Original Article

The Impact of Diabetes Mellitus on Clinical Outcomes after Percutaneous Coronary Intervention with Different Stent Sizes

Mohammad Javad Zibaeenezhad, MD[1], Mehrab Sayadi, PhD[1], Seyyed Saeed Mohammadi, MD[1], Soorena Khorshidi, MD[1], Ehsan Hadiyan, MD[1], Neda Rasouli, MD[2], Ali Karimi-Akhormeh, MS[1], Iman Razeghian-Jahromi, PhD[1*]

[1]*Cardiovascular Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.*
[2]*University of Colorado, School of Medicine, and VA Eastern Colorado Health Care System, Aurora, Colorado, USA.*

Received 03 January 2022; Accepted 06 August 2022

Abstract

Background: *This study aimed to investigate the possible relationship between different stent sizes and clinical outcomes after percutaneous coronary intervention (PCI) in patients with diabetes treated with drug-eluting stents (DESs) and dual antiplatelet therapy (DAPT).*

Methods: *Patients with stable coronary artery disease undergoing elective PCI with the DES were entered into a retrospective cohort between 2003 and 2019. Major adverse cardiac events (MACE), defined as the combined endpoint of revascularization, myocardial infarction, and cardiovascular death, were recorded. The participants were categorized according to the stent size: 27 mm for length and 3 mm for diameter. DAPT (aspirin and clopidogrel) was used for at least 2 years for diabetics and 1 year for nondiabetics. The median duration of follow-up was 74.7 months.*

Results: *Out of 1630 participants, 29.0% had diabetes. The diabetics constituted 37.8% of those with MACE. The mean diameter of the stents in the diabetics and nondiabetics was 2.81±0.29 mm and 2.90±0.35 mm, respectively (P>0.05). The mean stent length was 19.48±7.58 mm and 18.92±6.64 mm in the diabetics and nondiabetics, respectively (P>0.05). After adjustments for confounding variables, MACE was not significantly different between the patients with and without diabetes. Although MACE incidence was not affected by stent dimensions in the patients with diabetes, the nondiabetic patients implanted with a stent length exceeding 27 mm experienced MACE less frequently.*

Conclusion: *Diabetes did not influence MACE in our population. Additionally, stents of different sizes were not associated with MACE in patients with diabetes. We propose that using the DES supplemented by long-term DAPT and tight control of glycemic status after PCI could decrease the adverse consequences of diabetes.*

J Teh Univ Heart Ctr 2022;17(4):207-214

This paper should be cited as: Zibaeenezhad MJ, Sayadi M, Mohammadi SS, Khorshidi S, Hadiyan E, Rasouli N, et al. The Impact of Diabetes Mellitus on Clinical Outcomes after Percutaneous Coronary Intervention with Different Stent Sizes. J Teh Univ Heart Ctr 2022;17(4):207-214.

Keywords: *Diabetes mellitus; Myocardial infarction; Percutaneous coronary intervention; Stents*

[*]**Corresponding Author:** ***Iman Razeghian-Jahromi,*** *Assistant Professor of Cardiovascular Research Center, Shiraz University of Medical Sciences, 3rd Floor, Mohammad Rasoolallah Research Tower, Khalili Street, Shiraz, Iran. 71936-35899. Tel: +98 9173057849. Fax: +98 71 36122235. E-mail: razejahromi@yahoo.com.*

Introduction

Diabetes mellitus (diabetes) is deemed a global health emergency in that it has already involved 451 million people, a figure expected to rise to 693 million by the year 2045 (IDF Diabetes Atlas, Eighth edition 2017). Diabetes is known as one of the major risk factors for coronary artery disease (CAD). The prevalence of coronary involvement in diabetic patients was reported to be 10 times that in the general population, and the patterns of lesions in the coronary arteries of patients with diabetes are complex and diffuse. CAD is currently the leading cause of death in diabetics,[1] and diabetes has been historically considered a predictor of cardiac death.[2]

Percutaneous and surgical revascularization approaches are treatment options for CAD.[3] More than 25% of patients undergoing percutaneous coronary intervention (PCI) have diabetes. Long-term mortality and repeat revascularizations after PCI have been reported in diabetic patients.[4] Bare-metal stents (BMSs) have been used during PCI for years; nonetheless, recent years have witnessed the emergence of drug-eluting stents (DESs) with the additional capability to reduce restenosis rates. Indeed, CAD patients with diabetes have been reported to benefit from DES implantation compared with BMS implantation.[5,6]

Lesion complexity also plays a prominent role in the occurrence of post-PCI clinical events. Stent size (length and diameter) is a relatively representative of lesion complexity. The use of long stents, possibly reflecting more complex lesions, predicts poor clinical outcomes in general. Nevertheless, some studies have reported clinical outcomes independent of stent size.[6,7]

Substantial evidence demonstrates the beneficial efficacy of glycemic control in decreasing microvascular complications.[8] Still, it remains unclear whether glycemic control can reduce macrovascular complications and improve clinical outcomes.[9,10] Limited data are available on the effects of glycemic control after PCI, which is more valuable than preprocedural control, with respect to the incidence of adverse events.[8,11]

We conducted the present study to investigate the incidence of post-PCI clinical outcomes in diabetic patients with CAD treated with the DES and dual antiplatelet therapy (DAPT). We also evaluated the occurrence of clinical outcomes in relation to stent length and diameter.

