

# FACULDADE DE MEDICINA UNIVERSIDADE D COIMBRA

## MESTRADO INTEGRADO EM MEDICINA – TRABALHO FINAL

## Sara João Velho Moreira Machado Meirinhos

# Perioperative Morbi-mortality Analysis of Septal Myectomy during Aortic Valve Replacement

ARTIGO CIENTÍFICO ORIGINAL

ÁREA CIENTÍFICA DE CIRURGIA CARDIOTORÁCICA

Trabalho realizado sob a orientação de:

PROF. DOUTOR NUNO GONÇALO FREITAS COUTINHO

DR. PEDRO FILIPE MARQUES CORREIA

ABRIL 2021

# FACULDADE DE MEDICINA DA UNIVERSIDADE DE COIMBRA

# Perioperative Morbi-mortality Analysis of Septal Myectomy during Aortic Valve Replacement

Sara João Velho Moreira Machado Meirinhos<sup>1</sup>

Pedro Filipe Marques Correia<sup>1,2</sup>

Nuno Gonçalo Freitas Coutinho 1,2

 Faculdade de Medicina, Universidade de Coimbra, Portugal
 Serviço de Cirurgia Cardiotorácica, Centro Hospitalar e Universitário de Coimbra, Portugal

Morada Institucional: Polo III – Polo das Ciências da Saúde, Azinhaga de Santa Comba,

> Celas – 3000-548 Coimbra Endereço de Correio Eletrónico: goncalofcoutinho@gmail.com

"Ó Coimbra do Mondego E dos amores que eu lá tive Quem te não viu anda cego Quem te não amar não vive"

José Afonso

## INDEX

LIST OF ABBREVIATIONS	5
ABSTRACT	6
RESUMO	8
INTRODUCTION	
PATIENTS AND METHODS	
RESULTS	
DISCUSSION	
CONCLUSION	
ACKNOWLEDGEMENT	24
REFERENCES	25
APPENDICE I	

#### LIST OF ABBREVIATIONS

- AA Aortic Annulus
- AS Aortic Stenosis
- ASH Asymmetric Septal Hypertrophy
- AV Aortic Valve
- AVB Atrioventricular Block
- AVR Aortic Valve Replacement
- CSM Concomitant Septal Myectomy
- IVS Interventricular Septum
- LV Left ventricle
- LVEF Left Ventricular Ejection Fraction
- LVM Left Ventricular Mass
- LVOT Left Ventricular Outflow Tract
- NYHA New York Heart Association
- PPM Permanent Pacemaker
- RA Right Atrium
- SAVR Surgical Aortic Valve Replacement
- TAVR Transcatheter Aortic Valve Replacement
- TTE Transthoracic Echocardiography

#### ABSTRACT

**Introduction:** The treatment of aortic valve disease and, in particular, aortic valve stenosis (AS), has evolved significantly in the last decade with the development of percutaneous techniques, namely transcatheter aortic valve replacement (TAVR). Patients with severe AS usually have asymmetric septal hypertrophy (ASH), which can be treated by performing concomitant septal myectomy (CSM) during surgical aortic valve replacement (SAVR). The relevance of this project is the existence of scarce bibliography regarding this subject and the increasing number of TAVR procedures that are performed worldwide, which do not correct or deal with ASH. The aim of the study was to analyze the perioperative morbidity and mortality of patients submitted to CSM during SAVR compared to patients submitted to isolated SAVR.

**Methods:** This was a retrospective study of observationally collected data from patients undergoing either isolated SAVR (161) and SAVR combined with septal myectomy (97) at the Centro Hospitalar e Universitário de Coimbra (CHUC), from January 2018 to December 2019. Data were retrieved from clinical records during February 2021. Chi-square and t-student tests were used to establish associations and differences between variables, respectively, to determine causes of morbidity. The evaluation of perioperative echocardiographic data was analyzed using paired samples t-test and the comparison between groups was made by using the t-student test for independent samples. The Kaplan-Meier curves were used to analyze the mean overall survival between surgical groups. A p-value inferior to 0.05 was considered statistically significant.

**Results:** Patients submitted to CSM during SAVR were significantly older compared to patients undergoing isolated SAVR (71.5 $\pm$ 8.7 vs. 73.8 $\pm$ 7.3; p=.023). The majority of patients from both groups had heart failure NYHA class II. Hypertension was the most common comorbidity. Comparing the echocardiographic data between patients' groups, only the post-operative peak gradient was significantly higher in patients submitted to CSM (22.4 $\pm$ 10.8 vs. 29.9 $\pm$ 28.1; p=.028), but none of the groups showed to be superior in terms of change in echocardiographic perioperative data values. Age was found as the only variable associated with performing CSM (OR=1.037; 95% CI 1.003-1.071; p=.031). The mean cardiopulmonary bypass (p=.453) and aortic cross-clamp (p=.928) times did not differ between groups, supporting that CSM does not increase the duration of the surgery. Comparing CSM+SAVR versus isolated SAVR, postoperative complications and the duration of in-hospital stay were equivalent (p=.378). There was no difference in the survival distribution between groups (p=.161). This study agrees that

CSM is a safe and effective procedure. The importance of proceeding CMS can help the decision of the Heart Team between options like SAVR or TAVR for the treatment of AS.

