Mortality While Waiting for Aortic Valve Replacement

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Background. **Severe symptomatic aortic stenosis (AS) is associated with high mortality without intervention. The impact of waiting time for aortic valve replacement (AVR), either surgically or transcatheter, has not been reported.**

Methods. **From January 2008 to December 2012, we identified 1,005 patients with severe symptomatic AS. AVR was recommended for 823 patients (82%). Of these 823 patients, 721 (87.6%) underwent AVR. We modeled overall survival (OS) since AVR recommendation or intervention date using Cox and multistate models.**

Results. **Overall, the median (first, third quartiles) waiting time until operation was 2.9 (1.3, 5.1) weeks. Mortality at these times was lower ($p < 0.001$) in the AVR group (1.2%, 0.3%, 1.7%, respectively) than in the group that did not receive AVR (6.9%, 2.9%, 9.8%, respectively). Thirty-day mortality after AVR was 3.9% (3.2% surgical AVR [SAVR] and 7.0% transcatheter AVR [TAVR]). In patients receiving AVR, waiting time was not associated with increased mortality. Mortality while waiting for AVR was 3.7% and 11.6% at 1 and 6 months, respectively. Mortality while waiting for TAVR was higher than that for SAVR (1-, 6-, and 12-month mortality of 3.7%, 8.0%, and 9.6%, respectively, in SAVR group and 3.8%, 23.3%, and 27.5%, respectively, in TAVR group; $p < 0.001$).**

Conclusions. **Some patients do not receive AVR in a timely fashion, and prolonged waiting time for AVR is associated with mortality greater than the AVR operative mortality. Although waiting time was not associated with poor operative outcomes after AVR, many patients may die while waiting for AVR. Patients should receive AVR on a semiurgent, not elective, basis.**

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Patients with severe symptomatic aortic stenosis (AS) have poor overall survival (OS) without aortic valve replacement (AVR), whether surgical or transcatheter. Therefore, a class IA recommendation by major societies exists for AVR in patients with severe symptomatic AS, and there are class II recommendations for certain subsets of patients with severe but asymptomatic AS [1, 2].

Rapid progression of heart failure may result in hospitalization and death before intervention. Because many patients are evaluated electively on an outpatient basis, waiting time between recommendation for AVR and the actual intervention may place the patient at risk for progression of heart failure or death. Moreover, some patients may elect to wait for progression of symptoms before proceeding to AVR or for availability of new technology.

The quantification of this mortality risk may have important implications for avoidance of treatment delay and appropriate timing of AVR. We hypothesize that a prolonged delay in treatment introduces an unnecessary risk of mortality while the patient is waiting and that waiting time may be associated with increased mortality and morbidity in those patients who survive to intervention.

Patients and Methods

A total of 1,005 patients with symptomatic severe AS were evaluated between 2008 and 2012. Of these patients, 24 were deemed inoperable, and there was no recommendation date for 158 patients. We report on the remaining 823 patients who were recommended for an intervention. At surgical evaluation time, surgical AVR (SAVR) was recommended for 627 (76.2%) patients and transcatheter AVR (TAVR) was recommended for 196 (23.8%) patients. Of the 627 patients recommended for SAVR, 592 (94.4%) ultimately underwent the intervention, whereas 35 (5.6%) did not. In the group recommended for TAVR, 129 (65.8%) eventually underwent the intervention, whereas 67 (34.2%) did not undergo an intervention after recommendation. The cause of death could not be clearly

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Abbreviations and Acronyms

AF = atrial fibrillation
AS = aortic stenosis
AVR = aortic valve replacement
BMI = body mass index
CABG = coronary artery bypass grafting
CHF = congestive heart failure
CI = confidence interval
COPD = chronic obstructive pulmonary disease
HR = hazard ratio
LV = left ventricle
MI = myocardial infarction
NYHA = New York Heart Association
OR = odds ratio
OS = overall survival
SAVR = surgical aortic valve replacement
STS = The Society of Thoracic Surgeons
TAVR = transcatheter aortic valve replacement

established for the entire study cohort. Of the 102 individuals who did not have AVR (SAVR or TAVR), 11 (10.8%) had comorbidities not captured in The Society of Thoracic Surgeons (STS) Predicted Risk of Mortality but that otherwise elevated their surgical risk. These comorbidities included oxygen-dependent chronic obstructive pulmonary disease (COPD), dementia, cirrhosis, and frailty. Furthermore, 8 individuals (7.8%) refused intervention despite recommendations to proceed with AVR. This study has been approved by the Northwestern University Institutional Review Board (protocol STU00004896).

