Large and small artery crosstalk in patients with type 2 diabetes

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Introduction

Large artery stiffness is associated with microvascular disease in patients with type 2 diabetes.
Thus crosstalk between large and small blood vessels has been suggested to partake in the pathogenesis of microvascular complications to diabetes.
Indeed, vasoreactivity in the retina has been shown to be attenuated in patients with type 2 diabetes and to be associated with the degree of pathological changes in the retina's blood supply.

The mechanism behind this possible crosstalk is poorly understood though. In this study we examine a group of well regulated type 2 diabetics in an attempt to elucidate some of the early perturbations in the autoregulation of the retina's blood supply.

Hypothesis

Large artery stiffness and endothelial dysfunction is associated with dysfunction of the retinal vessels in type 2 diabetics.

Aim

To assess whether large artery stiffness and endothelial dysfunction is associated with perturbations in the retinal vessel function in patients with type 2 diabetes.

Method

16 type 2 diabetics and 14 controls have been recruited so far. 20+20 scheduled.

Arterial stiffness was assessed by carotid-femoral PWV using the SphygmoCor device. Endothelial function was assessed using EndoPAT.

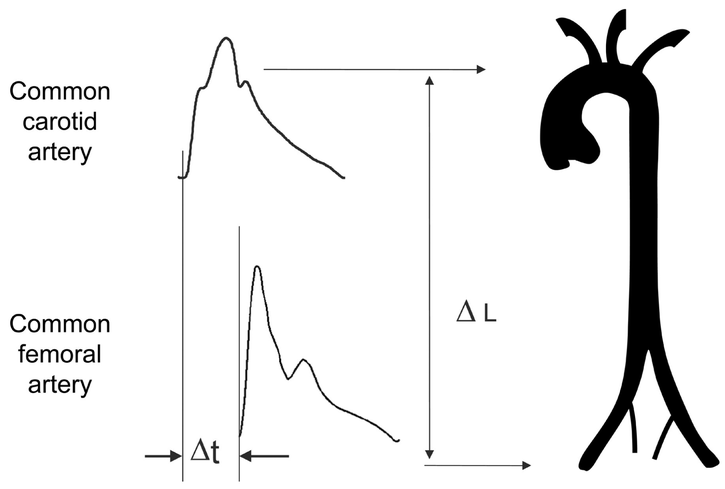

Figure 1. Background for measurement of cfPWV.
Laurent, S., et al. (2006). Eur Heart J **27**(21): 2588-2605

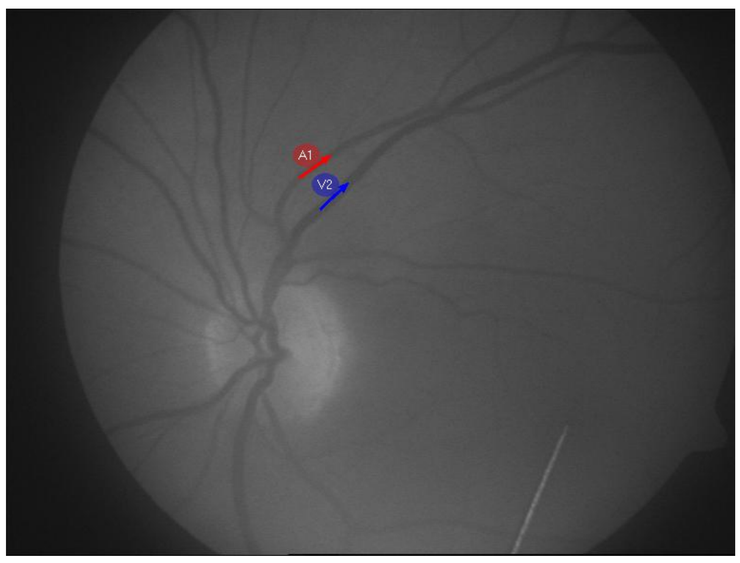

Figure 2. Still from the Retinal Vessel Analysis

Retinal blood regulation was examined using the Retinal Vessel Analyzer under three conditions:

i. Isometric exercise, that raises systemic blood pressure
ii. Flicker light stimulation, that raises the metabolic demand of the retina
iii. Combination of the two abovementioned interventions

Results

	T2DM (n = 16)	Controls (n = 14)	p-value
Age (y)	65.8±8.9	66.8±7.4	0.72
Male sex (%)	7 (44)	7 (50)	0.73
Diabetes duration (y)	9.5±1.8	n/a	
24h blood pressure (mm Hg)			
Systolic	121±12[1]	124±8[2]	0.41
Diastolic	71±7[1]	74±9[2]	0.37
HbA1C (mmol/mol)	50±7	39±3	<0.001
Total cholesterol, (mmol/L)	3.9±1.0	5.1±0.7	<0.001
HDL, (mmol/L)	1.43±0.51	1.81±0.48	0.045
LDL, (mmol/L)	1.84±0.90	2.92±0.86	<0.01
Triglycerides, (mmol/L)	1.39±0.49	0.85±0.25	<0.001
Urinary albumin:creatinine ratio	6.00±9.91[4]	9.93±24.55	0.22
Smoking status			
Current, n (%)	4 (25)	1 (7)	
Former n (%)	5 (31)	5 (36)	
Never, n (%)	7 (44)	8 (57)	
Previous CVD, n (%)	2 (13)	0 (0)	0.17
In antihypertensive treatment, n (%)	13 (81)	4 (29)	<0.01
Diabetes treatment			
Metformin, n (%)	13 (81)	n/a	
Sulfonylureas, n (%)	2 (13)	n/a	
GLP-1 agonist, n (%)	1 (6)	n/a	
DPP4 inhibitor, n (%)	4 (25)	n/a	
Insulin, n (%)	4 (25)	n/a	
Acetylsalicylic acid, n (%)	14 (88)	3 (21)	<0.001
Statin, n (%)	15 (94)	3 (21)	<0.001

[1] n = 15 [2] n = 12 [3] n = 13 [4] n = 15

Table 1. Baseline characteristics.

