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Distance between valvular leaflet and coronary ostium predicting risk of coronary obstruction during TAVR

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A R T I C L E I N F O

Keywords:
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A B S T R A C T

Background: The aim of this study was to evaluate the role of the distance between the aortic valve in projected position to the coronary ostium to determine risk of coronary artery obstruction after transcatheter aortic valve replacement (TAVR).
Methods: An Expected Leaflet-to-ostium Distance (ELOD) was obtained on pre-TAVR planning computed tomography by subtracting leaflet thickness and the distances from the center to the annular rim at annulus level and from the center to the coronary ostium at mid-ostial level. Variables were compared between patients with and without coronary obstruction and the level of association between variables was assessed using log odds ratio (OR).
Results: A total of 177 patients with 353 coronary arteries was analyzed. Mean annulus diameters (22.8 ± 2.8 mm and 23.4 ± 1.0 mm, $p > 0.05$) and mean sinus of Valsalva (SOV) diameters (31.2 ± 3.6 mm and 31.9 ± 3.6 mm, $p > 0.05$) were similar between patients with lower and higher coronary heights, respectively. There were three coronary obstruction cases. ELOD ≤ 2 mm in combination with leaflet length longer than mid-ostial height allowed for discrimination of cases with and without coronary obstruction. There was a significant association between coronary obstruction event and ELOD ≤ 2 mm (log OR = 6.180, $p < 0.001$).
Conclusions: Our study showed that a combination of ELOD < 2 mm and a longer leaflet length than mid-ostial height may be associated with increased risk for coronary obstruction during TAVR.

1. Introduction

Transcatheter aortic valve replacement (TAVR) was introduced more than a decade ago as an alternative option to surgical open aortic valve replacement for patients with high surgical risk. In the meantime, TAVR has not only gained wide acceptance in high risk patients, but its scope is also expanding to patients at low and intermediate surgical risk [1,2]. One of the most dreadful complications of TAVR is obstruction of the coronary artery ostium with a reported mortality of more than 50% [3]. Coronary obstruction is considered to be caused mainly by the displacement of thick calcified leaflets over the coronary ostium [4]. Several risk factors have been suggested including lower lying coronary

Abbreviations: CT, computed tomography; ELOD, Expected Leaflet-to-ostium Distance; PCI, percutaneous coronary intervention; SAVR, surgical aortic valve replacement; SHV, surgical heart valve; SOV, sinus of Valsalva; STS PROM, society of thoracic surgeons predicted risk of mortality; TAVR, transcatheter aortic valve replacement; TEE, transesophgeal echocardiography; THV, transcatheter heart valve; ViV, valve-in-valve.

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ostium less than 10–12 mm above the annulus plane ('coronary height'), narrow sinus of Valsalva (<30 mm), female sex, balloon-expandable TAVR devices, bulky calcified leaflet, and valve-in-valve procedure [5–8].

However, there have been numerous cases in previous studies where patients without those risk factors suffered coronary obstruction following TAVR, while some patients with risk factors underwent TAVR without compromising the ostium [6,9,10]. Thus, there remains a need for a more sophisticated tool to identify patients who are at truly high risk for coronary obstruction with TAVR.

We hypothesize that the Expected Leaflet-to-ostium Distance (ELOD) defined as the shortest distance between the coronary artery ostium and the corresponding aortic valve leaflet length when displaced by a transcatheter heart valve (THV) is associated with risk of coronary obstruction.

2. Methods

2.1. Patient selection

This study was approved by the Institutional Review Board of Stanford University, and written consent was obtained from all subjects. Patients who underwent a TAVR procedure between January 2016 and December 2017 were retrospectively included. Patients with high risk features for coronary obstruction (lower coronary height of<12 mm in at least either a left or right side coronary artery) on pre-planning computed tomography (CT) images were selected from the dedicated TAVR database of Stanford Hospital. To evaluate the performance of ELOD in predicting the corresponding actual distance after THV implantation, additional 14 patients with a follow-up CT examination after the index TAVR procedure from the database were included.

