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ADULT CARDIAC

Systolic anterior motion after mitral valve repair: a predictive computational model†

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Abstract

OBJECTIVES: Systolic anterior motion (SAM) can be an insidious complication after mitral repair. Predicting SAM represents a challenge, even for very experienced mitral valve surgeons. The goal of this pilot work was to illustrate for the first time, a computational software able to calculate and prevent SAM during mitral repair.

METHODS: Using MATLAB graphical user interface, a clinical software to predict SAM, we tested the performances of the software on 136 patients with degenerative mitral valves undergoing repair with standard techniques. A combination of 6 key echocardiographic parameters was used to calculate the SAM risk score. The discriminative performance of the model was assessed by the area under the receiver–operating characteristic curve. The receiver–operating characteristic was used to divide patients into low, medium and high risk for SAM. Simulation of virtual mitral repair (posterior leaflet resection and mitral ring annuloplasty) was also tested to reduce the risk of SAM.

RESULTS: The incidence of SAM was 8.1%; 73% were detected as high risk by the software. The area under the receiver–operating characteristic model discriminant performance was 0.87 (95% confidence interval: 0.78–0.95). Simulating a posterior leaflet resection with the leaflet length fixed at 15 mm, the estimated SAM risk was updated, and all patients were then classified at low risk.

CONCLUSIONS: This software is the first computational model designed to predict SAM during mitral repair to show excellent discrimination. This software has the potential to predict SAM risk preoperatively and, after a virtual step-by-step mitral repair simulation, depending on the technique adopted, to always achieve a low-risk SAM profile.

Keywords: Systolic anterior motion • Mitral regurgitation • Mitral valve repair • Posterior leaflet resection • Ring annuloplasty • Edge-to-edge technique • Computational model

INTRODUCTION

Systolic anterior motion (SAM) can be an insidious complication after surgical mitral valve (MV) repair. It is reported to occur in 4–10% of cases after mitral reconstruction [1]. SAM refers to the dynamic anterior movement of the MV towards the interventricular septum during systole, creating a left ventricular outflow tract obstruction (LVOTO), usually associated with mitral regurgitation. The degree of this complication is variable and can range from minor forms (such as chordal protrusion with mild LVOTO and trivial MR) to more serious clinical entities, with severe obstruction and massive MR, leading to haemodynamic instability, low cardiac output and refractory hypotension. When this last scenario happens, prompt surgical correction is mandatory. The post-repair SAM is detected in the operating room with transoesophageal echocardiography, usually once the cardiopulmonary bypass has been completed. Moreover, SAM is detected before or even after hospital discharge [2, 3] in only a few cases. Although the multifactorial pathophysiology of SAM is well recognized, the prediction risk of SAM still represents a challenge, even for experienced mitral surgeons. We illustrate for the first time a dedicated computational user-friendly software that calculates the risk of SAM using basal echocardiographic characteristics, either before or after mitral repair with posterior leaflet (PL) resection. The ultimate goal of this project is to guide surgeons to tailor the best repair for each specific mitral anatomy,

