Preoperative pulmonary function tests predict mortality after surgical or transcatheter aortic valve replacement

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ABSTRACT

Objectives: To determine the role of preoperative pulmonary function tests (PFTs) in patients with aortic stenosis (AS) evaluated for aortic valve replacement (AVR), and to evaluate the association between lung disease and mortality in specific subgroups.

Methods: Between 2008 and 2013, 535 patients with preoperative PFTs underwent AVR (transcatheter AVR [TAVR], n = 246; surgical AVR [SAVR], n = 289). The severity of lung disease determined by the Society of Thoracic Surgeons (STS) definition was evaluated in those with and without a clinical suspicion for lung disease (smoking, inhaled steroids/bronchodilators, or home oxygen). The association between lung disease and 1-year mortality was evaluated.

Results: Of the 186 patients (35%) without suspected lung disease, 39 (21%) had moderate/severe lung disease by PFT analysis. Among all patients, 1-year mortality was 12% in those with no lung disease, 17% in those with no mild lung disease, 22% in those with moderate lung disease, and 31% in those with severe lung disease ($P < .001$, log-rank test). After adjustment, moderate/severe lung disease was associated with increased 1-year mortality (adjusted hazard ratio, 2.07; 95% confidence interval, 1.30-3.29; $P = .002$); this association was not altered by smoking history, suspicion of lung disease, New York Heart Association class, or AVR type (interaction P value nonsignificant for all).

Conclusions: In patients with AS evaluated for AVR, the STS risk score is significantly influenced by the severity of lung disease, which is determined predominantly by PFT results. Even when lung disease is not suspected, PFTs are abnormal in many patients undergoing AVR. Moderate/severe lung disease, diagnosed predominantly by PFTs, is an independent predictor of mortality after SAVR or TAVR. Collectively, these findings suggest that PFTs should be a routine part of the risk stratification of patients considered for AVR. (J Thorac Cardiovasc Surg 2016;151:578-86)

Chronic lung disease severity and all-cause mortality after aortic valve replacement.

Central Message

Even when unsuspected, lung disease is common in patients undergoing AVR and is associated with increased mortality.

Perspective

There is no consensus on who should undergo preoperative PFTs before AVR. Our results demonstrate that even when lung disease is not suspected, PFTs are abnormal in many patients. Further, moderate/severe lung disease is an independent predictor of mortality after SAVR or TAVR. These findings suggest that PFTs should be a routine part of the risk stratification of patients considered for AVR.

See Editorial Commentary page 587.

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Chronic lung disease (CLD) is common in patients with aortic stenosis (AS) undergoing aortic valve replacement (AVR), and the presence and severity of CLD has been

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Abbreviations and Acronyms

AS	= aortic stenosis
AVR	= aortic valve replacement
BMI	= body mass index
CLD	= chronic lung disease
DLCO	= diffusion capacity of the lung for carbon monoxide
FEV1	= forced expiratory volume in 1 second
FVC	= forced vital capacity
HR	= hazard ratio
ICU	= intensive care unit
IQR	= interquartile range
NYHA	= New York Heart Association
PFT	= pulmonary function test
SAVR	= surgical aortic valve replacement
STS	= Society of Thoracic Surgeons
TAVR	= transcatheter aortic valve replacement

associated with increased mortality and morbidity after transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).¹⁻⁴ Accordingly, CLD is an important component of several preoperative risk prediction scores, including the Society of Thoracic Surgeons (STS) risk score.^{1,5,6} In the STS database, CLD is determined largely based on results of pulmonary function tests (PFTs).^{6,7} There is no established consensus regarding which patients should undergo preoperative PFTs, however, and many centers perform this testing only in patients with suspected lung disease. Moreover, in patients with significant AS, whether abnormal PFTs are the result of intrinsic lung disease or of heart failure is a matter of debate.⁸ Given the evidence suggesting that PFTs improve after AVR, there is uncertainty regarding the underlying pathophysiology that abnormal preoperative PFTs reflect, and how these tests should be incorporated into an assessment of patient risk and treatment decisions.⁸

The purpose of the present study was to determine the utility of preoperative PFTs in patients with severe AS who were treated with AVR (TAVR or SAVR), and to assess the prevalence of CLD and its effect on mortality in this population. We hypothesized that moderate or severe CLD as determined by preoperative PFT results would be associated with increased mortality after AVR, and that this association would not be altered by smoking status, suspicion for lung disease, or severity of heart failure symptoms in patients with severe AS undergoing SAVR or TAVR.

METHODS**Patient Population**

We retrospectively reviewed all patients age >40 years with severe AS (indexed valve area ≤ 0.6 cm²/m², transvalvular mean gradient >40 mm

Hg, or peak velocity >4 m/s) who underwent preoperative PFTs before SAVR (n = 289) or TAVR (transfemoral, n = 102; transapical, n = 98; transaortic, n = 46) between 2008 and 2013 at our institution. In the SAVR group, patients who underwent concomitant coronary artery bypass graft surgery (n = 82) were included, whereas patients undergoing any other valve procedures were excluded. Of the 1255 patients who underwent AVR at our institution during the study period, preoperative PFTs were performed in 91% (246 of 270) of those in the TAVR group and in 29% (289 of 985) of those in the SAVR group. PFTs were performed a median of 31 days before surgery. Outcomes were evaluated in the combined TAVR and SAVR groups and within each surgical approach. This study was conducted in accordance with the Declaration of Helsinki and was approved by Washington University School of Medicine's Institutional Review Board, from which a waiver of written informed consent was obtained, given the study's retrospective design.

