INTRODUCTION

Coronary CT angiography (CCTA) with a multidetector row computed tomography (MDCT) scanner holds diagnostic value in coronary artery disease (1-3). Even though many factors can affect the image quality of CCTA, including heart rate (HR), heart rate variability (HRV), breathing, obesity, and coronary calcification (4-7), a relatively low and regular HR is essential to optimal image quality (4). With advances in CT technology, 64-slice MDCT was designed to accommodate a wider range of HRs with improved temporal resolution; however, studies have shown that HRV during CT scanning has a strong influence on the image quality and can decrease the diagnostic accuracy of CCTA (4, 6).

β-blockers reduce sympathetic influences and have been widely used to optimize HR in patients with tachycardia (5).
β-blockers can amend HRV by stabilizing HR (6). Therefore, we assumed that administering a low dose β-blocker to patients with low HR could improve the image quality and diagnostic value of a prospective electrocardiography (ECG)-gated CCTA by reducing HR or HRV. We prospectively assessed the effectiveness of a low-dose β-blocker on HR, HRV and image quality of CCTA in subjects with a HR under 65 beats per minute (bpm), using a prospective ECG-triggered protocol (step-and-shoot technique) with a 64-slice MDCT scanner.

**MATERIALS AND METHODS**

**Patient Preparation**

The study was a prospective study that was approved by our Institutional Review Board. Written informed consent was obtained from all subjects. Healthy subjects with a HR of less than 65 bpm who underwent a prospective ECG-triggered CCTA using a 64-slice CT scanner to screen for coronary artery disease during the study period were enrolled. We excluded those who had a HR of greater than 65 bpm or less than 50 bpm before CT scan, history of coronary artery disease, known arrhythmia, previous allergic reaction to iodinated contrast media or β-blocker, renal insufficiency (serum creatinine > 150 µmol/L), hemodynamic instability, congestive heart failure, asthma, chronic obstructive pulmonary disease, systolic blood pressure of less than 100 mm Hg, and those taking an oral β-blocker at baseline (5). Enrolled subjects were randomly assigned to 2 groups (G1 and G2). Group 1 received a low-dose of β-blocker (Atenolol; 12.5 mg, Hyundai Pharmaceutical Ind. Co., Seoul, Korea) 30 minutes before the CCTA examination. Group 2 underwent CCTA without premedication.

**CT Scan Protocol**

All cardiac MDCT was performed with a 64-MDCT scanner (Philips Brilliance 64, Philips Medical System, Best, the Netherlands). Data acquisition was performed in the craniocaudal direction within a single breath-hold at end-inspiratory suspension. The scanning range covered the heart from the level of the carina to the diaphragm. A prospective ECG-triggered protocol was used with a step-and-shoot technique. The scanning parameters were as follows: step-and-shoot axial scanning direction, 420-msec gantry rotation time, 120 kV, 210 mAs, 64 × 0.625-mm slice collimation, 4-cm table feed per rotation, and the center of the imaging window set at 70–80% of the R-R interval. Seventy mL of iodinated contrast agent (Optiray 350; Tyco Healthcare, Kantata, Canada) was administered intravenously into an antecubital vein through an 18 gauge catheter at a rate of 5 mL/sec followed by 50 mL of normal saline at a rate of 5 mL/sec using a power injector (Nemoto; Nemoto Kyorindo, Tokyo, Japan). Imaging was performed using a real-time bolus tracking technique. The scans were started 7 seconds after a trigger threshold of 130 Hounsfield units was reached at the proximal descending aorta. The breath-hold maneuver was successfully performed by all patients. An ECG for each patient was recorded simultaneously.

**CT Image Reconstruction**

The image reconstruction was performed on the scanner’s workstation using commercially available software (Extended Brilliance Workstation, Philips Medical System, Best, the Netherlands). The reconstruction parameters used were as follows: 0.9 mm slice thickness, 0.45 mm increment, 512 × 512 pixels image matrix, XCC kernel, and 15–23 cm field of view. MDCT data were transferred and post processing was performed on an Aquarius Workstation V3.6 (TeraRecon, San Mateo, CA, USA). Multi-planar reformatted (MPR), curved-planar reformatted (CPR), and medial axis reformatted (MAR) images with orthogonal and perpendicular projections to the vessel courses of each coronary segment were generated for the evaluation.

