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*Research Article*

# The Association between Type-2 Diabetes Duration and Major Adverse Cardiac Events after Percutaneous Coronary Intervention

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*Background*. Diabetes is an independent risk factor for coronary artery disease and portends adverse prognosis in diabetic patients undergoing percutaneous coronary intervention (PCI) compared to nondiabetic patients. Few studies are currently available regarding the relationship between diabetes duration and major adverse cardiac events (MACEs) post-PCI. This study is aimed at assessing the association between diabetes duration and major adverse cardiac events after PCI. *Methods*. A total of 302 cases of diabetic patients undergoing an elective PCI with drug-eluting stent (DES) deployment and or percutaneous transluminal coronary angioplasty (PTCA) using a drug-coated balloon (DCB) were prospectively studied. We divided patients into three groups based on diabetes duration: <5 years group ($n = 165$), 5–10 years' group ($n = 72$), and ≥10 years' group ($n = 65$). Angiographic and clinical follow-up were conducted 12 months after the procedures for all the patients and at any given time during the study when needed. *Results*. A significantly higher rate of myocardial infarction (MI) in diabetic patients with the longest diabetes duration (7.7% vs. 0% and 0.6%, $P = 0.001$) was observed compared with groups of shorter duration. Repeat coronary revascularization was found to be significantly higher in the >10-year group than was it in groups with shorter duration of diabetes (23.1% vs. 19.4% and 9.10%, $P = 0.03$). After adjustment for confounding risk factors, longer diabetes duration remained an independent predictor of MI (hazard ratio (HR): 5.525, confidence interval (CI): 1.273-23.978, $P = 0.022$) and repeat revascularization (HR: 1.608, CI: 1.058-2.443, $P = 0.026$). Repeat revascularization was significantly related to the progression of nontreated lesions (De novo lesions 20% vs. 18% and 7.3%, $P = 0.009$) compared to previously treated lesions (target lesion revascularization (TLR) 3% vs. 1.3% and 2%, $P = 0.774$). However, all-cause mortality was not significantly different among the groups (3.1% vs. 5.6% and 0.6%, $P = 0.06$, HR: 2.403, CI: 0.464-12.436, $P = 0.293$). *Conclusion*. Diabetes duration was associated with significant differences in major adverse cardiac events after the percutaneous coronary intervention; the longest diabetes duration portended higher rates of MACEs than shorter duration at the 12-month follow-up.

## 1. Background

The ever-increasing diagnosis of diabetes worldwide has become a serious problem for public health with dramatic secondary complications. This increase is attributed to a growing and aging population, a sedentary lifestyle, and a higher prevalence of obesity. Diabetic patients are more likely to develop coronary artery disease and manifest it earlier in life than nondiabetic patients [1–3]. Type 2 diabetes is considered as coronary artery disease (CAD) equivalent, contributing to the death of a high proportion of type-2 diabetic patients from cardiovascular causes, and around one-third of patients undergoing percutaneous coronary intervention are made of diabetic patients [4, 5]. Advancements in revascularization procedures in the past decade have improved outcomes even in diabetic patients. However, compared to the nondiabetic group, studies consistently show worse outcomes in terms of cardiovascular events and death, and poor angiographical results post PCI in the diabetic group [6–13]. Despite the fact that diabetic patients often have concurrent risk factors that influence adverse outcomes following PCI, diabetes alone is a strong independent risk factor for

cardiovascular events [14]. Ongoing metabolic disturbances such as insulin resistance, hyperinsulinemia, hyperglycemia, and dyslipidemia associated with hematologic abnormalities and inflammatory response related to type 2 diabetes justify the complexity and severity of coronary lesions and faster progression of atherosclerotic disease, thus, poor outcomes even after the revascularization with the third generation of drug-eluting stent [5, 15]. The long-term exposure to these ongoing disturbances is an important parameter to consider when studying diabetes influences on coronary artery disease and revascularization procedures. This study is aimed at assessing the relationship between type 2 diabetes duration and major adverse cardiac events after percutaneous coronary intervention.

