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A high-volume study on the impact of diabetes mellitus on clinical outcomes after surgical and percutaneous cardiac interventions

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Abstract

Background Type I and type II diabetes mellitus (DM) patients have a higher prevalence of cardiovascular diseases, as well as a higher mortality risk of cardiovascular diseases and interventions. This study provides an update on the impact of DM on clinical outcomes, including mortality, complications and reinterventions, using data on percutaneous and surgical cardiac interventions in the Netherlands.

Methods This is a retrospective, nearby nationwide study using real-world observational data registered by the Netherlands Heart Registration (NHR) between 2015 and 2020. Patients treated for combined or isolated coronary artery disease (CAD) and aortic valve disease (AVD) were studied. Bivariate analyses and multivariate logistic regression models were used to evaluate the association between DM and clinical outcomes both unadjusted and adjusted for baseline characteristics.

Results 241,360 patients underwent the following interventions; percutaneous coronary intervention ($N=177,556$), coronary artery bypass grafting ($N=39,069$), transcatheter aortic valve implantation ($N=11,819$), aortic valve replacement ($N=8,028$) and combined CABG and AVR ($N=4,888$). The incidence of DM type I and II was 21.1%, 26.7%, 17.8%, 27.6% and 27% respectively. For all procedures, there are statistically significant differences between patients living with and without diabetes, adjusted for baseline characteristics, at the expense of patients with diabetes for 30-days mortality after PCI (OR = 1.68; $p < .001$); 120-days mortality after CABG (OR = 1.35; $p < .001$), AVR (OR = 1.5; $p < .03$) and CABG + AVR (OR = 1.42; $p = .02$); and 1-year mortality after CABG (OR = 1.43; $p < .001$), TAVI (OR = 1.21; $p = .01$) and PCI (OR = 1.68; $p < .001$).

Conclusion Patients with DM remain to have unfavourable outcomes compared to nondiabetic patients which calls for a critical reappraisal of existing care pathways aimed at diabetic patients within the cardiovascular field.

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Keywords Cardiovascular disease, Endocrinology, Percutaneous coronary intervention, Coronary artery bypass grafting, Aortic valve replacement, Transcatheter aortic valve implantation

Introduction

Over the years, the prevalence of diabetes mellitus (DM) is increasing as a result of ageing and lifestyle habits [1–6]. Both type I and II DM are associated with amongst others cardiovascular diseases (CVD) [1, 2, 7, 8]. Due to these co-morbidities, people with diabetes consume more care which is associated with higher healthcare costs compared to people without diabetes [3, 9, 10].

Cardiovascular disease is a common cause of death for people with diabetes [2, 9, 11, 12]. Earlier research showed that people with diabetes undergoing surgical and percutaneous cardiac procedures, compared to people without diabetes, are at higher risk of mortality, reinterventions, and complications like deep sternal wound infections (DSWI), stroke and kidney failure [3, 8, 13–15]. As the disease burden and healthcare consumption will further rise in the coming years due to the doubling of diabetes prevalence, care for patients with diabetes constitutes an ongoing concern [9, 11, 16]. Therefore, healthcare protocols, clinical pathways and drug treatment options in both primary and secondary (cardiac) care are continuously adjusted for patients with diabetes to optimize health outcomes [16, 17].

However, we lack recent, real-world data to evaluate outcomes in patients with diabetes. This study aims to assess the impact of diabetes mellitus on present-day clinical outcomes in patients undergoing surgical and percutaneous cardiac procedures in the Netherlands.

Method

Study design

This is a retrospective study using observational, real-world data from all hospitals participating in the voluntary public reporting program facilitated by the Netherlands Heart Registration (NHR) [18, 19]. This includes 14 out of 16 Dutch heart centres regarding CABG, TAVI, AVR and CABG+AVR, 21 out of 30 centres that perform PCI procedures (of which 14 do not have cardiothoracic surgery onsite) and 30 out of 30 centres that perform PCI after 2017. The NHR is a national mandatory quality registration in which hospitals register a standard set of baseline, procedural and outcome data of all invasive cardiac procedures. The NHR annually publishes outcome data of participating hospitals to improve the quality, safety and transparency of care in a voluntary reporting program [18, 19]. In the voluntary public reporting program, each hospital is responsible for the active follow-up per patient and each hospital must actively check for reinterventions and outcomes after discharge. The registered data and the data collection

process are checked by the NHR, amongst others in annual audits [20].

