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3D Transoesophageal echocardiography (TEE) versus computed tomography (MDCT) to guide prosthesis sizing in patients undergoing transcatheter aortic valve implantation (TAVI)

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I. TITLE PAGE

3D Transoesophageal echocardiography (TEE) versus computed tomography (MDCT) to guide prosthesis sizing in patients undergoing transcatheter aortic valve implantation (TAVI)

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II. ABSTRACT

BACKGROUND : In transcatheter aortic valve implantation (TAVI) procedures, aortic valve annulus sizing is a key-step in deciding prosthesis size. The main complication post TAVI remains paravalvular aortic regurgitation (PVR). Survival after TAVI is highly correlated with the presence of moderate/severe PVR. One of the causes of aortic leak is an inadequate choice of valve size.
Multi-detector row computed tomography (MDCT) is the first choice imaging method to calculate the annulus size. 3D transoesophageal echocardiography (TEE) is another emerging technique. As compared with 2D modalities, 3D modalities have been shown to be more accurate. However, 3D imaging modalities have so far rarely been compared.

AIM : We aim to compare measures of the aortic annulus by MDCT as compared to measures by 3D-TEE and evaluate the correlation between the imaging technique and the final annulus prosthesis size. Furthermore, we aim to investigate the correlation between the imaging technique chosen to decide the prosthesis size and the incidence of aortic regurgitation (AR) after TAVI.

METHODS : We established a cohort of patients who underwent TAVI between 2013 and 2016 in the Cardiology Department of the Lausanne University Hospital (CHUV).
We collected data in our defined cohort relating to each imaging techniques: Transthoracic echocardiography, MDCT, 2D-TEE and 3D-TEE.
We proceeded with a retrospective analysis of peri-procedural 3D-TEE data versus pre-procedural MDCT data and made comparisons with implanted prosthesis size.

RESULTS : Between 18.01.2013 and 14.09.2016, 199 patients underwent TAVI in our Department. Among them, results of MDCT were available in 165 patients whereas results of 3D-TEE were available in 106. As compared to MDCT, annulus size by 3D-TEE were significantly lower (22 [21;24.5]mm versus 24 [22;26]mm, $p<0.001$). Differences between implanted prosthesis size and the MDCT annulus size were significantly lower than those with 3D-TEE (1.5 [0;2.85]mm versus 3 [1.5;4.5]mm, $p<0.001$).

CONCLUSIONS : Annulus sizes assessed by 3D-TEE are significantly lower than annulus sizes assessed by MDCT. Operators should be aware of these differences and choose the annulus size consequently. Knowing these significant differences in prosthesis sizing between 3D-TEE and MDCT, TAVI can be performed without CT-scan and thus without contrast agent in population at risk of kidney failure.
Other large prospective trials should investigate if the imaging modality choice could impact the occurrence of paravalvular leak after TAVI.

III. ABBREVIATIONS

CHUV :	Centre hospitalier universitaire Vaudois (Lausanne University Hospital)
AS :	aortic sclerosis
AVR (or RVA) :	aortic valve replacement
TAVI :	transcatheter aortic valve implantation
LVEF (or EF):	left ventricular ejection fraction
ESC :	European Society of Cardiology
STS-PROM :	Society of Thoracic Surgeons-Predicted Risk of Mortality Score
EuroSCORE :	European System for Cardiac Operative Risk Evaluation
PVR :	paravalvular aortic regurgitation
AR :	aortic regurgitation
MDCT :	Multidetector row computed tomography
MSCT :	Multislice computed tomography
TTE :	Transthoracic echocardiography
2D :	two dimensional
3D :	three dimensional
TEE :	Transoesophageal echocardiography
CTA :	Computed tomography angiography
OR :	direct intraoperative
AA :	aortic annulus
LVOT :	left ventricular outflow tract
MSCT :	Multislice computed tomography
CMR :	Cardiovascular Magnetic Resonance
CCT:	Cardiac computed tomography
CT or CT-scan :	Computed tomography scanner

IV. ACKNOWLEDGMENTS

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V. INTRODUCTION

Valvular aortic stenosis (AS) consists in a narrowing of the outlet of the heart's left ventricle due to multiple etiologies such as sclerosis: thickening, calcification or fibrosis of the valve. It is the most common isolated valve disease (1). It affects between 2% and 9 % (2-3) of the population aged 65 years or older and its prevalence is increasing with ageing population. Symptoms are usually insidious and tend to appear when the aortic annulus valve size is critical (severe aortic stenosis) (4). Before this stage patients can stay asymptomatic for years. Angina, syncope and dyspnea are the primary symptoms.

AS has a bad prognostic when it is severe, particularly when it is symptomatic. This pathology which in western developed countries is mostly from a degenerative cause has a mortality rate of 50% (5) at the onset of the first symptoms if not treated. Severe symptomatic aortic stenosis has an average survival rate of two to three years with a high sudden death risk (6).

Treatments of aortic stenosis are multiple and different: the drug treatment alternative and the invasive valvular replacement treatment. Besides the drug treatment alternative, the more invasive treatment consists in a valve replacement either a surgical aortic valve replacement (AVR) or the latest and yet well-established transcatheter aortic valve implantation (TAVI).

Indications to treat an aortic stenosis by valvular replacement (either surgical or TAVI) are severity criteria: valvular surface less than $1cm^2$ ($0.6cm^2/m^2$ of body surface) and a medium transvalvular gradient of more than 40 mmHg (4) for symptomatic patients. For asymptomatic patient, severity criteria are needed and at least one of the following criteria will be added: a left ventricle ejection fraction (LVEF) lower than 50%, a concomitant indication of another cardiac surgery, a mean transaortic gradient higher than 60 mmHg (or maximum velocity superior to 5.5 m/s) with a low surgical risk (mortality estimated lower than 1.5%), a combination of a severely calcified valve with a quick progression of the stenosis (increasing of maximal transaortic velocity superior to 0.3 m/s per year) or an arterial pressure drop during a stress test in active patients (4).

