

SUPPLEMENTARY DATA

Supplementary Table 1. Baseline characteristics of the cohort stratified by presence of NAFLD at baseline.

Variables	Without NAFLD (n=130)	With NAFLD (n=131)	P value
Sex (M/F)	48/82	68/63	<0.05
Age (years)	38±12	45±12	<0.001
Diabetes duration (years)	14 (9-20)	21 (14-33)	<0.001
BMI (kg/m ²)	22.7±3.4	26.3±4.9	<0.001
Waist circumference (cm) ^a	80.8±15	98.6±17	<0.001
Current smokers (%)	22	27	0.41
Systolic blood pressure (mmHg)	124±16	133±17	<0.001
Diastolic blood pressure (mmHg)	76±8	80±9	<0.005
Fasting glucose (mmol/l)	10.3±4.1	10.8±4.2	0.39
A1C (%)	7.8±1.0	8.2±1.1	<0.005
A1C (mmol/mol)	61.7±7	66.1±7.7	<0.005
Triglycerides (mmol/l)	0.89 (0.66-1.21)	1.20 (0.84-1.81)	<0.001
HDL cholesterol (mmol/l)	1.49±0.4	1.33±0.4	<0.005
LDL cholesterol (mmol/l)	2.50±0.6	2.82±0.8	<0.005
eGFR _{MDRD} (ml/min/1.73 m ²)	92.1 (77-111)	85.9 (73-99)	<0.001
eGFR _{EPI} (ml/min/1.73 m ²)	104.8 (86-118)	96.9 (80-108)	<0.001
Urinary ACR (mg/mmol)	0.5 (0.2-2)	2.1 (0.5-3)	<0.001
Microalbuminuria (%)	3	18	<0.001
Hypertension (%)	27	60	<0.001
Diabetic retinopathy, any degree (%)	51	72	<0.001
Anti-hypertensive drug users (%)	17	48	<0.001
Metabolic syndrome (%)	18	52	<0.001
Insulin dose (U/day)	36 (25-48)	48 (32-62)	<0.001
AST (U/l)	17 (12-24)	18 (13-24)	0.11
ALT (U/l)	18 (14-24)	22 (14-28)	<0.05
GGT (U/l)	14 (10-19)	22 (13-38)	<0.005
ALT ≥30 U/l (%)	15	24	0.08

Cohort size: n=261. ^a Measurement of waist circumference was available in 102 patients only. All other parameters were available in all patients.

Data are expressed as means ± SD, medians (interquartile ranges) or proportions. Differences are assessed by the unpaired-*t* test (for continuous variables) and by the chi-squared test (for categorical measures). Hypertension was defined as blood pressure ≥140/90 mmHg or treatment. The metabolic syndrome was defined by a modified Adult Treatment Panel (ATP) III definition.

ACR, urinary albumin-to-creatinine ratio. BMI, body mass index. HbA1c, hemoglobin A1c. HDL, high density lipoprotein. LDL, low density lipoprotein. eGFR, estimated glomerular filtration rate. AST, aspartate aminotransferase. ALT, alanine aminotransferase. GGT, gamma-glutamyltransferase. NAFLD, non-alcoholic fatty liver disease.

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Supplementary Table 2. Univariate and multivariate Cox regression analyses showing associations of NAFLD and other factors with risk of incident CKD_{EPI} among type 1 diabetic adults.

	Univariate analysis	P-value	Multivariate model 1	P-value	Multivariate model 2	P-value	Multivariate model 3	P-value
NAFLD (yes vs. no)	10.8 (3.33-34.9)	<0.001	7.74 (2.25-26.6)	<0.005	7.23 (2.10-25.2)	<0.005	8.62 (1.73-42.9)	<0.01
Sex (F vs. M)	1.13 (0.60-2.14)	0.70	1.02 (0.52-2.01)	0.96	0.48 (0.21-1.10)	0.10	0.61 (0.20-1.91)	0.40
Age (years)	1.03 (1.02-1.05)	<0.005	1.01 (0.97-1.04)	0.81	0.98 (0.94-1.04)	0.31	0.99 (0.93-1.05)	0.69
Diabetes duration (years)	1.03 (1.01-1.05)	<0.005	1.01 (0.96-1.03)	0.51	1.01 (0.96-1.03)	0.80	1.01 (0.96-1.06)	0.72
Hypertension (yes vs. no)	6.34 (1.83-14.9)	<0.001	3.94 (1.54-10.1)	<0.005	3.71 (1.41-9.74)	<0.01	2.53 (0.85-7.89)	0.09
A1C (%)	1.25 (1.06-1.48)	<0.01	1.15 (0.92-1.42)	0.22	1.10 (0.90-1.35)	0.40	1.14 (0.87-1.50)	0.35
eGFR _{EPI} (ml/min/1.73 m ²)	0.93 (0.91-0.96)	<0.001			0.94 (0.92-0.97)	<0.001	0.95 (0.91-0.99)	<0.01
Urinary ACR (mg/mmol)	1.11 (1.08-1.15)	<0.001						
BMI (kg/m ²)	1.06 (1.01-1.12)	<0.05						
Smokers (yes vs. no)	1.41 (0.59-3.33)	0.44						
Triglycerides (mmol/l)	1.01 (1.01-1.03)	<0.005						
HDL cholesterol (mmol/l)	0.99 (0.97-1.01)	0.53						
LDL cholesterol (mmol/l)	1.01 (0.98-1.01)	0.55						

Cohort size: n=261. Data are expressed as hazard ratios (\pm 95% confidence intervals) by Cox regression analysis. Incident CKD was defined as occurrence of macroalbuminuria and/or e-GFR_{EPI} <60 ml/min/1.73 m² as estimated by the CKD-EPI study equation. CKD_{EPI} identified 38 subjects who developed CKD during the follow-up.

