4D-Flow MRI of aortic and valvular disease

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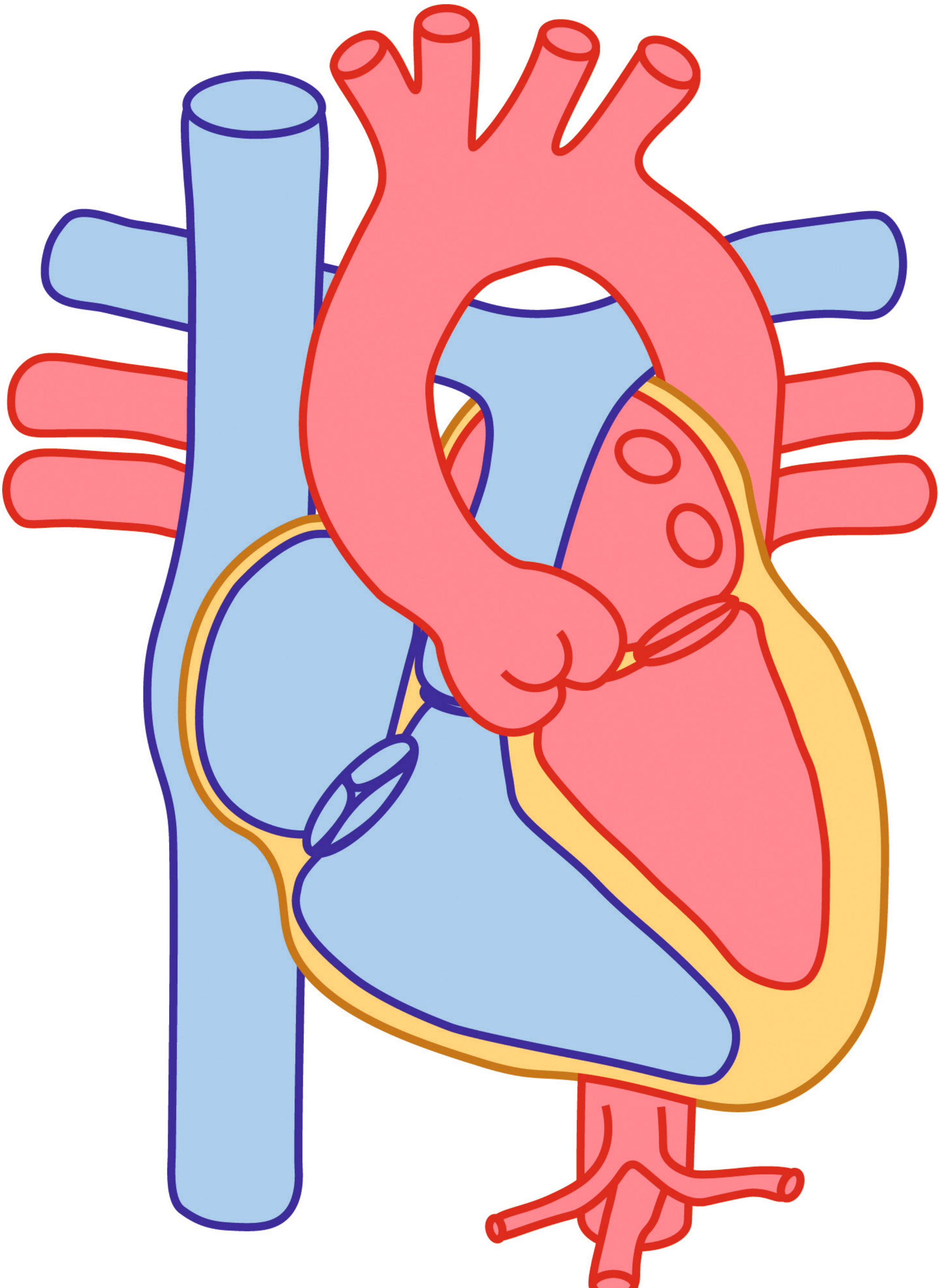

CHAPTER 1

General Introduction and Thesis Outline

INTRODUCTION

Aortic and valvular diseases encompass a wide range of conditions affecting the aorta and heart valves, posing significant challenges for healthcare professionals. These conditions include thoracic aortic aneurysm, aortic coarctation, valvular regurgitation, bicuspid aortic valve, and others. Management of these diseases involves accurate diagnosis, monitoring of disease progression, and deciding on the most suitable treatment approach. Corner stone clinical imaging modality for evaluation of aortic and valvular disease is cardiac ultrasound. 4D flow magnetic resonance imaging (MRI) is an emerging technique that is expected to improve management of patients with aortic and valvular disease.

