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One year clinical outcomes in patients with insulin-treated diabetes mellitus and non-insulin-treated diabetes mellitus compared to non-diabetics after deployment of the bio-engineered COMBO stent☆,☆☆

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ABSTRACT

Background: The COMBO stent is a novel sirolimus-eluting stent with a luminal anti-CD34+ antibody layer to promote vessel healing. No data is currently available on clinical outcomes after treatment with this novel bio-engineered device in diabetic patients. We evaluate clinical outcomes at twelve months after COMBO stent placement in patients without diabetes mellitus (non-DM), patients with non-insulin-treated diabetes mellitus (nITDM) and patients with insulin-treated diabetes mellitus (ITDM).

Methods: This study is a pre-specified subgroup analysis of the 1000 patient all-comers REMEDEE Registry. The primary endpoint is target lesion failure (TLF), which is a combined endpoint consisting of cardiac death, target vessel-myocardial infarction (tv-MI) and target lesion revascularization (TLR) at twelve months follow-up. Kaplan Meier method is used with log rank to compare outcomes between groups.

Results: This subgroup analysis includes 807 non-DM, 117 nITDM and 67 ITDM. Kaplan–Meier estimates for TLF at twelve months are 4.4% in non-DM, 6.8% in nITDM and 20.3% in ITDM, $p < 0.001$ (non-DM vs nITDM $p = 0.244$, non-DM vs ITDM $p < 0.001$).

Conclusions: This study gives the first insight into the impact of insulin-treated diabetes mellitus on clinical outcome of patients treated with the novel COMBO stent. At one year after COMBO stent placement significantly higher rates of target lesion failure are seen in patients with ITDM compared to patients with nITDM and patients without DM.

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1. Introduction

The prevalence of patient with diabetes mellitus (DM) is rising globally [1]. Patients with DM are at increased risk of atherosclerosis [2]. In patients with DM and coronary artery disease, clinical outcomes after percutaneous coronary intervention (PCI) improved with drug-eluting stent (DES) treatment compared to bare metal stenting [3–5]. However, numerous studies report on still existing less favorable outcome in patients with DM, compared to non-DM patients after DES placement [6–9]. Moreover, prognosis is known to be worse in insulin treated DM patients compared with non-insulin treated [10,11].

The novel COMBO stent has an anti-CD34+ antibody layer to promote vessel healing and a biodegradable abluminal polymer layer eluting sirolimus. The bio-engineered luminal layer attracts circulating endothelial progenitor cells (EPCs). These EPCs differentiate to endothelial cells and provide early endothelialization [12,13], which might facilitate safe shortening of dual antiplatelet therapy. The first clinical results with the COMBO stent from the REMEDEE Registry show high procedural success, low rates of cardiac death, target vessel myocardial infarction (tv-MI), and target lesion revascularization (TLR). Remarkably, no stent thrombosis was seen after nine days post stent placement [14].

We aim to provide more insight into the clinical outcomes twelve months after COMBO stent treatment in non-DM, nITDM and ITDM patients, as the dual therapy technology could possibly improve clinical outcomes in diabetic patients. No data is currently available on patients with DM treated with the COMBO stent, therefore this analyses will help establish the role of COMBO technology in diabetic patients undergoing PCI.

2. Methods

2.1. Study oversight and patient population

The REMEDEE Registry study design has been previously described [14]. In short, a total of 1000 patients in whom treatment with a COMBO stent in the setting of routine clinical care was attempted were enrolled in nine European sites between June 2013 and March 2014. Duration of dual antiplatelet therapy was recommended according to the European Society of Cardiology guidelines. The registry is an investigator-initiated, multicentre, prospective study and represents a true all-comers patient population. All patients provided written informed consent for data collection and the registry protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee. Follow-up was obtained through telephone contact or scheduled outpatient clinic visit at 30 days, 180 days, and one year. Hospital records were obtained and reviewed to complete event source documentation. An independent clinical event committee adjudicated all clinical events. The REMEDEE Registry is registered at ClinicalTrials.gov with identifier number NCT01874002.

