Optimizing Contrast Medium Injection for Coronary CT Angiography Using Myocardial CT Perfusion Data

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Objective: To derive and validate a formula to predict the optimal amount of contrast medium for coronary CT angiography (CTA) from CT perfusion (CTP) data during comprehensive cardiac CT.

Materials and Methods: The derivation and validation group consisted of 196 and 41 patients, respectively. Dynamic CTP was performed under adenosine triphosphate stress of 0.14 mg/kg/min, followed by rest coronary CTA. Time to peak (TTP) and peak enhancement (PE) in the left ventricle during CTP was recorded. The amount of contrast medium during CTA was 0.8×body weight (kg) in the derivation group. A formula to determine the amount of contrast medium needed to achieve an enhancement of 370 Hounsfield unit (HU) in CTA was derived using TTP, PE, body weight, and heart rate. The amount of contrast medium required during CTA in the validation group was determined by this formula.

Results: The mean amount of contrast medium during CTA did not differ between the derivation and validation groups (49.3±8.0 mL vs. 47.9±12.9 mL, $p=0.39$). The mean coronary artery enhancement was slightly lower in the validation group (400±55 HU vs. 380±46 HU, $p=0.03$) with smaller interpatient variability ($p=0.02$) than in the derivation group. The proportion of patients with an optimal enhancement of 320 HU to 420 HU significantly increased from 54% to 75% ($p=0.01$) when the formula was used.

Conclusion: Adjusting the amount of contrast medium using dynamic CTP data could reduce the interpatient variability of coronary enhancement during comprehensive cardiac CT.

Key words Contrast media · Computed tomography angiography · Myocardial perfusion imaging.

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INTRODUCTION

Coronary CT angiography (CTA) is a widely used method to diagnose coronary artery disease [1]. Coronary arteries need to be within an optimal enhancement to maintain a good diagnostic performance [2-4]. Body habitus, especially body weight, is an important factor in determining the total amount of contrast

medium required because more contrast medium is required to achieve an optimal enhancement in obese patients [5]. Even when the contrast medium is tailored to body weight, interpatient variability in coronary enhancement can still remain. Previous studies have attempted to tailor the contrast medium dose using other parameters, such as lean body weight [6], body surface area [7], and cardiac output [8,9].

Another approach for optimizing the dose of contrast medium to achieve the target enhancement is to use the test bolus data [10]. As the peak enhancement (PE) of the main bolus can

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be predicted from the PE of the test bolus, an optimal amount of contrast medium could be calculated. Comprehensive cardiac CT is a combination of dynamic myocardial CT perfusion (CTP) and coronary CTA. We sought to predict the enhancement of coronary CTA using CTP data. The test bolus scan to define the appropriate contrast medium dose and scan start time could be omitted using a prediction formula derived from CTP data. Therefore, the purpose of the present study was to derive and validate a formula to predict an optimal amount of contrast medium for coronary CTA from CTP data.

MATERIALS AND METHODS

Patients undergoing comprehensive cardiac CT (a combination of dynamic myocardial CTP under stress and coronary CTA) were entered in a prospective registry under the Protocol Registration System of the UMIN Clinical Trials Registry (UMIN000024245). In brief, the main objective of this registry was to test whether microvascular dysfunction estimated by the calculated myocardial blood flow during stress have additive value in predicting the prognosis of patients over coronary stenosis. Inclusion criteria were history of type 2 diabetes regardless of symptoms, suspected coronary artery disease due to multiple risk factors, or evaluation of coronary stenosis after percutaneous coronary intervention. Patients from the outpatient department who met the inclusion criteria without severe renal dysfunction (estimated glomerular filtration rate of >40 mL/min/1.73 m²) were invited to participate. The study protocol was approved by the local Ethics Committee and all patients gave written informed consent (No. 0085).