2.2. Image acquisition and reconstruction

Patients underwent a pre-planning CT angiography (CTA) exam on either a second or third generation dual source system (SOMATOM Definition Flash or SOMATOM Force, Siemens Healthineers, Forchheim, Germany) or a wide-detector system (Revolution, GE Healthcare, Chicago, IL). Low osmolar non-ionic iodinated contrast medium was administered intravenously (Isovue 370 mg/mL; 1.6 mL/kg body weight). Breathing instructions were provided resulting in image acquisition during inspiration. The total scan range of the CTA exam was from the lung apices to the greater trochanters. The chest part (lung apices to diaphragm) was acquired with retrospective electrocardiography gating and the abdomen/pelvis part (2 cm under the apex of the heart to the greater trochanters) without electrocardiography synchronization. Tube voltage depended on patient's body size. Thin-slice images were reconstructed (0.75 mm or 0.625 mm, respectively) allowing for multiplanar reconstructions with a vendor-recommended convolutional kernel (i26f or soft, respectively) for the Siemens and GE Healthcare systems, respectively. Dedicated heart images were reconstructed with a field of view around the heart and full cardiac cycle range of 0–90% of the RR-interval.

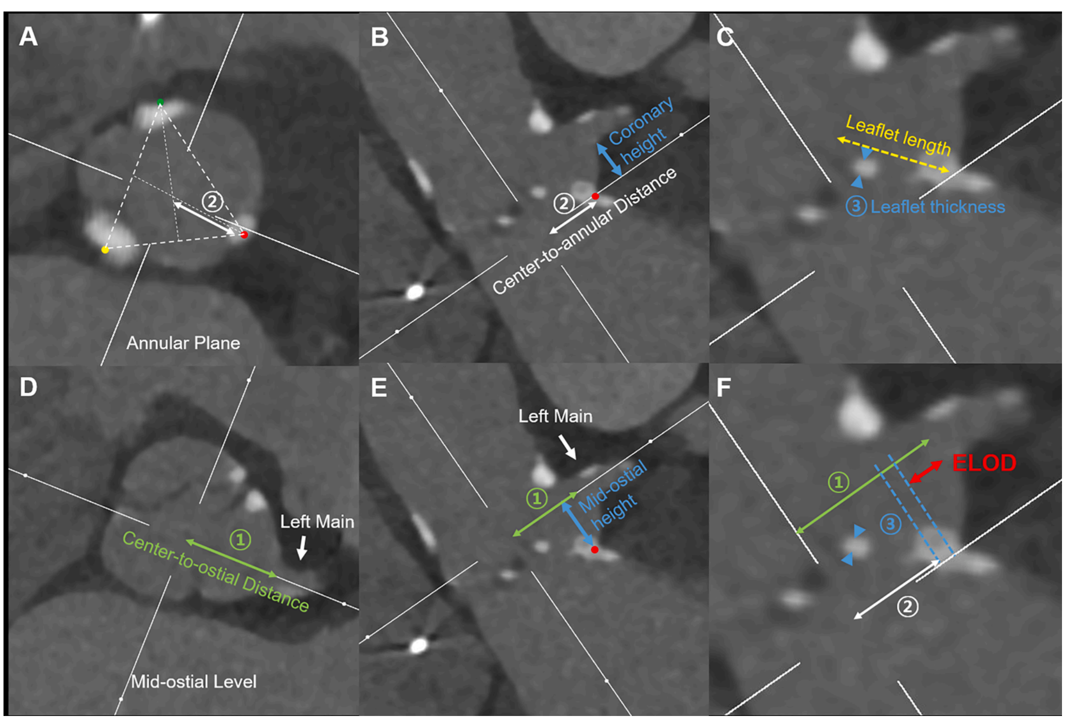

Fig. 1. Anatomical Analysis on Reconstructed CT Images. Step 1, identify the annular plane which accommodates the lowest insertion points of the three aortic valve cusps (A). Step 2, put the cross hairs at the geometric center of the triangle made by the three hinge points on the annular plane, which is defined by the intersection point of all the three medians drawn from its 3 vertices (white dashed lines, A). Step 3, rotate the cross hairs axially to visualize the coronary artery (B). Step 4, assess coronary height each for left and right, from the annular plane to the lowest insertion point of the coronary artery on the longitudinal view. The left coronary height was indicated by the blue double arrow (B). Step 5, scroll up the image to the coronary level and make the cross hair line aligned with the center of the ostium on both the axial and longitudinal views (D, E). Step 6, determine the distance between the hinge point of the leaflet and the center level of the coronary ostium on the longitudinal view (mid-ostial height, indicated by the blue double arrow) (E). Step 7, take the distance from the center to the ostium (Center-to-ostial Distance), indicated by the green double arrow (① in D and E). Step 8, scroll down the level to the annular plane and take the distance from the center to the inner margin of the aortic annulus (Center-to-annular Distance), indicated by the white double arrow (② in A and B). Step 9, assess the length (yellow dashed double arrow), the thickness (two blue arrow heads, ③) and the severity of the leaflet calcification (C). The Expected Leaflet-to-ostium Distance (ELOD, red double arrow) was calculated by subtracting ② and ③ from ① (F).

2.3. Measurements

The analyses for the anatomical features of the aortic root and aortic valve were conducted on reconstructed CT images during the systolic phase according to the recommendations of Society of Cardiovascular Computed Tomography, using dedicated image software (Aquarius iNtuition version 4.4, TeraRecon, CA, USA) [11].