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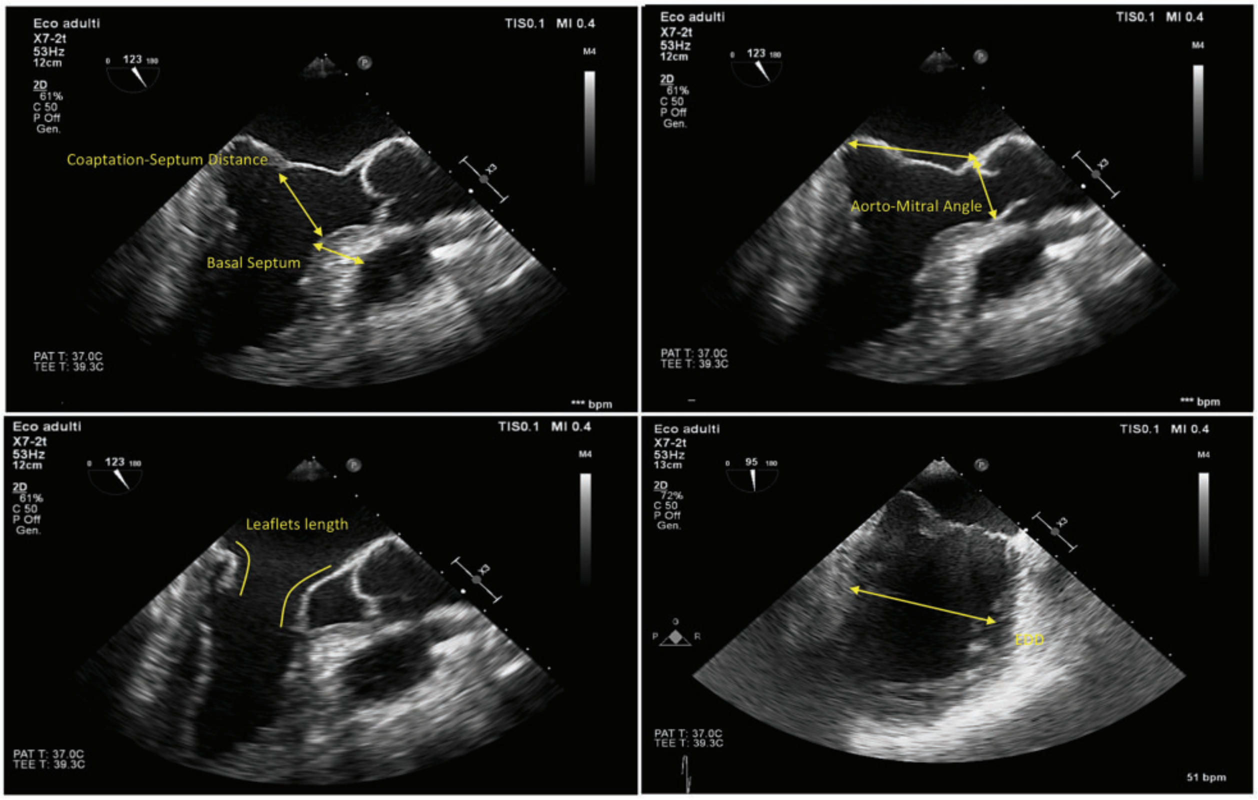

Figure 1: Transoesophageal echocardiographic views with the 6 parameters chosen as predictors of systolic anterior motion: coaptation–septum distance, basal septum, aortomitral angle, posterior leaflet length, anterior leaflet length and end-diastolic diameter.

using a software able to predict any potential mechanism of SAM derived from all mitral repair techniques.

MATERIALS AND METHODS

Study population

To test the software, we collected clinical data on 136 consecutive patients with severe MR operated on at San Raffaele University Hospital from September 2015 to August 2016. Patients undergoing the edge-to-edge repair were excluded from the analyses, because this technique is used either to prevent or to correct SAM during or after repair [4, 5]. Therefore, it is considered by definition a bias. Demographic, echocardiographic and intraoperative data were prospectively collected before and after surgery (Table 1). Six different echocardiographic parameters were selected from standard bidimensional echocardiographic views and inserted in the software: aortomitral angle (*A*), PL length, anterior leaflet (AL) length, end-diastolic diameter (EDD), basal septum (BS) and coaptation–septum distance (CS) (Table 2, Fig. 1). We detected the occurrence of SAM in the operating room after weaning from cardiopulmonary bypass for all patients. SAM was defined as follows: the dynamic anterior movement of the MV towards the interventricular septum during systole, creating an LVOTO associated with severe mitral regurgitation.

Descriptive analysis

All the clinical, intraoperative echocardiographic and annuloplasty data were reported with mean and standard deviation. The Shapiro–Wilk test of normality was performed to assess data distribution for both clinical and echocardiographic results. The patient population was divided into 2 groups: Group 1 with SAM after repair (SAM) and Group 2 without post-repair SAM (no SAM). The data of Group 1 (SAM) and Group 2 (no SAM) were compared using the Student's *t*-test if they had a normal distribution or the Mann–Whitney *U*-test if they did not have a normal distribution. Data that were expressed as percentages or frequency were compared with the χ^2 test or the Fisher's exact test. The latter was chosen if expected counts were less than 5. Univariable logistic regression was used to assess the association between SAM occurrence and the 6 echocardiographic parameters. All *P*-values <0.05 were considered statistically significant.

