Multimodality imaging in chronic coronary artery disease

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Summary and conclusions

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In the general introduction of this thesis, the various techniques used for non-invasive detection of coronary artery disease (CAD) are summarized. Chronic CAD can eventually lead to heart failure with considerable morbidity and mortality. Furthermore, the role of nuclear imaging in the evaluation of patients with heart failure is introduced, followed by the outline of the thesis.

Part I

In the first part of the thesis the value of multi-slice computed tomography (MSCT) in the detection and evaluation of CAD in patients with known or suspected CAD is discussed. MSCT has recently been introduced as an upcoming technique for non-invasive evaluation of the coronary arteries. Since the MSCT acquisition is gated to the patient's ECG, retrospective reconstruction throughout the cardiac cycle is possible, thus enabling the assessment of left ventricular (LV) volumes and function. **Chapter 1** provides an overview of the various techniques available for functional and anatomical imaging in coronary artery disease. Initially, the presence of CAD was evaluated by means of functional techniques, whereas more recently attention has been directed to direct visualization of the coronary arteries by means of anatomical imaging modalities. Both the advantages and the limitations are described for each technique. In **Chapter 2**, an extensive comparison between MSCT, gated single-photon emission computed tomography (SPECT) and 2D echocardiography is made for the assessment of global and regional LV function (LV ejection fraction and regional wall motion abnormalities) and volumes in patients with known or suspected CAD. Fairly good correlations between MSCT and gated SPECT were found, whereas correlations were excellent for MSCT compared with 2D echocardiography. In **Chapter 3**, a head-to-head comparison between 64-slice MSCT and 2D echocardiography is made for the assessment of LV volumes and function. Excellent correlations and agreement were shown, indicating that accurate evaluation of LV volumes and function is feasible with MSCT. **Chapter 4** focuses on the potential of MSCT to provide a comprehensive assessment of coronary artery stenosis, LV function and perfusion. In 21 patients with previous infarction, 16-slice MSCT was performed, in addition to conventional coronary angiography (to assess coronary anatomy) and gated SPECT imaging (to assess cardiac function and perfusion). In total, 98% of the coronary artery segments were interpretable on MSCT, and a sensitivity of 91% and a specificity of 97% for the detection of significant stenoses were observed. Moreover, excellent correlations and agreement for the assessment of LVEF and regional wall motion between MSCT and gated SPECT were demonstrated. Finally, with regard to perfusion, MSCT correctly identified a resting perfusion defect in 93% of the segments, whereas the absence of a perfusion defect was correctly noted in 98% of the segments. The evaluation of perfusion defects with MSCT is further investigated in **Chapter 5**. In 69 patients with healed myocardial infarcts, MSCT and gated SPECT were performed to assess the presence of myocardial infarct and to evaluate the infarct score. In 90% of the patients, a perfusion defect was identified on resting gated SPECT. In all of these patients, hypo-enhanced areas were

observed on MSCT. Moreover, in 43% of the patients without perfusion defects on SPECT, evidence of healed myocardial infarction could be demonstrated on MSCT. The total infarct score was calculated as the percentage of the LV. A mean infarct score of 12±10% was found for MSCT, compared to 16±13% of the LV as measured with gated SPECT, demonstrating an excellent correlation (r=0.93). In **Chapter 6**, the role of MSCT in the evaluation of patients presenting with suspected acute coronary syndrome (ACS) is assessed. In total, 40 patients underwent 64-slice MSCT to evaluate the atherosclerotic plaque burden and morphology in relation to the coronary calcium score. The majority of the patients was diagnosed as having low (46%) or intermediate (53%) risk of ACS, according to the TIMI risk score. In 33% of the patients with suspected ACS, no coronary calcium was observed on MSCT. However, in 85% of these patients coronary artery plaques were present, causing even significant stenosis in 39% of these patients. It was demonstrated that only 14% of the observed plaques were calcified, whereas 86% of the lesions contained non-calcified tissue. It seems that in patients presenting with suspected ACS, non-calcified plaques are highly prevalent, and absence of coronary calcium does not reliably exclude the presence of significant atherosclerosis.

