Cardiovascular magnetic resonance imaging techniques in hypertension and diabetes

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Summary and Conclusions

Summary

The aim of this thesis was to evaluate the functional and structural implications of aortic wall pathology and the association of these abnormalities with (early) left ventricular (LV) cardiac and cerebral disease in patients with hypertension and type-1 diabetes mellitus (DM1) using magnetic resonance imaging (MRI). Furthermore, the ability of more optimized cardiac MRI-techniques for assessment of cardiovascular disease was evaluated.

Chapter 1 provides a general introduction to the thesis, with a short description of the potential mechanism of development of cardiac and cerebral abnormalities in patients with hypertension and DM1, and MRI as a potential tool for assessment of diagnosis of cardiovascular abnormalities.

Chapter 2 evaluates the additional role of hypertension on aortic stiffness in patients with DM1. Aortic stiffness is measured by means of pulse wave velocity (PWV) using velocity-encoded (VE) MRI and compared between four groups: i.e. 32 healthy volunteers, 20 patients with DM1, 31 patients with hypertension and 28 patients having both DM1 and hypertension. Aortic PWV was similar in patients having DM1 and healthy volunteers, whereas aortic PWV was highest in patients with hypertension and patients having both DM1 and hypertension. This indicates that hypertension has an important effect on aortic stiffness in patients with DM1, whereas the role of DM1 itself on aortic stiffness seems marginal.

Chapter 3 describes the relationship between aortic stiffness and vessel wall thickness (VWT) in aorta and carotid arteries in 15 patients with hypertension and 15 age- and sex-matched healthy volunteers as studied by MRI. In both groups, increased aortic stiffness was associated with increased aortic VWT (Pearson correlation (r) 0.76 vs. 0.63) and to a lesser extent with increased carotid VWT (r 0.50 vs. 0.40). Furthermore, aortic stiffness, VWT in the aorta and carotid arteries, were all significantly increased in patients with hypertension versus healthy volunteers (7.0 ± 1.4 m/s vs. 5.7 ± 1.3 m/s, 0.12 ± 0.03 ml/m^2 vs. 0.10 ± 0.03 ml/m^2, 0.04 ± 0.01 ml/m^2 vs. 0.03 ± 0.01 ml/m^2, respectively all $p < 0.015$). In conclusion, MRI-measured aortic wall stiffness and VWT can be used for measurement of aortic and carotid wall pathology with important prognostic implications.

Chapter 4 reports on the association between aortic arch stiffness and cardiac and cerebral end organ damage in 50 patients with hypertension using MRI. After correction for age, sex, and hypertension duration, aortic arch stiffness was associated with LV mass index ($r = 0.37$, $p = 0.03$, beta regression coefficient (β) = 2.11), and lacunar brain infarcts (Odds ratio (OR) = 1.8, $p = 0.04$), whereas not with indices of LV systolic and diastolic function and periventricular and deep white matter hyperintensities. In conclusion, increased aortic stiffness is associ-

ated with LV hypertrophy and cerebral damage like lacunar brain infarcts in patients with hypertension. Thus MR-measured aortic arch stiffness can be used for cardiac and cerebral risk stratification in patients with hypertension.

Chapter 5 describes the association between aortic stiffness, LV function and cerebral small vessel disease in 86 patients with DM1 using MRI. After correction for confounding factors age, sex, mean arterial pressure, heart rate, BMI, smoking, DM duration and hypertension, aortic PWV was associated with LV ejection fraction (β = -0.406, $p < 0.05$), LV stroke volume (β = -0.407, $p < 0.05$), LV cardiac output (β = -0.458, $p < 0.05$), and with cerebral periventricular white matter hyperintensities (WMHs) (OR = 1.425, $p < 0.05$) and deep WMHs (OR = 1.479, $p = 0.02$), whereas not with LV mass, cerebral microbleeds or lacunar brain infarcts. Accordingly, in patients with DM1, increased aortic stiffness can be used as a marker for cardiac and cerebrovascular disease.

