

# Aortic Valve Replacement for Patients With Severe Aortic Stenosis: Risk Factors and Their Impact on 30-Month Mortality

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**Background.** Few studies have reported population-based outcomes for aortic valve replacement patients.

**Methods.** Patients with severe aortic valve stenosis who underwent aortic valve replacement with or without concomitant coronary artery bypass graft surgery from January 1, 2003, to December 31, 2005, were included in the study. Statistical models were developed to identify significant risk factors for mortality, to compare survival for patients with and without selected risk factors, and to compare survival to an age- and sex-matched group from US life tables.

**Results.** There was total of 6,369 patients in the study. The in-hospital and 30-day mortality rates were 3.97% for aortic valve replacement and 5.69% for aortic valve replacement with concomitant coronary artery bypass graft surgery. Significant risk factors for 30-month mortality included concomitant coronary artery bypass graft sur-

gery, advancing age, lower body surface area, emergency status, low ejection fraction, congestive heart failure, previous heart surgery, and several comorbidities. The 64.3% of patients with isolated aortic valve replacement who had neither congestive heart failure, ejection fraction less than 0.40, acute myocardial infarction less than 24 hours, nor hemodynamic instability had a risk-adjusted survival of 89.9% compared with the 90.0% survival rate of the age- and sex-matched general population ( $p = 0.28$ ).

**Conclusions.** For the large number of patients without high-risk conditions, the 30-month survival is essentially as high as that of an age- and sex-matched group of the US population.

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Aortic valve stenosis is the most frequent heart valve disease in developed countries [1, 2]. The prognosis for patients with severe aortic stenosis who do not undergo aortic valve replacement (AVR) is very poor, and much worse than the risk for patients undergoing AVR [1–15].

There is a continuing need to examine the significant risk factors for adverse outcomes after AVR, and to assess the prognosis for patients with several clinical features that frequently accompany aortic valve stenosis. Although numerous studies of this nature have been conducted, many are more than 10 years old, and the vast majority are single-institution studies [16–20].

The purposes of this study are (1) to identify the significant risk factors for 30-month mortality for patients with severe aortic valve stenosis who undergo AVR and (2) to compare risk-adjusted mortality for patients with and without each of several important risk factors to an age- and sex-matched group based on US census data [21]. The study is population-based and contains results

for all patients with severe aortic valve stenosis undergoing AVR in New York State between 2003 and 2005.

## Patients and Methods

### Database

The database used in the study was the New York State Department of Health's Cardiac Surgery Reporting System. This registry was created in 1989 for the purpose of collecting information on all New York patients undergoing cardiac surgery in nonfederal hospitals in the state to better understand risk factors for these procedures and to improve quality of care and outcomes. The registry contains information on type of procedure performed, demographics, comorbidities, left ventricular function, hemodynamic state, extent of coronary artery disease and attempted coronary vessels, hospital identifiers, and in-hospital adverse outcomes. Data are audited and cross-checked against the Department's acute care hospital discharge database, the Statewide Planning and Research Cooperative System to ensure accuracy and completeness. Definitions for these data elements are identical in the two systems.

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Table 1. Frequencies and Proportions of Short-Term Mortality and Preoperative Risk Factors in Severe Aortic Stenosis Patients Undergoing Isolated Aortic Valve Replacement or Aortic Valve Replacement With Coronary Artery Bypass Graft Surgery in New York State From 2003 to 2005

Risk Factors	Frequencies and Proportions (%) of Risk Factors by Type of Surgery		p Value
	Isolated AVR (n = 3,327)	AVR With CABG (n = 3,042)	
In-hospital or 30-day mortality	132 (3.97)	173 (5.69)	0.001
Demographic factors			
Age (mean ± SD)	68.91 ± 13.44	64.24 ± 8.90	<0.0001
Body surface area (mean ± SD)	1.95 ± 0.28	1.95 ± 0.26	0.85
Female	1,640 (49.29)	1,225 (40.27)	<0.0001
Race			0.25
White	3,139 (94.35)	2,897 (95.23)	
Black	135 (4.06)	108 (3.55)	
Other	53 (1.59)	37 (1.22)	
Hispanic	211 (6.34)	118 (3.88)	<0.0001
Cardiac risk factors			
Severe aortic valve incompetence	247 (7.42)	152 (5.00)	<0.0001
Severe mitral valve incompetence	49 (1.47)	50 (1.64)	0.58
Severe mitral valve stenosis	4 (0.12)	8 (0.26)	0.19
LMT disease	42 (1.26)	484 (15.91)	<0.0001
No. of vessels diseased			<0.0001
Less than two	3,161 (85.01)	1,491 (49.01)	
Two	67 (2.01)	896 (29.45)	
Three	99 (2.98)	655 (21.53)	
Ejection fraction			<0.0001
0.00-0.39	482 (14.49)	587 (19.30)	
0.40-0.49	429 (12.89)	514 (16.90)	
0.50 or more	2,416 (72.62)	1,941 (63.81)	
Shock or unstable	23 (0.69)	41 (1.35)	0.01
Angina class			<0.0001
None, CCS class I and II	2,381 (71.57)	1,278 (42.01)	
CCS class III	721 (21.67)	1,284 (42.21)	
CCS class IV	225 (6.76)	480 (15.78)	
Previous MI			<0.0001
<24 hours	2 (0.06)	7 (0.23)	
1-7 days	60 (1.80)	184 (6.06)	
8-20 days	33 (0.99)	127 (4.17)	
21 days or older	373 (11.21)	547 (17.98)	
None	2,859 (85.94)	2,177 (71.56)	
Current CHF	956 (28.73)	948 (31.16)	0.03
Comorbidities			
Cerebrovascular disease	513 (15.42)	753 (24.75)	<0.0001
Peripheral vascular disease	237 (7.12)	400 (13.15)	<0.0001
Malignant ventricular arrhythmia	21 (0.63)	18 (0.59)	0.84
COPD	633 (19.03)	686 (22.55)	0.001
Extensive aortic atherosclerosis	385 (6.04)	446 (14.66)	0.0003
Diabetes	746 (22.42)	840 (27.61)	<0.0001
Immunodeficiency	129 (3.88)	96 (3.16)	0.12
Organ transplant	18 (0.54)	9 (0.30)	0.13
Cardiomegalia	680 (20.44)	718 (23.60)	0.002
Endocarditis =	31 (0.93)	7 (0.23)	0.0003
Renal failure, creatinine > 1.6 mg/dL	182 (5.47)	206 (6.77)	0.03
Renal dialysis	72 (2.16)	72 (2.37)	0.59
Previous interventions			
Previous PCI	303 (9.11)	383 (12.59)	<0.0001
Previous cardiac surgery	545 (16.38)	238 (7.82)	<0.0001

