

ORIGINAL ARTICLE

Percutaneous management of long and diffused coronary lesions using newer generation drug-eluting stents in routine clinical practice: long-term outcomes and complication predictors

Elżbieta Paszek¹, Wojciech Zajdel¹, Piotr Musiałek², Andrzej Sokołowski³,
Bartłomiej Guzik¹, Anna Kablak-Ziembicka¹, Łukasz Niewiara¹,
Małgorzata Pankowska⁴, Aleksandra Mielimonka⁴, Krzysztof Żmudka¹

1 Department of Interventional Cardiology, Institute of Cardiology, Jagiellonian University Medical College, John Paul II Hospital, Kraków, Poland

2 Department of Cardiac and Vascular Diseases, Institute of Cardiology, John Paul II Hospital, Kraków, Poland

3 Cracow University of Economics, Department of Statistics, Kraków, Poland

4 Jagiellonian University Medical College, Kraków, Poland

KEY WORDS

coronary artery disease, newer generation drug-eluting stents, percutaneous coronary intervention

ABSTRACT

INTRODUCTION Long and diffuse coronary lesions (LDCLs) are routinely subjected to percutaneous management, but long-term clinical outcomes and complication predictors with the use of contemporary stents and techniques remain undetermined.

OBJECTIVES The aim of the study was to address long-term effects of percutaneous management of LDCLs, using contemporary devices and optimization techniques.

PATIENTS AND METHODS Long and diffuse coronary lesion was defined as a lesion requiring an implantation of 30 mm or longer total stent(s) length (TSL) into one coronary artery (bailouts excluded). There were 290 LDCL interventions with the use of newer generation drug-eluting stents (DESs; cobalt chromium everolimus- or zotarolimus-eluting stents) performed between January 2013 and January 2016.

RESULTS The mean (SD) TSL was 55.5 (16.8) mm. The use of intravascular ultrasound/optical coherence tomography was 17.1%, rotablation, 6.9%, and noncompliant balloon, 88.9%. The median (range) follow-up duration was 831 (390–1373) days. All-cause mortality and cardiac death rates were 11.7% and 6.9%, respectively. The myocardial infarction (MI) rate was 6.6%, including target-vessel MI in 4.1%. The rate of clinically-driven repeat revascularization was 13.8%, and of definite or probable LDCL stent thrombosis, 7.2%. Overall patient-oriented adverse event rate (any death, MI, or repeat revascularization) was 25.5%, and device-oriented rate (cardiac death, target vessel-MI, or target lesion restenosis), 13.4%. Adverse outcome predictors were chronic kidney disease, acute coronary syndrome as an indication for the procedure, chronic heart failure with reduced left ventricular ejection fraction, multivessel disease, and coexisting peripheral artery disease, but not lesion-related factors, such as bifurcation, calcification, chronic total occlusion, or TSL.

CONCLUSIONS Adverse outcomes following contemporary LDCL management using newer generation DESs in routine clinical practice are associated with clinical patient characteristics rather than lesion characteristics or TSL. We identified high-risk patient cohorts that may benefit from enhanced surveillance.

INTRODUCTION Coronary lesion length determines the length of stent(s) needed in percutaneous coronary revascularization (PCI). With bare

metal stents and first-generation drug-eluting stents (DESs), stent length was identified as a risk factor for clinical device failure, mostly

Correspondence to:
Elżbieta Paszek, MD, PhD,
Jagiellonian University,
Department of Interventional
Cardiology, John Paul II Hospital,
ul. Prądnicka 80, 31-202 Kraków,
Poland, phone: +48 12 614 35 01,
email: elzbieta.m.paszek@gmail.com
Received: March 20, 2019.
Revision accepted: May 29, 2019.
Published online: June 6, 2019.
Pol Arch Intern Med. 2019;
129 (6): 392-398
doi:10.20452/pamw.14864
Copyright by Medycyna Praktyczna,
Kraków 2019

due to increased restenosis and stent thrombosis rates, as well as a need for repeat revascularization.^{1,2} Clinical implementation of newer generation DES (everolimus-eluting stent [EES] or zotarolimus-eluting stent [ZES]) has led to a significant improvement in long-term outcomes.^{3,4} Although long stent(s) use is part of routine PCI today, the effect of total stent(s) length (TSL) used to treat long and diffuse coronary lesions (LDCLs) on the risk of adverse event remains undetermined.

