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Research Article

Evaluation of incidence of structural valve deterioration in patients with Freestyle aortic valve

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Abstract

Background: The Freestyle aortic root bio prosthesis is a complete porcine aortic root implanted by different techniques: sub coronary, root inclusion, or complete aortic root replacement. The choice among the three implant techniques depends on surgeon preference or upon the pathology encountered. Its implantation is done by open heart surgery. The study aimed to trace the prevalence of sub clinical leaflet thrombosis in patient underwent free style aortic valve replacement, and how far is the need for anticoagulation therapy to protect the patients from being involved in transient ischemic attacks (TIAs) or strokes. **Method**: This study enrolled 47 patients underwent Freestyle aortic valve and had MDCT at least with two follow up point interval post operative. We evaluated the cusp structure and possible sub clinical thrombosis using a retrospective ECG gated CT angiographic study. **Results**: We observed 22 cases with positive thrombus out of 47 with percentage of 46%, with negative relationship between thrombus formation and oral anticoagulant taking. The cumulative incidence of thrombus was increasing over years. **Conclusion**: Sub clinical thrombus formation is a common complication over Freestyle bioprosthetic valve and makes oral anti-coagulant taking mandatory.

Keywords: Freestyle aortic valve- sub clinical thrombus- oral anticoagulants

Introduction

Aortic valve lesions are the most common valvular pathology in the developed countries. The incidence of the pathology increases with growing ages after 65 years. Aortic valve replacement (AVR) is recommended for symptomatic aortic valve disease according to the guidelines of American Heart Association for management of patients with valvular heart disease, such as small aortic root, aortic aneurysm, or dissection. Also, it had been reported to be a successful treatment option in the destructive aortic valve endocarditis[1]

The Freestyle aortic root bio prosthesis is a complete porcine aortic root implanted by different techniques: sub coronary, root inclusion, or complete aortic root replacement. The choice among the three implant techniques depends on surgeon preference or upon the pathology encountered. Its implantation is done by open heart surgery[2].

It offers excellent hemodynamics in indicated patients, however, as with all biological prostheses, structural valve deterioration (SVD) limits its durability, eventually necessitating reintervention[3]

One of its complications is subclinical leaflet thrombosis which is predominantly hemodynamically silent and not detected by transthoracic Echocardiography in most patients. Echocardiography is used to assess transvalvular pressure gradient and effective valve orifice area. Mean aortic valve gradients is significantly higher in patients with reduced leaflet motion than in those with normal leaflet motion.[4]

Multi-slice computed tomography (MSCT) is needed for the accurate characterization of the valve. In post-contrast MSCT, subclinical leaflet thrombosis is defined as the presence of reduced leaflet motion, along with corresponding hypoattenuating lesions. We quantitatively assess leaflet

motion at maximal leaflet opening during systole using a three-dimensional volume-rendered en-face image of the prosthetic valve[5]

Aim of the work

We aimed in our study to trace the prevalence of sub clinical leaflet thrombosis in patient underwent free style aortic valve replacement, and how far is the need for anticoagulation therapy to protect the patients from being involved in transient ischemic attacks (TIAs) or strokes. This was done by using MSCT in evaluating the valve morphology, its function, and the possible complication.

Patients & Methods

This is a retrospective study conducted in Radio-diagnosis Department, at Aswan Heart Centre including the patients who underwent freestyle aortic root replacement between 2011-2019 and had MSCT.

Patients were selected according to the following inclusion and exclusion criteria:

Inclusion criteria: This study included patients underwent Freestyle aortic root replacement.

Exclusion criteria:

- Patient with one follow up study.
- Inadequate technique to examine the aortic valve area and leaflet mobility (using a prospective ECG gated technique)

Detailed description of the performed procedure:

a) Study planning.
b) Preprocedural preparations.
c) Technique of Examination; Data acquisition and Image reconstruction and post processing
d) Image interpretation.

a) Study planning:

- Measure the heart rate and blood pressure of the patients.
- Proper history taking focusing on usage of anticoagulant drugs and history of exposure to transient ischemic attacks TIAs, or strokes.
- ECG information was taken, either normal sinus rhythm or having arrhythmia.

b) Preprocedural preparations:

- The patient may need regulation of heart rate by beta blockers (we used IV metoprolol 5mg, or oral bisoprolol 5mg), and vasodilate the coronary arteries (by Isosorbide dinitrate 5mg), before the CT study for better evaluation of the coronary arteries. The heart rate should be <70 beats/min.
- The beta blocker is contra indicated for patients with true severe asthma and it was taken cautiously under supervision of cardiologist in cases of severe or worsened heart failure, and in hypotension (systolic blood pressure <90mmHg)[8].
- Insert 18- or 20-gauge cannula in the right or the left upper limb.

c) Technique of examination:

Data acquisition:

- Patients were scanned using 128-row multidetector CT scanner dual-energy source (SIEMENS, SOMATOM, Definition Flash, Germany).
- The patient lay supine on the CT table
- He was positioned on table to ensure the heart lies in the isocenter of the gantry for optimal spatial resolution.
- ECG electrodes were applied to chest wall and ECG trace was monitored to ensure good amplitude of R wave that was used for scan trigger.
- The intravenous (IV) line was connected and test injection with saline was done to

ensure good IV access with no extra-vasation.

- Thereafter, a scanogram (frontal view) was obtained where the scan ranges from the bifurcation of trachea down to the end of chest inferiorly.
- Ca score was taken in a prospective way (step and shoot manner) in the diastolic phase of the cardiac cycle (70% of the cardiac cycle) with 3mm slice thickness.
- Nonionic, non-diluted contrast material (Ultravist (Iopromide) 370 mg/ml) was injected in the peripherally inserted IV line using dual syringe mechanical power injector (Stellant, Medrad) with flow rate 5.5-6 ml/sec. The volume of contrast was at least 50ml and ideally to be 100ml with consideration of renal function factor of the patient.
- IV saline chaser injection of half the contrast dose was given immediately after the contrast injection to improve the contrast opacification and homogeneity. Particular care was taken to exclude air bubbles from the connection tube to prevent air embolism.
- All scans were performed in a cranio-caudal direction. The patients were scanned using a retrospective ECG gating for leaflet motion assessment. Dose modulation preferably not used; however, in some cases it was used.
- One-hundred twenty kilovolts is the standard scanner acquisition voltage used, but there may be some benefit in increasing this to 140 kV, particularly in the presence of a large body habitus, a denser bio-prosthetic frame.
- Scan slice thickness was sub-millimeter thickness.

Image reconstruction and post processing:

- By the end of examination, different phases including the best systolic and best diastolic phases were reconstructed in 0.6 mm slice thickness with interval 0.3mm. Post-processing of multi-detector CT (MDCT) scan was performed as multi-planar reconstruction (MPR) and curved planer reformations (CPR) as well as 3D volume rendering (VR) were used to display the heart and coronary arteries. Cine images for aortic valve were obtained for visual and mathematical evaluation of the cusps' mobility as well as the aortic valve area.

d) Image interpretation:

- Firstly, the Ca score was calculated using Agatston score protocol in different aortic segments (aortic annulus, along the right, left and non-coronary cusps, and ascending aorta).
- The maximum diameter of the aorta is measured from the external walls of the aorta, perpendicular to the long axis of flow and length of the aorta. The aortic measurements are made at the following sites:

1. Aortic annulus.
2. Aortic sinuses of Valsalva.
3. Sino tubular junction.
4. Mid-ascending aorta (midpoint in length between the Sino tubular junction and proximal aortic arch at the level of the main pulmonary artery).
5. Proximal aortic arch (at the origin of the innominate artery)

- Better evaluation of the annulus from all aspects searching for presence of left ventricular out flow tract aneurysms, with measuring its size over years.
- Evaluation of the coronary arteries ostia either normal or stenosed under the effect of operation and tracing each vessel along its course using the different MPR planes with proper axis on the vessel (coronal, sagittal and axial) to evaluate the lumen.