AVR = aortic valve replacement; CABG = coronary artery bypass graft; CCS = Canadian Cardiovascular Society; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; LMT = left main trunk; MI = myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation.

Table 2. In-Hospital or 30-Day Mortality in Selected Subsets of Patients With Severe Aortic Stenosis Undergoing Aortic Valve Replacement in New York State From 2003 to 2005<sup>a</sup>

Factor	No. of Cases (N = 6,369)	Adjusted Odds Ratio	p Value
Type of surgery			
Isolated AVR	3,327	1.00	Reference
AVR with CABG	3,042	1.27	0.056
Age			
Number of years > 60	...	1.04	<0.0001
Left ventricular ejection fraction			
Percent of LVEF < 0.55	...	1.02	0.0001
Congestive heart failure			
No	4,465	1.00	Reference
Yes	1,904	1.67	<0.0001
AMI < 24 hours or hemodynamically unstable			
No	6,299	1.00	Reference
Yes	70	3.37	0.0002
Body surface area	...	0.49	0.006
Comorbidities			
Cerebrovascular disease	1,266	1.42	0.007
Extensive aortic atherosclerosis	881	1.96	<0.0001
Diabetes	1,586	1.40	0.01
Renal failure	208	2.55	<0.0001
Previous cardiac operation	783	1.64	0.002

<sup>a</sup> Model performance C statistics for final model was 0.741.

AMI = acute myocardial infarction; AVR = aortic valve replacement; CABG = coronary artery bypass graft; LVEF = left ventricular ejection fraction.

Deaths occurring among New York State patients after discharge from the hospital were obtained by matching patients in the Cardiac Surgery Reporting System with New York's Vital Statistics Death file using patient identifiers.

#### Study Group and End Points

The study includes patients with severe aortic valve stenosis (regarded as aortic valve area < 1 cm<sup>2</sup> and jet velocity > 4.0 m/s) who underwent AVR from January 1, 2003, to December 31, 2005. Patients who underwent AVR with and without concomitant coronary artery bypass graft (CABG) surgery were included in the study. All patients were included except 620 patients from out of state and 30 patients with missing Social Security numbers. These two groups were excluded because they could not be followed for longer-term outcomes using New York Vital Statistics data. A total of 6,359 patients were included in the study. The end points of interest were in-hospital or 30-day mortality (death in the index admission at any time or death within 30 days after discharge after the index admission) and 30-month mortality.

#### Statistical Analysis

The main purposes of the study were to identify significant risk factors for medium-term (30-month) mortality and to compare age- and sex-adjusted 30-month mortality for patients with and without certain risk factors

(Canadian Cardiovascular Society class III or IV angina, congestive heart failure [CHF], concomitant CABG surgery, age 75 and older, and left ventricular ejection fraction [EF] < 0.40) with the age- and sex-matched population from the US life tables in 2004, which is based on 2004 final mortality statistics and US population estimates from the 2000 census [21].

Frequencies for a wide variety of risk factors (demographic, ventricular function, vessels diseased, previous myocardial infarction, previous interventions, and a large number of comorbidities) were computed, and differences in prevalence for each of these risk factors between patients undergoing isolated AVR and AVR with CABG surgery were examined. Significant differences were identified using Wilcoxon rank sum tests for continuous variables and  $\chi^2$  tests for categorical variables.

Significant independent risk factors for in-hospital or 30-day mortality of AVR patients were identified using logistic regression. The data were split in half, and a model was developed on the development sample using the variables in Table 1 as independent variables and mortality as the binary dependent variable. Stepwise selection was used with a significance criterion of 0.05 for entry and removal. The resulting model was applied to the validation sample to test for discrimination and calibration, and then a new model was developed for the entire data set using the variables that were significant in the development sample.