Our study was designed to evaluate long-term clinical outcomes and predictors of complications in newer-generation DESs used to treat LDCLs in routine clinical practice of PCI.

PATIENTS AND METHODS **Study design** This was a single-center retrospective study. Long and diffuse coronary lesion was defined as a lesion requiring a planned implantation of TSL of 30 mm or longer into a single coronary artery. We included consecutive patients with LDCL interventions performed between January 2013 and January 2016. We excluded bare metal stent use (rare in LDCL, 1.4%) and focused on newer-generation DESs (cobalt chromium EES or ZES) used to treat LDCLs in 290 patients with stable coronary artery disease (CAD) or acute coronary syndrome (ACS; including ST-segment elevation myocardial infarction [STEMI], non-ST-segment elevation myocardial infarction, and unstable angina). Patients presenting with cardiogenic shock or bailouts were excluded. As per standard at our center, elective patients with multivessel disease (MVD) or lesions in the left main (LM) or proximal left anterior descending artery (LAD) were consulted and referred by the heart team.

We analyzed the effect of procedure- and patient-related factors on the incidence of the following Academic Research Consortium (ARC) endpoints⁵: all-cause mortality, cardiac death, any myocardial infarction (MI), target lesion-related MI, target lesion restenosis (TLR), stent thrombosis, and repeat revascularization. Any death without a definite noncardiac cause was considered a cardiac death. Myocardial infarction was diagnosed according to the universal definition.⁶ An MI was treated as target lesion-related, unless there was clear evidence to the contrary. An event was coded as TLR when an angiographically confirmed lesion (50% or greater) was found within the primarily stented section of the vessel, and the patient had clinical symptoms or functional evidence of ischemia. Definite, probable, or possible, as well as subacute, acute, late, and very late stent thromboses were coded in accordance with the ARC.⁵ An intervention was coded as a repeat revascularization in cases that had not been planned beforehand as part of the treatment. We also analyzed composite endpoints in accordance with the ARC guidelines. We defined a device-oriented composite endpoint (DOCE) composed of cardiac death, target vessel-related MI and TLR, as well as a patient-oriented composite endpoint

(POCE), which is a composite of all-cause mortality, any MI, and any repeat revascularization.

Angiograms were analyzed and assessed by 2 independent operators, with any discrepancies resolved by consensus.

Procedures Percutaneous coronary intervention was performed according to guidelines current at the time of the study.⁷ The implanted devices were newer-generation DESs. Procedure strategy, including predilation, advanced imaging, particular stent use (EES or ZES), and optimization techniques were at the operator's discretion.

The following factors were analyzed as potentially affecting the outcomes: target vessel, number of stented vessels (including the LDCL), target lesion heavy calcifications defined as multiple opacifications surrounding the lumen in at least 2 projections, involvement of rotational atherectomy, chronic total occlusion (CTO) as the target lesion, major bifurcation(s) involvement (side branch of ≥ 1.5 mm in diameter), TSL, number of stents per lesion, use of kissing balloons technique, distal embolization, major side branch occlusion, and final flow in the target vessel in the Thrombolysis in Myocardial Infarction scale.

After the procedure, all patients were prescribed dual antiplatelet therapy (DAPT): acetylsalicylic acid plus clopidogrel or acetylsalicylic acid plus ticagrelor (none of the patients used prasugrel) and other medications, including typically a statin, β -blocker, and angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, as per current European Society of Cardiology (ESC) guidelines on the management of stable CAD. The duration of DAPT was based on the clinical presentation of CAD, according to ESC guidelines. Statin treatment was aimed to achieve guideline-recommended target low-density lipoprotein cholesterol levels.