## 2. Methods

We prospectively studied 302 cases of type-2 diabetic patients with coronary artery disease undergoing elective PCI with drug-eluting stent deployment (DES) and or PTCA using a drug-coated balloon (DCB) in the Department of Cardiology in The First Affiliated Hospital of Zhengzhou University. We considered as type-2 diabetic patients with fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L), and or two-hour plasma glucose ≥ 200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT) and or HbA1c ≥ 6.5%, in line with the American Diabetes Association diagnostic criteria for diabetes combined with clinical presentation [16]. We defined diabetes onset as the first time the above criteria were met. In addition to this, we considered diabetic patients, patients receiving treatment with oral hypoglycemic agents and or insulin, and those with a documented history of diabetes. The accurate period of diabetes onset was prospectively determined during the interview of patients with a known history of diabetes; however, for those with an unknown history, a medical record query was used. Diabetes duration was determined by counting the number of months from the first time the diagnostic criteria were meet to the time of revascularization and based on that duration; patients were divided into three groups: <5 years, 5-10 years, and >10 years.

*2.1. Exclusion Criteria.* We did not include in this study patients with type-1 diabetes, severe heart failure (EF < 35% , NYHA IV), emergent PCI for acute myocardial infarction, severe renal failure (eGFR <30 ml/L), contraindication for dual antiplatelet therapy, and failure to open a chronic total occlusion (CTO) lesion during PCI.

*2.2. Endpoints.* The endpoint of this study was the major adverse cardiac events (MACEs) defined as the composite of myocardial infarction, repeat coronary revascularization, and all-cause mortality. The diagnosis of myocardial infarction was made when the following criteria were met: detection of increase and/or decrease of cardiac biomarkers levels; at least one value above the 99th percentile of the upper reference limit (URL), together with evidence of myocardial ischemia, was recognized by at least one of the following: symptoms of ischemia, ECG changes of new ischemia or development of pathologic Q waves, and imaging evidence of new loss of viable myocardium or new regional wall motion abnormality [17]. We considered as repeat coronary revascularization any interventional (PCI, PTCA) or surgical (CABG) procedure used to restore adequate coronary blood supply within the 12-month period following the primary PCI/PCTA. We considered as a long lesion a coronary artery lesion of greater than 20 mm in length [18].

*2.3. Follow-Up.* We organized angiographic and clinical follow-up for assessment of angina recurrence, myocardial infarction, and cardiac death at the end of a period of 12 months from the procedure. However, without regard to the appointed time for follow-up, we advised patients to return to the hospital for further investigations and treatment at any time when necessary. Adjunctive pharmacological therapy. Every patient received a daily oral dual antiplatelet therapy of aspirin 100 mg plus clopidogrel 75 mg or ticagrelor 180 mg for a minimum period of 12 months for patients treated with DES and three months in those treated with DCB only. The initial loading dose for clopidogrel and ticagrelor was, respectively, 600 mg and 180 mg. We left the physician the discretion of using whether bivalirudin or heparin or glycoprotein IIb/IIIa inhibitors depending on specific conditions.

*2.4. Statistical Analysis.* Patients' baseline characteristics and MACEs parameters are presented in diabetic groups with 5-year increments in diabetes duration, with continuous and categorical variables, respectively, reported as means ± SD and as counts and percentages. We compared continuous variables between groups using ANOVA and post hoc analysis. Categorical variables were compared using X2 or Fisher's exact test. We constructed survival curves using the Kaplan-Meier method and compared with the log-rank test. To describe the relationship between the composite of MACEs and diabetes duration, multivariable Cox proportional hazards regression was used to calculate the hazard ratios (HR) with 95% confidence intervals (CI) first unadjusted and then adjusted for sex, age, hypertension, smoking, total cholesterol, high-density lipoprotein, low-density lipoprotein, glycated hemoglobin, and insulin therapy. Statistical analyses were performed using SPSS version 23, statistical software from IBM, and statistical significance was accepted for bilateral $P < 0.05$.

## 3. Results

*3.1. Demographic and Baseline Characteristics.* From a total of 302 type-2 diabetic patients studied, 165 had diabetes duration inferior to 5 years, 72 patients had diabetes for 5 to 10 years, and 65 had diabetes for more than ten years; there were more male than female patients in each group. Although without statistical significance, patients with longer duration of diabetes were older and were more likely to have a history of heart failure, stroke, myocardial infarction, and a higher level of blood urea and creatinine than patients with shorter duration. Still, without statistical significance, patients with shorter duration of diabetes were younger and were more likely smokers than those with a longer

Table 1: Demographic and baseline characteristics.