2.2. Definitions

DM was defined as a prior established diagnosis of DM and/or the use of medication to control blood glucose. Patients on insulin therapy were considered insulin-treated DM (ITDM) patients, patients taking oral medication and/or dietary measures only were considered as non-insulin treated DM patients (nITDM). Information on diabetes status and medication was entered into the electronic case report form by the local investigator. Blood samples were not collected routinely as part of the registry.

Definition of the primary outcome, target lesion failure (TLF), is the composite of cardiac death, non-fatal myocardial infarction (MI) (unless documented to arise from the non-treated coronary artery) or target lesion revascularization (TLR). TLR was defined as any repeat revascularization by percutaneous intervention of the treated lesion or CABG of the target vessel.

The third universal definition of myocardial infarction was used to define MI [15]. However, assessment of routine peri-procedural cardiac biomarkers was not mandated by the registry's protocol. Stent thrombosis was defined according to the Academic Research Consortium (ARC) criteria [16].

2.3. Statistical analysis

Categorical data are shown with counts and percentages, continuous variables are in mean ± standard deviation (SD), unless otherwise mentioned. Baseline characteristics were compared with one-way ANOVA or chi-squared test. For time-to-event data comparing non-DM, nITDM and ITDM patients, Kaplan–Meier estimates at the indicated time points are presented and compared using the log-rank test. Follow-up was censored at the last known date of follow-up, or at 12 months, whichever came first. All primary and secondary endpoints were evaluated in the unselected patient population, which consisted of all patients who were enrolled after signing an informed consent and in whom placement of a COMBO stent was attempted and in whom diabetes status was known. p-Values < 0.05 were considered statistically significant. All descriptive statistical analyses were performed using SPSS software package (version 23.0, SPSS Inc., Chicago, IL, USA).

Nine other risk factors were evaluated in the patient population: acute coronary syndromes (ACS), female sex, advanced age (≥65 years), smoking, hypertension, hypercholesterolemia, chronic renal failure, peripheral vascular disease and previous stroke. Univariate analysis was done for each risk factor with Kaplan–Meier estimates and log-rank tests. Backward multiple regression analysis was done with Cox regression analysis.

Table 1
Baseline characteristics for nondiabetic patients, non-insulin treated diabetics and insulin treated diabetics.

	Nondiabetic patients N = 807	Non-insulin treated diabetic patients N = 117	Insulin treated diabetic patients N = 64	p=
Age, y (SD)	64.8 ± 11.4	68.6 ± 9.4	64.8 ± 9.4	0.004
Sex, male n (%)	604 (74.8)	86 (72.9)	43 (67.2)	0.376
Body mass index, kg/m^2	23.8 ± 3.8	25.7 ± 4.2	26.6 ± 5.2	<0.001
History of hypertension	434 (53.8)	94 (79.7)	51 (79.7)	<0.001
History of hypercholesterolemia	429 (53.2)	80 (67.8)	51 (79.7)	0.031
Family history of CAD	373 (46.2)	46 (29.0)	33 (51.6)	0.563
Chronic renal failure	36 (4.5)	15 (12.7)	10 (15.6)	<0.001
Congestive heart failure (known LVEF <30%)	20 (2.5)	6 (5.1)	6 (9.4)	0.032
Current smoker	207 (25.7)	20 (16.9)	12 (18.8)	0.189
Prior myocardial infarction	191 (23.7)	38 (32.2)	23 (35.9)	0.064
Prior percutaneous intervention	231 (28.6)	42 (35.6)	26 (40.6)	0.165
Prior CABG	51 (6.3)	11 (9.3)	6 (9.4)	0.553
Indication for PCI				
Emergency PCI	249 (30.9)	33 (28.2)	13 (20.3)	0.033
STEMI	*150 (60.2)*	*16 (48.5)*	*5 (38.5)*	
NSTE-ACS	*69 (27.7)*	*7 (21.1)*	*6 (46.2)*	
Unstable angina	*30 (12.0)*	*10 (30.3)*	*2 (15.4)*	
Elective PCI	556 (69.1)	84 (71.8)	41 (79.7)	0.056
Stabilized STEMI	*20 (3.6)*	*1 (1.2)*	*0 (0.0)*	
Stabilized NSTE-ACS	*87 (15.6)*	*8 (9.5)*	*11 (21.6)*	
Stabilized unstable angina	*55 (9.9)*	*9 (10.7)*	*2 (3.9)*	
Stable angina and/or documented ischemia	*239 (42.9)*	*43 (51.2)*	*20 (23.5)*	
Angiographic driven	*134 (24.1)*	*16 (8.3)*	*12 (23.5)*	
Other	*22 (3.9)*	*7 (8.3)*	*6 (11.8)*	

