

## SUPPLEMENTAL MATERIAL

*Title:* Peripheral Artery Disease, Lower Limb Revascularization, and Amputation in Diabetes Patients with and without Coronary Artery Disease – A Cohort Study from the Western Denmark Heart Registry

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**Table S1.** International Classification of Diseases codes 10th revision (ICD-10), Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures Version 1.15, and Anatomical Therapeutic Chemical (ATC) codes used for baseline and outcome definition.

<i>Condition</i>	<i>ICD-10 code</i>
Myocardial infarction	DI21
Ischemic stroke	DI63, DI64
Peripheral artery disease	DI70, DI70.1–DI70.9. DI73.9
Heart failure	DI11.0, DI13.0, DI13.2, DI50
Renal disease	DI12, DI13, DN00–DN05, DN07, DN11, DN14, DN17–DN19, DQ61
Atrial fibrillation/flutter	DI48
Diabetes	DE10–DE14, DH36.0, DO24.0–24.3, DO24.5–24.9
Retinopathy	DE103, DE11.3, DE12.3, DE13.3, DE14.3, DH28.0, DH33.4B, DH34, DH35.0, DH36.0
Peripheral neuropathy	DE10.4, DE11.4, DE12.4, DE13.4, DE14.4, DG56, DG57, DG58, DG59, DG60.9, DG60.3, DG61, DG62, DG63, DG90.0, DG90.9, DG99
Nephropathy	DR80.9, DB28.9A, DE10.2, DE11.2, DE12.2, DE13.2, DE14.2, DE14.3, DN39.1, DN06, DN07, DN08, DN14, DN16, DM10.3, DM35.0E
<i>Procedure</i>	<i>NOMESCO classification</i>
Lower limb revascularization	KPDE-KPDF, KPDH, KPDN, KPDP, KPDQ, KPEE-KPEF, KPEH, KPEN, KPEP, KPEQ, KPFE-KPEG, KPFH, KPFN, KPFP, KPFQ, KPFQ, KPDU74, KPDU84

Lower limb amputation	KNFQ, KNGQ, KNHQ
Percutaneous coronary intervention	KFNG02, KFNG05, KFNG96
Coronary artery bypass grafting	KFNA–KFNE

<i>Drug</i>	<i>Anatomical Therapeutic Chemical code</i>
Aspirin	B01AC06, N02BA01
ADP-inhibitor	B01AC04, B01AC22, B01AC24
Statin	C10AA
Direct oral anticoagulant	B01AF02, B01AE07, B01AF01
Vitamin K-antagonist	B01AA03, B01AA04
β-blokkere	C07*
Angiotensin converting enzyme inhibitors	C09A*, C09B*
Angiotensin-II receptor blockers	C09C*, C09D*
Thiazides	C03AA*, C03AB*
Calcium channel blockers	C08C*, C08D*
Insulin	A10A*
Non-insulin glucose lowering drugs	A10B*

**Table S2.** Procedural baseline characteristics in non-diabetes and diabetes patients by coronary artery status.

	No DM, No CAD (n=41,878)		DM, No CAD (n=5,735)		No DM, CAD (n=59,427)		DM, CAD (n=11,747)	
	n	%	n	%	n	%	n	%
<b>Coronary artery disease extent</b>								
0 VD	41,878	100	5,735	100				
Diffuse VD					9,751	16.4	2,223	18.9
1 VD					26,442	44.5	4,179	35.6
2 VD					12,870	21.7	2,564	21.8
3 VD					10,364	17.4	2,781	23.7
<b>Procedural priority</b>								
Acute	3,234	7.7	298	5.2	16,319	27.5	2,081	17.7
Subacute	9,506	22.7	1,142	19.9	15,222	25.6	3,045	25.9
Elective	29,138	69.6	4,295	74.9	27,885	46.7	6,621	56.4
<b>Procedural indication</b>								
STEMI	1,760	4.2	153	2.7	14,641	24.6	1,769	15.1
NSTEMI	3,295	7.9	395	6.9	10,859	18.3	2,071	17.6
Unstable AP	1,395	3.3	197	3.4	1,714	2.9	352	3.0
Stable AP	17,264	41.2	2,575	44.9	21,127	35.6	4,890	41.6
Arrhythmia	2,031	4.8	224	3.9	1,224	2.1	241	2.1
Valve disease	5,341	12.8	632	11.0	3,570	6.0	848	7.2
Cardiomyopathy	3,854	9.2	593	10.3	2,129	3.6	680	5.8
Other incl. missing	6,938	16.4	966	16.8	4,163	6.9	897	7.6

