Using patient-specific contrast enhancement optimizer simulation software during the transcatheter aortic valve implantation-computed tomography angiography in patients with aortic stenosis

Takanori Masuda (takanorimasuda@yahoo.co.jp)
Kawasaki University of Medical Welfare

Takeshi Nakaura
Kumamoto University

Toru Higaki
Hiroshima University

Yoshinori Funama
Kumamoto University

Yoriaki matsumoto
Hiroshima University

Tomoyasu Sato
Tsuchiya General Hospital

Tomokazu Okimoto
Edogawa Hospital

Rumi Gotanda
Kawasaki University of Medical Welfare

Keiko Arao
Kawasaki University of Medical Welfare

Hiromasa Imaizumi
Kawasaki University of Medical Welfare

Shinichi ARAO
Kawasaki University of Medical Welfare

Atsushi Ono
Kawasaki University of Medical Welfare

Junichi Hiratsuka
Kawasaki University of Medical Welfare

Kazuo Awai
Hiroshima University
Research Article

**Keywords:** contrast enhancement optimizer simulation software, transcatheter aortic valve implantation, computed tomography angiography, contrast materials, contrast enhancement.

**Posted Date:** March 16th, 2023

**DOI:** [https://doi.org/10.21203/rs.3.rs-2676764/v1](https://doi.org/10.21203/rs.3.rs-2676764/v1)

**License:** 😇 ❗ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)
Abstract

**Purpose:** This study assessed whether patient-specific contrast enhancement optimizer simulation software (p-COP) can reduce the contrast material (CM) dose compared with the conventional body weight (BW)-tailored scan protocol during transcatheter aortic valve implantation-computed tomography angiography (TAVI-CTA) in patients with aortic stenosis.

**Methods:** We used the CM injection protocol selected by the p-COP in group A (n = 30). The p-COP uses an algorithm that includes data on an individual patient’s cardiac output. Group B (n = 30) was assigned the conventional BW-tailored CM injection protocol. We compared CM dose, amount of CM, injection rates, and computed tomography (CT) value in the abdominal aorta between the two groups and classified them as acceptable (>280 Hounsfield units (HU)) or unacceptable (<279 HU) based on the optimal CT value for TAVI-CTA.

**Results:** Group A received 56.2 ml CM and 2.6 ml/sec of injection, and group B received 76.9 ml CM and 3.4 ml/sec of injection (p < 0.01). The CT value for the abdominal aorta at the celiac level was 287.0 HU in group A and 301.7 HU in group B (p = 0.46). The rate of CT value for acceptable (280 HU or more) and unacceptable (less than 280 HU) were 22 and 8 patients in group A, and 24 and 6 patients in group B, respectively (p = 0.76).

**Conclusion:** The p-COP reduced the CM dosage, and the injection rate was approximately 30% in patients with aortic stenosis compared with the BW-tailored scan protocol during TAVI-CTA.

Introduction

Transcatheter aortic valve implantation (TAVI) is a treatment option for patients with severe symptomatic aortic stenosis (AS) at a high surgical risk or have contraindications to surgical valve replacement [1–4]. Additionally, assessment of the aortic root and access route must determine anatomical indications, and assessment using contrast tomography angiography (CTA) is a highly recommended criterion [5–7]. Chronic kidney disease is a significant comorbidity of the patients with AS [8]. Therefore, TAVI-CTA requires contrast materials (CMs) at a minimum while retaining at least 280 Hounsfield units (HU) of vessels [9, 10].

The patient-specific contrast enhancement optimizer simulation software (p-COP, Nemoto-Kyorindo) is an optimal scan protocol used for dynamic hepatic computed tomography (CT), coronary arteries, and whole-body CTA using patient characteristics, such as cardiac output (CO), body weight (BW), and height [11–13]. We hypothesized that p-COP would be a useful tool for optimizing the CMs injection protocol in patients with AS.

This study assesss whether p-COP can reduce the CMs dose compared with the conventional BW-tailored scan protocol during TAVI-CTA.
Materials And Methods

This retrospective study was approved by our institutional review board, and informed consent was waived for the BW-tailored conventional TAVI-CTA protocol (group B). Furthermore, this prospective study was approved by our institutional review board, and written informed consent was obtained from all patients in the new p-COP-tailored TAVI-CTA protocol (group A).