Methods

The present study was conducted in accordance with the Helsinki Declaration and was approved by our institutional research ethics committee (IR.sums.med.rec.1396.s113). Patients who underwent elective PCI (index PCI) for stable CAD in defined hospitals between March 2003 and January 2019 were included. Among CAD patients, those with multivessel disease, atrial fibrillation, and acute coronary syndromes were excluded. PCI was performed with the standard DES. The criterion for angioplasty was at least 75% narrowing in the left anterior descending, diagonal, left circumflex, obtuse marginal, right coronary, posterior descending, and posterior left ventricular branch arteries.[12] Based on availability, first-generation DESs (the sirolimus-eluting stent and the paclitaxel-eluting stent) or second-generation DESs (the zotarolimus-eluting tent and the everolimus-eluting stent) were applied.

Diabetes was defined as follows: a fasting plasma glucose level of 126 mg/dL (7.0 mmol/L) or higher, a 2-hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher during the oral glucose tolerance test, an A1C level of 6.5% (48 mmol/mol) or higher, the presence of the classic symptoms of hyperglycemia or the hyperglycemic crisis, a random plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher,[13] or the consumption of anti-diabetic medications. Patients who had a minimum systolic blood pressure of 130 mm Hg or a minimum diastolic blood pressure of 80 mmHg or both or those receiving antihypertensive medications before index PCI were considered patients with a history of hypertension.[14] Patients who had hyperlipidemia or used antihyperlipidemic medications were regarded as those with a history of hyperlipidemia.[15] Smokers were considered to be active smokers consuming any amount or type of smokables before the index PCI (at least 1 cigarette per day).

All the study subjects were followed up for cardiovascular death, myocardial infarction, and/or repeated revascularization (PCI or coronary artery bypass grafting), totally defined as major adverse cardiac events (MACE).

The participants attended the clinic for follow-up visits. In the case of nonadherence, phone calls were made to their spouse or first-degree relatives. Data were recorded in a dedicated online database. During the follow-up phase, diabetic patients were under the supervision of an endocrinologist for the close monitoring of their glycemic status. The type of medical therapy (oral or injectable) with or without diet changes was individualized. The time from the index PCI to the earliest MACE was defined as time-to-event. Age was defined as the age of the participants at the time of the index PCI. The length and diameter of stents were presented in their nominal value.

Clopidogrel (600 mg) and aspirin (ASA, 325 mg) were given before the index PCI and continued with clopidogrel (150 mg) and ASA (325 mg) for 3 weeks,[16] followed by clopidogrel (75 mg/d) and 80 mg (160 mg in the case of diabetes) of ASA for at least 2 years in diabetic patients and for at least 1 year in nondiabetics. Additionally, atorvastatin (40–80 mg) was administered to all the participants. Heparin (80–100 mg/kg) was given at the time of the index PCI. All the participants were under close follow-up surveillance through periodic visits for their health status and adherence to prescribed medications. Any patient experiencing MACE

was considered an event, and patients without MACE were regarded as censor cases.

Data were presented as the mean ± the standard deviation (SD) for continuous and as numbers (%) for categorical variables. The Student *t* and χ^2 tests were used to compare the continuous and categorical variables, respectively. The Cox proportional-hazard regression model and the unconditional multiple binary logistic regression model with 2-sided tests at a 5% level of significance were employed. For model building, all the variables were imported via the enter method due to the limited number of research variables. All the analyses were performed using the statistical Package for Social Sciences version 16 (SPSS Inc, Chicago, IL, USA).

Results

Overall, 1630 patients were eligible for participation. The minimum and maximum follow-up periods were 15 days and 201.4 months, respectively, with a median of 74.7 months. Moreover, the minimum and maximum time-to-event rates were 16 days and 105.6 months, respectively, with a median of 34.63 months. Diabetes was found in 485 CAD patients (29.8%). According to Table 1 and Table 2, the patients with diabetes were significantly younger at the time of the index PCI than their nondiabetic peers. There were also more females in the diabetes group. Hypertension and hyperlipidemia were more prevalent in the diabetes group, while smoking status was not different between the diabetics and nondiabetics.

MACE occurred in 126 patients (7.7%): revascularization in 69%, myocardial infarction in 5.6%, and cardiovascular death in 25.4%. the occurrence of MACE at 0.1% per person-month was confirmed. The rates of MACE and time-to-event were not statistically different between the diabetes and nondiabetes groups. Figure 1 shows the survival rate of the

Table 1. Unadjusted comparisons of characteristics between patients with and without DM*

Variables	DM (n=485)	Non-DM (n=1145)	P
Age (y)	59.8±10.48	60.41±11.65	0.319
Sex			
Female	248 (51.1)	390 (34.1)	<0.001**
HTN	325 (67.0)	587 (51.3)	<0.001**
HLP	368 (75.9)	457 (39.9)	<0.001**
Smoking	214 (44.1)	560 (48.9)	0.077
MACE	41/485 (8.5)	85/1145 (7.4)	0.477
Time-to-event (mon)[a]	50.31±50.65	50.24±47.80	0.569
Stent length	19.48±7.58	18.92±6.64	0.674
Stent diameter	2.81±0.29	2.90±0.35	0.210
Number of stents	1.41±0.61	1.39±0.52	0.501

*Data are presented as the mean ± the standard deviation (SD) or numbers (%).
**Values imply significant differences.
[a] This variable was measured only in patients with MACE.
DM, Diabetes mellitus; HTN, Hypertension; HLP, Hyperlipidemia; MACE, Major adverse cardiac events

Table 2. Adjusted comparisons of characteristics between patients with and without DM

