Identification of MR biomarkers to predict outcome in patients undergoing endoscopic third ventriculostomy

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Background: hydrocephalus is a common disorder classically treated by ventriculoperitoneal shunt. More recently endoscopic third ventriculostomy, creating an opening through the floor of the third ventricle has also been shown to be highly effective in many cases. The rationale for this success in patients with communicating hydrocephalus has been unclear since this is conventionally treated to overproduction of CSF within the ventricles, which would not respond to ventriculostomy. Previous researchers have suggested that communicating hydrocephalus results from increased transmission of the systolic pulse wave into cerebral capillaries and have suggested the term "increased capillary pulsatility hydrocephalus" [1]. We hypothesised that if this is indeed the aetiology and then measurements of physiological variables including cerebral blood flow and CSF flow should be able to predict response to ventriculostomy.

Methods: nine patients with communicating hydrocephalus and 10 age and sex matched controls were recruited. All patients underwent MRI before and two to four weeks after ventriculostomy. All subjects were scanned using a Philips 3 Tesla ACS-NT scanner. The imaging protocol included Axial Fluid Attenuated Inversion Recovery and Axial T1 weighted inversion recovery images. Arterial blood flow and CSF flow in the cerebral aqueduct and foramen magnum were measured using quantitative single-slice phase-contrast angiography (PCA) ECG gated with 16 cardiac phases. The assessment of white matter lesion load was based on the Scheltens' scale [1]. Virchow Robin spaces (VRS) were scored using a locally developed scoring scheme [2, 3]. PCA images were analysed to produce estimates of: 1) Aqueduct systolic peak width (aqWSP); 2) Aqueduct systolic stroke volume (Aq+ve); 3) Aqueduct diastolic stroke volume (Aq-ve) ;4) Aqueduct average stroke volume (SV), systolic flow through the foramen magnum(FM+ve) and diastolic flow through the foramen magnum (FM-ve). Effectiveness of the ventriculostomy was assessed using two objective measures; change in brain volume and ventriculostomy flow measured by PCA MRI.

Results: in normal volunteers there were significant correlations between total cerebral blood flow ($p < 0.01$), basilar bloodflow ($p < 0.01$) and the flow of CSF through the foramen magnum. In patients there was a close correlation between blood flow in the basilar artery and total cerebral blood flow ($p<0.01$). No correlations were seen between any measure of bloodflow and any measure of CSF flow. Direct comparison of normal and preoperative patient measurements demonstrated significant differences in cerebral blood flow ($p < .01$) and CSF flow through the foramen magnum ($p<0.01$) which were both reduced in the patient group. Multiple regression using a stepwise model showed a strong correlation between premorbid measurements and change in brain volume ($R2=0.927$, $p<0.001$). The model accounted for 94% of the variability in the change of brain volume occurring following treatment.

Model one: change in brain volume = -15.196 +(0.65xCBF)-(5.96xAQ-ve)

Multiple regression modelling also showed strong correlation between the model and the ventriculostomy flow (Square equals 0.979, p less than 0.001).

Model two: flow in the ventriculostomy=-0.456+(0.017xFM-ve)+(0.687xAQ+ve)

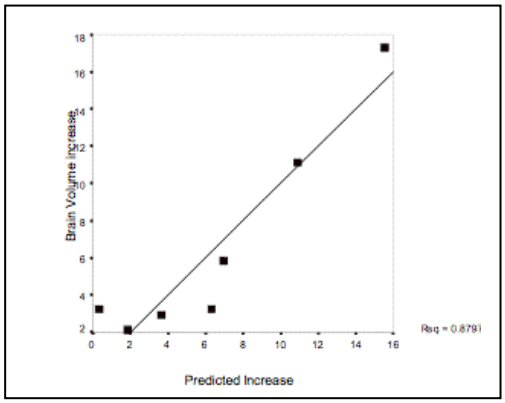

Figure 1: Scatterplot showing actual vs predicted changes in Brain volume from model 1

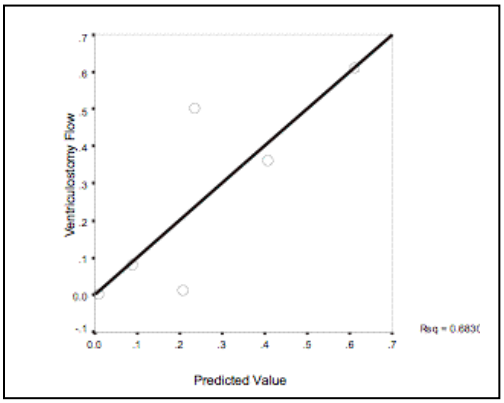

Figure 2: Scatterplot showing actual vs predicted ventriculostomy flow from model 2

Discussion: these findings support the hypothesis that ventricular dilatation in patients with communicating hydrocephalus results from increased capillary pulsatility. Furthermore although this is a preliminary study with a small number of patients they suggest that the physiological relationship between hydrocephalus and haemodynamic status can be assessed by simple PCA-MRI techniques allowing prediction of surgical outcome.

1. Greitz, D., The bulk flow model cannot explain communicating hydrocephalus and must be replaced by a new concept. Childs Nerv Syst, 2007. 23(11): p. 1229-31.