In short, a double oblique transverse aortic valve annular plane was created which encompasses the lowest hinge points of the three aortic cusps (Fig. 1A). The cross hairs was set at the centroid center of the triangle made up of the insertion points of aortic valve cusps, which was recognized as the intersection point of all the three medians drawn from its 3 vertices and rotated axially until the coronary artery was shown along its centerline. The distance from the established annular plane to the lower insertion point of the coronary ostium, designated as the coronary height (Fig. 1B), and the shortest distance between the mid-level of the ostium and the hinge point of the corresponding aortic cusp, i.e. mid-ostial height (Fig. 1B), were measured on the longitudinal images in a perpendicular fashion. Leaflet length was defined the distance between the tip and the hinge point to the aortic annulus of the corresponding aortic valve leaflet which was divided into three parts (base, mid, tip) and assessed for the distribution and severity of calcification as follows: none – no visible calcification; spotty – small isolated spots; moderate – measurable sized fragment without indications for the severe; severe – any chunk of calcium larger than 3 mm in diameter or thick plaque spanning across at least two contiguous parts (Supplementary Fig. 1).

Leaflet thickness was the maximal thickness at the tip within 2 mm at the same distance to the corresponding mid-ostial height from its base; when the leaflet was too thin to be recognizable it was set at the minimum thickness of 0.6 mm. The distance from the center to the inner most border of the annulus at the annular level, or Center-to-annular Distance, and the distance from the center to the coronary ostium at the mid-ostial level, or Center-to-ostial Distance, were taken respectively on axial images using longitudinal images for reference. Area, perimeter, and mean diameter of the annulus and mean diameter of the sinus of Valsalva (SOV) were measured. ELOD, the distance between the expected position of the leaflet after THV implantation and the coronary ostium was calculated by subtracting Center-to-annular Distance and leaflet thickness from Center-to-ostial Distance. In valve-in-valve (ViV) cases, the basal ring of surgically implanted valve was considered the annular plane. A dichotomized variable indicating whether the coronary ostium locates within or beyond the stent post height from the annular plane was used instead of leaflet length. CT measurements were obtained by two investigators (JH.O., G.K.). Interobserver and intraobserver intraclass correlation coefficients (ICC) for ELOD were 0.90 and 0.92, respectively. Among 22 patients who had CT images following TAVR, the actual distances from the complex of THV strut and leaflet to coronary ostium at the mid-ostial level were measured and compared with the corresponding ELOD. Routine echocardiography was performed the next day, after 30 days, and one year after the procedure. Coronary obstruction was defined as obstruction of a coronary ostium on any image study at the time of procedure or follow-up period (angiography, CT, echocardiography) proving the obstruction regardless of clinical symptoms or signs.