First choice treatment is primarily surgical. TAVI emerged in the early 2000s and is since then a less invasive and well-implanted treatment for asymptomatic or symptomatic aortic stenosis with severity criteria.

Percutaneous valvular replacement is an option that has proved to be successful in the treatment of aortic stenosis. It lowers the number of hospitalizations, the number of cardiac arrests and the mortality compared to standard drug treatment. Studies show a one year rate of death from any cause combined of 30.7% after TAVI against 50.7% after standard drug therapy (7) in patients who have contraindications for surgery.

Recent data regarding comparison between percutaneous and surgery approach for the treatment of aortic stenosis is growing and show similar outcomes for the population with an intermediate risk for surgery as assessed by the Society of Thoracic Surgeons-Predicted Risk of Mortality score (STS-PROM) (8) (reference ESC guidelines valvular 2017) (9). A number of variables are in favour of each approach and should be discussed in a Heart Team (including cardiologists, interventional cardiologists, cardiovascular surgeons, cardiologists specialized in imaging techniques, an anaesthetist and a geriatrician) for every patients for the best clinical decision making (comorbidities, porcelain aorta, history of thoracic radiation, age etc…) .

Like any operative procedures, TAVI present some risks. Complications of TAVI are of different kind: periprocedural complications (during or shortly after the procedure) related to vascular access, valve deployment, valve function, organ injury (including cerebrovascular events), arrhythmic complications and late complications. The main late complication after TAVI remains paravalvular aortic regurgitation (PVR) after the placing of the valve.

Survival rate after TAVI procedures is deeply correlated with the presence of moderate and/or severe PVR. Indeed PVR increases cardiovascular and all-cause mortality rate after TAVI (10). Although the two-year mortality rate after TAVI is 42.5% against 71.6% after standard drug therapy (10), the prognosis will not be as favourable if the patient suffers from an aortic insufficiency or regurgitation (AR).

One of the causes of aortic leak is a wrong choice of valve size. Multi-detector row computed tomography (MDCT) is the first choice imaging method to calculate the annulus size. MDCT and a transthoracic echocardiography (TTE) are both realized as routine analysis before the intervention in order to measure the dimensions of the annulus valve and to choose the right valve needed. The day of the intervention a 3-dimensional transoesophageal echocardiography (3D-TEE) will also be realized when the patient is on the operating table in order to take a final decision and to choose the right valve size.

3D-TEE is another emerging imaging technique. As compared with 2D modalities, 3D imaging modalities have been shown to be more accurate. 3D imaging has many benefits and its usefulness has been demonstrated in a large number of fields. An important benefit is the global perspective and visualization of cardiac valves. The visualization of the pathomorphological features of the cardiac valves has been shown to be enhanced by 3D-TEE. 3D-TEE also allows a real-time perception of valvular and subvalvular anatomic features from a single volume acquisition without need for offline reconstruction (11).

However, 3D imaging modalities have so far rarely been compared. As of this day few studies with small cohort have been realized on the matter. In literature aortic annulus size by 2D-TEE and computed tomography angiography (CTA) for noninvasive annular sizing were compared to direct intraoperative (OR) sizing the gold-standard in surgical replacement. The results obtained showed that CTA overestimated with 46.3% TAVI aortic annulus diameter valve-size (12). Another review compared the measurements of aortic annulus (AA) obtained by 3D-TEE automatic software and MDCT in patients undergoing TAVI. Their results on 31 patients concluded that 3D-TEE allows a high reproducibility (13). A third literature article compared 2D circular, 3D circular and 3D planimetered annular and left ventricular outflow tract (LVOT) areas by TEE with the so far "gold standard" multislice computed tomography (MSCT) before TAVI. Their results on a cohort of 53 patients demonstrated an underestimated AA/LVOT circular geometrics assumption by 2D and 3D-TEE before TAVI compared to the respective planimetered areas by MSCT (14). Finally a study correlating the imaging predictors of AR after TAVI and estimating agreement and reproducibility of aortic root assessment, asserts the association between presence and severity of AR after TAVI with larger AA measurements by both cardiovascular magnetic resonance (CMR) and cardiac computed tomography (CCT), but not TTE (15).

In this context, we aim to study the correlation between the size of the annulus aortic prosthesis calculated by ETT and MDCT or 3D-TEE. This correlation will allow us to see whether one imaging method is more precise to calculate the aortic surface and further on to reduce the rate of aortic insufficiency post implantation. Establishing the differences between those imaging techniques will allow a better choice of valve size. Furthermore, 3D-TEE is the only imaging technique possible in patients with chronic kidney disease, for whom MDCT and contrast agent use is contraindicated. Knowing these significant differences in prosthesis sizing between 3D-TEE and MDCT, operators will be able to perform TAVI without CT-scan and thus without contrast agent in population at risk of kidney failure.

VI. OBJECTIVES

- Identify every patient who underwent transcatheter aortic valve implantation (TAVI) between 2013 and 2016 in the Interventional Cardiac division of the University Hospital of Lausanne (CHUV) to form a retrospective cohort
- Collect and register data and measurements for each patient relating to each imaging technique: cardiac transthoracic echocardiography (TTE) performed as routine examination for each patient with aortic sclerosis, cardiac computed tomography (MDCT), so far the gold-standard method for aortic annulus sizing, transoesophageal echocardiography (TEE) 2D and 3D transoesophageal echocardiography performed during the procedure
- Examine the correlation between the size of the annulus aortic valve assessed by multi-detector row computed tomography (MDCT) as compared to measures by 3D transoesophageal echocardiography (TEE) in our defined retrospective cohort
- Investigate the correlation between the imaging technique chosen to assess the annulus prosthesis and the incidence of paravalvular aortic regurgitation after TAVI procedures

VII. METHODS

VII.1 Trial Design

Retrospective analysis of peri-procedural 3D transoesophageal echocardiography data versus pre-procedural multi-detector computed tomography data among a cohort of 199 patients undergoing TAVI in the Interventional Cardiology department in the CHUV and comparison with implanted prosthesis size.