Systolic anterior motion prediction

The combination of echocardiographic parameters was used to calculate the SAM risk score after repair. The echocardiographic parameters included in the prediction model were chosen from the literature [6–8]. For predictive purposes, we used a full logistic equation formula based on the results provided by Varghese *et al.* [7] to calculate the probability of SAM as follows:

$$P(\mathrm{SAM}=1)=\frac{\exp(-8.375631+1.00796\times A+1.36098\times \mathrm{EDD}+1.335\times \mathrm{PL}+1.74047\times \mathrm{AL}+1.31641\times \mathrm{BS}+1.62728\times \mathrm{CS})}{1+\exp(-8.375631+1.00796\times A+1.36098\times \mathrm{EDD}+1.335\times \mathrm{PL}+1.74047\times \mathrm{AL}+1.31641\times \mathrm{BS}+1.62728\times \mathrm{CS})}$$

Angle (A) < 120° = 1, EDD < 4.5 cm = 1, PL ≥ 1.5 cm = 1, AL ≥ 2.5 cm = 1, BS ≥ 1.5 cm = 1 and CS ≥ 2.5 cm = 1. The authors did not explicitly report the formula for their model, but it was possible to use it

Table 1: Demographics and clinical data of the population selected

	All	Group 1	Group 2	*P*-value
Demographic parameters				
Patient number	136	11 (8.1%)	125 (91.9%)	
EuroSCORE II (%)	1.17 ± 1.1	1.17 ± 0.6	1.17 ± 1.2	0.532
EF (%)	63.6 ± 8.1	67.5 ± 6.7	63.3 ± 8.1	0.115
Male gender	108 (79.4%)	9 (81.8%)	99 (79.2%)	0.843
Age (mean)	58 ± 11.6	57 ± 13.1	58 ± 11.5	0.764
Aetiology of MV disease				
Myxomatous degeneration	102 (75%)	10 (90.9%)	92 (73.6%)	0.182
Barlow's disease	10 (7.3%)	1 (9.1%)	9 (7.2%)	0.580
Fibroelastic deficiency	24 (17.6%)	0 (0%)	24 (19.2%)	0.111
MV disease				
Prolapse/flail	133 (97.8%)	11 (100%)	122 (97.6%)	0.773
Annular dilatation	3 (2.3%)	0 (0%)	3 (2.4%)	
Leaflet lesion				
Posterior leaflet	127 (93.4%)	9 (81.8%)	118 (94.4%)	0.160
Anterior leaflet	4 (2.9%)	0 (0%)	4 (3.2%)	0.710
Bileaflet	5 (3.7%)	2 (18.2%)	3 (2.4%)	0.052
Surgical techniques				
Posterior leaflet resection + folding/sliding	71 (52.2%)	7 (63.6%)	64 (51.2%)	0.807
Neochordal placement	55 (40.4%)	4 (36.4%)	51 (40.8%)	
Annuloplasty	10 (7.3%)	0 (0%)	10 (8%)	
Concomitant surgery				
AF ablation	3 (2.2%)	0 (0%)	3 (2.4%)	0.771
TV repair	14 (10.3%)	2 (18.2%)	12 (9.6%)	0.323
CABG	7 (5.1%)	0 (0%)	7 (5.6%)	0.552
AVR	2 (1.5%)	0 (0%)	2 (1.6%)	0.847

EF: ejection fraction; TV: tricuspid valve; CABG: coronary artery bypass grafting; AVR: aortic valve repair.

Table 2: Echocardiographic data acquisition and definitions

Echocardiographic parameters	Acquisition
Anteroposterior diameter	The distance between the origin of the 2 leaflets: it is measured from the mid-oesophageal long axis view at the end of diastole
Aortomitral angle	The angle between the mitral annulus plane and the aortic annulus plane: it is measured from the mid-oesophageal long axis view in mid-systole
Posterior and anterior leaflet length	It is recorded from the mid-oesophageal long-axis view by selecting the best frame to visualize the 2 leaflets completely (from the mitral annulus plane to the leaflet edge)
Left ventricular end-diastolic diameter	It is recorded from the mid-oesophageal 2-chamber or transgastric mid-papillary short-axis view
Basal septum values	It is measured from the mid-oesophageal long axis view at the end of diastole
Coaptation–septum distance	The distance between the basal septum and the point where leaflet tips touch themselves: these last values were acquired from the mid-oesophageal long axis view at the end of diastole

knowing the included covariates and the odds ratio (OR) [7]. The unknown parameter was the intercept, which was estimated using a univariable logistic regression with an offset term set equal to the linear predictor term without the intercept.