Variables	OR	95% Confidence Interval		P
		Lower limit	Upper limit	
Age (y)	0.98	0.97	0.99	0.031
Sex				
Female	1.47	1.15	1.89	0.002*
HTN	1.35	1.05	1.74	0.018*
HLP	4.14	3.23	5.30	<0.001*
Smoking	1.00	0.79	1.27	0.969
MACE	1.24	0.82	1.90	0.297
Stent length	1.00	0.98	1.02	0.553
Stent diameter	0.83	0.61	1.14	0.279
Number of stents	1.07	0.61	1.87	0.797

*Bold values imply significant differences. The multiple binary logistic regression model was used.
OR, Odds ratio; DM, Diabetes mellitus HTN, Hypertension; HLP, Hyperlipidemia; MACE, Major adverse cardiac events

Table 3. Characteristics of the diabetic patients according to MACE occurrence*

Variables	MACE (n=41)	Not MACE (n=444)	Unadjusted			Adjusted		
			HR	95% Confidence Interval for HR	P	HR	95% Confidence Interval for HR	P[b]
Age (at the time of the index PCI, y)	54.83±10.80	60.21±10.32	0.96	0.93-0.99	0.015	0.96	0.93-0.99	0.024**
Sex								
Male	23 (56.1)	214 (48.2)	0.94	0.59-1.51	0.333	0.94	0.49-1.80	0.858
HTN	30 (73.2)	295 (66.4)	1.45	0.72-2.89	0.292	2.35	1.14-4.84	0.021**
HLP	32 (78.0)	280 (63.4)	1.81	1.02-3.44	0.044	2.17	1.11-4.34	0.024**
Smoking	28 (68.3)	186 (41.9)	2.43	1.26-4.71	0.008	2.45	1.28-5.05	0.008**
Stent length (mm)	18.11±5.37	19.57±6.23	0.98	0.93-1.03	0.529	0.98	0.93-1.04	0.661
Stent diameter (mm)	2.86±0.32	2.80±0.35	1.36	0.63-2.91	0.424	1.06	0.49-2.26	0.873
Number of stents	1.41±0.61	1.39±0.52	1.06	0.61-1.87	0.797	1.08	0.62-1.88	0.745

*Data were presented as the mean ± the standard deviation (SD) or numbers (%).
**Values imply significant differences.
Pb, Obtained from the multiple Cox proportional hazard model. All the variables were adjusted via multiple models through the enter method.
HTN, Hypertension; HLP, Hyperlipidemia; MACE, Major adverse cardiac events; HR, Hazard ratio

patients up to MACE during the study. As the chart shows, the survival rate of the study participants was generally high (>80%) during the study. This rate was higher than 90% before 60 months.

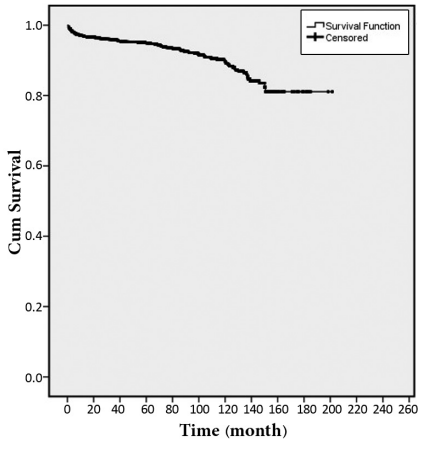

Figure 1. The image depicts the survival rate of the participants from enrollment to the occurrence of MACE during the study period. The vertical axis is the cumulative survival. The survival rate of the patients was generally high (>0%) during the study. This rate was higher than 90% before 60 months.

Stent length and diameter were not statistically different between the patients with and without diabetes. Even after adjustments for cardiovascular risk factors, such as hypertension, hyperlipidemia, smoking, age, and sex, there was no difference in the MACE rate between the 2 groups. Figure 2 demonstrates the unadjusted and adjusted hazard ratios of MACE, as well as related confidence intervals, for different variables. Age, hypertension, hyperlipidemia, and smoking were significantly different between the MACE and non-MACE groups among the diabetics. However, there was no difference in stent length and stent diameter between the MACE and non-MACE groups among the diabetics (Table 3).

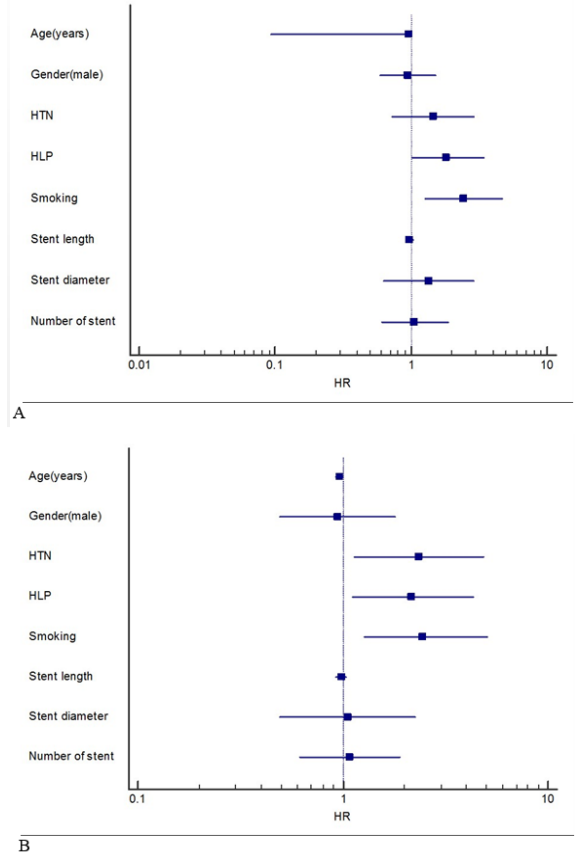

Figure 2. The images illustrate the forest plots of the unadjusted (A) and adjusted (B) hazard ratios of MACE and their confidence intervals for different variables (obtained from univariate (left) and multiple (right) Cox proportional hazard regression models).
Age, hypertension, hyperlipidemia, and smoking were significantly different between the MACE and non-MACE groups among the diabetics. However, there was no difference in stent length and stent diameter between the MACE and non-MACE groups among the diabetics.
HTN, Hypertension; HLP, Hyperlipidemia