AP: angina pectoris

NSTEMI: Non-ST segment elevation myocardial infarction

STEMI: ST segment elevation myocardial infarction

VD: vessel disease

**Table S3. Number events, event rates and incidence rate ratios of peripheral artery disease, lower limb revascularization, and lower limb amputation in diabetes patients by presence and extent of coronary artery disease.**

	Events	Events per 100 person years (95% CI)	10-year cumulative incidence (95% CI)	Unadjusted HR (95% CI)	Adjusted HR <sup>†</sup> (95% CI)
<i>Peripheral artery disease</i>					
No CAD				reference	reference
CAD				2.52 (2.22-2.85)	2.32 (2.03-2.65)
Diffuse VD	181	1.60 (1.39-1.86)	15.38 (12.67-18.61)	1.89 (1.57-2.28)	1.71 (1.42-2.06)
1 VD	423	1.75 (1.59-1.93)	15.03 (13.60-16.59)	2.11 (1.82-2.45)	2.07 (1.77-2.42)
2 VD	292	2.04 (1.82-2.28)	16.19 (14.40-18.19)	2.45 (2.08-2.87)	2.36 (1.99-2.80)
3 VD	458	3.13 (2.85-3.43)	24.59 (22.46-26.88)	3.73 (3.22-4.31)	3.45 (2.95-4.04)
					$p_{\text{trend}} < 0.001$
<i>Lower limb revascularization</i>					
No CAD				reference	reference
CAD				3.42 (2.62-4.46)	3.41 (2.58-4.52)
Diffuse VD	51	0.43 (0.33-0.57)	4.29 (3.07-5.97)	2.54 (1.75-3.67)	2.44 (1.68-3.55)
1 VD	111	0.44 (0.36-0.53)	4.35 (3.54-5.34)	2.56 (1.88-3.49)	2.71 (1.96-3.75)
2 VD	94	0.62 (0.51-0.76)	5.78 (4.62-7.22)	3.61 (2.63-4.97)	3.86 (2.76-5.40)
3 VD	143	0.90 (0.77-1.06)	8.30 (6.95-9.90)	5.25 (3.90-7.06)	5.47 (3.98-7.50)
					$p_{\text{trend}} < 0.001$
<i>Lower limb amputation</i>					
No CAD				reference	reference

CAD				1.78 (1.42-2.22)	1.80 (1.41-2.29)
Diffuse VD	47	0.40 (0.30-0.53)	4.42 (3.11-6.25)	1.31 (0.92-1.87)	1.35 (0.95-1.92)
1 VD	103	0.41 (0.33-0.49)	4.20 (3.40-5.18)	1.67 (1.25-2.23)	1.69 (1.26-2.26)
2 VD	65	0.43 (0.33-0.54)	4.11 (3.14-5.36)	1.71 (1.23-2.38)	1.73 (1.24-2.41)
3 VD	115	0.72 (0.60-0.86)	6.73 (5.44-8.16)	2.69 (2.01-3.60)	2.72 (2.03-3.64)
					$p_{\text{trend}} < 0.001$

†Adjusted for age, sex, hypertension, microvascular disease, active smoking (imputed), body mass index (imputed), oral anti-coagulant treatment, anti-platelet treatment, statin treatment, diabetes treatment, and diabetes duration.

