Clinical and magnetic resonance observations in cerebral small-vessel disease
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General introduction
General introduction

Hardening and thickening of the arterial walls probably begins after the second decade in human life and may eventually result in devastating diseases. This process is called arteriosclerosis, and occurs in all parts of the arterial system, from the large muscular arteries to the small arterioles and capillaries. Two main forms can be distinguished. Atherosclerosis is a disease of the intima, in which lipid-filled smooth muscle cells and macrophages (foam cells), and fibrous tissue accumulate.¹ This disease usually affects the abdominal aorta, the large renal and leg arteries, the coronary arteries and the large cerebral arteries and is therefore called large-vessel disease. The different clinical manifestations develop depending on the localization of the disease. Intermittent claudication results from large-vessel disease in the arteries of the legs, myocardial infarction from disease of the coronary arteries, and large territorial cerebral infarcts from atherosclerosis in the large cerebral arteries.

The second form of arteriosclerosis is characterized by hyaline depositions and degenerative changes in the intima and media of the small arteries of mainly the spleen, pancreas, adrenal glands, kidney and brain. This disease is also called arteriolosclerosis. In the brain affection of the small arteries may cause specific clinical symptoms: the lacunar syndromes. Why some patients develop large-vessel disease and others small-vessel disease, is unknown. Different vascular risk factors, like smoking, hypercholesterolemia and hypertension, may be associated with either small- or large-vessel disease.² Hypertension is assumed to be specifically associated with small-vessel disease. Hyalinization of the walls of the small arteries may be a more benign consequence of hypertension, and fibrous and elastic hyperplasia with necrosis of the media and intima a more malignant result. Other factors, like infections or genetic polymorphism may also play a role in the development of either small- or large-vessel disease.³ ⁴

Since decades small-vessel disease in the brain has been the subject of extensive study. Three clinical manifestations are considered specific
results of small-vessel disease: lacunar infarcts, white matter disease (also called Binswangers disease) and intracerebral hemorrhages. With CT-scans and MRI, these lesions can be studied in living individuals. In a prospective cohort of 229 patients with different manifestations of both small- and large-vessel arterial disease, we studied the clinical aspects and risk factors of cerebral small-vessel disease, as shown by MRI, in comparison to large-vessel disease. In addition, in a second prospective cohort of patients presenting with an ischemic stroke, we studied the differences in the early clinical course of infarcts due to small- and large-vessel disease.

This thesis will try to address the following questions:
1. Is it possible to detect genetic factors and vascular risk factors that are specifically associated with the development of small- or large-vessel disease?
2. Are the different clinical and MRI manifestations, that are attributed to small-vessel disease, like lacunar infarcts, white matter lesions and intracerebral hemorrhages, mutually related? Do the various consequences of small-vessel disease occur in one patient? Are there clinical and MRI manifestations of small-vessel disease that have been unnoticed until now?
3. What differences exist in the evolution of early clinical signs and symptoms between cerebral infarcts caused by small- or large-vessel disease?

Outline of the thesis
Chapter 1 gives a review of the history of the cerebral small-vessel disease and the controversies associated with the subject. In chapter 2 we investigate differences in vascular and genetic risk factors between patients with small-vessel disease and patients with large-vessel disease. In chapter 3 we study the risk factors of pontine hyperintense MRI-lesions. These lesions are considered to be a specific form of small-vessel disease in a hitherto hardly studied localization. In chapter 4 we examine the clinical significance of these pontine hyperintense lesions. In chapter 5 we describe the small, usually asymptomatic, intracerebral hemorrhages
that we observed on MRI of patients with atherosclerosis in our cohort. In chapter 6 we examine the differences in early symptom progression in patients with small-vessel (lacunar) cerebral infarcts and those with large territorial infarcts.

References


"In chapters 3, 4, and 5 of this thesis the term "atherosclerosis" is used to denote the whole spectrum of arterial ischemic disease, including small-vessel disease."
General Introduction

In this study, we aimed to investigate the clinical aspects of small- and large-vessel arterial disease by studying MRI in patients with various clinical presentations. We prospectively followed 239 patients with different manifestations of small- and large-vessel arterial disease. In patients with an acute ischemic stroke, we studied the clinical manifestations and the role of MRI in these patients. Additionally, in a second prospective cohort of 239 patients with an acute ischemic stroke, we studied the clinical and imaging manifestations of small-vessel disease.

Why is it important to study small-vessel arterial disease? The importance of small-vessel arterial disease lies in understanding the clinical and MRI manifestations of small-vessel disease, which have not been extensively studied until now.

3. What differences exist in the evolution of early clinical symptoms between cerebral infarcts caused by small- and large-vessel disease?

Outline of the thesis

Chapter 1 gives a review of the history of small-vessel arterial disease and the controversies associated with the subject. In chapter 2, we investigate differences in vascular and genetic risk factors between patients with small-vessel disease and patients with large-vessel disease. In chapter 3, we study the risk factors of peri-lesional hypointense MRI lesions. These lesions are considered to be a specific form of small-vessel disease, a topic that has not been extensively studied. In chapter 4, we examine the clinical significance of these peri-lesional hypointense lesions. In chapter 5, we summarize our findings and present future directions in the field of small-vessel disease.