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Myagmardorj, R.; Nabeta, T.; Hirasawa, K.; Singh, G.K.; Kley, F. van der; Weger, A. de; ... ; Delgado, V.

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# Association Between Chronic Obstructive Pulmonary Disease and All-Cause Mortality After Aortic Valve Replacement for Aortic Stenosis



Rinchyengkhand Myagmardorj, MD<sup>a</sup>, Takeru Nabeta, MD<sup>a</sup>, Kensuke Hirasawa, MD, PhD<sup>a</sup>, Gurpreet K. Singh, MD<sup>a</sup>, Frank van der Kley, MD, PhD<sup>a</sup>, Arend de Weger, MD<sup>b</sup>, Nina Ajmone Marsan, MD, PhD<sup>a</sup>, Jeroen J. Bax, MD, PhD<sup>a,\*</sup>, and Victoria Delgado, MD, PhD<sup>a,c</sup>

**Chronic obstructive pulmonary disease (COPD) and aortic stenosis (AS) are the most common diseases in which age plays a major role in the increase of their prevalence and when they co-exist, the outcomes prognosis worsens significantly. The aim of the present study was to evaluate the association between pulmonary functional parameters and all-cause mortality after aortic valve replacement (transcatheter or surgical). A total of 400 patients with severe AS and preoperative pulmonary functional test were retrospectively analyzed. Echocardiography and pulmonary functional parameters before aortic valve replacement were collected. COPD severity was defined according to criteria from the Society of Thoracic Surgeons. COPD was present in 128 patients (32%) with severe AS. Patients without COPD had smaller left ventricular (LV) mass and LV end-systolic volume and better LV function than the group with COPD. During a median follow-up of 32 months, 92 patients (23%) died. The survival rates were significantly lower in patients with moderate and severe COPD (log-rank  $p = 0.003$ ). In the multivariable Cox regression analysis, any grade of COPD was associated with an approximately 2-fold increased risk of all-cause mortality (hazard ratio 1.933; 95% confidence interval 1.166 to 3.204;  $p = 0.011$  for mild COPD and hazard ratio 2.028; 95% confidence interval 1.154 to 3.564;  $p = 0.014$  for moderate or severe COPD). In addition to other clinical factors, any grade of COPD was associated with 2-fold increased risk of all-cause mortality. © 2022 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>) (Am J Cardiol 2023;190:41–47)**

Chronic obstructive pulmonary disease (COPD) is the most prevalent chronic pulmonary disease and is the third cause of death and years of life lost after ischemic heart disease and stroke.<sup>1</sup> In addition, aortic stenosis (AS) is the most common valvular heart disease in the Western world.<sup>2</sup> For both diseases (COPD and AS), age plays a major role in the increase of their prevalence and percentual change in mortality over the years. In severe AS, aortic valve replacement (AVR) is the only treatment that has demonstrated to improve survival.<sup>3</sup> Yet, the presence of co-morbidities

increases the operative risk and influences the outcomes negatively after AVR.<sup>4</sup> The frequency of COPD among patients undergoing AVR due to severe AS ranges between 19% and 43%.<sup>5</sup> Notably, in a recent meta-analysis, COPD has been associated with an increased risk of all-cause mortality, with a hazard ratio of 1.34.<sup>6</sup> However, the definition of COPD varies across the studies and is not always based on the use of pulmonary function tests (PFTs). Accordingly, the aim of the present study was to evaluate the association between pulmonary functional parameters and all-cause mortality after AVR in a large cohort of patients with severe AS.

## Methods

Patients with severe AS who underwent surgical or transcatheter AVR between January 2001 and July 2017 were screened retrospectively for the presence of documented COPD with functional lung test. Patients who received only medical therapy or aortic valve balloon dilatation or had incomplete pulmonary functional data were excluded (Figure 1). The decision of performing surgical or transcatheter AVR was based on the heart team's discussions.<sup>7,8</sup> After AVR, patients were discharged from the hospital and followed up by the referring physician.

