Validation of a low-dose contrast 64-slice cardiac computed tomography angiography protocol for aortic valve annulus sizing

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ABSTRACT

Cardiac computed tomography angiography (CCTA) is the gold standard for accurately sizing the aortic valve annulus prior to aortic valve replacement. A reduction of contrast volume administered for CCTA, without sacrificing image quality, is desirable. Signal-to-noise ratio represents final CCTA image quality. Consecutive patients referred to CCTA for aortic valve annulus sizing were retrospectively analyzed. Patients were grouped into a low-dose contrast (LDCT) group and traditional dose contrast (TDCT) group. In the LDCT group, contrast dose was <50% of the maximal allowable dose ($3.7 \times$ estimated glomerular filtration rate). Guided by a time-density curve, the contrast was administered in a two-stage infusion, and retrospectively gated images were acquired with a 64-multidetector computed tomography scanner. Out of 123 patients (age 80 ± 9 years; 46% female), 65 (52.9%) underwent LDCT and 58 (47.2%) underwent TDCT. Contrast volume was significantly lower in the LDCT group (LDCT 41.2 ± 9.8 vs TDCT 76.2 ± 14.2 mL; $P < 0.001$). The signal-to-noise ratio of the aortic root was 10.4 ± 4.1 for the LDCT group and 8.4 ± 3.3 for the TDCT group ($P = 0.004$). Aortic root dimensions could be measured in both LDCT and TDCT groups. In conclusion, LDCT with 64-slice CCTA can effectively size the aortic valve annulus to direct aortic valve replacement while offering reduced contrast exposure.

KEYWORDS Aortic stenosis; cardiac computed tomography angiography; contrast dye; transcatheter aortic valve implantation

Transcatheter aortic valve implantation (TAVI) has been demonstrated to be an effective alternative to surgical aortic valve replacement for patients with severe aortic stenosis who have intermediate to extreme surgical risk.^{1–7} Tomographic imaging data guidance for patients being evaluated for TAVI plays an essential role in optimizing procedural and patient outcomes by providing accurate information about the aortic valve apparatus (AVA).^{8–10} Given the inherent dynamic shape deformation of the AVA, electrocardiographic gated cardiac computed tomographic angiography (CCTA), a robust dynamic 3-dimensional imaging modality, is now widely accepted as the gold standard for preprocedural evaluation.^{11–13} The volume of iodinated contrast medium administered for CCTA is of concern in many patients because candidates for TAVI frequently have impaired renal function or otherwise are at increased risk of dye-induced nephropathy.^{1,2,14} Previous

reports regarding reduced-dose CCTA have lacked comparison groups,¹⁵ included small sample sizes,^{16,17} or utilized advanced, high-slice computed tomography (CT) systems that are not available in most centers.^{18,19} Herein, we review our center's experience with a low-dose contrast CCTA protocol using a 64-slice CT scanner in a series of consecutive TAVI candidates.

METHODS

This study was approved by the local institutional review board, which waived the requirement for informed consent given the retrospective nature of the study. Consecutive TAVI candidates referred to CCTA for AVA sizing between January 1, 2011, and June 30, 2013, were retrospectively analyzed. Patients with increased risk of contrast dye-induced nephropathy were referred for a low-dose contrast study (LDCT) and patients not at risk underwent a traditional-

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Figure 1. Contrast CT angiography of the aortic annulus: (a) low-dose and (b) traditional dose.

dose contrast study (TDCT) based upon the fraction of the maximal allowable contrast dose administered during their CCTA study. Examples are shown in *Figure 1*.