Follow-up Patients were scheduled for routine clinical follow-up in a local outpatient clinic 4 to 8 weeks after the index procedure and annually thereafter. A total of 212 patients (73.1%) attended the final outpatient clinic follow-up visit. Another 55 patients (19.0%) were not able to attend due to logistic reasons (travel distance, satisfactory general practitioner care), and thus our final follow-up evaluation was performed via physician phone-call interview. Medical documentation regarding the presence of any definite or suspected endpoint was reviewed. For the remaining 23 patients, who were lost to follow up (7.9%), only the vital status was obtained via a national electronic database. If an endpoint was registered, the length of follow-up analyzed was the time that elapsed from the day of the procedure to the day when the endpoint occurred. The final follow-up for patients with no registered endpoints varied depending on the time of scheduled outpatient clinic visits. The final phone calls for patients outside the care of our outpatient clinic were made between January 16 and February 9, 2017, with

TABLE 1 Basic patient data

Parameter	Value
Age, y, mean (SD)	67 (10.6)
BMI, kg/m ² , mean (SD)	28.2 (4.5)
LVEF, %, mean (SD)	43.8 (15)
GFR on admission, ml/min/1.73 m ² , mean (SD)	68.9 (20.1)
Total cholesterol/LDL-C, mmol/l, mean (SD)	4.4/2.7 (1.3/1)
Male sex	208 (71.7)
Hypertension	265 (91.4)
Lipid disorders	254 (87.6)
Diabetes/diabetes with insulin use	101/37 (34.8/12.8)
Smoking	112 (38.6)
Obesity	94 (32.4)
Chronic kidney insufficiency	44 (15.2)
History of stroke or TIA	23 (7.9)
Peripheral artery disease	27 (9.3)
History of ACS	123 (42.4)
History of PCI/CABG	90/40 (31/13.8)
MVD	86 (29.7)
ACS as indication for procedure	157 (54.1)
STEMI/NSTEMI/UA	54/83/20 (18.6/28.6/6.9)

Data are presented as number (percentage) unless otherwise indicated.

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index, CABG, coronary artery bypass grafting; GFR, glomerular filtration rate; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; MVD, multivessel disease; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TIA, transient ischemic attack; UA, unstable angina

a final vital status check performed on February 11 to 13, 2017.

This study was approved by an institutional review board. Patients provided written informed consent to participate in the study.

Statistical analysis The Shapiro–Wilk test was used to check for normal distribution of the variables. The results were presented as the mean (SD) when the distribution was normal, or as median and interquartile range when the distribution differed from normal. Potential effects of patient- and procedure-related factors on the incidence of composite endpoints were evaluated using the univariate and multivariate Cox proportional hazard models. Multivariate models were estimated with the backward step-wise selection procedure with the variables with a *P* value of less than 0.1 from the univariate analysis as the initial list. Proportionality of hazards was evaluated by the Kaplan–Meier analysis and checking the dependence of residuals on time. In the final models, a *P* value of less than 0.05 was considered significant.

RESULTS Patients The mean (SD) age of patients at the time of the index procedure was 67.0 (10.6) years. Men constituted 71.7% of the study group. The representation of risk factors for CAD was typical (**TABLE 1**).

Procedures and devices The mean (SD) TSL was 55.5 (16.8) mm. For the majority of LDCLs, 2 stents were used (217 procedures, 74.8%). The EES (Xience, Abbott, Santa Clara, California, United States) was used in 159 procedures (54.8%), the ZES (Resolute Integrity, Medtronic, Minneapolis, Minnesota, United States) in 128 (44.1%), and a combination of EES and ZES was implanted in 3 patients (1%). The LDCL was predominantly located in the right coronary artery (40.7%) and LAD (39.7%). The left main artery was involved in 26 of the cases (9%), most of which were combined LM/LAD lesions. Overlapping stents were used in 83.1% of patients; a major bifurcation (side branch no smaller than 1.5 mm in diameter) was present in 41.8%, and the kissing technique was employed in 22% of the procedures. A CTO accounted for the long lesion in 20% of the cases. Heavily calcified lesions were present in 45.2% of the cases, with rotational atherectomy being used in 6.9% of all PCIs (heavily calcified lesions, 15.3%). A substantial number of patients had MVD (29.7%, with 13.8% postcoronary artery bypass grafting [CABG]). The SYNTAX score ranged from 2 to 44, with a median of 16. Distal vessel embolization or side branch occlusion occurred in 6.2% of the cases. A final Thrombolysis in Myocardial Infarction grade 3 flow was achieved in 96.2% of the procedures. Procedural details are presented in **TABLE 2**.