2.4. Statistical analysis

Normally distributed continuous variables are presented as means and standard deviations and were compared using Student *t* test. Non-parametric continuous variables proved with the Kolmogorov-Smirnov test were expressed as medians (interquartile range) and compared using the Mann-Whitney *U* test. Categorical variables are summarized as frequencies (percentages) and were analyzed using Fisher's exact test. The associations between coronary obstruction event and ELOD less than 2 mm or leaflet length longer than mid-ostial height treated as categorical variables were assessed using log odds ratio (OR) [12]. Linear regression analysis and Bland-Altman plot were used to evaluated correlation and agreement between two variables (ELOD and the corresponding actual distance after THV implantation). Pearson's correlations were classified as poor ($r \leq 0.20$), fair ($0.20 < r \leq 0.50$), moderate ($0.50 < r \leq 0.70$), very strong ($r > 0.80$) [13]. A p value < 0.05 was considered statistically significant. All statistical calculations were performed using SPSS software version 22.0 (IBM SPSS Inc., Chicago, IL).

3. Results

3.1. Study population

A total of 501 patients underwent a THV procedure between January 2016 and December 2017 at Stanford University Medical Center. Among them, 177 patients with a high-risk feature for coronary obstruction, i.e. having at least one coronary artery whose height was<12 mm, either the left or right side, or with CT examination following TAVR procedure constituted the study population and divided into two groups for comparison based on the minimum coronary height (≤10 mm for Group 1 and > 10 mm for Group 2) based on the suggestion of previous document [11]. Group 1 consisted of 93 patients with 49 (52.7%) females and Group 2 consisted of 84 patients with 36 (42.9%) females.

The mean age was 79.9 ± 9.3 years for Group 1 and 80.0 ± 10.9 years for Group 2 (p = 0.944), respectively (Supplementary Table 1). Baseline demographic and clinical characteristics were balanced well between the two groups except for the STS Predicted Risk Mortality (PROM) score which tended to be higher in the lower coronary height group (7.2 ± 4.3 vs. 6.0 ± 3.4, p = 0.052).

Table 1
Baseline CT Findings.

	Group 1 (n = 93)	Group 2 (n = 84)	p Value
Annulus mean diameter	22.8 ± 2.8	23.4 ± 1.9	0.106
SOV mean diameter	31.2 ± 3.6	31.9 ± 3.6	0.150
Coronary height of Lt	9.4 ± 2.2 (3.7–16.1) *	12.1 ± 1.7 (10.1–18.3) *	<0.001
Coronary height of Rt	11.7 ± 3.8 (2.2–20.4) *	14.2 ± 2.9 (10.1–21.5) *	<0.001
Mid-ostial height of Lt	11.7 ± 2.3	14.1 ± 1.8	<0.001
Mid-ostial height of Rt	13.8 ± 3.7	15.6 ± 2.9	<0.001
Leaflet length, Lt	12.7 ± 2.2	13.0 ± 1.8	0.379
Leaflet length, Rt	12.1 ± 1.9	12.4 ± 1.9	0.263
Leaflet length - Mid-ostial height, Lt	0.65 ± 2.37	−1.02 ± 2.08	<0.001
Leaflet length - Mid-ostial height, Rt	−1.83 ± 2.97	−3.22 ± 2.74	0.002
Leaflet thickness, Lt	1.20 [0.85–1.77]	1.40 [0.90–1.70]	0.347
Leaflet thickness, Rt	1.50 [1.10–1.98]	1.40 [1.16–1.90]	0.916
Calcium deposition on leaflet			
Tip	50 (53.8%)	40 (47.6%)	0.453
Middle	58 (62.4%)	54 (64.3%)	0.876
Base	49 (52.7%)	63 (75.0%)	0.003
Severe calcification	42 (45.2%)	34 (40.5%)	0.547
Center-to-annular Distance, Lt	10.9 ± 1.9	11.1 ± 1.5	0.391
Center-to-annular Distance, Rt	11.0 ± 1.7	11.5 ± 1.6	0.063
Center-to-ostial Distance, Lt	16.9 ± 2.4	17.1 ± 2.4	0.630
Center-to-ostial Distance, Rt	18.2 ± 2.7	18.4 ± 2.8	0.573
ELOD, Lt	4.6 ± 2.3	4.6 ± 2.4	0.887
ELOD, Rt	5.5 ± 2.5	5.3 ± 2.5	0.513