**Table S4. Number events, event rates and incidence rate ratios by diabetes treatment**

	Patients	Events	Events per 100 person years (95% CI)	Unadjusted HR (95% CI)	Adjusted HR <sup>†</sup> (95% CI)
<i>Peripheral artery disease</i>					
Non-pharmacological treatment	3,457	236	1.09 (0.96-1.24)	1	1
Non-insulin treatment	8,875	722	1.43 (1.33-1.54)	1.30 (1.12-1.50)	1.20 (1.03-1.39)
Insulin treatment	5,150	689	2.43 (2.25-2.61)	2.19 (1.89-2.54)	1.60 (1.33-1.91)
<i>Lower limb revascularization</i>					
Non-pharmacological treatment	3,457	65	0.29 (0.23-0.37)	1	1
Non-insulin treatment	8,875	192	0.37 (0.32-0.42)	1.26 (0.95-1.68)	1.23 (0.92-1.64)
Insulin treatment	5,150	205	0.68 (0.59-0.78)	2.34 (1.77-3.10)	1.86 (1.32-2.62)
<i>Lower limb amputation</i>					
Non-pharmacological treatment	3,457	37	0.16 (0.12-0.23)	1	1
Non-insulin treatment	8,875	123	0.23 (0.20-0.28)	4.27 (3.49-5.24)	1.10 (0.75-1.61)
Insulin treatment	5,150	279	0.90 (0.80-1.01)	16.34 (13.99-19.09)	2.11 (1.40-3.18)

\*10-year cumulative incidence proportion accounting for the competing risk of death.

<sup>†</sup>Adjusted for age, sex, hypertension, microvascular disease, active smoking (imputed), body mass index (imputed), oral anti-coagulant treatment, anti-platelet treatment, statin treatment, coronary artery disease, and diabetes duration.

CI: confidence interval

CIP: cumulative incidence proportion

**Table S5. Number events, event rates and hazard ratio by duration of diabetes.**

	Patients	Events	Events per 100 person years (95% CI)	Unadjusted HR (95% CI)	Adjusted HR <sup>†</sup> (95% CI)
<i>Peripheral artery disease</i>					
0-4 years	9,185	682	1.20 (1.11-1.29)	1	1
5-9 years	3,683	370	1.82 (1.65-2.02)	1.50 (1.31-1.70)	1.22 (1.06-1.40)
≥10 years	4,614	595	2.56 (2.36-2.77)	2.08 (1.86-2.32)	1.35 (1.17-1.56)
<i>Lower limb revascularization</i>					
0-4 years	9,185	197	0.33 (0.29-0.38)	1	1
5-9 years	3,683	105	0.49 (0.41-0.60)	1.47 (1.16-1.87)	1.13 (0.88-1.46)
≥10 years	4,614	160	0.65 (0.55-0.76)	1.93 (1.57-2.38)	1.09 (0.82-1.43)
<i>Lower limb amputation</i>					
0-4 years	9,185	97	0.16 (0.13-0.20)	1	1
5-9 years	3,683	104	0.49 (0.40-0.59)	3.01 (2.28-3.97)	2.08 (1.54-2.82)
≥10 years	4,614	229	0.93 (0.82-1.06)	5.80 (4.57-7.35)	2.64 (1.94-3.59)

\*10-year cumulative incidence proportion accounting for the competing risk of death.

†Adjusted for age, sex, hypertension, microvascular disease, microvascular disease, active smoking (imputed), body mass index (imputed), oral anti-coagulant treatment, anti-platelet treatment, statin treatment, coronary artery disease, and type of diabetes treatment.

DM: diabetes mellitus

CAD: coronary artery disease



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CI: confidence interval

CIP: cumulative incidence proportion

**Figure S1. Distribution of first lower limb amputation by diabetes and coronary artery disease.**