Patients

The records of 212 patients in the registry from December 2016 to November 2018 were included for derivation. The exclusion criteria were as follows: arrhythmia (n=6), unable to hold breath (n=2), history of coronary artery bypass grafting (n=3), extravasation (n=2), technical errors present (n=2), and informed consent unavailable (n=1). Thus, the final derivation group included 196 patients. The derived formula was validated by 45 patients during December 2018 and March 2019, but the following patients were excluded: history of coronary artery bypass grafting (n=3) and arrhythmia (n=1). All patients were requested to discontinue caffeine intake at least 12 hours before the exam. We included 4 parameters in the equation: iodine dose, heart rate, PE, and time to peak (TTP). We believed that approximately 50 patients for each parameter would be feasible to produce a robust equation. Therefore, we included 196 patients in the derivation group. For the validation group, we determined that one-fifth of the derivation group would include patients with various body habitus and circulation status.

CT acquisition

All patients underwent cardiac CT using a single-source scanner (Somatom Definition AS+; Siemens Healthineers, Forchheim, Germany) with collimation of 64×0.6 mm and flying-focal spot, resulting in 128 slices. All scans were performed at the fastest gantry rotation time of 300 ms. Two intravenous lines were placed in both antecubital veins for the administration of contrast medium and adenosine triphosphate. We used a self-monitoring device for patients to visually control respiration (Abches; APEX Medical, Tokyo, Japan). We trained each patient before the scan to keep the end-inspiratory position at the same position. We used iopamidol 370 mg iodine/mL (Iopamiron 370; Bayer, Osaka, Japan) when the body weight was <70 kg, otherwise iomeprol 350 mg iodine/mL (Iomeron 350; Eisai, Tokyo, Japan). Iomeprol was used in obese patients because the amount of contrast medium included was 135 mL compared to 100 mL for iopamidol.

Myocardial CTP was initiated 3 min after administration of adenosine triphosphate (Adetphos; Kowa Company, Tokyo, Japan) at 0.14 mg/kg/min. When the heart rate increase was <10 beats/min or blood pressure decreased to <10 mm Hg, we increased the injection rate of adenosine to 0.20 mg/kg/min. The scanning parameters were as follows: tube potential, 100 kVp; reference mAs, 190 mAs; scan coverage 68.5 mm; acquisition window, 30–40% of the R-R interval. A total of 38–60 mL of contrast medium was injected at a flow rate of 3.2–5.0 mL/s, followed by a saline chaser. Excessive injection of contrast medium in lean patients would cause streak artifacts from the right atrium. This would negatively influence the calculated myocardial blood flow. Therefore, we changed the injection speed according to body weight. The scan initiation timing after the contrast medium injection was optimized with the stress heart rate: 6, 8, and 10 s when >90 , 65–90, and <65 beats/min, respectively. During the data acquisition of 25 s, 5 sets of 2-slab prospective electrocardiogram-gated axial scans were performed. The time interval between each slab was ≈ 1 s and the interval was ≈ 3 s between each set. Adenosine infusion was discontinued after the acquisition was completed. Half-reconstruction images were acquired with a slice thickness of 0.75 mm and an increment of 0.4 mm using a cardiac kernel (I36f) with sinogram-affirmed iterative reconstruction (SAFIRE) strength 2.

Coronary CT angiography was performed by prospective electrocardiogram-gated axial scan. When the tube current-time product of the CTP scan exceeded 150 mAs, the tube potential and the reference mAs was set as 120 kVp and 250 mAs, otherwise these were set as 100 kVp and 350 mAs. The acquisition window initiated at 60–75% of the R-R interval when the heart rate was below 65 beats/min, otherwise it initiated at 30–75%. In the derivation group, the total amount of contrast medium was determined by body weight ($0.8 \times$ body weight, kg). The