From the electronic medical records of the Leiden University of Medical Center (EPD-vision and Hix, Leiden, The Netherlands), demographic and clinical data, including

<sup>a</sup>Department of Cardiology; <sup>b</sup>Department of Cardio-Thoracic Surgery, Heart Lung Center, Leiden University Medical Center, Leiden, The Netherlands; and <sup>c</sup>Department of Cardiovascular Imaging, University Hospital Germans Trias i Pujol, Barcelona, Spain. Manuscript received June 16, 2022; revised manuscript received and accepted November 4, 2022.

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See page 46 for disclosure information.

\*Corresponding author: Tel: + 31 (0)71 526 2020.

E-mail address: [J.J.Bax@lumc.nl](mailto:J.J.Bax@lumc.nl) (J.J. Bax).

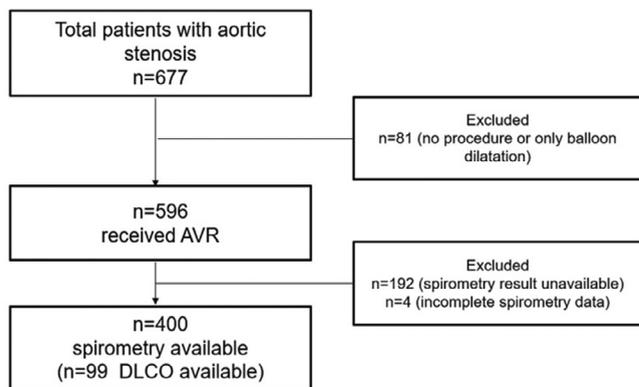


Figure 1. Study flow chart.

symptoms, co-morbidities, and medications, were collected. Furthermore, echocardiographic and PFTs were retrieved and analyzed. For the retrospective analysis of clinically collected data, the institutional review board approved the study and waived the need for patient written informed consent.

PFTs (including plethysmography) were performed before AVR, according to the European Respiratory Society and American Thoracic Society recommendations.<sup>9</sup> Forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), Tiffeneau index (ratio of FEV1/FVC), vital capacity (VC), peak expiratory flow, and inspiratory capacity were expressed as absolute values and percentage of a theoretical value calculated by the Global Lung Function 2012 equations.<sup>10</sup> Patients were divided according to the results of FEV1 and the categories defined in the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database: normal pulmonary function was defined by an FEV1 >75% of predicted, mild COPD if FEV1 was 60% to 75% of predicted, moderate COPD if FEV1 was 50% to 59% of predicted, and severe COPD when FEV1 <50% of predicted.<sup>11</sup>

Patients underwent transthoracic echocardiography before AVR. Echocardiographic data were acquired with available ultrasound systems (Vivid-7, E9 and E95; GE Healthcare), triggered to electrocardiographic signal, and stored for subsequent offline analysis. The ultrasound systems were equipped with the MS5 and 4Vc-D 4-D matrix cardiac probes. The 2-dimensional, color, spectral continuous and pulsed-wave Doppler images were obtained from the parasternal, apical, and subcostal views. All images were digitally stored for offline analysis (EchoPAC version 203; GE-Vingmed, Horten, Norway). Left ventricular (LV) dimensions and function were assessed by measuring the end-diastolic diameter, end-systolic diameter, and interventricular septal thickness, as well as the posterior wall thickness on parasternal M-mode recordings, whereas the LV end-diastolic volume and end-systolic volume were measured from the apical 2- and 4-chamber views and the LV ejection fraction was derived using the biplane Simpson method. LV mass was calculated according to the Devereux formula and indexed for body surface area.<sup>12</sup> The peak jet velocity estimation was based on the continuous wave Doppler data from the apical 5- or 3-chamber views.<sup>13</sup> The mean and peak transvalvular pressure gradients were

calculated using the Bernoulli equation. The aortic valve area was calculated using the LV outflow tract diameter and velocity time integrals of the aortic valve and LV outflow tract.<sup>13</sup> All other standard measurements were performed based on the recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging.<sup>12</sup>

Patients were followed up for the occurrence of all-cause mortality after AVR. Survival data were completed for all patients and collected from the departmental cardiology information system, which is linked to municipal civil registries.