VII.2 Inclusion and exclusion criteria

First stage of the analysis was to identify all the patients who underwent an aortic valve replacement with a transcatheter implantation since 2013 at the CHUV. Those were the enrolled patients and they were registered in a chart. Informed consent was obtained. Another inclusion criteria was the presence of MDCT and/or 3D-TEE.

The exclusion criteria concerned deceased patients following the implantation from a non-cardiologic etiology. At the end no patients were excluded.

VII.3 Variables

Variables registered were multiple: date of procedure, operators, material, size of implanted valve. Multiple variables were also registered depending on each imaging method.

TTE variables: date of TTE, left ventricle ejection fraction (LVEF), mean and maximum transvalvular gradient, aortic planimetered opening surface, continuous aortic opening surface, annulus size, annulus aortic valve diameter. TEE variables: date of TEE, regurgitation flow, LVEF, mean and maximum gradient, aortic planimetered opening surface, continuous aortic opening surface, annulus size, 3D telediastolic maximum annulus diameter, telesystolic minimum aortic diameter, mean diameter, annulus surface, annulus perimeter. MDCT variables: date of imaging, maximum diameter, minimum diameter, mean diameter, surface, perimeter. TEE post-intervention variables: date of examination, maximum and mean transvalvular gradient, aortic regurgitation grade (0 to 4). TTE post intervention variables: date of examination, maximum and mean transvalvular gradient, aortic regurgitation grade.

VII.4 Transthoracic echocardiography

All subjects had a transthoracic echocardiography (TTE) performed pre-operatively using a GE Vivid E9 ultrasound machine and equipment. All images were digitally stored for subsequent analysis and a TTE medical report was completed for each examination. A complete 2-dimensional color, pulsed, and continuous-wave Doppler echocardiography was also performed as a pre-operative routine according to standard methods. The ejection fraction was calculated using standard techniques. Transaortic gradient was measured by continuous-wave Doppler and the annulus aortic valve area was obtained using the continuity equation.

VII.5 Transoesophageal echocardiography imaging

TEE was performed peri-operatively using Philips Epiq 7 transoesophageal transducers. All images were digitally stored for posterior analysis. The aortic annulus surface was calculated using two different methods: the continuity equation and/or the planimetered equation. Using 3D imaging we calculated the minimum telesystolic diameter, maximum telediastolic diameter and mean diameter as well as the aortic annulus surface and perimeter.

VII.6 Multidetector computed tomography imaging

Preoperative MDCT imaging was performed in order to measure the minimum aortic annulus diameter, maximum aortic annulus diameter and mean aortic annulus diameter, aortic annulus surface and perimeter using 3mensio Software (Pie Medical Imaging BV The Netherlands).

VII.7 Statistical analysis

Statistical analysis was carried out using SPSS 24.0 software (SPSS Inc., Chicago, Illinois) and figures were realized with Prism 6.0h (GraphPad Software, La Jolla, California, USA). Significance was defined as a p value <0.05. Continuous variables are expressed as mean ± SD or median (P25 ; P75) as appropriate, whereas categorical variables are reported as frequencies and percentages. Student *t* test was used to compare normally distributed continuous variables as appropriate, whereas Mann-Withney test was used to compare non-normally distributed continuous variables. Comparisons between categorical variables were evaluated using Pearson's χ^2 test

VIII. RESULTS

VIII.1 Baseline characteristics

From January 2013 to September 2016, 199 patients with severe aortic stenosis underwent TAVI in our institution. They were retrospectively included in our study. They were all evaluated in an interdisciplinary “Heart Team” meeting.

Two different brands of aortic bioprosthesis were implanted: Edwards SAPIEN XP valve (ESV) (Edwards Lifesciences, Irvine, California) and Medtronic Corevalve Evolut System (MCV) (Medtronic, Minneapolis, Minnesota). Six different sizes of aortic valves were implanted: 21 mm, 23 mm, 25 mm, 26 mm, 29 mm and 31 mm.

Clinical characteristics	n = 200
Female sex (%)	52
Age (years)	81.39 (39-97)
TAVI characteristics	
Type of prosthesis	
21 mm (%)	0.5 (1)
23 mm (%)	37.4 (74)
25 mm (%)	2.0 (4)
26 mm (%)	40.4 (80)
29 mm (%)	18.7 (37)
31 mm (%)	1.0 (2)

Table 1

Majority of prosthesis implanted were 26 mm (40.4%), 23 mm (37.4%) and 29 mm (18.7%). In total those three sizes represent 96.5 % (191) of all valves implanted.

VIII.2 Transthoracic echocardiography imaging results

Transthoracic echocardiography was performed preoperatively in 193 patients. The mean opening surface assessed by TTE is 0.76 cm^2 by planimetered equation and 0.65 cm^2 by continuous equation. The mean left ventricular ejection fraction (LVEF) is 54.1%. Mean aortic transvalvular gradient is 38.84 mmHg.

Transthoracic echocardiography characteristics	n = 193
Planimetered surface (cm^2)	0.76 (± 0.18)
Surface by continuity equation (cm^2)	0.65 (± 0.19)
Left ventricular ejection fraction (%)	54.1 (± 15)
Mean aortic transvalvular gradient (mmHg)	38.84 (± 17.03)
Mean annulus aortic valve diameter (mm)	23.22 (± 2.81)

Table 2

Results and characteristics assessed by transthoracic echocardiography expressed as mean ± SD.
Results of TTE were obtained in 193 patients.

VIII.3 Transoesophageal echocardiography imaging results

Transoesophageal echocardiography were performed peri-operatively in 148 patients. Among those results, results of aortic annulus diameter by 3D-TEE were available in 105 patients. Result of mean aortic flow velocity is 36.51 cm/s, result of mean left ventricular ejection fraction (LVEF) is 50.21%, result of mean opening surface calculated by planimetered equation is 0.76 cm^2, result of mean opening surface calculated by continuous equation is 0.55 cm^2, result of mean aortic transvalvular gradient is 38.22 mmHg, result of mean aortic diameter is 22.66 mm, result of mean aortic perimeter is 71.75 mm.