The incidence of MACE in relation to different stent dimensions was sought in the patients with and without diabetes using the χ^2 test (Table 4). In the diabetes group, MACE incidence was similar both in patients treated with different stent lengths (≤27 or >27 mm) or those treated with different stent diameters (≤3 or >3mm). In the nondiabetic group, MACE incidence was similar between those treated with stent diameters of 3 mm less and those implanted with stent diameters exceeding 3 mm. In contrast, nondiabetic patients stented with a DES length of greater than 27mm experienced MACE less frequently than those who received stents of 27 mm or less.

Table 4. MACE occurrence in the diabetic and nondiabetic patients with different stent sizes*

Stent Dimensions	MACE		P
	Yes	No	
DM			
Length ≤27 (mm)	34 (9.4%)	327 (90.6%)	0.193
Length >27 (mm)	7 (5.6%)	117 (94.4%)	
Diameter ≤3 (mm)	38 (8.7%)	400 (91.3%)	0.591
Diameter >3 (mm)	3 (6.4%)	44 (93.6%)	
Non-DM			
Length ≤27 (mm)	75 (8.3%)	824 (91.7%)	0.023**
Length >27 (mm)	10 (4.1%)	326 (95.9%)	
Diameter ≤3 (mm)	71 (7.3%)	896 (92.7%)	0.807
Diameter >3 (mm)	14 (7.9%)	164 (92.1%)	

*Data are presented as numbers (%).
**Stent size unit is millimeter. Bold values imply significant differences. The χ^2 test was used for comparison.
MACE, Major adverse cardiac events; DM, Diabetes mellitus

Discussion

The present study was designed to reflect the real-world practice in patients with diabetes who underwent PCI with the DES.[17] Data were collected by trained individuals from a considerable sample size with an acceptable follow-up period (median =74.7 mon). The key findings of the study are as follows: Patients with diabetes were more likely to be younger and female; stent length and stent diameter were not statistically different between patients with and without diabetes; although the majority of the diabetic group had hypertension and hyperlipidemia, no statistical difference in MACE existed between diabetics and nondiabetics; diabetes did not change MACE occurrence; and MACE was not influenced by different stent sizes among diabetic patients.

The adverse effects of diabetes on the cardiovascular system are multifaceted. Diabetes can reduce fibrinolytic capacity, elevate the concentrations of hemostatic proteins, and induce endothelial dysfunction in terms of intimal hyperplasia and vascular inflammation.[18,19] The early onset and development of multifocal atherosclerotic plaques, especially in small-caliber coronary arteries, is a progressive process in diabetic patients.[20] Accordingly, it is plausible that diabetics are at an increased risk of coronary atherosclerosis, plaque burden, and accelerated maturation of multivessel CAD compared with nondiabetics.[21]

A general belief corroborates the association between diabetes and MACE events, such as mortality.[22] The corresponding higher risk of diabetic patients is attributable to such factors as elevated prothrombotic states, platelet hyperactivation, hypercoagulation, and exacerbated endothelial dysfunction.[23,24] However, reports in this area are conflicting. According to a previous study, the adjusted mortality rate and the target lesion revascularization rate were not significantly different between patients with and without diabetes. Further, late stent thrombosis was not associated with diabetes.[25] Another real-world registry on 5115 patients treated with the DES showed that long-term mortality was not adversely affected by diabetes.[25] The discrepancies between studies may also be linked to differences in ethnicity, clinical indications, medication variations, and versatility of practice patterns. The small number of participants and events in the diabetes arm of some studies could be regarded as other influencing factors.

Diabetes is also known as an established risk factor for restenosis after PCI.[26] Restenosis is one of the major long-term complications of PCI in such patients.[27,28] Nonetheless, the correlation between diabetes and in-stent restenosis is not well documented.[29,30] A cohort study on patients with chronic total occlusion indicated that the post-PCI complication rate was the same in diabetics and nondiabetics.[31] Another study showed that the rates of angiographic restenosis and target lesion revascularization were similar in diabetics and nondiabetics.[32] Our findings showed that MACE incidence was not different between patients with diabetes and those without it. Notably, this inconsistency may partly be related to lesion complexity. The relationship between diabetes and revascularization is stronger in complex lesions, whereas diabetic patients with more simple lesions tend to have nearly similar lesion and vessel revascularization rates to nondiabetics during 1 year after DES implantation.[33] The correlation between diabetes and repeat revascularization has been reported only vis-à-vis complex lesions. In addition, the duration of diabetes, the number of diseased vessels, and stent length are also considered the most significant angiographic and clinical determinants of restenosis.[34]

The emergence of the DES into interventional cardiology ushered in promising hopes, particularly with regard to the attenuation of BMS-related complications. The long-term durability of the DES has been reported in diabetic patients.[25] A prior investigation reported that the DES exhibited outstanding benefits, such as similar rates of MACE incidence, late lumen loss, and binary restenosis, when compared with invasive surgery.[35] New-generation stents possess pronounced impacts in terms of safety and efficacy against balloon angioplasty, the BMS, and early-generation

DESs, not least in diabetic patients.[26] It seems that the DES mitigates diabetes-related vascular proliferation in simple lesions. In the present study, all the patients received the DES, either first or second-generations, irrespective of diabetes status.

