Cardiovascular magnetic resonance imaging techniques in hypertension and diabetes

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Chapter 01

General introduction and outline

Introduction

Cardiovascular disease is the main cause of death in patients with hypertension and in patients with type-1 diabetes mellitus (DM1)(1-3). Early recognition of patients at risk for developing cardiovascular disease with the use of an accurate and non-invasive imaging tool may result in more optimal early treatment of those most likely to suffer from the detrimental consequences of hypertension and DM1. Increased aortic stiffness may be one important pathway linking hypertension and or DM1 to the increased cardiovascular risk (3-8), which is supported by recent reports indicating that increased aortic stiffness predicts the development of cardiovascular disease and mortality in patients with hypertension and DM1 (9-11).

The mechanism of aortic wall stiffness is generally dependent on the disruption in elastin collagen proportion and smooth muscle cell dysfunction (12). The arterial wall alterations in both hypertension and DM1 probably involve different disease mechanisms. In hypertension, continuous stress upon the arterial wall causes structural and functional alterations in the arterial wall resulting in diminished elastin elasticity, leading to wall thickening and diminished compliance of large arteries including the aorta (13,14). In DM1, the accumulation of advanced glycation end products on the arterial wall, a direct hyperglycemic and hyperinsulinemic stimulating effect on the renine-angiotensin-aldosteron system, low-grade inflammation and endothelial dysfunction have all been proposed to decrease the collagen elasticity and promote the development of vascular wall hypertrophy and fibrosis eventually leading to increased arterial wall stiffness (3). Despite the differences in underlying mechanisms, the resultant effect in both disease entities may lead to structural aortic wall abnormalities, associated with increased vascular stiffness. Still, in contrast to the prominent effect of hypertension on aortic stiffness, the role of DM1 on aortic stiffness remains to be established (15).

Aortic stiffness leads to a number of adverse hemodynamic consequences, including elevation of systolic blood pressure and lowering of diastolic blood pressure and consequent widening of pulse pressure, which, in turn, increases left ventricular (LV) afterload and alters coronary perfusion (8,16-18). These changes may lead to LV hypertrophy and diminished coronary perfusion. A wide pulse pressure is also transmitted to more distal arteries like the carotid arteries, where - in order to reduce shear stress - the carotid wall will undergo a process of remodeling, by intima-media thickening, which on itself is associated with increased cardiovascular risk (8,19). Even more importantly, increased pulse pressure has been postulated to be involved in the development of microvascular cerebral abnormalities (17). Thus, aortic stiffness represents an attractive target for demonstrating functional and structural alterations in the heart and the brain in patients with hypertension and DM1, which could improve cardiovascular risk stratification both in patients with hypertension and DM1.

Pulse wave velocity (PWV) is considered as the “gold” standard for aortic stiffness measurement (7,8,18). PWV is defined as the propagation speed with which the systolic pressure

wave form propagates along the aorta. Until now, several techniques including intravascular pressure measurement, ultrasound and tonometry, are available for assessment of aortic PWV. However, intravascular pressure measurement has been hampered by its invasiveness, whereas ultrasound and tonometry only provide an estimation of global aortic function due to the limited availability to obtain acoustic windows and the inability to spatially register the distance between the acquisition sites along the length of the aorta (20). Magnetic resonance imaging (MRI) provides a non-invasive, accurate alternative with unlimited access to the thoracic cavity, enabling quantification of global and regional (i.e. ascending, descending and total) aortic function without the need for geometrical assumptions. In addition, aortic diameter, aortic vessel wall thickness, carotid vessel wall thickness and LV function (systolic and diastolic) can be accurately and reliably assessed with MRI (21,22). MRI is the gold standard for assessment of brain abnormalities.

In addition, imaging at higher magnetic field strengths (like 3T and 7T MRI) and further technical innovations in software and hardware should increase the signal-to-noise ratio, allowing for improved spatial and temporal resolution and better imaging quality.

This thesis describes the structural and functional alterations in the aortic wall as well as the association between these aortic vessel wall abnormalities and cardiac and cerebral end organ damage in patients with hypertension and DM1 with the use of MRI. Furthermore, the ability of more optimized cardiac MR-techniques for assessment of cardiovascular disease is evaluated.

Chapter 2 describes the effect of hypertension and DM1 on aortic stiffness as measured by pulse wave velocity using velocity-encoded MRI. **Chapter 3** evaluates the associations between vessel wall thickness (VWT) in the aorta and carotid arteries and aortic PWV with a comprehensive MRI-approach in subjects with and without hypertension. In **chapter 4,** the associations between aortic arch PWV, cardiac function and cerebral end-organ damage are reported in patients with hypertension by using MRI. **Chapter 5** describes the application of MRI for assessment of the association between aortic PWV, cardiac function and cerebral small vessel disease in patients with DM1. **Chapter 6** studies vascular mechanisms of brain atrophy in DM1 patients by investigating the relationship between brain volumes, cerebral perfusion and aortic stiffness using MRI. **Chapter 7** evaluates the accuracy and reproducibility of flow velocity and volume measurements in a phantom and in human coronary arteries using breathhold velocity-encoded (VE) MRI with spiral k-space sampling at 3T. In **chapter 8**, the ability of 7T cardiac MRI to quantitatively assess LV volumes, mass, and function from cine short-axis series and LV diastolic filling from velocity-encoded MRI is tested in healthy volunteers. **Chapter 9** compares parameters describing diastolic function obtained with 3-dimensional three-directional velocity-encoded MRI using retrospective valve tracking and 2-dimensional one-directional velocity-encoded MRI in patients with ischemic heart failure.

Furthermore, transmitral flow rate indices obtained with both MRI techniques are compared with Doppler echocardiography to evaluate the clinical value of velocity-encoded MRI for diastolic function assessment.

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