Significant independent risk factors for 30-month mor-

Table 3. Multivariable Predictors for 30-Month Survival in Patients With Severe Aortic Stenosis Undergoing Aortic Valve Replacement Surgery in New York State From 2003 to 2005

Predictor	Prevalence	Coefficient	p Value	Adjusted Hazard Ratio
Type of surgery				
Isolated AVR	52.24	Reference	1.00	
AVR with CABG	47.76	0.2334	0.002	1.26
Demographic factors				
Age				
<65 y	17.57	Reference	1.00	
65–74 y	28.75	0.453	0.003	1.57
75–84 y	44.36	0.7807	<0.0001	2.18
≥85 y	9.33	1.3767	<0.0001	3.96
Body surface area	...	–0.7225	<0.0001	0.49
Cardiac risk factors				
Emergency status				
Hemodynamically stable and no AMI within 24 hours	98.90	Reference	1.00	
Hemodynamically unstable or AMI within 24 hours	1.10	1.135	<0.0001	3.11
Left ventricular ejection fraction				
0.40 or more	83.22	Reference	1.00	
0.30–0.039	8.93	0.3859	0.0002	1.47
<0.30	7.85	0.5452	<0.0001	1.72
Current congestive heart failure				
No	70.11	Reference	1.00	
Yes	29.89	0.3973	<0.0001	1.49
Comorbidities				
Cerebrovascular disease	19.88	0.293	0.0003	1.34
Peripheral vascular disease	10.00	0.2862	0.003	1.33
COPD	20.71	0.4926	<0.0001	1.64
Extensive aortic atherosclerosis	13.05	0.4563	<0.0001	1.58
Diabetes	24.90	0.3713	<0.0001	1.45
Immunodeficiency	3.53	0.5569	0.0001	1.75
Organ transplant	0.42	0.7814	0.0203	2.18
Renal failure	3.69	1.0606	<0.0001	2.89
Previous interventions				
Previous heart surgery	12.29	0.3024	0.002	1.35

AMI = acute myocardial infarction; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease.

AMI = acute myocardial infarction; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease.

tality for AVR patients were identified by developing a stepwise Cox proportional hazards model after having confirmed that the proportional hazards assumption was justified [22]. Candidate independent variables included the baseline risk factors in Table 1.

Thirty-month risk-adjusted survival curves were then constructed for patients with and without each of several important risk factors (concomitant CABG surgery, age > 75 years, CHF, EF < 0.40, acute myocardial infarction [AMI] < 24 hours, or hemodynamic instability) using Cox proportional hazards models and methods for calculating adjusted survival [23]. The risk-adjusted survival rates for patients with and without the risk factor of interest were then compared with the survival of the age- and sex-matched general population in the years 2003 to 2005 [21].

All tests were conducted at the 0.05 level, all confidence limits were two-sided, and all analyses were conducted in SAS 9.1 (SAS Institute Inc, Cary, NC).

## Results

There was total of 6,369 patients in the study. A total of 3,327 patients (52.2%) were isolated aortic valve patients and the remainder underwent AVR with CABG surgery. As noted in Table 1, patients with combined AVR and CABG surgery were younger (64.2 years versus 68.9 years;  $p < 0.0001$ ), less likely to be female (40.3% versus 49.3%;  $p < 0.0001$ ), less likely to be Hispanic (3.9% versus 6.3%;  $p < 0.0001$ ), and less likely to have severe aortic valve incompetence (5.0% versus 7.4%;  $p < 0.0001$ ). Also, they were more likely to have left main disease (15.9% versus 1.3%;  $p < 0.0001$ ), had more vessels diseased (eg, 21.5% with three-vessel disease versus 3.0% with fewer than three vessels diseased), had significantly lower ejection fractions, had more severe angina (eg, 15.8% versus 6.8% for Canadian Cardiovascular Society class IV), were more likely to have had a previous myocardial