Reports are conflicting regarding the contribution of clinical outcomes after PCI with the DES to diabetes status and the complexity of coronary lesions.[26] The involvement of small vessels with long lesions increases the risk of restenosis; hence, a poor prognosis is anticipated.[36] Given that no difference was seen in stent size between patients with and without diabetes in our study, it may be concluded that lesion complexity was not considerably different between the 2 groups, at least according to stent size.

Coronary lesions in diabetic patients typically appear long and diffuse, more likely in small-diameter arteries. Consequently, lesion complexity could be relatively presented by the length and diameter of the stent. Consistent with our findings that there was no correlation between stent size and MACE in patients with diabetes, another study showed that the different stent lengths had no impact on 30-day mortality, all-cause mortality, MACE, target lesion revascularization, and target vessel revascularization.[37] However, another study suggested that a 1 mm increase in stent length translated into higher restenosis risks.[36] Accordingly, longer stents are associated with elevated risks of thrombosis.[38,39] In line with our findings concerning the higher incidence of MACE with stents of shorter length among nondiabetic patients, another study revealed that MACE, target lesion revascularization, and target vessel revascularization were more frequent in patients treated with small stents (<3 mm) than in patients treated with larger stents (≥3 mm).[40,41]

Satisfactory results of coronary revascularization in patients with diabetes are also dependent on adequate adjunctive medications.[42] In the post-PCI setting with the DES, DAPT possesses a protective role against early and late ischemic events.[42] Indeed, platelet hyperactivity in diabetic patients necessitates the use of more potent antiplatelet medications.[43,44] DAPT with aspirin and P_2Y_{12} inhibitors has been drawn upon for many years as the main treatment option after PCI. This treatment is associated with a significant reduction in MACE, particularly in patients with diabetes.[45]

The duration of DAPT after PCI has been discussed in diabetic patients. In this regard, stent thrombosis was significantly reduced upon long-term DAPT in a prior study.[46] These trials mostly included early and second-generation stents and showed that an extended DAPT duration (>24 mon) was associated with a reduction in the MACE rate.[47] The most recent guidelines on the duration of DAPT in stable ischemic heart disease recommend a period of at least 12 months after an acute coronary syndrome and at least 6 months after revascularization. In the case of lower bleeding risks, this duration could be lengthened beyond 6 and 12 months, respectively. There is no recommendation about the continuation of DAPT after these periods, and the decision is left to clinicians to individualize the duration based on the balance of risks and benefits.[10] We used long-term DAPT with ASA and clopidogrel for at least 2 years for diabetics (1 year for nondiabetics). Meanwhile, no increased rates of bleeding complications or hemorrhagic events were seen in our studied population.

As the glycemic index affects the outcome of PCI in diabetic patients,[48] optimal glycemic control reduces the rate of restenosis.[42] Notably, the presence of hyperglycemia is known as an independent variable that favors the long-term use of DAPT.[49] A previous investigation reported that the periprocedural control of plasma glucose significantly reduced restenosis in a 6-month follow-up, primarily due to the downregulation of inflammatory cytokines and oxidative stress. Such meticulous control probably had beneficial effects on endothelial function, even more than DES implantation.[50] In the current study, an endocrinologist tightly controlled the glycemic status of the patients during the follow-up phase.

We tried to resolve the major limitations of such studies, including the lack of adequate sample size, short follow-up duration, and consideration of primary angiographic endpoints rather than clinical endpoints. The strengths of the current study are the long and close follow-up and the acceptable sample population size, facilitating the demonstration of real-world post-PCI clinical outcomes in patients with diabetes. Our investigation was, however, limited by the inherent restrictions of nonrandomized retrospective studies. We evaluated only patients with diabetes and excluded those who became diabetic after PCI. Further, it was not feasible for us to measure the glycemic status of the patients in the follow-up phase via more precise indices, such as HbA1C. The duration of diabetes in each study participant was not known to us. Our results would have been bolstered had we analyzed the diabetic population according to glycated hemoglobin and the class of antidiabetic drugs. The generalizability of our results needs comparisons with similar investigations from other regions of the world.

Conclusion

In the present study, the MACE rate exhibited no rise in patients with diabetes compared with nondiabetics. Moreover, no association was found between MACE and stent size in diabetics. Using the DES and long-term DAPT (ASA and clopidogrel) for at least 2 years, along with tight control of plasma glucose, may reduce MACE in diabetics.

Acknowledgments

The present study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics

Committee of Shiraz University of Medical Sciences. This work was financially supported by the Vice Chancellorship of Research of Shiraz University of Medical Sciences.