The discriminative performance of the model was assessed by the area under the receiver–operating characteristic (AUROC) curve. The receiver–operating characteristic curve and Youden's index were computed and used to choose cut-offs to individuate 3 ranges of SAM risk: 'low risk' (patients with very low chance of SAM), 'medium risk' (moderate chance of SAM) and 'high risk' (high chance of SAM). Cut-off values were chosen as follows: first, we selected as the cut-off the value that maximized sensitivity and specificity according to Youden's index. This value has been used to discriminate patients developing SAM from patients not developing SAM. We classified the former as low risk. Then, we chose another cut-off among the range of risks calculated for patients classified as SAM developed according to the criteria previously described. This value is the one with the maximum Youden's index and was used to identify patients at high risk, requiring greater attention by the surgeon. Medium-risk patients are those with risk scores between these 2 cut-offs. All statistical analyses were performed using SPSS Statistics version 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0, IBM Corp., Armonk, NY, USA).

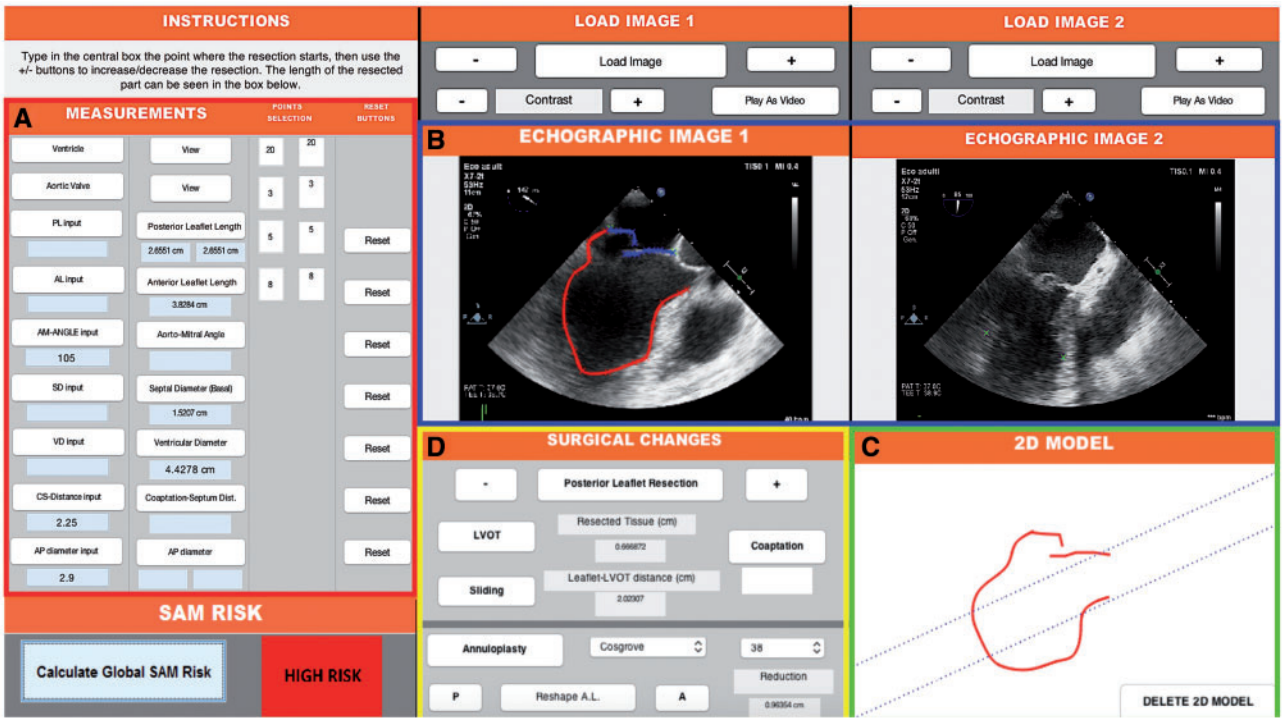

Figure 2: Software graphical user interface developed with MATLAB used to predict systolic anterior motion and virtual simulation of the surgical correction. (**A**) Echocardiographic measurements box. (**B** and **C**) Echocardiographic image and corresponding 2D model. (**D**) Surgical changes box. PL: posterior leaflet; AL: anterior leaflet; SD: standard deviation; CS: coaptation–septum distance; AP: anteroposterior; SAM: systolic anterior motion; LVOT: left ventricular outflow tract.