Inclusion criteria

The study population consisted of all patients with CVD, treated with an invasive cardiac intervention for coronary artery disease (CAD), aortic valve disease (AVD), or combined CAD and AVD between January 1st 2015 and December 31st 2020. Patients undergoing the following cardiac procedures are included: percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), aortic valve replacement (AVR), transcatheter aortic valve implantation (TAVI) and combined CABG and AVR.

Per invasive cardiac intervention, only the first CABG, AVR, TAVI or CABG+AVR per patient in the period 2015–2020 is included. Likewise, if a patient underwent multiple PCIs within one year, only the first PCI (within 365 days) is included in the dataset. A second procedure within one year was excluded or was considered a reintervention if the procedure meets the NHR-definition of reintervention.

Baseline characteristics and outcome measures

The baseline characteristics and outcome measures (mortality, complications and reinterventions) per invasive cardiac intervention are presented in Table 1 in the supplementary materials. These variables are standard parameters within the NHR [18, 19, 21].

Definitions

Diabetes mellitus (DM) is defined as having chronic hyperglycaemia, diagnosed prior to cardiac intervention, demonstrating one of the following criteria; (1) fasting plasma glucose ≥ 7.0 mmol/l (2) 2-hour post-load (75 mg glucose) plasma glucose ≥ 11.1 mmol/l (3) symptoms of hyperglycaemia and plasma glucose ≥ 11.1 mmol/l and (4) glycated haemoglobin (HbA1c) $\geq 6.5\%$ [21–23]. If a patient is considered diabetic, the treatment method is registered as well: insulin, oral medication, diet, other treatment, no treatment or treatment unknown.

The following six other variables are worth defining; an urgent procedure, myocardial infarction (MI), cerebrovascular accident (CVA) with a residual deficit, re-exploration, DSWI, and Target Vessel Revascularization (TVR).

First, urgent procedures are patients who are not electively admitted for surgery but for medical reasons require intervention within the current admission [21].

Second, MI is defined as an increase and subsequent decrease in one or more biomarkers (preferably troponin) by at least one value above the 99th percentile of the upper limit where at least one of the following symptoms is present; (1) symptoms appropriate to ischemia (2) new significant ST-segment or T-wave abnormalities or bundle branch block (3) development of pathological waves on the electrocardiogram (4) new loss of viable myocardial tissue or new wall motion abnormalities demonstrated by imaging technologies and/or (5) identification of intracoronary thrombus on angiography or autopsy [21, 24, 25].

Third, CVA with residual deficit during hospital admission is a permanent, neurological dysfunction as determined by a neurologist due to focal ischemia of the brain, spinal cord or retina caused by acute infarction of the neurological tissue due to thrombosis, embolism, systemic hypoperfusion or haemorrhage [21, 26].

Fourth, re-exploration within 30 days after the intervention is defined as the first rethoracotomy after the initial closing of the thorax due to bleeding, tamponade or cardiac problems [21].

Fifth, DSWI within 30 days after the intervention covers muscle, sternum and mediastinum and is positive if one or more of the following criteria applies: (1) surgical drainage or fixation sternum due to deep sternal wound (2) positive wound cultures and (3) antibiotics-therapy for sternum wound treatment [21].

Last, TVR within one year after the intervention is defined as revascularization by PCI in the same vessel (or vessels) that had been treated at the index PCI within 1 year (≤ 365 days) of the index PCI, or; revascularization by CABG in the same vessel (or vessels) that had been treated at the current PCI after 1 day and within 1 year (≤ 365 days) of the PCI. An urgent CABG performed within 1 day of the current PCI is recorded as an outcome indicator of urgent CABG and not as an occurrence of TVR [21].

The definitions of other included variables are aligned with the European Society of Cardiology's (ESC) Guidelines [18].

Statistical analyses

Following current guidelines on the imputation of data by The Dutch Journal of Medicine (2013) and BMC Medical Research Methodology (2017), missing values of baseline characteristics were imputed [27, 28]. The baseline characteristics, that are missing at random and missing less than 35%, were imputed using ten iterations and ten imputations using both baseline characteristics and outcomes as predictors [27, 28]. An overview of all available variables and the rate of completeness can be found in Table 1 of the Supplementary materials. Outcome variables only served as predictors and were not imputed.