Variables are expressed as mean ± standard deviation or medians with interquartile range for continuous variables and number (percentage) for categorical variables. *Variables are expressed with minimum and maximum values.
SOV = sinus of Valsalva; Lt = left; Rt = right; ELOD = Expected Leaflet-to-ostium Distance.

3.2. Anatomical CT findings and procedural outcome

The mean annulus diameters were 22.8 ± 2.8 and 23.4 ± 1.9 mm, and the mean SOV diameters were 31.2 ± 3.6 and 31.9 ± 3.6 mm, without statistical significances between the two groups (Table 1). The mean coronary heights were significantly lower for Group 1 compared to Group 2 (for the left coronary artery, 9.4 ± 2.2 mm vs. 12.1 ± 1.7 mm, $p < 0.001$; for the right coronary artery, 11.7 ± 3.8 mm vs. 14.2 ± 2.9 mm, $p < 0.001$). There were no significant differences in leaflet length, leaflet thickness, distribution and severity of leaflet calcification, Center-to-annular and Center-to-ostial Distances as well as Expected Leaflet-to-ostium Distance (ELOD) between the two groups.

Most of the procedures were performed via transfemoral route except one case that was performed with apical approach (Supplementary Table 2). Balloon expandable Sapien valves were more commonly used than self-expandable valves in both groups with the predominant sizes of 23 and 26 mm. The coronary artery was protected in 3 (3.2%) cases in Group 1. Coronary artery obstruction occurred in 3 cases; all of them belonged to Group 1.

The first one had partial obstruction of the left main ostium (Supplementary Figure 3A and B) which aggravated the insufficiency of the blood flow down to the diseased left anterior descending coronary artery (LAD) in a sequential manner and required a coronary stent. The second case had a chunk of calcium abutting on the right coronary artery ostium, but there was a furrow on the surface of that calcium (Supplementary Figure 3C and D) which allowed enough amount of blood flow not to create any ischemic signs or symptoms without deteriorating the LV function. The last case had an obvious obstruction of left main ostium by the displaced piece of calcium on the leaflet and received cardio-pulmonary bypass support immediately and open heart surgery (Table 2). All those three patients have been well up to 989, 700, and 379 days of follow-up, respectively, since the index procedures.

3.3. Valve-in-Valve cases

There were 17 cases of ViV of stented surgical bioprosthesis including Mosaic, Perimount, Hancock, Carpentier, Magna, Biocor, Trifecta, and Mitroflow (Supplementary Table 3). When compared to TAVR in native valve, it had smaller annulus size, lower coronary height, shorter Center-to-annular Distance, and lesser amount of calcium but significantly longer ELOD in both the right and the left side. In 14 cases, 23 ostia of either the right or left coronary artery were found within the post height from the annular plane with mean coronary height of 7.3 ± 3.2 mm. However, with the observed mean ELOD of 7.1 ± 2.6 mm (minimum and maximum values of 2.7 and 14 mm) none of those cases had coronary obstruction.