contrast medium was injected for 14 s followed by a saline flush. A bolus tracking method was performed to determine the scan timing. The scan started 6 s after the descending aorta reached 60 Hounsfield unit (HU) above the initial value. In the validation group, the total amount of contrast medium and the start of scan timing was determined by the formula derived from the derivation group. The contrast medium injection time was shortened to 12 s because the time for the breath-holding announcement after the trigger of the bolus tracking method could be omitted [11]. As the maximum injection speed was 5.0 mL/s, we extended the injection time when the injected contrast medium exceeded 60 mL. If the heart rate was over 65 beats/min, a maximum dose of 12.5 mg of landiolol (Corebeta; Ono Pharmaceutical, Tokyo, Japan) was given intravenously [12]. There were no reported side-effects using beta-blockers, including vasospasm. All patients received 0.3 mg sublingual nitroglycerin (Nitrophen; Nippon Kayaku, Tokyo, Japan). Half-reconstruction was performed with a slice thickness of 0.75 mm and an increment of 0.4 mm using a cardiac kernel (I36f) with SAFIRE strength 2. Dose length product was recorded from the console. A conversion factor of 0.014 mSv/mGy cm was used to calculate the effective dose.

Images were transferred to a workstation for processing (Synapse Vincent Ver 5.2; Fujifilm Medical, Tokyo, Japan).

CTP data analysis

The time density curve of the left ventricle was analyzed using software (Perfusion Analysis; Fujifilm Medical). To increase

the precision of the fit, double sampling of the arterial input was performed (Fig. 1). The input function was sampled in the left ventricle at every table position and combined into one arterial input function that had twice the sampling rate of the original position. TTP and PE were recorded.

CTA data analysis

The enhancement within the lumen of the proximal right coronary artery and left main trunk was measured by placing a circular region of interest (ROI). The ROI was placed as large as possible while carefully avoiding the vessel wall. The mean value of the two coronary arteries was used for further analysis. Another ROI was placed at the aortic root. The SD within this ROI was determined as the image noise. Signal to noise ratio was determined as coronary enhancement divided by the image noise. The scan start time was also recorded. The time was defined as the time between the start of contrast medium injection and the initiation of the scan.

Derivation group analysis

Multivariable logistic regression analysis was performed to derive a formula to predict coronary enhancement during CTA and the scan start time. In a model to predict coronary enhancement, we included the following parameters: PE during CTP, CTA heart rate/CTP heart rate, and CTP iodine dose/CTA iodine dose. We performed a forced entry analysis because these parameters theoretically influence coronary enhancement. As coronary CTA of most patients in the derivation group was per-

Fig. 1. The input function was sampled in the left ventricle at each table position (A and C). Time density curves were produced at each position (B and D) and these curves were combined into one arterial input function (E) that had twice the sampling rate of each position. TTP and PE were recorded. PE: peak enhancement, TTP: time to peak, HU: Hounsfield unit.

formed with 100 kVp, only these patients were used for derivation of the optimal amount of contrast medium. The optimal amount of contrast medium was calculated to achieve a target enhancement of 370 HU. Previous studies showed that an optimal coronary enhancement would be between 320 HU and 420 HU [2-4], because a low enhancement would overlook non-calcified plaques and a high enhancement would make it difficult to detect calcified plaques. Therefore, we determined the target enhancement as the median value of the upper and lower limits. When the tube voltage of 120 kVp was selected for CTA, we increased the amount of contrast medium by 20% based on a phantom study (data not shown). In a model to predict the scan start time, we included the following parameters: TTP during CTP and CTA heart rate/CTP heart rate. We performed a forced entry analysis because these parameters theoretically influence arrival time.

Statistical analysis

Continuous variables are shown as means $\pm$ SD and categorical variables as a number unless otherwise described. Student's t-test was used to compare continuous variables. Fisher's exact test or the chi-square test was used to compare categorical and skewed variables. Levene's test was used to compare the interpatient variability in coronary enhancement between the derivation and validation groups. Multivariable logistic regression analysis was performed to derive a formula that would predict the appropriate scan timing and contrast medium dose. We determined the range of optimal coronary enhancement to be between 320 HU and 420 HU [2-4]. All statistical analyses were performed using JMP software (ver. 12.2.0; SAS, Cary, NC, USA). In all analysis, $p < 0.05$ was taken to indicate statistical significance.