Software development

In 2015, a dedicated software was developed to automate the prediction of SAM after MV repair (Fig. 2A–D). The graphical user interface of MATLAB (The Mathworks Inc., Natick, MA, USA) was used to design this software and provide a user-friendly version. The software has the capability to predict SAM risk both from the simulation of a virtual PL resection and from baseline echocardiographic views. The 2 echocardiographic images are loaded at the same time, and the echocardiographic parameters can be either entered manually, as input, or directly measured by the software (Fig. 2B). Once the predictive parameters of the SAM are entered, the software elaborates them with the predictive formula and gives the SAM risk score as output. A 2D model of the echocardiographic view is also automatically drawn during parameter acquisition, giving instantaneous feedback of where the coaptation point (CP) is placed with respect to the LVOT projection (Fig. 2C).

Virtual mitral valve repair

Software clinical application I: posterior mitral valve leaflet resection simulation. This software can calculate the risk of SAM after the simulation of a virtual PL resection. This tool is particularly useful in those patients showing increased probability of post-repair SAM (marked as medium risk or high risk) by the integrated algorithm. In the 'surgical changes' box (Fig. 2D), the surgeon can choose the extension of the PL resection, progressively decreasing the PL length. Once the virtual resection is performed, the SAM risk score is re-updated by the software according to the new anatomical parameters.

Software clinical application II: ring annuloplasty. After having done the virtual PL resection with the software, we can quantify the degree of residual SAM by calculating the anteroposterior mitral annular diameter reduction after the ring annuloplasty. The choice of the ring should be based on the anteroposterior diameter measured in the preoperative echocardiographic image, which is provided by a dedicated output. Once the ring type and size are selected, the software updates the SAM risk according to the value of the CS distance. The updated CP is shown in a 2D model.

RESULTS

Clinical and intraoperative data

The mean age of the population used to validate the software was 58 ± 11.6 years; New York Heart Association Class I–II was present in 94.8% (129 patients); atrial fibrillation was present in 2.2% (3 patients); and the mean preoperative left ventricular ejection fraction was 63.6% ± 8.1%. All patients had primary (degenerative) MV disease. MV disease aetiology was myxomatous degeneration in 102 patients (75%), Barlow's disease in 10 patients (7.4%) and fibroelastic deficiency in 24 patients (17.6%). The MR was caused by bileaflet prolapse in 5 patients (3.7%), AL prolapse in 4 patients (2.9%) and PL prolapse in 127 patients (93.4%). All patients in our study underwent intraoperative transoesophageal echocardiography to record these values according to the American Society of Echocardiography Guidelines [9]. The overall incidence of SAM was 8.1% (11 of 136 patients). Seventy-one patients (52.2%) were treated with PL resection associated with folding or sliding plasty techniques, 55 (40.4%) patients were treated with artificial chordae, and 7 of 10 (5.4%) patients were

Table 3: Details of patients developing systolic anterior motion after mitral valve repair (Group 1)

Patient number	Aetiology of MV disease	Leaflet lesion	First repair technique	Ring	New CPB	Medical correction	Surgical correction	SAM/LVOTO resolution
1	Mixomatous degeneration	PL	Posterior leaflet resection	Cosgrove 38 mm	Yes		Edge to edge	Yes
2	Mixomatous degeneration	PL	Posterior leaflet resection	Cosgrove 34 mm	No	Hypervolaemia		Yes
3	Mixomatous degeneration	PL	Posterior leaflet resection	Cosgrove 36 mm	Yes		Edge to edge	Yes
4	Mixomatous degeneration	PL	Posterior leaflet resection, neochordal placement and tricuspid valve repair	Cosgrove 36 mm	Yes		Edge to edge	Yes
5	Mixomatous degeneration	PL	Neochordal placement	Cosgrove 38 mm	No	Beta-blockers		Yes
6	Mixomatous degeneration	PL	Neochordal placement	Cosgrove 28 mm	No	Hypervolaemia		Yes
7	Barlow's disease	BL	Neochordal placement	Tailor 35 mm	Yes		Edge to edge	Yes
8	Mixomatous degeneration	PL	Posterior leaflet resection	Tailor 35 mm	Yes		Edge to edge	Yes
9	Mixomatous degeneration	PL	Posterior leaflet resection, edge-to-edge and tricuspid valve repair	Tailor 33 mm	No	Beta-blockers		Yes
10	Mixomatous degeneration	BL	Neochordal placement	Simulus flexible 35 mm	Yes		Edge to edge	Yes
11	Mixomatous degeneration	PL	Posterior leaflet resection	Tailor 33 mm	Yes		Edge to edge	Yes