- Estimation of leaflet possibility of thrombosis as follows:

➢ We defined sub clinical leaflet thrombosis as reduced leaflet motion (RELM) together with the presence of hypo attenuated leaflet[6]

➢ Hypo attenuated leaflet thrombosis (HALT) was defined as an increased leaflet thickness with meniscal appearance on long-axis views at the time of leaflet coaptation (in diastole)[54] . The thickening which resolved after oral anti-coagulant is considered evidence of a thrombus as well[55-44]

➢ **statistical analysis:**

The analysis of the data was carried out using the IBM SPSS version 20.0 statistical package software (IBM; Armonk, New York, USA). Normality of the data was

tested using the Kolmogorov-Smirnov test. Data were expressed as mean ± SD for parametric quantitative data and median (IQR) for non-parametric quantitative data, in addition to both number and percentage for qualitative data. Paired samples t-test and Wilcoxon signed rank test were done to compare parametric and non-parametric data, quantitative data of follow ups respectively. While independent samples t-test was done to compare parametric quantitative data between two groups. The Chi-square test and Fisher's exact test were used to compare categorical variables. Pearson's correlation was done for non-parametric data. A p-value less than 0.05 was considered significant.

Results

Demographic data:

This study enrolled 47 patients (23 males and 24 females), underwent replacement of aortic valve with Freestyle aortic valve and had at least two follow up studies post-operative (table1).

Ca score:

Regarding calcification (Figure 1), it was measured from different parts of the aortic root, the data of Ca score from some cases were missed as they had not been scanned with Ca score. It was obvious that the calcification was a common complication, and it was increasing significantly over years with P value=0.001 (Chart 1). It is figured out that the annulus is the most affected part to be calcified with percentage of affection in comparison with all other areas= 69.6% (Chart 2).

Aortic diameters:

The ascending aorta diameters were measured at every follow up study. All aortic measurements were within average diameter with no stenosis or dilatation. There was significant increase in the diameters of sinus of Valsalva and STJ as well as proximal aortic arch with P value <0.05, while no significant changes in other segments of the ascending aorta. (Table 2).

Leaflet thrombosis:

Thrombosed leaflet was observed in 22 cases from the 47 cases with percentage of 46% (table 3). There was a strong negative relationship between thrombus formation and use of oral anti-coagulants (chart 3). The cumulative probability of a thrombus was increasing over years from 1 year follow up post-operative to 10 years (chart 4).

Table (1): Criteria of age, gender, rhythm, and age at operation

Demographic data	**Cases N= 47**
Age	41.0 ± 12.2
Gender:	
Males	23 (48.9%)
Females	24 (51.1%)
Age at operation	32.3 ± 12.2
Rhythm:	
AF	8 (17.0%)
NSR	39 (83.0%)