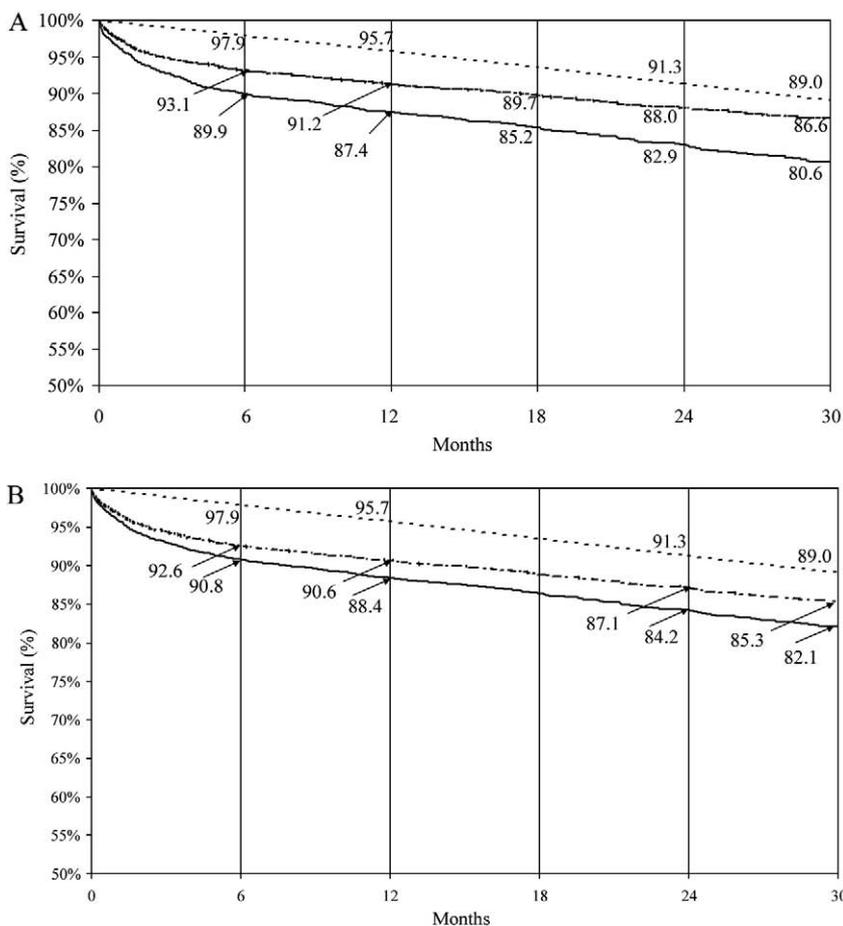


Fig 1. Survival after isolated aortic valve replacement versus aortic valve replacement with concomitant coronary artery bypass grafting. Dashed lines are survival for age- and sex-matched US population. Solid and dash-dotted lines represent survival for aortic valve replacement patients with and without concomitant coronary artery bypass grafting, respectively. (A) Unadjusted Kaplan-Meier survival curves. (B) Adjusted Kaplan-Meier survival curves.

infarction (71.6% with no previous myocardial infarction versus 85.9%;  $p < 0.001$ ). Furthermore, AVR with concomitant CABG patients had significantly higher prevalence of several comorbidities (cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease, extensive aortic atherosclerosis, diabetes, cardiomegaly, and renal failure), had a significantly lower rate of endocarditis (0.2% versus 0.9%;  $p = 0.03$ ), and were more likely to have had previous percutaneous coronary intervention (12.6% versus 9.1%;  $p < 0.0001$ ), but were less likely to have undergone previous open heart surgery (7.8% versus 16.4%;  $p < 0.0001$ ).

Table 2 indicates that significant risk factors for in-hospital or 30-day mortality were advancing age greater than 60 years, EF (adjusted odd ratio for each year EF  $< 0.55$ , 1.02;  $p = 0.0001$ ), CHF (adjusted odd ratio, 1.67;  $p < 0.0001$ ), AMI less than 24 hours or hemodynamically unstable (including shock cases, adjusted odd ratio, 3.37;  $p = 0.0002$ ), lower body surface area, previous cardiac operations (adjusted odd ratio, 0.49 for each unit increase;  $p = 0.001$ ), and several comorbidities (cerebrovascular disease, extensive aortic stenosis, diabetes, and renal failure).

Table 3 demonstrates that significant predictors of 30-month mortality for patients undergoing AVRs include concomitant CABG surgery (adjusted hazard ratio

[AHR], 1.26;  $p = 0.002$ ), advancing age, body surface area (AHR, 0.49 per unit increase;  $p < 0.0001$ ), emergency status (AHR for hemodynamically unstable or AMI within 24 hours, 3.11;  $p < 0.001$ ), low EF, CHF (AHR, 1.49;  $p < 0.001$ ), and numerous comorbidities (cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease, extensive aortic stenosis, diabetes, immunodeficiency, organ transplant, and renal failure). Also, patients with previous heart surgery were more likely to die within 30 months (AHR, 1.35;  $p = 0.002$ ). Valve type (mechanical versus tissue) was not a significant predictor of 30-month mortality.

Figure 1 provides respective unadjusted and adjusted Kaplan-Meier survival curves for patients with AVR and AVR with concomitant CABG surgery compared with an age- and sex-matched US population. As indicated in Figure 1A, AVR patients had a 30-month unadjusted survival of 86.6% and AVR with concomitant CABG patients had an 80.6% 30-month survival, in contrast to an 89.0% survival for patients with the age and sex distribution of the AVR and AVR with concomitant CABG population. When AVR and AVR with concomitant CABG patients were adjusted to take into account that AVR with concomitant CABG patients were sicker on average with regard to other risk factors, the respective adjusted 30-month AVR and AVR with concomitant