Values are mean ± SD or n (valid %). CAD: coronary artery disease. LVEF: left ventricular ejection fraction. CABG: coronary artery bypass graft. PCI: percutaneous coronary intervention. STEMI: ST elevation myocardial infarction. NSTEMI: non ST elevation myocardial infarction.

3. Results

3.1. Baseline characteristics

From the 1000 patient REMEDEE Registry, 807 patients were non-diabetic, 117 patients were nITDM and 67 patients were ITDM. For nine patients diabetes mellitus status was unknown and therefore these patients were not included in this analysis. Baseline characteristics are shown in Table 1. Mean age was higher in nITDM-patients 68.6 ± 9.4 years versus 64.8 ± 11.4 years in non-DM and 64.8 ± 9.4 years in ITDM. The prevalence of women was highest in ITDM (32.8%) compared to and 27.1% in nITDM and 25.2% in non-DM. ITDM had highest BMI (26.6 ± 5.2, versus 23.8 ± 3.8 in non-DM and 25.7 ± 4.2 in nITDM). A medical history of hypertension, hypercholesterolemia, prior myocardial infarction, prior PCI and prior CABG were all more frequent in DM patients, both in ITDM and nITDM. The amount of current smokers was highest in non-diabetics. Emergency PCI as indication for PCI was higher in non-DM patients (30.9% versus 28.2% in nITDM and 20.3% in ITDM, p = 0.033).

3.2. Angiographic characteristics

A total of 1011 lesions were treated in non-diabetic subjects, 149 lesions in nITDM and 81 lesions in ITDM. Lesion and procedural characteristics are presented in Table 2. Pre-procedure reference vessel diameter did not differ between all groups (3.2 ± 0.5 mm). There were no differences in the location of lesion, AHA/ACC lesion classification or mean stent length. 56.9% of lesions of DM patients were AHA/ACC lesion type B2 or C, compared to 58.0% in non-DM patients, lesion length was 20.9 ± 9.4 in DM patients versus 21.6 ± 10.8 mm in non-DM patients. Similar rates of device success (98.2% in nITDM, 98.4% in ITDM and 97.9% in non-DM) and procedural success (97.4% in nITDM, 98.4% in ITDM and 98.0% in non-DM) were observed.

3.3. Clinical outcomes

In Fig. 1 the Kaplan Meier estimates are shown for the primary endpoint TLF. TLF at twelve months was 4.4% in non-DM, 6.8% in nITDM and 20.3% in ITDM (p < 0.001). This difference is attributed to higher rates of the individual clinical endpoints in ITDM. TLR in non-DM-patients is 3.5%, in nITDM-patients 4.3%, and in ITDM-patients 14.1% with p < 0.001. Cardiac death was 1.0%, 3.4% and 7.8%, p < 0.001. Target vessel MI occurred in 0.4% in non-DM, 1.7% in nITDM and 3.1% in ITDM, p = 0.015. All endpoints are presented in Table 3. Kaplan Meier plots are shown in Fig. 2a–c. Difference in TLF rate between nITDM and non-DM is not significant, with a p value of 0.244. Comparison of TLF between IDTM and non-DM shows a highly significant difference with p < 0.001. Cardiac death is the only endpoint which is significantly higher in the nITDM compared to non-DM. All endpoints are significantly higher in the ITDM group compared with the non-DM group.