MV: mitrovalve; CPB: cardiopulmonary bypass; SAM: systolic anterior motion; LVOTO: left ventricular outflow tract obstruction; PL: posterior leaflet; BL: bileaflet.

Table 4: Echocardiographic parameters of the population selected calculated with software

Echocardiographic parameters	All	Group 1	Group 2	*P*-value
AP diameter pre-surgery (cm)	3.7 ± 0.5	3.5 ± 0.5	3.7 ± 0.5	0.184
AP diameter post-surgery (cm)	2.6 ± 0.4	2.4 ± 0.4	2.6 ± 0.3	0.240
Aortomitral angle (°)	114 ± 10.7	105 ± 9.5	114.3 ± 10.5	0.043
PL length (cm)	1.9 ± 0.4	2.4 ± 0.5	1.8 ± 0.4	<0.012
AL length (cm)	3.0 ± 0.4	3.3 ± 0.5	2.9 ± 0.4	0.021
EDD (cm)	5.1 ± 0.7	4.7 ± 0.4	5.1 ± 0.8	0.020
Basal septum (cm)	1.5 ± 0.3	1.8 ± 0.2	1.4 ± 0.3	<0.014
Coaptation-septum distance (cm)	2.7 ± 0.5	2.3 ± 0.6	2.8 ± 0.5	0.011

AP: anteroposterior; PL: posterior leaflet; AL: anterior leaflet; EDD: end-diastolic diameter.

treated with isolated ring annuloplasty and posterior cleft closure. No statistically significant difference was found with demographic data, MV aetiology, MV disease and leaflet lesion between the 2 groups. Demographic and surgical details of the patients who had SAM after repair are reported in detail below (Table 3). Seven of the patients with SAM (63.6%) required surgical correction with the edge-to-edge technique (mean time, 15 ± 4 min) to successfully abolish the LVOTO, whereas the others were treated conservatively (Table 3).

Preoperative echocardiographic findings

The comparison between Group 1 and Group 2 showed a significant difference for the following parameters: aortomitral angle ($P = 0.043$), PL length ($P < 0.012$), AL length ($P = 0.021$), EDD ($P = 0.020$), BS ($P < 0.014$) and CS ($P = 0.011$) (Table 4). Univariable logistic regression also showed significant association between SAM occurrence and the following echocardiographic parameters: aortomitral angle [OR 0.36; 95% confidence interval (CI): 0.038–25.96], PL length (OR 3.11; 95% CI: 0.39–24.85), AL length (OR 2.64; 95% CI: 0.42–16.44), EDD (OR 0–80; 95% CI: 0.29–2.24), BS (OR 2.54; 95% CI: 0.15–43.78) and CS (OR 0.24; 95% CI: 0.34–1.71).

Systolic anterior motion prediction and model performance

The discriminant performance of the model, measured with the area under the receiver–operating characteristic curve, was 0.87

(95% CI: 0.78–0.95) (Fig. 3). Using the optimal cut-offs, patients were divided into 3 ranges according to their chance of post-repair SAM as follows: 28 high-risk, 20 medium-risk and 88 low-risk subjects. Eleven patients had post-repair SAM in the operating room; of these, 8 patients were labelled as high risk, whereas the other 3 patients were recognized as medium risk. No patients considered low risk showed post-repair SAM, which means that 73% of the patients who developed SAM were properly detected as high risk by the software. On the other hand, a considerable portion of intraoperative SAM was derived from patients labelled as medium risk (27%).