**Conclusion:** Perioperative morbidity and mortality is not increased by the procedure of CSM during SAVR.

**Keywords:** Aortic Valve Replacement; Septal Myectomy; Aortic Stenosis; Asymmetric Septal Hypertrophy; Morbi-mortality; Perioperative.

#### RESUMO

**Introdução:** O tratamento da doença valvular aórtica e, em particular, da estenose valvular aórtica (AS), evoluiu significativamente na última década com o desenvolvimento das técnicas percutâneas, nomeadamente a TAVR (transcatheter aortic valve replacement). Pacientes com AS grave apresentam, geralmente, hipertrofia septal assimétrica (ASH), que pode ser tratada pela realização de miectomia septal concomitante (CSM) durante a substituição valvular aórtica (SAVR). A relevância do projeto passa pela existência de uma bibliografia escassa relativa a este assunto e do aumento, quase exponencial, de realização da TAVR um pouco por todo o mundo, sendo importante enfatizar que esta técnica não corrige nem aborda a ASH. O objetivo do estudo foi analisar a morbi-mortalidade peri-operatória de pacientes submetidos a miectomia septal durante a substituição valvular aórtica em comparação a doentes submetidos a substituição valvular aórtica isolada.

**Métodos:** Tratou-se de um estudo observacional retrospetivo, que analisou dados de doentes submetidos a SAVR isolada (161) e SAVR associada a miectomia septal (97) no Centro Hospitalar e Universitário de Coimbra (CHUC), de janeiro de 2018 a dezembro de 2019. Os dados clínicos foram colhidos a partir dos processos clínicos hospitalares durante fevereiro de 2021. Testes qui-quadrado e t-student foram usados para estabelecer associações e diferenças entre as variáveis, respetivamente, para determinar as causas de morbilidade. A avaliação dos dados ecocardiográficos perioperatórios foi realizada por meio do método paramétrico t-teste e a comparação entre os grupos foi feita pelo teste t-student para amostras independentes. As curvas de Kaplan-Meier foram utilizadas para analisar a sobrevida global média entre os grupos cirúrgicos. Um p-value inferior a 0,05 foi considerado estatisticamente significativo.

**Resultados:** Os pacientes submetidos a CSM+SAVR mostraram ser significativamente mais velhos, quando comparados com os pacientes submetidos a SAVR isolada (71,5  $\pm$  8,7 vs. 73,8  $\pm$  7,3; p = 0,023). A maior parte dos pacientes de ambos os grupos apresentaram insuficiência cardíaca classe II da NYHA. A hipertensão arterial foi a comorbilidade mais comum. Comparando os dados ecocardiográficos entre os grupos de pacientes, apenas o gradiente máximo pós-operatório foi significativamente superior nos pacientes submetidos a CSM (22,4  $\pm$  10,8 vs. 29,9  $\pm$  28,1; p = 0,028), mas nenhum dos grupos mostrou ser superior em termos de mudança nos valores de dados ecocardiográficos perioperatórios. Apenas a idade mostrou ser uma variável associada à realização de CSM (OR = 1,037; IC95% 1,003-1,071; p = 0,031). Os tempos médios de circulação extracorpórea (p=.453) e de clampagem aórtica (p=.928) não diferiram entre grupos, o que suporta o facto de que a CSM não aumenta a duração da cirurgia. Comparando os grupos CSM+SAVR versus SAVR isolada, a frequência de complicações pós-cirúrgicas e a duração do internamento hospitalar são equivalentes entre ambos (p=.378). Não houve diferença na distribuição de sobrevivência entre os grupos (p = 0,161). O presente estudo corrobora a tese de que a CSM é um procedimento seguro e eficaz. A importância de proceder à CSM ajuda na decisão da equipa médica e cirúrgica a optar entre técnicas como a SAVR ou TAVR para o tratamento da AS.

**Conclusão:** A morbi-mortalidade perioperatória da SAVR não é aumentada pela realização da CSM durante a SAVR.

**Palavras-Chave:** Substituição Valvular Aórtica; Miectomia Septal; Estenose Aórtica; Hipertrofia Septal Assimétrica; Morbi-mortalidade; Perioperatória.

#### INTRODUCTION

Aortic Stenosis (AS) is the most common primary valve disease treated by surgery or catheter intervention in Europe and North America, with a rising prevalence due to the ageing population.<sup>1</sup>

Moreover, AS is the most prevalent heart valve disease worldwide. Although interventional treatment options have speedily improved in recent years, symptomatic aortic valve stenosis is still associated with high morbidity and mortality. Calcific aortic valve stenosis is characterized by a progressive fibro-calcific remodeling and thickening of the aortic valve cusps, which subsequently leads to valve obstruction. Calcification is the consequence of the complex and fundamental pathophysiology that involves endothelial dysfunction, immune cell infiltration, myofibroblastic and osteoblastic differentiation.<sup>2</sup>

Echocardiography is the key diagnostic instrument. It confirms the presence of AS, assesses the degree of valve calcification, left ventricle (LV) function and wall thickness, detects the presence of other associated valve disease or aortic pathology and provides prognostic information. The key element for assessing the severity of aortic stenosis is doppler echocardiography. For clinical decision making, flow rate, mean pressure gradient - the most robust measurement -, ventricular function, size and wall thickness, degree of valve calcification, blood pressure and functional status have also to be considered. Exercise testing is recommended in physically active patients for revealing symptoms and for risk stratification of asymptomatic patients with severe aortic stenosis.