Transoesophageal echocardiography characteristics	n = 148
Aortic flow (cm/s)	36.51 (± 18.06)
Left ventricular ejection fraction (%)	50.21 (± 15.81)
Planimetered surface (cm^2)	0.76 (± 0.27)
Surface by continuity equation (cm^2)	0.55 (± 0.18)
Mean aortic transvalvular gradient (mmHg)	38.22 (± 21.49)
Aortic diameter (mm)	22.66 (± 2.52)
Mean 3D annulus surface (mm^2)	409.25 (± 86.04)
Perimeter (mm)	71.75 (± 9.13)

Table 3

Results and characteristics assessed by transoesophageal echocardiography expressed as mean ± SD. TEE results were obtained in 148 patients.

VIII.4 Multidetector computed tomography imaging results

176 patients underwent multi-detector row computed tomography preoperatively. Maximum and minimum aortic annulus diameter were calculated. Mean aortic annulus diameter is 24.28 mm. Mean aortic annulus surface obtained in 142 patients is 443 mm^2. Mean aortic perimeter patients is 76.47 mm.

Multidetector row computed tomography characteristics	n = 176
Maximum annulus diameter (mm)	27.13 (± 3.29)
Minimum annulus diameter (mm)	21.43 (± 3.07)
Mean annulus diameter (mm)	24.28 (± 2.87)
Mean annulus surface (mm^2)	443 (± 99.11)
Perimeter (mm)	76.47 (± 11.12)

Table 4

Measurements and characteristics assessed by Multidetector row computed tomography expressed as mean ± SD. Multidetector row computed tomography results were obtained in a total of 176 patients.

VIII.5 Assessment of aortic annulus valve size and comparison with implanted prosthesis

Between 18.01.2013 and 14.09.2016, 199 patients underwent TAVI in our institution. Among them, results of annulus aortic valve size by MDCT were available in 165 patients whereas results by 3D-TEE were available in 106 patients. With both imaging techniques aortic annulus valve surface, valve diameter and perimeter were calculated. Results show a mean opening surface calculated by planimetered equation of 0.76 cm^2 assessed by 3D-TEE and by continuity equation of 0.55cm^2 compared to a mean surface of 443 mm^2 assessed by MDCT. Mean aortic annulus valve perimeter is 71.75 mm assessed by 3D-TEE as compared to 76.47 mm by MDCT. Mean aortic annulus valve diameter assessed by 3D-TEE is 22.66 mm as compared to 24.28 mm by MDCT.

As compared to MDCT, annulus diameter sizes by 3D-TEE were significantly lower (22 [21;24.5]mm versus 24 [22;26]mm, p<0.001, **Figure 1**). Differences between implanted prosthesis size and the MDCT annulus size were significantly lower than those with 3D-TEE (1.5 [0;2.85] mm versus 3 [1.5;4.5] mm, p<0.001, **Figure 2**).

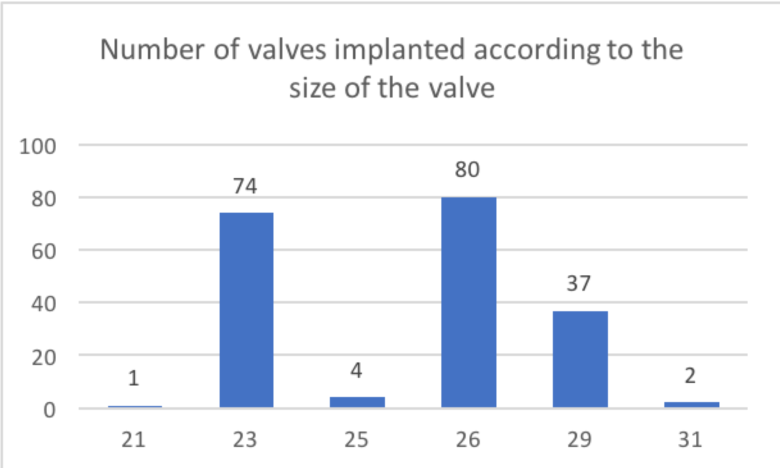

Chart 1

Bar chart indicating each valve size model implanted (21 mm, 23 mm, 25 mm, 26 mm, 29 mm and 31 mm) in our retrospective cohort and the total number of aortic prosthesis implanted according to each valve size. The total number of valves implanted represents the total number of patient enrolled in our cohort. 80 (40.19%) 26 mm valves were implanted among the 199 valves implanted, 74 (37.18%) 23 mm valves, 37 (18.58%) 29 mm valves and less than 10 valves were sizes 21 mm, 25 mm or 31 mm.

Chart 1 shows that there were mainly 26 mm and 23 mm prosthesis implanted among our cohort. Those two different valve sizes represent for themselves 154 from the 199 valves implanted, which is 77.39% of the implanted valves.

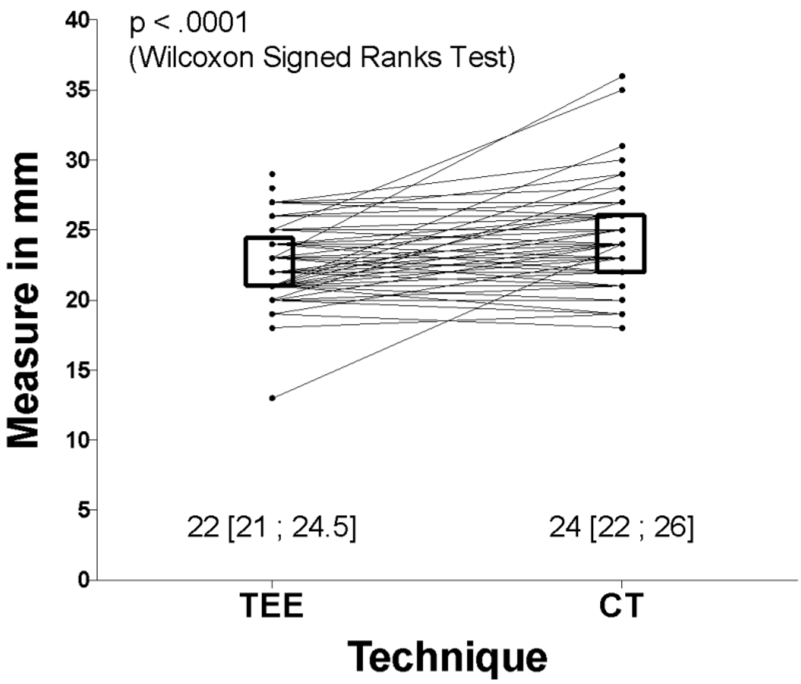

Figure 1

Wilcoxon Signed Ranks Test demonstrating aortic annulus size measurements in mm assessed by 3D-TEE as compared to aortic annulus size measurements assessed by MDCT (CT). Mean aortic annulus size assessed by TEE is 22 [21;24.5]mm as compared to 24 [22;26]mm by MDCT.