3.4. Performance of Expected Leaflet-to-ostium (ELOD) distance

A total of 353 coronary arteries from 177 patients (excluding 1 unrecognizable right coronary artery) were analyzed to evaluate the performance of coronary height and SOV diameter for the prediction of coronary obstruction (Fig. 2A). Most of the cases (162, 45.9%) had coronary height and SOV diameter greater than 10 mm and 30 mm, respectively, 81 (22.9%) cases with coronary height > 10 mm and SOV diameter ≤ 30 mm, 61 (17.3%) cases with coronary height ≤ 10 mm and

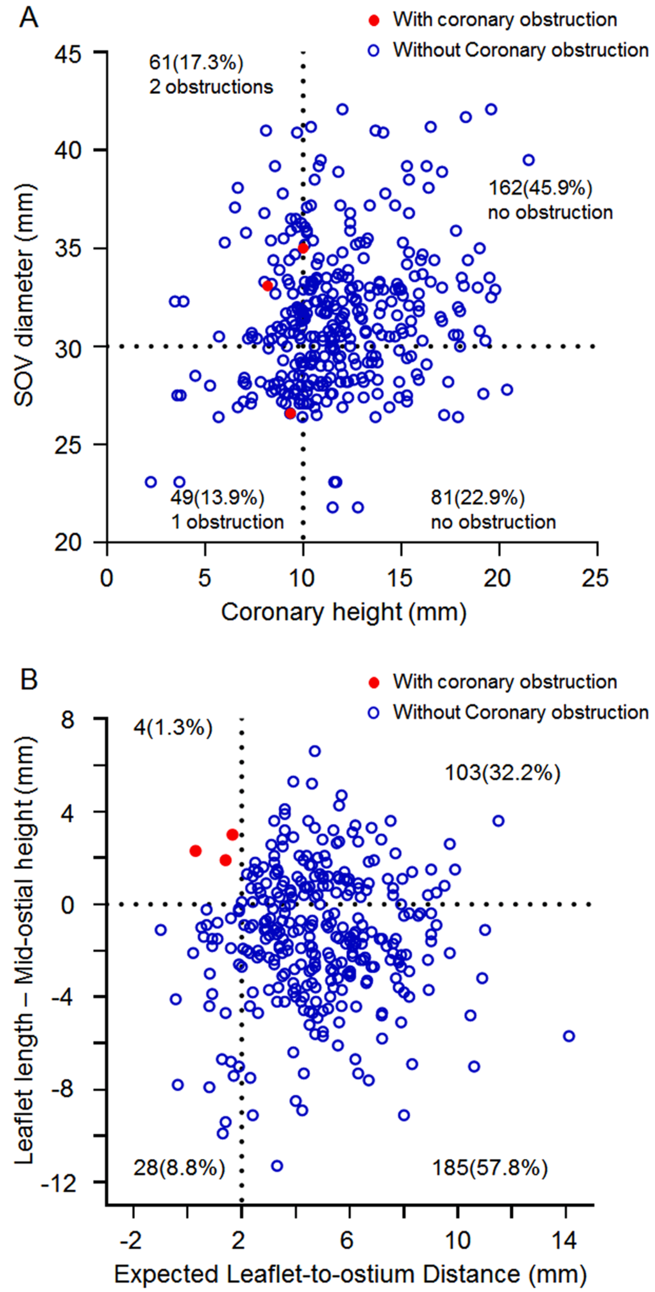

Fig. 2. Scatter Plots for Cases with and without Coronary Obstruction. (A) Scatter plot for SOV diameter against coronary height. The three coronary obstruction cases (red closed circle) spread out the different quadrants defined by the cut-off values of 30 mm for SOV diameter and 10 mm for coronary height. (B) The three coronary obstruction cases were clearly differentiated from others in the left upper quadrant with Expected Leaflet-to-ostium Distance of less than or equal to 2 mm and positive value of leaflet length minus mid-ostial height.