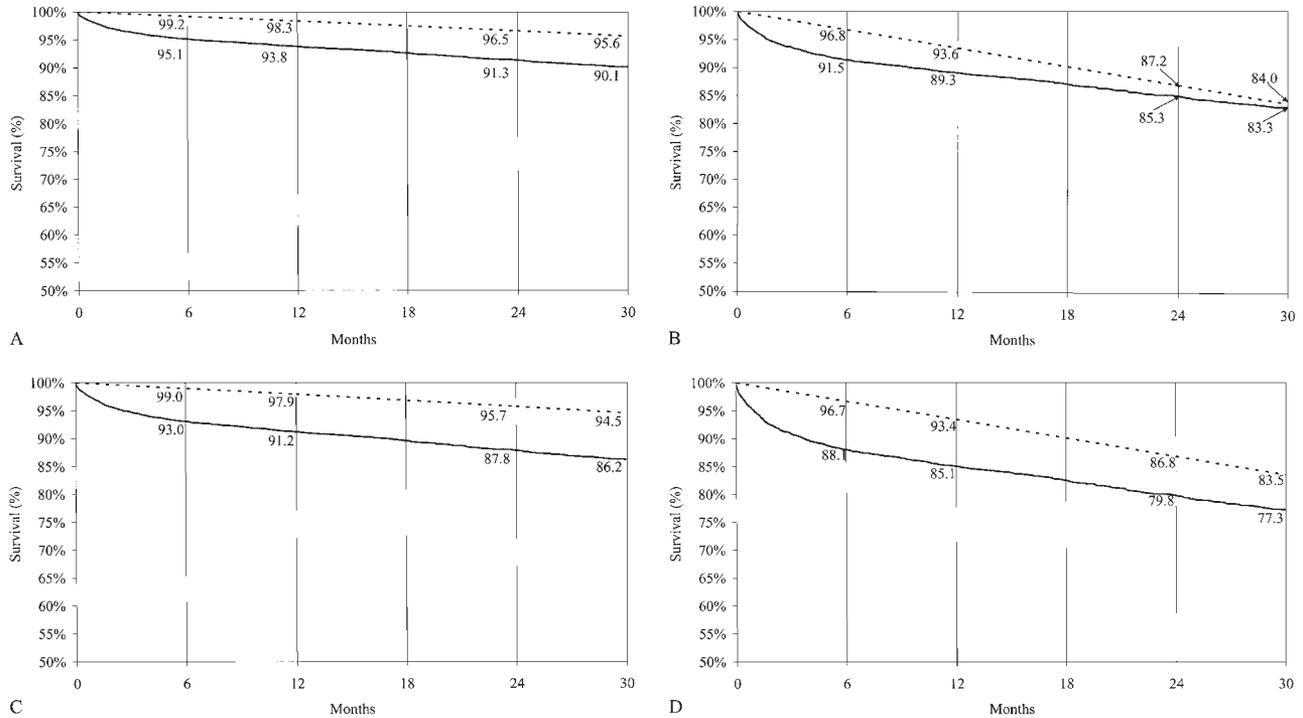


Fig 2. Survival after aortic valve replacement according to patient age. Dashed lines are survival for age- and sex-matched US population. Solid lines represent risk-adjusted survival in selected age and surgery subgroups. (A) Nonelderly patients (age < 75 years) with isolated aortic valve replacement. (B) Elderly patients (age > 75 years) with isolated aortic valve replacement. (C) Nonelderly patients undergoing aortic valve replacement with coronary artery bypass graft surgery. (D) Elderly patients undergoing aortic valve replacement with coronary artery bypass graft surgery.

CABG surgery survival rates were 85.3% and 82.1% (Fig 1B).

After 30 months, patients with isolated AVR who were younger than 75 had a 30-month survival of 90.1%, compared with 95.6% for people from the general population who were age and sex matched to this group (Fig 2). Patients with isolated AVR who were 75 or older had a 30-month survival of 86.2% compared with 94.5% for their age- and sex-matched counterparts. Patients with AVR with concomitant CABG who were 75 or older had a 30-month survival of 77.3% compared with 83.5% for their age- and sex-matched counterparts. All differences in Figure 2 were statistically significant except for the difference between patients with AVR with concomitant CABG surgery who were younger than 75 (30-month survival of 83.3%) and compared with people from the general population who were age and sex matched to this group (84.0% survival;  $p = 0.69$ ). However, it should be noted that the two curves were quite different initially as a result of the short-term mortality related to AVR with concomitant CABG surgery.

The following rates apply to patients with isolated AVR (Fig 3). Patients with AMI less than 24 hours or hemodynamically unstable had a risk-adjusted 30-month survival of 69.8%, compared with 88.4% for patients with neither AMI less than 24 hours nor hemodynamic instability, and a rate of 90.0% for the general population age and sex matched to all patients in our study. Isolated

AVR patients with CHF had a risk-adjusted 30-month survival of 81.8%, compared with 87.5% for patients without CHF. Patients with EF less than 0.40 had a risk-adjusted 30-month survival of 83.4%, compared with 88.2% for patients with EF greater than 0.40. Patients who had CHF, EF less than 0.40, or AMI less than 24 hours or were hemodynamically unstable had a risk-adjusted survival of 81.7%, and patients with none of those conditions had a risk-adjusted survival of 89.9%, almost identical to the 90.0% survival rate of the age- and sex-matched general population. This was the only difference in Figure 3 that was not statistically significant ( $p = 0.28$ ).

For patients with AVR with concomitant CABG surgery, the following were the survival rates (Fig 4). Patients with AMI less than 24 hours or who were hemodynamically unstable had a risk-adjusted 30-month survival of 59.6%, compared with 83.6% for patients with neither AMI less than 24 hours nor hemodynamic instability, and a rate of 88.0% for the general population age and sex matched to all patients in our study. The AVR with concomitant CABG patients with CHF had a risk-adjusted 30-month survival of 74.6%, compared with 82.5% for patients without CHF. Patients with EF less than 0.40 had a risk-adjusted 30-month survival of 76.7%, compared with 83.2% for patients with EF greater than 0.40. Patients who had CHF, EF less than 0.40, or AMI less than 24 hours or were hemodynamically unstable had a

