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General introduction

Stroke is a major cause of death and a devastating disorder that puts a large burden on health care systems. Stroke occurs particularly in the elderly.¹ Most studies on the incidence of stroke have focused on persons aged younger than 85 years and limited data exist on the occurrence of stroke in the very old.² Since populations are growing older, an increase in the burden of stroke is expected in coming decades. A challenge for medical research is the question whether and how this devastating disease can be prevented. This requires identification of modifiable risk factors that are amenable to intervention. Moreover, it requires possibilities to recognize those who may benefit most from preventive interventions.

The main risk factor for stroke is atherosclerosis, which accumulates with age. Several non-invasive measures of atherosclerosis exist. Despite research that has been done in this field, the strength and nature of the relation between measures of atherosclerosis and stroke subtypes is not yet fully understood. Further, it is not clear whether other risk factors are related to stroke through unrelated mechanisms, or that they trigger the presence or progression of atherosclerosis. Besides atherosclerosis, there are other putative risk factors for stroke such as sex hormones and genetic factors.³ The relevance of these factors in relation to stroke still needs to be established. The work described in this thesis aims to further quantify the incidence of stroke in the elderly and the relation between atherosclerosis, sex hormones and genetic markers and stroke. The studies were based on the Rotterdam Study, a large population-based cohort study among 7,983 persons aged 55 years or over that started in 1990. Since then, the cohort was followed for morbidity and mortality, including stroke.

Chapter 2 describes the occurrence of stroke in elderly men and women in this cohort. Chapter 3 focuses on the relation between non-invasive measures of atherosclerosis and risk of stroke. Structural as well as functional measures of atherosclerosis will be dealt with. For each measure we aim to assess the strength of the relation with stroke. In chapter 3.2, 3.3 and 3.4 the relation between structural measures of atherosclerosis and risk of stroke is assessed. In particular we examine the effect of carotid intima media thickness (chapter 3.2), plaques in the carotid artery (chapter 3.3) and coronary calcifications (chapter 3.4). In chapter 3.5 we describe the relation between functional measures of atherosclerosis and stroke risk, in particular measures of arterial stiffness. In the last paragraph of this chapter we evaluate and compare the strength of the relation between different measures of atherosclerosis in relation to stroke

(chapter 3.6). In chapter 4, we investigate the relation between sex hormone levels and stroke in men and in women. Both estrogen and testosterone are evoked to be related to the risk of cardiovascular disease, but the relation with stroke is not yet clear.⁴⁻⁶ In chapter 5 we investigate the role of two candidate genes, namely mutations in the hemochromatosis gene and the angiotensin-converting enzyme polymorphism. Finally in chapter 6 we review our findings and we comment on the strength and limitation of our studies. Further, we discuss the clinical relevance of our findings and make recommendations for further research.

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