Using descriptive statistics, QQ-plots and Kolmogorov-Smirnov tests, the structure of the dataset was studied and checked for outliers and normal distribution. Continuous variables are shown as mean (standard deviation (SD)) or median (interquartile range (IQR)) while categorical variables are shown as absolute and relative frequencies. Bivariate analyses were performed to study differences between patients with diabetes and patients without diabetes for baseline characteristics and outcome measures using Mann-Whitney U and Pearson χ^2 -tests. Logistic regression analyses were used to analyse the association between diabetes mellitus and short-term outcome measures while adjusting for all applicable baseline characteristics and the year of intervention. An overview of the applicable baseline characteristics per intervention that were used in the logistic regression analyses is presented in Table 1 in the Supplementary materials. Per invasive cardiac intervention, for each (short-term) outcome measure, the odds ratio (OR) and p-value for diabetes are shown. Furthermore, two additional logistic regressions were performed as sensitivity analyses; one analysis while making cohorts for the year of intervention (2015–2017 versus 2018–2020) to study differences in time and one by making cohorts for the different treatment of diabetes (as seen in Supplementary Table 2 and as defined above) for each intervention [21–23]. Furthermore, a propensity score (PS) matching analysis was executed to study if we adequately adjusted for differences in baseline characteristics. The PS included all baseline characteristics listed in Table 1. For each patient with DM, a propensity score matched patient without DM was selected (ratio 1:n) using the nearest neighbour (with a calliper width of 0.2 of the pooled SD of the logit of the propensity score) and no replacement. Covariate balance was evaluated with standardised mean differences, and a standardised mean difference < 0.1 was considered a negligible difference between cohorts.

Last, to study the relationship between patients with diabetes and patients without diabetes in relation to survival and reintervention during follow-up, Cox regression curves with 95% CI were used while correcting for baseline characteristics (as seen in Table 1 in Supplementary materials). The proportional hazards assumption was checked by plotting a log minus log survival curve stratified for each covariate per intervention.

Results for all analyses were considered statistically significant with a two-tailed p-value $< \alpha$ 0.05. All analyses were performed using SPSS 29 (SPP Inc., Chicago IL, USA) and Rstudio (Rstudio Inc., Boston, MA, USA).

Results

A total of 241,360 invasive cardiac interventions were analysed, divided among the following interventions: PCI ($N=177,556$), CABG ($N=39,069$), AVR ($N=8,028$),

Table 1 (continued)

Variable	Coronary artery disease (CAD)			Aortic valve disease (AVD)			Combined CAD and AVD				
	PCI n = 177,556	CABG N = 39,069	AVR N = 8,028	TAVI N = 11,819	CABG + AVR N = 4,888	DM	No DM	p-value	DM	No DM	p-value
Prior CABG, n (%)	5,864 (15.3)	10,818 (7.8)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
PCI (STEMI), n (%)	7,770 (20.3)	45,529 (32.7)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
NYHA-class IV, n (%)	n/a	n/a	n/a	n/a	n/a	247 (7.6)	416 (5.0)	<0.001	n/a	n/a	n/a

*n/a = not applicable (not part of NHR indicators), eGFR = Estimated Glomerular Filtration Rate, LVEF = Left ventricular ejection fraction, BMI = body mass index, COPD = chronic obstructive pulmonary disease, Prior. Card. Pro. = prior cardiac procedure, Multi vessel dis. = multi vessel disease, prior MI = prior myocardial infarction, log. EuroSCORE I = logistic EuroSCORE I, log. EuroSCORE II = logistic EuroSCORE II, prior CVA = cerebrovascular accident, OHCA = out of hospital arrest. An overview of the available baseline characteristics per procedure is shown in Table 1 of the Supplementary materials

TAVI (N=11,819), and CABG+AVR (N=4,888). Of all patients undergoing PCI, 21.1% has diabetes, 26.7% of CABG patients, 17.8% of AVR, 27.6% of TAVI and 27.8% of CABG+AVR. Oral medication is the most common medical treatment for DM, ranging between 6.7 – 14.4% of patients with diabetes, and subsequently insulin treatment, ranging between 4.2 – 9.7% of patients with diabetes. More information regarding diabetes within the study population is presented in Table 2 in the Supplementary Materials.

