The role of coronary artery calcification testing in incident coronary artery disease risk prediction in type 1 diabetes

ESM Table 1. Baseline clinical characteristics of participants between those with and without repeated CAC measures

Characteristics (N=292)	Had repeated CAC measures	
	No (n=93)	Yes (n=199)
Age, years	40.5 (7.5)	36.5 (7.1)**
Diabetes duration, years	33.0 (7.7)	27.9 (6.8)**
Age at diabetes onset, years	7.5 (4.1)	8.7 (4.1)*
Female, % (*n*)	45.2 (42)	53.3 (106)
Ever smoker, % (*n*)	41.9 (39)	35.2 (70)
High WHR, % (*n*)[a]		
Male sex	19.6 (10)	7.5 (7)
Female sex	31.0 (13)	21.7 (23)
BMI, kg/m^2	26.8 (4.3)	25.2 (3.6)**
Pulse rate, beats/min	118.7 (15.6)	114.1 (15.2)*
Systolic BP, mmHg	69.7 (10.9)	69.7 (10.2)
Diastolic BP, mmHg	28.0 (26)	21.1 (42)
Hypertension, % (*n*)	66 (8.2%)	67 (8.3%)
AER, μg/min[b]	11.4 (5.6, 64.0)	10.5 (5.3,44.5)
HDL-cholesterol, mmol/l		
Male sex	1.3 (0.3)	1.2 (0.3)
Female sex	1.7 (0.5)	1.6 (0.4)
Non-HDL-cholesterol, mmol/l	3.4 (1.0)	3.5 (0.9)
Statin use, % (*n*)	24.7 (23)	2.0 (4)**
Baseline CAC score		
Agatston[b]	6.6 (0, 116.2)	0 (0, 28.1)**
Volume[b]	6.7 (0, 143.2)	0 (0, 32.9)**
Density	1.7 (2.0)	1.1 (1.4)**

Categorical variables are presented as percentage (number) and continuous variables as mean (SD) or median (first and third quartiles)

[a]High WHR was defined as >1.0 for men or >0.85 for women

[b]Log_e transformed before statistical testing

*p<0.05 and **p<0.01 for the comparison between those with and without repeated CAC measures

WHR, waist–hip ratio

ESM Table 2. Associations between annual CAC progression (in quantiles) and incident CAD events (including cases occurred between the two CAC scans)

CAC measures (n=199, events=55 [18 out of the 55 events occurred between the two CAC scans])		Unadjusted		Adjusted[a]	
		HR (95%CI)	*p* value	HR (95%CI)	*p* value
Volume					
Progression[b]	Q1	ref		ref	
	Q2	1.7 (0.5, 6.1)	0.421	1.9 (0.5, 7.1)	0.327
	Q3	4.0 (1.3, 11.8)	0.013	4.0 (1.2, 13.3)	0.024
	Q4	5.5 (1.8, 17.0)	0.003	5.1 (1.4, 18.7)	0.013
Baseline	0	ref		ref	
	1-99	2.0 (0.9, 4.2)	0.078	1.9 (0.8, 4.4)	0.141
	100-399	1.9 (0.8, 4.7)	0.168	1.6 (0.6, 4.7)	0.360
	≥ 400	6.2 (2.3, 16.6)	<0.001	5.5 (1.7, 17.9)	0.004
Agatston score					
Progression[b]	Q1	ref		ref	
	Q2	1.3 (0.3, 5.4)	0.750	1.4 (0.3, 6.0)	0.674
	Q3	3.5 (1.1, 10.9)	0.028	4.0 (1.2, 14.0)	0.029
	Q4	6.1 (1.9, 19.7)	0.003	4.8 (1.3, 17.6)	0.019
Baseline	0	ref		Ref	
	1-99	1.7 (0.8, 3.8)	0.188	1.6 (0.7, 3.9)	0.300
	100-399	1.5 (0.6, 4.0)	0.452	1.4 (0.5, 4.4)	0.525
	≥ 400	4.1 (1.5, 11.7)	0.006	4.1 (1.3, 12.8)	0.014