Categorical variables are presented as numbers and percentages. Normally distributed continuous variables are expressed as mean with standard deviation, whereas non-normally distributed continuous variables are presented as median and interquartile range. The distribution of normality was verified using the Kolmogorov-Smirnov test and visual assessment of histograms. Continuous data were compared with 1-way analysis of variance for normally distributed variables and Kruskal-Wallis test was used for variables with non-normal distribution. For both continuous and categorical data, a Bonferroni post hoc analysis was added for 1-way ANOVA for comparison. Survival analysis was performed with the Kaplan-Meier curve method, taking the time of AVR as the onset of follow-up. Cumulative event-free rates were compared across groups with the log-rank test. To evaluate the association between COPD severity and all-cause mortality in patients treated with AVR, the univariable and multivariable Cox proportional hazards analysis was used. Clinically relevant variables were selected for univariable analysis, and statistically significant ( $p \leq 0.05$ ) variables were introduced as covariates in multivariable Cox proportional hazards models. A 2-sided  $p$  value <0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS version 25.0 (SPSS Inc., IBM Corp, Armonk, New York).

## Results

Of 677 patients diagnosed with severe AS undergoing AVR, 400 patients (aged 78.0 years [71.0 to 84.0], 56.7% men) had documented preoperative PFT results. Demographic and clinical characteristics of the overall population, as well as the groups divided according to the STS definition of COPD severity are presented in Table 1. Mild, moderate, and severe COPD was present in 75 patients (19%), 31 patients (8%), and 22 patients (5%), respectively, whereas the remaining 68% had a normal PFT. Compared with patients without COPD, patients with moderate and severe COPD were more frequently male (56.7%) and more often received diuretics (53.3%) and statins (61.3%). In addition, New York Heart Association class III or IV heart failure symptoms were more frequent among patients with moderate and severe COPD than those without COPD.

In terms of echocardiographic characteristics, patients without COPD had smaller LV mass (117.1 vs 126.9 g/m<sup>2</sup>) and LV end-systolic volume (21.1 vs 24.1 ml/m<sup>2</sup>) and superior LV function (LVEF 58.0% vs 53.1%) than the group with mild COPD in Table 2. For the remaining echocardiographic variables, the groups of patients were comparable.

Table 1  
Patient characteristics

	Overall (n = 400)	STS classification			p Value*
		None (n = 272)	Mild COPD (n = 75)	Moderate & severe COPD (n = 53)	
Age, years	78.0 (71.0-84.0)	79.0 (71.0-84.0)	77.0 (71.3-82.0)	76.0 (68.0-81.0)	0.118
Male, n (%)	227 (57)	138 (52)	51 (64)	38 (72)	<b>0.010</b>
Body mass index, kg/m <sup>2</sup>	25.8 (23.8-28.7)	26.0 (24.0-29.1)	26.0 (23.6-28.6)	24.6 (23.2-27.8)	0.114
Beta-blocker, n (%)	219 (55)	153 (57)	40 (50)	26 (49)	0.347
ACEi/ARB, n (%)	203 (51)	136 (51)	43 (54)	24 (45)	0.631
Calcium antagonist, n (%)	83 (21)	55 (21)	17 (21)	11 (21)	0.992
Diuretics, n (%)	213 (53)	127 (48)	49 (61)	37 (70)	<b>0.003</b>
Aspirin, n (%)	192 (48)	135 (51)	34 (43)	23 (43)	0.348
OAC/NOAC, n (%)	127 (32)	77 (29)	29 (36)	21 (40)	0.192
Statin, n (%)	245 (61)	174 (65)	40 (50)	31 (59)	<b>0.046</b>
Hypertension, n (%)	275 (69)	185 (69)	59 (74)	31 (59)	0.169
Diabetes mellitus, n (%)	104 (26)	65 (24)	21 (28)	14 (26)	0.467
Hyperlipidemia, n (%)	244 (61)	172 (64)	41 (51)	31 (59)	0.098
CAD, n (%)	205 (51)	144 (54)	37 (46)	24 (45)	0.314
Previous MI, n (%)	70 (18)	50 (19)	9 (11)	11 (21)	0.244
Smoking history, n (%)	148 (37)	94 (35)	29 (36)	25 (47)	0.256
Active smoker, n (%)	37 (9)	19 (7)	9 (11)	9 (17)	0.061
Atrial fibrillation, n (%)	119 (30)	70 (26)	30 (38)	19 (36)	0.089
Stroke, n (%)	25 (6)	17 (6)	7 (9)	1 (2)	0.277
SAVR, n (%)	127 (32)	87 (33)	24 (30)	16 (30)	0.827
TAVR, n (%)	273 (68)	183 (67)	53 (70)	37 (70)	
NYHA class, %					<b>&lt;0.0001</b>
I	44 (11)	39 (15)	5 (6)	0 (0.0)	
II	155 (39)	106 (40)	27 (35)	22 (42)	
III	164 (42)	106 (40)	35 (45)	23 (44)	
IV	31 (8)	13 (5)	11 (14)	7 (14)	
Logistic	10.4	10.2	10.9	10.5	0.667
EuroSCORE, %	(6.4-16.3)	(6.4-15.9)	(6.7-19.0)	(6.5-19.6)	
Concomitant CABG, n (%)	51 (13)	33 (12)	10 (13)	8 (15)	0.860
Creatinine, $\mu$ mol/L	88.0 (74.0-111.0)	87.0 (73.0-107.0)	93.5 (77.0-121.5)	91.0 (77.0-118.0)	0.156