According to echocardiography results, severe aortic stenosis is defined as an aortic valve area <1 cm<sup>2</sup>, mean gradient >40mmHg, and/ or peak flow velocity > 4 m/s.<sup>3</sup>

Protocols for severe aortic valve stenosis treatment include surgical aortic valve replacement (SAVR), balloon valvuloplasty, transcatheter aortic valve replacement (TAVR), and medical treatment. The success rates are getting higher among the well adapted SAVR and the lately popular TAVR, so it's important to suit the best treatment for the right patient.<sup>3</sup>

To date, no pharmacotherapy has been established to prevent aortic valve calcification.<sup>2</sup> Medical therapy don't block the development of aortic stenosis process. Although progression of degenerative AS is an active process, sharing a number of similarities with atherosclerosis, randomized trials have consistently shown that statins do not affect the progression of aortic stenosis. Patients with symptoms of heart failure who are unsuitable candidates for surgery or TAVR and the ones who are currently awaiting surgical or catheter intervention, should be medically treated according to the heart failure guidelines.<sup>1,4</sup>

TAVR has emerged as a safe and effective therapeutic option for patients with severe AS who are at prohibitive, high, or intermediate risk for SAVR. However, in low-risk patients, SAVR remains the standard therapy in current clinical practice. A recent study has suggested comparable outcomes with TAVR and SAVR in low-risk patients with severe AS.<sup>5</sup> However, long-term valve durability of transcatheter heart valves remains uncertain.<sup>5</sup>

The findings about the trend in morbidity and mortality in SAVR support the hypothesis that mortality and morbidity rates following SAVR have significantly improved over the years, even for patients at high risk and it is substantially lower than those observed in trials comparing TAVR with SAVR. Improvements in surgical and postoperative care have translated into a significant reduction in mortality rate and in periprocedural complications. These results along with the better long-term benefit given by SAVR provide more evidence when deciding for future TAVR indications.<sup>6</sup>

Patients with severe AS usually have asymmetric septal hypertrophy (ASH).<sup>7,8,9</sup> A routine of intraoperative inspection of left ventricular outflow tract (LVOT) strategy for SAVR can be adopted because of low sensitivity of echocardiography for detecting dynamic LVOT obstruction in severe AS, in order to know if there are criterions to perform concomitant septal myectomy (CSM). This type of hypertrophy combined with severe AS can be related to residual LVOT obstruction following SAVR and a deteriorating postoperative course. Intraoperative findings of ASH in patients undergoing SAVR for moderate-to-severe AS do not seem to be uncommon, and CSM for ASH can be performed without additional risks. Preoperative echocardiographic measurement of the LVOT/ AA (Left Ventricular Outflow Tract / Aortic Annulus) ratio may be helpful in corroborating the intraoperative finding of ASH. As the implanted valve size  $\leq 21$  mm was the only risk factor for CSM, a careful assessment of the LVOT is important in patients with a small AA and small LVOT/AA ratio (LVOT/AA <0.7) at the time of AVR.<sup>7</sup>

Related conditions such as female sex, history of hypertension, and high aortic gradients in patients with severe aortic stenosis should raise a suspicion for the presence of ASH. <sup>8</sup> Surgeons should inspect the LVOT for possible concomitant myectomy at the time of SAVR.<sup>7,8</sup> CSM can be the simple additional procedure that does not increase the operative risk to resect obstructive muscle mass. Therefore, CSM should be considered for patients with a preoperative or intraoperative diagnosis of ASH, even though dynamic obstruction is not demonstrated.<sup>8</sup>

The echocardiographic sensitivity for detecting dynamic left ventricular obstruction in severe AS is low, but there are compilations of preoperative echocardiographic parameters that correlate with the SAH findings, for later determination of the predictors for performing the septal myectomy.<sup>7</sup> Moreover, there is a recent study that evaluated the surgical results of septal myectomy and considered it safe and effective.<sup>9</sup>

The relevance of this project is the existence of scarce bibliography regarding this subject and the increasing number of TAVR procedures that are performed worldwide, which do not correct or deal with ASH.

Therefore, the aim of this study was to compare the perioperative morbidity and mortality in patients undergoing CSM during SAVR versus isolated SAVR.

### PATIENTS AND METHODS

#### Ethical Statement

Ethical and legal requirements were met, the study was approved and a waiver for patients' consent for using clinical information was obtained.

This project is a retrospective observational study of perioperative collected data from patients undergoing either isolated SAVR or SAVR combined with CSM at the Centro Hospitalar e Universitário de Coimbra (CHUC), from 1<sup>st</sup>January 2018 to 31<sup>st</sup> December 2019.

#### Patient Population

Patients included in the study cohort underwent SAVR or SAVR+CSM using mechanical or stented biological valves.

Patients with concomitant procedures and previous heart surgeries of any type were excluded. Patients undergoing multiple valves, or another major non-valve and redo surgery were also excluded.

The study population included 258 patients, of whom 97 were submitted to SVAR+CSM and 161 to isolated SVAR.