Thoracic Aortic Aneurysm

Thoracic aortic aneurysm (TAA) is associated with adverse events such as aortic dissection, rupture and death. The risk of these adverse events increase with maximal cross-sectional diameter of the aortic aneurysm, resulting in yearly rates of 14.1%, 6.5%, and 5.3% for aortas with a diameter of >60 mm, >50 mm, and >40 mm, respectively (1). Since the risk of these adverse events exceeds the risk of preemptive surgical aortic replacement (1), surgical repair is recommended for aortic diameters >55mm for asymptomatic patients (2, 3). However, the majority (60%–96%) of dissections occur in aortas with diameters below this threshold (4, 5). Therefore, more comprehensive risk stratification methods for patients with TAA are needed to predict aneurysm growth, aortic dissection and rupture (4, 6). It has been hypothesized that aneurysm formation and growth as well as the risk of aortic dissection and rupture are influenced by alterations in aortic hemodynamics which affect hemodynamic forces on the arterial wall (7-15).

Aortic hemodynamics can be assessed by 4D flow MRI which comprises a three dimensional velocity vector field over the entire cardiac cycle, wherein 4D represent three velocity encoding directions and time (16, 17). From the velocity vector field various patient-specific parameters of aortic hemodynamics can be mathematically derived (18). Quantification of hemodynamic parameters is affected, among other factors, by manual post-processing of the images by an observer (19).

Valvular Regurgitation

Evaluation, management, and procedural guidance of patients with valvular heart disease rely on accurate and consistent quantification of valvular flow (20-22). Although Doppler echocardiography is the primary clinical imaging modality for assessing valvular flow(23, 24), complementary magnetic resonance imaging is used to quantitatively assess valvular flow and regurgitation severity (22, 25).

From a single intracardiac 4D flow MRI acquisition, valvular flow and regurgitation jets through all 4 valves can be quantified with retrospective valve tracking (25, 26).

To allow this tracking method, 1 or 2 (orthogonally oriented) complementary valvular cine acquisitions of the valve motion are acquired per valve. In contrast to multiple 2D flow MRI, retrospective valve tracking allows quantification of eccentric regurgitation jets and correction for annular valve plane motion (26-30). Furthermore, retrospective valve tracking has also demonstrated a superior accuracy with a lower variation in net forward flow assessment among the cardiac valves (i.e., intervalvular variation) (27-34). To support clinical applicability, retrospective valve tracking was recently automated, which reduced analysis time and improved intervalvular consistency (27). Because of the international variation of locally used CMR scanners and protocols, it remains uncertain whether previously published reproducibility and consistency results of automated retrospective valve tracking hold for other clinical centers (19).

Aortic Coarctation

Aortic coarctation is a congenital obstruction of aorta (35-37), typically located in the distal part of the aortic arch after branching of the left arteria subclavia (36-41). With a prevalence of approximately 3 to 4 per 10,000 live births (41-43), aortic coarctation accounts for 5 to 8% of all congenital heart defects (35-37, 40). The most commonly associated abnormality is a (functionally) bicuspid aortic valve, with a prevalence rate between 60 and 85% in patients with aortic coarctation (37-40, 42). After curative reconstruction, patients are at risk to develop late hypertension and residual or recurrent obstruction of the aorta (37, 44), the latter with a prevalence up to 30% (38).

Before intervention, the local aortic narrowing results in an increased afterload of the heart and a pressure gradient over the obstruction with associated formation of abnormal aorta flow patterns (35). The viscous friction of the blood on the vessel wall regulates the endothelium lining properties, which by high wall shear stress promotes vascular dilatation and remodeling (45). In addition, more collagen tissue and less smooth muscle fibers are observed within the aortic wall proximally towards the lesion compared to distally (46). It is unclear whether the abnormal hemodynamic situation prior to intervention is related to aortic wall deterioration (47). Knowledge of this association is important in order to identify the ideal time for intervention (41).

4D Flow MRI

Phase-contrast MRI is currently utilized to create three-dimensional flow images with velocity encoding in all three spatial directions resolved over the entire cardiac cycle, see Figure 1. This MRI sequence is commonly referred to as 4D flow MRI. In typical clinical practice, only conventional hemodynamic parameters, such as peak velocities, flow volumes, and regurgitation fractions, are evaluated for diagnosing and monitoring certain aortic and valvular diseases (21). While echocardiography, 2D, and 4D flow MRI all can assess these conventional hemodynamic parameters, it is only the three-dimensional velocity vector field captured by 4D flow MRI that enables a comprehensive evaluation of more advanced hemodynamic parameters (18).

