Computed tomography coronary angiography : from quantification of coronary atherosclerosis to risk stratification of patients

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Chapter 1

General introduction and outline

Introduction

Around 1970 computed tomography (CT) entered the field of clinical imaging tools. In those days both the spatial and temporal resolution of CT were insufficient for cardiac imaging. With the introduction of 4-slice CT in the late 1990s, visualization of coronary arteries became feasible. Nowadays computed tomography coronary angiography (CTA) is considered a suitable non-invasive method for the assessments of coronary atherosclerosis; its clinical applicability is widely incorporated in current guidelines.[1, 2] Coronary stenosis severity on CTA is strongly correlated with invasive coronary angiography, and the diagnostic accuracy for the presence of coronary artery disease (CAD) is excellent. Especially the high sensitivity (~ 98%) allows for accurate rule-out of disease in patients with suspected CAD.[3] Additionally, the prognostic value of CTA has been established in the past years.[4] The prognosis of patients is decreased with increasing number of obstructive (≥50% stenosis) lesions.[5] Most importantly, the prognosis of patients without CAD on coronary CTA is excellent. Moreover, it has been noted, that also the presence of non-obstructive CAD is associated with impaired prognosis.[6] This has led to an increasing interest in the clinical value of coronary atherosclerosis burden in addition to only assessing the presence of obstructive CAD. On coronary CTA, plaque composition can also be assessed. Traditionally, coronary plaque is classified as non-calcified, partially plaque or calcified plaque. In several studies, the prognostic implications of the presence of different plaque types have been established.[7, 8] Patients with non-calcified and partially calcified plaque have a worse prognosis compared to patients with only calcified plaques. Currently the field of research in cardiac CT is shifting towards assessment of overall atherosclerotic burden and incorporating additional features of coronary CTA, besides obstructive CAD, for risk stratification of patients.

Quantification of coronary atherosclerosis.

In current practice the assessment of CAD on coronary CTA is performed visually. However, for accurate and reproducible assessment of the dimension and composition of coronary atherosclerosis, a quantitative approach would be favorable. Recently, novel software algorithms have become available which allow for such a quantitative analysis.[9] Using this software, the burden of coronary atherosclerosis, the three-dimensional dimensions (i.e. diameters and volumes) and the exact degree of stenosis can be quantified. Moreover, this software allows for assessment of composition of coronary atherosclerosis using Hounsfield Unit (HU) thresholds. The accuracy of this software for quantification of atherosclerosis dimensions has been recently established.[10]

This thesis further investigates the accuracy of this software, especially for quantification of coronary plaque composition. Additionally, the clinical value of this quantification algorithm will be explored.

Diabetic patients without chest pain syndrome.

Cardiovascular death is the main cause of death in patients with diabetes mellitus (DM).[11] Additionally, patients with DM often have silent myocardial ischemia and CAD in an advanced stage before becoming manifest.[12] However, in these patients traditional cardiovascular risk factors fail to accurately predict diabetic patients' risk.[13] In the past years the value of different imaging modalities in the specific setting of asymptomatic patients with DM has been addressed.[14]

This thesis explores the prognostic value of coronary CTA in these high risk diabetic patients. Furthermore, the change in ischemia over-time is investigated, focusing on the role of coronary CTA to predict these changes.

Outline

This thesis focuses on the clinical value of quantification of coronary atherosclerosis on coronary CTA. Moreover, the value of coronary CTA in high risk diabetic patients without chest pain syndrome in clinical practice is assessed. This thesis is preceded by **Chapter 2** which provides an overview of the clinical use of computed tomography coronary angiography (CTA) and the application in acute cardiac care.

Part 1 of this thesis focuses on the quantitative assessment of coronary atherosclerosis on coronary CTA.
Chapter 3 describes the different imaging techniques for analysis of coronary atherosclerosis. In **Chapter 4** the feasibility of an automatic algorithm for coronary atherosclerotic tissue characterization is established and compared to IVUS VH. **Chapter 5** continues the study of Chapter 4 and discusses a novel method to enhance the characterization of calcified areas in IVUS VH by quantification of the acoustic shadow. This acoustic shadow is the result of the inability of the IVUS signal to penetrate calcium, and considered a major limitation of this technique. **Chapter 6** assesses the accuracy of a novel algorithm to automatically detect and quantify the Agatston coronary artery calcium score on contrast CTA. In **Chapter 7** the parameters of coronary atherosclerosis as derived from quantitative coronary computed tomography (QCT) are correlated to the presence of myocardial ischemia on gated myocardial perfusion single photon emission computed tomography (SPECT). In **Chapter 8**, a novel CTA risk score is introduced which integrates the location, severity

and composition of coronary atherosclerosis on CTA in one score. The value of this automated QCT-derived risk score for risk stratification is assessed in patients with suspected coronary artery disease. In **Chapter 9**, the value of CTA for serial imaging of coronary atherosclerosis is investigated. For this purpose, QCT is performed in patients who underwent serial CTA with a 2-year interval.