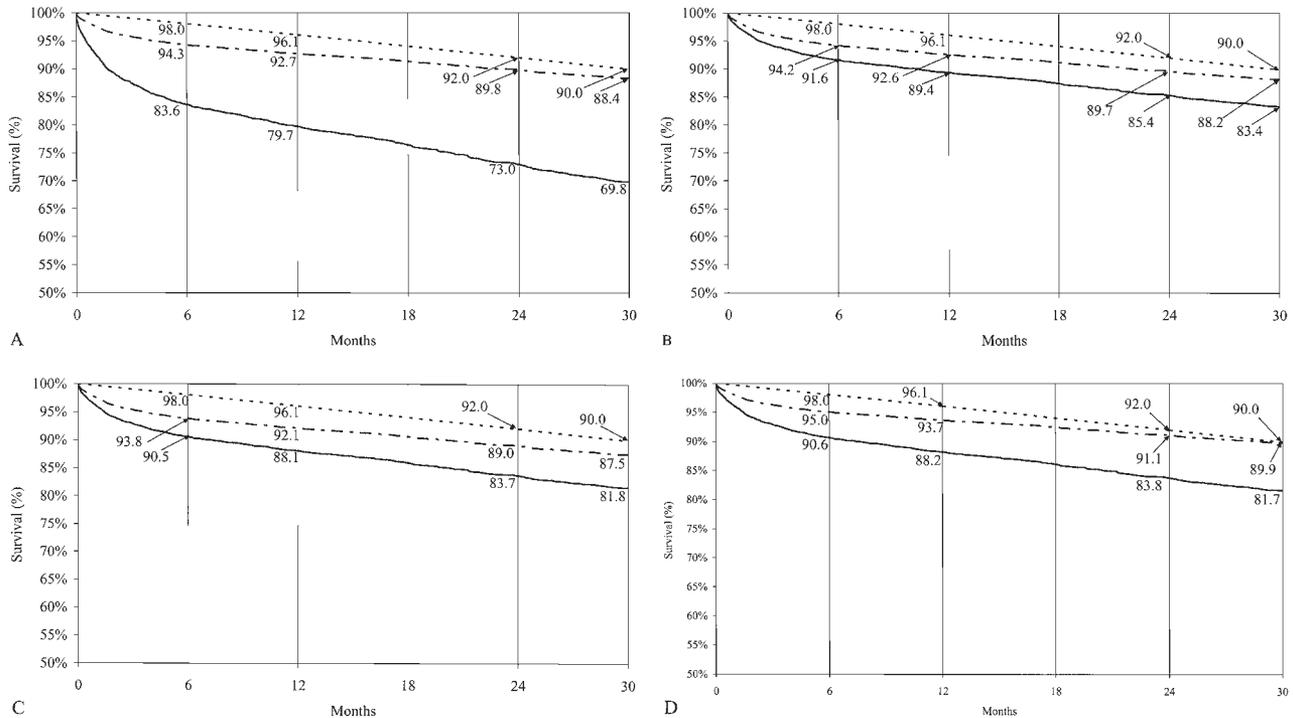


Fig 3. Survival after isolated aortic valve replacement according to preoperative cardiac risk factors. Dashed lines are survival for age- and sex-matched US population. Solid and dash-dotted lines represent risk-adjusted survival for patients with and without each risk factor, respectively. (A) Acute myocardial infarction less than 24 hours or hemodynamically unstable. (B) Congestive heart failure. (C) Left ventricular ejection fraction less than 0.40. (D) Combination of congestive heart failure, left ventricular ejection fraction less than 0.40, and acute myocardial infarction less than 24 hours or hemodynamically unstable.

risk-adjusted survival of 74.7%, and patients with none of those conditions had a risk-adjusted survival of 85.7%.

### Comment

Aortic valve stenosis is a common problem in developed countries, particularly among the elderly. A total of 6,369 patients underwent AVR in New York State between 2003 and 2005, with 3,327 (52.2%) of those patients undergoing isolated AVR and the remainder undergoing AVR with CABG surgery.

The purposes of our study were to use population-based data from New York to (1) identify significant short-term and medium-term risk factors for patients undergoing AVR and (2) compare risk-adjusted mortality for patients with and without each of several important risk factors and to contrast this mortality with an age- and sex-matched group based on census data.

There were numerous significant risk factors for in-hospital or 30-day mortality, including advanced age, lower body surface area, compromised hemodynamic state, low ventricular function, previous myocardial infarction, previous heart surgery, and several comorbidities. Significant risk factors for 30-month mortality included concomitant CABG surgery, advancing age, lower body surface area, emergency status, low EF, CHF, previous heart surgery, and several comorbidities (cerebrovascular disease, peripheral vascular disease, chronic

obstructive pulmonary disease, extensive aortic stenosis, diabetes, immunodeficiency, organ transplant, and renal failure).

Concomitant CABG surgery has been identified in some studies to be a significant risk factor for patients undergoing AVR [2], whereas other studies have not found CABG surgery to be an independent predictor of mortality [16, 18]. We found concomitant CABG surgery to be highly significant, with AVR with concomitant CABG surgery procedures having an adjusted 30-month mortality hazard ratio of 1.26 ( $p = 0.002$ ) in comparison with isolated AVR.

Many earlier studies have identified age as a significant medium-term risk factor for AVR [3, 4, 7, 8, 14, 17-19]. A few have also identified low ventricular function as a risk [4, 7, 8, 12, 14]. Renal failure or insufficiency was also found to be a risk factor for mortality [4], as was diabetes [8] and extensive aortic atherosclerosis [14, 18]. Although we were unable to find any studies that identified lower body surface area as a risk factor for medium-term mortality, two studies did identify female sex, which may or may not be a proxy for lower body surface area [4, 7]. The inability of other studies to identify as many comorbidities as our study did may be related to most other studies having lower statistical power resulting from smaller sample sizes.