P-value is inferior to 1; meaning a significant result.

Results in this test demonstrate a significant difference in aortic annulus diameter sizing assessed by 3D-TEE as compared to the size assessed by MDCT.

Results in measurements of aortic annulus valve size by 3D-TEE are significantly lower (22 [21;24.5]mm versus 24 [22;26]mm , $p<0.001$) assessed by MDCT.

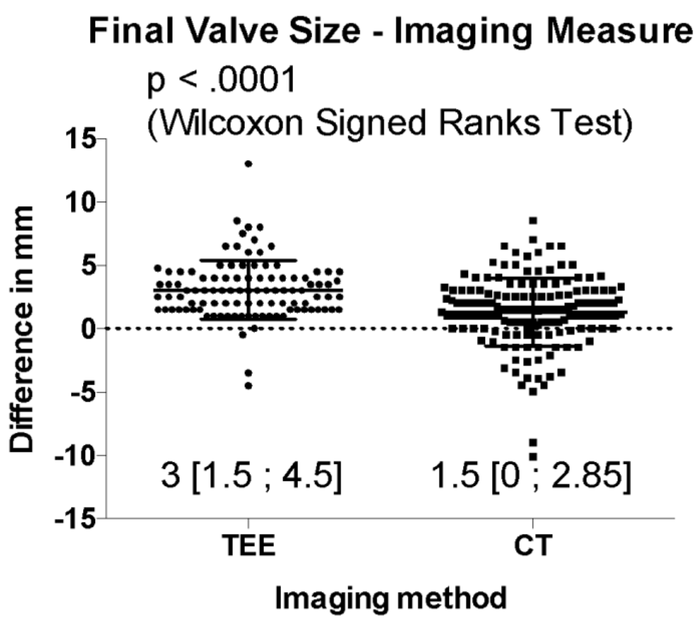

Figure 2

Wilcoxon Signed Ranks Test demonstrating the difference in millimetre between the aortic annulus valve size assessed by 3D-TEE or by MDCT (CT) and the final valve size implanted during the TAVI procedure.

The test demonstrates a 3 [1.5 ; 4.5] mm valve size difference with the final valve implanted when the imaging method is 3D-TEE as compared to a 1.5 [0 ; 2.85] mm valve size difference when the imaging method assessing the valve size is MDCT.

Differences between implanted prosthesis size and the MDCT annulus size were significantly lower than those with 3D TEE (1.5 [0;2.85] mm versus 3 [1.5;4.5] mm, $p<0.001$, **Figure 2**).

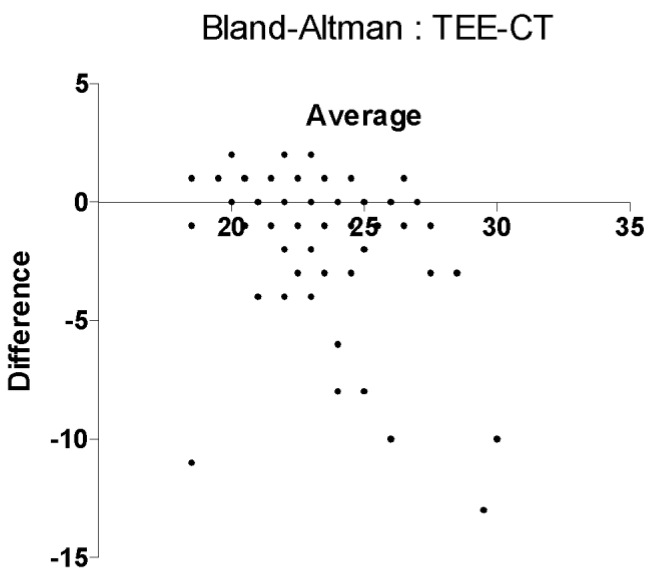

Figure 3

Bland-Altman plot: the graph indicates mean aortic annulus diameter measurements by 3D-TEE and MDCT between 20 and 25 mm. X axis indicates the average sizes calculated by 3D-TEE and MDCT and Y axis the difference between aortic annulus diameter calculated by TEE or MDCT and the implanted valve.

The interest of Bland-Altman plot in this case is to see which imaging technique has the most size differences. We can see that most of the time differences are small and rather well-distributed. Most of the differences are negative. This means that most of the time 3D-TEE aortic annulus diameter measurements values are smaller than the values obtained by MDCT.