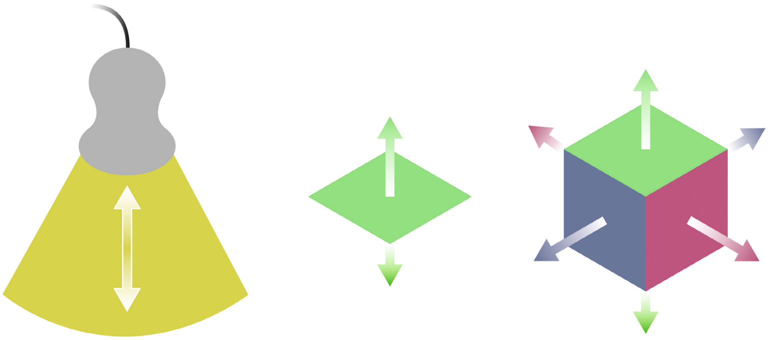

Figure 1. Schematic diagram of the velocity encoding directions of Doppler Echocardiography, 2D flow MRI, and 4D Flow MRI.

These advanced hemodynamic parameters encapsulate more complex flow phenomena that have been previously described by fluid dynamics studies. For instance, when a fluid travels through a tube, it may undergo a transition into laminar flow, wherein the flow velocity vector (i.e., flow direction and magnitude) of the fluid particles aligns parallel to the tube's wall. Due to interaction between fluid particles and the tube's wall, the highest velocities within a laminar flow are observed at the center of the tube, with the velocity magnitude of the fluid particles gradually diminishing to zero as it approaches the tube's wall, see Figure 2. When the flow velocity vectors of the fluid particles become eccentric and deviate from the center, the highest velocities of the flow profile will shift towards the tube's wall [48]. Consequently, this flow displacement can induce a secondary rotational flow overlaying the primary forward flow [49]. As a result, the motion of the fluid particles can be decomposed into translation and rotation components. The rotation of the fluid particles is denoted by the curl of the velocity field, commonly known as vorticity. The topological relationship between the translation and rotation of the fluid particles can be delineated by the helicity of the flow, which distinguishes between clockwise and counterclockwise rotating flows [50]. Moreover, fluid particles located near the tube's wall exert a shear force on the vessel wall, referred to as wall shear stress [51]. The wall shear stress can be broken down into its axial and circumferential components, along with the angle that exists between these two components. These fluid dynamic parameters are studied in patients with aortic or valvular diseases (18).

Quantification of hemodynamic parameters derived from 4D flow MRI is influenced by various factors such as patient preparation, MRI sequence, and manual post-processing (19). However, reproducibility and consistency of 4D flow MRI to assess conventional and advanced hemodynamic parameters in patients with aortic or valvular disease is largely unknown. Although there is a hypothesis that 4D flow MRI can enhance management of patients with aortic and valvular diseases, the clinical potential of aortic hemodynamics for diagnosis and disease progression monitoring in patients with aortic and valvular disease are currently mostly unexplored.