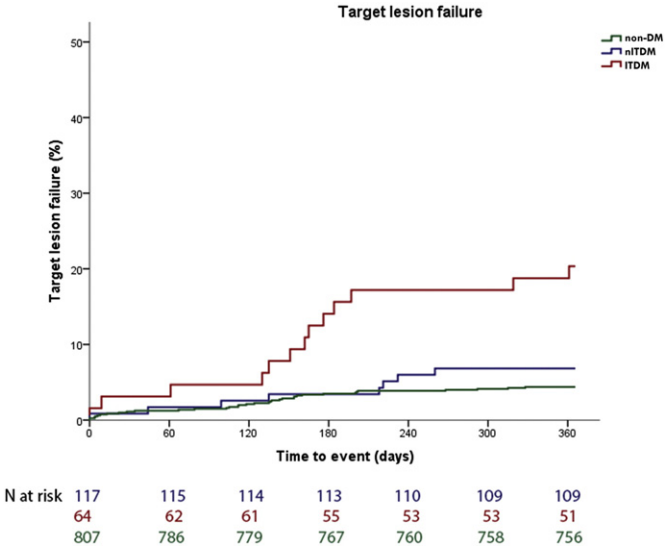

Fig. 1. Comparison of target lesion failure in non-diabetic, non-insulin treated DM and insulin treated DM by cumulative event rate by Kaplan Meier method.

3.4. Multiple regression analysis

Acute coronary syndromes (ACS), female sex, advanced age (≥65 years), smoking, hypertension, hypercholesterolemia, chronic renal failure (CKD), peripheral vascular disease (PVD) and previous stroke were evaluated in the patient population. Univariate analyses showed higher TLF in patients with CKD (13.1% versus 5.3%, p = 0.010) compared to patients without CKD. ACS, smoking, CKD, hypertension and DM had the strongest association with backward multiple regression analysis. DM, CKD and hypertension were predictors, DM (HR = 2.96, 95% CI: 1.58–5.53 p = 0.001), CKD (HR = 2.91, 95% CI: 1.29–6.60 p = 0.010) and hypertension (HR = 0.51, 95% CI: 0.27–0.95 p = 0.036).

Table 2
Lesion and procedural characteristics.

	Nondiabetic patients N = 1011	Non-insulin treated diabetic patients N = 149	Insulin treated diabetic patients N = 81	p=
Pre-procedure reference vessel diameter, mm	3.2 ± 0.5	3.2 ± 0.5	3.2 ± 0.5	0.953
Stent length, mm	21.6 ± 10.8	20.7 ± 9.9	21.5 ± 8.5	0.733
Location of lesion				
RCA	288 (28.5)	48 (32.2)	22 (27.2)	0.163
LAD	463 (45.8)	52 (34.9)	31 (38.3)	0.046
LCX	227 (22.5)	41 (27.5)	25 (30.9)	0.132
LMCA	17 (1.7)	2 (1.3)	1 (1.2)	0.971
Graft	16 (1.6)	6 (4.0)	2 (2.5)	0.229
AHA/ACC lesion classification				
A	164 (17.0)	22 (15.7)	10 (12.3)	0.693
B1	239 (24.8)	38 (27.1)	23 (28.4)	0.112
B2	357 (37.0)	52 (37.1)	28 (34.6)	0.471
C	205 (21.2)	28 (20.0)	20 (24.7)	0.619
Device success	759 (97.9)	112 (98.2)	62 (98.4)	0.983
Procedural success	788 (98.0)	114 (97.4)	62 (98.4)	0.960

Values are N (valid %) and mean ± SD. RCA: right coronary artery, LAD: left anterior descending artery, LCx: left circumflex artery, and LMCA: left main coronary artery.

Table 3
Primary endpoint and clinical outcomes at one-year follow-up according to non-diabetics, non-insulin treated diabetics and insulin treated diabetic patients.