Clinical Data

Baseline, perioperative, and postoperative clinical data were obtained from the STS database and from chart abstraction. The diagnosis of CLD was based on the STS definition, and the stratification of severity of lung disease was as follows⁷: none; mild, forced expiratory volume in 1 second (FEV1) 60% to 75% of predicted, and/or on chronic inhaled or oral bronchodilator therapy; moderate, FEV1 50% to 59% of predicted, and/or on chronic inhaled steroid therapy; severe, FEV1 <50% of predicted and/or room air oxygen tension <60 mm Hg or room air carbon dioxide tension >50 mm Hg.

All patients were also stratified by suspicion of lung disease regardless of their STS classification of CLD. For this study, suspected lung disease was defined as a history of smoking (current or past), bronchodilator or inhaled steroid use, or supplemental oxygen use. Based on these criteria, the patients were classified as with or without suspected lung disease, and the severity of CLD based on the STS definition was evaluated in each group.

Statistical Analysis

Patients with no lung disease or mild lung disease were combined into a single group and compared with those with moderate or severe lung disease. Comparisons of baseline clinical, procedural, and postprocedural characteristics between groups were performed using the Student 2-sample *t* test or Fisher's exact test for continuous and categorical data, respectively. For nonnormal and ordinal data, summary statistics are provided as median and interquartile range, and between-group comparisons were performed using the Kruskal-Wallis test.

Surgery date served as the start time, and follow-up was completed through October 2014. Kaplan-Meier estimates were stratified by lung disease severity, and the log-rank test was used to compare survival distributions. A multivariable Cox proportional hazards model was constructed to evaluate the association between lung disease severity and 1-year all-cause mortality in the combined SAVR and TAVR population while adjusting for covariates including age, sex, body mass index (BMI), diabetes, previous infarct, New York Heart Association (NYHA) class, atrial fibrillation, smoking, glomerular filtration rate, left ventricular ejection fraction, and AVR type, all of which have been associated with mortality in this population.

In addition, a multivariable Cox proportional hazards model was built with the aforementioned covariates along with the appropriate corresponding interaction, to determine whether the association between moderate/severe CLD and mortality differed with respect to subgroups defined by the following variables: smoking status, AVR type (TAVR vs

TABLE 1. Suspected versus actual lung disease based on PFT results

Variable	No suspected lung disease	Suspected lung disease*	P value
TAVR-treated, n	91	155	
Lung disease severity, n (%)†			<.001
None	49 (54)	37 (24)	
Mild	19 (21)	39 (25)	
Moderate	14 (15)	27 (17)	
Severe	9 (10)	52 (34)	
Moderate/severe lung disease, n (%)†	23 (25)	79 (51)	<.001
SAVR-treated, n	95	194	
Lung disease severity, n (%)†			<.001
None	61 (64)	57 (29)	
Mild	18 (19)	46 (24)	
Moderate	10 (11)	36 (19)	
Severe	6 (6)	55 (28)	
Moderate/severe lung disease, n (%)†	16 (17)	91 (47)	<.001

TAVR, Transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement. *Suspected lung disease based on history of smoking, inhaled bronchodilator/steroids, or home oxygen. †Lung disease severity based on the STS definitions of none, mild, moderate, and severe.

SAVR), suspicion of lung disease, and NYHA class III or IV heart failure. A separate multivariable model was built for each interaction comparing subgroups. A 2-sided *P* value < .05 was considered significant. All statistical analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

In the entire cohort (*n* = 535), the prevalence of lung disease determined by STS definition was as follows: none, 38% (*n* = 204); mild, 23% (*n* = 122); moderate, 16% (*n* = 87); severe, 23% (*n* = 122). Of the 186 patients (35%) without suspicion for lung disease, 39 (21%) had moderate or severe CLD according to the STS definition. Among the 349 patients with some suspicion for lung disease, 255 (73%) had some degree of CLD based on STS criteria, including 63 with moderate CLD (18%) and 107 with severe CLD (31%). Regardless of any suspicion for lung disease, 39% of the entire cohort (209 of 535) had moderate/severe CLD based on preoperative PFTs and the STS criteria for CLD. The presence and severity of lung disease in the TAVR and SAVR groups according to whether or not lung disease was suspected are reported in Table 1.

Patient Demographics for TAVR and SAVR

Overall, patients with moderate/severe CLD were sicker in both the TAVR and SAVR groups. In the overall AVR cohort, compared with patients with no/mild CLD, those with moderate/severe CLD were younger (mean age, 76.2 years vs 78.9 years; *P* = .003) and had more NYHA

class III/IV heart failure (90% [189 of 209] vs 78% [254 of 326]; *P* < .001), more atrial arrhythmias (42% [88 of 209] vs 31% [100 of 326]; *P* = .007), and higher STS risk scores (10.2 vs 7.4; *P* < .001). In the TAVR group, compared with patients with no/mild CLD, those with moderate/severe CLD were younger, had higher STS risk scores, and more NYHA class III/IV heart failure (Table 2). These results were consistent with those in the SAVR group; however, in that group, patients with moderate/severe CLD also had more peripheral artery disease and atrial arrhythmias compared with those with no/mild CLD (Table 2).