Nephrotoxicity is more likely when the contrast volume-to-creatinine clearance ratio exceeds 3.7:1.^{20,21} Therefore, the maximal allowable contrast dose for the CCTA was calculated using 3.7 times the estimated glomerular filtration rate (eGFR). Patients in the LDCT group had a dose of contrast that was <50% of the maximal allowable dose, whereas patients in the TDCT group received the maximal allowable dose. eGFR was calculated using the Modification of Disease in Renal Diet (MDRD) eGFR formula.²² The MDRD formula can underestimate the actual glomerular filtration rate by approximately 6% in patients with chronic kidney disease and by approximately 29% in healthy individuals. Given the formula's tendency to underdose contrast, the MDRD formula was felt to be a suitable approach to conservatively calculating the contrast dosing.²³ Patients with MDRD eGFR <25 were excluded. This cutoff of 25 was chosen since the maximal allowable dose of contrast for an MDRD eGFR of 25 would be approximately 90 mL ($3.7 \times \text{eGFR of } 25$), and half of that maximal allowable contrast would be 45 mL (the minimum we require to obtain a CCTA with acceptable signal-to-noise ratio [SNR] for postprocessing).

Images were acquired with a Brilliance 64-slice CT scanner (Philips Healthcare). Based on the recommendations for radiation protection in CCTA by the Society of Cardiovascular Computed Tomography,²⁴ a tube potential of 100 kV was implemented for patients weighing ≤ 90 kg or with a body mass index (BMI) ≤ 30 kg/m², whereas a tube potential of 120 kV was used for patients weighing >90 kg and with a BMI >30 kg/m². The tube potential was adjusted, based on each individual patient's size, to the lowest setting that guaranteed acceptable image noise for a suitable SNR.²⁴

A total contrast dose of 45 mL is essential for electrocardiogram (ECG)-synchronized CCTA that utilizes a 64-multislice CT scanner in order to obtain satisfactory image quality and SNR of the aortic root. Therefore, two separate acquisitions (ECG synchronized for the aortic root and nongated for the aorta and peripheral vessels) may be preferable to an ECG-synchronized acquisition of the entire volume to reduce the amount of contrast agent. Depending on the remaining amount of allowable contrast after CCTA, a decision was made to perform a nongated CT of the aorta and peripheral vessels with either no contrast or low-dose contrast to selectively enhance the iliofemoral arteries. The resulting DICOM data were post-processed by a workstation capable of advanced image processing, manipulation, and optimal multiplanar reformatting.

Baseline characteristics were tabulated, and unadjusted comparisons were made between participants receiving LDCT and participants receiving TDCT using Wilcoxon signed sum-rank tests for continuous variables and Pearson's chi-squared tests for categorical variables. For the main outcomes of contrast volume, signal, noise, and SNR, four unadjusted linear regression models were used with contrast dose (LDCT vs TDCT) as the sole independent variable.

To adjust for confounding, a propensity score was formed by regressing select risk factors in a logistic regression model with contrast dose (LDCT vs TDCT) as the outcome. This propensity score was then fitted, along with contrast dose, into four linear regression models (with outcomes of contrast volume, signal, noise, and SNR, respectively) using a five-knot restricted cubic spline. The adjusted differences in means were reported along with the Wald chi-squared *P* value for contrast dose.

RESULTS

During the study period, 123 patients underwent CCTA for TAVI evaluation: 65 (52.8%) with LDCT and 58 (47.2%) with TDCT. Baseline characteristics and procedural

Table 1. Study cohort baseline characteristics, procedures, and outcomes by contrast dose

