

SUPPLEMENTARY DATA

Supplementary Table S1. Characteristics of participants at baseline by the requirement of lower extremity revascularization during follow-up in the Type 2 diabetes cohorts

	No revascularization	Revascularization	P
n (%)	4438	115	-
Cohort: DIABHYCAR, n (%)	2991 (96.4)	110 (3.6)	<0.0001
SURDIAGENE, n (%)	1452 (93.3)	98 (6.7)	
Sex: male, n (%)	2950 (68)	160 (77)	0.006
Age, y	65 ± 9	67 ± 9	0.02
Duration of diabetes, y	12 ± 9	14 ± 9	0.002
BMI, kg/m ²	30.1 ± 5.3	28.9 ± 4.7	0.001
Systolic BP, mmHg	141 ± 16	141 ± 17	0.96
Diastolic BP, mmHg	79 ± 10	76 ± 12	<0.0001
Arterial hypertension, n (%)	2779 (64)	164 (79)	<0.0001
Current tobacco smoking, n (%)	557 (13)	39 (19)	0.02
Previous MI, n (%)	361 (8.3)	34 (16.4)	0.0002
Previous stroke, n (%)	187 (4.3)	16 (7.7)	0.04
Previous LEA, n (%)	58 (1.3)	14 (6.7)	<0.0001
Copeptin, pmol/l	7.0 [7.1]	8.4 [9.3]	<0.0001
HbA1c, %	7.8 ± 1.7	8.0 ± 1.8	0.08
HbA1c, mmol/mol	62 ± 18	64 ± 20	0.08
Total cholesterol, mmol/l*	5.5 ± 1.2	5.5 ± 1.3	0.80
HDL cholesterol, mmol/l	1.3 ± 0.4	1.2 ± 0.3	<0.0001

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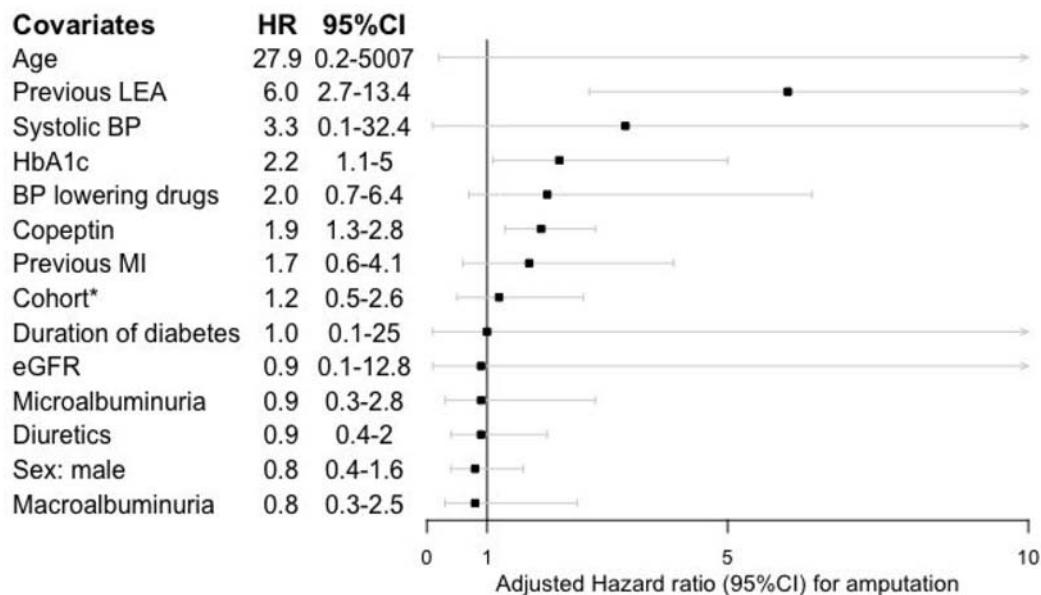
Triglycerides, mmol/l*	1.8 [1.3]	1.9 [1.6]	0.09
Plasma creatinine, µmol/l	87 [29]	94 [37]	<0.0001
eGFR, ml/min/1.73 m ²	74 ± 20	67 ± 23	<0.0001
UAC, mg/l	60 [128]	102 [314]	<0.0001
UAC stages: Normoalbuminuria, n (%)	621 (14)	33 (16)	<0.0001
Microalbuminuria, n (%)	2743 (63)	103 (49)	
Macroalbuminuria, n (%)	974 (23)	72 (35)	
Use of antiplatelet or anticoagulation drugs, n (%)	1223 (28)	117 (56)	<0.0001
Use of lipid lowering drugs, n (%)	1154 (27)	56 (27)	0.94
Use of BP lowering drugs, n (%)	2775 (64)	166 (80)	<0.0001
Use of ACE-I or ARB, n (%)	1019 (23)	80 (38)	<0.0001
Use of diuretics, n (%)	1274 (29)	85 (41)	0.0006
Use of insulin, n (%)	804 (19)	70 (34)	<0.0001

