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Transcatheter Mitral Valve Replacement: Factors Associated with Screening Success and Failure.

Short Title: Screening for Transcatheter Mitral Valve Replacement

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ABSTRACT

Aims. Transcatheter mitral valve replacement (TMVR) is a promising therapeutic solution to treat high-risk patients with severe mitral regurgitation (MR) contraindicated to surgery. Optimal selection of patients who will benefit from the procedure is of paramount. We aimed at investigating factors associated with TMVR screening.

Methods and Results. From November 2016 to July 2018, we examined conditions associated with TMVR screening success in patients referred to the two French Heart Valve Clinics with the greatest TMVR experience. Among a total of 40 consecutive screened patients, 16 (40%) were selected for TMVR (8 Twelve Intrepid, 7 Tendyne and 1 HighLife), while 24 patients (60%) were refused for TMVR mainly for too large mitral annulus (MA) (n=15,62% of refusal), or too small anatomy and risk of neo-left ventricular outflow tract (LVOT) obstruction (n=6,25% of refusal). Patients with suitable anatomy for TMVR were more often male and suffered more frequently from secondary MR (p=0.01) associated with previous myocardial infarction and presented commissure-to-commissure diameter lower than 39mm (AUC=0.72, p=0.0085) and LVESD larger than 32mm (AUC=0.83, p<0.0001) on transthoracic echocardiography and MA area lower than 17.6cm² (AUC=0.95, p<0.0001) and anteroposterior diameter higher than 41.6mm (AUC=0.87, p<0.001) on CT-scan.

Conclusion. Despite several prostheses available, most patients referred to Heart Valve Clinics and good candidate regarding their clinical profile cannot be implanted with TMVR because of mismatch between their anatomy and prosthesis characteristics. Our findings suggest the need to develop new prosthesis adapted to larger MA but with lower impact on the LVOT.

CONDENSED ABSTRACT

Transcatheter mitral valve replacement (TMVR) is a promising therapeutic solution to treat high-risk patients with severe mitral regurgitation contraindicated to surgery. Optimal selection of patients who will benefit from the procedure is of paramount. We examined patients referred to the two French Heart Valve Clinics allowed to propose TMVR with dedicated prosthesis (Twelve Intrepid, Tendyne and HighLife). Most patients cannot be implanted with TMVR because of mismatch between their anatomy and prosthesis characteristics. Our findings urge on the development of new prosthesis adapted to larger mitral annuls together with lower impact on the left ventricular outflow tract.

Keywords: Mitral Regurgitation, Imaging Modalities, Innovation, Multidisciplinary Heart Team

ABBREVIATIONS LIST

AP: Anteroposterior

C-C: Commissure to commissure

LV: Left Ventricle

LVEF: Left Ventricle Ejection Fraction

LVESD: Left Ventricle End Systolic Diameter

LVOT: Left Ventricle Outflow Tract

MA: Mitral Annulus

MR: Mitral Regurgitation

TMVR: Transcatheter Mitral Valve Replacement

TTE: Transthoracic Echocardiography

VHD: Valvular Heart Disease

INTRODUCTION

Mitral regurgitation (MR) is the most prevalent valvular heart disease (VHD) in Western countries, with an age-dependant prevalence and affecting up to 10% of people older than 75 years old (1,2). Without treatment, severe MR is associated with excess morbidity and mortality and a significant socio-economic impact (3,4). Despite these poor outcomes and the undeniable advances in the surgical management, only a small portion of patients suffering from MR undergo surgery, paving the way for percutaneous management strategies (5,6).

While several repair techniques have emerged the last decade, percutaneous mitral valve repair is mostly limited nowadays to the edge-to-edge technique by the MitraClip system (7–10). Nevertheless, some patients are not suitable for this technique because of primary MR with severe calcification, cleft, rheumatic restriction or Barlow's disease (11). Additionally, conflicting data exist on the benefit of treating secondary MR with left ventricular dysfunction. (12,13)

Recent studies have shown that transcatheter mitral valve replacement (TMVR) using dedicated prosthesis is a promising therapeutic solution to treat high-risk patients contraindicated to surgery (14–16). This technique may offer several advantages considering the complexity and the wide variety in the presentation of mitral valve disease. However, the development of TMVR is confronted with several challenges including a careful selection of patients to get an adapted sizing to fit with the dimensions and the geometry of the mitral annulus (MA) and to minimize the risk of left ventricular outflow tract (LVOT) obstruction (17,18).

In the present study, we aimed at investigating the factors associated with TMVR screening failure in the two French Heart Valve Centers allowed to propose TMVR with dedicated prosthesis: the Twelve Intrepid (Medtronic, Minneapolis Minnesota), the Tendyne (Abbott Vascular, Santa Clara, California) and the HighLife (HighLife, Paris, France) systems.

METHODS

Study population and design

From November 2016 to July 2018, we prospectively studied all consecutive patients with severe MR referred to the two French Heart Valve Centres, CHU Lille & Clinique Pasteur, Toulouse, for percutaneous implantation because of high-risk for MR surgery. Inclusion criteria were: age > 18 years with severe (grade III-IV) and symptomatic (New York Heart Association functional class ≥ 2) chronic MR. Patients with severe mitral annulus calcification, left atrial or LV thrombus, prior mitral valve surgery, indicated for standard cardiac surgery or suitable for mitral valve repair using the MitraClip system according to our Heart Team decision were not considered for TMVR screening. The local ethics committee approved the protocol and patients gave informed consent

Echocardiography

A comprehensive transthoracic (TTE) and transoesophageal echocardiography (TEE) using 2- and 3-dimensional imaging was performed according to current guidelines (19) using state-of-the-art echocardiographic ultrasound systems (Vivid 9 or Vivid 95, GE Healthcare, Little Chalfont, UK). A special attention was paid to the mechanism, severity and consequences of MR as well as the dimensions and calcifications of the MA.

