B, Ayad D, Royzman R. Extremely late in-stent thrombosis 12 years after implantation of a drug-eluting stent. Cureus. 2020; 12(7): e9053. doi: 10.7759/cureus.9053.

29. Barbato E, Mehilli J, Sibbing D, Siontis GCM, Collet JP, Thiele H,et al. ESC Scientific Document Group. Questions and answers on antithrombotic therapy and revascularization strategies in non-ST-elevation acute coronary syndrome (NSTE-ACS): a companion document of the 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021; 42(14): 1368-78. doi: 10.1093/eurheartj/ehaa601.

Correspondence to/Autor za korespondenciju
Nart Zafer Baytugan, MD
Department of Cardiology, Gebze Fatih State Hospital
Osman Yilmaz Neighborhood, Istanbul Street, 127, Kocaeli, Turkey
E-mail: nartzafer@hotmail.com
Telephone number: +902625022240
ORCID: https://orcid.org/0000-0003-4732-9367