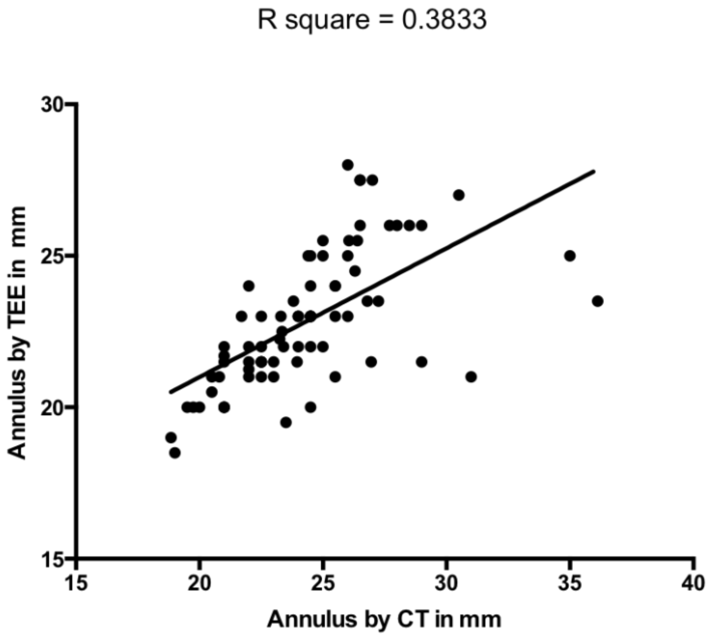

Figure 4

Aortic annulus diameter measurements by MDCT or 3D-TEE and their linear regression.

X axis indicates the aortic annulus diameter sizes assessed by MDCT (CT) in millimetre; Y axis indicates the aortic annulus diameter sizes assessed by 3D-TEE in millimetre.

Line graph demonstrating a linear correlation. We can assess a difference between measurements obtained by 3D-TEE and measurements obtained by MDCT.

VIII.6 Aortic regurgitation post TAVI depending on imaging method

Aortic regurgitation grade was measured in 129 patients by transthoracic echocardiography post TAVI and in 109 patients by 3D-TEE. Most of the patients who didn't get a measure of the AR grade after TAVI either by TTE or TEE, usually didn't have any signs of regurgitation directly after the implantation and there were no indications to perform TTE or TEE. Aortic regurgitation is classified according to a grade from 0 to 4 or small, moderate, important or severe which correlate with the numbered grade.

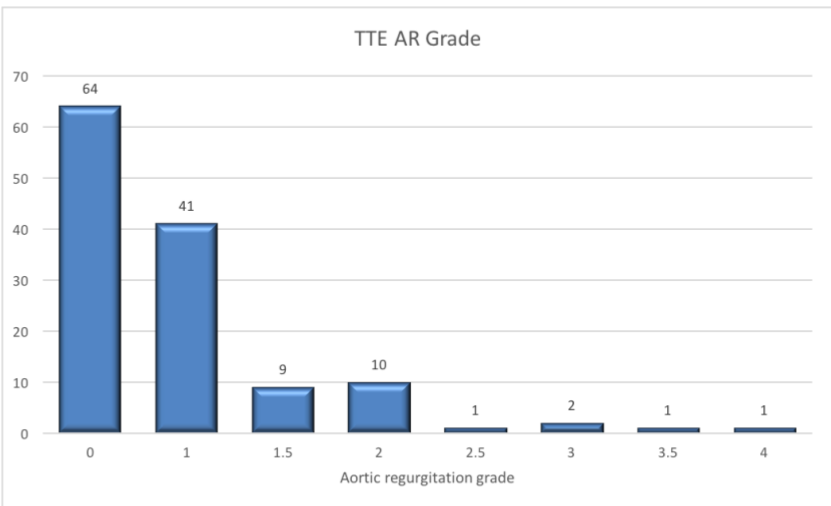

Chart 2

Bar chart representing the number of aortic regurgitation among our cohort assessed by TTE according to aortic regurgitation grade (0 to 4). Among 129 results of AR measurements obtained by TTE post TAVI, 64 (49.22%) AR observed were grade 0 (no AR) and 10 (7.68%) AR were grade 1 (small regurgitation). Very few AR were moderate or important.

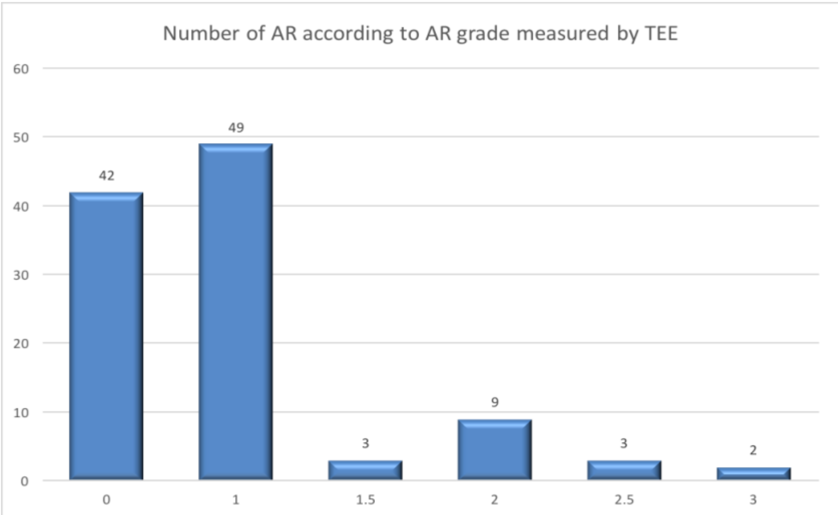

Chart 3

Bar chart representing the number of aortic regurgitation post TAVI assessed by 3D-TEE according to AR grade (0 to 4). 109 results of AR assessed by 3D-TEE post-TAVI were obtained among our cohort. 42 (38.17%) AR were grade 0 (no AR) and 49 (44.54 %) were grade 1 (small regurgitation). 9 AR were moderate and very few were important. None were severe.

Chart 2 and chart 3 both illustrate the fact that most of the AR post TAVI assessed either by TTE or TEE are grade 0 or 1 which corresponds to no regurgitation or small and very few AR are moderate or important.