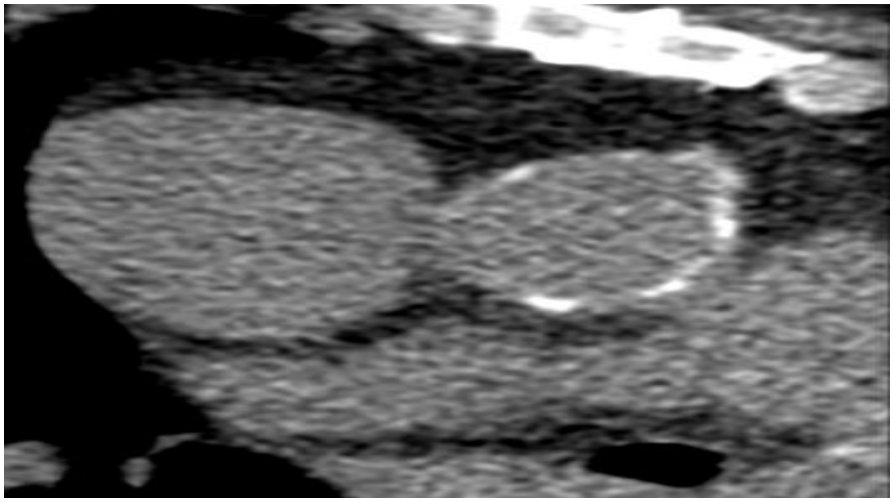

Figure (1): calcification affecting the sinus of valsava

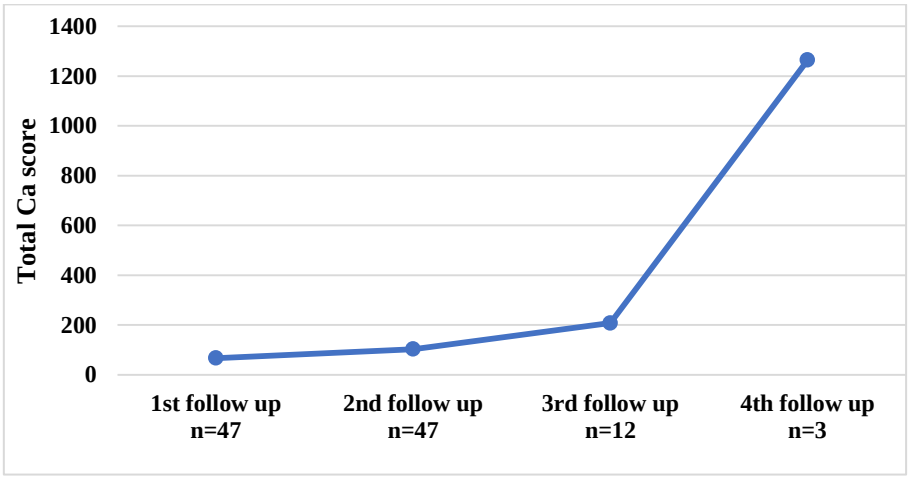

Chart (1): total ca score over years.

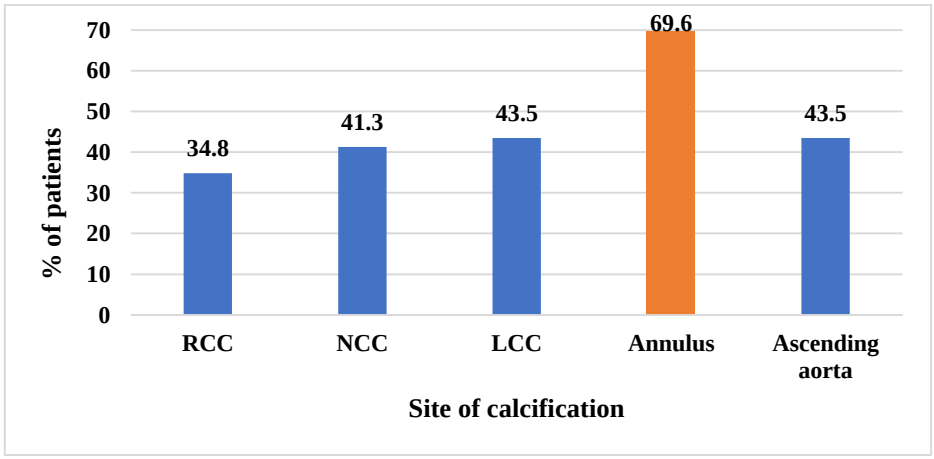

Chart (2): percentage of calcification among different parts of the ascending aorta

Table (2): aortic diameters over years

Aortic diameters	Cases N= 47			
	1st follow up N= 47	2nd follow up N= 47	3rd follow up N= 12	4th follow up N= 3
	Mean ± SD			
Aortic annulus	20.7 ± 3.5	20.7 ± 3.4	21.4 ± 4.6	22.3 ± 6.6
Sinus	30.1 ± 3.1	31.0 ± 4.3	31.3 ± 5.3	32.5 ± 8.3
STJ	24.0 ± 2.6	24.5 ± 3.1	25.6 ± 5.2	24.5 ± 6.6
Ascending aorta	30.9 ± 4.4	31.1 ± 4.7	31.5 ± 4.5	30.3 ± 3.8
Proximal aortic arch	29.5 ± 3.8	30.2 ± 4.3	30.0 ± 3.6	31.0 ± 1.8
	p value 1st vs 2nd follow up			
Aortic annulus	0.761			
Sinus	**0.024***			
STJ	**0.022***			
Ascending aorta	0.176			
Proximal aortic arch	**<0.001***			