Table 1 shows descriptive and univariable analyses of baseline characteristics between patients with diabetes and patients without diabetes for each cardiac procedure. All baseline characteristics within the PCI cohort are statistically significantly different between patients with diabetes and patients without diabetes (p<.001). For CABG there is a statistically significant difference for all baseline characteristics (p<.001) except for urgency of procedure (p=.112). In the AVR cohort, the variables age, eGFR, body mass index (BMI) and chronic obstructive pulmonary disease (COPD), logistic EuroSCORE I, logistic EuroSCORE II (p<.001) and CVA (p=.03) were significantly different between the two groups. Regarding TAVI, there is a significant difference for all baseline characteristics (p<.001) except EuroSCORE I (p=.112). Lastly, the CABG+AVR cohort shows a statistically significant difference in age, eGFR, BMI, chronic lung disease, EuroSCORE II (p<.001) and left ventricular ejection fraction (LVEF) (p=.005), multivessel disease (p=.016), prior myocardial infarction (p=.043) and EuroSCORE I (p=.004).

Table 2 shows descriptive and univariable analyses of outcome variables between patients with diabetes and patients without diabetes for each cardiac procedure. For PCI, there is a significant difference between patients with and without diabetes in 30-day mortality, 1-year mortality, myocardial infarction within 30 days after the procedure and TVR within 1 year after the procedure (p<.001). For CABG, 120-day mortality, 1-year mortality, CVA, DSWI within 30 days (p<.001) and coronary reintervention during follow-up (p<.001) are statistically significant. In the AVR cohort, there is a statistically significant difference between 120-day mortality (p=.003), 1-year mortality (p=.031), and DSWI within 30 days (p<.001). Concerning TAVI, 120-day mortality (p=.035), 1-year mortality (p<.001) and implantation of a new permanent pacemaker within 30 days post-procedure (p=.014) are statistically different between the two groups. Last, CABG+AVR has a statistically significant difference between patients with diabetes and patients without diabetes regarding 120-day mortality (p<.001), 1-year mortality (p=.023) and DSWI within 30 days (p=.030).

Table 2 Univariable analyses of outcome variables between diabetics and non-diabetics for each cardiac procedure

	Coronary artery disease (CAD)				Aortic Valve Disease (AVD)				Combined CAD and AVD					
	PCI n = 177,556		CABG N = 39,069		AVR N = 8,028		TAVI N = 11,819		CABG + AVR N = 4,888		No DM		DM	
	No DM	p-value	No DM	p-value	No DM	p-value	No DM	p-value	No DM	p-value	No DM	DM	No DM	p-value
Mortality														
Proc. mortality (3-days), n (%)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
30-day mortality, n (%)	1,332 (3.5)	<0.001	3,385 (2.5)	<0.001	n/a	n/a	n/a	n/a	26 (0.8)	89 (1.0)	0.217	n/a	n/a	n/a
120-day mortality, n (%)	n/a	n/a	n/a	n/a	264 (2.6)	438 (1.6)	<0.001	43 (3.1)	117 (1.8)	0.003	192 (6.1)	420 (5.1)	0.035	82 (6.2)
1-year mortality (2015–2019), n (%)	2,745 (8.5)	<0.001	5,782 (4.9)	<0.001	334 (3.8)	546 (2.3)	<0.001	52 (4.2)	165 (3.0)	0.031	334 (12.9)	698 (10.2)	<0.001	83 (7.2)
Complications														
CVA, during admission n (%)	n/a	n/a	n/a	n/a	95 (0.9)	169 (0.6)	<0.001	15 (1.1)	57 (0.9)	0.547	61 (2.0)	157 (1.9)	0.884	26 (1.9)
Re-exploration < 30 days, n (%)	n/a	n/a	n/a	n/a	50 (0.5)	129 (0.7)	0.334	79 (5.7)	361 (5.7)	0.944	n/a	n/a	n/a	115 (8.8)
DSWI < 30 days, n (%)	n/a	n/a	n/a	n/a	171 (1.7)	198 (0.7)	<0.001	14 (1.0)	20 (0.3)	<0.001	n/a	n/a	n/a	20 (1.5)
PM < 30 days, n (%)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	33 (3.7)	168 (4.1)	0.613	371 (11.6)	842 (10.1)	0.014	22 (2.6)
Maj. vasc. compl. < 30 days, n (%)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	73 (2.6)	243 (3.2)	0.097	n/a
MI < 30 days, n (%)	219 (0.9)	<0.001	568 (0.7)	<0.001	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Urgent CABG < 1 day, n (%)	69 (0.2)	0.323	262 (0.2)	0.323	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
TVR < 1 year (2015–2019), n (%)	2,109 (7.3)	<0.001	5,678 (5.3)	<0.001	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

