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Cerebral blood flow distribution, collateral function and pulsatility in healthy and in patients with symptomatic carotid stenosis

A magnetic resonance imaging approach

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Akademisk avhandling

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Abstract
Background: For the detection and treatment of early cerebral vascular disease it is of paramount importance to first understand the normal physiology of the cerebral vasculature, and subsequently, to understand how and when pathology can develop from that. This is especially important as the population above 65 years of age is increasing and aging itself is an established risk factor for the development of cerebral vascular disease. This, however, is not always an easy task, since there is a subtle balance and overlap between age-related physiological and pathophysiological changes in the arterial system. Atherosclerotic changes that lead to the development of carotid artery stenosis are responsible for about one fifth of all ischemic strokes. Today, the current state of evidence and the algorithm for carotid revascularization is mainly focused on the degree of carotid stenosis and not on its impact on cerebral hemodynamics. One reason for this is the lack of a non-invasive method, that allows for repeated investigations and provides accurate and reliable results to study cerebral hemodynamic changes. The overall aim of this thesis was to explore and develop a comprehensive approach to investigate the cerebral blood flow distribution, collateral function and pulsatility in healthy subjects and in patients with symptomatic carotid stenosis using a phase-contrast magnetic resonance imaging (PCMRI) platform. The thesis is based on four scientific papers (papers I—IV).
Methods: In papers I and II, 49 healthy young (mean 25 years) and 45 healthy elderly (mean 71 years) subjects were included. 2D PCMRI was used to assess cerebral blood flow rate (BFR), pulsatility index (PI) and dampening factor (DF) in 15 cerebral arteries and in the ophthalmic arteries (OA). Thirty-eight patients (mean 72 years) with symptomatic carotid stenosis were included in paper III. Nineteen of these patients (mean 71 years) underwent carotid endarterectomy (CEA) (paper IV). 4D PCMRI was used for BFR assessment in papers III and IV. BFR, its distribution and collateral routes, was measured in 17 cerebral arteries and in the OA. The BFR on ipsilateral side (with symptomatic stenosis) was compared to the contralateral side (papers III and IV). BFR laterality was defined as contralateral BFR minus ipsilateral BFR in paired arteries and, BFR was compared before and after CEA (paper IV).
Results: On average, in healthy subjects, 72% of the total cerebral blood flow (tCBF) was distributed through the anterior circulation and 28% through the posterior circulation. The distribution was symmetrical and not affected by age, sex, or brain volume (paper I). Aging resulted in lower BFRs, increased pulsatility and reduced dampening capacity in cerebral arteries. Anatomical variations in the circle of Willis resulted in an asymmetrical distribution of blood flow (papers I and II). In patients with carotid stenosis, a lower BFR was found in the internal carotid artery (ICA) and its branches on the ipsilateral side. The anterior cerebral artery territory was bilaterally, primarily, supplied by the contralateral ICA. In addition to the supply through the ICA, the middle cerebral artery (MCA) territory on the ipsilateral side was secured by collateral supply from the OA and the posterior communicating arteries, seen as retrograde flow in those arteries. Despite these compensations, BFR in ipsilateral side MCA was lower, and this laterality was more pronounced in patients with severe carotid stenosis (≥70%). After CEA, the distribution of BFR going into the cerebral arteries was found to be symmetrically distributed. Total CBF increased postoperatively in patients with collateral recruitment preoperatively (n=9). The BFR laterality in MCA observed prior to CEA, was found only in the group of patients with collateral recruitment preoperatively (paper IV). The degree of stenosis did not differ between the groups with and without collateral recruitment.
Conclusions: This thesis provides a new and comprehensive approach to mapping and quantifying normal cerebral blood flow and pulsatility. By presenting the distribution of tCBF going into cerebral arteries, instead of using absolute values, the effect of age could be neutralized and the results can be applicable when describing healthy cerebral blood flow, regardless of age. 4D PCMRI made it possible to describe the altered blood flow distribution and collateral ranking in patients with carotid stenosis prior to CEA and its normalization after the procedure. Our findings highlight the importance of BFR quantification for understanding cerebral hemodynamics in patients with carotid stenosis. 4D PCMRI technique is a promising clinical tool for investigations of cerebral hemodynamics in patients with stroke.

Keywords
Aging, Arterial pulsatility, Carotid stenosis, Cerebral arteries, Cerebral blood flow, Cerebral collateral blood flow, Circle of Willis, Phase contrast magnetic resonance imaging.

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