CABG = coronary artery bypass graft; CAD = coronary artery disease; EuroSCORE = the logistic European System for Cardiac Operative Risk Evaluation; MI = myocardial infarction; NYHA = New York Heart Association; SAVR=Surgical aortic valve replacement; STS = Society of Thoracic Surgeons.

Values are presented as median (25th to 75th percentile) if not normally distributed.

\* p values comparing among all 3 severity groups.

The results of the PFTs are presented in Table 3. The FVC, FEV1, Tiffeneau index, vital capacity, peak expiratory flow, and inspiratory capacity were the worst among patients with moderate and severe COPD (per definition) ( $p < 0.0001$ ).

Over a median follow-up of 32 months (interquartile range 17 to 60 months), 92 patients (23%) died. The cumulative 1-, 2-, and 5-year survival rates for the overall population were 92%, 88%, and 81%, respectively. The survival rates were significantly lower in patients with moderate and severe COPD than patients without COPD (log-rank  $p = 0.004$ , Figure 2). There were significant differences in all-cause mortality between the no COPD group and mild COPD group ( $p = 0.007$ ), as well as the no COPD group and moderate/severe COPD group ( $p = 0.008$ ), respectively. The univariable and multivariable Cox regression analyses were constructed with variables known to be associated with outcomes in patients with COPD after AVR

(Table 4). In univariable analysis, older age, higher body mass index, active smoking, diabetes mellitus, previous myocardial infarction, higher creatinine level, lower LV ejection fraction, and COPD were significantly associated with all-cause mortality. On multivariable Cox regression analysis, older age (hazard ratio [HR] 1.048; 95% confidence interval [CI] 1.022 to 1.075;  $p < 0.0001$ ), higher body mass index (HR 0.942; 95% CI 0.889 to 0.998;  $p = 0.041$ ), active smoking (HR 2.115; 95% CI 1.198 to 3.732;  $p = 0.010$ ), diabetes mellitus (HR 2.557; 95% CI 1.626 to 4.022;  $p < 0.0001$ ), creatinine level (HR 1.004; 95% CI 1.002 to 1.007), and COPD were independently associated with all-cause mortality. Remarkably, any grade of COPD was associated with approximately 2-fold increased risk of all-cause mortality (HR 1.933; 95% CI 1.166 to 3.204;  $p = 0.011$  for mild COPD and HR 2.028; 95% CI 1.154 to 3.564;  $p = 0.014$  for moderate and severe COPD, respectively).