	Non-DM N = 807	nITDM N = 117	ITDM N = 64	Between all groups p=	Non-DM vs nITDM p=	Non-DM vs ITDM p=
Primary endpoint: TLF	35 (4.4)	8 (6.8)	13 (20.3)	<0.001	0.244	<0.001
Cardiac death	8 (1.0)	4 (3.4)	5 (7.8)	<0.001	0.032	<0.001
Target vessel MI	3 (0.4)	2 (1.7)	2 (3.1)	0.015	0.067	0.005
TLR	28 (3.5)	5 (4.3)	9 (14.1)	<0.001	0.669	<0.001
TVR	32 (4.0)	6 (5.2)	9 (14.4)	0.001	0.568	<0.001
TVF	39 (4.9)	9 (7.7)	13 (20.3)	<0.001	0.209	<0.001
Stent thrombosis	3 (0.4)	1 (0.9)	2 (3.1)	0.023	0.457	0.005

Values are in N (%). Non-DM: patients without diabetes mellitus. nITDM: non-insulin treated diabetic patients. ITDM: diabetic patients with insulin treatment. TLF: target lesion failure: a composite of cardiac death, myocardial infarction (MI) (unless documented to arise from the non-treated coronary artery), and target lesion revascularisation (TLR). *Definite and probable stent thrombosis.

4. Discussion

4.1. Main finding

We present the first clinical results of diabetic patients treated with the COMBO stent in the REMEDEE Registry. Our main findings are that in patients treated with a sirolimus eluting bio-engineered EPC capturing stent: 1) high rates of TLF remain in patients with ITDM (20.3%) compared to patients with nITDM (6.8%) and patients without DM (4.4%), 2) All individual secondary endpoints are frequently observed in ITDM, and 3) there is a need for improvement of clinical outcomes after PCI with stenting in patients with ITDM.

4.2. Comparison with previous DES studies in diabetics

Comparing results between studies evaluating clinical outcomes in diabetics is hampered by differences in baseline characteristics, including the number of insulin-dependent DM patients and patient comorbidities, and trial design (e.g. availability of angiographic follow-up or the use of functional assessment). The REMEDEE Registry is a true all-comers registry, with an overall high risk of TLF patient population, but with lack of follow-up re-angiography. SORT OUT IV [17] compared randomized patients with either everolimus-eluting stent (EES) or sirolimus-eluting stent at 18 months follow-up, MACE (composite of cardiac death, MI, definite ST and TVR) was 10.3% in DM patients treated with EES and 15.8% in DM patients treated with SES, compared to 6.6% and 6.3% in non-DM patients. A pooled analyses of the ISAR-TEST3, ISAR-TEST4 and LEADERS trials in diabetics [18] showed combined cardiac death, MI or TLR rate of 15.3% in biodegradable polymer drug-eluting stents (BP-DES) and 15.6% in durable polymer sirolimus-eluting stents (DP-SES) at 12 months follow-up. Pooled patient-level data from the RESOLUTE Global Clinical Program showed lower rate of TVF in DM patients treated with zotarolimus-eluting stent at 2 year follow-up (12.1%), but still significantly higher than the 8.9% in patients without DM (p = 0.01) [10]. The TUXEDO trial compared outcomes after EES and paclitaxel-eluting stents (PES) in Indian diabetic patients. The non-inferiority of PES compared to EES was not met, but the study showed very low rates of TVR at one year follow-up (5.6% versus 2.9%) [19]. The secondary analysis of the same cohort comparing the insulin versus the non-insulin requiring patients evaluated the influence of the insulin treated patients. In an unadjusted model insulin treated patients had a significant increase of cardiovascular event rate, but after propensity score adjustment this increased risk was not observed [20]. A systematic review and meta-analysis of 21,759 insulin treated diabetics and 15,509 non-insulin treated DM patients reports the association of significant higher short and long-term adverse cardiovascular outcomes after PCI in DM patients with insulin treatment compared with non-insulin treated DM patients [21].