Table 2
Cases of Coronary Artery Obstruction.

Case	Age/Gender	THV	Cause	Site	Clinical Presentation	Treatment	ELOD
1	88/M	S3 26 mm	Leaflet displacement	LM, partial	delayed AMI	PCI	1.4 mm
2	89/F	S3 20 mm	Leaflet displacement	RCA, partial	none	none	0.3 mm
3	80/F	S3 29 mm	Leaflet displacement	LM, total	Shock	OHS	1.6 mm

AMI = Acute Myocardial Infarction; ELOD = Expected Leaflet-to-ostium Distance; LM = Left Main; OHS = Open Heart Surgery; PCI = Percutaneous Coronary Intervention; RCA = Right Coronary Artery; THV = Transcatheter Heart Valve.

SOV diameter > 30 mm, and 49 (13.9%) cases with coronary height ≤ 10 mm and SOV diameter ≤ 30 mm. Two coronary obstruction cases occurred in the group with SOV > 30 mm and coronary height ≤ 10 mm and one obstruction case occurred in the group with SOV ≤ 30 mm and coronary height ≤ 10 mm. The association between coronary obstruction event and low coronary height (≤10 mm) treated as dichotomous variable when SOV was ≤ 30 mm was not statistically significant (log OR = 1.618, p = 0.325, Supplementary Table 4).

Fig. 2B depicts the location of each case in relation to ELOD and the difference in length between leaflet and mid-ostial height. 33 arteries from ViV cases were excluded in which leaflet lengths were not available. Among 107 cases with longer leaflet length than mid-ostial height, one case with ELOD ≤ 2 mm did not experience coronary obstruction complication and three cases with ELOD ≤ 2 mm experienced the complication giving a significant association between coronary obstruction event and ELOD ≤ 2 mm (log OR = 6.180, p < 0.001, Supplementary Table 4).

3.5. Agreement of Expected Leaflet-to-ostium distance with actual distance

In order to assess how well the ELOD correlated with the actual distance following TAVR, the CT images from 22 patients who had CT examinations both before and after the index TAVR procedure were analyzed. We measured the shortest distance, or actual distance, from the THV strut or displaced leaflet to the coronary ostium at the mid-ostial level on axial images. There was a very strong correlation between ELOD taken from pre-planning CT images and the corresponding actual distance on follow-up CT scan (r = 0.837, Supplementary Figure 3A). The mean difference was + 0.199 mm indicating that the actual distance tended to be slightly longer than the ELOD (Supplementary Figure 3B). Most of the analyzed arteries (n = 38, 97.4%) fit within the limits of agreement but one case which had a large calcification of the leaflet sitting in the SOV after TAVR, impeding full extension of the TAVR valve. It resulted in increased space than expected between the coronary ostium and the displaced native leaflet (Supplementary Figure 3C-F).

3.6. Proposed algorithm

Based on the results of this study we suggest a systematic approach to the risk assessment for coronary artery obstruction during TAVR procedure (Supplementary Figure 4). First, consider the location of the ostium of coronary artery in relation to the leaflet length in native valve case or stent post in ViV case. If the ostium is more distant from the annulus plane than the length of the leaflet or is in higher position than the stent post then the risk for coronary obstruction is considered very low. Second, once the above condition is failed, calculate ELOD. If the ELOD is less than 2 mm, the risk of coronary obstruction should be taken seriously and coronary protection or alternative therapy should be considered.