The high negative predictive value has always been considered to be the major strength of MSCT coronary angiography and a normal MSCT scan virtually excludes CAD on a conventional coronary angiography. However, concern has been raised that ruling out of the disease will only be possible in a minor proportion of patients since coronary atherosclerosis may be encountered in a considerable number of patients. **Chapter 7** focuses on the prevalence of a normal MSCT scan in patients with suspected coronary artery disease. Observations were related to both clinical presentation and pretest likelihood of CAD. In total, 340 consecutive patients without a history of CAD were included in the analysis, of whom 46% had no coronary calcium and 40% had a completely normal MSCT coronary angiogram. Importantly, MSCT allowed ruling out CAD in 33% of the patients with intermediate pretest likelihood.

Part II

In **Part II** attention is directed to heart failure and the role of nuclear imaging in the evaluation of heart failure patients. **Chapter 8** provides a review of the various nuclear techniques to evaluate the success of cardiac resynchronization therapy (CRT), and also which imaging modalities can be useful in the patient selection for CRT. In **Chapter 9**, phase analysis with gated perfusion SPECT is described as a nuclear technique for the evaluation of LV dyssynchrony in 75 patients with heart failure, impaired LV function and wide QRS complex. The measurements with phase analysis have been compared with the LV dyssynchrony as evaluated with tissue Doppler imaging (TDI). It was shown that, of the 4 parameters that can be derived from phase analysis, the histogram bandwidth and phase SD correlated best with LV dyssynchrony as assessed with LV dyssynchrony on TDI. Finally, in **Chapter 10** is investigated whether the degree of LV dyssynchrony as assessed with phase analysis from gated perfusion SPECT could predict which heart failure patients would benefit from CRT. In total, 42 patients with severe heart failure, depressed LV ejection fraction and wide

QRS complex underwent both gated perfusion SPECT and 2D echocardiography with TDI before implantation of a CRT device. It was observed that responders to CRT had significantly higher values of histogram bandwidth and phase SD than the nonresponders. Moreover, it was demonstrated that a cutoff value of 135º for histogram bandwidth and a cutoff value of 43º for phase SD can predict response to CRT with high sensitivity and specificity (70% sensitivity and specificity for histogram bandwidth and 74% sensitivity and specificity for phase SD). Gated perfusion SPECT can therefore not only provide valuable information on the presence of viable myocardium and the presence of scar tissue in the posterolateral myocardium, but can also provide important knowledge on the presence or absence of LV dyssynchrony.

Conclusions

MSCT imaging can provide important information on global as well as regional LV function, without the need for additional data sets. LV functional assessment with MSCT correlates well with LV functional assessment as performed with 2D echocardiography and gated SPECT. This information is of clinical importance as it offers more insight in patients' prognosis. Moreover, in patients with prior myocardial infarction, hypoenhanced areas can be detected with MSCT imaging, indicating areas with reduced perfusion during rest.

MSCT coronary angiography is mostly used to exclude CAD in patients with suspected CAD. The coronary calcium score is also used for this purpose.
In patients presenting with suspected acute coronary syndrome, non-calcified plaques are highly prevalent on MSCT coronary angiography and the absence of coronary calcium may therefore not reliably exclude the presence of (significant) atherosclerosis. Importantly, the use of MSCT in the setting of suspected ACS needs further study to determine if MSCT has a role in the work up of this patient population.

MSCT can detect significant CAD with high sensitivity and specificity. Its high negative predictive value is considered to be its major strength and it renders the technique suitable for ruling out CAD in a non-invasive manner in patients with suspected CAD and a low to intermediate pretest likelihood for CAD. Indeed, in a substantial number of patients MSCT coronary angiography can reliably exclude the presence of CAD.

In patients with heart failure, gated SPECT not only provides valuable information on viability and the presence of scar tissue in the posterolateral area, but also on the presence of LV dyssynchrony by means of phase analysis. The assessment of LV dyssynchrony with phase analysis on gated SPECT correlates well with the evaluation of LV dyssynchrony with tissue Doppler echocardiography. The parameters histogram bandwidth and phase SD have higher values in patients who respond to CRT and both parameters can aid in the patient selection for CRT.