**CT Image Analysis**

Fifteen coronary segments were subdivided according to the American Heart Association guidelines (8); proximal right coronary artery (pRCA), middle RCA (mRCA), distal RCA (dRCA), right posterior descending artery (RPD), left main coronary artery, proximal left anterior descending artery (LAD), middle LAD, distal LAD, 1st diagonal branch (D1), 2nd diagonal branch, proximal left circumflex artery (pLCx), distal LCx (dLCx), obtuse marginal artery (OM), posterolateral artery and left posterior descending artery. The segments with a diameter of at least 1.5 mm at their origin were included.

Two radiologists assessed the image quality of 15 coronary segments in consensus. We evaluated all reconstructed images using axial source images, as well as MPR, CPR, and MAR im-
The image quality was assessed using the following 4-point grading scale by the 2 radiologists who were blinded to the HR and HRV: grade 1 (poor), severe degree of image degradation or discontinuation of vessel contour that prevented vessel lumen evaluation; grade 2 (adequate), moderate degree of image degradation with some obstacle to vessel lumen evaluation; grade 3 (good), minor degree of image degradation without compromising vessel lumen evaluation, and grade 4 (excellent), no image degradation (Fig. 1). Any segment with grade 1 was regarded as non-diagnostic.

Radiation Dose

The dose-length product was recorded for each cardiac CT examination by the CT scanner. The mean effective radiation dose was calculated by multiplying the dose-length product by the conversion coefficient (0.017) for the chest and expressed as millisieverts (9).

Heart Rate and Heart Rate Variability Analyses

The initial HR (HR_{pre}) prior to β-blocker administration, was measured 30 minutes before the CCTA exam after sufficient rest in all patients. HRs were also checked during data acquisition of CCTA. Mean HR during scanning (HR_{mean}) was obtained from the ECG-gated data. HR change (HR_{chg}) was defined as difference between HR_{pre} and HR_{mean} (i.e., HR_{chg} = HR_{pre} - HR_{mean}). HRV was calculated as 1 standard deviation (SD) of the HR during CT scanning (10).

Statistical Analysis

Continuous variables were expressed as mean ± SD and categorical variables as frequencies or percentages. Student’s t-test or Mann-Whitney U test was used to evaluate the statistical significance of differences for the demographic data, HR, HRV and image quality scores between the 2 groups. Paired t-test was used to evaluate the statistical significance of difference between HR_{pre} and HR_{mean} in each group. Chi-square test was used to evaluate the statistical significance of differences for the number of segments in each score between the 2 groups. A linear regression and Pearson correlation were used to determine the correlations between the mean image quality score and HR_{mean} or HRV. A p value of less than 0.05 was considered as statistically significant. All statistical analyses were performed with the commercially-available software (SPSS 20; Statistical Package for the Social Science, Chicago, IL, USA).

RESULTS

Heart Rate and Heart Rate Variability

CCTA was performed in all subjects without complications. Demographic data including HR and HRV were summarized in Table 1. Mean age and body mass index were not statistically different between the 2 groups (p > 0.05). HR_{pre} was not different in
group 1 and group 2 (60.4 ± 4.2 bpm vs. 58.8 ± 3.6 bpm, \( p = 0.08 \)). HR\(_{\text{mean}}\) was significantly lower than HR\(_{\text{pre}}\) in group 1 (50.3 ± 5.6 bpm vs. 60.4 ± 4.2 bpm, \( p = 0.011 \)) but not in group 2 (53.3 ± 4.8 bpm vs. 58.8 ± 3.6 bpm, \( p = 0.193 \)). HR\(_{\text{CHG}}\) was significantly higher in group 1 than in group 2 (10.1 ± 5.4 bpm vs. 5.5 ± 5.5 bpm, \( p < 0.001 \)). HR\(_{\text{mean}}\) during CCTA in group 1 was significantly lower than that of group 2 (50.3 ± 5.6 bpm vs. 53.3 ± 4.8 bpm, \( p = 0.016 \)) (Table 1, Fig. 2). During CCTA, HR\(_{\text{V}}\) was not different in group 1 and group 2 (1.1 ± 0.5 vs. 1.3 ± 0.7, \( p = 0.147 \)) (Table 2, Fig. 3). The mean radiation dose of CCTA was 4.0 ± 0.4 mSv (range, 3.7–4.6 mSv). The radiation dose of group 1 was not different with that of group 2 (3.9 ± 0.5 mSv vs. 4.0 ± 0.4 mSv, \( p = 0.98 \)).