| | Diabetes duration | | | $P$ for trend[#] |
|---|---|---|---|---|
| | <5 years | 5 to 10 years | >10 years | |
| Number ($n = 302$) | 165 (54.6%) | 72 (23.8%) | 65 (21.5%) | |
| Gender: male, % | 107 (55.7%) | 42 (21.9%) | 43 (22.4%) | 0.561 |
| Gender: female, % | 58 (52.7%) | 30 (27.3) | 22 (20%) | |
| Age | 60.2 ± 9.6 | 61.4 ± 9.5 | 62.6 ± 8.1 | 0.141[$] |
| Life style modification % | 164 (99.4%) | 72 (100%) | 65 (100%) | 0.546 |
| OHA % | 112 (67.9%) | 63 (87.5%) | 56 (86.2%) | 0.001 |
| Insulin % | 35 (21.2%) | 27 (37.5%) | 33 (50.8%) | 0.001 |
| OHA and insulin % | 28 (17%) | 22 (30.6%) | 27 (41.5%) | 0.001 |
| Smoking % | 55 (33.3%) | 19 (26.4%) | 20 (30.8%) | 0.568 |
| Hypertension % | 111 (67.3%) | 50 (69.4%) | 43 (66.2%) | 0.913 |
| Heart failure % | 103 (62.4%) | 50 (69.4%) | 46 (70.8%) | 0.372 |
| Prior MI % | 24 (14.5%) | 14 (19.4%) | 13 (20%) | 0.489 |
| Prior stroke % | 21 (12.7%) | 14 (19.4%) | 11 (16.9%) | 0.380 |
| EF % | 60.6 ± 5.4 | 58.7 ± 8 | 59.1 ± 6.3 | 0.141[$] |
| BNP Pg/ml | 758.3 ± 1075 | 1403.4 ± 2572 | 1555.3 ± 2235.8 | 0.006[$] |
| CK-MB, U/L | 15.3 ± 9.2 | 16.2 ± 11.4 | 13.74 ± 6.2 | 0.351[$] |
| cTnT, ng/L | 0.2 ± 1.4 | 0.2 ± 0.5 | 0.2 ± 0.5 | 0.982[$] |
| HGB, g/L | 129.7 ± 17 | 125.1 ± 21 | 127.2 ± 17 | 0.178[$] |
| Glucose, mmol/L | 11.9 ± 56.5 | 7.2 ± 2.7 | 8.6 ± 3.1 | 0.707[$] |
| HbA1C, % | 7.5 ± 1.4 | 9 ± 9.1 | 8.7 ± 1.7 | 0.069[$] |
| Urea, mmol/L | 5.2 ± 1.9 | 5.2 ± 2.3 | 6.2 ± 5.4 | 0.075[$] |
| Creatinine, mmol/L | 73.4 ± 47.8 | 76.4 ± 52.7 | 93.1 ± 129.8 | 0.203[$] |
| eGFR, mL/min/1.73m$^2$ | 92.79 ± 15.31 | 90.75 ± 24.03 | 86.35 ± 20.86 | 0.088[$] |
| T. Cholesterol, mg/dL | 3.7 ± 0.8 | 3.9 ± 1.1 | 3.7 ± 1 | 0.444[$] |
| HDL, mmol/L | 1 ± 0.9 | 1 ± 0.2 | 0.9 ± 0.2 | 0.763[$] |
| LDL, mmol/L | 3.5 ± 15.2 | 2.3 ± 1 | 2.2 ± 0.7 | 0.656[$] |
| Triglyceride, mmol/L | 1.9 ± 1.1 | 1.6 ± 0.8 | 1.7 ± 1.2 | 0.153[$] |
| Albumin, g/L | 40.9 ± 4 | 40 ± 5 | 39.8 ± 4 | 0.152[$] |
| Medication | | | | |
| Aspirin + clopidogrel | 110 (67%) | 36 (50%) | 35 (54%) | 0.034 |
| Aspirin + ticagrelor | 55 (33.3%) | 36 (50%) | 30 (46.1%) | |
| ACE inhibitor | 29 (18%) | 17 (24%) | 13 (20%) | 0.497 |
| Beta blockers | 123 (75%) | 48 (67%) | 44 (68%) | 0.321 |
| Statin | 165 (100%) | 72 (100%) | 65 (100%) | 0.000 |

Data are reported as mean ± SD or $n$ (%). OHA: oral hypoglycemic agent; MI: myocardial infarction; EF: ejection fraction; BNP: brain natriuretic peptide; CK-MB: creatinine kinase myocardial band; cTnT: cardiac troponin T; HGB: hemoglobin; HbA1C: glycosylated hemoglobin; eGFR: estimated glomerular filtration rate; T. cholesterol: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; ACE: angiotensin-converting enzyme. [#]Statistical significances for categorical variables were tested using X2 test for trend. [$]Statistical significances were tested by one-way ANOVA with trend analysis for continuous variables.

duration. The usage of insulin (50.8% vs. 37.5% vs. 21.2%, $P = 0.001$), the combination of insulin and oral hypoglycemic agents (41.5% vs. 30.6% vs. 17%, $P = 0.001$), and higher BNP level (1555.3 ± 2235.8 vs. 1403.4 ± 2572 vs. 758.3 ± 1075, $P = 0.006$) were significantly higher in patients with longer duration of diabetes. Table 1 presents the demographic and baseline characteristics of diabetic patients before revascularization.

