Quantitative carotid blood flow and response to pharmacological stress in pre-diabetes and type-2 diabetes

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Introduction: High stroke risk is associated with type-2 diabetes mellitus (T2DM). Post-stroke recovery is particularly poor in people with T2DM. Arterial cerebral blood flow and the ability to increase the brain's arterial blood supply under vascular stress (cerebrovascular reserve or CVR) are vital in the context of potential cerebral ischemia. This study sought to quantify internal carotid artery (ICA) blood flow and any response to a potent carbonic anhydrase inhibitor (pharmacological vasodilator)[1] in subjects with T2DM, Impaired Glucose Tolerance (IGT or pre-diabetes) and normative controls.

Method: The cohort consisted age– and sex-matched, stroke-free groups of subjects with T2DM, IGT and healthy volunteers (HV) [see table]. Flow assessment was performed at 3T (Achieva 3.0T, Philips, Netherlands) on each subject pre and 30min post intravenous infusion of 1g acetazolamide (Diamox sodium perenteral). An 8-chanel array receive-only head coil was used for quantitative flow assessment, based on a single-slice, multi-phase, fast-field echo sequence encoding flow parallel to the slice-encode direction, approximately 3cm distal to the carotid bifurcation. The resultant cine sequence (TE = 3.7ms; TR = 7.7ms; field echo single shot interval = 16ms; flip angle = 100^0; in-plane acquisition resolution = 1.72mm x 1.60mm, interpolated to 0.86mm x 0.86mm; slice thickness = 5mm) sampled k-space using a continuous, linear ordered, phase-encoded scheme. Vector ECG was used to retrospectively gate 40 time points over the cardiac cycle. A constant velocity encoding factor was used for all subjects (120cm/s). Second-order residual background phase offset errors were minimized by using low-pass filtering and concomitant gradient correction techniques. Quantitative flow-encoded information (flow and velocity) was extracted via region of interest (ROI) analysis. Macrovascular CerebroVascular Reactivity within the carotid artery was calculated as:

$CVR_{ICA} = [(flow_{post} – flow_{pre})/flow_{pre}] \times 100$

	Healthy volunteers (n=18)	Impaired glucose tolerance (n=12)	Type 2 Diabetes (n= 13)	p-value
Age (years)	52.6 (10.5)	54.8 (5.3)	56.9 (13.4)	0.677
Height (m)	1.69 (0.1)[*]	1.7 (0.08)[*]	1.68 (0.08)	0.839
Weight	72.9 (10.8)[*]	93.3 (13.3)[†]	87.7 (10.6)	<0.001
BMI (Kg/m^2)	25.7 (4.2)[*]	32.3 (3.2)[*]	31.2 (3.9)	<0.001

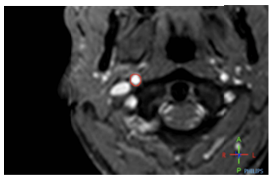

Figure 1. ICA ROI placement.

Results: Resting ICA velocity was significantly lower in patients with T2DM [14.4(2.6)cm/s] compared to HV's [17.6(3.2)cm/s] (p=0.05). All groups demonstrated significant increases in flow and velocity post-ACZ (p=<0.001, Fig 2). CVR_{ICA} was significantly greater in HV [59(15)%] compared to T2DM [46(16)%; p<0.05] and IGT [40(20)%; p<0.01], Fig 3.

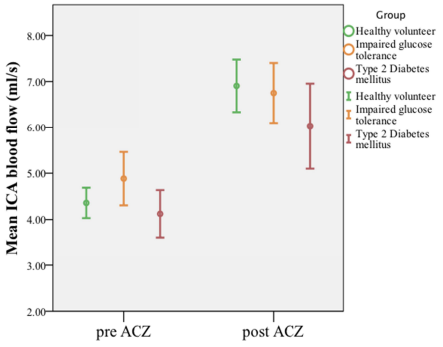

Fig 2. ICA blood flow pre and post acetazolamide (ACZ).

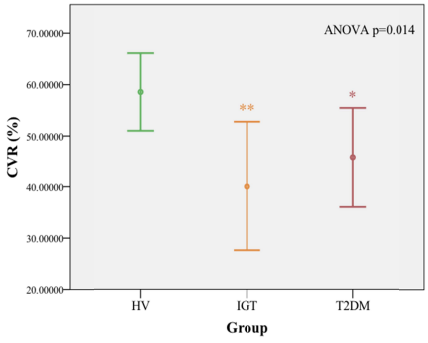

Fig 3. ICA-cerebrovascular reserve (CVR_{ICA}) * p<0.05, **p<0.01

Discussion: Neuro-macrovascular response to pharmacological stress appears to be lower in T2DM *and* IGT than in HV's. The ability to adapt to vascular demand may be a factor in stroke risk and post-stroke recovery and our observations may thus be important. This technique may provide a useful marker of vascular functional abnormality in the context of T2DM, particularly in early-stage, IGT (pre-diabetes).

Reference: 1. Reeve J.M. et al. Quantification of carotid artery blood flow before and after the acetazolamide challenge. ISMRM Stockholm, 2010.