4.3. Prognostic implications of diabetes mellitus

A recent patient-level pooled analysis of more than 6000 patients comparing patients with and without DM showed that the presence of DM was the driver of high TLR and MACE and not the severity of the coronary artery disease [22]. The FREEDOM trial showed the superiority of CABG to PCI for patients with multi-vessel disease and DM in reducing rates of death and MI, with a higher rate of stroke [23]. Moreover, long term clinical outcomes in the subgroup analyses of this trial showed a significant higher death/stroke/MI rate in insulin treated DM patients compared to non-insulin DM patients in both patients treated with

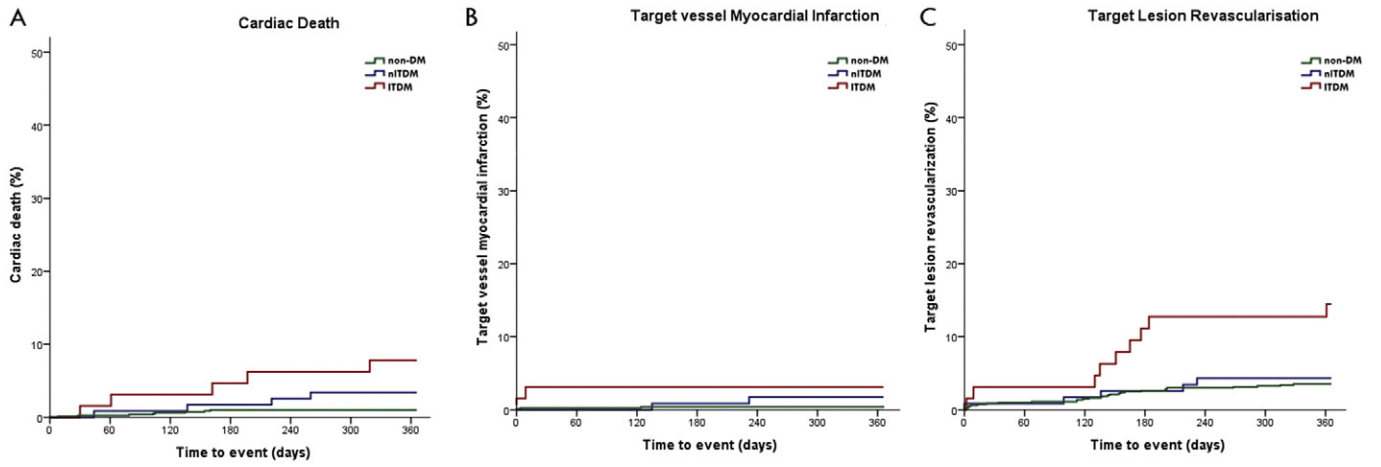

Fig. 2. Comparison of cardiac death, vessel myocardial infarction, target vessel revascularisation and target lesion revascularisation by Kaplan Meier method in non-diabetic, non-insulin treated DM and insulin treated DM. a: Time to event curves for cardiac death b: Time to event curves for target vessel myocardial infarction c: Time to event curves for target lesion revascularisation.

PCI and CABG. They report a 1-year repeat revascularization rate of 16.1% in the insulin treated DM PCI-arm and 4.9% in the insulin treated DM CABG-arm, compared to 10.8% in non-insulin treated DM PCI-arm and 4.7% in non-insulin treated CABG-arm [24].

4.4. Future perspectives

The REMEDEE Registry pre-specified subgroup analyses confirms that with new generation DES the presence of ITDM is associated with high TLF, compared to nITDM and non-DM patients. We conclude that current DES technology is not sufficient to guarantee the same clinical outcome for patients with ITDM compared to patients without DM. New treatment strategies are being developed to alter this clinical equipoise, first results with Amphilimus Eluting Stent (AES), Cre8 (Alvimedica, Turkey) specifically designed for DM patients are promising [25], but larger randomized controlled trials are needed.

The ongoing randomized HARMONEE trial (enrolment completed: NCT02073565), will allow comparison of clinical outcomes with COMBO stent to the EES, Xience stent (Abbott Vascular, Japan), also in diabetic patients.

4.5. Limitations

Limitation of the study remains the registry design, which limits us to compare these results to other DES treatment strategies. Also, this subgroup analyses, although pre-specified, is not designed or powered to evaluate clinical outcomes. Another limitation is that diabetic status is investigator reported, no differentiation was made into DM type I and DM type II, and no laboratory test were measured e.g. hemoglobin A1C/no data on glycemic control were available.

However, this is the first study to report on clinical outcomes after placement of the novel COMBO stent comparing patients without DM, patients with nITDM and patients with ITDM. Novel stent technologies must be evaluated in all-comers patient cohorts, especially in high risk patient groups, to determine the real clinical performance.

