Radiation-Dose-Lowering Effects of Landiolol Hydrochloride in Coronary Angiography Using Computed Tomography (DELIGHT)  
– A Prospective Multicenter Study –

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Background: Controlling and decreasing the heart rate (HR) of patients during coronary computed tomography angiography (CCTA) is necessary to reduce radiation exposure and improve image quality. This prospective multicenter study aimed to investigate whether HR control with landiolol hydrochloride is useful for reducing radiation exposure during CCTA.

Methods and Results: We investigated 219 patients with suspected ischemic heart disease whose pretest HRs were 50–80 beats/min. We measured the HR before and after administration of landiolol hydrochloride and compared the estimated exposure inferred from the HR before administration of landiolol hydrochloride with the actual dose. After administration of landiolol hydrochloride, the mean HR (59.9±6.4 beats/min) at the time of CCTA was significantly lower than before administration (69.3±7.3 beats/min; P<0.001); 80% of the patients had controlled HRs at ≤65 beats/min. HR and blood pressure of all the patients recovered after the scan. The mean radiation dose in all patients was approximately 50% derived from the inferred dose before use of landiolol hydrochloride (4.5±3.2 vs. 9.0±3.7 mSv; P<0.001). There were no adverse events during this study.

Conclusions: The use of landiolol hydrochloride during CCTA was safe and resulted in approximately 50% decrease in radiation exposure dose, suggesting the clinical usefulness of this drug. (Circ J 2016; 80: 1225–1231)

Key Words: Beta-blockers; Coronary computed tomography angiography; Ischemic heart disease; Landiolol hydrochloride

The recent development of multislice computed tomography (CT) devices and scanning technology has led to the widespread use of coronary CT angiography (CCTA) in the clinical field as an essential diagnostic modality for cardiovascular imaging. In particular, the latest multislice CT devices have played a major role in advancing the diagnostic accuracy for ischemic heart disease.1–7

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As the use of CCTA has increased, radiation exposure has become a concern. Several methods have been developed to reduce the doses of radiation used for cardiac CT, including prospective electrocardiogram (ECG)-gating techniques to target a certain cardiac phase and low-voltage scanning with iterative reconstitution. However, inadequate doses of radiation may degrade image quality and cause deterioration of diagnostic performance. Therefore, it is important to control and reduce the heart rate (HR) so that ECG-gating acquisition can be applied to reduce the radiation dose.6,8

Oral β-blockers are widely used to control and reduce HR during CCTA.9–11 For this purpose, landiolol hydrochloride, a short-acting β1-selective β-blocker, has recently emerged and is being used in the clinical setting.12,13 Landiolol hydrochloride
has its maximum effect approximately 4 min after intravenous administration, allowing the HR to return to the initial value at the end of the scan. Therefore, this drug is useful for CCTA. Several reports have already described the diagnostic accuracy of CCTA achieved with good HR control using landiolol hydrochloride. However, no reports have described the reduction in radiation exposure via landiolol hydrochloride-dependent HR control.

In this study, we investigated the ability of landiolol hydrochloride to reduce radiation exposure during CCTA. We hypothesized that the use of landiolol hydrochloride may reduce not only HR but also radiation dose, reducing particularly the necessity of another scan because of poor image quality, and thus making this procedure safer.

### Methods

#### Patients

The study protocol was approved by the local ethics commit-
Figure 1. Mean heart rate (beats/min) of the patients during coronary computed tomography (CT) angiography, before and after administration of landiolol hydrochloride. bpm, beats/min.

Figure 2. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) (mmHg) of the patients during coronary computed tomography (CT) angiography, before and after administration of landiolol hydrochloride. bpm, beats/min.
Figure 3. Absorbed dose (mGy), dose-length product (DLP) (mGy*cm) and effective dose (mSv) for the calculated and actual radiation doses during coronary computed tomography angiography under landiolol hydrochloride administration.
Landiolol Hydrochloride in CCTA

and the mean HR of these patients decreased to 59.9 ± 6.4 beats/min (46–76 beats/min) after administration of landiolol hydrochloride. HR was reduced to <65 beats/min in 170 patients (77.6%) at the time of CCTA, and 49 patients (22.4%) had a HR ≥ 65 beats/min at the time of CCTA (Figure 1).

HR showed the greatest decrease during the scan, which was after completion of intravenous administration of landiolol hydrochloride (Figure 1), although the percent decrease in BP was minimal (Figure 2). Systolic and diastolic BPs of all patients returned to baseline levels after the CCTA examination.

Effective Radiation Dose

Among 219 patients, axial scanning with prospective gating was performed in 175 (79.9%), and 44 patients (20.1%) underwent helical scan with retrospective gating. The mean actual effective dose in the 219 patients was 4.5 ± 3.2 mSv, 4.1 ± 2.7 mSv in the 175 patients subjected to prospective gating, and 8.8 ± 4.4 mSv in the 44 patients subjected to helical scan with retrospective gating. Based on the assumption that helical scanning with retrospective gating was performed in patients on a 3-point scale (1=poor: motion artifact present and impossible to diagnose; 2=fair: motion artifact present but diagnosable; 3=excellent: no motion artifact and diagnosable) semiquantitatively and independently. Image quality was scored by consensus of both readers.

Statistical Analysis

For statistical testing, SPSS version 19.0 (SPSS, Inc, Chicago, IL, USA) was used. Paired t-tests were used to determine statistical significance. Differences with P<0.05 were considered significant.