*n/a = not applicable (not part of NHR indicators), proc. Mortality (3-days) = procedural mortality within 3 days, PM < 30-days = implantation of new permanent pacemaker within 30 days, maj. vasc. compl < 30-days = major vascular complication within 30 days, MI < 30 days = myocardial infarction within 30 days, TVR < 1 year = Target Vessel Revascularization within 1 year. An overview of the available baseline characteristics per procedure is shown in Table 1 of the Supplementary materials

The results of the logistic regression analyses with diabetes as an independent variable are shown in Table 3. Diabetes mellitus is a statistically significant variable in the PCI-cohort for 30-day mortality ($p < .001$; OR=1.668), 1-year mortality ($p < .001$; OR=1.682), myocardial infarction within 30-days ($p < .001$; OR=1.431) and TVR within 1 year ($p < .001$; OR=1.307). In the CABG-cohort, diabetes mellitus is significantly associated with the following outcome measures: 120-day mortality ($p < .001$; OR=1.421), 1-year mortality ($p < .001$; OR=1.494), CVA ($p = .015$; OR=1.371) and DWSI within 30-days post-procedure ($p < .001$; OR=2.203). Concerning TAVI, 1-year mortality ($p < .010$; OR=1.122) and implantation of a new permanent pacemaker within 30 days post-procedure ($p = .007$; OR=1.200) are significantly associated with diabetes. Lastly, for AVR, diabetes is a statistically significant variable for 120-day mortality ($p = .030$, OR=1.493), DWSI within 30-days ($p = .003$; OR=2.873) and for CABG+AVR the variables 120-day mortality ($p = .005$; OR=1.520) and DSWI within 30-days ($p = .022$; 1.996).

Results of the additional sensitivity analyses and propensity score matching can be found in Tables 3, 4, 5 and 6 in the Supplementary materials; all analyses led to similar findings.

Last, Fig. 1 below shows the cox regression survival curves for each intervention. Survival time in days for patients living with diabetes and patients living without diabetes is plotted over a follow-up period of five years, adjusted for all baseline characteristics. All figures show patients with diabetes have lower survival rates compared to patients without diabetes.

Discussion

The current study provides the latest report on the relationship between diabetes mellitus and clinical outcomes after different invasive cardiac interventions in the Netherlands. This study uses recent, real-world data from multiple years (2015–2020) from a nationwide registry covering almost the entire Dutch CVD population that underwent invasive cardiac interventions. It thus forms

Table 3 Results of the multivariate logistic regression analyses with correlation between diabetes mellitus and all early outcomes

Outcome measure	Coronary artery disease (CAD)				Aortic valve disease (AVD)				Combined CAD and AVD	
	PCI n = 177,556		CABG N = 39,069		AVR N = 8,028		TAVI N = 11,819		CABG + AVR N = 4,888	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Mortality										
Proc. mortality (3-days)	n/a	n/a	n/a	n/a	n/a	n/a	0.72 (0.46-1.13)	0.15	n/a	n/a
30-day mortality	1.68 (1.56-1.82)	< 0.001	n/a	n/a	n/a	n/a	1.03 (0.81-1.31)	0.81	n/a	n/a
120-day mortality	n/a	n/a	1.35 (1.15-1.58)	< 0.001	1.50 (1.04-2.15)	0.03	1.13 (0.95-1.36)	0.18	1.42 (1.05-1.90)	0.02
1-year mortality (2015-2019)	1.68 (1.6-1.77)	< 0.001	1.43 (1.24-1.65)	< 0.001	1.22 (0.88-1.69)	0.23	1.21 (1.05-1.4)	0.01	1.21 (0.91-1.61)	0.19
Complications										
CVA during admission	n/a	n/a	1.32 (1.02-1.7)	0.04	1.15 (0.65-2.04)	0.64	1.05 (0.77-1.42)	0.77	1.02 (0.65-1.62)	0.93
Re-exploration < 30 days	n/a	n/a	0.92 (0.82-1.03)	0.15	0.99 (0.77-1.28)	0.94	n/a	n/a	1.14 (0.91-1.44)	0.26
DSWI < 30 days	n/a	n/a	2.18 (1.77-2.68)	< 0.001	2.86 (1.43-5.69)	0.003	n/a	n/a	1.92 (1.06-3.48)	0.03
PM < 30 days	n/a	n/a	n/a	n/a	0.88 (0.60-1.29)	0.51	1.20 (1.05-1.37)	0.01	0.68 (0.42-1.10)	0.11
Maj. vasc. compl. < 30 days	n/a	n/a	n/a	n/a	n/a	n/a	0.82 (0.63-1.08)	0.16	n/a	n/a
MI < 30 days	1.44 (1.24-1.67)	< 0.001	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Urgent CABG < 1 day	0.94 (0.72-1.22)	0.64	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
TVR < 1 year (2015-2019)	1.30 (1.23-1.37)	< 0.001	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