Interestingly, there was no difference in the prevalence of smoking between patients with no/mild CLD and those with moderate/severe CLD in either the TAVR or SAVR group (Table 2). There were also no differences in BMI, ejection fraction, glomerular filtration rate, or in the prevalence of cerebrovascular disease, coronary disease, or diabetes (Table 2).

Perioperative Morbidity and Mortality

In the overall AVR cohort, compared with patients with no/mild CLD, those with moderate/severe CLD had higher 30-day mortality (7% vs 3%; *P* = .035), a longer median intensive care unit (ICU) stay (48 hours [interquartile range (IQR), 26-116 hours] vs 30 hours [IQR, 24-68 hours]; *P* < .001), more ICU readmissions (11% vs 5%; *P* = .009), and more ICU readmissions secondary to respiratory failure (56% [12 of 22] vs 20% [3 of 15]; *P* = .036).

In the SAVR group, patients with moderate/severe CLD had significantly longer ICU stays compared with those with no/mild CLD (median, 76 hours [IQR, 44-142 hours] vs 47 hours [IQR, 25-78 hours]; *P* < .001) and longer hospital stays (median, 8 days [IQR, 6-12 days] vs 11 days [IQR, 7-17 days]; *P* < .001). In the TAVR group, compared with patients with no/mild CLD, those with moderate/severe CLD had a longer ICU stay (median 28 hours [IQR, 24-52 hours] vs 25 hours [IQR, 23-44 hours]; *P* = .024), more ICU readmissions (9% vs 2%; *P* = .017), and a trend toward a longer hospital stay (Table 3). In both populations, there were no differences in intraoperative blood product administration, intra-aortic balloon pump insertion, acute kidney injury, perioperative stroke, intubation for >24 hours, or 30-day mortality (Table 3).

One-Year Mortality

Based on a Kaplan-Meier estimates, 1-year mortality was 12% in patients with no lung disease, 17% in those with mild lung disease, 22% in those with moderate lung disease, and 31% in those with severe lung disease

TABLE 2. Baseline clinical characteristics

Characteristic	TAVR				SAVR			
	Overall (n = 246)	No/mild CLD (n = 144)	Moderate/ severe CLD* (n = 102)	P value	Overall (n = 289)	No/mild CLD (n = 182)	Moderate/ severe CLD* (n = 107)	P value
Age, yr, mean $\pm$ SD	81 $\pm$ 9	83 $\pm$ 8	80 $\pm$ 9	.005	75 $\pm$ 11	76 $\pm$ 11	73 $\pm$ 10	.023
Female sex, n	49	45	54	.20	43	38	50	.08
Body mass index, mean $\pm$ SD	27.6 $\pm$ 6.1	27.0 $\pm$ 5.0	28.5 $\pm$ 7.3	.07	30.6 $\pm$ 8.2	30.7 $\pm$ 8.0	30.2 $\pm$ 8.4	.62
STS score, mean $\pm$ SD	10.4 $\pm$ 5.6	9.0 $\pm$ 4.6	12.5 $\pm$ 6.2	<.001	6.9 $\pm$ 5.5	6.2 $\pm$ 4.8	8.0 $\pm$ 6.3	.010
Diabetes, n	41	39	45	.36	43	42	44	.81
Insulin treated, n	20	17	23	.33	16	15	18	.62
Hypertension, n	93	95	91	.29	84	87	79	.13
Coronary disease, n	85	86	82	.48	67	67	66	1.00
Previous cardiovascular surgery, n	54	56	51	.52	26	29	21	.13
NYHA class III/IV, n	88	84	93	.047	79	73	88	.003
Atrial arrhythmia, n	38	35	41	.42	33	27	43	.006
Smoker, n	49	44	55	.12	56	52	62	.14
Immunocompromised state, n†	12	11	14	.56	8	6	10	.25
Peripheral arterial disease, n	61	63	57	.35	37	32	46	.023
Cerebrovascular disease, n	34	33	35	.79	26	27	25	.78
Laboratory values, mean $\pm$ SD								
Hemoglobin, g/dL	11.4 $\pm$ 1.5	11.5 $\pm$ 1.5	11.3 $\pm$ 1.6	.44	12.0 $\pm$ 1.7	12.2 $\pm$ 1.7	11.6 $\pm$ 1.7	.004
Glomerular filtration rate, mL/min/1.73 m ²	64 $\pm$ 27	62 $\pm$ 20	67 $\pm$ 34	.18	68 $\pm$ 27	65 $\pm$ 23	71 $\pm$ 32	.09
Albumin, g/dL	4.1 $\pm$ 0.4	4.0 $\pm$ 0.4	4.1 $\pm$ 0.4	.042	4.0 $\pm$ 0.4	4.1 $\pm$ 0.4	3.9 $\pm$ 0.5	.009
Pulmonary function tests, mean $\pm$ SD								
Forced expiratory volume in 1 s, L	1.6 $\pm$ 0.6	1.9 $\pm$ 0.5	1.3 $\pm$ 0.6	<.001	2.0 $\pm$ 0.8	2.2 $\pm$ 0.7	1.6 $\pm$ 0.8	<.001
Percent predicted, %	72 $\pm$ 25	86 $\pm$ 20	52 $\pm$ 18	<.001	74 $\pm$ 24	87 $\pm$ 17	53 $\pm$ 18	<.001
Forced vital capacity, L	2.3 $\pm$ 0.8	2.6 $\pm$ 0.8	2.0 $\pm$ 0.8	<.001	2.8 $\pm$ 0.9	3.0 $\pm$ 0.8	2.4 $\pm$ 1.0	<.001
Percent predicted, %	77.1 $\pm$ 23.4	87.2 $\pm$ 18.9	62.6 $\pm$ 21.5	<.001	82.2 $\pm$ 22.0	90.9 $\pm$ 18.5	67.4 $\pm$ 19.4	<.001
DLCO percent predicted, %	103.8 $\pm$ 36.9	105.3 $\pm$ 33.4	101.5 $\pm$ 41.7	.48	98.8 $\pm$ 30.5	104.7 $\pm$ 27.6	87.5 $\pm$ 32.7	<.001
Pao ₂ , mmHg, on room air	76.4 $\pm$ 13.2	80.6 $\pm$ 8.9	71.0 $\pm$ 15.8	<.001	73.6 $\pm$ 12.5	78.7 $\pm$ 9.1	66.2 $\pm$ 13.1	<.001
Paco ₂ , mmHg, on room air	41 $\pm$ 7	39 $\pm$ 5	43 $\pm$ 9	.006	40 $\pm$ 6	39 $\pm$ 4	42 $\pm$ 7	<.001
Echocardiography								
Ejection fraction, %, mean $\pm$ SD	53 $\pm$ 15	53 $\pm$ 15	54 $\pm$ 15	0.84	54 $\pm$ 15	54 $\pm$ 14	53 $\pm$ 16	.45
Mean gradient, mmHg, mean $\pm$ SD	42 $\pm$ 13	43 $\pm$ 13	41 $\pm$ 13	.32	42 $\pm$ 14	42 $\pm$ 13	42 $\pm$ 16	.76
Moderate or severe AR, %	13	12	14	.70	16	13	21	.13
Moderate or severe MR, %	20	21	19	.74	14	12	17	.21
Moderate or severe TR, %	11	6	19	.004	7	8	4	.22
Pulmonary artery systolic pressure, mm Hg, mean $\pm$ SD	48 $\pm$ 16	46 $\pm$ 15	51 $\pm$ 17	0.05	46 $\pm$ 15	43 $\pm$ 14	50 $\pm$ 15	.003