*3.2. Lesion Characteristics and Devices Used.* Angiographic characteristics of coronary lesions showed no statistical significance between groups regarding the number of vessels diseased lesion length and CTO lesion. However, we observed a higher numerical frequency of CTO and long-lesions in patients with longer diabetes duration (CTO: 37% vs. 31% and 30%, $P = 0.604$, long lesions: 60% vs.54.2% and 52.4%, $P = 0.584$). There was a significant association

Table 2: Baseline lesions characteristics and devices used.

| | Diabetes duration | | | $P$ for trend |
|---|---|---|---|---|
| | <5 years | 5 to 10 years | >10 years | |
| Number ($n = 302$) | 165 (54.6%) | 72 (23.8%) | 65 (21.5%) | |
| Coronary artery | | | | |
| LM | 11 (6.7%) | 9 (12.5%) | 4 (6.2%) | 0.260 |
| LAD | 149 (90.3%) | 67 (93.1%) | 58(89.2%) | 0.714 |
| Proximal | 119 (72.1%) | 53 (73.6%) | 53 (81.5%) | 0.330 |
| Middle | 117 (70.9%) | 37 (51.4%) | 42 (64.6%) | 0.015 |
| Distal | 48 (29.1%) | 23 (31.9%) | 20 (30.8%) | 0.900 |
| LCX | 104 (63%) | 48 (66.7%) | 47 (72.3%) | 0.404 |
| Proximal | 68 (41.2%) | 31 (43.1%) | 26 (40%) | 0.934 |
| Middle | 64 (38.8%) | 28 (38.9%) | 26 (40%) | 0.985 |
| Distal | 35 (21.2%) | 19 (26.4%) | 21 (32.3%) | 0.202 |
| RCA | 107 (64.8%) | 46 (63.9%) | 46 (70.8%) | 0.639 |
| Proximal | 60 (36.4%) | 24 (33.3%) | 22 (33.8%) | 0.878 |
| Middle | 60 (36.4%) | 31 (43.7%) | 30 (46.2%) | 0.313 |
| Distal | 43 (26.1%) | 23 (31.9%) | 25 (38.5%) | 0.169 |
| Severity of CAD | | | | |
| 1VD | 32 (19.4%) | 12 (17%) | 8(16.9) | 0.497 |
| 2VD | 54 (32.7%) | 22 (30.5%) | 26 (40%) | 0.609 |
| 3VD | 78 (47.3%) | 38 (52.9%) | 32 (49.2%) | 0.772 |
| Long lesion | 86 (52.4%) | 39 (54.2%) | 39 (60%) | 0.584 |
| CTO | 50 (30.3%) | 22 (31%) | 24 (37%) | 0.604 |
| Treatment | | | | |
| DES-DCB | 27 (16.3%) | 10 (14%) | 12 (18.4%) | 0.767 |
| DES alone | 130 (79%) | 55 (76.3%) | 48 (74%) | 0.713 |
| DCB alone | 8 (5%) | 7 (10%) | 5 (8%) | 0.364 |
| DES and DCB length | 23.88 ± 7.173 | 23.952 ± 7.874 | 23.443 ± 6.911 | 0.765 |
| DES and DCB diameter | 2.94 ± 0.464 | 2.935 ± 0.493 | 2.932 ± 0.492 | 0.909 |

Data are presented as $n$ (%). LM: left main; LAD: left anterior descendant; LCX: left circumflex; RCA: right coronary artery; 1VD: 1 vessel disease; 2VD: 2 vessels disease; 3VD: 3 vessels disease; CAD: coronary artery disease; CTO: chronic total occlusion; DES: drug-eluting stent; PTCA: DCB: drug-coated balloon. All statistical significances were tested using X2 test for trend.

between shorter diabetes duration and middle LAD lesion (70.9% vs. 51.4% vs. 64.6%, $P = 0.015$) compared to patients with longer duration of diabetes. Although without significance, PTCA with a drug-coated balloon was used more frequently in diabetic patients with longer diabetes duration. Table 2 presents baseline lesions characteristics and devices used during revascularization.