* n/a = not applicable (not part of NHR indicators), proc. Mortality (3-days) = procedural mortality within 3 days, PM < 30-days = implantation of new permanent pacemaker within 30 days, maj. vasc. compl < 30-days = major vascular complication within 30 days, MI < 30 days = myocardial infarction within 30 days, TVR < 1 year = Target Vessel Revascularization within 1 year. An overview of the available baseline characteristics per procedure is shown in Table 1 of the Supplementary materials

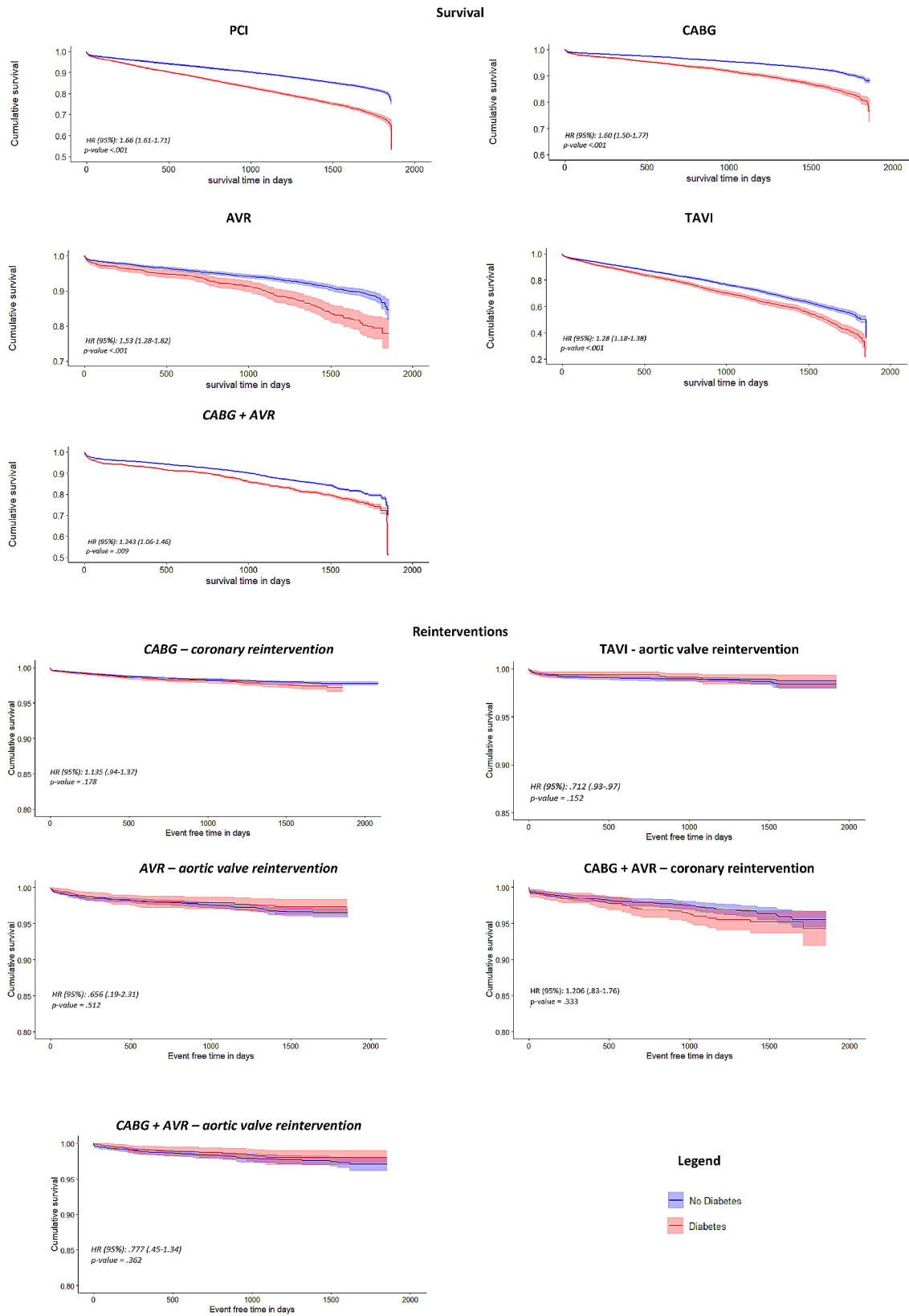


Fig. 1 Cox regression curves per intervention of the study regarding survival and reinterventions. Blue lines; no diabetes mellitus, Red lines; diabetes mellitus

a representative sample of all cardiac procedures on a nearby nationwide level. Results show that people with diabetes have statistically significantly worse outcomes in terms of mortality, complications and reinterventions compared to people without diabetes.

From a pathophysiologic point of view, these findings could be expected as DM patients share similar risk factors for CAD (such as hypercholesterolemia, obesity, etc.) and DM itself is associated with endothelial damage as a result of glucose-related tissue toxicity and circulating inflammatory cytokines [29]. Quantitative histologic analysis of aortic valves after explantation for AVR shows worse calcifications in DM patients and a recent animal study points in the direction of faster progression to calcification of the aortic valve in DM-hyperglycemic hamsters [30]. The association between DM and AVD is not well understood but given that calcification of the aortic valve and DM both are related to inflammatory pathways, an association is likely [31].