Groups were compared using the Student 2-sample *t* test or Fisher's exact test for continuous and categorical variables, respectively. Nonnormal and ordinal variables were compared using the Kruskal-Wallis test. TAVR, Transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; CLD, chronic lung disease; SD, standard deviation; STS, Society of Thoracic Surgeons; NYHA, New York Heart Association; DLCO, diffusion capacity of the lung for carbon monoxide; Pao₂, arterial oxygen tension; Paco₂, arterial carbon dioxide tension; AR, aortic regurgitation; MR, mitral regurgitation; TR, tricuspid regurgitation. *Moderate/severe CLD includes moderate or severe chronic lung disease based on STS criteria. †Excludes any one-time administration of corticosteroids perioperatively.

($P < .001$, log-rank) (Figure 1 and Table E1). In subgroup analysis, no, mild, moderate, and severe lung disease were associated with a 1-year mortality of 12%, 18%, 20%, and 36%, respectively, in the TAVR group ($P = .011$, log-rank test) and 11%, 14%, 21%, and 25%, respectively, in the SAVR group ($P = .034$, log-rank test) (Figure 1 and Table E1). Also based on Kaplan-Meier estimates, the survival of patients with no/mild CLD and those with moderate/severe CLD remained significantly different in

the overall cohort ($P < .001$, log-rank test), the SAVR group ($P = .011$, log-rank test), and the TAVR group ($P = .005$, log-rank test).

When all patients were stratified into quartiles based on raw PFT data, 1-year mortality was significantly different in the 4 quartiles of FEV1 percent predicted ($P = .006$, log-rank test) and in the 4 quartiles of diffusion capacity of the lung for carbon monoxide (DLCO) percent predicted ($P = .005$, log-rank test) (Figure E1 and Table E2);