Table 2  
Baseline echocardiographic characteristics

	Total (n = 400)	STS classification			P Value
		None (n = 272)	Mild COPD (n = 75)	Moderate & Severe COPD (n = 53)	
<b>LVEDD index, mm/m<sup>2</sup></b>	25.1 (22.4-28.5)	24.8 (22.4-27.6)	25.6 (23.1-29.0)	26.0 (21.8-29.5)	0.170
<b>LVESD index, mm/m<sup>2</sup></b>	17.6 (14.4-21.2)	17.3 (14.0-20.5)	18.6 (14.5-23.8)	18.6 (15.1-22.9)	0.114
<b>IVST, mm</b>	13.0 (11.0-14.0)	13.0 (12.0-14.00)	13.0 (11.0-14.0)	12.0 (11.0-14.0)	0.316
<b>LV mass index, g/m<sup>2</sup></b>	119.1 (100.9-142.2)	117.1 (97.8-137.5)	126.9 <sup>†</sup> (106.4-151.5)	119.6 (95.5-146.7)	<b>0.037*</b>
<b>LVEDV index, mL/m<sup>2</sup></b>	51.3 (40.6-67.1)	50.5 (40.5-66.3)	55.1 (40.3-77.1)	51.3 (41.1-61.5)	0.505
<b>LVESV index, mL/m<sup>2</sup></b>	22.3 (15.2-38.4)	21.1 (14.7-32.9)	24.1 <sup>†</sup> (16.8-50.2)	24.1 (17.8-45.6)	<b>0.008*</b>
<b>LV stroke volume index, mL/m<sup>2</sup></b>	35.0 (26.4-43.5)	34.9 (27.1-44.1)	34.9 (25.5-43.4)	33.3 (24.6-41.7)	0.492
<b>LVEF, %</b>	57.0 (43.0-64.0)	58.0 (46.0-65.0)	53.1 <sup>†</sup> (36.0-60.5)	54.5 (39.7-61.8)	<b>0.005*</b>
<b>LAVI, mL/m<sup>2</sup></b>	38.9 (27.1-52.2)	38.4 (26.4-50.2)	42.4 (32.1-58.2)	38.2 (25.6-51.9)	0.050
<b>AoV mean gradient, mmHg</b>	41.0 (31.0-52.0)	41.6 (31.3-52.0)	40.8 (30.4-55.4)	41.0 (26.6-51.2)	0.663
<b>AVA index, cm<sup>2</sup>/m<sup>2</sup></b>	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.951

AoV = aortic valve; AVA = aortic valve area; IVST = intraventricular septal thickness; LAVI = left atrial volume index; LV = left ventricular; LVEDD = left ventricular end-diastolic dimension; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic dimension; LVESV = left ventricular end-systolic volume.

Values are presented as mean ± SD with percentage (%) or median (25th to 75th percentile) if not normally distributed.

\* p values represent significant difference between COPD groups and are calculated by ANOVA (for normal distribution) and Kruskal-Wallis H (for non-normal distribution) test for continuous variables, and by chi-square test for categorical variables.

<sup>†</sup> p < 0.05 vs none COPD group with Bonferroni post hoc analysis.

## Discussion

In this study, 1/3 of patients with severe AS undergoing AVR had COPD. COPD was independently associated with all-cause mortality after AVR.

As the population ages, cardiovascular and pulmonary diseases become more frequent. AS and COPD are the most frequent valvular heart disease and pulmonary diseases in Western countries. The presence of COPD increases the surgical risk of patients with severe AS. The

frequency of COPD among patients with severe AS undergoing AVR has been explored in several studies.<sup>14,15</sup> From the STS Adult Cardiac Database analysis, of 29,344 patients undergoing isolated AVR for AS, 9,177 patients with PFTs were selected and the frequency of mild, moderate, and severe COPD was documented in 26%, 13%, and 11%, respectively.<sup>16</sup> Similarly, in a prospective registry of 319 consecutive patients with severe AS undergoing transcatheter AVR, Mok et al<sup>5</sup> identified 94 patients (29%) with