Demographics and perioperative characteristics were extracted from patient's records and analyzed across February 2021.

### Perioperative (preoperative, Intra-operative and postoperative) Evaluations

The pathology of the AV was preoperatively confirmed by transthoracic echocardiography (TTE). Severe AS was diagnosed with TTE by measuring the AV peak transvalvular pressure gradient, mean transvalvular pressure gradient and the AV orifice area in the systolic phase. Ventricular septal diameter and posterior free wall diameter were also measured preoperatively in the parasternal long-axis view.

### **Operative Technique**

Median sternotomy. Opening and suspension of the pericardium. Establishing standard extracorporeal circulation by cannulation of the ascending aorta and right atrium (RA). LV decompression by cannulation through the upper right pulmonary vein and left atrium,

cooling down to 28°C. Aortic clamping. Administration of cardioplegia directly in the coronary ostia, if significant aortic regurgitation was present, or in the ascending aorta through a catheter if not. Oblique aortotomy, excision of the native aortic valve and evaluation of the LV outflow tract for subvalvular obstruction or bulging of the interventricular septum. If present, myectomy was performed consisting of resection of septal muscle from the nadir of the right aortic sinus to the commissure between the left and right cusps. We generally take a generous piece of myocardial septum (2—3 cm long, 1—2 cm wide, and 0.5—0.7 cm deep). Implantation of the aortic prosthesis was made usually with interrupted simple 2/0 polyester sutures.

#### **Statistical Analysis**

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 25. Descriptive statistics included mean and standard deviation for continuous variables, and absolute and relative frequency for categorical variables. Chisquare and t-student tests were used to establish associations and differences between variables, respectively. The change between pre-operative and post-operative echocardiographic data was analyzed using paired samples t-test and the comparison between groups was made by using the t-student test for independent samples. The Kaplan-Meier curves were used to analyze the mean overall survival between surgical groups. Univariate logistic regression was used to determine predictors for performing CSM during SAVR. A p-value inferior to 0.05 was considered statistically significant.

#### RESULTS

This study included data of a total of 258 patients, 97 of whom underwent CSM during SAVR. The sample's features before surgery are shown in Table 1. Patients submitted to CSM during SAVR were significantly older compared to patients undergoing isolated SAVR (71.5±8.7 vs. 73.8±7.3; p=.023). The majority of patients from both groups had heart failure NYHA class II and hypertension was the most common comorbidity. There were no other significant differences between the two groups regarding demographic data and comorbidities.

	S		
Variable	SAVR (n=161)	SAVR+CSM (n=97)	P-value
Age (years), mean±SD	71.5±8.7	73.8±7.3	.023*
Gender, n (%)			.849
Female	75 (46.6%)	44 (45.4%)	
Male	86 (53.4%)	53 (54.6%)	
NYHA class, n (%)			.219
1	12 (7.5%)	11 (11.3%)	
Ш	89 (55.3%)	42 (43.3%)	
ш	54 (33.5%)	36 (37.1%)	
IV	6 (3.7%)	7 (7.2%)	
Comorbidities, n (%)			
Heart failure	11 (6.8%)	8 (8.2%)	.673
Diabetes mellitus	49 (30.4%)	30 (30.9%)	.959
Hypertension	128 (79.5%)	85 (87.6%)	.096
Dyslipidemia	109 (67.7%)	72 (74.2%)	.267
COPD	11 (6.8%)	3 (3.1%)	.199
Stroke	11 (6.8%)	9 (9.3%)	.332
Peripheral Vascular Disease	7 (4.3%)	5 (5.2%)	.774
Chronic Kidney Disease	9 (5.6%)	2 (2.1%)	.174
Atrial Fibrillation	22 (13.7%)	10 (10.3%)	.428
Creatinine (mg/dL), mean±SD	1.1±1.0	0.9±0.3	.098

#### TABLE 1 | Preoperative features of patients submitted to SAVR.

\* **p-value<0,05**; COPD, Chronic obstructive pulmonary disease; CSM, Concomitant septal myectomy; NYHA, New York Heart Association; SAVR, Surgical aortic valve replacement; SD, standard deviation.

The mean cardiopulmonary bypass (p=.453) and aortic cross-clamp (p=.928) times did not differ between groups. The frequency of post-surgical complications and the duration of in-hospital stay (p=.378) was also comparable irrespectively to the procedure (Table 2).

	Surgical treatment		
Variable	SAVR (n=161)	SAVR+CSM (n=97)	P-value
Cardiopulmonary bypass duration (min), mean±SD	71.3±20.4	74.9±54.5	.453
Aortic cross-clamp duration (min), mean±SD	44.8±11.3	44.7±9.8	.928
Creatinine (mg/dL), mean±SD	1.4±1.0	1.3±1.0	.556
Complications, n (%)			
Atrial Fibrillation	33 (20.5%)	18 (18.6%)	.734
Stroke	3 (1.9%)	2 (2.1%)	.902
Chronic Kidney Disease	14 (8.7%)	7 (7.2%)	.691
Pacemaker implantation	6 (3.7%)	4 (4.1%)	.860
Inotropic support	2 (1.2%)	2 (2.1%)	.598
In-hospital stay duration (days), mean±SD	8.8±4.4	9.5±7.1	.378

TABLE 2 | Intraoperative and postoperative features of patients submitted to SAVR.