TABLE 3. Procedural and postprocedural characteristics

Characteristic	TAVR				SAVR			
	Overall (n = 246)	No/mild CLD (n = 144)	Moderate/ severe CLD* (n = 102)	P value	Overall (n = 289)	No/mild CLD (n = 182)	Moderate/ severe CLD* (n = 107)	P value
CABG, n					28	29	28	1.00
Cardiopulmonary bypass, n	4	6	2	.20	99	99	99	1.00
Bypass time min, mean $\pm$ SD	N/A	N/A	N/A		123 $\pm$ 39	124 $\pm$ 40	121 $\pm$ 37	.53
Crossclamp time, min, mean $\pm$ SD	N/A	N/A	N/A		85 $\pm$ 30	86 $\pm$ 31	83 $\pm$ 29	.33
Intraoperative blood products used, n	41	43	39	.51	88	87	89	.71
Red blood cells	37	40	34	.42	80	80	79	1.00
Fresh frozen plasma	3	3	3	1.00	40	41	39	.90
Cryoprecipitate	1	1	1	1.00	26	26	26	1.00
Platelets	11	13	8	.22	60	62	57	.46
Fibrinolytics (intraoperative), n	2	2	3	.69	90	89	92	.68
IABP (preoperative or intraoperative), n	2	1	3	.31	6	5	8	.31
Vascular complications, n	21	20	22	1.00	0	0	0	1.00
Intubation >24 h, n	1	1	1	1.00	11	10	13	.33
Postprocedural								
Stroke within 24 h of AVR, n	1	1	1	1.00	1	1	1	1.00
Acute kidney injury, n	12	9	17	.08	20	20	21	.88
Hospital LOS, d, median (IQR)	5 (4, 8)	5 (4, 7)	6 (5, 9)	.12	9 (7, 14)	8 (6, 12)	11 (7-17)	<.001
ICU hours, mean $\pm$ SD	26.3 (23.2-47.3)	25.3 (23.0-43.9)	28.0 (23.8-51.8)	.024	52.4 (27.0-109.3)	47.2 (25.2-78.0)	76.3 (43.8-142.0)	<.001
ICU readmission, n (%)	12 (5)	3 (2)	9 (9)	.017	25 (9)	12 (7)	13 (12)	.13
Respiratory readmission,† n (%)	7 (58)	1 (33)	6 (67)	.52	8 (32)	2 (17)	6 (46)	.20
Perioperative mortality, n (%)	13 (5)	5 (3)	8 (8)	.15	12 (4)	5 (3)	7 (7)	.13

TAVR, Transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; CLD, chronic lung disease; CABG, coronary artery bypass graft; SD, standard deviation; N/A, not applicable; IABP, intra-aortic balloon pump; AVR, aortic valve replacement; LOS, length of stay; IQR, interquartile range; ICU, intensive care unit. *Moderate/severe CLD includes moderate or severe CLD based on Society of Thoracic Surgeons criteria. †Number and percent of ICU readmissions secondary to respiratory distress. Groups were compared using the Student 2-sample *t* test or Fisher's exact test, for continuous and categorical variables, respectively. Nonnormal and ordinal variables were compared using the Kruskal-Wallis test.

however, 1-year mortality was not significantly different among the 4 quartiles of forced vital capacity (FVC) percent predicted ($P = .06$, log-rank test). When evaluated as continuous variables, all 3 PFT metrics (FEV1, FVC, and DLCO) were associated with increased 1-year mortality per 10% decrease (Table E3).

After adjustment for age, sex, BMI, diabetes, previous infarct, NYHA class, atrial fibrillation, smoking, glomerular filtration rate, left ventricular ejection fraction, and AVR type, moderate/severe CLD was associated with increased risk for 1-year mortality (adjusted hazard ratio [HR], 2.07; 95% CI, 1.30-3.29; $P = .002$) (Table 4). Of note, there was no interaction between CLD severity and smoking history, AVR type, NYHA class, or suspicion of lung disease with respect to 1-year mortality (interaction P value nonsignificant for all) (Table 4). Finally, among patients with moderate/severe CLD, there was no difference in risk for

mortality at 1 year between patients who underwent nontransfemoral TAVR and those who underwent transfemoral TAVR (adjusted HR, 2.42; 95% CI, 1.14-5.12 vs adjusted HR, 1.57; 95% CI, 0.69-3.58; $P = .45$); however, the present study was underpowered to fully evaluate this interaction.

DISCUSSION

In our study population, the majority of patients treated with TAVR or SAVR had lung disease according to a PFT-based definition. Even when lung disease was not suspected, PFTs are abnormal in many of these patients, including approximately 20% with moderate/severe lung disease. Moderate/severe lung disease is an independent predictor of mortality after SAVR or TAVR regardless of smoking history, suspicion for lung disease, or severity of heart failure symptoms. In

FIGURE 1. CLD and mortality after AVR. Time-to-event curves are shown based on Kaplan-Meier estimates with patients stratified by STS lung disease severity for (A) TAVR and SAVR combined, (B) TAVR alone, and (C) SAVR alone. AVR, Aortic valve replacement.

additionally, moderate/severe lung disease is associated with increased ICU utilization. Collectively, these findings demonstrate that a PFT-based diagnosis of lung disease has consistent prognostic significance and suggest that PFTs should be a routine part of the risk stratification of patients considered for AVR.