Table 3  
Pulmonary function test

	Overall (n = 400)	STS classification			p Value
		None (n = 272)	Mild COPD (n = 75)	Moderate & Severe COPD (n = 53)	
<b>FVC, % predicted</b>	93.3 ± 22.1	102.8 ± 17.9	77.0 ± 11.1 <sup>†</sup>	69.9 ± 19.4 <sup>†‡</sup>	<b>&lt; 0.0001*</b>
<b>FEV 1, % predicted</b>	87.4 ± 25.0	100.6 ± 18.6	68.3 ± 4.7 <sup>†</sup>	49.3 ± 8.5 <sup>†‡</sup>	<b>&lt; 0.0001*</b>
<b>Tiffeneau Index (FEV1/FVC)</b>	73.7 (67.2-79.8)	76.4 (71.4-81.4)	69.0 <sup>†</sup> (63.3-75.3)	56.8 <sup>†‡</sup> (47.2-70.9)	<b>&lt; 0.0001*</b>
<b>VC, % predicted</b>	98.4 ± 45.8	107.5 ± 51.4	79.0 ± 13.8 <sup>†</sup>	80.5 ± 24.5 <sup>†‡</sup>	<b>&lt; 0.0001*</b>
<b>PEF, % predicted</b>	90.7 ± 42.8	101.4 ± 45.8	74.6 ± 19.3 <sup>†</sup>	63.6 ± 12.6 <sup>†‡</sup>	<b>&lt; 0.0001*</b>
<b>IC, % predicted</b>	96.6 ± 23.1	103.3 ± 21.1	87.0 ± 14.8 <sup>†</sup>	78.6 ± 29.5 <sup>†‡</sup>	<b>&lt; 0.0001*</b>

FEV1 = Forced expiratory volume in 1 second; FVC = Forced vital capacity; IC = inspiratory capacity; PEF = peak expiratory flow; VC = vital capacity.

Values are presented as mean ± SD with percentage (%) or median (25th to 75th percentile) if not normally distributed.

\* p values represent significant difference between COPD groups and are calculated by Analysis of variance (ANOVA) (for normal distribution) and Kruskal-Wallis H (for non-normal distribution) test for continuous variables, and by chi-square test for categorical variables.

<sup>†</sup> p < 0.05 vs none COPD group with Bonferroni post hoc analysis.

<sup>‡</sup> p < 0.05 vs mild COPD group with Bonferroni post hoc analysis.