Historically, treatment of DM focused on drug therapy, aimed to control glycemic control, hypertension and cholesterol levels. In recent years, a paradigm shift toward a more patient-centred approach addressing lifestyle-related risks such as increasing physical activity levels, adopting a healthy and varied diet to control weight, and smoking cessation [9, 16, 32, 33]. Since 2019, the European Society of Cardiology included Sodium-glucose co-transporter 2 (SGLT2-inhibitors) in the ESC Clinical Practice guidelines, based on new evidence that SGLT2-inhibitors benefit patients with cardiovascular diseases and reduce the risk of cardiovascular mortality [34, 35]. Nevertheless, the present study shows that differences between patients with diabetes and patients without diabetes still exist; patients with diabetes have worse outcomes and mortality statistics than patients without diabetes. As shown in our study, patients with diabetes have higher odds of mortality compared to patients without diabetes. People with diabetes show higher health-care utilization and higher healthcare costs compared to people without diabetes, whereas the prevalence of DM is deemed to strongly incline in the upcoming decades [3, 9, 10, 16].

With regard to CAD interventions, the results align with two recent meta-analyses by Head et al. 2018 [36] and Zhou et al. 2019 [14] and two cohort studies by Rogan et al. 2018 [37] and Raza et al. 2015 [3]. These studies, covering both randomized controlled trials (RCT) and observational studies for a period ranging between 1972 and 2018, state people with diabetes have significantly worse outcomes concerning short-term mortality and 1-year mortality [3, 14, 36–38]. Concerning complications and reinterventions in literature; patients with diabetes have more strokes, bleeding complications, DSWI, MI and reinterventions [14, 39–42]. Our study confirms

these results, although it is worth noting that our study uses more recent data, has a higher number of total interventions and the data exist of observational real-world data.