Follow-up The median follow-up was 831 days (range, 390–1373; interquartile range, 459). Death occurred in 34 patients (11.7%), with the underlying cardiac cause in 21 (6.9%). A total of 19 patients had MI (6.6%), and in 12 cases (4.1%), the event was related to the target vessel. Repeat revascularization was required 45 times in 40 patients (13.8%), and target-vessel revascularization occurred in 18 of the cases (6.2%). The majority of those revascularizations was repeated PCI. Restenosis within the target vessel was confirmed in 9 cases (3.1%). In 9 patients (3.1%), a target lesion definite stent thrombosis was established, and in 12 (4.1%) the ARC criteria for probable stent thrombosis were met. Of the episodes of definite stent thrombosis 3 were acute, 3 subacute, 2 late, and 1 very late. In 1 case of subacute stent thrombosis, the underlying cause was noncompliance to DAPT. In patients on acetylsalicylic acid plus ticagrelor therapy (3.8%), neither definite nor probable stent thrombosis occurred.

The DOCE occurred in 39 patients (13.4%) whereas the POCE in 74 (25.5%). Follow-up data are presented in **TABLE 3**.

Results of univariate and multivariate analysis In the univariate analysis (**TABLE 4**), the strongest predictor of DOCE was CKD (*P* = 0.002, Supplementary material, *Figure S1*). In particular, a 1-point decrease in glomerular filtration rate was associated with a 2% increase in the risk of DOCE. Other factors related to DOCE were ACS (*P* = 0.01;

TABLE 2 Procedural characteristics

Parameter		Value
Stent length, mm, mean (SD)		55.5 (16.8)
Radiation/body mass, Gy/kg, mean (SD)		0.03 (0.02)
SYNTAX score, median (min–max range)		16 (2–44)
Number of stents / lesion	1	25 (8.6)
	2	217 (74.8)
	3	39 (13.4)
	>3	9 (3.1)
Target vessel	RCA	118 (40.7)
	LAD	115 (39.7)
	Cx	46 (15.8)
	LM	26 (9.0)
Overlap		241 (83.1)
Major bifurcation		119 (41.8)
Kissing technique		64 (22.0)
NC balloon postdilation		258 (88.9)
IVUS optimization		41 (14.1)
IVUS and/or NC balloon optimization		266 (91.7)
CTO as target lesion		58 (20.0)
Heavy calcifications		131 (45.2)
Rotational atherectomy		20 (6.9)
>1 stented vessel		140 (48.3)
Distal embolization		18 (6.2)
Side branch occlusion		18 (6.2)
Final TIMI grade 3		279 (96.2)
GP IIb/IIIa inhibitor use		11 (3.8)
P2Y ₁₂ inhibitor: clopidogrel/ticagrelor		279/11 (96.2/3.8)

Data are presented as number (percentage) unless otherwise indicated.

Abbreviations: CTO, chronic total occlusion; Cx, circumflex artery; GP, glycoprotein; IVUS, intravascular ultrasound; LAD, left anterior descending artery, LM, left main artery; NC, noncompliant; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction

Supplementary material, *Figure S2*), MVD ($P = 0.03$; Supplementary material, *Figure S3*), and the coexistence of peripheral artery disease (PAD) ($P = 0.046$, Supplementary material, *Figure S4*). The single procedure-related variable with an influence on DOCE was CTO as the target lesion ($P = 0.01$; Supplementary material, *Figure S5*). Device-oriented composite endpoints occurred less frequently in patients with CTO than in those with non-CTO target lesion.

For POCE, the strongest predictor was CKD ($P = 0.002$; Supplementary material, *Figure S6*) and ACS as the clinical indication ($P = 0.002$; Supplementary material, *Figure S7*). A 1-point rise in the glomerular filtration rate decreased the risk of POCE by 1.9%. This was followed by MVD ($P = 0.01$; Supplementary material, *Figure S8*), PAD ($P = 0.03$; Supplementary material, *Figure S9*), and congestive heart failure (CHF) ($P = 0.04$; Supplementary material, *Figure S10*). Single-vessel disease was associated with a lower risk of POCE ($P = 0.049$).