Characteristic	Low-dose CT (<i>n</i> = 65)	Traditional-dose CT (<i>n</i> = 58)	<i>P</i> value ^a
Age (y) ^b	81 ± 10	78 ± 9	0.08
Body mass index (kg/m ²) ^b	26 ± 5	29 ± 6	0.002
Women	29 (45%)	27 (47%)	0.86
Hypertension	56 (86%)	51 (88%)	0.77
Diabetes mellitus	23 (35%)	17 (29%)	0.55
Hyperlipidemia	57 (88%)	52 (90%)	0.71
Atrial fibrillation	21 (32%)	15 (26%)	0.43
Chronic lung disease	14 (22%)	12 (21%)	0.87
Prior chronic kidney disease	7 (11%)	7 (12%)	0.85
Congestive heart failure	28 (43%)	25 (43%)	0.92
Coronary artery disease	62 (95%)	57 (98%)	0.37
Previous stroke	14 (22%)	22 (38%)	0.05
Previous PCI	30 (46%)	16 (28%)	0.03
Previous valve surgery	4 (6%)	1 (2%)	0.21
Ejection fraction ^b	54 ± 14	58 ± 13	0.26
Valve procedures			0.002
TAVI	34 (52%)	11 (19%)	
SAVR	18 (28%)	31 (53%)	
BAV	12 (19%)	16 (28%)	
TAVI complications			
Annular rupture	0	0	>0.99
Paravalvular leak			0.73
Trace	9 (14%)	3 (5%)	
Mild	3 (5%)	1 (2%)	
Moderate to severe	2 (3%)	0	

^aUnadjusted chi-squared for categorical variables, Wilcoxon signed sum-rank for continuous variables.

^bMean ± SD.

BAV indicates balloon aortic valvuloplasty; CT, computed tomography; PCI, percutaneous coronary intervention; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

outcomes are summarized in [Table 1](#). LDCT patients had lower mean BMI and more commonly had previous percutaneous coronary intervention than TDCT patients, but otherwise there were no significant differences in baseline characteristics.

CCTA results are summarized in [Table 2](#). Mean dose of contrast volume was significantly lower in the LDCT group than in the TDCT group (41.2 ± 9.8 vs 76.2 ± 14.2 mL; *P* < 0.0001). After adjustment for confounding factors, the LDCT protocol reduced contrast volume by a mean of 33.7 mL (95% confidence interval: −28.8 to −38.7; *P* < 0.001), a 44% reduction in contrast volume. The SNR was significantly higher in the LDCT group than in the TDCT group (10.4 ± 4.1 vs 8.4 ± 3.3; *P* = 0.004). However,

subjective assessment of image quality identified no clinically significant differences, and all LDCT images were sufficient for measurement of the aortic annulus.

Ultimately, most LDCT patients—34 of 65 (52.3%)—underwent TAVI, whereas most TDCT patients—31 of 58 (53.4%)—underwent surgical aortic valve replacement (*P* = 0.002). For those patients undergoing TAVI, there was no difference between the groups in the incidence of post-procedural paravalvular leak, and no annular ruptures occurred during the study.

DISCUSSION

Reduction of contrast volumes for CCTA of the AVA can be achieved by using lower flow rates than for coronary

Table 2. Imaging results in the aortic root stratified by contrast dose

Outcomes	Low-dose CT (n = 65)	Traditional-dose CT (n = 58)	Unadjusted <i>P</i> value	Adjusted mean difference ^a (95% CI)	Adjusted <i>P</i> value
Contrast volume (mL) ^a	41 ± 10	76 ± 14	< 0.0001	−33 (−39 to −29)	< 0.001
SNR (HU)	10 ± 4	8 ± 3	0.004	2 (0.2–3)	0.03
Signal (HU) ^b	288 ± 57	311 ± 56	0.03	−24 (−48 to 1)	0.06
Noise (HU) ^b	31 ± 10	41 ± 12	< 0.0001	−11 (−15 to −6)	< 0.001

^a(Low-dose CT – high-dose CT): Adjusted using a propensity score containing the following variables: age (y), body mass index (kg/m²), female, hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, chronic obstructive pulmonary disease, chronic kidney disease, congestive heart failure, coronary artery disease, previous stroke, previous percutaneous coronary intervention, previous valve surgery, left ventricular ejection fraction.

^bMean ± SD.

CI indicates confidence interval; CT, computed tomography; HU, Hounsfield units; SNR, signal-to-noise ratio.