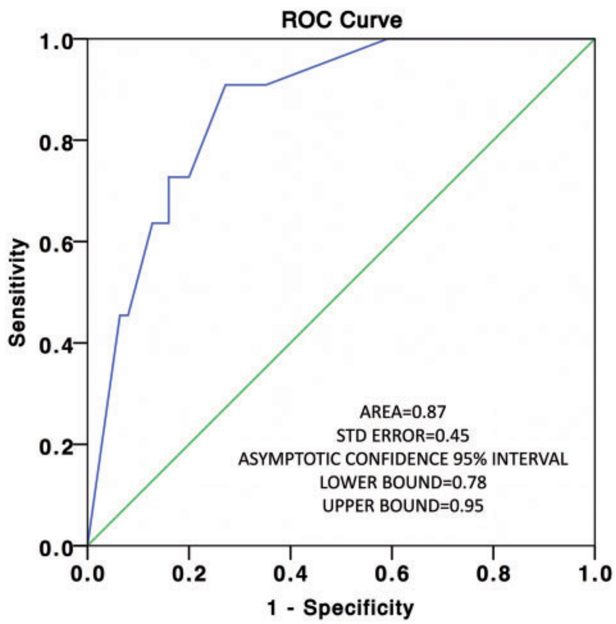

Figure 3: ROC curve and software output. ROC: receiver-operating characteristic.

Software application surgical correction

We revised every echocardiogram of the 7 patients developing SAM after PL resection in the operating room. The new length of the resected PL was then measured, and this value was inserted as PL length in the virtual resection simulator. The software predicted 5 patients at high and 2 at medium risk for SAM among these patients. We then performed the virtual PL resection in these patients, in order to detect how to abolish the SAM risk. The virtual resection changed the CP position, the posterior and AL shape and the PL length: All these changes are elaborated by the software and could be instantaneously visualized in the 2D model (Fig. 4). When the virtual resection was repeated, fixing the PL length at 15 mm, all 7 patients were reported as low risk by the software. Also, we performed in all patients the virtual simulation of ring annuloplasty. When the desired MV ring is chosen, the value of the CS distance is updated, with a visual feedback in the 2D model of where the new CP will be in respect to the LVOT projection (Figs 1D and 4).

DISCUSSION

The prediction of SAM after mitral repair still represents a challenging and insidious issue, even for very experienced mitral surgeons, eventually leading to surgical correction [1, 4, 6–8]. It is well known that SAM is a multifactorial entity and that its incidence is higher when several anatomical predisposing factors coexist. Having the chance to calculate the risk of SAM before MV repair is desirable and clinically useful. Hence, the development of a dedicated software programme, which can also indicate how much of the PL should be resected and which specific ring annuloplasty should be used (model and size) to abolish SAM, represents an innovative solution. Indeed, this software is, to the best of our knowledge, the first computational model specifically developed for this clinical application. The software elaborates the SAM risk score on the basis of 6 key echocardiographic parameters, selected as strong predictors of SAM after

