Pulse wave velocity is an independent risk factor for cardiovascular events, mortality and diabetic kidney disease in patients with type 1 diabetes

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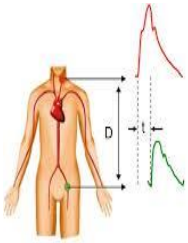
Objective

- The prognostic significance of carotid-femoral pulse wave velocity (cfPWV) - the gold standard measure of arterial stiffness - remains to be determined in patients with type 1 diabetes (T1D)

- We investigated the predictive value of cfPWV for development of cardiovascular events, mortality and decline in renal function in T1D

Methods

- Prospective study including 652 patients recruited at Steno Diabetes Center Copenhagen and stratified by levels of albuminuria (normo-, micro- and macroalbuminuria)
- Eligibility:
  - Type 1 DM
  - ≥18 years of age
  - No ESRD and eGFR ≥ 15 ml/min/1.73m2
- cfPWV was measured at baseline using the SphygmoCor device



Methods

- Endpoints were traced through National Registers until 31st December 2016 and comprised:
  - Composite CVE (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and coronary or peripheral arterial interventions)
  - All-cause mortality
- Information regarding eGFR and UAER during follow up was obtained at outpatient visits and electronic laboratory records. The renal endpoints comprised:
  - Decline in eGFR >30%
  - Progression from normo- to micro/macroalbuminuria or from micro-to macroalbuminuria
  - Yearly changes in eGFR and UACR
- Median follow-up: 5.2-6.2 years

Baseline characteristics

	cfPWV in quartiles				P
	< 7.9 m/s	≥ 7.9 ≤ 9.8 m/s	> 9.8 < 12.4 m/s	≥ 12.4 m/s	
Number	160	168	158	166	
Male, %	50	54	53	65	**0.036**
Age (years)	43.0 ± 12.3	52.0 ± 9.1	58.3 ± 8.8	63.81 ± 9.0	**< 0.001**
Diabetes duration (years)	20.3 ± 14.5	30.3 ± 12.6	35.8 ± 13.8	44.1 ± 11.8	**< 0.001**
BMI (kg/m^2)	25.1 ± 9.2	25.1 ± 4.5	25.2 ± 4.0	25.7 ± 3.9	0.34
Smokers,%	18	25	26	16	0.18
HbA_{1c} (mmol/mol)	63 ± 13	65 ± 12	66 ± 13	63 ± 11	0.38
UAER (mg/24-h)	11 (7-19)	13 (7-39)	25 (9-123)	35 (12- 129)	**< 0.001**
eGFR (ml/min/1.73m^2)	96.5 ± 22.6	85.9 ± 22.4	75.6 ± 24.9	67.2 ± 24.8	**< 0.001**
Mean arterial pressure (mmHg)	89 ± 8	93 ± 10	95 ± 10	98 ± 11	**< 0.001**
LDL cholesterol (mmol/L)	2.5 ± 0.7	2.5 ± 0.8	2.4 ± 0.7	2.5 ± 0.8	0.52

Data are %, mean ± SD or geometric mean (IQR). P for trend across quartiles

Results of Cox regression analyses

	Composite CVE (n=81)		All-cause mortality (n=48)		Decline in eGFR>30% (n=90)		Progression in albuminuria (n=34)	
Model	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Unadjusted	1.75 (1.48-2.08)	**<0.001**	1.97 (1.58-2.45)	**<0.001**	1.57 (1.52-1.86)	**<0.001**	1.19 (1.10-1.29)	**<0.001**
Adjusted	1.31 (1.01-1.70)	**0.045**	1.39 (1.03-1.89)	**0.033**	1.39 (1.07-1.81)	**0.015**	1.09 (0.96-1.22)	0.17
rIDI, %	1.4	0.74	2.3	0.48	8.3	**<0.001**	8.8	0.49

Hazard ratios represent risk related to 1 SD increase in cfPWV (3.38 m/s) .
Adjustment included sex, age, mean arterial pressure, LDL cholesterol, smoking, HbA1c, UACR and eGFR
rIDI: relative integrated discrimination improvement.

Association between cfPWV and yearly change in eGFR and UACR

	Yearly change in eGFR (n=492)		Yearly change in UACR (n=489)	
Model	**β (SE)**	**P**	**β (SE)**	**P**
Unadjusted	- 0.35 (0.11)	**0.0022**	0.0037 (0.009)	**<0.001**
Adjusted	- 0.39 (0.15)	**0.0090**	0.038 (0.012)	**0.0019**

The β estimates represent the effect 1 SD increase in cfPWV (3.38 m/s)
Adjustment included sex, age, mean arterial pressure, LDL cholesterol, smoking, HbA1c, UACR and eGFR at baseline

Conclusions

- In patients with T1D, higher arterial stiffness was consistently associated with at higher risk of CVE, mortality and decline in kidney function independent of traditional risk factors
- In addition, it contributes significant discrimination, beyond traditional risk factors for decline in kidney function