*3.3. Relationship between Diabetes Duration and MACEs.* We observed a significantly higher rate of myocardial infarction (7.7% vs. 0% and 0.6%, $P = 0.001$) and repeat revascularization (23.1% vs. 19.4% and 9.1%, $P = 0.03$) in patients with longer duration of diabetes compared to those with shorter duration. Adjustment for confounding risk factors was needed to clarify the independent association between diabetes duration and MACEs: MI (HR: 5.525, CI: 1.273-23.978, $P = 0.022$) and repeat revascularization (HR: 1.608, CI: 1.058-2.443, $P = 0.026$). The higher repeat revascularization rate observed in patients with longer diabetes duration was significantly related to de novo lesion than in those with shorter duration of diabetes (De novo lesion: 20% vs. 18% and 7.3%, $P = 0.009$, TLR: 3.1% vs. 1.3% and 2%, $P = 0.774$). However, all-cause mortality did not significantly differ between groups (3.1% vs. 5.6% and 0.6%, $P = 0.06$, HR: 2.403, CI: 0.464-12.436, $P = 0.293$). Table 3 and Figure 1 present an unadjusted relationship between MACEs and diabetes duration, Figure 2 and Table 4 show, respectively, and Kaplan-Meier survival curves and calculated hazard ratios with 95% confidence intervals, first unadjusted and then adjusted for confounding risk factors.

## 4. Discussion

The main finding of this study is that diabetes duration > 10 years is significantly and independently associated with major adverse cardiovascular events 12 months postrevascularization by PCI and PTCA compared to a shorter duration of diabetes. We observed a significantly higher prevalence of myocardial infarction (7.7% vs. 0% and 0.6%, $P = 0.001$) in diabetic patients with longer duration of diabetes than those

Table 3: Relationship between diabetes duration and MACEs.

| | Diabetes duration | | | $P$ for trend |
|---|---|---|---|---|
| | <5 years | 5 to 10 years | >10 years | |
| Number ($n = 302$) | 165 (54.6%) | 72 (23.8%) | 65 (21.5%) | |
| Death | 1 (0.6%) | 4 (5.6%) | 2 (3.1%) | 0.06 |
| MI | 1 (0.6%) | 0 (0%) | 5 (7.7%) | 0.001 |
| Revascularization: | 15 (9.1%) | 14 (19.4%) | 15 (23.1%) | 0.03 |
| De novo | 12 (7.3%) | 13 (18%) | 13 (20%) | 0.009 |
| TLR | 3 (2%) | 1 (1.3%) | 2 (3.1%) | 0.774 |
| TVR | 11 (7%) | 8 (11.1%) | 5 (8%) | 0.506 |

Data are presented as $n$ (%). MI: myocardial infarction; TLR: target lesion revascularization; TVR: target vessel revascularization. Variables were compared using X2 or Fisher's exact test; $P < 0.05$ is significant.