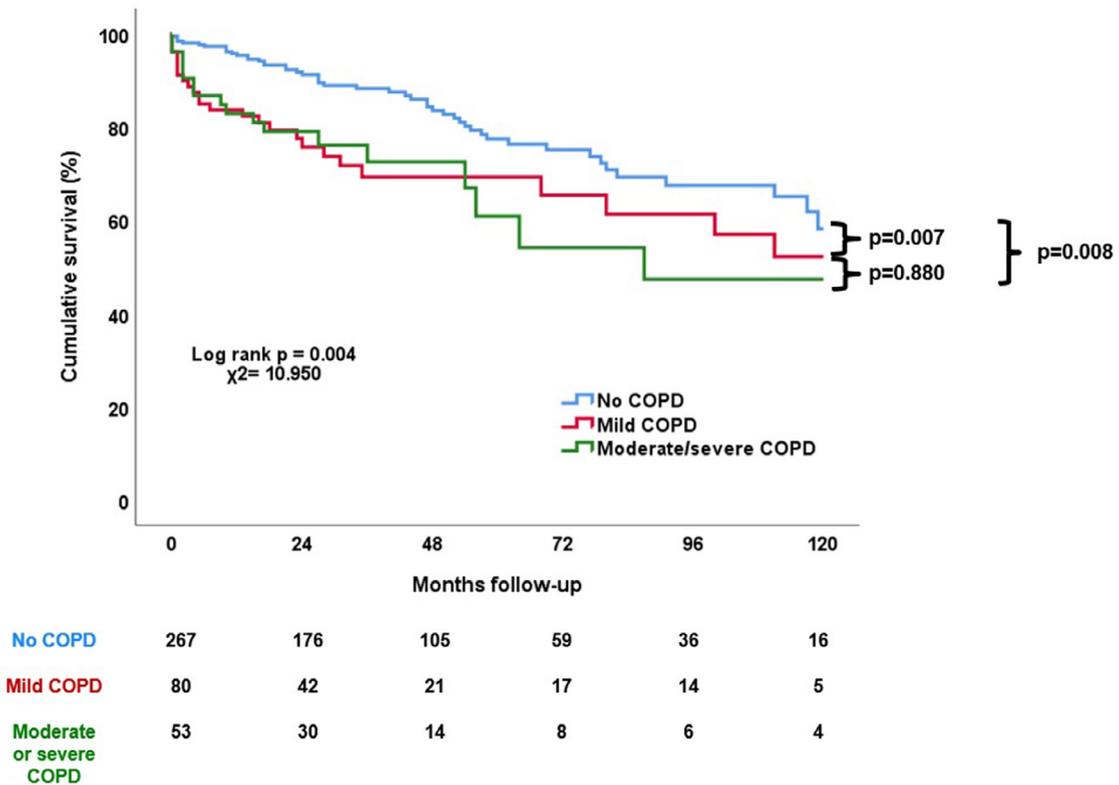


Figure 2. Comparison of overall survival according to STS classification. Kaplan-Meier cumulative frequency of all-cause mortality at 10 y stratified by severity of chronic obstructive pulmonary disease. p value calculated using log-rank test.

Table 4  
Associates of all-cause mortality after aortic valve replacement

	Univariate analysis		Multivariate Analysis*	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Baseline variables				
Age (per 1 year increase)	1.034 (1.011-1.058)	<b>0.003</b>	1.048 (1.022-1.075)	<b>&lt; 0.0001</b>
Gender (yes/no)	1.071 (0.704-1.630)	0.748		
Body mass index, (per 1 kg/m <sup>2</sup> increase)	0.938 (0.888-0.990)	<b>0.020</b>	0.942 (0.889-0.998)	<b>0.041</b>
Beta-blocker (yes/no)	0.903 (0.600-1.359)	0.625		
Hypertension (yes/no)	1.123 (0.713-1.769)	0.617		
Smoking history (yes/no)	1.237 (0.810-1.889)	0.326		
Active smoker (yes/no)	2.218 (1.293-3.803)	<b>0.004</b>	2.115 (1.198-3.732)	<b>0.010</b>
DM (yes/no)	1.921 (1.257-2.937)	<b>0.003</b>	2.557 (1.626-4.022)	<b>&lt; 0.0001</b>
Hyperlipidemia (yes/no)	0.977 (0.646-1.478)	0.912		
Previous MI (yes/no)	1.912 (1.181-3.095)	<b>0.008</b>	1.593 (0.955-2.658)	0.075
CAD (yes/no)	1.416 (0.937-2.141)	0.099		
Atrial fibrillation (yes/no)	1.318 (0.832-2.089)	0.240		
Creatinine (per 1 μmol/L increase)	1.002 (1.001-1.004)	<b>0.011</b>	1.004 (1.002-1.007)	<b>0.001</b>
LVEF (per 1% increase)	0.977 (0.964-0.990)	<b>0.000</b>	0.979 (0.966-0.993)	<b>0.004</b>
COPD by STS definition				
None	-	<b>ref</b>	-	<b>ref</b>
Mild COPD	1.926 (1.188-3.121)	<b>0.008</b>	1.933 (1.166-3.204)	<b>0.011</b>
Moderate and severe COPD	2.157 (1.256-3.706)	<b>0.005</b>	2.028 (1.154-3.564)	<b>0.014</b>

DM = diabetes mellitus; MI = myocardial infarction; CAD = coronary artery disease; LVEF = left ventricular ejection fraction; COPD = chronic obstructive pulmonary disease; STS = Society of Thoracic Surgeons; CI = confidence interval.

\* Univariate predictors with a p < 0.05 were included in multivariate analysis.

COPD (based on PFTs or requirement for bronchodilator therapy). Among randomized clinical trials evaluating the efficacy of transcatheter AVR, Dvir et al<sup>14</sup> performed a pooled analysis including 2,553 patients from the Placement of Aortic Transcatheter Valve (PARTNER I) trial cohorts A and B and from the nonrandomized continuous access registry; in this large cohort, the authors showed a frequency of COPD of 43%. Among patients enrolled in the CoreValve US Pivotal Extreme Risk or High Risk Trial and treated with transcatheter AVR, 55% presented with COPD, including mild in 20%, moderate in 13%, and severe in 22%.<sup>17</sup> The present study reports similar frequencies of COPD and its respective grades of COPD compared with the registries and randomized clinical trials. The present study population was based on the presence of PFTs, which may have led to selection bias; however, this also occurred in the STS Adult Cardiac Database, where 65% of patients with severe AS undergoing isolated AVR did not have the lung function documented.<sup>16</sup>