CT angiography. Although 5 mL/s is typically recommended for coronary imaging, 3 mL/s may sometimes be sufficient for imaging patients in the workup for TAVI.²⁵ Although suggested, these CCTA lower flow rates have not been systematically used and validated in a population being evaluated for candidacy for TAVI/TAVI. And as recommended by guidelines, a standard bolus of 80 mL to 120 mL of low-osmolar iodinated contrast is usually necessary for optimal TAVI CCTA scanning.²⁶ In these patients, reducing the dose of iodinated contrast at the time of CCTA acquisition in an attempt to minimize renal injury, and at the same time being able to accurately assess the AVA, will be of paramount importance. Some reduction of contrast nephropathy can be accomplished by minimizing contrast volume and the use of iso-osmolar or low-osmolar contrast agents.^{20,27} It has been suggested that the contrast volume threshold can be estimated by using the ratio of contrast volume to creatinine clearance. Nephrotoxicity is more likely when the contrast volume/creatinine clearance ratio exceeds 3.7:1.²¹ And using this, $3.7 \times \text{eGFR}$ can be set as the maximal contrast dose for an imaging test or invasive procedure.

CCTA analysis is a key component of candidate evaluation, valve selection, and procedural planning for patients referred for evaluation for TAVI.¹³ Because many patients with aortic stenosis have impaired renal function, the volume of iodinated contrast medium injected for CCTA should be minimized while still ensuring adequate image quality for analysis. Our study has demonstrated that an LDCT protocol is capable of reducing contrast volume for CCTA while maintaining acceptable imaging quality for measurement of the aortic root.

Baseline characteristics between patients in the LDCT and TDCT groups were similar. No difference in postprocedural paravalvular leak was apparent between patients in each study group undergoing TAVI and no annular ruptures occurred during the study, suggesting that all CCTA images using the LDCT protocol were of sufficient quality for accurate assessment and valve sizing. However, given the small size of this study, there is not sufficient power to detect a difference in these endpoints.

This study adds to previous reports on LDCT protocols for several reasons. First, the majority of these studies have examined small numbers of patients, ranging from 8 to 33 patients undergoing an LDCT protocol—less than half of the number of patients included in our analysis.^{16–19} Second, prior reports have focused on specific patient populations such as octogenarians¹⁶ or patients with chronic kidney disease,¹⁸ whereas our study included all TAVI candidates. One published protocol required direct injection of contrast into the aorta through a pigtail catheter inserted through the femoral or radial artery.¹⁶ Another study assessed image quality in the aorta and access vessels rather than the aortic annulus.¹⁹ The most comprehensive study to date utilized a 320-slice volumetric CT scanner that is not currently available in most centers.¹⁸ Thus, our study offers information that matches real-world scenarios in terms of patient population as well as imaging capabilities.

Spagnolo et al reported an LDCT protocol utilizing a more readily available 64-slice CT scanner in a large sample of patients, but their study lacked a comparison group to validate the techniques. Moreover, their LDCT technique relied on an overly complex contrast injection protocol composed of 5 boluses of varying volumes administered at different flow rates without a saline flush.¹⁵ Our study enrolled a large sample of all-comer TAVI candidates to validate a simple and practical LDCT protocol for 64-slice CT scanners against a control group. Thus, these data suggest that our LDCT protocol for CCTA for evaluation for TAVI is feasible for real-world implementation, including in centers that may not have advanced high-slice CT scanners available or the ability to carry out complex contrast injection protocols.

Limitations of this study include those expected of a single-center, retrospective review. However, our data represent a real-world experience with an LDCT protocol that can be practically adapted by most centers performing TAVI. A further limitation is the subjective assessment of image quality from a clinical perspective, but the fact that there was no difference in incidence of postprocedural paravalvular leak among the LDCT and TDCT groups and no cases of annular rupture does provide indirect confirmation that our subjective assessment of image quality was accurate.

In conclusion, we have validated an LDCT protocol that enables comprehensive assessment of the aortic annulus via CCTA in patients under consideration for TAVI. The LDCT protocol significantly reduces contrast volume and provides images of sufficient quality for measurement of the aortic annulus. The LDCT protocol is safe and can be practically adapted by virtually all centers performing TAVI.

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