CSM, Concomitant septal myectomy; SAVR, Surgical aortic valve replacement; SD, standard deviation.

Table 3 compares the echocardiographic data between patients undergoing CSM during SAVR and patients submitted to isolated SAVR. Only the post-operative peak gradient was significantly higher in patients submitted to CSM ( $22.4\pm10.8$  vs.  $29.9\pm28.1$ ; p=.028), but no significant differences were registered concerning the remaining pre-operative or post-operative data. In fact, the post-operative interventricular septum (IVS) thickness was similar in both groups ( $12.6\pm4.4$  vs.  $12.3\pm4.2$ ; p=.863). Both groups showed a significant decrease in the mean (p<.001) and peak gradient (p<.001) values after surgery, but not concerning the IVS thickness or the left ventricular ejection fraction LVEF. None of the groups showed to be superior in terms of change in echocardiographic data between pre-operative and post-operative values.

	Surgical treatment		
Variable, mean±SD	SAVR (n=161)	SAVR+CSM (n=97)	P-value
Pre-operative			
Aortic valve area (cm²)	0.8±0.7	0.8±1.1	.855
IVS (mm)	13.5±2.8	14.2±3.3	.207
LVEF (%)	59.8±10.0	62.0±9.0	.253
Mean gradient (mmHg)	50.9±12.8	51.5±10.0	.665
Peak gradient (mmHg)	88.4±71.6	81.0±15.1	.361
Post-operative			
Aortic prothetic valve area (cm <sup>2</sup> )	0.8	1.7±1.7	.662
IVS (mm)	12.6±4.4	12.3±4.2	.863
LVEF at discharge (%)	59.3±13.0	62.8±9.1	.157
Mean gradient (mmHg)	12.2±6.5	14.2±8.8	.061
Peak gradient (mmHg)	22.4±10.8	29.9±28.1	.028
Change in values			
∆IVS (mm)	-1,2±5,5	-4,0±5,4	.315
∆LVEF (%)	1,5±11,6	1,7±11,8	.953
∆Mean gradient (mmHg)	-38,8±13,7	-37,8±13,0	.617
∆Peak gradient (mmHg)	-67,2±76,5	-52,0±27,9	.128

 TABLE 3 | Echocardiographic findings of patients submitted to SAVR.

CSM, Concomitant septal myectomy; IVS, Interventricular septum; LVEF, Left ventricular ejection fraction; SAVR, Surgical aortic valve replacement; SD, standard deviation.

Table 4 shows the univariate logistic regressions results for predicting CSM during SAVR. Age was found as the only variable associated with performing CSM (OR=1.037; 95% CI 1.003-1.071; p=.031).

Variables	OR	CI 95%	P-value
Age (for each 1 year)	1.037	1.003-1.071	.031
Male	1.050	0.634-1.742	.849
NYHA class III-IV	1.366	0.817-2.283	.234
Comorbidities			
Heart failure	1.226	0.475-3.162	.674
Diabetes mellitus	1.014	0.587-1.751	.959
Hypertension	1.826	0.893-3.734	.099
Dyslipidemia	1.374	0.783-2.411	.268
COPD	0.435	0.118-1.601	.211
Stroke	1.411	0.562-3.539	.463
Peripheral Vascular Disease	1.188	0.366-3.852	.774
Chronic Kidney Disease	0.356	0.075-1.681	.192
Atrial Fibrillation	0.726	0.328-1.607	.430
Creatinine	0.472	0.197-1.131	.092
Pre-operative ecochardiographic findings			
Interventricular septum	1.077	0.964-1.204	.188
LVEF	1.025	0.996-1.056	.093
Valve area	1.031	0.741-1.435	.854
Peak gradient	0.996	0.985-1.007	.446
Mean gradient	1.005	0.983-1.027	.682

TABLE 4 | Univariate logistic regression for predictors of CSM during SAVR.

COPD, Chronic obstructive pulmonary disease; CSM, Concomitant septal myectomy; LVEF, Left ventricular ejection fraction; NYHA, New York Heart Association; SAVR, Surgical aortic valve replacement.

The mean survival time was 159.8 weeks (95% CI 155.9-163.7) for patients undergoing CSM during SAVR and 154.6 weeks (95% CI 149.1-160.2) for those not submitted to CSM (Figure 1). There was no difference in the survival distribution between groups (p=.161). Two patients submitted to SAVR exclusively died during the in-hospital stay, 7 and 21 days after surgery.



#### FIGURE 1 | Survival after surgery.

#### DISCUSSION

AS predominantly affects the elderly, with a prevalence of severe status ranging from 0.2% for those aged 50–59years to 9.8% for those aged 80–89years.<sup>10</sup> However, age is considered an independent determinant of post-operative mortality and complications. Comparison between age groups is used to report long-term survival, stratifying patients based on established risk scores. Guidelines recommend that the selection and modes of intervention for AS should be founded on established preoperative risk scores rather than just age, which is supported by data that reveals that all age groups had satisfactory survival outcomes after SAVR.<sup>10</sup> These conclusions are validated by this project because despite the fact that patients submitted to CSM during SAVR were significantly older compared to patients undergoing isolated SAVR, there was no significant difference in the survival distribution between groups (p=.161).