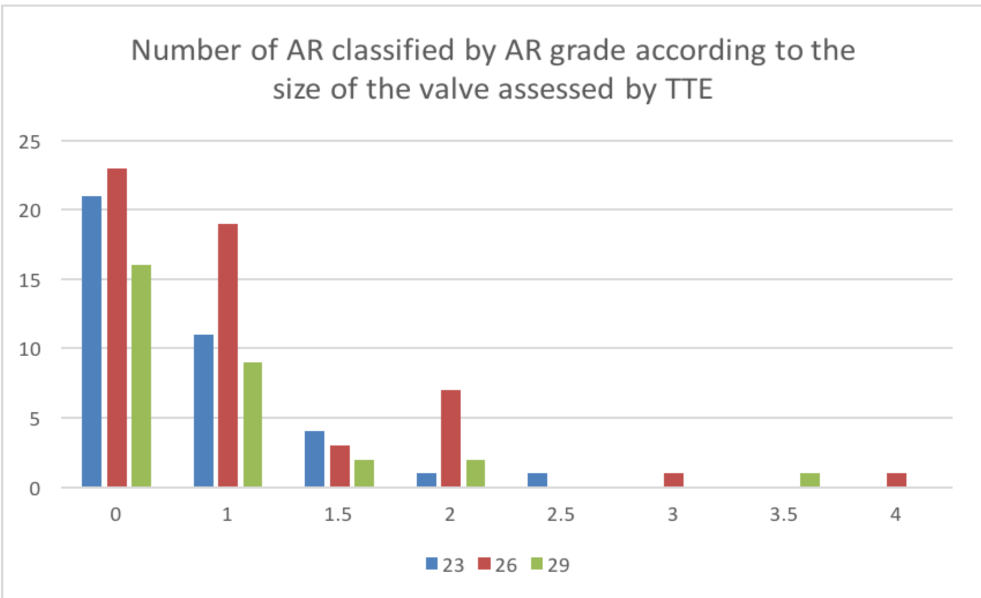

Chart 4

Bar chart demonstrating the total number of aortic regurgitation assessed by transthoracic echocardiography after TAVI. AR are classified by AR grade (0-4) and by valve prosthesis size (23, 26 and 29; as there were only 4 valves of 25 mm implanted, 2 valves of 31 mm and one valve of 21 mm they are not represented in the chart).

Most of AR assessed by TTE are represented in the first six columns which corresponds with conclusions from chart 2 and 3 demonstrating that most AR are grade 0 and 1. We can also see that 26 mm valve has more AR grade 1 and grade 2.

Chart 1 showed that there were mainly 26 mm (40%) and 23 mm (37%) prosthesis implanted among our cohort. Those two different valve sizes represent for themselves 154 from the 199 valves implanted, which is 77.39% of the implanted valves. It can possibly explain the fact that there are mostly AR after implantation of 23 mm and 26 mm valves. But there were only 6 more 26 mm valves implanted as 23 mm valves which doesn't explain why there are more AR grade 1 when 26 mm valves were implanted.

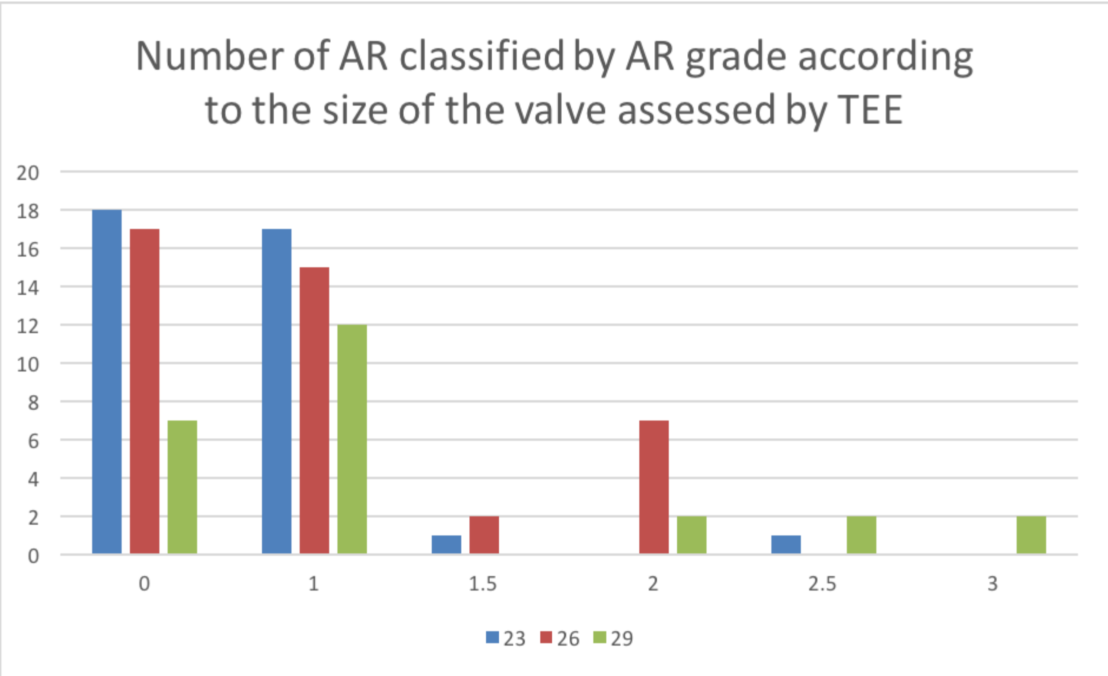

Chart 5

Bar chart demonstrating the total number of aortic regurgitation assessed by 3D-TEE after TAVI. AR are classified by AR grade (0-3, no grade 4) and by valve prosthesis size (23, 26 and 29; as there were only 4 valves of 25 mm implanted, 2 valves of 31 mm and one valve of 21 mm they are not represented in the chart).

Most AR post TAVI are grade 0 and 1, no matter which valve was implanted. When the AR is assessed by TEE no valve causes significantly more AR than another.

IX. DISCUSSION

Aortic sclerosis is a pathology growing with the ageing population and its incidence is increasing in parallel. Treatment of severe aortic stenosis consists so far of the surgical valvular replacement and the newly well-established transcatheter aortic valve implantation. Indications to treat AS are precise. Severity criteria and discussion in a Heart Team formed by diverse specialists is needed for a patient to be eligible for a TAVI procedure.

One of the late complications of aortic annulus replacement by TAVI procedure which considerably decreases the survival and increases the all-cause combined death rate after TAVI is aortic regurgitation. The main cause of aortic leak is choosing the wrong valve size.

