UMEÅ UNIVERSITET

CEREBRAL HEMODYNAMIK VID STROKE, CEREBRAL SMÅKÄRLSSJUKDOM OCH FARMAKOLOGISKA INTERVENTIONER

En 4D flow MRI-studie

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Akademisk avhandling

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Cerebral Hemodynamics in Stroke, Cerebral Small Vessel Disease and Pharmacological Interventions – a 4D Flow MRI study

Abstract
Background and aim: Current cerebrovascular imaging techniques provide important information on arterial anatomy and structural pathologies, such as stenoses and occlusions, but physicians are left to infer how the blood flow is affected. In addition, the relationship between blood pressure and cerebral blood flow (CBF) is complex and poorly understood. Increased transmission of cardiac pulsatility to the cerebral microvasculature has been suggested as a causative factor of cerebral small vessel disease (CSVD) but previous research have yielded conflicting results regarding this relationship. 4D flow magnetic resonance imaging (MRI) is a novel and promising technique enabling time-resolved blood flow quantification with whole-brain coverage and relatively short scan times. However, despite its obvious potential, there is not yet an evidence-based application for the use of 4D flow MRI within stroke or CSVD. This dissertation aimed to apply 4D flow MRI to describe blood flow patterns in posterior circulation stroke and CBF responses to common pharmacological agents used to alter arterial blood pressure as well as to examine the relationship between cerebral arterial pulsatility and CSVD.
Methods and Results: This doctoral dissertation consisted of four papers, referred to by roman numerals. 4D flow MRI and computed tomography angiography (CTA) were applied in 25 patients with acute ischemic stroke in the posterior circulation and a reference population of 15 healthy elderly (**paper I**). Individual flow profiles were created for each stroke patient and hemodynamic disturbances as well as collateral compensation were described. We show that hemodynamic findings were related to structural findings from CTA. The cross-sectional relationship between cerebral arterial pulsatility (quantified using 4D flow MRI as pulsatility index [PI] and flow volume pulsatility [FVP]) and features of CSVD were examined using regression analysis in 89 patients with acute ischemic stroke (**paper II**) and a population-based sample of 862 elderly (**paper III**). Internal carotid artery FVP was associated with increasing white matter hyperintensity (WMH) volume in patients with stroke and TIA (**paper II**). In addition, increasing middle cerebral artery FVP and PI were associated with worse cognitive function. In the population sample, high FVP and PI were associated with increasing WMH volume, lower brain volume and the presence of lacunes, but not the composite MRI-CSVD (**paper III**). Among subjects with MRI-CSVD, displaying symptoms consistent with CSVD was associated with higher WMH volume, lower brain volume and active smoking, but not any measure of pulsatility. Eighteen healthy volunteers were administered noradrenaline to increase mean arterial pressure by 20% above baseline, and labetalol to decrease mean arterial pressure to 15% below baseline (**paper IV**). CBF was measured using phase-contrast MRI at each blood pressure level and compared to baseline. Despite a marked increase in blood pressure, noradrenaline administration caused a reduction in CBF and cardiac output. Meanwhile, labetalol treatment caused no change in CBF but an increased cardiac output.
Conclusions: 4D flow MRI can detect hemodynamic disturbances and discriminate between hemodynamic disturbances and normal flow in patients with structural vascular pathologies. This additional information compared to structural imaging alone could potentially be used for prognosis and selection for procedures in clinical care. Cerebral arterial pulsatility is modestly associated with several MRI and clinical features of CSVD but not all. Cerebral arterial pulsatility as the main risk factor of CSVD seems unlikely but its involvement in the pathophysiology cannot be ruled out. Raising the blood pressure with noradrenaline decreases CBF and cardiac output without any redistribution from peripheral to cerebral flow. This highlights the pitfalls of using blood pressure as a surrogate for CBF and questions the validity of our understanding of cerebral autoregulation. Lowering the blood pressure with labetalol does not affect CBF, reassuring its use in clinical routine. 4D flow MRI can be integrated into an in-patient work-up in selected cases of acute ischemic stroke and into the workflow of large epidemiological studies.

Keywords
4D flow MRI, cerebral blood flow, cerebral arterial pulsatility, pulsatility index, stroke, cerebral small vessel disease, noradrenaline, labetalol, white matter hyperintensities, lacunes, perivascular spaces

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