RESULTS

Patient and scan characteristics

The patients were dominantly male in both derivation and validation groups (Table 1). The mean age in the validation group was slightly higher (68.9 ± 10.0 yr vs. 64.4 ± 11.7 yr, $p = 0.02$) and the body weight was lower (61.8 ± 12.4 kg vs. 68.2 ± 14.8 kg, $p = 0.01$) than in the derivation group but the interpatient variability was not significantly different ($p = 0.15$). A 100-kVp protocol was adopted in 77% and 66% of the patients in the derivation and validation group, respectively. The mean amount of contrast medium during CTP was slightly higher in the derivation group (52.3 ± 3.8 mL vs. 49.4 ± 5.3 mL, $p = 0.001$) but did not differ during CTA (49.3 ± 8.0 mL vs. 47.9 ± 12.9 mL, $p = 0.39$). The iodine injection dose per body weight during CTP (294 ± 46 mg Iodine/kg vs. 298 ± 36 mg Iodine/kg, $p = 0.64$) and CTA (281 ± 34 mg Iodine/kg vs. 279 ± 36 mg Iodine/kg, $p = 0.74$) was not

Table 1. Patient and scan characteristics

Parameter	Derivation group	Validation group	P
Number of patients	196	41	
Male/female	138/58	27/14	0.58
Age (yr)	64.4 ± 11.7	68.9 ± 10.0	0.02 [†]
Body weight (kg)	68.2 ± 14.8	61.8 ± 12.4	0.01 [†]
Body mass index (kg/m ²)	25.5 ± 4.7	23.6 ± 3.4	0.02 [†]
Tube voltage of CTA			
100 kVp	151 (77)	27 (66)	0.16
120 kVp	45 (23)	14 (34)	
Contrast medium (mL)*			
CTP	52.3 ± 3.8	49.4 ± 5.3	0.001 [†]
CTA	49.3 ± 8.0	47.9 ± 12.9	0.39
Iodine dose (mg Iodine/kg)*			
CTP	294 ± 46	298 ± 36	0.64
CTA	281 ± 34	279 ± 36	0.74
Injection speed (mL/s)*			
CTP	4.1 ± 0.3	4.0 ± 0.4	0.09
CTA	3.5 ± 0.6	3.8 ± 0.8	0.01 [†]
Heart rate (beats/min)			
CTP	77.7 ± 13.6	76.9 ± 11.9	0.37
CTA	64.4 ± 9.4	63.8 ± 7.5	0.36
Effective dose (mSv)			
CTP	2.7 ± 0.8	2.7 ± 0.8	0.81
CTA	3.1 ± 1.5	2.8 ± 1.3	0.38

Data are means $\pm$ SD or n (%). *only 100 kVp patients are included in the derivation group, [†]statistically significant, $p < 0.05$. CTA: CT angiography, CTP: CT perfusion

significantly different between the derivation and validation groups. The mean injection speed during CTP was similar in the derivation and validation groups (4.1 ± 0.3 mL/s vs. 4.0 ± 0.4 mL/s, $p = 0.09$) but the speed during CTA was higher in the validation group than the derivation group (3.5 ± 0.6 mL/s vs. 3.8 ± 0.8 mL/s, $p = 0.01$). The mean effective dose of CTP (2.7 ± 0.8 mSv vs. 2.7 ± 0.8 mSv, $p = 0.81$) and CTA (3.1 ± 1.5 mSv vs. 2.8 ± 1.3 mSv, $p = 0.38$) did not differ between the derivation and validation groups.