Statistical Analyses

Baseline characteristics in the entire cohort and by intervention status are presented in Table 1. Continuous variables were summarized in using means and standard deviations or medians, first and third quartiles. Variables with discrete distributions were presented using counts and percentages. Group comparisons were based on the standard 2-sample t test (unequal variance), Wilcoxon rank-sum test, χ^2 test, or Fisher exact test. Thirty-day mortality, morbidity (major complications), and postsurgical discharge location were modeled using logistic regression with stepwise variable selection.

Overall survival (OS) since time of recommendation or time of intervention was summarized using the Kaplan-Meier estimator. For patients receiving AVR (SAVR or TAVR), we summarize the percent undergoing an intervention in Figure 1. The association of AVR and OS since recommendation was studied using Cox regression models, with waiting time (from recommendation to intervention or death) as a time-dependent covariate (Table 2; Fig 2). For patients receiving AVR alone, Cox models adjusting for age, sex, previous myocardial infarction (MI), COPD, renal failure, congestive heart failure (CHF), and history of atrial fibrillation (AF) were used to assess whether waiting time was associated with OS. Figure 3 presents OS since the intervention date.

Based on a 3-state Markov model (Aalen-Johansen estimator), we estimated patient risk of mortality while waiting

Table 1. Summary of Patient Characteristics Stratified by Intervention Status

Variable	N	Entire AVR Cohort (n = 823)	No Intervention (n = 102)	Intervention (n = 721)	p Value
Age at recommendation (y)	823	75.7 ± 11.8	81.4 ± 11.1	74.9 ± 11.7	<0.001
Female sex	823	357 (43%)	44 (43%)	313 (43%)	0.96
Body mass index (kg/m^2)	810	28.5 ± 6.8	24.1 ± 8.1	29.0 ± 6.5	<0.001
LVEF	812	55.9 ± 13.5	54.0 ± 14.2	56.2 ± 13.4	0.13
Congestive heart failure	821	412 (50%)	72 (72%)	340 (47%)	<0.001
STS score	618	5.9 ± 4.8	8.4 ± 4.9	5.4 ± 4.6	<0.001
NYHA functional class	823	. . .	. . .	. . .	<0.001
III/IV		467 (57%)	73 (72%)	394 (55%)	
Missing		3 (0%)	3 (3%)	0 (0%)	
Creatinine level	779	1.3 ± 1.1	1.8 ± 2.3	1.2 ± 0.9	<0.001
Hypertension	822	677 (82%)	75 (74%)	602 (83%)	0.023
Previous sternotomy	823	193 (23%)	35 (34%)	158 (22%)	0.006
Mitral valve operation	721	75 (10%)	NA	75 (10%)	NA
Coronary artery bypass grafting	721	205 (28%)	NA	205 (28%)	NA
Tricuspid valve operation	721	35 (5%)	NA	35 (5%)	NA
Chronic obstructive pulmonary disease	822	227 (28%)	26 (26%)	201 (28%)	0.65
Renal failure	822	89 (11%)	35 (35%)	54 (7%)	<0.001
Previous myocardial infarction	822	111 (14%)	18 (18%)	93 (13%)	0.18
History of atrial fibrillation	823	284 (35%)	31 (30%)	253 (35%)	0.35
Coronary artery disease	810	477 (59%)	62 (61%)	415 (59%)	0.68

LVEF = left ventricular ejection fraction; NA = not available; NYHA = New York Heart Association; STS = The Society of Thoracic Surgeons.