Cardiac computed tomography for valvular heart disease and non-coronary percutaneous interventions

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10

Summary and conclusions

This thesis investigated how computed tomography (CT), a 3-dimensional (3D) non-invasive imaging technique, may be used in clinical practice to better characterize valvular heart disease and to plan transcatheter therapeutic techniques. In the introduction, **Chapter 1** of this thesis, the state-of-the-art of non-coronary structural heart disease and the recommendations and guidelines for the diagnosis, evaluation and treatment of valvular heart disease are reviewed. In addition, the development of transcatheter therapies for valvular heart disease is summarized. Remaining difficulties, current gaps in knowledge and potential future directions of transcatheter valvular repair are discussed. Additionally, the current status of transcatheter therapies to prevent stroke, particularly left atrial appendage closure, are appraised.

This thesis is divide in two parts. **Part I** explores how the high-spatial, volumetric resolution images of CT may be used to evaluate in great anatomical detail the pathophysiological mechanisms and geometrical distortions underlying valvular heart disease. The additional and integrated value that 3D imaging analysis by CT may provide over a 2-dimensional (2D) imaging evaluation alone is investigated. In **Chapter 2**, the calcification process of the aortic valve in relation to coronary artery calcification was studied with CT in patients with a bicuspid aortic valve and these calcification processes were compared to patients with a tricuspid aortic valve who were matched for cardiovascular risk factors and age. In the 70 patients with a bicuspid aortic valve, the calcification process, as reflected by the presence of aortic valve calcification on non-contrast calcium score, started at an earlier age than in the 210 propensity score matched patients with a tricuspid aortic valve. The first aortic valve calcification deposits in the patients with a bicuspid aortic valve were seen in the age quintile of 35-51 years whereas the first aortic valve calcification deposits in the patients with a tricuspid aortic valve were seen in the age quintile of 51-60 years. Median calcification volume of the deposits were larger in the patients with a bicuspid aortic valve (391 [43-2.028] mm^3 vs. 0 [0-1.844] mm^3, $p < 0.001$). The differences in aortic valve calcification process between the bicuspid and tricuspid aortic valve patients was independent of the process of coronary calcification.

In **Chapter 3**, the feasibility of using CT to analyze the geometrical remodeling process of the tricuspid valve and right ventricle in patients who have functional tricuspid regurgitation was investigated. CT analysis showed a geometrically distorted right valvulo-ventricular complex with larger tricuspid annuli (cross-sectional annulus area of 1539.7±260.2 mm2 vs.1228.4±243.5 mm2, $p<0.001$), more severe tricuspid leaflet tethering (degree of anterior leaflet tethering: 18.1±4.9° vs. 15.4±4.1°, $p=0.003$) and right ventricular dilatation (end systolic volume of 93.2±29.8 mL vs. 64.2±23.6 mL, $p<0.001$) in the patients who had moderate or severe tricuspid regurgitation compared to those with a normal or less regurgitant tricuspid valve. CT analysis revealed that particularly tricuspid annulus dilation in an antero-posterior direction was independently associated with the occurrence of moderate/severe tricuspid regurgitation.

In **Chapter 4** the novel concept of combining anatomical data from CT with haemodynamical data from 2D echocardiography for a quantitative assessment of the grade of mitral regurgitation was investigated. The anatomical mitral regurgitant orifice area was measured in a full heart beat CT data by analyzing the regurgitant orfice area in the systolic phase where the regurgitant orifice was maximal. The measurement of the anatomical mitral regurgitant area overcomes the geometrical assumption of the regurgitation orifice area used with 2D echocardiography. By incorporating this CT measurement in the formula for the calculation of the mitral regurgitant volume the anatomical-haemodynamical fused regurgitant volume was obtained. Compared to the regurgitant volume of mitral regurgitation by 2D echocardiography alone, assessment of the fused mitral regurgitant volume resulted in reclassification of mitral regurgitant grade from severe to non-severe in 10% and and vice versa in 14%. The clinical impact of combining anatomical CT data and haemodynamical echocardiography data to quantify mitral regurgitation remains to be further investigated.

