Heart rate reduction in non-invasive coronary angiography with multi-detector computed tomography
INTRODUCTION

In recent years, multi-detector computed tomography coronary angiography (CTA) has emerged as a rapidly advancing imaging technique for the non-invasive assessment of coronary artery disease (CAD). This technique not only allows the evaluation of the degree of coronary stenosis, but also enables the identification atherosclerotic changes in the vessel wall, including the identification of plaque type. Figure 1 shows an example of a CTA investigation of a patient showing severe stenosis in the left anterior descending artery (LAD). With each new scanner generation, acquisition times, spatial and temporal resolution improved resulting in superior image quality and diagnostic accuracy in the detection of CAD.

Figure 1. CTA of a 54 year-old male patient who presented at the outpatient clinic with chest pain at exertion. Examination was performed using 320-row CTA. Heart rate during image acquisition was 50 beats per minute resulting in excellent image quality. A) Three dimensional volume rendered reconstruction of the heart, showing an overview of the LCx and LAD. B) Severe non-calcified plaque in the LAD (arrow). C) The stenosis was confirmed on invasive coronary angiography.

DIAGNOSTIC ACCURACY OF CTA

Excellent diagnostic accuracy has been reported for 64-row CTA. In a prospective multicenter trial, sensitivity, specificity, positive and negative predictive values of 95%, 83%, 64%, and 99%, respectively, were reported for the detection of significant CAD (defined as ≥ 50% luminal narrowing) on a patient level. As a result, with a high negative predictive value, approaching 100%, this technique is particularly useful to rule out CAD. However, accurate detection and evaluation of CAD is entirely dependent on good image quality and image quality degradation remains one of the main challenges in CTA. Using 64-row CTA, important reasons for CTA image quality degradation are cardiac motion, breathing and stair-step artifacts. Moreover, with novel radiation dose
Importance of heart rate reduction

limiting techniques, such as prospective ECG triggering, stair-step artifacts may be more pronounced.6 With the introduction of novel CTA technology, such as 320-row CTA and dual-source CTA several of these problems have been reduced or eliminated.7 8 Novel 320-row CTA allows scanning of the entire heart in a single heart beat, thereby eliminating stair-step artifacts and reducing total time of breath hold, thus decreasing motion artifacts. Furthermore, with the introduction of dual-source CTA the temporal resolution increased even further, thereby decreasing the problem of cardiac motion, even at increased heart rates.9 10 More recently prospectively ECG-triggered high-pitch spiral coronary CTA has been introduced and excellent image quality has been reported with sub-millisievert radiation doses. However to achieve such low radiation doses, a stable and low heart rate is essential.11 As a result, even with state-of-the-art CTA technologies, heart rate reduction remains important to optimize CTA image quality and limit radiation exposure.

NEED FOR HEART RATE REDUCTION

Image Quality
Also with new generation CTA technology, an important predictor of image quality remains heart rate. High or irregular heart rate may cause image quality degradation and decrease diagnostic accuracy.12-14 In particular, an elevated heart rate will increase the

Figure 2. Coronary artery motion velocities according to heart rate. Patients were grouped according to heart rate: lower than 60 beats per minute, between 60 and 75 beats per minute, and higher than 75 beats per minute. Velocities of all coronary arteries were plotted against percentages of the R-R interval. Arrows indicate shifts of first velocity trough and second velocity peak and decrease of width of the second velocity trough with increasing heart rate. Reproduced with permission from.15
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likelihood of cardiac motion during image acquisition, while the diastolic rest-period shortens, or even disappears. As a result, to minimize coronary artery motion artifacts, image acquisition should be performed at a low heart rate during the diastolic phase during which the heart is relatively motionless. Figure 2 illustrates that heart rate significantly affects coronary artery motion. Several previously published CTA image acquisition protocols suggest that optimal vessel visibility is obtained at heart rate below 65 beats per minute.

Radiation Dose

With the introduction of novel radiation dose limiting acquisition techniques, heart rate has become an important determinant of patient radiation exposure. Although CTA is inherently associated with radiation exposure, techniques have been developed to reduce patient radiation exposure while at the same time maintaining CTA image quality. As a result, prospective ECG triggered image acquisition has been introduced, enabling image acquisition during only a small portion of the R-R interval, thus significantly lowering radiation burden as compared to retrospective ECG gating techniques. It is important to note, however, that to use this technique effectively, the patient should have a low heart rate.

STRATEGIES FOR HEART RATE REDUCTION

Since heart rate reduction is essential for optimal image quality and dose reduction, heart rate lowering medication is routinely administered prior to CTA investigations. In order to achieve heart rate control, different strategies may be used.

Beta-blockade

Previous studies have shown that roughly half of all patients referred for CTA require heart rate reduction. Beta-blockers are routinely used to lower heart rate, and may be administered sublingually or intravenously. Beta-blockers lengthen the diastolic interval, during which the heart is relatively quiescent, thereby reducing cardiac motion artifacts and improving CTA image quality. Additionally beta-blockers decrease heart rate variability, which is also an important factor determining image quality. As a result, beta-blockers are an effective and commonly used agent to reduce heart rate and heart rate variability prior to CTA and thus to improve image quality. Nevertheless, contraindications to beta-blocking medication are common, thereby limiting its use. Reported percentages for the presence of contraindications to beta-blockers range from 16% to 24%, and contraindications include asthma, advanced AV block, severe left ventricular systolic dysfunction, severe aortic stenosis and known allergy to beta-blockers.
Recent data have shown that, in patients with contraindications to beta-blockers, mean heart rate during CTA was significantly higher resulting in a decrease in overall CTA image quality as compared to patients without contraindications to this agent (Figure 3).20 As a result, careful individual assessment prior to CTA is important, and, in the presence of contraindications to beta-blockers, alternatives should be considered.

Ivabradine

Recently, ivabradine has been suggested as a potential heart rate lowering agent that may serve as an alternative when contraindications to beta-blockers are present. Ivabradine reduces heart rate in patients by specific inhibition of the $I_f$ current in the sinoatrial node.24 Accordingly, it selectively inhibits the sinus node and does not alter other aspects of cardiac function, such as blood pressure 25 and cardiac contractility.26 The BEAUTIFUL trial, a double-blind, randomized, placebo-controlled trial, tested whether lowering the heart rate with ivabradine reduces cardiovascular death and morbidity in patients with CAD and left ventricular systolic dysfunction. It was shown that ivabradine safely and effectively lowered heart rate by 6 beats per minute at 12 months use and that it did not affect clinical outcomes. These data confirm that ivabradine has the potential to effectively reduce heart rate. Consequently, prior to CTA investigation, ivabradine may be a potential alternative to reduce heart rate when beta-blockers are contraindicated. At present however, data on the use of ivabradine in this setting are not yet available, but soon expected.

Figure 3. The presence of contraindications to beta-blockers was associated with a significant decrease in CTA image quality. The percentage of examinations with poor image quality was higher in patients with contraindications to beta-blockade than in patients without contraindications to this agent. Reproduced with permission from.20
CONCLUSION

CTA mage quality is inversely related to heart rate and radiation dose. As a result, heart rate lowering medication is routinely administered prior to CTA. Beta-blockers are routinely administered for the purpose of heart rate control. Inadequate beta-blockade due to contraindications, which are frequently present, may significantly reduce CTA image quality, indicating the need for alternative approaches. Ivabradine has been shown to safely and effectively reduce heart rate and may therefore be a potential alternative to reduce heart rate prior to CTA investigation.
REFERENCES