Our results also underline the importance of the current problem, in a world where diabetes mellitus is a fast growing epidemic, that better treatment options for ITDM patients presenting at the catheterization laboratory for PCI are needed.

5. Conclusion

This is the first study to evaluate clinical outcomes of diabetic patients (ITDM and nITDM) treated with the COMBO stent. At one year after COMBO stent placement significantly higher rates of target lesion failure are seen in patients with ITDM compared to patients with nITDM and patients without DM. These results emphasize that new technologies need to be explored to serve this high risk patient group.

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References

[1] G. Danaei, M.M. Finucane, Y. Lu, G.M. Singh, M.J. Cowan, C.J. Paciorek, et al., National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2·7 million participants, Lancet 378 (9785) (2011) 31–40.
[2] J.A. Beckman, M.A. Creager, P. Libby, Diabetes and atherosclerosis: epidemiology, pathophysiology, and management, JAMA 287 (19) (2002) 2570–2581.
[3] A.J. Kirtane, A. Gupta, S. Iyengar, J.W. Moses, M.B. Leon, R. Applegate, et al., Safety and efficacy of drug-eluting and bare metal stents comprehensive meta-analysis of randomized trials and observational studies, Circulation 119 (2009) 3198–3206.
[4] U. Stenestrand, S.K. James, J. Lindback, O. Frobert, J. Carlsson, F. Schertsen, et al., Safety and efficacy of drug-eluting vs. bare metal stents in patients with diabetes mellitus: long- term follow-up in the Swedish coronary angiography and angioplasty registry (SCAAR), Eur. Heart J. 31 (2010) 177–186.
[5] P. Jimenez-Quevedo, L. Hernando, J. Antoni, A. Iniguez, A. SanRoman, F. Alfonso, et al., Sirolimus-eluting stent versus bare metal stent in diabetic patients: the final five-year follow-up of the DIABETES trial, EuroIntervention 9 (3) (2013) 328–335.
[6] C. Stettler, S. Allemann, S. Wandel, A. Kastrati, M.C. Morice, M.E. Pfisterer, et al., Drug eluting and bare metal stents in people with and without diabetes: collaborative network meta-analysis, BMJ 337 (a) (2008) 1331.
[7] O. Fröbert, B. Lagerqvist, J. Carlsson, J. Lindbäck, U. Stenestrand, S.K. James, Differences in restenosis rate with different drug-eluting stents in patients with and without diabetes, JACC 53 (18) (2009) 1660–1667 (American College of Cardiology Foundation).
[8] S. Kang, K.H. Park, H. Ahn, K.W. Park, Y.J. Hong, B. Koo, et al., Everolimus-eluting versus sirolimus-eluting coronary stents in patients with and without diabetes mellitus, EuroIntervention 10 (2014) 74–83.
[9] S.M. Donahoe, G.C. Stewart, C.H. Mccabe, S. Mohanavelu, S.A. Murphy, C.P. Cannon, et al., Diabetes and mortality following acute coronary syndromes, JAMA 298 (7) (2007) 765–775.
[10] S. Silber, P.W. Serruys, M.B. Leon, I.T. Meredith, S. Windecker, F.J. Neumann, et al., Clinical outcome of patients with and without diabetes mellitus after percutaneous coronary intervention with the resolute zotarolimus-eluting stent: 2-year results from the prospectively pooled analysis of the international global RESOLUTE program, JACC Cardiovasc. Interv. 6 (4) (2013) 357–368.
[11] L.P. Hoebers, B.E. Claessen, P. Woudstra, J.H. DeVries, J.J. Wykrzykowska, M.M. Vis, et al., Long-term mortality after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction in patients with insulin-treated versus non-insulin-treated diabetes mellitus, EuroIntervention 10 (1) (2014) 90–96.