Results

HR and BP Evaluation During CCTA

All 219 patients enrolled in the present study received the study drug (landiolol hydrochloride), without any withdrawals or dropouts. The demographic characteristics of the patients are summarized in Table 1.

The mean HR in 219 patients before administration of landiolol hydrochloride was 69.3 ± 7.3 beats/min (52–80 beats/min), and the mean HR of these patients decreased to 59.9 ± 6.4 beats/min (46–76 beats/min) after administration of landiolol hydrochloride. HR was reduced to <65 beats/min in 170 patients (77.6%) at the time of CCTA, and 49 patients (22.4%) had a HR ≥ 65 beats/min at the time of CCTA (Figure 1).

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<table>
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<th>2</th>
<th>3</th>
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<th>356 (41.3%)</th>
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<tr>
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Score: 1, poor: motion artifact present and impossible to diagnose; 2, fair: motion artifact present but diagnosable; 3, excellent: no motion artifact and diagnosable. #, segment; 4AV, atrioventricular; 4PD, posterior-descending; CCTA, coronary computed tomography angiography; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; LMT, left main trunk; RCA, right coronary artery.
whose HR was ≥65 beats/min after landiolol hydrochloride administration, the mean estimated effective dose was 14.5±4.5 mSv without dose modulation technology, and 9.0±3.7 mSv with dose modulation technology. Results showed that without the use of landiolol hydrochloride, patients may have received nearly twice as much radiation, even if dose modulation technology was applied (Figure 3).

Furthermore, we performed CCTA at 120 kV for 174 patients, and at 100 kV for 45 patients in this study. In our analysis of voltage base, the actual effective doses were 4.6±3.3 mSv and 4.1±2.9 mSv at 120 kV and 100 kV, respectively. There was no significant difference between the scan voltages because the prevalence of a 100-kV scan differed among the prospective scan, retrospective modulation and retrospective scan groups.

Image Quality
From among 3,504 theoretically possible segments in 219 patients with 16 coronary segments, 270 were eliminated because of anatomic variants or diameter <1.5 mm at their origins, and 199 had severe calcification and stents. As a result, we evaluated 3,035 segments.

The image quality of 2,962 segments (97.6%) was diagnostic (score 2–3), with excellent image quality rated in 2,092 segments (68.9%) and fair image quality rated in 870 segments (28.7%); 73 segments (2.4%) in 37 of the 219 patients were not diagnosed because of motion artifacts. Table 2 summarizes the image quality scoring of each coronary vessel and segment.

Additionally, we evaluated the difference in image quality between the prospective (2.01±0.59) and retrospective ECG-gating methods (2.02±0.63); there were no observed differences between them. Use of landiolol can reduce the radiation dose without reducing image quality.

Discussion
In this study, we examined the effects of landiolol hydrochloride on HR during CCTA. We found that administration of landiolol hydrochloride resulted in a significant decrease in HR, which yielded reduced exposure to radiation. These results are expected to facilitate the development of improved protocols for reducing radiation exposure in patients undergoing CCTA.

Advances in CT devices and technology have resulted in improved CCTA methods with superior diagnostic accuracy in patients with increased HR. However, increased radiation exposure dosages are required when the HR is elevated in order to obtain static images wherein the influence of the elevated HR is minimized. According to previous studies, the mean HR without HR control ranges from 74 to 76 beats/min. Therefore, it is possible to obtain sufficient diagnostic accuracy using the latest CT scanners, but the HR should be <65 beats/min when imaging in prospective gating mode in order to reduce radiation exposure. In other words, it is important to control the HR during CCTA with β-blockers in order to decrease the HR from 75 beats/min at the time of entering the CT room to 65 beats/min while imaging.

Using landiolol hydrochloride during CCTA in this study, we were able to decrease the percentage of patients with a HR ≥65 beats/min from 70.8% before drug administration to 22.4% after administration. Thus, it was possible to obtain a significant effective dose reduction of 50%. In addition, we succeeded in maintaining diagnosable image quality in 97.6% of segments by correctly controlling HR when using radiation exposure reduction mode. This yielded nearly the same level of diagnostic accuracy as in the past studies, indicating that it was both clinically and diagnostically useful to reduce radiation exposure in CCTA by using landiolol hydrochloride. Landiolol hydrochloride, which was used to reduce HR in this study, is a short-acting β1-blocker with a very short half-life (4 min). Long-acting β-blockers will remain effective after the end of the CT scan, so they are associated with risks such as decreasing BP. However, our study results suggested that landiolol hydrochloride could be used as a pretreatment for CCTA to rapidly decrease the HR for scanning and then having the HR return to baseline soon after, thus making CCTA safer by lowering the radiation exposure while maintaining diagnostic capability. In fact, in our study, the decrease in BP was not significant, and none of the patients required special treatment, demonstrating the safety of landiolol hydrochloride usage for CCTA. However, we cannot distinguish the reason why approximately 20% of the patients did not achieve a HR <65 beats/min. Additional studies are required to explain the observed data.

In conclusion, use of landiolol hydrochloride, a short-acting β1-blocker, enabled us to choose an appropriate prospective ECG-gating technique for CCTA with at least 50% reduction in the dose of radiation. Landiolol hydrochloride is safe and useful in terms of both radiation exposure reduction and image quality maintenance for CCTA in the clinical setting.

Conflicts of Interest
The authors have no conflicts of interest to declare.

Funding Declaration
The authors have no sources of funding to declare.

References