Baseline and progression of CAC were included in the same model

[a]Adjusted for sex, diabetes duration, ever smoking, BMI, HbA1c, cholesterol (HDL and non-HDL), urinary AER, hypertension and the use of statins

[b]CAC progression was defined as the annualised difference in square root between baseline and follow-up CAC measures

ESM Table 3. Likelihood ratio tests for model fit evaluation

Subjects	Model[a]	-2Log Likelihood	*p* value
Total (n=292)	Base	692.542	_
	Base+ baseline Agatston	677.988	<0.001 (vs Base)
	Base+ baseline volume	675.307	<0.001 (vs Base)
In those baseline CAC>0 (n=144)	Base	470.385	_
	Base+ baseline volume	466.666	0.054 (vs Base)
	Base+ baseline volume+density	460.050	0.006 (vs Base) 0.010 (vs Base+ volume)
In those with two CAC scans (n=181)	Base	292.420	_
	Base+ baseline Agatston	288.975	0.063 (vs Base)
	Base+ baseline and progression in Agatston	285.800	0.010 (vs Base) 0.074 (vs Base + baseline Agatston)
	Base+ baseline volume	288.216	0.040 (vs Base)
	Base+ baseline and progression in volume	284.120	0.004 (vs Base) 0.043 (vs Base+ baseline volume)

[a]Base model was adjusted for sex, diabetes duration, ever smoking, BMI, HbA_{1c}, cholesterol (HDL and non-HDL), urinary AER, hypertension and the use of statins.

ESM Table 4. C-statistics for Cox model comparison

Participants	Model [a]	CAD C statistic (SE)	*p* value
Total (n=292)	Base	0.795 (0.047)	_
	Base+ baseline Agatston	0.847 (0.041)	0.045 (vs Base)
	Base+ baseline volume	0.848 (0.041)	0.037 (vs Base)
In those with two CAC scans (n=181)	Base	0.764 (0.129)	_
	Base+ baseline Agatston	0.822 (0.115)	0.363 (vs Base)
	Base+ baseline and progression in Agatston	0.829 (0.106)	0.352 (vs Base) 0.783 (vs Base + baseline Agatston)
	Base+ baseline CAC volume	0.820 (0.114)	0.388 (vs Base)
	Base+ baseline and progression in volume	0.827 (0.106)	0.329 (vs Base) 0.571 (vs Base+ baseline volume)

[a]Base model was adjusted for sex, diabetes duration, ever smoking, BMI, HbA_{1c}, cholesterol (HDL and non-HDL), urinary AER, hypertension and the use of statins.

SE: standard error

ESM Table 5. Continuous net reclassification improvement (NRI) for Cox model comparison

Participants	Model[a]	CAD NRI (95% CI)	*p* value
Total (n=292)	Base+ baseline Agatston vs Base	0.283 (0.001, 0.513)	0.048
	Base+ baseline volume vs Base	0.315 (0.038,0.530)	0.028
In those with two CAC scans (n=181)	Base+ baseline Agatston vs Base	0.202 (-0.158, 0.553)	0.209
	Base+ baseline and progression in Agatston vs Base	0.380 (-0.159, 0.639)	0.189
	Base+ baseline and progression in Agatston vs Base + baseline Agatston	0.281 (-0.553, 0.591)	0.458
In those with two CAC scans (n=181)	Base+ baseline volume vs Base	0.226 (-0.199, 0.539)	0.299
	Base+ baseline and progression in volume vs Base	0.255 (-0.131, 0.584)	0.159
	Base+ baseline and progression in volume vs Base + baseline volume	0.091 (-0.434, 0.455)	0.697

[a]Base model was adjusted for sex, diabetes duration, ever smoking, BMI, HbA1c, cholesterol (HDL and non-HDL), urinary AER, hypertension and the use of statins.