References

1. Yang Y, Park GM, Han S, Kim YG, Suh J, Park HW, Won KB, Ann SH, Kim SJ, Kim DW, Park MW, Her SH, Lee SG. Impact of diabetes mellitus in patients undergoing contemporary percutaneous coronary intervention: Results from a Korean nationwide study. PLoS One 2018;13:e0208746.
2. Sanguineti F, Garot P, O'Connor S, Watanabe Y, Spaziano M, Lefèvre T, Hovasse T, Benamer H, Unterseeh T, Chevalier B, Morice MC, Louvard Y. Chronic total coronary occlusion treated by percutaneous coronary intervention: long-term outcome in patients with and without diabetes. EuroIntervention 2017;12:e1889-e1897.
3. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Jüni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferovic PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO; ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019;40:87-165.
4. Kappetein AP, Head SJ, Morice MC, Banning AP, Serruys PW, Mohr FW, Dawkins KD, Mack MJ; SYNTAX Investigators. Treatment of complex coronary artery disease in patients with diabetes: 5-year results comparing outcomes of bypass surgery and percutaneous coronary intervention in the SYNTAX trial. Eur J Cardiothorac Surg 2013;43:1006-1013.
5. Fukutomi M, Takahashi M, Toriumi S, Ogoyama Y, Oba Y, Funayama H, Kario K. Evaluation of stent length on the outcome of ST-segment elevation myocardial infarction receiving primary percutaneous coronary intervention. Coron Artery Dis 2019;30:196-203.
6. Konigstein M, Ben-Yehuda O, Smits PC, Love MP, Banai S, Perlman GY, Golomb M, Ozan MO, Liu M, Leon MB, Stone GW, Kandzari DE. Outcomes Among Diabetic Patients Undergoing Percutaneous Coronary Intervention With Contemporary Drug-Eluting Stents: Analysis From the BIONICS Randomized Trial. JACC Cardiovasc Interv 2018;11:2467-2476.
7. Maeng M, Jensen LO, Tilsted HH, Kaltoft A, Kelbaek H, Abildgaard U, Villadsen A, Aarøe J, Thayssen P, Krusell LR, Christiansen EH, Bøtker HE, Kristensen SD, Ravkilde J, Madsen M, Sørensen HT, Rasmussen K, Thuesen L, Lassen JF. Outcome of sirolimus-eluting versus zotarolimus-eluting coronary stent implantation in patients with and without diabetes mellitus (a SORT OUT III Substudy). Am J Cardiol 2011;108:1232-1237.
8. ADVANCE Collaborative Group, Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, Marre M, Cooper M, Glasziou P, Grobbee D, Hamet P, Harrap S, Heller S, Liu L, Mancia G, Mogensen CE, Pan C, Poulter N, Rodgers A, Williams B, Bompoint S, de Galan BE, Joshi R, Travert F. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med 2008;358:2560-2572.
9. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, Elkind MS, George MG, Hamdan AD, Higashida RT, Hoh BL, Janis LS, Kase CS, Kleindorfer DO, Lee JM, Moseley ME, Peterson ED, Turan TN, Valderrama AL, Vinters HV; American Heart Association Stroke Council, Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular and Stroke Nursing; Council on Epidemiology and Prevention; Council on Peripheral Vascular Disease; Council on Nutrition, Physical Activity and Metabolism. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013;44:2064-2089.
10. Ahmed A, Husain A, Love TE, Gambassi G, Dell'Italia LJ, Francis GS, Gheorghiade M, Allman RM, Meleth S, Bourge RC. Heart failure, chronic diuretic use, and increase in mortality and hospitalization: an observational study using propensity score methods. Eur Heart J 2006;27:1431-1439.
11. Rawshani A, Rawshani A, Franzén S, Sattar N, Eliasson B, Svensson AM, Zethelius B, Miftaraj M, McGuire DK, Rosengren A, Gudbjörnsdottir S. Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med 2018;379:633-644.
12. Esper RB, Farkouh ME, Ribeiro EE, Hueb W, Domanski M, Hamza TH, Siami FS, Godoy LC, Mathew V, French J, Fuster V. SYNTAX Score in Patients With Diabetes Undergoing Coronary Revascularization in the FREEDOM Trial. J Am Coll Cardiol 2018;72(23 Pt A):2826-2837.
13. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2019. Diabetes Care 2019;42(Suppl 1):S13-S28.
14. Zibaeenezhad MJ, Mohammadi SS, Sayadi M, Khorshidi S, Bahramali E, Razeghian-Jahromi I. The impact of diabetes mellitus and hypertension on clinical outcomes in a population of Iranian patients who underwent percutaneous coronary intervention: A retrospective cohort study. J Clin Hypertens (Greenwich) 2019;21:1647-1653.
15. Nelson RH. Hyperlipidemia as a risk factor for cardiovascular disease. Prim Care 2013;40:195-211.
16. Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, Jüni P, Kastrati A, Kolh P, Mauri L, Montalescot G, Neumann FJ, Petricevic M, Roffi M, Steg PG, Windecker S, Zamorano JL, Levine GN; ESC Scientific Document Group. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. Eur J Cardiothorac Surg 2018;53:34-78.
17. Zibaeenezhad MJ, Ghaem H, Parsa N, Sayadi M, Askarian M, Kasaei M, Sohrabi Z, Dehghani-Firouzabadi A, Nariman A, Radmanesh S, Mani A, Bahramali E, Nikoo MH, Moaref AR, Razeghian-Jahromi I. Analysing cardiovascular risk factors and related outcomes in a middle-aged to older adults population in Iran: a cohort protocol of the Shiraz Heart Study (SHS). BMJ Open 2019;9:e026317.
18. Konigstein M, Ben-Yehuda O, Smits PC, Love MP, Banai S, Perlman GY, Golomb M, Ozan MO, Liu M, Leon MB, Stone GW, Kandzari DE. Outcomes Among Diabetic Patients Undergoing Percutaneous Coronary Intervention With Contemporary Drug-Eluting Stents: Analysis From the BIONICS Randomized Trial. JACC Cardiovasc Interv 2018;11:2467-2476.
19. Byrne RA, Banai S, Colleran R, Colombo A. Challenges in Patients with Diabetes: Improving Clinical Outcomes After Percutaneous Coronary Intervention Through EVOlving Stent Technology. Interv Cardiol 2018;13:40-44.
20. Messerli A, Whayne TF Jr. Impact of Diabetes Mellitus on Percutaneous Coronary Intervention Outcomes: Real-World Lessons From a Large Chinese Single-Center Registry. Angiology 2018;69:749-751.
21. Loutfi M, Sadaka MA, Sobhy M. Outcomes of DES in Diabetic and Nondiabetic Patients with Complex Coronary Artery Disease after Risk Stratification by the SYNTAX Score. Clin Med Insights Cardiol 2016;10:103-110.
22. Iijima R, Ndrepepa G, Mehilli J, Markwardt C, Bruskina O, Pache J, Ibrahim M, Schömig A, Kastrati A. Impact of diabetes mellitus on long-term outcomes in the drug-eluting stent era. Am Heart J 2007;154:688-693.
23. Osende JI, Badimon JJ, Fuster V, Herson P, Rabito P, Vidhun R, Zaman A, Rodriguez OJ, Lev EI, Rauch U, Heflt G, Fallon JT, Crandall JP. Blood thrombogenicity in type 2 diabetes mellitus patients is associated with glycemic control. J Am Coll Cardiol 2001;38:1307-1312.
24. Neergaard-Petersen S, Hvas AM, Kristensen SD, Grove EL, Larsen SB, Phoenix F, Kurdee Z, Grant PJ, Ajjan RA. The influence of type 2 diabetes on fibrin clot properties in patients with coronary artery