Cardiac computed tomography

Contrast-enhanced cardiac computed tomography (CT) images were also acquired for screening and procedure planning. CT examinations were performed using a multiphase retrospectively electrocardiogram-gated data acquisition. Mitral annular segmentation was performed (20) using a dedicated software (3mension, Pie Medical Imaging. Bilthoven, The Netherlands), as previously described. Briefly, mitral annular segmentation was performed at

60% of the cardiac cycle, yielding a D-shaped mitral orifice contour with the several parameters including annular area, perimeter, septal-to-lateral and intercommissural diameters.

Statistical analysis

Continuous variables were tested for normality with Shapiro test, and were given as mean±SD. Continuous variables with no Gaussian distribution are given as median (IQR). Categorical variables were given as percentages of individuals. Patients were separated in three groups according to their anatomy. A too large MA was defined by a compression rate lower than the threshold defined by the constructor. One-way ANOVA analysis of variance was used for comparison of the three groups with Bonferroni post hoc t-test. Receiver Operating Characteristics (ROC) curve analysis were used to predict the TTE or CT-scan parameter and cut-off with the higher discriminating power to predict a refusal for too large or too small anatomy. Statistics were performed using MedCalc v16.4 (Olstead, Belgium).

RESULTS

Characteristics of patients referred to the Heart Team and eligible for TMVR screening

A total of 40 patients were included. Characteristics of the population are summarized in Table 1. Mean age was 79±7 years. The population was made of 58% of male and 18% had diabetes. Most of the patients (70%) were in NYHA 3 or 4. Almost two third had chronic kidney disease and 18% had previous cardiac surgery. Median EuroScore II and STS predicted risk of mortality were 4.7 [3.0-7.3] and 6 [3.9-8.7], respectively. MR mechanism was mainly secondary (53%) and in case of primary MR, posterior mitral valve leaflet was mainly involved (63%) (Table 2). LV function was normal (ejection fraction>60%) in 15 patients (37.5%) and moderately impaired (ejection fraction 30% and 60%) in 25 patients (62.5%). No patient had severe LV dysfunction (ejection fraction <30%). CT analysis showed a mean aorto-mitral angulation

measured at 132±12.6°, a MA area at 15.5±4.2cm² and a total MA perimeter at 143.1±31.1mm (Table 3). The anteroposterior and the orthogonal diameter were measured by CT-scan at 42.6±6.6mm and 45.6±6.7mm, respectively.

Screening results

Among the 40 patients screened, 16 (40%) were selected for TMVR (8 Twelve Intrepid, 7 Tendyne and 1 HighLife), while the remaining 24 patients (60%) were not considered for TMVR, because of too large anatomy (n=15) or too small anatomy (n=8, small annulus diameter (n=2) and/or predicted neoLVOT obstruction (n=6)) for TMVR (Figure 1 & 2, Supplemental Table 1). One patient had too poor LV function and one died during the screening process. The mean time between the Heart Team decision and TMVR was 113 ± 87 days. Examples of screening results are given in Figure 3.

Parameters according to screening results

Patients with suitable anatomy for TMVR were more often male and suffered more frequently from secondary MR (p=0.01) associated with previous myocardial infarction (p=0.06). They were thus more frequently treated with aspirin or antiplatelet agent (p=0.005) (Table 1 and 2). Conversely, patients with either too large or too small anatomy were mainly those with primary MR (75% and 60% vs. 25%, p=0.01 respectively). While the severity of the MR was not different, suitable patients for TMVR had greater LV dysfunction (ejection fraction 41±10% vs. 56± 5% and 66±17 %, p<0.0001 respectively) and more enlarged LV (end-systolic diameter 48.9±10.1mm vs. 42.5±11.8mm and 32.9±9.9mm, p=0.006 respectively) than patients with either too large or too small anatomy. Regarding the MA dimensions assessed by TTE, A2-P2 and commissure to commissure (C-C) diameters logically discriminated the 3 groups

(34.1±5.7mm vs. 38.2±7.3mm and 28.9±8.6 mm, p=0.03 for A2-P2 diameter and 37.9±5.7mm vs. 42.1±4.0mm and 37.6±6.0mm, p=0.05 for C-C diameter). ROC curve analysis showed that a cut-off of 39mm for C-C diameter by TTE and of 40mm for A2-P2 diameter by TTE had the higher discriminating power to predict a refusal for too large anatomy (area under the curves (AUC)=0.72, p=0.0085 and AUC=0.71, p=0.018 respectively) (Supplemental Figure 1A and B). A cut-off of 32 mm for LV end-systolic diameter was predictive of a refusal for too small anatomy (AUC=0.83, p<0.0001) (Supplemental Figure 1C). The CT parameters to differentiate suitable patients from patients with either too large or too small anatomy were the anteroposterior diameter (40.9±5.1mm vs. 48.3±4.5mm and 35.7±4.3mm, p<0.001 respectively), the orthogonal diameter (43.1±4.9mm vs. 51.1±5.6mm and 40.4±5.1mm, p<0.001 respectively), the MA area (13.4±2.7cm² vs. 19.5±2.9m² and 12.1±2.8cm², p<0.001 respectively), the total MA perimeter (130.1±35.2mm vs. 163.2±22.4mm and 131.3±17.9mm, p=0.004 respectively), and the projected MA perimeter (124.7±18.8mm vs. 155.9±19.9mm and 125.3±17.4mm, p<0.001 respectively). ROC curve analysis showed that a cut-off of 17.6cm² for MA area had the higher discriminating power to predict a refusal for too large anatomy (AUC=0.95, p<0.0001) (Supplemental Figure 2A) and a cut-off of 41.6mm for the anteroposterior diameter to predict a refusal for too small anatomy (AUC=0.87, p<0.001) (Supplemental Figure 2B). The individual CT parameters of the patients refused for TMVR are given in Supplemental Table 2. ROC-curve analyses to predict a too small or a too large anatomy are summarized in Supplemental Table 3.