Derivation of a formula to predict the optimal contrast medium amount and start time

Multivariable logistic regression analysis to predict enhancement during CTA showed that PE during CTP ($p < 0.001$) and CTA heart rate/CTP heart rate ($p = 0.03$) were significant parameters, but CTP iodine dose/CTA iodine dose lacked significance ($p = 0.09$). When measured against predicted coronary enhancement, a strong correlation ($R^2 = 0.33$, $p < 0.001$) was shown between the predicted and measured coronary enhancement. Based on this result, the following formula was used to predict coronary enhancement during CTA:

Predicted enhancement (HU)

$$= 441 + 0.397 \times \text{PE} - 80.4 \times \frac{\text{CTA heart rate}}{\text{CTP heart rate}} - 132 \times \frac{\text{CTA iodine dose}}{\text{CTA iodine dose}},$$

where CTA iodine dose was defined as the iodine dose included in an amount of contrast medium that was $0.8 \times \text{body weight (kg)}$. The optimal amount of contrast medium was calculated to achieve a target enhancement of 370 HU.

Contrast medium (mL)

$$= 0.8 \times \text{body weight (kg)} \times \frac{370}{\text{Predicted enhancement}}.$$

When a tube voltage of 120 kVp was selected for CTA, we increased the amount of contrast medium by 20%.

Multivariable logistic regression analysis to predict the scan start time showed that TTP during CTP was a strong predictor

Table 2. Coronary enhancement and start time

Parameter	Derivation group	Validation group	p
Coronary enhancement (HU)*	400±55	380±46	0.03†
Comparison of SD			0.02†
High (>420 HU)	57 (38)	6 (15)	0.01†
Optimal (320–420 HU)	81 (54)	31 (75)	
Low (<320 HU)	13 (9)	4 (10)	
Image noise*	27.6±9.4	30.6±5.1	0.05
Signal to noise ratio*	16.0±5.3	12.8±3.0	0.001†
CTA start time (s)	25.0±2.9	24.5±1.4	0.33

Data are means±SD or n (%). *only 100 kVp patients are included in the derivation group, †statistically significant, $p < 0.05$. CTA: CT angiography; HU: Hounsfield unit

($p < 0.001$), but CTA heart rate/CTP heart rate was not significant ($p = 0.19$). Measured against the predicted scan start time a moderate correlation ($R^2 = 0.23$, $p < 0.001$) was shown between the measured and predicted scan times. Based on this result, the following formula was used to predict the start time of the CTA scan:

$$\text{Scan start time (s)} = 15 + 0.49 \times \text{TTP} - 2.3 \times \frac{\text{CTA heart rate}}{\text{CTP heart rate}}.$$

Validation of the formula

The mean coronary artery enhancement (400 ± 55 HU vs. 380 ± 46 HU, $p = 0.03$) and signal to noise ratio (16.0 ± 5.3 vs. 12.8 ± 3.0 , $p = 0.001$) were slightly higher in the derivation group than in the validation group (Table 2, Fig. 2A). The interpatient variability was significantly smaller ($p = 0.02$) in the validation group than in the derivation group. The proportion of patients with an optimal enhancement was 75% in the validation group, which was 21% higher ($p = 0.01$) than the derivation group (Table 2). The mean coronary enhancement was significantly higher when the 100-kVp protocol was adopted than the 120-kVp protocol (396 ± 43 HU vs. 350 ± 36 HU, $p = 0.01$) (Figs. 2A and 3). The scan start time (25.0 ± 2.9 s vs. 24.5 ± 1.4 s, $p = 0.33$) was not significantly different between the groups (Table 2, Fig. 2B).