The multivariate analysis (**TABLE 5**) showed that only coexistent PAD was an independent predictor of DOCE. For POCE, ACS as the clinical indication, CHF, and single-vessel disease (protective role in the case of the latter) remained significant after adjustment for other factors.

Importantly, neither TSL nor other procedural factors influenced any of the endpoints. There were no differences in outcomes between EESs and ZESs.

DISCUSSION The main finding of this study is that in contemporary routine management of LDCL, PCI with the use of newer-generation DESs as well as imaging and optimization techniques, lesion and procedural factors (including TSL) do not determine long-term outcomes. Despite guideline-indicated medical management, patient-related factors such as MVD, CKD, CHF, and PAD remain risk factors for long-term adverse events.

Traditionally, LDCLs have been considered to be associated with an increased risk of complications following PCI.^{1,2} Still, specific data on LDCL PCI in contemporary clinical practice are lacking. A subanalysis of the RESOLUTE all-comers (Randomized Comparison of a Zotarolimus-Eluting Stent with an Everolimus-Eluting Stent for Percutaneous Coronary Intervention) trial, focused on complex coronary lesions as compared with simple ones, indicated no differences in 1-year clinical outcomes irrespective of the particular newer-generation DES type. In that study, the definition of complex patient/lesions involved a number of patient-related and angiographic factors including lesion length with the cutoff value of 27 mm as one of the complexity criteria (only 1 was required to meet the complexity definition).³ A sub-study of the prospective, randomized, multicenter CENTURY II (Clinical Evaluation of New Terumo Drug-Eluting Coronary Stent System in the Treatment of Patients with Coronary Artery Disease) trial has shown very satisfactory short-term results in patients with long lesions treated with bioresorbable polymer sirolimus-eluting stent or EES.⁸ This study, however, dealt with a different population than ours. The mean lesion length was approximately 33 mm, and there was a 3-fold smaller number of patients with STEMI. Although a significant percentage of patients in the CENTURY II substudy had MVD, the mean SYNTAX score was lower and fewer patients were post-CABG. Furthermore, the percentage of patients with a multivessel PCI was 2-fold higher in our study, all of which probably influenced the results.

Recently, the results of a single-center, retrospective study on 71 patients with extremely long lesions (60–106 mm) with the use of ZES and biolimus A9-eluting stents have been published, also showing good clinical outcomes.⁹ Still, lesion length was not sufficiently evaluated as a separate risk factor, and thus the impact of this variable on long-term PCI outcome with newer-generation DES remains unknown.

TABLE 3 Follow-up data

Endpoint	Value	
All-cause mortality	34 (11.7)	
Cardiac death	21 (6.9)	
MI	19 (6.6)	
MI (definitely or possibly target lesion-related)	12 (4.1)	
Repeat revascularization (target and nontarget lesion)	40 (13.8)	
PCI	39 (13.4)	
CABG	6 (2.1)	
Target vessel revascularization	18 (6.2)	
Target lesion restenosis	9 (3.1)	
Target lesion definite ^a thrombosis	All lesions	9 (3.1)
	Acute	3 (1.0)
	Subacute	3 (1.0)
	Late	2 (0.6)
Very late	1 (0.3)	
Probable ^a thrombosis	12 (4.1)	
Possible ^a thrombosis	14 (4.8)	
Definite and probable thrombosis	21 (7.2)	
DOCE	39 (13.4)	
POCE	74 (25.5)	

Data are presented as number (percentage).

a In accordance with the Academic Research Consortium definitions

Abbreviations: DOCE, device-oriented composite endpoint; MI, myocardial infarction; POCE, patient-oriented composite endpoint; others, see **TABLE 1**

TABLE 4 Univariate analysis of patient- and procedure-related factors with a significant effect on endpoints

Parameter	P value	
	DOCE	POCE
Patient-related factors		
Peripheral artery disease	0.046	0.03
Chronic kidney disease	0.002	0.002
Multi-vessel disease	0.03	0.01
Acute coronary syndrome	0.01	0.002
Chronic heart failure	0.32	0.04
Procedure-related factors		
Chronic total occlusion	0.008	0.20