Implantation results

Among the 16 patients who underwent TMVR, 14 patients (87.5%) had successful implantation without complication, 1 (6.25%) presented severe paravalvular leak, and 1 (6.25%) moderate intravalvular leak. After a mean follow-up of 365 ± 287 days, 5 (31%) patients died after TMVR (4 cardiovascular and 1 non-cardiovascular deaths). Among the 24 patients not suitable for

TMVR, 4 patients were lost to follow-up, 8 underwent compassionate MitraClip implantation and 5 patients died (25%) (2 after MitraClip).

DISCUSSION

Exploring all consecutive patients referred to high volume French Heart Valve Clinics during a period of 18 months, we found that i) a majority of patients (60%) was refused for TMVR mainly for too large annulus (62% of refusal) and less frequently for too small anatomy and subsequent risk of neo-LVOT obstruction (25% of refusal), ii) patients with a C-C diameter >39mm measured by TTE and a MA area >17.6 cm² measured by CT-scan were at higher risk of being refused for a too large anatomy and iii) patients with a LV end-systolic diameter <32mm measured by TTE and a anteroposterior diameter less than 41.6mm measured by CT-scan were at higher risk of being refused for a too small anatomy.

Controversial results in secondary MR, complexity of the procedure mainly performed with transapical access and anatomical constraints make the development of TMVR more laborious than for transcatheter aortic valve replacement (18,21). To date, TMVR is restricted to high-risk and inoperable patients as defined by the Heart Team and the experience of TMVR is still very limited with few hundred patients included in feasibility studies (14–16).

Decreasing the time between the decision of the Heart Team and TMVR (4 months in our study) is warranted to suit a target population that requires a rapid decision, i.e. frail patients exposed to frequent cardiac events such as death and hospitalization for recurrent heart failure. A better understanding of screen failure reasons in real-life patients will allow to avoid screening many patients in vain. We thus propose that C-C diameter and LV end-systolic diameter measured by TTE as relevant first-line parameters to avoid further tedious and time-consuming CT-scan. The threshold values we showed should be tested in further studies.

Our rate of screen failure is in line with previous studies with the Tendyne (14) and Twelve systems (15), reporting a rate of 60% and 70%, respectively. The main anatomical reason for refusal was a too large MA (62% of refusal) in patients likely at a end-stage of their mitral disease with significant LV and atrial dilatation. The second major concern with screening was the small anatomy with a risk of obstruction of the LVOT. Of note, the evaluation of the risk of LVOT obstruction is challenging as a result of the D- or saddle shape of the MA and its dynamic variation during the cardiac cycle (22). A dynamic evaluation of the mitral annulus will probably be useful to better assess the real impact of the prosthesis on the LVOT.

In the future, since there is currently a mismatch between the anatomical reality of the candidate patients and the size and the clutter of existing prostheses, the propagation of TMVR implantation will depend on the design of the prostheses. Our findings suggest the need to develop new prosthesis adapted to larger MA but with lower impact on the LVOT.

Limitations

The small number of our population is the main limitation. Our findings should be validated and confirmed in larger clinical trial. The final suitability decision was given by the manufacturer leading the feasibility study. The criteria for suitability was the same for the 3 devices. However, this criterion must be confirmed in the future according to each center experience. Moreover, atients with Barlow's disease were deemed inappropriate for MitraClip. This relative contra-indication must be confirmed with recent MitraClip innovations (MitraClip XTR). **Finally, given the small size of our population and the short period of follow-up, it is not possible to draw any conclusion regarding outcomes.**

IMPACT ON DAILY PRACTICE

C-C diameter and LV end-systolic diameter measured by TTE and MA area measured by CT-scan could be proposed as first line criteria in the pre-selection process to avoid vain screening for TMVR.

CONCLUSION

Despite several prostheses available, most of patients referred to Heart Valve Clinics and good candidate regarding their clinical profile cannot be implanted with TMVR mainly for a too large annulus. C-C diameter and LV end-systolic diameter measured by TTE and MA area measured by CT-scan could be proposed as first line criteria in the pre-selection process to avoid vain screening. Our findings suggest the need to develop new prosthesis adapted to larger MA but with lower impact on the LVOT.