Previously reported estimates of the prevalence of CLD in patients undergoing aortic valve intervention for severe AS have ranged from 16% to 30%.^{3,9,10} In the present study, we found a higher percentage of patients with CLD than was previously reported, likely owing to a sicker cohort of patients. With the introduction of TAVR, more high-risk patients are being offered intervention, which is likely increasing the number of patients with CLD receiving intervention.^{11,12} Our numbers are more consistent with recent studies from the PARTNER trial, which report CLD in nearly 45% of patients who underwent TAVR.^{2,13,14}

In the present study, moderate/severe CLD is associated with increased mortality, which is consistent with literature reports in patients undergoing TAVR^{2,3,15,16} and

SAVR.^{1,4,17} A study from the STS database that included 9177 patients with preoperative PFTs who underwent SAVR for AS demonstrated independent associations between moderate/severe CLD and operative mortality (OR, 2.88; 95% CI, 2.0-4.5), pulmonary morbidity (OR, 2.33; 95% CI, 1.93-2.8), and prolonged hospital stay (OR, 7.73; 95% CI, 2.17-3.45).¹ Dvir and colleagues² reported data from the PARTNER trial, which included 2553 patients who underwent TAVR, and found a higher mortality rate at 1-year follow-up for patients with CLD compared with those without CLD (23.4% vs 19.6%; $P = .02$). In contrast to those reports, however, several other trials did not identify CLD as an independent predictor for mortality.^{8,18}

The diagnosis of CLD according to the STS definition⁷ is based primarily on PFT results, particularly FEV1; however, there is some evidence that airway edema from congestive heart failure in patients with AS may cause elevated FEV1 and lead to overestimation of the prevalence of CLD in this population.^{1,8} Magee and colleagues⁸ reported that 42% to 50% of patients enrolled in the PARTNER trial at their institution demonstrated at least a 10% improvement in FEV1 values after intervention. This finding has raised concerns about the prognostic significance of a PFT-based diagnosis of lung disease in patients with severe AS; however, our data suggest that regardless of the reason for the abnormal PFT results, and despite the fact that they may improve after AVR in some patients, the prognostic significance of moderate/severe CLD (based largely on PFTs) is consistent regardless of smoking history, suspicion of lung disease, NYHA class, or AVR type.

Despite the association of CLD with mortality and other clinical outcomes after AVR, there is no current consensus on which patients being evaluated for SAVR or TAVR should undergo preoperative PFTs. Although we acknowledge the importance of a cost-effective preoperative evaluation, in an era when TAVR is a viable alternative to SAVR for higher-risk patients, it is important to accurately assess each patient's preoperative risk to clarify his or her treatment options.¹⁹ Clinical history alone has

TABLE 4. Impact of lung disease on 1-year mortality in adjusted analyses for SAVR and TAVR combined

Variable	HR (95% CI)	P value
Overall adjusted moderate/severe lung disease*	2.069 (1.302-3.285)	.002
Interactions with lung disease severity on 1-y mortality		
Smoker	2.288 (1.288-4.064)	.56
Nonsmoker	1.729 (0.812-3.683)	
TAVR	2.033 (1.120-3.692)	.93
SAVR	2.116 (1.074-4.168)	
NYHA class I/II	1.058 (0.109-10.278)	.55
NYHA class III/IV	2.138 (1.329-3.439)	
Suspected lung disease	2.001 (1.176-3.405)	.76
Not suspected lung disease	1.687 (0.622-4.576)	

HR, Hazard ratio; CI, confidence interval; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; NYHA, New York Heart Association. *After adjustment for age, sex, body mass index, diabetes, previous infarct, NYHA class, atrial fibrillation, smoking, glomerular filtration rate, left ventricular ejection fraction, and type of aortic valve replacement.

proven inadequate for accurately identifying risk secondary to CLD in patients undergoing cardiac surgery. Adabag and colleagues²⁰ reviewed 1169 patients undergoing cardiac surgery and demonstrated that PFTs reclassified the COPD status in 31% of patients, including identifying new CLD in 16% of the cohort. Ad and colleagues²¹ reported similar results in a prospective cohort of 220 patients undergoing cardiac surgery who were at high risk for CLD based on smoking status, history of asthma, home oxygen use, or persistent cough. They found a significant underestimation of the prevalence and severity of CLD when using the STS definitions without spirometry, including detecting severe CLD in 12% of patients previously classified as having no CLD or mild CLD. These results are consistent with the present study, which is the first to report that in patients with severe AS undergoing either TAVR or SAVR, 21% of those without suspected lung disease had moderate/severe CLD based on PFT results.

Other PFT indices besides FEV1 have been explored as predictors of outcomes in the severe AS population. In the SAVR-treated population, low predicted DLCO and low arterial oxygen tension have been associated with increased mortality and pulmonary complications,^{1,20} whereas low predicted FVC also has been loosely associated with in-hospital mortality.²² Other PFT indices besides FEV1 have not been closely evaluated in the TAVR population, however. In the present study, we were able to demonstrate significant differences in 1-year mortality in patients stratified into quartiles based on preoperative DLCO and FEV1 values, but the quartiles of FVC did not reach statistical significance. Further studies are needed to determine whether there are better ways to refine risk stratification related to CLD for patients evaluated for AVR.

The present study has some limitations. It is based on preoperative PFTs, which are not obtained routinely in every patient undergoing either TAVR or SAVR. This introduces a selection bias that may select for patients with some clinical suspicion of lung disease other than the criteria that we used, particularly in the SAVR population. However, with the widespread application of TAVR, every patient referred to our institution for TAVR undergoes preoperative PFTs, which reduces this selection bias. Another limitation is the possibility of potential unidentified confounding variables despite multivariate adjustments. Still another is the lack of standardization of the interval between PFTs and surgery, which potentially could confound our results. Finally, this was a single-center, retrospective study from a high-volume TAVR and SAVR institution, and so the results might not be generalizable.