disease. Thromb Haemost 2014;112:1142-1150.
25. Park DW, Flaherty JD, Davidson CJ, Yun SC, Lee SW, Kim YH, Lee CW, Hong MK, Cheong SS, Kim JJ, Park SW, Park SJ. Prognostic influence of diabetes mellitus on long-term clinical outcomes and stent thrombosis after drug-eluting stent implantation in asian patients. Am J Cardiol 2009;103:646-652.
26. Koskinas KC, Siontis GC, Piccolo R, Franzone A, Haynes A, Rat-Wirtzler J, Silber S, Serruys PW, Pilgrim T, Räber L, Heg D, Jüni P, Windecker S. Impact of Diabetic Status on Outcomes After Revascularization With Drug-Eluting Stents in Relation to Coronary Artery Disease Complexity: Patient-Level Pooled Analysis of 6081 Patients. Circ Cardiovasc Interv 2016;9:e003255.
27. Wang JL, Qin Z, Wang ZJ, Shi DM, Liu YY, Zhao YX, Yang LX, Cheng WJ, Zhou YJ. New predictors of in-stent restenosis in patients with diabetes mellitus undergoing percutaneous coronary intervention with drug-eluting stent. J Geriatr Cardiol 2018;15:137-145.
28. Megaly M, Ali A, Abraham B, Khalil C, Zordok M, Shaker M, Tawadros M, Hennawy BS, Elbadawi A, Omer M, Saad M. Outcomes with Drug-Coated Balloons in Percutaneous Coronary Intervention in Diabetic Patients. Cardiovasc Revasc Med 2020;21:78-85.
29. Billinger M, Räber L, Hitz S, Stefanini GG, Pilgrim T, Stettler C, Zanchin T, Pulver C, Pfäffli N, Eberli F, Meier B, Kalesan B, Jüni P, Windecker S. Long-term clinical and angiographic outcomes of diabetic patients after revascularization with early generation drug-eluting stents. Am Heart J 2012;163:876-886.
30. Mahmud E, Ormiston JA, Turco MA, Popma JJ, Weissman NJ, O'Shaughnessy CD, Mann T, Hall JJ, McGarry TF, Cannon LA, Webster MW, Mandinov L, Baim DS. TAXUS Liberté attenuates the risk of restenosis in patients with medically treated diabetes mellitus: results from the TAXUS ATLAS program. JACC Cardiovasc Interv 2009;2:240-252.
31. Martinez-Parachini JR, Karatasakis A, Karmpaliotis D, Alaswad K, Jaffer FA, Yeh RW, Patel M, Bahadorani J, Doing A, Nguyen-Trong PK, Danek BA, Karacsonyi J, Alame A, Rangan BV, Thompson CA, Banerjee S, Brilakis ES. Impact of diabetes mellitus on acute outcomes of percutaneous coronary intervention in chronic total occlusions: insights from a US multicentre registry. Diabet Med 2017;34:558-562.
32. Yang TH, Park SW, Hong MK, Park DW, Park KM, Kim YH, Han KH, Lee CW, Cheong SS, Kim JJ, Park SJ. Impact of diabetes mellitus on angiographic and clinical outcomes in the drug-eluting stents era. Am J Cardiol 2005;96:1389-1392.
33. Kedhi E, Généreux P, Palmerini T, McAndrew TC, Parise H, Mehran R, Dangas GD, Stone GW. Impact of coronary lesion complexity on drug-eluting stent outcomes in patients with and without diabetes mellitus: analysis from 18 pooled randomized trials. J Am Coll Cardiol 2014;63:2111-2118.
34. Heper G. The comparison of different clinical, laboratory, and angiographical parameters in diabetic stent restenosis. Heart Dis 2002;4:147-151.
35. Morice MC, Serruys PW, Sousa JE, Fajadet J, Ban Hayashi E, Perin M, Colombo A, Schuler G, Barragan P, Guagliumi G, Molnàr F, Falotico R; RAVEL Study Group. Randomized Study with the Sirolimus-Coated Bx Velocity Balloon-Expandable Stent in the Treatment of Patients with de Novo Native Coronary Artery Lesions. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. N Engl J Med 2002;346:1773-1780.
36. Hong SJ, Kim MH, Ahn TH, Ahn YK, Bae JH, Shim WJ, Ro YM, Lim DS. Multiple predictors of coronary restenosis after drug-eluting stent implantation in patients with diabetes. Heart 2006;92:1119-1124.
37. Fukutomi M, Takahashi M, Toriumi S, Ogoyama Y, Oba Y, Funayama H, Kario K. Evaluation of stent length on the outcome of ST-segment elevation myocardial infarction receiving primary percutaneous coronary intervention. Coron Artery Dis 2019;30:196-203.