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CONFLICT OF INTEREST

ND is consultant for Abbott Vascular, Boston Scientific, Edwards Life Sciences and Medtronic
TM is consultant for Abbott Vascular and Medtronic

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FIGURE LEGENDS

Figure 1. Flow Chart

Figure 2. Screening results

Figure 3. Example of screening results: A) Screening failure and B) Screening success

Table 1. Patients' characteristics and comorbidities

Table 1. Patients' characteristics and comorbidities					
	All population (n=40)	Suitable anatomy (n=16)	Too large anatomy (n=15)	Too small anatomy (n=8)	P value
Age (years)	78.9 ± 7.4	76.1 ± 6.6	79.8 ± 7.5	83.3 ± 4.8	0.08
Gender Male n (%)	23 (57.5)	11 (68.7)	10 (66.7)	1 (12.5)	**0.02**
BMI (kg/m^2)	25.0 ± 3.5	25.3 ± 2.5	24.4 ± 4.2	24.6 ± 3.4	0.76
Diabetes mellitus n (%)	7 (17.5)	3 (18.7)	3 (20)	0 (0)	0.30
Hypertension n (%)	29 (72.5)	10 (62.5)	12 (80)	7 (87.5)	0.25
Atrial Fibrillation n (%)	23 (57.5)	10 (62.5)	11 (73.3)	2 (25)	0.16
Prior Stroke n (%)	1 (2.5)	0 (0)	0 (0)	1 (12.5)	0.11
Prior Myocardial Infarction n (%)	7 (17.5)	5 (31.3)	0 (0)	2 (25)	0.06
Prior Cardiac surgery (except mitral) n (%)	7 (17.5)	4 (25)	2 (13.3)	1 (12.5)	0.63
CKD, eGFR <60 ml/min n (%)	24 (60)	9 (56.3)	11 (73.3)	3 (37.5)	0.24
NYHA n %					0.50
1	0 (0)	0 (0)	0 (0)	0 (0)	
2	12 (30)	6 (37.5)	4 (26.7)	1 (12.5)	
3	22 (62.5)	7 (43.8)	10 (66.7)	5 (62.5)	
4	6 (15)	3 (18.7)	1 (6.7)	2 (25)	
ACE inhibitors or ARBs n (%)	26 (65)	13 (81.3)	7 (46.7)	6 (75)	0.11
Beta-receptor antagonist n (%)	27 (67.5)	12 (75)	11 (73.3)	3 (37.5)	0.15
Aspirin or antiplatelet agent n (%)	13 (32.5)	9 (56.3)	4 (26.7)	0 (0)	**0.005**
Oral anticoagulant n (%)	9 (22.5)	4 (25)	2 (13.3)	3 (37.5)	0.66
Diuretics n (%)	30 (75)	13 (81.3)	11 (73.3)	6 (75)	0.67
Statins n (%)	16 (40)	10 (62.5)	5 (33.3)	1 (12.5)	**0.01**
Euroscore II (%)	4.7 [3.0;7.3]	4.9 [2.6;8]	4.7 [3.3;8.7]	4.4 [2.7;6.0]	0.86
STS predicted risk of mortality (%)	6.0 [3.9;8.7]	5.3 [3.5;7.8]	6.6 [4.0;16.5]	6.3 [4.4;13.6]	0.18

ACE: Angiotensin-Converting Enzyme; ARB: Angiotensin Receptor Blocker; BMI: Body Mass Index; CKD; Chronic Kidney Disease; eGFR: Estimated Glomerular Filtration Rate; NYHA: New York Heart Association; STS: Society of Thoracic Surgery. P-value by one-way ANOVA analysis of variance

Table 2. Echocardiography parameters

Table 2. Echocardiography parameters					
	All population (n=40)	Suitable anatomy (n=16)	Too large anatomy (n=15)	Too small anatomy (n=8)	P value
MR mechanism n (%)					**0.01**
Primary	19 (47.5)	4 (25)	9 (60)	6 (75)	
Secondary	21 (52.5)	12 (75)	6 (40)	2 (25)	
Mitral Valve Prolapse n (%)					0.75
Anterior	5 (26.3)	2 (50)	2 (13.3)	1 (12.5)	
Posterior	12 (63.2)	2 (50)	6 (40)	4 (50)	
Both	2 (10.5)	0 (0)	1 (6.7)	1 (12.5)	
Regurgitant Volume (ml)	67.1 ± 30.5	51.5 ± 24.4	76.3 ± 36.2	71.6 ± 28.2	0.19
ERO Area (mm²)	46.7 ± 17.7	43.1 ± 17	50.1 ± 20.2	49.5 ± 15.5	0.51
LVEF (%)	51.6 ± 16.6	41.2 ± 9.8	56.3 ± 15.1*	66 ± 16.5 *#	**<0.001**
LVEF > 60% n (%)	15 (37.5)	1 (6.25)	7 (33.3)	7 (87.5)	**0.0001**
LVEF 30-60% n (%)	25 (62.5)	15 (93.8)	8 (53.3)	1 (12.5)	**0.001**
LVEF < 30% n (%)	0 (0)	0 (0)	0 (0)	0 (0)	--
LV EDD (mm)	59.0 ± 9.0	60.9 ± 8.3	58.9 ± 7.2	52.6 ± 9.4	0.07
LV ESD (mm)	43.6 ± 12.2	48.9 ± 10.1	42.5 ± 11.8	32.9 ± 9.9 *	**0.006**
Max aortic velocity (m/s)	1.57 ± 0.49	1.60 ± 0.54	1.81 ± 1.75	1.63 ± 0.5	0.88
A2-P2 diameter (mm)	34.8 ± 8.2	34.1 ± 7.5	38.2 ± 7.3	28.9 ± 8.6 #	**0.03**
C-C diameter (mm)	39.5 ± 5.4	37.9 ± 5.7	42.1 ± 4.0	37.6 ± 6.0	**0.05**
Anterior leaflet length (mm)	28.0 ± 6.9	27.5 ± 7.1	30.1 ± 7.2	25.1 ± 5.8	0.25
Calcifications n (%)					0.27
No	27 (67.5)	11 (68.8)	11 (7.3)	4 (50)	
Mild	11 (27.5)	3 (18.8)	4 (26.7)	4 (50)	
Moderate	2 (5)	2 (12.5)	0 (0)	0 (0)	
Severe	0 (0)	0 (0)	0 (0)	0 (0)	
Mitral mean gradient (mmHg)	3.2 ± 1.4	3.0 ± 1.7	3.6 ± 1.1	3.0 ± 1.2	0.67
SPAP (mmHg)	56.7 ± 14.9	58.3 ± 13.0	58.9 ± 15.3	48.6 ± 17.4	0.25
TAPSE (mm)	19.8 ± 9.2	22.3 ± 12.3	17.9 ± 7.5	18.5 ± 4.1	0.41