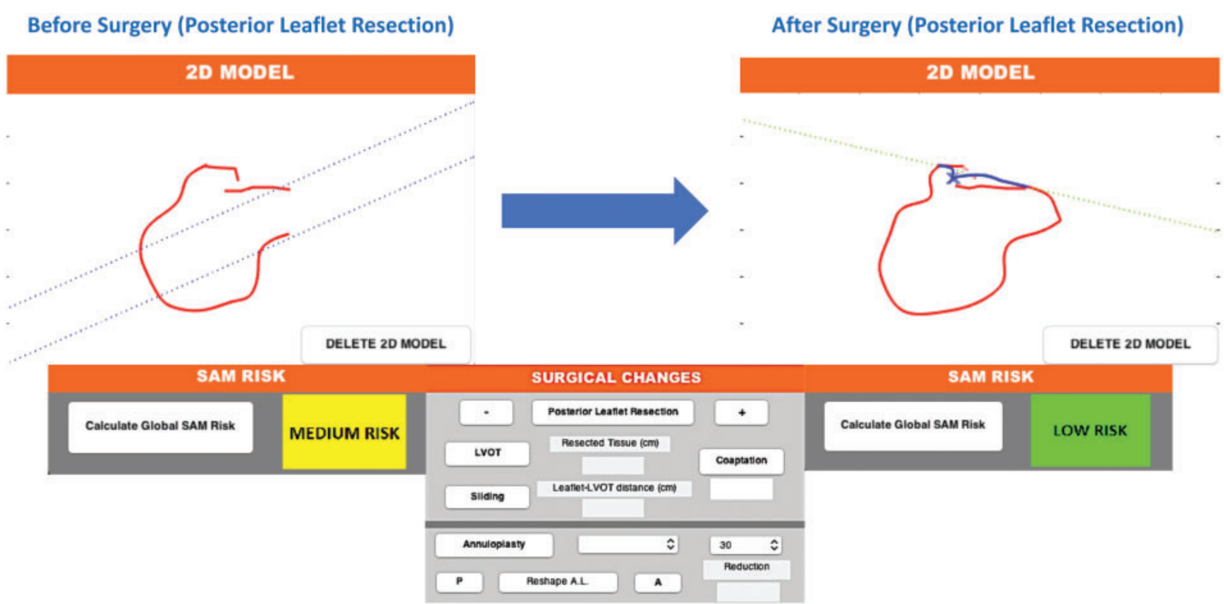

Figure 4: Virtual simulation of posterior leaflet resection with annulopasty and changes in 2D model and systolic anterior motion risk score. SAM: systolic anterior motion; LVOT: left ventricular outflow tract.

repair, from information found in the literature [6, 7]. It has a user-friendly layout and presents the outputs through a multi-functional graphical user interface (Fig. 2). This intuitive interface automatically creates a 2D model of the mitral and left ventricular complex; meanwhile, the echocardiographic parameters are acquired. More, it provides instantaneous feedback as to where the CP will fall in respect to the LVOT projection (Fig. 2B). This 2D model is used to simulate the position of the new CP, calculated after the virtual PL resection and prosthetic ring annuloplasty (Fig. 2B). We tested the performance of the software on 136 consecutive patients with degenerative mitral valves who had repair with classic techniques (artificial chordae, PL resection and ring annuloplasty) at our institution. Seven patients undergoing ring annuloplasty had in addition closure of posterior clefts. Overall, in our study, the incidence of SAM was 8.1% (11 of 136 patients), which is in accordance with the rate reported by dedicated mitral repair centres [4]. Using a modified predictive model to apply the software to our data [7], we evaluated the detection of post-repair SAM, showing an area under the receiver–operating characteristic curve equal to 0.87, which is an excellent discrimination result. Of the 11 patients with SAM identified in the operating room, 8 patients were categorized as high risk and 3 patients were labelled as medium risk. No low-risk patients developed SAM after mitral repair. The software showed its potential: The 7 patients who developed SAM after PL resection were classified as high risk (5 patients) and medium risk (2 patients) on the basis of the measured length of the resected PL. When the virtual PL resection was performed, fixing the PL length at 15 mm, all these patients were classified as low risk. This finding indicates that, if the software had been used preoperatively, a more aggressive PL resection would have been taken into account during the first cardiopulmonary bypass run, potentially avoiding SAM occurrence. We are currently developing virtual simulation of other techniques that are used to prevent the risk of SAM (edge-to-edge, artificial chordae and/or septal myectomy) and an algorithm to predict LVOTO after transcatheter mitral valve replacement [4, 5, 10, 11].

Limitations

We were unable to perform a full external validation, including a proper calibration check, for the SAM predictive model because the intercept value was unknown and estimated by our data. Anyway, this procedure is not the main purpose of this paper, and it does not significantly affect the discriminatory ability of the model and the validity of the software features. The software was not tested in patients undergoing the edge-to-edge procedure, because this technique is currently used to prevent SAM after repair. It is considered by definition a bias [4, 5], which obviously led to a tested population with slightly less prevalence of bileaflet prolapses, usually considered at high risk for SAM. In addition, the current model should be implemented with different surgical techniques and eventually calibrated with a larger population with degenerative mitral valves. PL resection and ring annuloplasty are the only techniques currently available for the virtual simulation.

CONCLUSION

Every mitral repair technique has the intrinsic risk of SAM. This risk depends on the correct application of these techniques in each specific anatomical presentation. This software has the potential to predict the risk of SAM preoperatively and, after a virtual step-by-step mitral repair simulation, depending on the technique adopted, always to achieve a low-risk SAM profile.

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Conflict of interest: none declared.

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