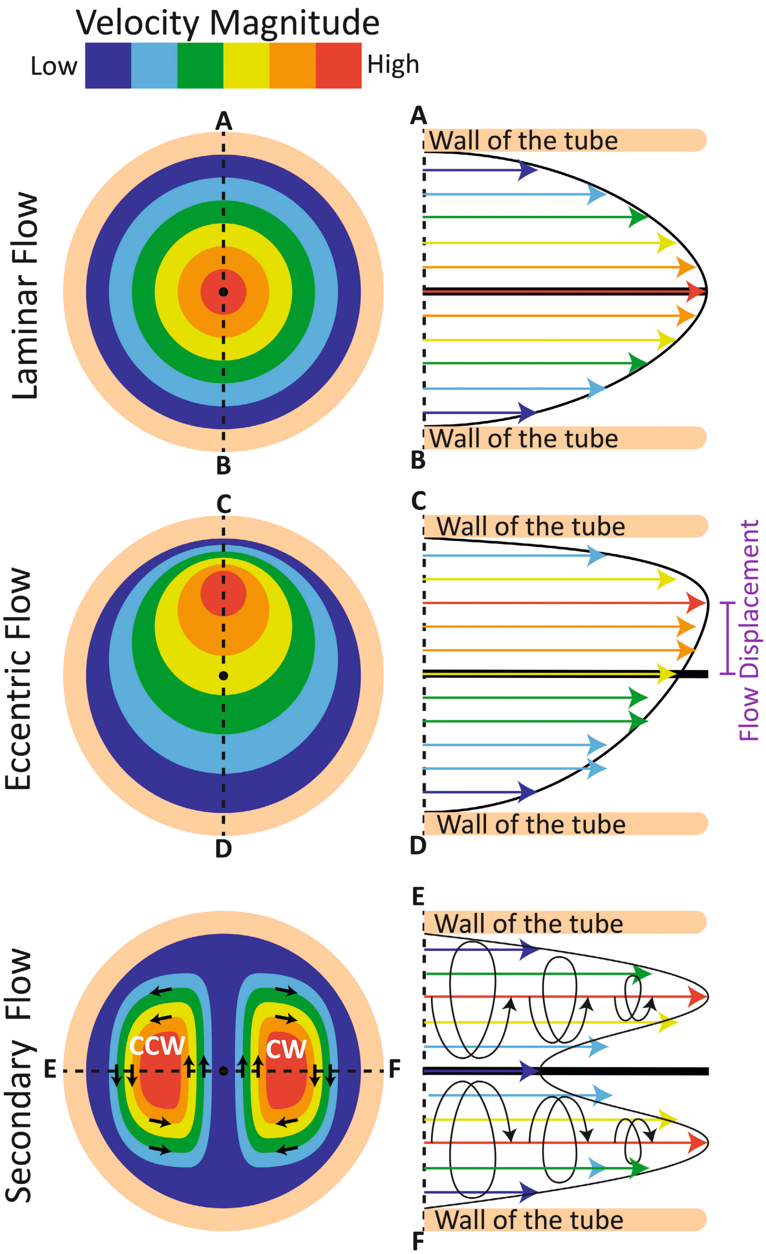

Figure 2. Schematic diagram of the laminar, eccentric and secondary flow through a tube. Left and right columns display orthogonal and longitudinal cross-sections of a tube, respectively. Velocity vectors are represented by arrows which indicate the direction and magnitude of the velocity. Abbreviation; CW – clockwise helicity, CCW – counter-clockwise helicity.

Aims of the thesis

The aims of this thesis are to assess the reproducibility and consistency of 4D flow MRI for evaluating the aortic hemodynamics and valvular flow, and to explore the clinical potential of aortic hemodynamics for diagnosis and disease progression monitoring in patients with aortic and valvular disease.

THESIS OUTLINE

This thesis is divided into two parts. **Part 1 (Chapter 2 – 4)** focusses on reproducibility and consistency of 4D flow MRI for evaluation of aortic hemodynamics and valvular flow. **Part 2 (Chapter 5 – 7)** explores the clinical potential of aortic hemodynamics for diagnosis and disease progression monitoring in patients with aortic and valvular diseases.

Part 1. Reproducibility and Consistency

Hemodynamic parameters of the aorta can be extracted from 4D flow MRI, but this requires an aortic lumen segmentation (19). These lumen segmentations are mostly semi-automatically created and subsequently manually improved. In **Chapter 2**, the reproducibility of aortic lumen segmentation on 4D flow MRI was assessed in healthy volunteers.

The observer-dependent variability of lumen segmentation will affect 4D flow MRI-derived hemodynamic parameters. In **Chapter 3**, reproducibility of 4D flow MRI-derived hemodynamic parameters was assessed in patients with a thoracic aortic aneurysm. In addition, reproducibility of aortic lumen segmentation was assessed.

Automated retrospective valve tracking in 4D flow MRI allows assessment of valvular flow through all intracardiac valves (27). However, it remains uncertain if valvular flow quantification can be performed consistently with automated retrospective valve tracking, independent of used MRI type and protocols. In **Chapter 4** inter-observer agreement and valvular flow variation of automated retrospective valve tracking in 4D flow MRI was assessed at multiple sites.

Part 2. Clinical Potential

The long-term progression of aortic hemodynamics remain unexplored, leaving us uncertain about the impact of increasing aortic diameter on the changes in aortic hemodynamics as individuals age. It is unclear whether aortic dilation rate will increase, decrease, or remain constant in relation to these hemodynamic changes. In **Chapter 5** we present the hemodynamic course of a patient with an ascending aortic aneurysm and a healthy volunteer with a decade and eight years of follow-up by 4D flow MRI, respectively.

Previous studies have demonstrated that aortic hemodynamics are associated with aneurysm growth in patients with tricuspid aortic valves (7, 8). In **Chapter 6** hemodynamic phenotypes were determined of aortic root dilatation, ascending aorta dilation patients and healthy volunteers.

Patients with a coarctation of the aorta before curative reconstruction are exposed to abnormal flow patterns which potentially could cause wall deterioration (35, 47). In **Chapter 7** we evaluated the effect of the age at correction on the aortic hemodynamics in adolescent patients with corrected coarctation. In addition, the effect of aortic valve morphology and presence of reobstruction were also evaluated.

In **Chapter 8** the main findings of this thesis are discussed and summarized.

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