C-C diameter: Commissure to commissure diameter; EDD: End diastolic parameter; ESD: End systolic parameter; ERO: Effective Regurgitant Orifice; MR: Mitral regurgitation; LV: Left Ventricle; LVEF: Left Ventricular Ejection Fraction; SPAP: Systolic Pulmonary Artery Pressure; TAPSE: Tricuspid Annular Plane Systolic Excursion. P-value by one-way ANOVA analysis of variance

** p<0.05 between suitable anatomy*

 # p<0.05 between too large anatomy

Table 3. Computed tomography parameters

Table 3. Computed tomography parameters					
	All population (n=40)	Suitable anatomy (n=16)	Too large anatomy (n=15)	Too small anatomy (n=8)	P value
Aortomitral angulation (°)	132.0 ± 12.6	135.6 ± 10.7	127.1 ± 15.1	132.8 ± 9.8	0.17
Anterior leaflet length (mm)	29.8 ± 12.6	32.9 ± 16.8	30.1 ± 9.1	23.6 ± 7.0	0.25
Anteroposterior diameter (mm)	42.6 ± 6.6	40.9 ± 5.1	48.3 ± 4.5*	35.7 ± 4.3 *#	**<0.001**
Orthogonal diameter (mm)	45.6 ± 6.7	43.1 ± 4.9	51.1 ± 5.6 *	40.4 ± 5.1 #	**<0.001**
Trigon to trigon distance (mm)	28.3 ± 8.3	27.7 ± 7.5	31.2 ± 10	24.8 ± 5.9	0.20
MA area (cm²)	15.5 ± 4.2	13.4 ± 2.7	19.5 ± 2.9 *	12.1 ± 2.8 #	**<0.001**
Total MA perimeter (mm)	143.1 ± 31.1	130.1 ± 35.2	163.2 ± 22.4 *	131.3 ± 17.9 #	**0.004**
Projected MA perimeter (mm)	137.2 ± 23.7	124.7 ± 18.8	155.9 ± 19.9 *	125.3 ± 17.4 #	**<0.001**
Basal IVS (mm)	14.9 ± 3.2	14.9 ± 2.9	14.7 ± 3.9	15.0 ± 2.9	0.99
Sub valvular apparatus abnormalities					0.30
No	34 (85)	12 (75)	14 (93.3)	7 (87.5)	
Yes	6 (15)	4 (25)	1 (6.7)	1 (12.5)	
Calcifications n (%)					0.77
No	21 (52.5)	9 (56.3)	8 (53.3)	4 (50)	
Yes	19 (47.5)	7 (43.7)	7 (46.7)	4 (50à	

IVS: Interventricular septum, MA: Mitral Annulus. P-value by one-way ANOVA analysis of variance

