The use of non-invasive MRI to quantify the effect of secretin on pancreatic blood flow and perfusion in healthy volunteers

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Background: Alterations in pancreatic blood flow have been implicated in pancreatic inflammation and pain [1]. However, there are few methods to assess pancreatic blood flow and these are generally invasive, using ionising radiation or intravenous contrast media [2], limiting repeat measures. Secretin stimulation is used to assess alterations in blood flow [3], and used clinically in the assessment of sphincter of Oddi dysfunction [4]. In this study non-invasive MRI is used to assess the temporal response to secretin stimulation. Flow within the arteries supplying the pancreas is assessed using Phase Contrast MRI (PC-MRI) and pancreatic perfusion using Arterial Spin Labeling (ASL) [5], with a respiratory-triggered ASL method employed to minimise motion artefacts which otherwise limit abdominal ASL [6].

Methods: The study was approved by the local ethics committee, and all volunteers gave informed, written consent. 12 healthy male volunteers (median age 24 yrs (18-60 yrs)) attended following an overnight fast. Imaging was performed using a 1.5T Philips Achieva scanner (body transmit coil, 16-channel SENSE torso receive coil). The MR protocol consisted of repeated non-invasive measurements of: vessel flow in the superior mesenteric artery (SMA), common hepatic artery (HA), splenic artery (SA) and gastroduodenal artery (GDA); pancreatic tissue perfusion; and pancreatic volume, data collected in this order. An equilibrium M0 scan and IR data for T1 mapping [6] were also acquired for perfusion quantification. Flow, pancreatic perfusion and volume measures were acquired prior to intravenous (IV) secretin (11U/kg) administration and repeated every 10 minutes following administration.

Vessel flow: Multi-slice balanced Turbo Field Echo (bTFE) images were initially acquired in 3 orthogonal planes to locate the vessels of interest to aid slice positioning. PC-MRI, with a single slice perpendicular to the vessel of interest, was acquired with 15 phases across the cardiac cycle (TFE, TE/TR = 4.1/7.3-8.6 ms, FA 25°, NSA 2, SENSE 3, resolution 1.17x1.17x6 mm3, TFE factor = 3-4 (dependent on subjects’ heart rate), Venc = 70/100/120/200 cm/s for GDA/HA/SA/SMA). Each PC measurement was acquired in a single 15-20 s breath hold.

Perfusion: Respiratory-triggered FAIR ASL (288x324 mm FOV, 3x3x8 mm3 voxel, 3 sagittal-oblique slices across the body and tail of the pancreas, label delay = 1100 ms, in-plane saturation) with True-FISP readout was used (TE/TR = 1.8/3.6 ms, SENSE 2, FA 60°, linear acquisition, and half-Fourier acquisition) [6]. Each ASL measurement was acquired with 30 ASL pairs, taking approximately 4 mins.

Volume: Transverse bTFE with 35 contiguous slices to cover the whole pancreas (FOV 400x400 mm, 2x1.76x5 mm3, TE/TR = 1.7/3.3 ms, FA 80°, SENSE 2) were collected in a single 15 s breath hold.

Data Analysis: Vessel flow: Philips Q-flow software (Philips Medical Systems) was used to draw a region of interest (ROI) over the vessel of interest, and the mean artery flow (ml/s) over the cardiac cycle, across the vessel, was calculated.

Perfusion: For each time point, ASL tag and control images were motion corrected to the base M0 image using FSL (FMRI Research Library Software) and individual difference images (label-control) calculated [7] and averaged to create a single perfusion weighted difference map (ΔM). A mask was formed from the base M0 image to encompass the pancreatic tissue (body and tail of the pancreas) whilst avoiding major vessels. Mean values of ΔM, M0 and T1 were then used in the kinetic model [8] to calculate pancreatic tissue perfusion (f).

Volume: Analyze® software was used to manually trace around the pancreas, excluding vessels, volume measures were then summed across all slices and the total pancreatic volume calculated.

Results: Median (IQR) baseline parameters were: pancreatic perfusion (N=10) = 186 (176-264) ml/100g/min, pancreatic volume (N=12) = 89 (75-106) ml, SMA flow (N=12) = 6.4 (4.9-5.5) ml/s, GDA flow (N=9) = 0.9 (0.8-1.5) ml/s, HA flow (N=11) = 4.4 (2.8-5.3) ml/s and SA flow (N=12) = 7.0 (5.3-9.7) ml/s. Figure 1 shows the response of each parameter to secretin administration at time 0 min. There was a significant change in pancreatic perfusion from baseline (Fig 1A, p=0.025, ANOVA), with a maximal rise seen at 4 min (36 (8-39) ml/100g/min). There was no significant change in the pancreatic volume (Fig 1B). A significant increase from baseline in arterial blood flow was seen immediately after injection in both the SMA (Fig 1C, p<0.0001, ANOVA) and GDA (Fig 1D, p=0.015, ANOVA), with maximum SMA flow of 15 (12-18) ml/s above baseline (~235% increase), and maximum GDA flow of 1.1 (0.7-1.8) ml/s above baseline (~122% increase). A reduction from baseline in hepatic artery blood flow was observed (Fig 1E, not significant) with a maximum decrease of 1.3 (1.8-0.3) ml/s below baseline. No change in splenic artery flow was seen (Fig 1F), however this may be due to the tortuous nature and small size of this vessel limiting the assessment of such changes.

Discussion and Conclusion: Our baseline pancreatic perfusion values are in agreement with those in the literature [2,5,9]. Bali et al [2] used dynamic contrast enhanced (DCE) MR to study the change in pancreatic perfusion 1 minute after secretin administration, a large increase in perfusion was measured but this can be expected immediately following administration compared to our later ASL measure. However, using DCE method only a single timepoint following secretin administration was assessed, prohibiting the monitoring of serial changes. Here, using non-invasive PC-MRI and ASL, we have demonstrated significant temporal changes in pancreatic perfusion and arterial blood flow in response to IV secretin. These methods have potential benefit to study pancreatic diseases with a putative vascular pathophysiology and to monitor the effects of therapy.