4. Discussion

This study demonstrated several key factors that were associated with coronary artery obstruction following TAVR: leaflet length, mid-ostial height or ostial location in relation to stent post in ViV case, leaflet thickness, and ELOD. Leaflet length longer than the corresponding mid-ostial height was one prerequisite for coronary obstruction. The ELOD less than 2 mm posed an increased risk of coronary obstruction along with short mid-ostial height compared to the corresponding leaflet length. Ostial locations positioned lower than the stent-post may have an equivalent implication of longer leaflet length in ViV cases because the possibility of prosthesis valvular leaflets reaching and covering the coronary ostium when displaced by a newly deployed THV.

Although coronary artery obstruction after TAVR procedure occurs rarely with the reported incidences of 0.34%−4.1%, the consequences are devastating with a mortality rate of 50% [3,9,14,15]. Since the first case report of coronary artery obstruction after TAVR in humans was described by Webb et al. in 2006, it has still been challenging to predict the risk [16]. Several characteristics have been suggested as relevant risk factors such as low lying coronary ostium, shallow SOV, bulky calcification on the leaflet, long leaflet length, women, ViV procedure or certain types of surgical bioprosthesis (Mitroflow and Trifecta), balloon-expandable valve, and oversized THV [6,7,14,17,18]. However, there is no definitive criteria or evidence-based evaluation of the appropriate patient-adjusted coronary height which put a patient at high-risk for coronary obstruction at this time. The manufacturer's recommendations for minimum coronary height were 10 mm for Edwards Sapien XT system and 14 mm for CoreValve system [11]. A comprehensive review work on the complications after TAVR suggested that the coronary ostium should be located at least 14 mm away from the leaflets insertion to avoid coronary obstruction [18]. Ribeiro et al. suggested a threshold value of 12 mm for lower-lying coronary ostium based on the observation that most of the patients suffered coronary obstruction (80% of the study population) had left coronary artery heights less than 12 mm and also SOV diameters of < 30 mm as the synergistic cofactor [6]. On one prospective study Conzelmann et al. reported TAVR could be performed prudently in patient with extremely low coronary height of ≤ 7 mm (the mean coronary height of 6.4 ± 1.1 mm) with a relatively low rate of coronary obstruction (3 out of 86 patients), in which one of the obstruction cases was caused by aortic dissection whose flap covered the right coronary artery ostium [8]. On the other hand, a large multicenter registry study revealed that 14.3% of the obstruction case had a higher coronary heightgreater than 12 mm [6]. These results highlighted the need for considering other factors to predict coronary obstruction like length of the valvular leaflet, the amount of calcification on the leaflet and the size of SOV as well. It seems that valvular leaflets need to be long enough to reach the coronary ostium given the fact that most of the coronary obstructions were caused by the displaced calcified valvular leaflet covering the coronary ostium.

This study showed that all the coronary obstruction occurred only when the leaflet length was longer than the mid-ostial height. In addition to the above mentioned prerequisites, we found that short distance between the shifted leaflet and the coronary ostium can compromise coronary artery blood flow. ELOD represents the space by taking account of the Center-to-ostial Distance at the coronary ostial level and the leaflet thickness. Our findings suggested an ELOD cut-off value of 2 mm, which in combination with longer leaflet length put the patients at high risk for coronary obstruction.

5. Study limitations

This study has several limitations. First of all, the number of the coronary obstruction cases was too small to draw robust conclusions and compare the characteristics between those patients with and without. Additionally, the quantification of valve calcification was assessed in a semi-quantitative manner, which might not estimate the risk appropriately as volumetric quantitative assessment dose. Due to the fact that this is a single center study, the results should be replicated in other larger studies.

6. Conclusions

Leaflet length, mid-ostial height, leaflet thickness and Expected Leaflet-to-ostium Distance (ELOD) were the key risk factors for coronary obstruction following TAVR. ELOD less than 2 mm, and leaflet length longer than the corresponding mid-ostial height posed an increased risk of coronary obstruction to the patients. Coronary obstruction was not found in any ViV cases even with lower coronary height presumably due to large ELOD.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2021.100917.

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