** p<0.05 between suitable anatomy*

 # p<0.05 between too large anatomy

Figure 1. Flow Chart

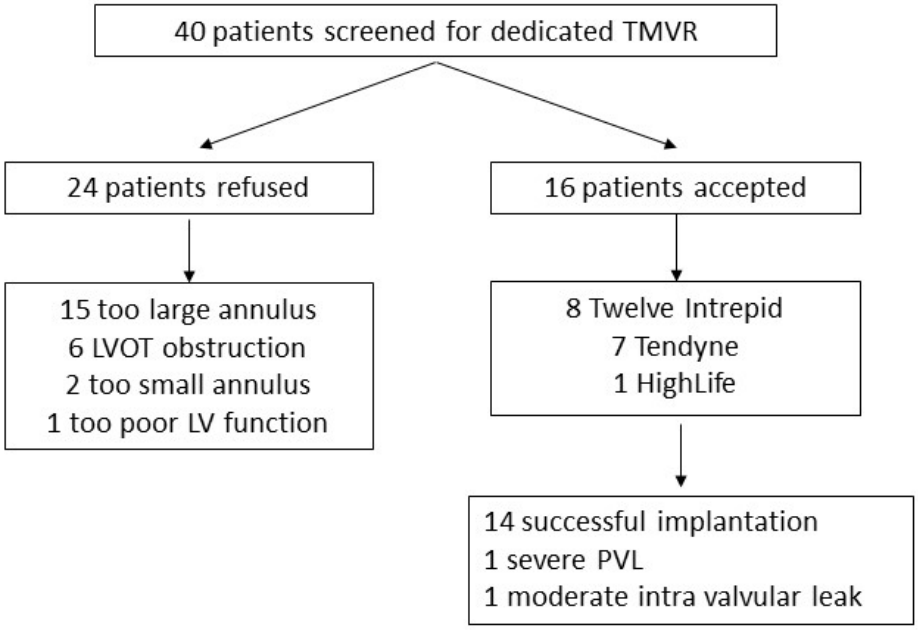


Figure 2. Screening results

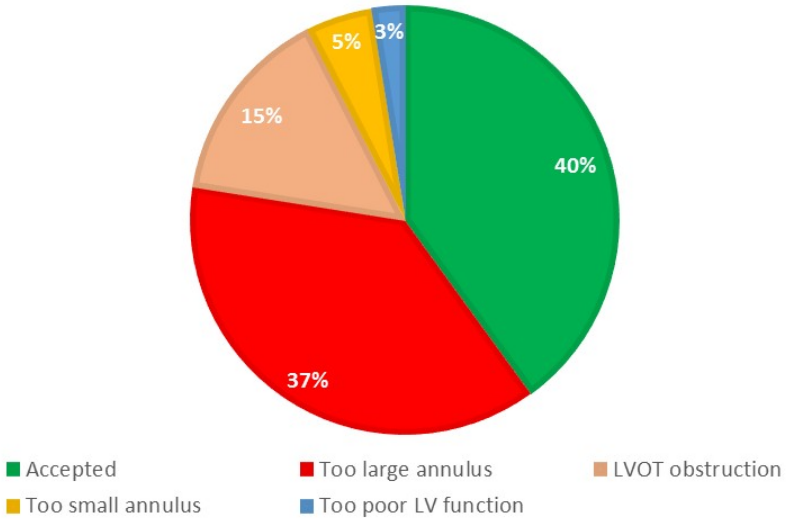
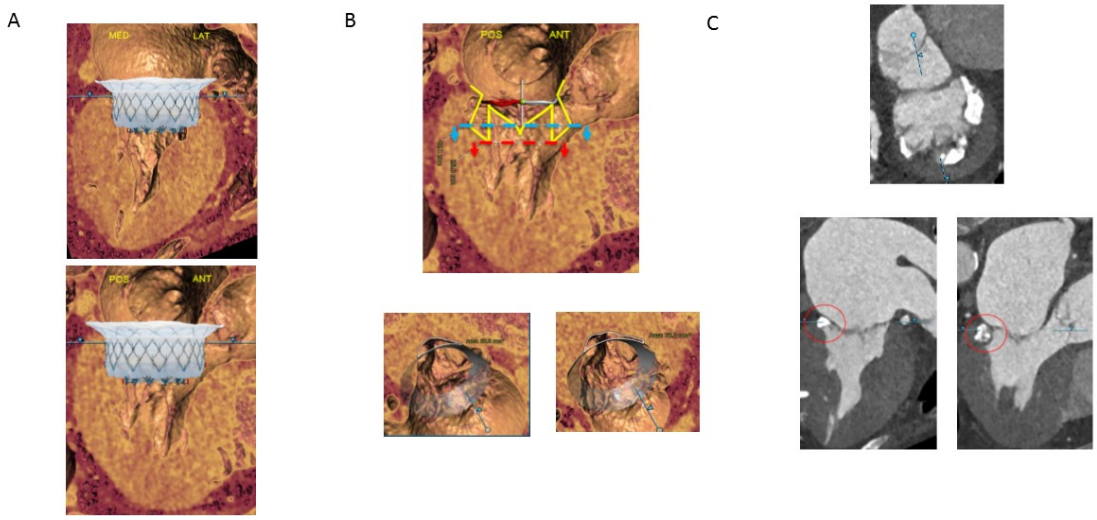


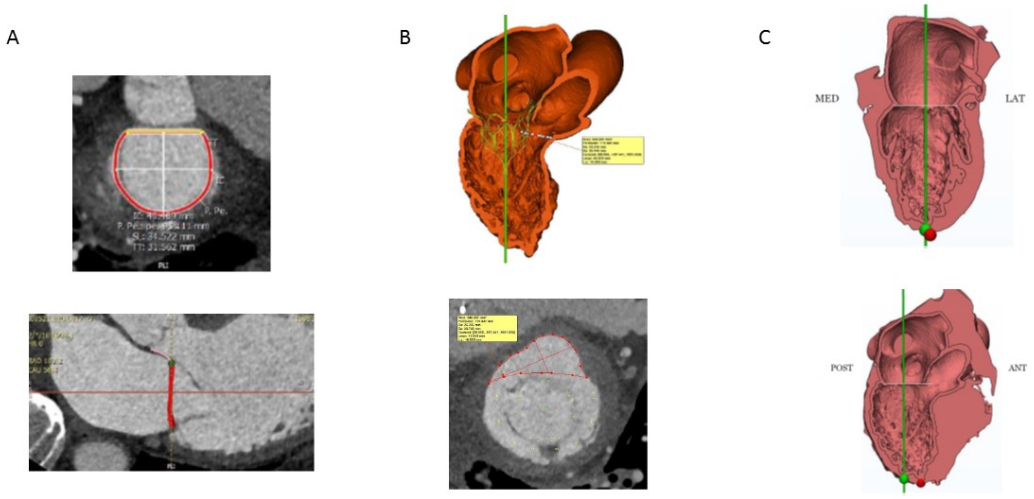
Figure 3. Example of screening results: A) Screening failure and B) Screening success

A. Screening failure



A. Valve modelization with 43mm Twelve Intrepid prosthesis to calculate oversizing and compression rate, B. Calculation of the predicted neo LVOT at 0.6cm² at end systole, C. Substantial amount of calcium observed at the level of the annulus and the posterior commissure

B. Screening success



A. Measurements of annulus dimensions, B. Valve modelization with the Tendyne prosthesis and calculation of the predicted neo LVOT at 540mm² at end systole, C. Target access site (green) and true LV apex (red)

Supplemental Table 1. Suitablity for all patients with each device used at the centre.