STJ: sino-tubular junction

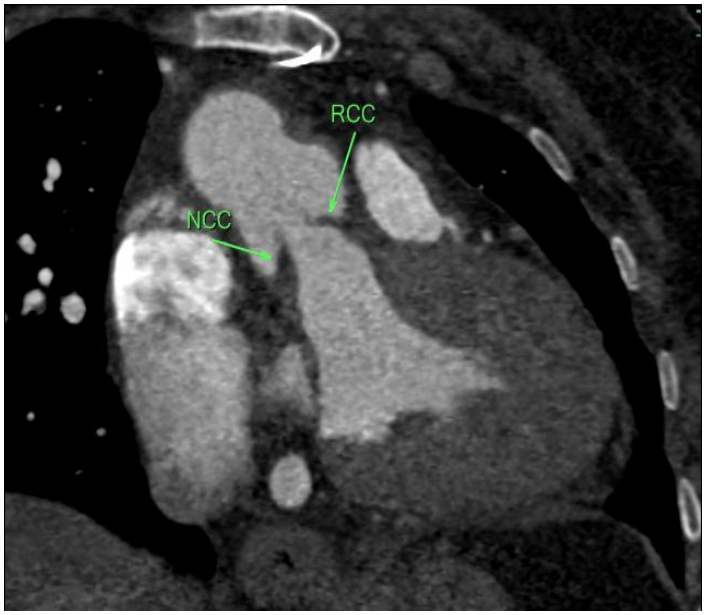

Figure (2): thrombosis is notices along NCC

Table (3): the incidence of thrombus along different aortic cusps, and its follow up over years

Thrombus	Cases N= 47			
	1st follow up N= 47	2nd follow up N= 47	3rd follow up N= 12	4th follow up N= 3
	N %			
RCC	5 (10.6%)	6 (12.8%)	2 (16.7%)	0
LCC	2 (4.3%)	7 (14.9%)	0	0
NCC	9 (19.1%)	7 (14.9%)	2 (16.7%)	0

RCC: right coronary cusp. LCC: left coronary cusp. NCC: non coronary cusp

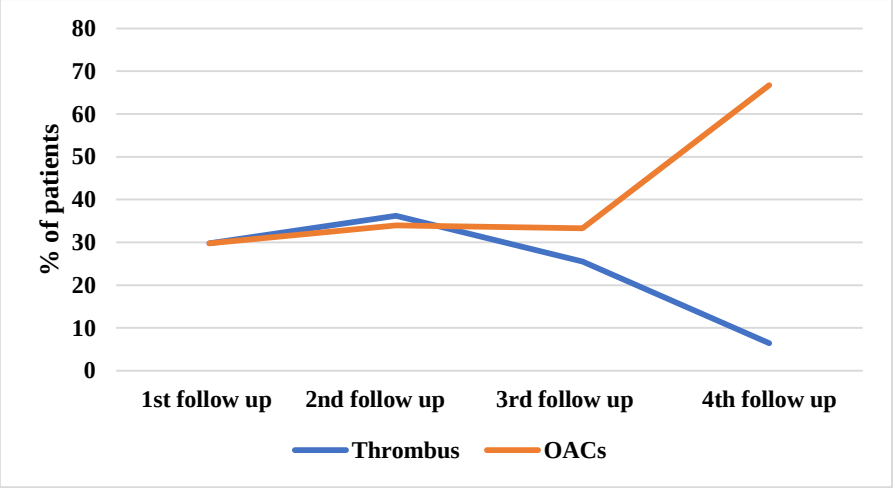

Chart (3): relation between oral anticoagulant and thrombus formation

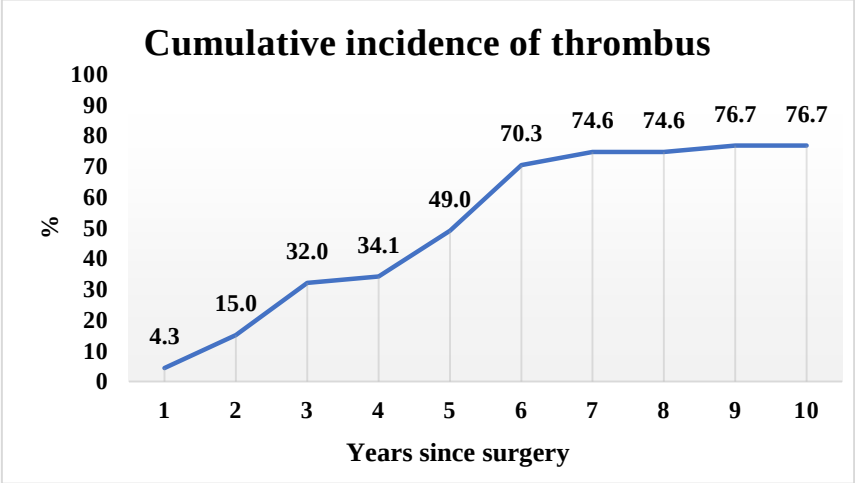

Chart (4): Cumulative incidence of thrombus over years since surgery.