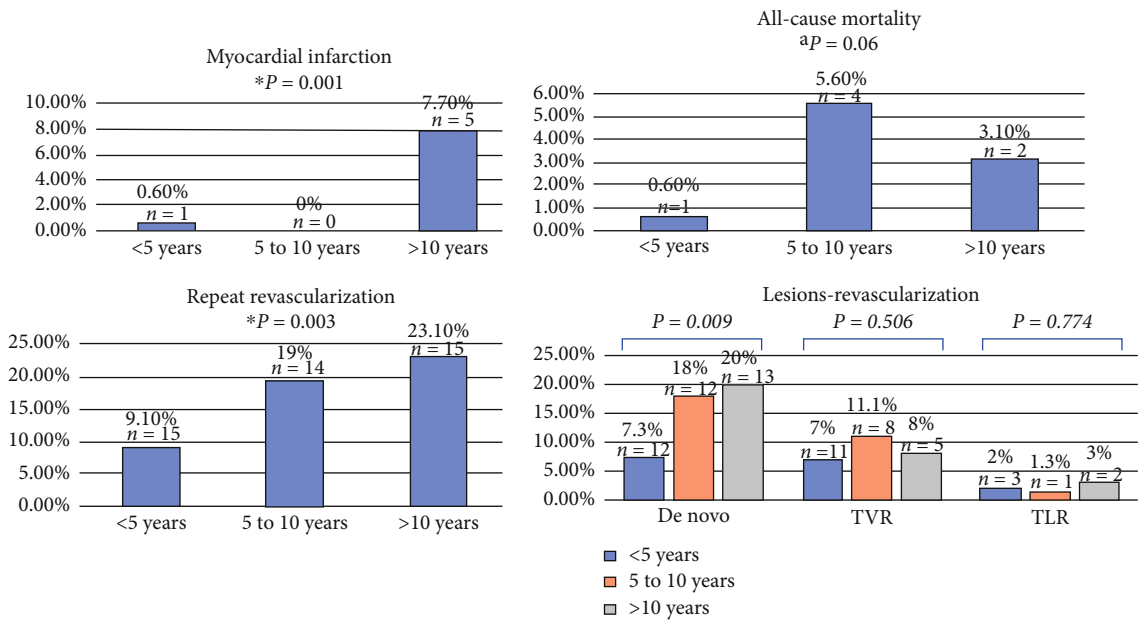


Figure 1: Relationship between diabetes duration and MACEs. Statistical significance was tested using X2 test for trend; $P < 0.05$ is significant. *Statistical significances were tested by ANCOVA with linear trend analysis adjusting confounding cardiovascular risk factors such as age, sex, smoking, systolic blood pressure, and cholesterol. [a]Statistical significance was tested using X2 test for trend. TVR: target vessel revascularization; TLR: target lesion revascularization.

with shorter duration, and the rate of repeat revascularization (23.1% vs. 19.4% and 9.1%, $P = 0.03$) whether PCI or PTCA or both was significantly higher in diabetic patients with diabetes duration > 10 years compared to those with diabetes duration < 10 years. To determine whether diabetes duration was independently associated with MACEs, adjustment for sex, age, hypertension, smoking, total cholesterol, high-density lipoprotein, low-density lipoprotein, glycated hemoglobin, and insulin therapy was conducted using multivariable Cox proportional hazards regression. After adjustment, longer diabetes duration remained an independent predictor of MI (HR: 5.525, CI: 1.273-23.978, $P = 0.022$) and repeat revascularization (HR: 1.608, CI: 1.058-2.443, $P = 0.026$).

These findings validate our hypothesis, stating that the long-term exposure to ongoing metabolic and hematologic disturbances observed in type 2 diabetes is an important factor to consider when studying the influence of type 2 diabetes in the outcomes of coronary revascularization procedures.

The incidence of a thrombotic event is higher in diabetic patients; available literature state that a mortality rate up to 80% in diabetic patients is related to a thrombotic event, myocardial infarction, or stroke [19]. As discussed previously, diabetes is associated with a widespread endothelial dysfunction resulting in pronounced plaque instability, enhanced clotting, platelet activator factors, and increased platelet aggregation in response to platelet agonists, thus, a hypercoagulability state [20, 21]. Diabetic patients exhibit impaired development of collateral coronary circulation, which is an important myocardial protective mechanism endothelium mediated in response to significant myocardial ischemia [22]. In addition, longer diabetes duration increases autonomic diabetic neuropathy involving sympathetic afferent fibers, a key component of