	Screening Result	Reason	Prosthesis implanted	Center
Patient 1	refused	Too small		LILLE
Patient 2	accepted		Twelve Intrepid	LILLE
Patient 3	accepted		Tendyne	LILLE
Patient 4	refused	Too large		LILLE
Patient 5	refused	Poor LV function		LILLE
Patient 6	accepted		Twelve Intrepid	LILLE
Patient 7	refused	Too large		LILLE
Patient 8	refused	LVOT obstruction		LILLE
Patient 9	refused	Too large		LILLE
Patient 10	accepted		Tendyne	LILLE
Patient 11	refused	Too large		LILLE
Patient 12	refused	Too large		LILLE
Patient 13	refused	LVOT obstruction		LILLE
Patient 14	refused	Too large		LILLE
Patient 15	accepted		Tendyne	LILLE
Patient 16	refused	LVOT obstruction		LILLE
Patient 17	refused	Too large		LILLE
Patient 18	accepted		HighLife	LILLE
Patient 19	accepted		Twelve Intrepid	LILLE
Patient 20	accepted		Twelve Intrepid	LILLE
Patient 21	refused	Too large		LILLE
Patient 22	accepted		Tendyne	LILLE
Patient 23	accepted		Twelve Intrepid	LILLE
Patient 24	accepted		Twelve Intrepid	LILLE
Patient 25	refused	Too large		LILLE
Patient 26	accepted		Tendyne	TOULOUSE
Patient 27	refused	LVOT obstruction		TOULOUSE
Patient 28	refused	Too large		TOULOUSE
Patient 29	refused	Too large		TOULOUSE
Patient 30	accepted		Tendyne	TOULOUSE
Patient 31	refused	LVOT obstruction		TOULOUSE
Patient 32	accepted		Twelve Intrepid	TOULOUSE
Patient 33	refused	Too large		TOULOUSE
Patient 34	refused	Too large		TOULOUSE
Patient 35	accepted		Tendyne	TOULOUSE
Patient 36	refused	Too large		TOULOUSE
Patient 37	refused	LVOT obstruction		TOULOUSE
Patient 38	accepted		Twelve Intrepid	TOULOUSE
Patient 39	refused	Too small		TOULOUSE
Patient 40	refused	Too large		TOULOUSE

Supplemental Table 2. CT parameters according to refusal reason

Refusal reason	Aortomitral angulation (°)	AP diameter (mm)	Orthogonal diameter (mm)	MA area (cm²)	Total MA perimeter (mm)	Projected MA perimeter (mm)
Too large anatomy (n=15)						
Patient 1	107.5	53.3	52.9	22.8	182.2	173.7
Patient 2	143.1	46.8	43.3	16.3	151.6	148.3
Patient 3	128.5	43.7	51.2	17.8	155.4	141.2
Patient 4	114	52	59	25	203	181
Patient 5	113	51	52	19.4	167	160
Patient 6	116	50	48	18.6	168	156
Patient 7	96.8	50	64	23.8	169	179
Patient 8	134.7	44.1	48.7	18.1	157.2	152.9
Patient 9	145	53.3	55.1	22.4	173.8	168.4
Patient 10	137	44	52	21	115.5	109.3
Patient 11	141	38.6	46	15.4	146.2	144.4
Patient 12	120	47	50	19.8	181.7	170.6
Patient 13	131	49.7	53	18	134.6	128.5
Patient 14	147	55	50	19	173.8	169.7
Patient 15	132	46.5	41.8	15.9	149.6	143.1
Too small anatomy (n=8)						
Patient 16	120.7	30.2	36.7	9	119.2	109
Patient 17	128.4	36.4	39.1	11.5	132.5	132
Patient 18	137.6	41.3	47.5	15.6	150	142
Patient 19	118	38	37	11	129	120
Patient 20	136	32.6	40.6	12	119	114
Patient 21	136	33.3	39.5	12.4	142.5	132.8
Patient 22	139	41.6	48.3	16.6	156.2	152.2
Patient 23	147	32.5	34.2	8.8	102.3	100.7

AP: Anteroposterior; MA: Mitral annulus

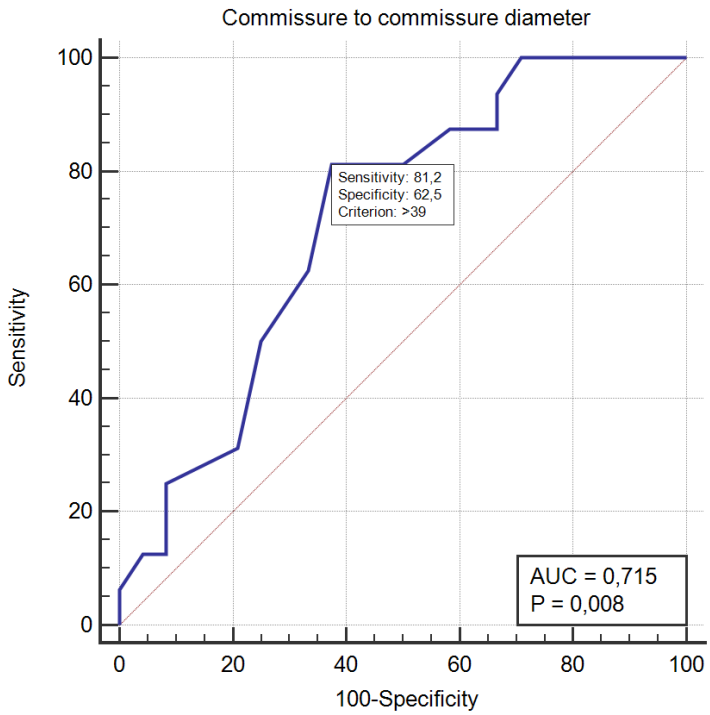
Supplemental Table 3. ROC-curve analyses. TTE and CT parameter to predict a too small or a too large anatomy