Indeed, annulus aortic sizing is a key step in prosthesis sizing. Multi-detector row computed tomography (MDCT) is the first-choice imaging method to calculate the annulus size. The day of the intervention a 3D transoesophageal echocardiography (TEE), a new emerging imaging technique, is performed. As compared with 2D modalities, 3D imaging modalities have been shown to be more accurate.

Up until now no agreement has been made on the optional imaging strategy for planning TAVI and few comparative multimodality imaging data has been done.

In our retrospective analysis, we collected data of 199 patients who underwent TAVI in the CHUV between 18.01.2013 and 14.09.2016. Results of aortic annulus diameter assessed by MDCT were available in 165 patients whereas results of aortic annulus diameter assessed by 3D-TEE were available in 106 patients. This study demonstrates that aortic annulus measurements by MDCT, ETT and 3D-TEE are highly reproducible. Variability in the aortic annulus measurements is low.

Aortic annulus diameter measurements assessed by 3D-TEE were significantly lower than measurements by MDCT. This result has clinical implication for predicting outcome such as paravalvular regurgitation after TAVI. Using a statistical analysis, important differences between implanted prosthesis size and MDCT annulus size were significantly lower than those with 3D-TEE.

IX.1 Aortic valve annulus measurements

The most precise imaging technique for measuring aortic annulus valve diameter remains to be determined by larger studies. A highly reproducible and effective imaging method is necessary without so far any gold standard assessed method. In our study the intra-observer variability and inter-observer variability of both MDCT and 3D-TEE are low. Our analysis demonstrates that 3D-TEE imaging significantly underestimates the aortic annulus diameter compared to MDCT imaging. Annulus aortic diameters obtained by 3D-TEE are systematically lower than the annulus diameters obtained by MDCT.

IX.2 TAVI planning strategy

The appropriate prosthetic valve size is crucial in preventing paravalvular regurgitation after TAVI. Although TAVI techniques using 3D-TEE imaging techniques for aortic annulus sizing are associated with good clinical results, data has so far not been clear on the reproducibility of 3D-TEE. Studies have demonstrated an underestimation of aortic annulus diameter by 3D-TEE as compared to MDCT (14) and other studies have assessed a larger aortic annulus by CCT and CMR but not by TEE. Our study demonstrates in a significant way a lower aortic annulus diameter assessed by 3D-TEE as compared to the aortic annulus diameter measurements assessed by MDCT.

As 3D-TEE always calculates a lower diameter, 3D-TEE imaging can be used as an imaging technique for aortic annulus sizing either as a complementary imaging technique to the MDCT imaging which is the standard method or as the only imaging technique in patients who cannot undergo MDCT. Indeed, patients suffering from chronic kidney failure cannot undergo MDCT which is performed with contrast product. Assessing the reproducibility of 3D-TEE in aortic annulus prosthesis sizing as a standard imaging technique will allow a larger and more diverse category of patients to undergo

TAVI. Given the fact that 3D-TEE predicts a lower aortic annulus diameter, we suggest that 3D-TEE be used as an additional imaging technique to MDCT and as a standard technique for patients suffering from chronic kidney failure. As a standard or unique imaging technique, operators should be aware that 3D-TEE significantly underestimates the aortic annulus diameter (22 [21;24.5]mm versus 24 [22;26]mm, $p<0.001$) as compared to MDCT and should choose the aortic annulus prosthesis consequently.

IX.3 Impact on outcome: predicting aortic regurgitation

Significant paravalvular regurgitation post TAVI is a predictor of higher mortality and lower survival. In our study the presence of AR is not correlated with one type of valve size. Furthermore, very few severe or important paravalvular regurgitations were found which limits our assessment of predicting factors of severe AR. Whatsoever our study demonstrates differences between implanted prosthesis size and the 3D-TEE annulus size were larger than those with MDCT (3 [1.5;4.5]mm versus 1.5 [0;2.85]mm; $p<0.001$).

As larger differences between implanted prosthesis size and the aortic annulus are known to be a cause of paravalvular aortic regurgitation, we suggest that 3D-TEE imaging should be used as an additional imaging method to MDCT or as a standard one for patients suffering from chronic kidney failure and for operators knowing the limits of 3D-TEE and proceeding in annulus sizing consequently.

IX.4 Strengths and study limitations

Our study has several strengths: firstly, different operators implanted the aortic valves. The results obtained are therefore not operator dependant. The results whether good or not and whether the rate of aortic regurgitation is high or low is not dependant on one interventional cardiologist only. The same example is valid for every exam (TTE, MDCT and 3D-TEE).

Secondly our study includes data from a long time period and nearly two hundred patients were retrospectively enrolled in our cohort. Previous studies had between thirty and sixty patients enrolled in their research.

The study also has several limitations worth acknowledging, most of which were data limitations. Being a retrospective study, we did not have any impact on the data we collected. Not every patient who underwent a TAVI implantation had both an MDCT pre-operatively and a 3D-TEE per-operatively. For a better comparison of both imaging techniques, data of both imaging techniques for each patient in our cohort should have been done.

Another limitation concerns the lack of information in a few reports. A few TTE, MDCT or 3D-TEE reports were not totally complete which led to a few missing values in our final database. Retrospectively those missing values could not be filled. However, the incomplete reports or missing data had little or no impact on our final results.

X. CONCLUSION

Annulus sizes assessed by 3D-TEE are significantly lower than annulus sizes assessed by MDCT. Operators should be aware of these differences and choose the annulus size consequently.

Knowing these significant differences in prosthesis sizing between 3D-TEE and MDCT, transcatheter aortic valve implantation can be performed without CT-scan and thus without contrast agent in population at risk of kidney failure.

Other large prospective trials should investigate if imaging modality choice could impact the occurrence of paravalvular leak after TAVI.

XI. PERSPECTIVE

- Assessment of 3D-TEE as a standard imaging method for annulus aortic valve sizing
- Lower the number of paravalvular aortic regurgitation due to wrong choice of valve size

XII. DISCLOSURES

The authors report no conflict of interest.

XIII. REFERENCES

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