Considering that the incidence of AS is increasing and is the most common valvular heart disease, ASH combined with severe AS is not a rare condition.<sup>7</sup> Hospital mortality for aortic valve surgery in the elderly has been declining over the past decades, probably due to better myocardial protection, anesthesia and postoperative care techniques, which encourage the performance of this procedure in elderly patients.<sup>11</sup>

There is no consensus for the strategy for managing ASH at the time of SAVR because of scarce literature and no large cohort or a randomized controlled trial. Some studies suggest the procedure of CSM in the cases of dynamic LVOT obstruction with septal anterior motion and recommend no routine resection of ASH at the time of AV surgery because of possible CSM related complications such as the need for permanent pacemaker (PPM) or septal perforation.<sup>7</sup>

This report provides that postoperative complications and the duration of in-hospital stay (p=.378) were comparable between isolated SAVR and CSM+SAVR (Table 2), confirming that CSM for ASH can be performed without additional risks, as demonstrated by other studies.<sup>7</sup>

The mean cardiopulmonary bypass (p=.453) and aortic cross-clamp (p=.928) times did not differ between groups, supporting that CSM does not increase the duration of the surgery. In fact, this statement can be important because of the impact of longer surgeries. Other studies suggest that prolonged cardiopulmonary bypass time of >180 minutes, in patients over 80 years, were associated with a >50% probability of death within 1 year.<sup>12</sup> None of the groups showed to be superior in terms of change in echocardiographic data between pre-operative and post-operative values. It could be interesting to analyze the evolution for longer time than perioperative, to have more robust conclusions about septal myectomy impact on imaging exams.

The fact that there was no difference in the survival distribution between groups (p=.161) is important to improve the evidence that CSM doesn't increase the probability of mortality. The study reported that two patients submitted to isolated SAVR died during the in-hospital stay, 7 and 21 days after surgery.

The choice of intervention in symptomatic aortic stenosis must be based on careful individual evaluation of technical suitability and weighing of risks and benefits of each modality. SAVR is recommended in patients at low surgical risk (STS or EuroSCORE II < 4% or logistic EuroSCORE I < 10% and no other risk factors not included in these scores, such as frailty, porcelain aorta, sequelae of chest radiation). TAVR is recommended in patients who are not suitable for SAVR as assessed by the Heart Team.<sup>1</sup> To date, new articles provide the evidence that TAVR may be preferred over SAVR in low-risk patients, who are candidates for bioprosthetic SAVR, although the durability of the valve remains uncertain. Therefore, it is pertinent to identify the advantages of CSM during SAVR and its impact on morbidity and mortality of patients' candidate to open surgery practice, in order to treat not only the calcification of the valve by the replacement, but also the degree of subvalvular obstruction resulting from ASH.

One of the weaknesses of this study is being a retrospective observational study, not a randomized controlled one. Randomized controlled trials are considered the highest quality of scientific evidence.<sup>13</sup> Also, the decision for septal myectomy was mostly based on intraoperative assessment by the operating surgeon, not measured predictors.

Limitations can be related to the relatively small population, partly because of strict inclusion criteria, which were adopted to improve the homogeneity of the study population and to verify the strategy of our surgical approach to ASH with AS. Also, the follow-up duration was short, just including perioperative time for morbidity and until three years for mortality. Longer follow-up with a larger population may provide enough statistical power to demonstrate differences in LV mass regression between CSM+SAVR and isolated SAVR, and the evolution of interventricular septum itself. LV remodeling due to the severe AS was documented by an increase left ventricular mass (LVM), LVM

index, and interventricular septum thickness preoperatively. Di Tommaso et al found that, at 5 years of follow-up, patients with added myectomy had a more favorable reduction in the LVM, LVM index and interventricular septum thickness than the patients with isolated SAVR. The study showed that in patients with a hypertrophied septum, CSM during SAVR improves the regression of the LVM and diastolic function and does not increase the operative risk.<sup>9</sup>

#### CONCLUSION

Increasing age was found to be associated with performing CSM. Postoperative complications and the duration of in-hospital stay between groups of isolated SAVR and CSM+SAVR were comparable. CSM did not prolong cardiopulmonary bypass time and there was no difference in the survival distribution between groups. The findings support the hypothesis that perioperative morbidity and mortality is not increased by the procedure of septal myectomy during SAVR.

More studies within this area should be encouraged. In particular, performing metaanalysis or randomized controlled trials on the impact on log-term survival of doing CSM during SAVR would be interesting to determine the importance of septal myectomy on full treatment of AS. In fact, these projects could help the Heart Team to make the decision between AS treatment options.

#### ACKNOWLEDGEMENT

Ao Prof. Doutor Gonçalo Coutinho, por ter aceitado o convite para ser meu Orientador. Ao Dr. Pedro Correia, pela assistência. Terminada a elaboração do Trabalho Final de Mestrado, voltaria a fazer a mesma escolha.