CONCLUSIONS

This study demonstrates that a majority of patients who undergo TAVR or SAVR for severe AS have abnormal PFT results, and that 21% of patients without any suspicion for lung disease had moderate or severe lung disease on evaluation. The consistency of the adverse association between moderate/severe lung disease and mortality after AVR suggests that PFTs should be a routine part of the preoperative workup for patients with severe AS undergoing AVR.

Conflict of Interest Statement

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You can watch a Webcast of this AATS meeting presentation by going to: http://webcast.aats.org/2015/Video/Monday/04-27-15_608_1630_Henn.mp4.

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Key Words: aortic valve replacement, pulmonary function tests, preoperative evaluation, aortic stenosis, TAVR

Discussion

Dr T. Dewey (Dallas, Tex). Thank you. I'd like to congratulate Dr Henn and his coauthors from Washington University on an interesting and well-presented study. I'd also like to thank the Association for the opportunity to comment on this paper.

Pulmonary function tests are one of the few diagnostic studies that make two specific demands on the patients. First, they must be compliant with somewhat detailed instructions in the performance of the test, and second, they must give maximal effort in order to achieve accurate results. Thus, conditions such as frailty and debility, severe heart failure, neurocognitive decline from dementia or previous strokes or age or musculoskeletal abnormalities such as kyphoscoliosis can have profound effects on the results on these tests but no actual correlation with intrinsic lung disease.

I have 3 questions. The first of which would be, one would expect that your patients with moderate to severe chronic lung disease would have a higher incidence of smoking, longer post-procedure intubation times, and more frequent readmission to the ICU for respiratory complications. However, neither in your surgical AVR group or your transcatheter AVR group demonstrated this. Can you comment on this finding especially in light of the fact that based on their pulmonary function tests they should have had higher risks for each of these complications?

Dr Henn. Thank you, Dr Dewey, for reviewing our work and for your excellent question. We were also surprised to find no correlation between those with moderate or severe lung disease and history of smoking, intubation time, or ICU respiratory readmissions in the individual SAVR and TAVR populations. These findings are consistent with the notion that the suspicion of underlying lung disease based on clinical history is not very good at predicting lung disease when the lung disease is diagnosed by STS criteria and PFTs. One would usually suspect bad lung disease if a patient comes into the office who is a chronic smoker, however our data suggest this may not necessarily be the case.

When combining both the TAVR and SAVR population, there actually was a significant difference in moderate to severe lung disease compared to none and mild lung disease in current or chronic smokers. Those with moderate to severe lung disease had 58% smokers while those with none or mild had 49% smokers.

Prolonged intubation did not reach significance in the combined group, but there was a trend toward more prolonged intubations in the moderate or severe lung disease group.

Finally, respiratory readmissions to the ICU were significantly different when looking at the combined TAVR and SAVR population. We suspect this did not reach significance in the individual populations because of the relatively low numbers of readmissions in each group.

Dr Dewey. Sure. Second question, pulmonary function tests in a high-risk group of patients often appear to be more a marker of severity of illness and not particularly a predictor of perioperative pulmonary complications. As such, how would you recommend using this data in terms of your decision-making when deciding whether to offer a patient a surgical aortic valve versus a transcatheter aortic valve or even a transcatheter aortic valve and deciding on the approach, either transfemoral or an alternative access?

Dr Henn. Thank you for that question. This is something we are interested in evaluating in our patient population. Like most centers, our preferred approach is transfemoral, but it would be very interesting to evaluate whether preoperative PFTs have affected our choice in alternative access routes.

In terms of this particular study, we didn't necessarily compare TAVR to SAVR in outcomes. However, we do routinely use preoperative PFTs to help risk stratify patients and to help decide between TAVR or SAVR.

Dr Dewey. And, finally, longer-term survival appeared to be significantly affected by having either moderate or severe chronic lung disease in both the surgical AVR and the transcatheter AVR groups. However, these groups also had significantly higher STS predicted risk scores in differences between the groups in terms of peripheral vascular disease and New York Heart Association Class, which also is directly related to poor survival.

Do you have any data that indicates that these late deaths could be directly attributable to pulmonary complications within these groups?

Dr Henn. That's a great question, but we were unable to evaluate pulmonary complications resulting in death because of the limitations in identifying true cause of death in this retrospective study.

Dr Dewey. Thank you.

Dr G. Whitman (*Baltimore, Md*). Dr Henn, I have a slightly different question. As a result of the trial for the TAVR patients, we performed pulmonary function studies on patients who normally would not have gotten them because their clinical history would not have indicated a need for them. A quarter of these patients, though, had moderate to severe COPD as defined by an FEV1 of less than 60% or less than 50%.

Were these results to have been entered into the STS database, the individual's expected mortality would have risen. I think you even showed an increased mortality rate

of 6 to 8%. This generalizes to CABG surgery as well. An 80-year-old diabetic woman who is having an urgent operation has a 2% mortality, but if she has just moderate COPD, she has a 4% mortality.

It seems to me that your data suggests that all of our patients, in order to be appropriately risk stratified, should be getting pulmonary function studies. This is crucial in determining quality of care, as one of the ways we judge that is via our O/E ratios. Is that a reasonable thing to expect of programs when, in fact, in the Choosing Wisely campaign, for example, we are being advised to forego unnecessary pulmonary function studies?