Simulation software for contrast enhancement

Bae et al. proposed a representative physiology-based pharmacokinetic (PBPK) model for contrast enhancement [14–16]. We used p-COP and Nemoto–Kyorindo, which uses PBPK. The p-COP outputs the CMs volume, injection rate, and injection duration for the optimal contrast enhancement of the target organs. The input parameters required to calculate the optimal CMs injection protocol include the target organ, target CT value, sustained time, admissible maximal CMs dose, patient factors [17], CMs factors, and CT scanning factors (Fig. 1). We defined the target CT value as the minimum CT value necessary for diagnosing the target organ, and sustained time as the duration at which the CT value of the target organ is higher than the target CT value.

Study population

Our study retrospectively considered 30 consecutive patients who underwent TAVI-CTA to evaluate the preoperative TAVI in April 2020 with the conventional TAVI-CTA protocol using BW (group B), and prospectively considered 34 patients who underwent TAVI-CTA to evaluate the preoperative TAVI in January 2021 with the new TAVI-CTA protocol for the p-COP (group A). The exclusion criteria were as follows: (1) hemodialysis (n = 2) and (2) severe renal failure (estimated glomerular filtration rate < 40 mL/min/1.73 m² and n = 2). Thus, the final study population comprised 60 patients (median age, 72 years; range, 42–89 years; 30 males and 30 females). The BW, height, and CO of the patients were recorded immediately before the TAVI-CTA examination. The CO was measured using a non-invasive cardiovascular monitor (Aesculon mini; Peace Bussan). The COs obtained with the electrical velocimeter were recorded and displayed continuously on the monitor at the average of more than 10 valid cardiac cycles.

CT scanner

We used a 64-detector row CT scanner (LightSpeed VCT; GE Healthcare, Milwaukee, WI, USA) to scan all the patients. Retrospective electrocardiogram-gating helical scans were performed to assess the aortic valve and coronary arteries. Scanning parameters were as follows: 100 kVp, 300 to 770 mA, 0.35 s rotation, 0.625 mm detector row width, 0.20–0.22 helical pitch (beam pitch), 8.0 mm table movement and 50 cm scan field of view with cardiac filter, and adaptive statistical iterative reconstruction (30% standard). After table migration, helical scans were performed to assess the entire aortic vessels from the
subclavian artery to the femoral artery. Scanning parameters were as follows: 100 kVp, 200 to 770 mA (noise index: 10) with an automatic tube current modulation, 0.4 s rotation time, 5-mm detector row width, 1.375 helical pitch, and 50-cm scan field of view. Image reconstruction was performed with a slice thickness of 0.625 mm and slice spacing of 0.625 mm.

**Contrast material injection protocol**

With a power injector (Dual Shot, Nemoto–Kyorindo, Tokyo, Japan), we delivered a CM (Omnipaque-300; Daiichi Sankyo, Tokyo, Japan) via a 22-gauge catheter into the antecubital vein. In both groups, the CMs volume were delivered during 22 s, followed by the 20 mL saline chaser for the same injection rates. In group A, the CMs dose was determined by p-COP based on CO, BW, and height. Patient characteristics were recorded before the TAVI-CTA examination, and CO was measured using a cardiovascular monitor [18, 19]. The abdominal aorta at the celiac artery level was the target of CE. The target CT value was 280 HU, and sustained time were 20 s for simulated 100 kVp.

For group B, we used standard injection protocol for TAVI-CTA: An iodine dose for 450 mgI/kg was injected during 22 s, followed by 20 mL of saline chaser. The minimum CT value of the abdominal aorta was 280 HU [9, 10]. As in group A, the patient characteristics were recorded before the CT examination, and CO was measured using cardiovascular monitor.

**Data analysis**

Intravascular CT value were measured for all patients by using workstation (Advantage Workstation ver. 4.4; GE Healthcare). On TAVI-CTA scans, we recorded the CT value in the abdominal aorta within an approximately 1.0 cm$^2$ circular region of interest. The CT value of the abdominal aorta at the level of the celiac artery was compared between the two groups based on the optimal CT value of TAVI-CTA scans [9, 10].