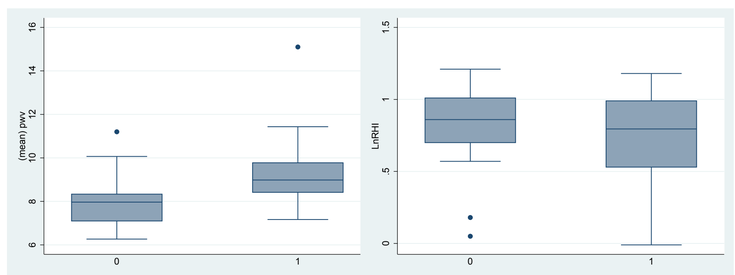

Figure 3. 0: Controls 1: T2DM
Left: Patients with type 2 diabetes have significantly higher cfPWV than controls (p=0.045).
Right: There is no significant difference in LnRHI (a measure of endothelial function) between the two groups (p=0.67).

There was no significant difference among the groups in vasoreactivity to any of the three interventions. Nor among the groups as to change in diameter during interventions or any association between diameter change and cfPWV or LnRHI.

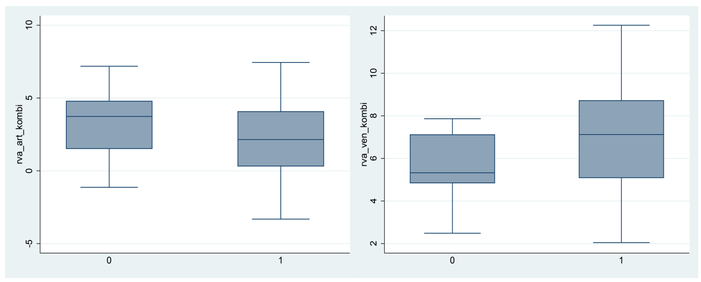

Figure 4. 0: Controls 1: TDM
Retinal vessel analysis during combination of isometric exercise and flicker light stimulation. Diameter change is shown in percentage.
Left: Arteriole (p=0.21). Right: Venule (p=0.23).

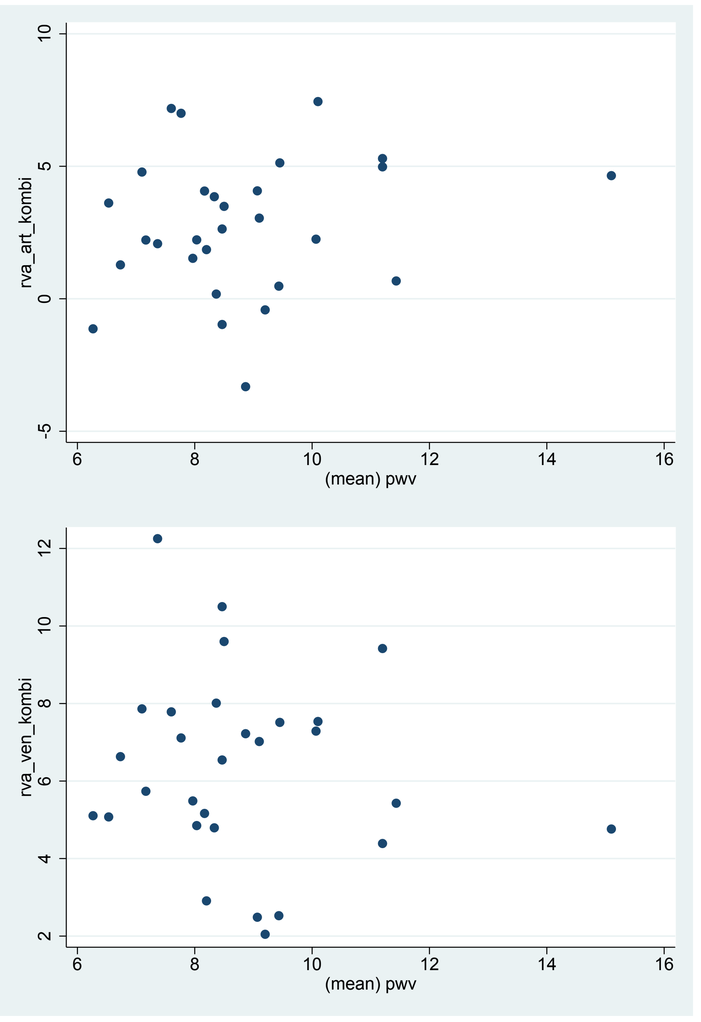

Figure 5. Scatter plots of data from the retinal vessel analysis. Diameter change in percentage and mean cfPWV.
Top: Arteriole (p=0.33). Bottom: Venule (p=0.50).

Conclusions

Type 2 diabetics had significantly higher measures of arterial stiffness than controls. There was, however, no difference among the groups regarding endothelial function or vasoreactivity.
There was no association between vasoreactivity and arterial stiffness or endothelial function in the two groups. We did not find any evidence of crosstalk between large and small arteries in this group of type 2 diabetics.

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