Aos meus pais, Berta e Francisco, que são o verdadeiro motivo e razão para que eu seja aspirante a médica, escritora, ativista, política. À Madrinha Antónia, que me ensina a ser mais persistente do que insistente na luta pelas minhas próprias causas. Ao meu Padrinho de vida, Célio, por ser um brilhante clínico e médico, que me inspira a ser sempre um pouco mais. À Tia Olga, que me incita a encarar o mundo com delicadeza e graça, sem perder a determinação.

Aos amigos que me mostram diariamente o que significa ser Médica na verdadeira aceção da palavra, no sentido de altruísmo e humanismo: Maria, Rita, Sofia, Catarina, Beatriz, Mafalda, Filipe, Miguel Pacheco, Miguel Oliveira, Filipa, Pedro.

Aos amigos que me ensinaram a ser estudante da Academia Coimbrã, e a pertencer-Ihe verdadeiramente: Rodrigo, João Vasco, João Maria, Sofia, David e Alexandre.

Às amigas que me proporcionaram a melhor experiência enquanto Estudante de Medicina na Invicta e sem as quais eu não seria quem sou hoje: Inês, Maria Cunha, Filipa, Carolina, Maria Cameira.

Às amigas do colégio, ao lado de quem tantas vezes sonhei e com as quais tenho visto os ideais ganharem concretização e forma: Catarina Sá, Catarina Reis, Catarina Magalhães, Catarina Silva e Rafaela.

### REFERENCES

- 1. Baumgartner H, Hung J, Bermejo J, et al. Recommendations on the echocardiographic assessment of aortic valve stenosis: A focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *Eur Heart J Cardiovasc Imaging*. 2017;18(3):254-275. doi:10.1093/ehjci/jew335
- Goody PR, Hosen MR, Christmann D, et al. Aortic valve stenosis: From basic mechanisms to novel therapeutic targets. *Arterioscler Thromb Vasc Biol.* 2020;(April):885-900. doi:10.1161/ATVBAHA.119.313067
- Ali Yesiltas M, Haberal I, Kuserli Y, Yildiz A, Koyuncu AO, Özsoy SD. Comparison of short and mid-term mortality and morbidity in patients with severe aortic stenosis (intermediate/high risk) who underwent transcatheter aortic valve replacement and surgical aortic valve replacement. *Heart Surg Forum*. 2020;23(2):E212-E220. doi:10.1532/HSF.2913
- 4. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2016;37(27):2129-2200m. doi:10.1093/eurheartj/ehw128
- Kolte D, Vlahakes GJ, Palacios IF, et al. Transcatheter Versus Surgical Aortic Valve Replacement in Low-Risk Patients. *J Am Coll Cardiol*. 2019;74(12):1532-1540. doi:10.1016/j.jacc.2019.06.076
- 6. Dimagli A, Sinha S, Caputo M, Angelini GD, Benedetto U. Trend in morbidity and mortality in surgical aortic valve replacement: A retrospective, observational, single-centre study. *Interact Cardiovasc Thorac Surg.* 2021;31(6):796-802. doi:10.1093/icvts/ivaa189
- Yong Lim J, Choi JO, Jae Kon O, Li Z, Park SJ. Concomitant septal myectomy in patients undergoing aortic valve replacement for severe aortic stenosis. *Circ J*. 2015;79(2):375-380. doi:10.1253/circj.CJ-14-0672
- 8. Kayalar N, Schaff H V., Daly RC, Dearani JA, Park SJ. Concomitant Septal Myectomy at the Time of Aortic Valve Replacement for Severe Aortic Stenosis. *Ann Thorac Surg.* 2010;89(2):459-464. doi:10.1016/j.athoracsur.2009.10.065
- 9. Di Tommaso L, Stassano P, Mannacio V, et al. Asymmetric septal hypertrophy in patients with severe aortic stenosis: The usefulness of associated septal myectomy. *J Thorac Cardiovasc Surg.* 2013;145(1):171-175. doi:10.1016/j.jtcvs.2011.10.096
- 10. Hussain AI, Auensen A, Brunborg C, Beitnes JO, Gullestad L, Pettersen KI. Agedependent morbidity and mortality outcomes after surgical aortic valve replacement. *Interact Cardiovasc Thorac Surg.* 2018;27(5):650-656. doi:10.1093/icvts/ivy154
- 11. Valle FH, Costa AR, Pereira EMC, et al. Morbidity and mortality in patients aged over 75 years undergoing surgery for aortic valve replacement. *Arq Bras Cardiol*. 2010;94(6):720-725. doi:10.1590/S0066-782X2010005000052
- 12. Atladottir HO, Modrau IS, Jakobsen CJ, Torp-Pedersen CT, Gissel MS, Nielsen DV. Impact of perioperative course during cardiac surgery on outcomes in patients 80 years and older. *J Thorac Cardiovasc Surg*. Published online 2020. doi:10.1016/j.jtcvs.2020.03.005
- 13. Chow JTY, Lam K, Naeem A, Akanda ZZ, Si FF, Hodge W. The pathway to RCTs: How many roads are there? Examining the homogeneity of RCT justification. *Trials*. 2017;18(1):1-7. doi:10.1186/s13063-017-1804-z