DISCUSSION

The present study showed that interpatient variability of coronary enhancement during CTA could be reduced by adjusting the amount of contrast medium using dynamic CTP data. Although the condition between stress and rest is different, especially in heart rate, the optimal amount of contrast medium could be predicted by regression analysis. The mean amount of con-

Fig. 2. Comparison of coronary enhancement (A) and scan start time (B) between derivation and validation groups. The coronary enhancement of the validation group is further subdivided into 100-kVp and 120-kVp protocols. Box, 1st to 3rd quartiles; bold line, median; whiskers, minimum and maximum values; filled circle, outlier.

Fig. 3. A 71-year-old female with effort chest pain. The body weight was 44 kg and the injected contrast medium during CT perfusion was 38 mL. The time to peak and peak enhancement were 21 s and 360 Hounsfield unit (HU), respectively (A). The heart rate dropped from 80 to 70 beats/min after adenosine triphosphate was discontinued. Coronary CT angiography started 23 s after the injection with 33 mL contrast medium for 12 s. Surface maximal intensity projection image (B) and curved planar reconstruction images of right coronary (C), left anterior descending (D), and left circumflex (E) arteries show good enhancement with a mean value of 397 HU.

trast medium and scan start time did not differ between the derivation and validation cohorts. Body weight would be the most important factor in optimizing these parameters, but it is influenced by various factors such as the position of the iv route, pulmonary circulation, vessel volume, etc. The strength of the present formula is that it included various factors which might influence the enhancement of coronary arteries.

The timing bolus method was initially used to optimize the scan timing of the main acquisition using a low dose contrast medium. A target enhancement could be achieved with a shorter injection time than the bolus tracking technique [11]. However, interpatient variability in coronary enhancement still remains because the TTP of the main bolus differs due to different injection duration. An algorithm to predict the time density curve of the main bolus was devised using the short test bolus data [13]. The prediction error of coronary enhancement was less than 50 HU in 80% of the patients using this algorithm. Because we optimized the scan timing using the formula, optimal coronary enhancement was achieved with a shorter injection time in the validation cohort.

A timing bolus method with the injection of a diluted contrast medium was introduced. The amount of contrast medium during the test injection ranged from 0.2 mL/kg to 0.3 mL/kg [3,10] and the injection duration was the same as for the main bolus. The relationship between the predicted and actual coronary enhancement was better when diluted contrast medium was used than with undiluted contrast medium [10]. Coronary CTA with the amount of contrast medium calculated from the time density curve of the diluted contrast medium method resulted in smaller interpatient variability and more patients within optimal enhancement than the body weight adjusted protocol [3,14]. Including the cardiac function index in the prediction function enabled the achievement of a more precise PE value [9].

As more contrast medium is used during the comprehensive cardiac CT than in the coronary CTA alone [15], an additional test injection should be avoided. The present study is meaningful in that no additional contrast medium was injected to determine the optimal parameters for coronary CTA. As coronary enhancement differs with the hemodynamic status even within the same patient [16], the formula derived in the present study

would help to manage the difference between stressed and resting state.

We acknowledge the following limitations in the present study. First, this study was a single-center study with a single CT machine. Further studies using other CT machines and different patient populations are necessary to confirm the results of this study. Second, the sampling rate during the dynamic CTP was lower than protocols using high-end scanners. The PE during the CTP might be missed, but this study obtained positive results in predicting enhancement during CTA. Third, patients with arrhythmia were excluded from this study because it is difficult to determine the heart rate in these patients. Fourth, the body weight in the validation cohort was significantly smaller than the derivation cohort. Fifth, the rate-pressure product rather than just using the heart rate would be better to derive a more precise formula. Finally, the narrow body weight range might be a limitation for the formula derived in this study. Further studies that include obese patients are necessary to confirm the results.