With regard to our findings on risk-adjusted 30-month survival, we found that most subgroups of patients un-

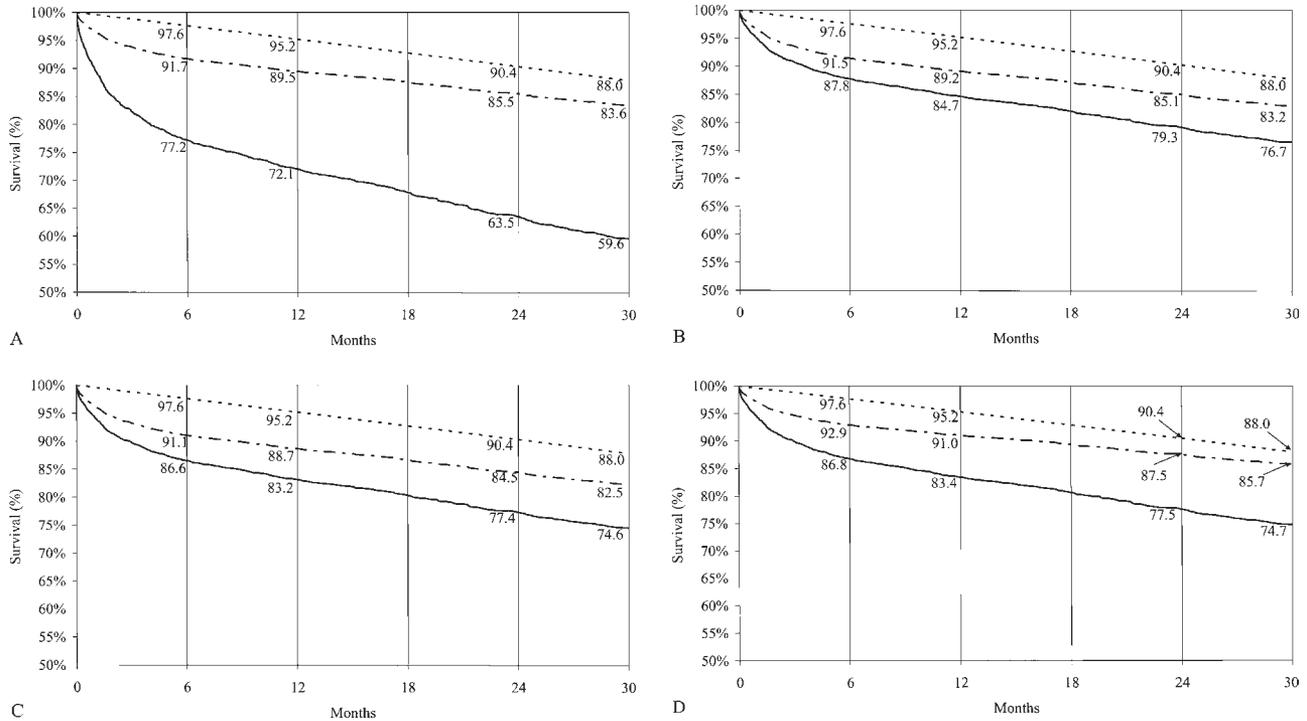


Fig 4. Survival after aortic valve replacement with concomitant coronary artery bypass graft surgery according to preoperative cardiac risk factors. Dashed lines are survival for age- and sex-matched US population. Solid and dash-dotted lines represent risk-adjusted survival for patients with and without each risk factor, respectively. (A) Acute myocardial infarction less than 24 hours or hemodynamically unstable. (B) Congestive heart failure. (C) Left ventricular ejection fraction less than 0.40. (D) Combination of congestive heart failure, left ventricular ejection fraction less than 0.40, and acute myocardial infarction less than 24 hours or hemodynamically unstable.

dergoing AVR had lower survival rates than a group of people from the general population who were age and sex matched to the AVR group of interest. It is difficult to interpret these findings because in addition to healthy patients, the age- and sex-matched group of people from the general population includes people with severe aortic stenosis who did not undergo AVR as well as people with other serious health conditions. However, it is expected that the number in the former group is not very large because numerous studies have shown that patients with severe aortic stenosis fare better with AVR than without it [1, 3, 6-12]. Also, a reasonable assumption is that AVR patients are as likely to have other serious medical conditions as age- and sex-matched patients from the general population.

It was especially notable that patients with AVR with concomitant CABG surgery who were 75 or older had a risk-adjusted survival of 83.3%, not statistically different from the 84.0% survival for people from the general population who were age and sex matched to this group.

Also, the 64.3% of patients with isolated AVR who had neither CHF, EF less than 0.40, AMI less than 24 hours, nor hemodynamic instability had a risk-adjusted survival of 89.9%, statistically equivalent to the 90.0% survival rate of the age- and sex-matched general population. This is especially important because it means that this group of patients without major symptoms is very strongly indicated for AVR.

Of the different individual risk factors for 30-month mortality after isolated AVR, the one that was clearly the most dangerous was AMI less than 24 hours or hemodynamic instability. As indicated in Table 3, it had the highest adjusted hazard ratio (AHR, 3.11;  $p < 0.0001$ ). Also, whereas patients without this risk factor fared nearly as well as patients from the age- and sex-matched general population on 30-month adjusted survival (88.4% versus 90.0%), patients with the risk factor had a much lower 30-month survival (69.8%). For patients with AVR with concomitant CABG surgery, patients with AMI less than 24 hours or who were hemodynamically unstable had an even lower risk-adjusted 30-month survival of 59.6%, compared with 83.6% for patients with neither AMI less than 24 hours nor hemodynamic instability, and a rate of 88.0% for the age- and sex-matched general population. However, less than 2% of patients in the isolated AVR group and in the AVR with concomitant CABG group had either an AMI within 24 hours or were hemodynamically unstable.