### Image Quality

A total of 921 segments with a diameter greater than 1.5 mm were evaluated (431 segments in group 1 and 490 in group 2). Group 1 was diagnostic in 429 coronary segments (99.3%); excellent (score 4) in 190 (44.1%), good (score 3) in 184 (42.7%), and adequate (score 2) in 54 (12.5%). Three segments (0.7%) were non-diagnostic (score 1) due to severe degradation of vessel contours. Group 2 was diagnostic in 474 (97.7%); excellent (score 4) in 192 (39.2%), good (score 3) in 216 (44.1%), and adequate (score 2) in 66 (13.5%). Sixteen segments (3.3%) were non-diagnostic (score 1). On the segment-based analysis, the image quality scores for mRCA and D1 segments were higher in group 1 than in group 2 (3.0 ± 0.9 vs. 2.5 ± 1.1, \( p = 0.039 \) in mRCA, 3.4 ± 0.6 vs. 3.1 ± 0.7, \( p = 0.024 \) in D1). However, the mean scores of image quality were not different between group 1 and group 2 (3.3 ± 0.4 vs. 3.2 ± 0.3, \( p = 0.199 \)), and the image quality scores on the vessel-based analysis were not different between group 1 and group 2 (Table 2). The mean image quality score of the coronary artery segments in both groups was nega-
β-blocker on HR and HRV, as well as the image quality of a prospective ECG-gated CCTA in healthy subjects with low HR. Our study demonstrated that the use of low dose β-blocker could improve the image quality of mRCA and D1 segments by reducing HR, even when the HR was less than 65 bpm. The step-and-shoot technique using a prospective ECG-gated algorithm is one of the most powerful methods for radiation dose reduction. Dosage can be reduced up to 70–90% from that of retrospective ECG-gated CCTA (9, 11-13). However, a prospective ECG-gated CCTA mandates a low and regular HR of less than 60 to 65 bpm for optimal images (14). We postulated that the administration of low dose β-blocker could improve the image quality of a prospective ECG-gated CCTA by reducing the step-and-shoot dose while maintaining adequate image quality.

**DISCUSSION**

The aim of this study was to evaluate the effect of a low-dose β-blocker on HR and HRV, as well as the image quality of a prospective ECG-gated CCTA in healthy subjects with low HR. Our study demonstrated that the use of low dose β-blocker could improve the image quality of mRCA and D1 segments by reducing HR, even when the HR was less than 65 bpm. The step-and-shoot technique using a prospective ECG-gated algorithm is one of the most powerful methods for radiation dose reduction. Dosage can be reduced up to 70–90% from that of retrospective ECG-gated CCTA (9, 11-13). However, a prospective ECG-gated CCTA mandates a low and regular HR of less than 60 to 65 bpm for optimal images (14). We postulated that the administration of low dose β-blocker could improve the image quality of a prospective ECG-gated CCTA by reducing the step-and-shoot dose while maintaining adequate image quality.
HR or HRV, even in low HR subjects. We administered 12.5 mg oral atenolol that is less than the usual dose of 50–100 mg depending on the patient's weight for heart rate control (15). In group 1, the HR reduction (HR$_{\text{chg}}$) was 11 bpm after low dose β-blocker administration. In group 2, the HR$_{\text{chg}}$ was 5.5 bpm without premedication, probably due to the increased vagal tone by breath-holding (16). Zhang et al. (17) reported that breath-holding reduced the mean HR by about 4 bpm. Low dose β-blocker affected the image quality of CCTA. Non-diagnostic segments were lower in group 1 (0.7%) than in group 2 (3.3%). Image quality on segmental analysis was better in group 1 at the mRCA, which was known to be easily degraded by motion artifact (18), and D1 branch. However, image quality improvement was only observed in mRCA and D1 segments. Also, there was no difference in image quality between the 2 groups on vessel based analysis. Leschka et al. (4, 6) reported that 64-slice MDCT had reasonable image quality over a wide range of HRs, and HRV has more effect than the HR. Earls (19) reported that a small dose of β-blocker might be helpful in minimizing HRV in patients with low HR and high HRV. HRV was not related directly to the image quality in our study. These findings may be the result of low HR and small HRV in the study subjects. Low HR provides sufficient duration of diastole for good quality images, and the HRV may have been too small to significantly affect the image quality in patients with low HR (20). Furthermore, there was no difference of HRV between the 2 groups, hence the effect of low dose β-blocker on HRV was hard to compare. The radiation dose of our study was similar to those of previous studies with a prospective ECG-gating technique (9, 21). Lowering HR could increase the radiation dose of prospective ECG-gated CCTA by lengthening the R-R interval. However, the radiation dose in group 1 and 2 were not significantly different.