Abbreviations: see **TABLE 3**

TABLE 5 Multivariate Cox model

	Variables	HR	95% CI	P value
DOCE	PAD	3.16	1.15–8.66	0.03
POCE	CHF	2.37	1.31–4.28	0.004
	ACS	1.99	1.16–3.44	0.01
	Single-vessel disease	0.47	0.23–0.96	0.04

Abbreviations: CHF, congestive heart failure; HR, hazard ratio; PAD, peripheral artery disease; others, see **TABLES 1 and 3**

The focus of our study was to assess the influence of TSL of 30 mm or longer with the use of newer-generation DESs in LDCL in an all-comer cohort. We found that TSL was not associated with the risk of periprocedural or long-term complications. Specifically, none of the procedural factors analyzed (**TABLE 1**) increased the risk of DOCE and POCE. On the other hand, a number of patient-related factors did influence the long-term results, indicating that these variables should still be considered. The overall number of major acute and/or adverse cardiovascular events (MACEs) in our study is comparable to that from other contemporary reports.^{3,4}

Peripheral artery disease Peripheral artery disease was present in 9.3% of patients, which is consistent with contemporary data reported by Midwall et al.¹⁰ Our analysis demonstrates a negative impact of PAD on both DOCE and POCE in patients with LDCL PCI. Earlier studies in PCI populations showed that PAD increased the risk of in-hospital MI and death, as well as cardiac and overall mortality rates in the long-term follow-up.^{10,11} Patients with multilevel atherosclerosis probably have a larger genetic and environmental burden predisposing to a more dynamic development and progression of plaques or a less favorable vessel-wall response, hence a larger probability of TLR, stent thrombosis, and MI (composites of DOCE). On the other hand, in the case of POCE, the effect of PAD may have been overshadowed by comorbidities, as was suggested before.^{10,11}

Kidney disease We found a significant link between CKD and both composite endpoints. Although in-hospital complications in patients with renal failure undergoing PCI have been well described,¹² long-term data are scarce and include a potential relationship between in-stent restenosis and microalbuminuria. Microalbuminuria is a marker of microvascular damage in CKD and thus a predictor of small-vessel damage in other organs, implicating an association with worse final outcome.¹³

Indication for the procedure Acute coronary syndrome appeared to be a predictor of DOCE, but the significance was lost in the multivariate analysis. It was also found to be a strong predictor of POCE, and remained significant after adjustment for other factors in the multivariate analysis. This outcome is consistent with the fact that patients with ACS represent a high-risk profile group.¹⁴

Multivessel disease versus single-vessel disease Multivessel disease was found to be a predictor of both DOCE and POCE. This is consistent with previous findings.¹⁵ However, it is probable that individuals with MVD who were referred for PCI rather than CABG were more likely to have multiple comorbidities, which contributed to POCE. The fact that MVD fell below

the significance threshold in the multivariate analysis supports this explanation.

Chronic heart failure Chronic heart failure was found to increase the risk of POCE in the univariate and multivariate analyses. This is consistent with previous reports, where CHF was shown to increase both short- and long-term PCI complications.¹⁶ This could be justified by a reduced cardiac reserve, higher risk of life-threatening arrhythmias and comorbidities, but also by more intricate pathophysiological mechanisms, such as enhanced activation of the coagulation system, which has been described in individuals with CHF.¹⁷ This could predispose to thrombotic events, additionally increasing the frequency of the assessed endpoints.

Diabetes mellitus Diabetes mellitus has been long known to increase the risk of coronary restenosis^{18,19} and MACE.⁹ We found that with the use of newer-generation DES to treat long coronary lesions, diabetes mellitus did not come across as a risk factor of poor long-term outcome. This result may reflect the impact of improved stent technology, overall PCI strategy, and better glycaemic control with new, more effective drugs. Still, this is somewhat controversial and would require further studies, especially to determine LDCL PCI outcomes in the context of the efficacy of medical treatment of diabetes mellitus.

Procedure-related factors The only procedure-related factor associated with the long-term outcome of LDCL PCI was CTO as the target lesion. Interestingly, patients with CTO had a significantly lower risk of DOCE. This could be explained by a possibility that any restenosis or target vessel-related MI were clinically silent due to well-developed collaterals and remained unnoticed. No other procedure-related variables, including TSL, proved to predict the long-term outcome in LDCL PCI. This is similar to the findings by Çoner et al,⁹ where TSL, stent diameter, and number of stents / vessels was also not found to impact the MACE rate.