	AUC	p-value	Sensitivity	Specificity
TOO LARGE ANATOMY				
TTE C-C diameter > 39mm	0.715	0.008	81.2	62.5
TTE A2-P2 diameter > 40mm	0.707	0.018	50.0	87.5
CT MA area > 17.6cm²	0.949	<0.001	75.0	100.0
TOO SMALL ANATOMY				
TTE LVESD < 32mm	0.832	<0.001	75.0	87.5
CT AP diameter <41.6	0.873	<0.001	100.0	65.6

AP: Anteroposterior; AUC: Area under the curve; C-C: Commissure to commissure; LVESD: Left ventricular end systolic parameter; MA: Mitral annulus; NPV: Negative predictive value; PPV: Positive predictive value

Supplemental Figure 1. ROC-curve. TTE parameter with the highest discriminating power to predict A, B) a too large anatomy and C) a too small anatomy

A.



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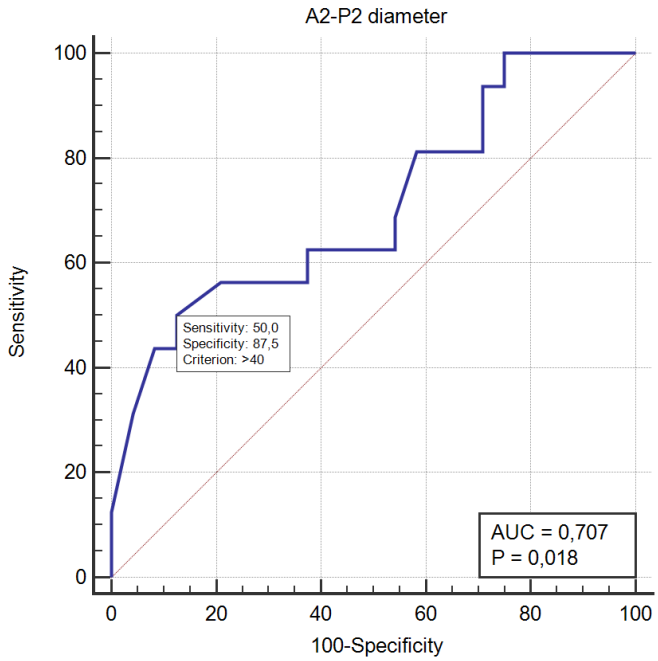

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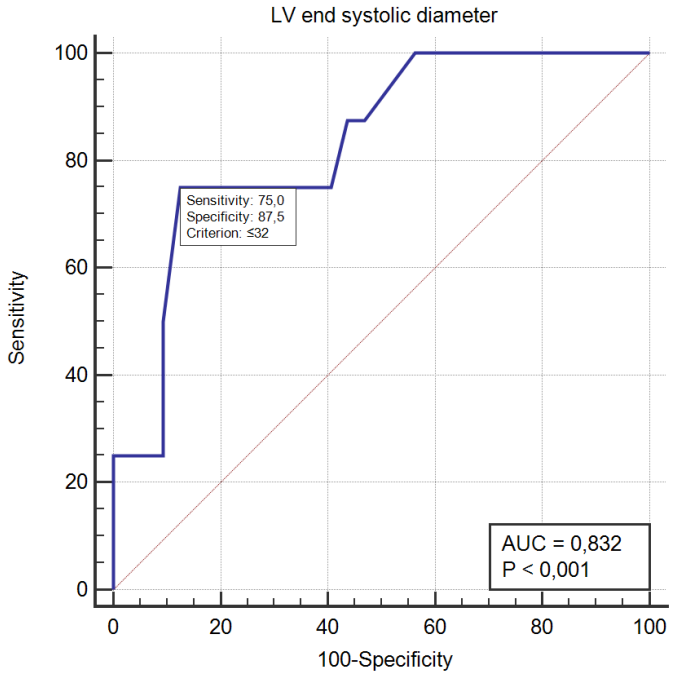
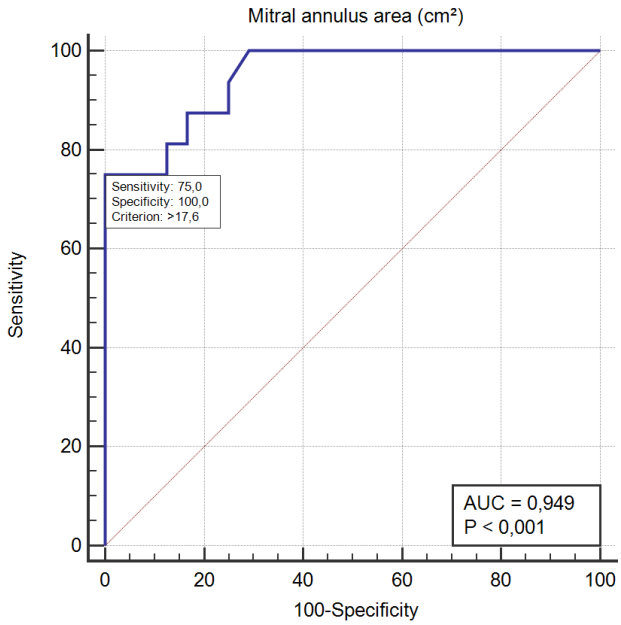


Supplemental Figure 2. ROC-curve analysis. CT-scan parameter with the highest discriminating power to predict A) a too large anatomy and B) a too small anatomy

A.



B.