Qualitative data expressed as means ± SD, except for UAC, copeptin, plasma creatinine and triglycerides expressed as median and interquartile range [IQR]. Statistics are Student's t test, Wilcoxon test (UAC, copeptin, creatinine and triglycerides) or Fisher's exact test. BP, blood pressure. MI, myocardial infarction. eGFR, estimated glomerular filtration rate computed by the CKD EPI formula. UAC: urinary albumin concentration. ACE-I: angiotensin converting enzyme inhibitor. ARB: angiotensin receptor blocker. p<0.05 was significant.

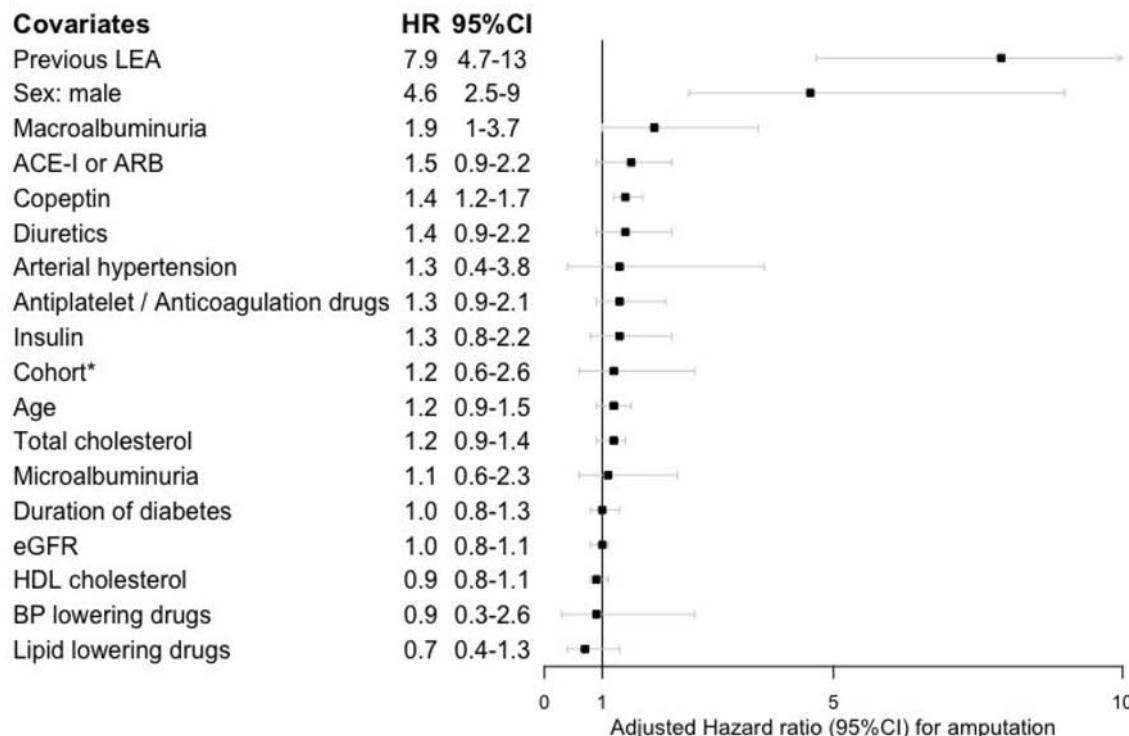
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Supplementary Figure S1. Baseline covariates and risk for LEA during follow-up for Type 1 (A) and Type 2 (B) diabetes cohorts

A



B



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Cox proportional hazards survival regression analysis. Hazard ratio (HR) computed for 1 SD of log for quantitative covariates. Regression models for Type 1 or Type 2 diabetes cohorts correspond to model 2 as shown in Table 2. BP: blood pressure. UAC: urinary albumin concentration. ACE-I: angiotensin converting enzyme inhibitor. ARB: angiotensin receptor blocker. *Data expressed for GENEDIAB for Type 1 diabetes cohorts and SURDIAGENE for Type 2 Diabetes cohorts. p<0.05 is significant.

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Supplementary Figure S2. Kaplan-Meier curves (cumulative incidence) for the requirement of lower extremity revascularization during follow-up by tertiles (T) of baseline plasma copeptin in Type 2 diabetes cohorts. Log-rank test chi-square = 24.4, p<0.0001.