Chapter 6 evaluates the relationship between aortic stiffness, brain volumes and cerebral perfusion in 51 DM1 patients and 34 age- and sex matched healthy volunteers. White matter (WM) and grey matter (GM) brain volumes, total cerebral blood flow (tCBF) and aortic PWV were assessed with MRI. Aortic PWV was similar in both groups. WM and GM brain volumes were decreased (WM: $p = 0.04$; GM: $p = 0.03$) and tCBF was increased (tCBF: $p < 0.05$) in DM1 patients versus healthy volunteers. Furthermore tCBF and aortic PWV were independent predictors of WM brain volume in DM1 patients (β = 0.352, $p = 0.024$ for tCBF; β = -0.458, $p = 0.016$ for aortic PWV). Age was the independent predictor of GM brain volume (β = -0.695, $p < 0.001$). This study shows that in DM1, WM and GM brain volumes are decreased concomitant with increased brain perfusion. WM brain atrophy is predicted by tCBF and aortic PWV, whereas GM brain atrophy is determined by age.

Chapter 7 studies accuracy and reproducibility of flow velocity and volume measurements in a phantom and in human right coronaries using breathhold VE MRI with spiral k-space sampling at 3T. In vitro, MRI-measured flow rates correlated strongly with volumetric collection ($r = 0.99$; $p < 0.01$). Due to limited sample resolution, VE MRI overestimated the flow rate by 47% on average when non-constricted region-of-interest segmentation was used. Using constricted region-of-interest segmentation with lumen size equal to ground-truth luminal size, less than 13% error in flow rate was found. In vitro right coronary artery flow velocity assessment was successful in 82% of the applied studies. High interscan, intra- and inter-observer agreement was found for almost all indices describing coronary flow velocity. In conclusion, 3T breathhold VE MRI with spiral k-space sampling enables accurate and reproducible assessment of right coronary artery flow velocity.

Chapter 8 describes the ability of 7T cardiac MRI to quantitatively assess LV volumes, mass, and function from cine-short axis series and LV diastolic function from VE MRI in 10 healthy volunteers. The corresponding measures obtained at 1.5T were taken as the "gold standard". Imaging at 7T was successful in 80% of the examinations. Good agreement between LV volumes, function and mass at 7T and 1.5T was found with no significant difference between variables describing LV volumes, function and mass and intraclass correlation coefficients (ICCs) ranging from 0.77 to 0.96. Trans-mitral stroke volume and the ratio between early and atrial peak filling rate showed strong agreement at the two field strengths (no significant differences between stroke volumes and filling ratios at 7T MRI and 1.5T MRI, with ICCs of 0.92 and 0.77, respectively). This study shows that assessment of LV volumes, function and flow is feasible at 7T MRI and that standardized MRI protocols provide similar quantitative results when compared to 1.5T MRI.

Chapter 9 compares parameters describing LV diastolic function obtained with 3-dimensional (3D) three-directional VE MRI with retrospective valve tracking and 2-dimensional (2D) one-directional VE MRI in patients with ischemic heart failure. Secondly, classification of LV diastolic function, in particular for discriminating restrictive filling patterns, with both MRI techniques was compared versus Doppler echocardiography. All flow rate parameters determined with 3D three-directional VE MRI were systematically lower than when assessed with 2D one-directional VE MRI, except for E/A filling ratio and E deceleration time. Agreement between 3D three-directional VE MRI and Doppler echocardiography in classifying LV diastolic filling patterns was superior to the agreement between 2D one-directional VE MRI and Doppler echocardiography (i.e. kappa agreement (κ) = 0.91 versus κ = 0.79 respectively). Accordingly, 3D three-directional VE MRI with retrospective valve tracking better describes LV diastolic function as compared to 2D one-directional VE MRI in patients with ischemic heart failure.

Conclusions

This thesis evaluates the relationship between structural and functional aortic vessel wall alterations and end-organ damage in cross-sectional patient studies with use of MRI. These studies show that aortic PWV in DM1 patients is mainly determined by hypertension, whereas the effect of DM1 itself on aortic PWV is marginal. Increased aortic PWV in patients with hypertension is associated with aortic and carotid vessel wall alterations. Also, increased aortic PWV is associated with cardiac as well as cerebral damage both in hypertensive and DM1 patients.

Furthermore, this thesis describes and evaluates the ability of more optimized cardiac MRI-techniques for assessment of cardiovascular disease. Right coronary artery flow can be accurately and reproducibly assessed using 3T VE MRI in healthy control subjects. Furthermore, the use of standardized 7T MRI protocols for assessment of LV volumes, function and flow provides similar quantitative results when compared to 1.5T MRI. Finally, 3D three-directional VE MRI better describes LV diastolic function as compared to 2D one-directional VE MRI in patients with ischemic heart failure.