Chapter 5 analyses with CT the impact of mitral annulus dilatation in patients with atrial fibrillation on the occurrence and grade of mitral regurgitation in patients whose left ventricle was functionally and anatomical considered to be normal by 2D echocardiography. Specifically patients with a preserved ejection fraction and a non-dilated left ventricle were selected to investigate the concept of "atrial" mitral regurgitation in contrast to mitral valve regurgitation that originates due to left ventricular distortion or dysfunction. Using CT, parallel en-face views of the mitral valve annulus were reconstructed and these views were selected for the annulus measurements. The CT data showed more mitral annulus dilatation in the patients who had significant mitral regurgitation compared to the patients without significant mitral regurgitation: mitral annulus area indexed to body surface area of 665.0±100.6mm^2/m^2 compared to 530.5±66.6mm^2/m^2, $p<0.001$. In these patients with atrial fibrillation, the mitral regurgitation occurred independent of left ventricular dilatation or dysfunction providing anatomical concepts for "atrial" mitral regurgitation.

Part 2 investigates how CT images may be used to better understand potential complications of currently available and upcoming cardiac transcatheter treatments. It is important to emphasize that transcatheter procedures rely on periprocedural non-invasive imaging modalities as echocardiography and CT.

In **Chapter 6** the anatomy of the left atrial appendage of patients with atrial fibrillation was studied with CT in order to propose a systematic imaging approach for the geometrical planning of transcatheter left atrial appendage occlusion as a prophylactic treatment for embolic stroke prevention in patients with atrial fibrillation. It was hypothesized that the 3D dimensional analysis of left atrial appendage morphology would provide more accurate measurements for sizing and planning than that would be acquired with 2D angiography or echocardiography. According to the specific product characteristics and available different sizes of the two, in 2013 commercially available left atrial appendage occlusion systems, the percentage of patients whose left atrial appendage morphology would be anatomically suitable for left atrial appendage occlusion was determined. In **Chapter 7** the relation between the amount of thoracic aorta and aortic valve atherosclerosis and the occurrence of acute kidney injury after transcatheter aortic valve implantation was investigated. It was hypothesized that procedural catheter manoeuvring through a severely atherosclerotic thoracic aorta might result in kidney injury due to peripheral cholesterol embolization. In 210 patients who had undergone a CT scan before transcatheter aortic valve implantation, acute kidney injury occurred in 24% of these patients and although that acute kidney injury is obviously multifactorial, more thoracic atherosclerosis on the CT scan was independently associated with acute kidney injury. These data may be used for the development of arterial embolic filter devices that protect the kidneys for procedural injury due to atheroembolization.

In **Chapters 8** and **9** the focus was shifted to upcoming, transcatheter treatment techniques for tricuspid valve regurgitation. **Chapter 8** reviews the rationale and technical characteristics of the transcatheter repair techniques under development. Several different imaging aspects and imaging techniques evaluating the right side of the heart that may become important for the evaluation and selection of patients for these techniques were discussed. **Chapter 9** provides a detailed proposal for a systemic pre-procedural CT analysis approach for the planning of the different available transcatheter tricuspid valve repair techniques. The geometrical distribution of crucial anatomical landmarks such as distance between the right coronary artery and the tricuspid annulus was provided by CT analysis of 250 patients.

In conclusion, the volumetric, high resolution CT images provide valuable geometrical insights in the pathophysiology of valvular heart disease. In current clinical practice, cardiac CT is key in the evaluation of patients with valvular heart disease who are considered for structural valvular intervention, either surgical or transcatheter.

CT will help to further individualize each transcatheter repair procedure.

Furthermore, the incremental and prognostic value of combining anatomical CT and hemodynamical echocardiography data for a more precise quantification of valvular heart disease remains to be further clarified.