MR and CT evaluation of cardiovascular risk in metabolic syndrome

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SUMMARY AND CONCLUSIONS

The aim of this thesis was to identify risk factors and subclinical disease in metabolic syndrome, by using MRI and CT.

Familial longevity is marked by an exceptionally healthy metabolic profile and low prevalence of cardiometabolic disease observed already at middle age. In **chapter 2** the association between abdominal fat distribution and longevity was evaluated. Offspring of long-lived siblings and controls underwent CT imaging to assess the amount of abdominal visceral and subcutaneous fat. In male offspring of long-lived siblings, total abdominal fat and abdominal visceral fat areas were smaller compared to controls. These differences persisted after adjusting for several factors affecting adipose tissue deposition. Consistent with a potential link between abdominal visceral fat and health outcomes, in our study prevalence of hypertension and type 2 diabetes was lower in male offspring of long-lived siblings compared to controls. Male individuals who have genetically determined prospect to become long-lived may be protected against development of cardiovascular disease by relatively low amounts of visceral fat.

Chapter 3 describes the association of liver steatosis with longevity. Nonfasting liver enzymes were measured in offspring of long-lived siblings and controls. In addition, in two random subgroups, fasting liver enzymes and liver to spleen CT attenuation ratios as a measure of liver steatosis were obtained. Except for nonfasting levels of alanine transaminase, which were slightly higher in the offspring of long-lived siblings compared to controls, no differences were found between groups in the extent of liver steatosis. Our study findings indicate that decreased liver steatosis is not an early metabolic phenotype that associates with the more favourable glucose metabolism in familial longevity.

Chapter 4 evaluates the association between liver steatosis and brain tissue integrity in middle-aged to older persons. All study participants underwent CT imaging to assess liver fat and abdominal visceral fat as well as MTI to assess brain tissue integrity. In addition, total body fat was estimated from bioelectrical impedance analysis. Liver to spleen CT attenuation ratio as a measure of liver fat was related to reduced brain tissue integrity in overweight study participants. This finding was independent of the amount of visceral fat and total body fat, indicating that the observed relation between liver fat and brain tissue integrity in overweight individuals cannot be accounted for by overall adiposity nor differences in visceral abdominal fat deposition. Although future studies should future elucidate these associations, current study findings could improve understanding of the mechanisms underlying the relation between obesity and dementia.

Chapter 5 reports the relation between imaging measures of brain tissue integrity and aortic arch stiffness in hypertension patients. In sixty-six hypertension patients without clinically manifest cerebrovascular disease, aortic arch PWV was assessed using VE-MRI. Brain tissue integrity was assessed using DTI. Increased aortic arch PWV was associated with several DTI measures of brain injury. These effects were independent of age, sex, BMI, smoking, and white matter hyperintensity volume. The study findings suggest that increased aortic arch stiffness may play a role in causing subclinical brain injury in hypertension patients observed already at midlife.

In **chapter 6** the association between metabolic syndrome risk factors and brain tissue integrity is evaluated. All study participants underwent conventional structural MRI, MTI, and DTI. Metabolic syndrome was not associated with brain volume, white matter lesion volume, or the presence of lacunar infarcts or cerebral microbleeds. In contrast, metabolic syndrome was associated with MTI and DTI measures of microstructural brain injury. Serum high density lipoprotein cholesterol, triglycerides, BMI, and diastolic blood pressure were independent factors in these brain changes. Future studies should determine whether these changes evolve in more pronounced structural deterioration or cognitive decline.

MTI nowadays has become increasingly useful in detecting microstructural cerebral changes that correlate with cognitive decline in a variety of neurodegenerative diseases. However, there are no longitudinal data on the association between MTI measures of brain structure and cognition in nondemented individuals. **Chapter 7** evaluates the association between brain microstructure and two longitudinal measures of cognition in older persons. In one hundred ninety three nondemented older individuals at increased risk for vascular, MTI and cognitive function testing was performed. Magnetization transfer ratio (MTR) histogram peak height, a MTI measure of brain tissue integrity, was associated with cognitive test performance at baseline and 3.3-year follow-up. MTR histogram peak height may be a potentially useful marker of cognition in future clinical intervention studies.

Chapter 8 describes the effect of temporal resolution on the accuracy of aortic PWV assessed by VE-MRI. Imaging was performed in five patients referred for cardiac MRI and ten healthy volunteers. Temporal downsampling was achieved by repeated reconstructions of the reference PWV data set while reducing the number of phases and by repeated scanning with decreasing temporal resolution. Sparse temporal sampling was associated with increased variation and bias in aortic arch PWV. The study findings indicate that, when allowing an error in PWV assessment that does not exceed the physiological variation, temporal resolution of at least 20 ms is required.

CONCLUSION

The key clinical implication of a diagnosis of metabolic syndrome is identification of a patient who needs aggressive lifestyle modification focused on weight reduction and increased physical activity. The studies described in this thesis show the potential of MRI and CT for identifying risk factors and subclinical disease in metabolic syndrome.

It is demonstrated that relatively low amounts of abdominal visceral fat assessed by CT relate to familial longevity, which in turn has been associated with an exceptionally healthy metabolic profile and low prevalence of cardiometabolic disease observed already at middle age. Furthermore, it is described that liver to spleen CT attenuation ratio as a measure of liver fat relates to MRI evidence of subclinical brain tissue decline in overweight individuals without manifest cerebrovascular disease. Although future studies should future elucidate these associations, current study findings could improve understanding of the mechanisms underlying the relation between obesity and dementia.

This thesis extends knowledge on subclinical brain injury in hypertension patients by showing an association between DTI measures of brain injury and aortic arch PWV. In addition, it is shown that metabolic syndrome as a risk factor per se relates to microstructural brain injury. Future studies should determine whether these MRI measures of brain damage evolve in more pronounced structural deterioration or cognitive decline.

Finally, this thesis provides a technical evaluation of the effect of temporal resolution on the accuracy of aortic arch PWV, a surrogate marker of vascular stiffness, assessed by VE-MRI. Aortic arch stiffness integrates and reflects the long-term effects of all identified as well as currently unknown cardiovascular risk factors and can be detected at a stage when organ damage may be reversible.