In conclusion, adjusting the contrast medium amount using dynamic CTP data could reduce the interpatient variability of coronary enhancement during comprehensive cardiac CT. No additional contrast medium is necessary to perform the prediction.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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REFERENCES

1. Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (assessment by coronary computed tomographic angiography of individuals undergoing invasive coronary angiography) trial. *J Am Coll Cardiol* 2008;52:1724-1232.
2. Cademartiri F, Maffei E, Palumbo AA, Malagò R, La Grutta L, Meijboom WB, et al. Influence of intra-coronary enhancement on diagnostic accuracy with 64-slice CT coronary angiography. *Eur Radiol* 2008;18:576-583.
3. Kidoh M, Nakaura T, Nakamura S, Awai K, Utsunomiya D, Namimoto T, et al. Novel contrast-injection protocol for coronary computed tomographic angiography: contrast-injection protocol customized according to the patient's time-attenuation response. *Heart Vessels* 2014;29:149-155.
4. Komatsu S, Kamata T, Imai A, Ohara T, Takewa M, Miyaji K, et al. Controlling intracoronary CT number for coronary CT angiography. *J Cardiol* 2013;61:155-161.
5. Awai K, Hiraishi K, Hori S. Effect of contrast material injection duration and rate on aortic peak time and peak enhancement at dynamic CT involving injection protocol with dose tailored to patient weight. *Radiology* 2004;230:142-150.
6. Guerrisi A, Marin D, Barnhart H, Ho L, Toth TL, Catalano C, et al. Optimization of contrast material dose for abdominal multi-detector row CT: predicting patient lean body weight by using preliminary transverse CT images. *Adv Comput Tomogr* 2014;3:1-10.
7. Yanaga Y, Awai K, Nakaura T, Utsunomiya D, Oda S, Hirai T, et al. Contrast material injection protocol with the dose adjusted to the body surface area for MDCT aortography. *AJR Am J Roentgenol* 2010;194:903-908.
8. Tomizawa N, Komatsu S, Akahane M, Torigoe R, Kiryu S, Ohtomo K. Influence of hemodynamic parameters on coronary artery attenuation with 320-detector coronary CT angiography. *Eur J Radiol* 2012;81:230-233.
9. Higaki T, Nakaura T, Kidoh M, Yuki H, Yamashita Y, Nakamura Y, et al. Effect of contrast material injection duration on arterial enhancement at CT in patients with various cardiac indices: Analysis using computer simulation. *PLoS One* 2018;13:e0191347.
10. Masuda T, Funama Y, Imada N, Sato T, Yamagami T, Tatsugami F, et al. Prediction of aortic enhancement on coronary CTA images using a test bolus of diluted contrast material. *Acad Radiol* 2014;21:1542-1546.
11. Nakaura T, Awai K, Yanaga Y, Namimoto T, Utsunomiya D, Hirai T, et al. Low-dose contrast protocol using the test bolus technique for 64-detector computed tomography coronary angiography. *Jpn J Radiol* 2011;29:457-465.
12. Tomizawa N, Hayakawa Y, Inoh S, Nojo T, Nakamura S. Clinical utility of landiolol for use in coronary CT angiography. *Res Reports Clin Cardiol* 2015;145-152.
13. Mahnken AH, Rauscher A, Klotz E, Mühlenbruch G, Das M, Günther RW, et al. Quantitative prediction of contrast enhancement from test bolus data in cardiac MSCT. *Eur Radiol* 2007;17:1310-1319.
14. Kawaguchi N, Kurata A, Kido T, Nishiyama Y, Kido T, Miyagawa M, et al. Optimization of coronary attenuation in coronary computed tomography angiography using diluted contrast material. *Circ J* 2014;78:662-670.
15. Tomizawa N, Chou S, Fujino Y, Kamitani M, Yamamoto K, Inoh S, et al. Feasibility of dynamic myocardial CT perfusion using single-source 64-row CT. *J Cardiovasc Comput Tomogr* 2019;13:55-61.
16. Komatsu S, Imai A, Kamata T, Ohara T, Takewa M, Minamiguchi H, et al. A CT number-controlling system for reproducibility of intracoronary CT number on follow-up coronary CT angiography. *J Cardiol* 2013;62:82-86.