38. Jim MH, Yiu KH, Ho HH, Chan WL, Ng AK, Siu CW, Chow WH. Angiographic and clinical outcomes of everolimus-eluting stent in the treatment of extra long stenoses (AEETES). J Interv Cardiol 2013;26:22-28.
39. Nakagawa Y, Kimura T, Morimoto T, Nomura M, Saku K, Haruta S, Muramatsu T, Nobuyoshi M, Kadota K, Fujita H, Tatami R, Shiode N, Nishikawa H, Shibata Y, Miyazaki S, Murata Y, Honda T, Kawasaki T, Doi O, Hiasa Y, Hayashi Y, Matsuzaki M, Mitsudo K; j-Cypher Registry Investigators. Incidence and risk factors of late target lesion revascularization after sirolimus-eluting stent implantation (3-year follow-up of the j-Cypher Registry). Am J Cardiol 2010;106:329-336.
40. Tarantini G, Facchin M, Capodanno D, Musumeci G, Saia F, Menozzi A, Meliga E, Mancone M, Lettieri C, Tamburino C. Paclitaxel versus sirolimus eluting stents in diabetic patients: does stent type and/or stent diameter matter?: long-term clinical outcome of 2,429-patient multicenter registry. Catheter Cardiovasc Interv 2013;81:80-89.
41. Kornowski R, Fort S, Almagor Y, Silber S, Lewis BS; Nirtop investigators. Impact of vessel size, lesion length and diabetes mellitus on angiographic restenosis outcomes: insights from the NIRTOP study. Acute Card Care 2008;10:104-110.
42. Bernelli C, Chan J, Chieffo A. Drug-eluting stent outcomes in diabetes. Expert Rev Cardiovasc Ther 2014;12:95-109.
43. Ferreiro JL, Angiolillo DJ. Diabetes and antiplatelet therapy in acute coronary syndrome. Circulation 2011;123:798-813.
44. Wiviott SD, Braunwald E, Angiolillo DJ, Meisel S, Dalby AJ, Verheugt FW, Goodman SG, Corbalan R, Purdy DA, Murphy SA, McCabe CH, Antman EM; TRITON-TIMI 38 Investigators. Greater clinical benefit of more intensive oral antiplatelet therapy with prasugrel in patients with diabetes mellitus in the trial to assess improvement in therapeutic outcomes by optimizing platelet inhibition with prasugrel-Thrombolysis in Myocardial Infarction 38. Circulation 2008;118:1626-1636.
45. Rivas Rios JR, Franchi F, Rollini F, Angiolillo DJ. Diabetes and antiplatelet therapy: from bench to bedside. Cardiovasc Diagn Ther 2018;8:594-609.
46. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, McFadden E, Lansky A, Hamon M, Krucoff MW, Serruys PW; Academic Research Consortium. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007;115:2344-2351.
47. Alonso JJ, Durán JM, Gimeno F, Ramos B, Serrador A, Fernández-Avilés F. Angioplastia coronaria en el paciente diabético. Situación actual y perspectivas futuras [Coronary angioplasty in diabetic patients. Current and future perspectives]. Rev Esp Cardiol 2002;55:1185-1200.
48. Corpus RA, George PB, House JA, Dixon SR, Ajluni SC, Devlin WH, Timmis GC, Balasubramaniam M, O'Neill WW. Optimal glycemic control is associated with a lower rate of target vessel revascularization in treated type II diabetic patients undergoing elective percutaneous coronary intervention. J Am Coll Cardiol 2004;43:8-14.
49. Yeh RW, Secemsky EA, Kereiakes DJ, Normand SL, Gershlick AH, Cohen DJ, Spertus JA, Steg PG, Cutlip DE, Rinaldi MJ, Camenzind E, Wijns W, Apruzzese PK, Song Y, Massaro JM, Mauri L; DAPT Study Investigators. Development and Validation of a Prediction Rule for Benefit and Harm of Dual Antiplatelet Therapy Beyond 1 Year After Percutaneous Coronary Intervention. JAMA 2016;315:1735-1749.
50. Marfella R, Sasso FC, Siniscalchi M, Paolisso P, Rizzo MR, Ferraro F, Stabile E, Sorropago G, Calabrò P, Carbonara O, Cinquegrana G, Piscione F, Ruocco A, D'Andrea D, Rapacciuolo A, Petronella P, Bresciani A, Rubino P, Mauro C, Paolisso G. Peri-procedural tight glycemic control during early percutaneous coronary intervention is associated with a lower rate of in-stent restenosis in patients with acute ST-elevation myocardial infarction. J Clin Endocrinol Metab 2012;97:2862-2871.