[12] J.F. Granada, S. Inami, M.S. Aboodi, A. Tellez, K. Milewski, D. Wallace-Bradley, et al., Development of a novel prohealing stent designed to deliver sirolimus from a biodegradable abluminal matrix, Circ. Cardiovasc. Interv. 3 (3) (2010) 257–266.
[13] K. Larsen, C. Cheng, D. Tempel, S. Parker, S. Yazdani, W.K. Den Dekker, et al., Capture of circulatory endothelial progenitor cells and accelerated re-endothelialization of a bio-engineered stent in human ex vivo shunt and rabbit denudation model, Eur. Heart J. 33 (1) (2012) 120–128.
[14] P. Woudstra, D.N. Kalkman, P. den Heijer, I.B.A. Menown, A. Erglis, H. Suryapranata, et al., 1-year results of the REMEDEE registry, JACC Cardiovasc. Interv. 9 (11) (2016) 1127–1134 (Internet). (Available from:) http://linkinghub.elsevier.com/retrieve/pii/S193687981630142X.
[15] K. Thygesen, J.S. Alpert, A.S. Jaffe, M.L. Simoons, B.R. Chaitman, K.T. Denmark, et al., Third universal definition of myocardial infarction, J. Am. Coll. Cardiol. 60 (16) (2012).
[16] D.E. Cutlip, S. Windecker, R. Mehran, A. Boam, D.J. Cohen, G.-A. van Es, et al., Clinical end points in coronary stent trials: a case for standardized definitions, Circulation 115 (17) (2007) 2344–2351.
[17] L.O. Jensen, P. Thayssen, A. Junker, M. Maeng, H.H. Tilsted, A. Kaltoft, et al., Comparison of outcomes in patients with versus without diabetes mellitus after revascularization with everolimus- and sirolimus-eluting stents (from the SORT OUT IV trial), Am. J. Cardiol. 110 (11) (2012) 1585–1591.
[18] A. De Waha, G.G. Stefanini, L.A. King, R.A. Byrne, P.W. Serruys, S. Kufner, et al., Long-term outcomes of biodegradable polymer versus durable polymer drug-eluting stents in patients with diabetes a pooled analysis of individual patient data from 3 randomized trials, Int. J. Cardiol. 168 (6) (2013) 5162–5166.
[19] U. Kaul, S. Bangalore, A. Seth, P. Arambam, R.K. Abhaychand, T.M. Patel, et al., Paclitaxel-eluting versus everolimus-eluting coronary stents in diabetes, N. Engl. J. Med. 373 (18) (2015) 1709–1719.
[20] S. Bangalore, A. Bhagwat, B. Pinto, P.K. Goel, P. Jagtap, S. Sathe, et al., Percutaneous coronary intervention in patients with insulin-treated and non–insulin-treated diabetes mellitus, JAMA Cardiol. 10 (016) (2016) 1–8.
[21] P.K. Bundhun, N.L. Chen, M-H., Adverse cardiovascular outcomes between insulin-treated and non-insulin treated diabetic patients after percutaneous coronary intervention: a systematic review and meta-analysis, Cardiovasc. Diabetol. 14 (135) (2015) 1–11.
[22] K. Koskinas, G. Siontis, R. Piccolo, A. Franzone, A. Haynes, J. Rat-wirtzler, et al., 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. 9 (2) (2016).
[23] M.E. Farkouh, M. Domanski, L.A. Sleeper, F.S. Siami, G. Dangas, Strategies for multivessel revascularization in patients with diabetes, N. Engl. J. Med. 367 (25) (2012) 2375–2384.
[24] G.D. Dangas, M.E. Farkouh, L.A. Sleeper, M. Yang, M.M. Schoos, C. Macaya, et al., Long-term outcome of PCI versus CABG in insulin and non-insulin-treated diabetic patients: results from the FREEDOM trial, J. Am. Coll. Cardiol. 64 (12) (2014) 1189–1197.
[25] R. Romaguera, J.A. Gomez-Hospital, J. Gomez-Lara, S. Brugaletta, E. Pinar, P. Jimenez-Quevedo, et al., A randomized comparison of reservoir-based polymer-free amphilimus-eluting stents versus everolimus-eluting stents with durable polymer in patients with diabetes mellitus the RESERVOIR clinical trial, JACC Cardiovasc. Interv. 9 (1) (2016) 42–50.