**Statistical analysis**

We used the Mann–Whitney U-test, to compare the patient characteristics to assess the interpatient variability of subjects exposed to both groups. To compare the male/female ratio and the number of patients in both groups whose CT value of the abdominal aorta at the celiac artery level was acceptable ($\geq$ 280 HU) or unacceptable (less than 280 HU), we used the chi-square test. Differences were considered statistically significant at $P < 0.05$. Statistical analyses were performed using free statistical software (R version 3.0.2, R Project for Statistical Computing; http://www.r-project.org/).

**Results**

The CM dose, amount of CM, and injection rates were 318.0 mgI/kg, 56.2 mL, and 2.6 mL/sec for group A and 450.0 mgI/kg, 76.9 mL, and 3.4 mL/sec for group B, respectively ($p < 0.01$). In group A, the CM dose, amount of CM, and injection rates were significantly lower than those in group B.
The CT values for the ascending aorta, abdominal aorta at the celiac level, and mean femoral arteries were 270.0, 287.0, and 332.0 HU for group A, and 289.2, 301.7, and 337.8 for group B, respectively (p = 0.22, 0.46, and 0.47). There were no significant differences in the CT values for the abdominal aorta at the celiac level between the two groups.

The rate of CT value for acceptable (≥ 280 HU) or unacceptable (< 280 HU) was 22 and 8 patients for group A, and 24 and 6 patients for group B, respectively (p = 0.76). There were no significant differences in the rate of CT values for acceptable or unacceptable in two groups.

**Discussion**

The p-COP scan protocol can reduce the CM and injection rates by approximately 30% in patients with AS compared with the conventional BW-tailored scan protocol during TAVI-CTA.

The AS is associated with low CO levels [20]. The severity of AS is generally assessed by calculating the aortic valve area (< 1.0 cm²), transvalvular gradient (≥ 40 mmHg), and maximal aortic valve flow velocity (≥ 4.0 m/sec). However, these three criteria are often unfulfilled, especially in conditions where the pressure gradient does not increase owing to the reduced CO, which is referred to as low flow, low-pressure gradient AS (low flow, low gradient AS) [21]. Our study might have included patients with low-flow, low-gradient AS. From a previous study [13], it was found that in patients with low CO, a reduction in injection rates and CMs dose did not lead to reduce imaging quality; particularly in patients with low CO, CMs dose can be reduced by p-COP. In this study, the CM dose was reduced by approximately 30% compared with the BW-tailored CM protocol. Therefore, p-COP can reduce the CM dose in patients with AS during TAVI-CTA.

In our results, the injection rates were significantly lower in the p-COP protocol than in the BW-tailored conventional CM injection protocols. Reducing the injection rate increases the choice of the puncture needle. Furthermore, because TAVI-CTA requires longer ranges, longer injection times must be adjusted to obtain a stable CT value. Therefore, p-COP may be useful in reducing the injection rate in patients with AS during TAVI-CTA.

The p-COP calculates the optimal CT value protocol based on pharmacokinetic modeling [14–17]. Factoring patient height and CO into BW may provide a more accurate estimate of extracellular fluid volume and reduce the variability in CT values among patients. Therefore, p-COP is a superior predictor of CT value than the body mass index, for which BW is widely used to determine the appropriate size.

However, our study had some limitations. First, we used a single-vendor scanner. Second, the mean BW of our Japanese study subjects was lower than those of the North American and European patients. Finally, we did not evaluate the diagnostic capabilities of CT in the two group.

In conclusion, the p-COP was useful for reducing the CMs dosage, and the injection rate was approximately 30% in patients with AS compared with the BW-tailored scan protocol during TAVI-CTA.
Abbreviations

Transcatheter aortic valve implantation (TAVI)
aortic stenosis (AS)
contrast tomography angiography (CTA)
contrast materials (CMs)
Hounsfield units (HU)
opimizer simulation software (p-COP)
computed tomography (CT)
cardiac output (CO)
body weight (BW)

Declarations

Funding: No funding

Ethics approval: This retrospective study was approved by our institutional review board; informed consent was waived.

References


**Figures**

Figure 1

The p-COP output the contrast material (CM) volume, injection duration, and injection rates for the optimal CE of the target organs