Part 2 of this thesis focuses on the clinical aspects of coronary atherosclerosis on coronary CTA in high risk diabetic patients without chest pain syndrome.
Chapter 10 investigates the changes in ischemia over time as assessed with SPECT myocardial perfusion imaging in relation to characteristics of coronary atherosclerosis on coronary CTA. In **Chapter 11** the long-term prognostic value of coronary CTA in high risk diabetic patients without cardiac symptoms is assessed.

References

(1) Montalescot G, Sechtem U, Achenbach S *et al.* 2013 ESC guidelines on the management of stable coronary artery disease: The Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013 August 30.

(2) Taylor AJ, Cerqueira M, Hodgson JM *et al.* ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 appropriate use criteria for cardiac computed tomography. A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the Society of Cardiovascular Computed Tomography, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of Nuclear Cardiology, the North American Society for Cardiovascular Imaging, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance. *J Am Coll Cardiol* 2010 November 23;56(22):1864-94.

(3) von Ballmoos MW, Haring B, Juillerat P, Alkadhi H. Meta-analysis: diagnostic performance of low-radiation-dose coronary computed tomography angiography. *Ann Intern Med* 2011 March 15;154(6):413-20.

(4) Bamberg F, Sommer WH, Hoffmann V *et al.* Meta-analysis and systematic review of the long-term predictive value of assessment of coronary atherosclerosis by contrast-enhanced coronary computed tomography angiography. *J Am Coll Cardiol* 2011 June 14;57(24):2426-36.

(5) Min JK, Shaw LJ, Devereux RB *et al.* Prognostic value of multidetector coronary computed tomographic angiography for prediction of all-cause mortality. *J Am Coll Cardiol* 2007 September 18;50(12):1161-70.

(6) Lin FY, Shaw LJ, Dunning AM *et al.* Mortality risk in symptomatic patients with nonobstructive coronary artery disease: a prospective 2-center study of 2,583 patients undergoing 64-detector row coronary computed tomographic angiography. *J Am Coll Cardiol* 2011 July 26;58(5):510-9.

(7) Gaemperli O, Valenta I, Schepis T *et al.* Coronary 64-slice CT angiography predicts outcome in patients with known or suspected coronary artery disease. *Eur Radiol* 2008 June;18(6):1162-73.

(8) van Werkhoven JM, Schuijf JD, Gaemperli O *et al.* Incremental prognostic value of multi-slice computed tomography coronary angiography over coronary artery calcium scoring in patients with suspected coronary artery disease. *Eur Heart J* 2009 November;30(21):2622-9.

(9) Boogers MJ, Broersen A, van Velzen JE *et al.* Automated quantification of coronary plaque with computed tomography: comparison with intravascular ultrasound using a dedicated registration algorithm for fusion-based quantification. *Eur Heart J* 2012 April;33(8):1007-16.

(10) Voros S, Rinehart S, Qian Z *et al.* Coronary atherosclerosis imaging by coronary CT angiography: current status, correlation with intravascular interrogation and meta-analysis. *JACC Cardiovasc Imaging* 2011 May;4(5):537-48.

(11) Morrish NJ, Wang SL, Stevens LK, Fuller JH, Keen H. Mortality and causes of death in the WHO Multinational Study of Vascular Disease in Diabetes. *Diabetologia* 2001 September;44 Suppl 2:S14-S21.

(12) Zellweger MJ, Hachamovitch R, Kang X *et al.* Prognostic relevance of symptoms versus objective evidence of coronary artery disease in diabetic patients. *Eur Heart J* 2004 April;25(7):543-50.

(13) van Dieren S, Beulens JW, Kengne AP *et al.* Prediction models for the risk of cardiovascular disease in patients with type 2 diabetes: a systematic review. *Heart* 2012 March;98(5):360-9.

(14) Bax JJ, Young LH, Frye RL, Bonow RO, Steinberg HO, Barrett EJ. Screening for coronary artery disease in patients with diabetes. *Diabetes Care* 2007 October;30(10):2729-36.