#### **APPENDICE I** PERCURSO ACADÉMICO DURANTE A ELABORAÇÃO DO TRABALHO FINAL DE MESTRADO

#### 6º ano curricular - escrita, entrega e dissertação do Trabalho Final de Mestrado

- Oradora na Conferência "Vacinação: Portugal, Europa e Mundo", ao lado do Dr. Ricardo Baptista Leite, evento promovido pelo Núcleo de Estudantes Sociais-Democratas do Instituto de Estudos Políticos da Universidade Católica Portuguesa.
- Publicação de artigo de opinião no Jornal "Público", intitulado "A importância de ser Europa".
- Oradora no Congresso "In2ME", desenvolvido pelo Núcleo de Estudantes de Medicina da Universidade da Beira Interior sobre "O Futuro da Educação Médica em Portugal", juntamente com o Prof. Doutor Miguel Castelo Branco, Diretor da Faculdade de Ciências da Saúde da Universidade da Beira Interior e Prof. Doutora Isabel Neto, Docente Agregada e Investigadora da mesma Instituição de Ensino.
- Membro da Direção da Associação Nacional de Estudantes de Medicina (ANEM), enquanto Diretora de Educação Médica e National Officer on Medical Education na International Federation of Medical Students Association (IFMSA):
  - Moderadora Mesa Redonda "Medical Students Acess to Clinical ecords: At What Cost", na presença do Prof. Doutor Rui Guimarães, que tem funções na Administração Pública na Área da Saúde, e é, atualmente, o Responsável pelo Acesso à Informação do Centro Hospitalar Universitário de São João e Professor Auxiliar da Faculdade de Medicina da Universidade do Porto, Dr. Luís Goes pinheiro, Presidente do Conselho de Administração dos Serviços Partilhados do Ministério da Saúde, Eng.ª Maria João Campos, Diretora dos Serviços de Sistemas e Tecnologias de Informação e Comunicação do centro Hospitalar e Universitário São João e Dr.ª Sónia Dória Braga, Data Protection Officer no Hospital de Braga;
  - Investigadora Principal dos Estudos da Área de Educação Médica da ANEM "Aferição das Intenções Emigratórias dos Estudantes de medicina Nacionais na Vinculação Profissional em Portugal ou no Estrangeiro" e "Condições Pedagógicas de Ensino em Meio Clínico das Escolas Médicas Portuguesas";

 Oradora no Congresso "Beyond MEd", promovido pela Associação de Estudantes de Medina de Lisboa e Conselho Pedagógico da Faculdade de Medicina da Universidade de Lisboa, palestra subordinada ao tema "The Covid-19 Pandemic and its Impact on Medical Education", ao lado da Professor Trudie E. Roberts, presidente *da Association for Medical Education in Europe* até agosto de 2019 e membro do Conselho Educacional da RCPS Glasgow, bem como do Prof. Doutor Fausto Pinto, Presidente do Conselho das escolas Médicas Portuguesas e Prof.a Doutora Suzane Ono, graduada em Medicina pela Universidade Federal do Panamá, mestre em Gastroenterologia Clínica pela Universidade de São Paulo e doutoranda em Medicina Interna - Tokyo University (2000).

#### 5º ano curricular – elaboração e entrega do Projeto do Trabalho Final de Mestrado

- Membro da Direção da Associação Nacional de Estudantes de Medicina (ANEM), enquanto Diretora de Educação Médica e National Officer on Medical Education na International Federation of Medical Students<sup>2</sup> Association (IFMSA):
  - Oradora no Webinar organizado pela "Rede de Investigação em Educação Médica - RIEM", sob o mote "O Ensino Clínico no contexto da retoma da pandemia: que desafios e soluções?", juntamente com o Sr. Presidente do Conselho de Escolas Médicas Portuguesas e o Sr. Bastonário da Ordem dos Médicos;
  - Oradora num webinar organizado pela empresa UpHILL, em debate com o Presidente do Conselho Pedagógico da Faculdade de Medicina da Universidade de Lisboa (FMUL);
  - Entrevistadora na atividade TalkMedToMe da ANEM, ao Presidente do Conselho de Escolas Médicas Portuguesas.
- Membro da redação da Revista "aNEMia" do Núcleo de Estudantes da Medicina da Associação Académica de Coimbra (NEM/AAC):
  - Apresentação oral sobre a existência de Médicos Não Especializados na presença do Presidente do Conselho de Escolas Médicas Portuguesas, Diretor da Faculdade de Medicina da Universidade de Coimbra, Diretor Clínico Centro Hospitalar ((CHUC) e Universitário de Coimbra e Diretor do Internato Médico CHUC, a propósito do evento de lançamento da 55<sup>a</sup> edição revista "aNEMia";
  - Entrevista à banda "Os Quatro e Meia".

- Vencedora do concurso do Congresso "Call ME", e publicação de uma Carta Aberta ao Primeiro Ministro sobre a afetação política nacional e europeia das medidas em saúde, com posterior publicação na "Acta Médica Portuguesa -Student", a 4 de novembro de 2019;
- Membro da Comissão de Curso do 5º ano Faculdade de Medicina da Universidade de Coimbra (FMUC), em representação de duas valências de Unidades Curriculares Integradas;
- Membro da Comissão Organizadora do Congresso Médico-científico "In4Med" do Núcleo de Estudantes de Medicina da Associação Académica de Coimbra (NEM/AAC);
- Formanda da informação da Rádio Universidade de Coimbra (RUC).