In this study, the majority (91.7%) of procedures were optimized using noncompliant balloons and / or intravascular imaging. Moreover, 6.9% of all lesions were adapted by use of rotational atherectomy. This may explain the lack of any significant effect of lesion length, calcification, or bifurcation on long-term outcome in our analysis. The disproportion between heavily calcified lesions (45.2%) and the rate of rotational atherectomy (6.9%) might be explained by the fact that most of these lesions were crossable and sufficiently adaptable with a noncompliant balloon, which is a first choice in accordance with the current ESC guidelines dedicated to revascularization, including rotablation.²⁰ Although the frequency of rotablation use is growing, it is seldom used upfront, as not all operators feel completely comfortable using rotational atherectomy

and prefer a less aggressive approach. Based on a national registry from 2017 (the National Registry of Procedures of Invasive Cardiology, not published), the rate of rotablation in Poland was only roughly 0.7% of all PCIs.

Finally, we found only 9 definite stent thromboses (3.1%), 1 of which was attributable to premature DAPT discontinuation. The remaining 8 occurred after the standard period of DAPT use. The percentage of definite and probable stent thrombosis was rather high (7.2%). This might be due to the fact that a large proportion of these patients were admitted due to ACS (54.1%), especially STEMI (18.6% of the whole cohort, 34.4% of ACS). Also, ticagrelor was prescribed only in 3.8% of the cases, none of which presented in-stent thrombosis.

Study limitations This was a retrospective analysis. Our definition of TSL of no less than 30 mm does not consider overlap implantations. However, in cases where the overlap was present, the actual length of the covered artery segment was approximately 1 to 2 mm shorter than the sum of stents. However, this is unlikely to have significantly affected our findings. TSL was determined through operator assessment, which may be a source of some heterogeneity. Even though the analyzed data came from a large-volume center, due to the specific inclusion criteria, the sample size was moderate, which could be a source of error. The median follow-up time in this study was 27.7 months with a minimum of 13 months, which is significantly longer than the majority of contemporary stent studies, which routinely report 12-month data.³ This was not a randomized study. A proportion of patients was referred by cardiac surgeons to our and other centers due to the number and severity of comorbidities. Hence, the analyzed population reflects day-to-day reality in the catheterization laboratory.

Conclusions This study shows that with the routine use of newer generation of DESs and current optimization techniques, LDCL stenting is not associated with an increased risk of device-oriented endpoints. Patient-related factors that need careful consideration when deciding on treating LDLC percutaneously include CKD, CHF, PAD, and MVD. With newer-generation DESs used to treat LDLC, long-term clinical outcomes appear superior to those previously published for bare metal stents and first-generation DESs. Time will tell whether continued device improvements such as fully resorbable polymers, abluminal drug coating, or new-generation bioresorbable scaffolds with standard application of proper lesion adaptation, post-implantation optimization, and wider adoption of intracoronary imaging will further improve long-term outcomes in long lesions.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

CONTRIBUTION STATEMENT EP, WZ, PM, AK-Z, BG, and KZ designed the study. EP, AM, MP, and LN collected the data. AS performed the statistical analysis. EP, WZ, PM, KZ, and AK-Z interpreted the data. EP and LN prepared the manuscript draft. PM, WZ, AK-Z, and KZ critically reviewed the final version of the manuscript. All authors approved the final version of the manuscript.

CONFLICT OF INTEREST None declared.

OPEN ACCESS This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material, provided the original work is properly cited, distributed under the same license, and used for noncommercial purposes only. For commercial use, please contact the journal office at pamw@mp.pl.