Concerning aortic valve interventions, two studies Besch., 2019 [43], an observational study of 18,154 patients, and Mendez-Bailion et al., 2019 [44], a randomized controlled trial (RCT), show no statistically significant difference between patients with diabetes and patients without diabetes in short-term and long-term mortality as well as post-procedural complications. The RCT studies of both Abramowitz [15] and Layrer [45] reported no significant difference between patients with diabetes and patients without diabetes regarding short-term and long-term mortality as well as complications after TAVI. However, after correcting the data for baseline characteristics, diabetes was significantly associated with mortality. This partly contradicts our study, covering more recent years, more interventions and is an observational study instead of an RCT; we did not find an association between diabetes mellitus and 30-day mortality, but we did find a negative association in relation to 1-year mortality and pacemaker implantation. Results specifically in relation to AVR are contradicting some previous publications; to our knowledge, there is no consensus in the literature on the difference between patients with diabetes and patients without diabetes in terms of mortality, complications or reinterventions. A recent systematic review by Banovic et al., 2019 [46] reports that results on short-term and long-term mortality and complications differ per study while other studies, such as Ram et al., 2019 [13], an observational study covering 1,053 patients, do not report differences between patients with diabetes and patients without diabetes. Our study, which includes recent data on more AVR patients, does show a significant difference in terms of 120-day mortality and DSWI within 30 days when correcting for baseline characteristics.

Over the years, mortality in cardiovascular diseases is decreasing for both patients with and without diabetes [9]. The systematic review of Htay et al., 2019 [9] found the gap between patients with diabetes and patients without diabetes to decrease; mortality among diabetics is declining at a higher rate than among non-diabetics. The study states developments in the treatment of diabetes and diabetic complications, together with improved management of individual risk factors, are the main influences for this decline [9]. In general, according to the studies mentioned above and the results of this study, people with diabetes have statistically significantly worse outcomes in terms of mortality, complications and reinterventions compared to people without diabetes. To prevent a rapid incline in disease burden and healthcare consumption, it is key to optimize healthcare protocols

for this target group and increase focus on prevention. A possible solution is to create and optimize regional collaboration between healthcare providers to align healthcare pathways [47].

Strengths and limitations

One of the strengths of this study is its size; in total 214,360 surgical and percutaneous cardiac procedures were included in a period of six years. It uses observational, real-world data from populations in daily practice instead of data received from included patients in an RCT. Hence, patients from almost the entire Dutch surgical and percutaneous cardiovascular disease population are included, which ensures a recent and proportionate representation. However, this dataset can also be seen as a limitation, since observational retrospective data have potential bias; arguably, not all relevant risk factors have been included in the dataset. In this study, a standard set of variables, as selected by medical experts in the registration committees of the NHR, was used. This selection of the most relevant outcomes and baseline characteristics is based on a published methodology. However, as this is a limited set it possibly excludes some baseline characteristics that might also influence outcomes (e.g. TAVI prior to PCI, SYNTAX score and STS PROM-scale). Also, relevant biomedical parameters, such as perioperative and postoperative blood plasma glucose levels, and data on diabetic medication as well as on antiplatelet treatment, are not collected in the NHR which made it impossible to correct for these variables in the multivariate analysis. This can potentially affect the reported association. For future research, it is recommended to include more variables if possible. Furthermore, quality of life is not included in these analyses due to the fact that the majority of hospitals have insufficiently collected these variables. Hence, a recommendation for future research is to study the difference between patients with diabetes and patients without diabetes after different invasive cardiac interventions. Additionally, due to multiplicity, there is a potential for an increased risk of a type I error. Last, although differences over time were studied, showing no statistical differences, the impact of the COVID-19 pandemic on the study results of 2020 is unknown. This should be included in future research, as SARS-CoV-2 could be associated with a higher risk of in-hospital mortality [48].

This study has shown that real-world, clinical outcomes after cardiac procedures still differ between patients with diabetes and patients without diabetes. It is vital to critically assess existing care pathways and protocols targeted to patients with diabetes to minimize these differences.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12933-024-02356-2>.

Supplementary Material 1
Supplementary Material 2
Supplementary Material 3
Supplementary Material 4
Supplementary Material 5
Supplementary Material 6
Supplementary Material 7
Supplementary Material 8
Supplementary Material 9

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None.

Author contributions

SS contributed to the paper by conceptualizing the study design, overseeing data collection, conducting formal analysis, interpreting results, and drafting the original manuscript. DS and GS collaborated on data analysis and the interpretation of results, and reviewed the manuscript. During the literature review stage, MS, GS and KT provided valuable input. The manuscript underwent review and editing by DS, MT, JK, MS, GS, KT, LD and DV. LD and DV provided project supervision.

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Data availability

The data underlying this article were provided by the Netherlands Heart Registration (NHR) by permission. A request can be submitted to NHR to access these data.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors whose names are listed certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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