Although the various studies that have reported on the association between COPD and increased morbidity and mortality of patients with severe AS treated with surgical or transcatheter AVR have not evaluated the pathophysiologic aspects, it is conceivable that the association is multifactorial and not only explained by COPD.<sup>5,14,16,17</sup> Patients with COPD present with local inflammation of the lungs and there is a spill-over of acute phase proteins (i.e., interleukin-6, C-reactive protein, and fibrinogen) to the systemic circulation, which contribute to the atherosclerotic process, inducing plaque formation and growth in the arterial vascular system. In addition, this systemic inflammation is associated with increased platelet count and reactivity, increasing the risk of thrombotic events.<sup>18</sup> The pathophysiology of AS shares some pathways of the atherosclerosis process, and therefore, it may be expected that the prevalence of AS among COPD patients is higher than the general population. However, the systemic inflammation and prothrombotic status that characterize COPD may influence significantly the outcomes of patients with severe AS and probably as much as the airway obstruction.

In the present study, patients with COPD had significantly worse survival than patients without COPD, which is in line with previous studies.<sup>5,14,16,17</sup> In the study by Crestanello et al<sup>16</sup> including patients undergoing isolated surgical AVR, the operative mortality of patients with moderate and severe COPD varied between 3% and 6%. In the series of Mok et al<sup>5</sup> including only patients undergoing transcatheter AVR, the cumulative mortality rate at 1-year follow-up of patients with COPD was significantly higher than patients without COPD (39.4% vs 25.3%, respectively;  $p = 0.042$ ). It is important to note that this was related to a higher rate of noncardiac deaths caused by respiratory failure among patients with COPD. The substudy of the PARTNER I trial and the analysis of the nonrandomized continuous access registry showed that patients with COPD had worse outcomes than patients without COPD.<sup>14</sup> However, it is important to note that among patients with severe AS and COPD, transcatheter AVR was associated with better survival than medical therapy, whereas no differences between transcatheter and surgical AVR were observed. Similarly, the results

of the subanalysis of the CoreValve US Pivotal Extreme Risk or High Risk Trial showed that patients with COPD and treated with transcatheter AVR had worse survival than patients without COPD.<sup>17</sup> Importantly, the majority of patients with COPD who were treated with transcatheter AVR experienced an improvement in functional status and quality of life, which suggested that associated co-morbidities, such as a frailty, low stroke volume index, and the presence of significant paravalvular regurgitation, had a higher impact on survival than COPD alone.

The results of the present study and previous subanalyses of large registries and randomized clinical trials suggest the need of careful evaluation of lung function and co-morbidities of patients with severe AS who have COPD in whom surgical or transcatheter AVR is indicated. Patients with severe AS and COPD have a higher prevalence of co-morbidities that influence outcomes of the intervention than patients without COPD. Furthermore, patients with COPD have a systemic inflammatory status that may increase the risk of thrombotic complications and cardiovascular events.<sup>19</sup> Therefore, preventive strategies that control the inflammatory status and reduce the risk of these complications should be considered before AVR. In patients with moderate and severe COPD, transcatheter AVR may be preferred over surgical AVR because it can be performed under local anesthesia without the need for orotracheal intubation. PFTs are useful examinations to risk stratify patients with suspected COPD and help to select the optimal therapeutic approach.

The present study has some limitations. Due to the retrospective design, there may be confounders that could not be adjusted for in the statistical analysis. Preoperative PFT was not obtained routinely in patients undergoing AVR, leading to selection bias. Discrepant results of the COPD proportion can be caused by different definitions of chronic lung disease and/or COPD. The Global Initiative for Chronic Obstructive Lung Disease (COPD) uses postbronchodilator FEV1/FVC ratio  $<0.70$  and FEV1, whereas the STS uses only FEV1 to define COPD.

In conclusion, any grade of COPD was associated with 2-fold increased risk of all-cause mortality in patients with severe AS undergoing AVR. COPD severity based on documented PFT may improve risk stratification for patients with severe AS and identify patients who will benefit from AVR.

## Disclosures

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