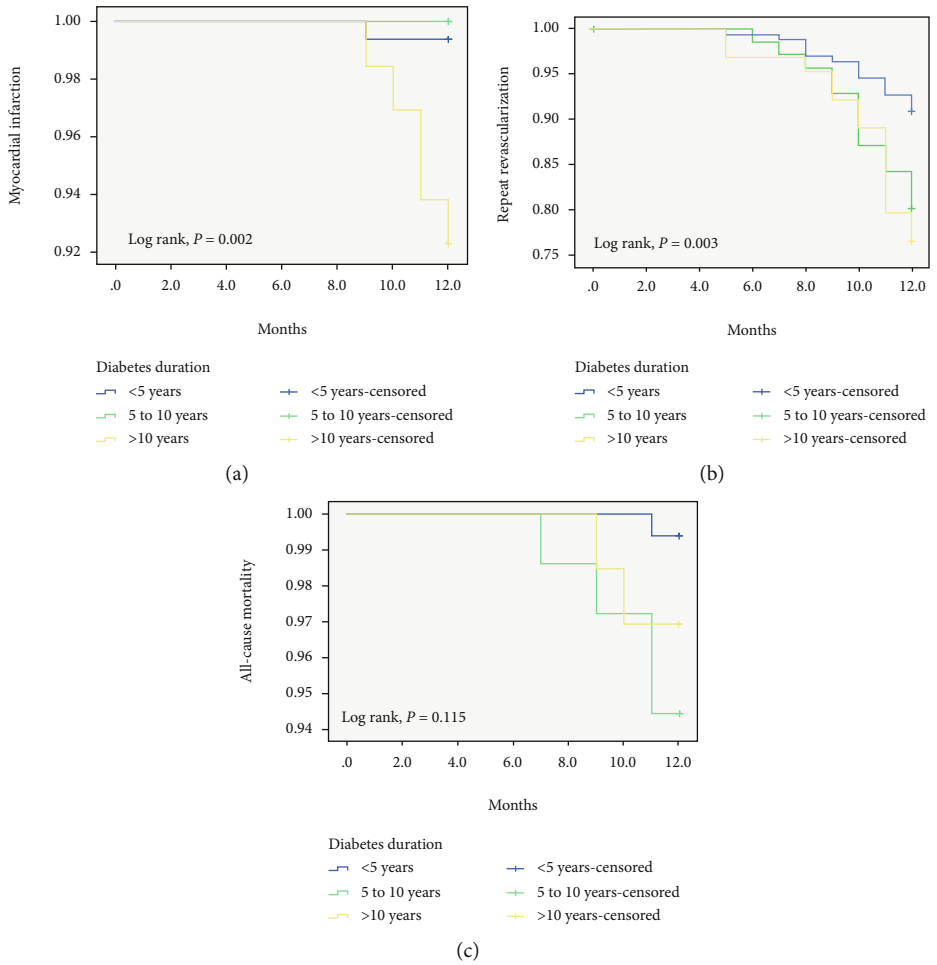


Figure 2: Kaplan-Meier survival curves for MACEs based on diabetes duration. (a) Patients with the most extended duration of diabetes have a significantly increased risk of myocardial infarction compared to those with shorter duration. (b) A significantly higher risk of repeat revascularization was observed in patients with longer duration of diabetes compared to those with shorter duration. (c) Diabetes duration was not significantly associated with an increased risk of all-cause mortality at 1 year.

Table 4: Hazard ratios for MACEs based on diabetes duration.

| MACEs—months | Number of events DD < 5 years | DD 5 to 10 years | DD > 10 years | *Unadjusted HR (95% CI) | *P* value | #Multivariable adjusted HR (95% CI) | *P* value |
|---|---|---|---|---|---|---|---|
| MI | 1 (0.6%) | 0 (0%) | 5 (7.7%) | 4.907 (1.346-17.881) | 0.016 | 5.525 (1.273-23.978) | 0.022 |
| Revascularization | 15 (9.1%) | 14 (19.4%) | 15 (23.1%) | 1.653 (1.175 - 2.325) | 0.004 | 1.608 (1.058-2.443) | 0.026 |
| All-cause mortality | 1 (0.6%) | 4 (5.6%) | 2 (3.1%) | 1.948 (0.817-4.644) | 0.132 | 2.403 (0.464-12.436) | 0.293 |

*Hazard ratios unadjusted per event according to diabetes duration. #Hazard ratios per event based on diabetes duration after adjustment for sex, age, hypertension, smoking, total cholesterol, high-density lipoprotein, low-density lipoprotein, glycated hemoglobin, and insulin requiring. DD: diabetes duration; HR: hazard ratio; CI: confidence interval; MI: myocardial infarction.

cardiac pain perception leading to the absence or impaired warning of anginal symptoms during ischemia, thus, silent infarction [23–25].

Accelerated atherosclerosis results in rapid disease progression, and restenosis accounts for the higher rates of repeat revascularization. Although restenosis after coronary stenting remains still higher in diabetic patients compared to nondiabetic, the use of drug-eluting stents and drug-coated balloons have improved the outcomes among diabetic patients and shifted the occurrence of restenosis to a longer period from the coronary intervention [26–29]. When lesions treated with DES and DCB benefit from the local effect of antiproliferative drugs eluted by the stents or the balloon, nontreated lesions not benefiting from it continue their normal progression and are more likely to cause future events in a relatively short period after coronary intervention. We found that repeat revascularization at one year was significantly related to the progression of nontreated lesions

(De novo lesions 20% vs. 18% and 7.3%, $P = 0.009$) compared to previously treated lesions (TLR 3% vs. 1.3% and 2%, $P = 0.774$). This indicates a more accelerated atherosclerosis process with faster coronary lesion progression in diabetic patients with the most extended duration of diabetes compared to those with shorter duration.