HOW TO CITE Paszek E, Zajdel W, Musialek P, et al. Percutaneous management of long and diffused coronary lesions using newer generation drug-eluting stents in routine clinical practice: long-term outcomes and complication predictors. *Pol Arch Intern Med.* 2019; 129: 392-398. doi:10.20452/pamw.14864

REFERENCES

- 1 Mauri L, O'Malley AJ, Cutlip DE, et al. Effects of stent length and lesion length on coronary restenosis. *Am J Cardiol.* 2004; 93: 1340-1346. A5.
- 2 Serruys PW, Morice M-C, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med.* 2009; 360: 961-972.
- 3 Stefanini GG, Serruys PW, Silber S, et al. The impact of patient and lesion complexity on clinical and angiographic outcomes after revascularization with zotarolimus- and everolimus-eluting stents: a substudy of the RESOLUTE All Comers Trial (a randomized comparison of a zotarolimus-eluting stent with an everolimus-eluting stent for percutaneous coronary intervention). *J Am Coll Cardiol.* 2011; 57: 2221-2232.
- 4 Palmerini T, Benedetto U, Biondi-Zoccai G, et al. Long-term safety of drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *J Am Coll Cardiol.* 2015; 65: 2496-2507.
- 5 Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation.* 2007; 115: 2344-2351.
- 6 Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *J Am Coll Cardiol.* 2012; 60: 1581-1598.
- 7 Authors/Task Force members, Windecker S, Kolh P, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J.* 2014; 35: 2541-2619.
- 8 Lesiak M, Araszkiwicz A, Grajek S, et al. Long coronary lesions treated with thin strut bioresorbable polymer drug eluting stent: experience from multicentre randomized CENTURY II Study. *J Intervent Cardiol.* 2016; 29: 47-56.
- 9 Çoner A, Çiçek D, Akıncı S, et al. Mid-term clinical outcomes of new generation drug-eluting stents for treatment of diffuse coronary artery disease. *Türk Kardiyol Dern Ars.* 2018; 46: 659-666.
- 10 Midwall S, Swaminathan RV, Charitakis K, et al. Impact of peripheral vascular disease on short- and long-term outcomes in patients undergoing non-emergent percutaneous coronary intervention in the drug-eluting stent era. *J Invasive Cardiol.* 2013; 25: 132-136.
- 11 Singh M, Lennon RJ, Darbar D, et al. Effect of peripheral arterial disease in patients undergoing percutaneous coronary intervention with intra-coronary stents. *Mayo Clin Proc.* 2004; 79: 1113-1118.
- 12 Gupta T, Paul N, Kolte D, et al. Association of chronic renal insufficiency with in-hospital outcomes after percutaneous coronary intervention. *J Am Heart Assoc.* 2015; 4: e002069.
- 13 Heper G, Durmaz T, Namik Murat S, et al. Clinical and Angiographic Outcomes of Diabetic Patients After Coronary Stenting: A Comparison of Native Vessel Stent Restenosis Rates in Different Diabetic Subgroups. *Angiology.* 2002; 53: 287-295.
- 14 Pilgrim T, Vranckx P, Valgimigli M, et al. Risk and timing of recurrent ischemic events among patients with stable ischemic heart disease, non-ST-segment elevation acute coronary syndrome, and ST-segment elevation myocardial infarction. *Am Heart J.* 2016; 175: 56-65.
- 15 Habib RH, Dimitrova KR, Badour SA, et al. CABG versus PCI: greater benefit in long-term outcomes with multiple arterial bypass grafting. *J Am Coll Cardiol.* 2015; 66: 1417-1427.
- 16 Holper EM, Blair J, Selzer F, et al. The impact of ejection fraction on outcomes after percutaneous coronary intervention in patients with congestive heart failure: an analysis of the National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry and Dynamic Registry. *Am Heart J.* 2006; 151: 69-75.
- 17 Jafri SM, Ozawa T, Mammen E, et al. Platelet function, thrombin and fibrinolytic activity in patients with heart failure. *Eur Heart J.* 1993; 14: 205-212.

18 Elezi S, Kastrati A, Pache J, et al. Diabetes mellitus and the clinical and angiographic outcome after coronary stent placement. *J Am Coll Cardiol.* 1998; 32: 1866-1873.

19 Abizaid A, Kornowski R, Mintz GS, et al. The influence of diabetes mellitus on acute and late clinical outcomes following coronary stent implantation. *J Am Coll Cardiol.* 1998; 32: 584-589.

20 Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *EuroIntervention J Eur Collab Work Group Interv Cardiol Eur Soc Cardiol.* 2019; 14: 1435-1534.