Multivariable regression model 1: adjustment for age, sex, duration of diabetes, A1C and hypertension (blood pressure \geq 140/90 mmHg or drug treatment).

Multivariable regression model 2: adjustment for age, sex, duration of diabetes, A1C, hypertension and baseline eGFR_{EPI}

Multivariable regression model 3: adjustment for the same covariates as model 2 after excluding those (n=27) with microalbuminuria at baseline.

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Supplementary Table 3A. Reclassification of risk based on regression model 1 according to the inclusion or exclusion of NAFLD for subjects in whom CKD_{MDRD} developed and for those in whom CKD_{MDRD} did not develop.

OUTCOME: CKD _{MDRD}		Regression model 1 with NAFLD				Total at risk
		0 to 5%	5 to 10%	10 to 20%	>20%	
Regression model 1 without NAFLD						
0 to 5%	CKD follow-up: No	53	2	0	0	55
	CKD follow-up: Yes	8	1	0	0	9
5 to 10%	CKD follow-up: No	18	24	5	0	47
	CKD follow-up: Yes	1	8	4	0	13
10 to 20%	CKD follow-up: No	0	21	24	9	54
	CKD follow-up: Yes	0	0	6	2	8
>20%	CKD follow-up: No	0	0	10	34	44
	CKD follow-up: Yes	0	0	2	29	31
Total no.	CKD follow-up: No	71	47	39	43	200
	CKD follow-up: Yes	9	9	12	31	61
NRI (%)		10.5				
P value		<0.001				

Multivariable regression model 1: adjustment for age, sex, diabetes duration, A1C and hypertension. NRI, net reclassification improvement.

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Supplementary Table 4A. Reclassification of risk based on regression model 1 according to the inclusion or exclusion of NAFLD for subjects in whom CKD_{CKD-EPI} developed and for those in whom CKD_{CKD-EPI} did not develop.

OUTCOME: CKD _{CKD-EPI}		Regression model 1 with NAFLD				Total at risk
		0 to 5%	5 to 10%	10 to 20%	>20%	
Regression model 1 without NAFLD						
0 to 5%	<i>CKD follow-up: No</i>	109	7	1	0	117
	<i>CKD follow-up: Yes</i>	5	2	0	0	7
5 to 10%	<i>CKD follow-up: No</i>	25	3	15	0	43
	<i>CKD follow-up: Yes</i>	0	4	4	0	8
10 to 20%	<i>CKD follow-up: No</i>	14	0	10	8	32
	<i>CKD follow-up: Yes</i>	0	0	6	2	8
>20%	<i>CKD follow-up: No</i>	2	5	4	20	31
	<i>CKD follow-up: Yes</i>	0	2	0	13	15
Total no.	<i>CKD follow-up: No</i>	150	15	30	28	223
	<i>CKD follow-up: Yes</i>	5	8	10	15	38
NRI (%)		10.2				
P value		<0.005				

Multivariable regression model 1: adjustment for age, sex, diabetes duration, A1C and hypertension. NRI, net reclassification improvement.

SUPPLEMENTARY DATA

Supplementary Table 4B. Reclassification of risk based on regression model 2 according to the inclusion or exclusion of NAFLD for subjects in whom CKD_{CKD-EPI} developed and for those in whom CKD_{CKD-EPI} did not develop.

OUTCOME: CKD _{CKD-EPI}		Regression model 2 with NAFLD				Total at risk
		0 to 5%	5 to 10%	10 to 20%	>20%	
Regression model 2 without NAFLD						
0 to 5%	<i>CKD follow-up: No</i>	132	7	0	0	139
	<i>CKD follow-up: Yes</i>	5	1	0	0	6
5 to 10%	<i>CKD follow-up: No</i>	18	7	8	0	33
	<i>CKD follow-up: Yes</i>	0	2	4	0	6
10 to 20%	<i>CKD follow-up: No</i>	11	0	7	5	23
	<i>CKD follow-up: Yes</i>	0	0	4	3	7
>20%	<i>CKD follow-up: No</i>	2	6	2	18	28
	<i>CKD follow-up: Yes</i>	0	0	1	18	19
Total no.	<i>CKD follow-up: No</i>	163	20	17	23	223
	<i>CKD follow-up: Yes</i>	5	3	9	21	38
NRI (%)						
P value		=0.01				

Multivariable regression model 2: adjustment for age, sex, diabetes duration, A1C, hypertension and baseline eGFR.

NRI, net reclassification improvement.