Dr Henn. Thank you for that excellent question. Certainly having full knowledge of a patient's risk prior to taking them to the operating room is ideal. Particularly if you look at the future of medicine with the possibility of reimbursement for outcomes, having an adequate picture of how risky an operation is going to be is extremely important now more than ever. Our data suggest that there is a significant portion of this population where we are underestimating the risk of intervention.

Whether it's going to be financially feasible to do preoperative PFTs in everybody, particularly in the aortic stenosis population where your preoperative PFTs may be a surrogate for underlying heart failure, certainly needs to be evaluated. We definitely do know that abnormal preoperative PFTs is a predictor of mortality, so certainly it would be reasonable to get preoperative PFTs in patients with aortic stenosis to accurately stratify their risk.

Dr Whitman. Thank you very much.

FIGURE E1. PFT metrics and mortality after AVR. Time-to-event curves are shown based on Kaplan-Meier estimates when patients who underwent TAVR or SAVR are stratified into quartiles based on (A) percent predicted forced expiratory volume in 1 second (*FEV1*), (B) diffusion capacity of the lung for carbon monoxide (*DLCO*), and (C) forced vital capacity (*FVC*).

TABLE E1. Kaplan-Meier survival estimates for chronic lung disease and mortality after aortic valve replacement

Procedure	None	Mild	Moderate	Severe
TAVR and SAVR				
30 d	0.97 (0.93-0.98)	0.96 (0.91-0.98)	0.94 (0.86-0.97)	0.91 (0.85-0.95)
6 mo	0.93 (0.88-0.96)	0.91 (0.84-0.95)	0.83 (0.73-0.90)	0.76 (0.67-0.83)
1 y	0.88 (0.83-0.92)	0.83 (0.74-0.89)	0.78 (0.67-0.86)	0.69 (0.59-0.77)
TAVR only				
30 d	0.97 (0.90-0.99)	0.97 (0.87-0.99)	0.95 (0.82-0.99)	0.90 (0.79-0.95)
6 mo	0.92 (0.83-0.96)	0.88 (0.76-0.94)	0.85 (0.70-0.93)	0.75 (0.62-0.84)
1 y	0.87 (0.78-0.93)	0.80 (0.67-0.88)	0.80 (0.64-0.90)	0.64 (0.50-0.75)
SAVR only				
30 d	0.97 (0.92-0.99)	0.97 (0.88-0.99)	0.93 (0.81-0.98)	0.93 (0.83-0.97)
6 mo	0.95 (0.88-0.98)	0.95 (0.85-0.98)	0.82 (0.66-0.91)	0.78 (0.64-0.87)
1 y	0.89 (0.82-0.94)	0.86 (0.73-0.93)	0.76 (0.58-0.87)	0.75 (0.61-0.85)

Data are presented as survival proportion (95% confidence interval). TAVR, Transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement.

TABLE E2. Kaplan-Meier survival estimates for pulmonary function test metrics and mortality after aortic valve replacement

Metric	Quartile 1	Quartile 2	Quartile 3	Quartile 4
FEV1				
30 d	0.92 (0.86-0.96)	0.95 (0.89-0.97)	0.98 (0.93-0.99)	0.96 (0.91-0.98)
6 mo	0.78 (0.70-0.85)	0.88 (0.81-0.93)	0.91 (0.84-0.95)	0.92 (0.86-0.96)
1 y	0.72 (0.62-0.79)	0.81 (0.73-0.87)	0.83 (0.75-0.89)	0.88 (0.81-0.93)
DLCO				
30 d	0.94 (0.88-0.97)	0.95 (0.89-0.98)	0.97 (0.91-0.99)	0.97 (0.92-0.99)
6 mo	0.80 (0.71-0.87)	0.88 (0.81-0.93)	0.91 (0.85-0.95)	0.93 (0.86-0.96)
1 y	0.71 (0.61-0.79)	0.81 (0.72-0.87)	0.85 (0.77-0.91)	0.89 (0.81-0.93)
FVC				
30 d	0.92 (0.86-0.96)	0.96 (0.92-0.99)	0.96 (0.91-0.98)	0.96 (0.91-0.98)
6 mo	0.80 (0.71-0.86)	0.89 (0.82-0.93)	0.89 (0.83-0.94)	0.91 (0.84-0.95)
1 y	0.74 (0.65-0.81)	0.82 (0.74-0.87)	0.83 (0.75-0.89)	0.86 (0.79-0.91)

Data are presented as survival proportion (95% confidence interval). *FEV1*, Percent predicted forced expiratory volume in 1 second; *DLCO*, diffusion capacity of the lung for carbon monoxide; *FVC*, forced vital capacity.

TABLE E3. Univariate Cox model results for 1-year mortality

Pulmonary function test		
metric	HR (95% CI)*	P value
FEV1% predicted	1.158 (1.058-1.267)	.001
FVC% predicted	1.127 (1.027-1.237)	.011
DLCO% predicted	1.163 (1.080-1.254)	<.001

HR, Hazard ratio; CI, confidence interval; *FEV1*, forced expiratory volume in 1 second; *FVC*, forced vital capacity; *DLCO*, diffusion capacity of the lung for carbon monoxide. *HR for 1-year all-cause mortality per 10% decrease in pulmonary function test metric.