Discussion

Freestyle aortic valve is a porcine bioprosthetic valve implanted by several techniques regarding surgeon's preferences. The ideal valve substitute for the aortic valve should have superior hemodynamics, no pressure gradients, no leaks, and normal laminar flow. It should be easy to be implanted, silent, biocompatible, and resistant to thromboembolic problems. Lastly, it should be durable enough to last the patient's lifetime. The disadvantages of a stent include an increase in stress forces associated with leaflet opening and closing, with possibility of leaflet abrasion adjacent to the cloth covering the stent.[9].

Imaging modalities to assess the function and structure of the valve are several. Among those modalities is multi-detector computed tomography MDCT which identifies the leaflet thrombus as combined hypo attenuated leaflet together with reduced its mobility to 50% and more[10]

Moreover, the calcification with specific details regarding its distribution and density could be measured using CT to trace the possible increased calcification over years as one of Freestyle aortic valve complication.

As one of the steps of implanting the Freestyle aortic valve is manipulation of coronary artery ostia; both coronary ostia are mobilized on generous buttons of aortic wall, then the coronary arteries on their buttons of aortic wall are sewn end to side to the corresponding sinus of Valsalva of the bio prosthesis with a continuous 5–0

polypropylene suture[11], that is why CT is important to evaluate the coronary ostia whether patent or stenotic.

Some reported that generally subclinical leaflet thrombosis occurred frequently in bioprosthetic aortic valves. And oral anticoagulants are prescribed for treatment and prevention of thrombosis.

David S. Bach et al., 2004[12] made a prospective study on 700 patients (93% >60 years of age) at 8 centers in North America having aortic valve replacement with the Freestyle stent-less bio prosthesis using the three methods of the implant technique. Follow-up was yearly till 8 years post operatively and they used clinical and echocardiographic study. They reported 100% freedom from structural valve deterioration using total root replacement. The effective orifice area was decreasing in 1 and 6 years post operative; however, with no significance (P=0.02). So, they concluded that the Freestyle stent less aortic root bio prosthesis is a versatile option for aortic valve replacement.

In the current study, Regarding calcification: we reported that the calcification over the leaflets was increasing over follow up periods, with calcification over the cusps: RCC ranging from (12-206), NCC (19-332), and LCC (4-44).

Regarding thrombus formation: we concluded that 22 cases out of 47 (46%) had positive thrombus formation. The thrombus had negative relationship with oral anticoagulants, and it had no association with size of Freestyle valve.

Jagdish Butany et al., 2007[13] Freestyle valves were reviewed to assess the reasons for bio prosthesis failure by using histochemistry and immunohistochemistry. Average implant duration was 52.8+-35.5 months. Four valves were explanted for infective endocarditis, three for aortic insufficiency, two for aortic stenosis with cusp calcification seen in five valves, pannus, and thrombus in all valves
Although it was done in very small sample size, the duration of the valve implantation was short to develop the above-mentioned complication with thrombus in all valves.

Adriaan W. Schneider 2019[14] they analyzed their experience with reinterventions after stent less AVR. A total of 75 patients with previous AVR using a Freestyle stent less bio prosthesis that underwent reintervention. In 47 (63%) patients, SVD was the failure mode of the stent less prosthesis. These patients typically presented with subacute dyspnea due to sudden increase of aortic regurgitation caused by leaflet tear or perforation. Non-SVD was the failure mode in 13(17%) patients and prosthesis endocarditis in 15(20%).

Conclusion

Although Freestyle aortic valve is a bioprosthetic valve, sub clinical thrombosis in it is a common complication and requires usage of oral anticoagulants. It has less durability with a need for redo surgery. MDCT is a valuable method for detection of structural valve deterioration.

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