There were several limitations to the study. First, the number

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Fig. 3. Heart rate variability (HRV) in group 1 and 2. Boxplots show HRV in subjects with low dose β-blocker (group 1) and without β-blocker (group 2). During coronary CT angiography scanning, HRV was not different in group 1 and group 2 ($p = 0.147$).

Note.—Box = 1st–3rd quartiles, Bold line = median, Whiskers = minimum and maximum values, o = outlier

Fig. 4. Linear regression plots of mean image quality scores over the mean heart rate and heart rate variability (HRV) in 75 patients.

A. The mean image quality score of the coronary artery segments in both groups is negatively correlated with mean heart rate ($r = -0.449$, $p < 0.001$).

B. The mean image quality scores for all coronary artery segments and HRV shows no significant correlation ($r = -0.013$, $p = 0.913$). Dotted lines represent 95% confidence limits.
of enrolled subjects was too small to be generalized to all patients. Second, the comparative study was not performed in the same patient groups due to the concern of radiation exposure. Nevertheless, there was no significant difference in demographic data and HRs prior to the administration of β-blocker between the 2 groups. Third, we evaluated the image quality based on motion artifact but not the diagnostic performance for detecting coronary artery disease. A future study has been planned to analyze the diagnostic accuracy of a prospective ECG-gated CCTA under the effect of a low dose β-blocker.

In conclusion, low-dose β-blocker could reduce the HR, including resting HRs of less than 65 bpm that are not usually indicated for β-blocker. The image quality of CCTA using a prospective gating technique was improved in the mRCA and D1 segments with a low-dose β-blocker by reducing HR. However, on the per-vessel analysis, the overall image quality was not changed. Therefore, usefulness of a low-dose β-blocker appears to be limited in healthy subjects with low HR.

REFERENCES


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Note.—dLAD = distal LAD, dLCx = distal LCx, dRCA = distal RCA, D1 = 1st diagonal branch, D2 = 2nd diagonal branch, LAD = left anterior descending artery, LCx = left circumflex artery, LM = left main coronary artery, LPD = left posterior descending artery, mLAD = middle LAD, mRCA = middle RCA, OM = obtuse marginal artery, PL = posterolateral artery, pLAD = proximal LAD, pLCx = proximal LCx, pRCA = proximal RCA, RCA = right coronary artery, RPD = right posterior descending artery
저용량 베타차단제가 낮은 심박수 무증상 환자의 심박수, 심박변화, 그리고 전향적 동조화 심장 CT에 미치는 영향

박철환1 · 이상민2 · 홍유진3 · 김태훈1

목적: 저용량 베타차단제가 분당 65회 이하의 느린 심박수 무증상 환자에서 전향적 동조화 심장 CT의 영상 질을 높일 수 있는지 알아본다.

대상과 방법: 심박수가 65회 이하인 무증상 환자 75명을 두 군으로 나누어 전향적 동조화 심장 CT를 시행하였다. 1군 35명은 검사 30분 전, 저용량 베타차단제를 구강투여 후 시행하였으며, 2군 40명은 투약 없이 시행하였다. 각 환자에서 검사 전 심박수, 검사 중 심박수, 검사 중 심박변화를 측정하였다. 심장 CT 관상동맥 각 분절마다 영상 질을 평가하여 1점에서 4점까지 점수를 매겼으며, 4점이 가장 좋은 영상을 의미하였다.

결과: 두 군의 검사 전 심박수는 차이가 없었다. 심장 CT 시행 중 평균 심박수(bpm)는 1군이 2군에 비해 유의하게 낮았다(50.3 ± 5.6 vs. 53.3 ± 4.8, p = 0.016), 검사 중 심박변화는 두 군 간 차이가 없었다. 분절별 분석에서 1군의 우관상동맥 중분절(3.0 ± 0.9 vs. 2.5 ± 1.1, p = 0.039)과 좌전하행동맥 제1사선분절(3.4 ± 0.6 vs. 3.1 ± 0.7, p = 0.024)의 영상 질이 2군에 비해 유의하게 좋았다. 영상 질은 심박수와 음의 상관관계를 보였으나 심박변화와는 상관관계를 보이지 않았다. 혈관별 분석에서 영상 질은 두 군 간 차이가 없었다.

결론: 저용량 베타차단제는 느린 심박수 무증상 환자에서 심박수 감소효과가 있으며, 전향적 동조화 심장 CT 일부 분절의 영상 질을 높일 수 있으나, 그 효과는 제한적이다.

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