In line with the findings of our study, previous studies strongly suggested that a longer diabetes duration was associated with adverse cardiovascular events. However, less data is currently available concerning the outcomes post-PCI and PTCA. Wannamethee et al. studying the impact of diabetes on cardiovascular disease risk and all-cause mortality concluded that only diabetes associated with >10 years duration appears to be a coronary heart disease (CHD) equivalent [30]. The study on the impact of diabetes duration on the extent and severity of coronary atheroma burden by Kim et al. observed a higher rate of MACCE in patients with diabetes duration > 10 years [$P = 0.025$] [31]. Onuta et al. reported that long-term diabetes significantly increased the development of in-stent restenosis (ISR), thus, increasing the rate of repeat revascularization than in patients with short duration of diabetes [32]. However, contrary to the findings of our study and previous studies, a more recent study by Gao observed a higher incidence of MACCE in patients with diabetes at least five years (HR 2.13, 95% CI 1.34-3.39, $P < 0.01$) [33]. This conflicting result may be explained by the fact that in our study and previous studies cited earlier, diabetes duration was divided into three groups: <5 years, 5 to 10 years, and >10 years, when the study conducted by Gao et al. has diabetes patients divided only in two groups: < 5 years and at least five years. With this classification, all the patients with diabetes duration > 10 years in our study and previous studies are found in at least five years group according to their classification, so this result is not contradicting our observation.

D'Ascenzo et al. found that pharmacologic-induced regression of atherosclerotic plaque burden is associated with reduction of midterm (18 months) myocardial infarction and revascularization [34]. This finding goes hand in hand with our observation of the fact that there was significantly less repeat revascularization of DES- or DCB-treated lesions at 1 year. As previously stated, the coronary treated segment benefits both from the anti-inflammatory effect of oral medication and the in situ antiproliferative effect of drugs eluted by stent or balloon. The combined action can produce a more significant effect in reducing the plaque burden on the treated segment compared to the nontreated segment. To further elucidate our observation, there is a need for IVUS study of plaque burden in diabetic patients undergoing PCI with DES and or DCB.

It is interesting to note that diabetes duration was not significantly associated with all-cause mortality at one year (3.1% vs. 5.6% and 0.6%, $P = 0.06$). The results from previous studies remain controversial in this matter [30–32, 35]. Our finding is consistent with the Framingham Heart Study, which reported that for each 10-year increase in diabetes duration, there was no increase in the risk of all-cause mortality (1.21, 0.91–1.60; $P$ 0.19) [35]. However, in their studies, Wannamethee et al. and Kim et al. reported, respectively, that diabetes with >8 years and >10 years of duration was significantly associated with all-cause mortality (30, 31). The difference in results between studies may be attributed to differences in sample size, follow-up period, criteria of patient selection, and ethnicity. Further studies are needed to clarify this point while taking into consideration of all these parameters.

*4.1. Limitations.* The present study is a single-center study; it is uncertain whether its results may be applied to other populations. The relatively short period of follow-up and the small sample size of this study may explain the lack of statistical significance observed in some of our analyses. The accuracy of diabetes duration utilized in this study may be affected by the fact that a considerable number of our patients' diabetes duration was self-reported or obtained by medical record query, carrying the possibility of being underestimated or overestimated. It is also important to note that type-2 diabetes is frequently not diagnosed (at the accurate onset time) until the complications appear and that in some cases it is hard to differentiate type-1 diabetes from type-2 in the acute onset setting. In the future, there is a need for multicenter studies with a larger sample size and a more extended period of follow-up to confirm the results obtained.

## 5. Conclusion

Longer diabetes duration (>10 years) is a significant independent predictor of major adverse cardiovascular events at one year after coronary intervention using DES and DCB. This would suggest that the decision-making process among diabetic patients undergoing coronary intervention should always be individualized, and diabetes duration can serve as an important parameter for risk stratification among diabetic patients. There is no significant association between diabetes duration and all-cause mortality at one year following PCI or PTCA. The observed higher rate of repeat revascularization in diabetic patients during a relatively short period following coronary intervention with DES and or DCB is significantly attributed to new lesion progression rather than restenosis, indicating the more accelerated atherosclerosis processes with faster lesion progression in diabetic patients with the most extended duration.

## Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Additional Points

*To Be Noted.* This is to inform that the earlier version of this study abstract was accepted to be presented as conference abstract, in the 26th International Student Congress Of (bio) Medical Sciences, held in Groningen at the University Medical Center Groningen, the Netherlands, from the 3$^{rd}$ to 7$^{th}$ of June 2019. However, it is important to note that for personal reasons, I was not able to join the conference;

therefore, this abstract was not presented at that conference. This information is true and can be verified.

## Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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