The 30-month survival for patients of age 75 and younger was 90.1% if they underwent an isolated AVR and 83.3% if they underwent AVR with concomitant CABG surgery. For patients older than 75, the 30-month survival was 86.2% for isolated AVR and 77.3% for AVR with concomitant CABG surgery. These percentages are similar to findings of other studies. For example, for isolated AVR, Mihaljevic and colleagues [15] reported a

1-year survival of 91%, and He and associates [20] and Morris and coworkers [19] reported respective 5-year survival rates of 74% and 81%.

In conclusion, we found that the medium-term mortality of AVR patients in a population-based study is excellent, and that for the large number of patients without high-risk conditions like CHF, low EFs, recent AML, or hemodynamic instability, the 30-month survival is essentially as high as that of an age- and sex-matched group of the US population. Although we were not able to compare AVR patients with patients with aortic stenosis who did not undergo AVR, the fact that many AVR patients have been demonstrated to fare as well as an age- and sex-matched group of patients without aortic stenosis certainly indicates that AVR is an appropriate intervention for these patients.

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## References

- Grimard BH, Larson JM. Aortic stenosis: diagnosis and treatment. *Am Fam Physician* 2008;78:717-24.
- Varadarajan P, Kapoor N, Bansal RC, Pai RG. Survival in elderly patients with severe aortic stenosis is dramatically improved by aortic valve replacement: results from a cohort of 277 patients aged  $\geq 80$  years. *Eur J Cardiothorac Surg* 2006;30:722-7.
- Tarantini G, Buja P, Scognamiglio R, et al. Aortic valve replacement in severe aortic stenosis with left ventricular dysfunction: determinants of cardiac mortality and ventricular function recovery. *Eur J Cardiothorac Surg* 2003;24:879-85.
- Aronow WS. Recognition and management of aortic stenosis in the elderly. *Geriatrics* 2007;62:23-32.
- Bach DS, Cimino N, Deeb GM. Unoperated patients with severe aortic stenosis. *J Am Coll Cardiol* 2007;50:2018-9.
- Kojodjojo P, Gohil N, Barker D, et al. Outcomes of elderly patients aged 80 and over with symptomatic, severe aortic stenosis: impact of patient's choice of refusing aortic valve replacement on survival. *QJM* 2008;101:567-73.
- Aronow WS, Ahn C, Kronzon I, Nanna M. Prognosis of congestive heart failure in patients aged  $\geq 62$  years with unoperated severe valvular aortic stenosis. *Am J Cardiol* 1993;72:846-8.
- Pereira JJ, Lauer MS, Bashir M, et al. Survival after aortic valve replacement for severe aortic stenosis with low transvalvular gradients and severe left ventricular dysfunction. *J Am Coll Cardiol* 2002;39:1356-63.
- Dal-Bianco JP, Khanvdheria BK, Mookadam F, et al. Management of asymptomatic severe aortic stenosis. *J Am Coll Cardiol* 2008;52:1279-92.
- Otto CM. Valvular aortic stenosis: disease severity and timing of intervention. *J Am Coll Cardiol* 2006;47:2141-51.
- Mohan SB, Stouffer GA. Timing of surgery in aortic stenosis. *Curr Treat Options Cardiovasc Med* 2006;8:421-7.
- Hachicha Z, Dumesnil JG, Bogaty P, Pibarot P. Paradoxical low-flow, low-gradient severe aortic stenosis despite preserved ejection fraction is associated with higher afterload and reduced survival. *Circulation* 2007;115:2856-64.
- Pai GR, Varadaraian P, Razzouk A, Lagazzi L. Survival benefit of aortic valve replacement in patients with severe aortic stenosis with low ejection fraction and low gradient with normal ejection fraction. *Ann Thorac Surg* 2008;86:1781-9.
- Pellikka PA, Sarano ME, Nishamura RA, et al. Outcome of 622 adults with asymptomatic, hemodynamically significant aortic stenosis during prolonged follow-up. *Circulation* 2005;111:3290-5.
- Mihaljevic T, Nowicki ER, Rajeswaran J, et al. Survival after valve replacement for aortic stenosis: implications for decision making. *J Thorac Cardiovasc Surg* 2008;135:1270-9.
- Brown ML, Pellikka PA, Schaff HV, et al. The benefits of early valve replacement in asymptomatic patients with severe aortic stenosis. *J Thorac Cardiovasc Surg* 2008;135:308-15.
- Sharon R, Grossi EA, Saunders PC, et al. Aortic valve replacement in patients with impaired ventricular function. *Ann Thorac Surg* 2003;75:1808-14.
- He GW, Acuff TE, Ryan WH, et al. Aortic valve replacement: determinants of operative mortality. *Ann Thorac Surg* 1994;57:1140-6.
- Morris JJ, Schaff HV, Mullany CJ, et al. Determinants of survival and recovery of left ventricular function after aortic valve replacement. *Ann Thorac Surg* 1993;56:22-30.
- He GW, Grunkemeier GL, Starr A. Aortic valve replacement in elderly patients: influence of concomitant coronary grafting on late survival. *Ann Thorac Surg* 1996;61:1746-51.
- Arias E. United States life tables, 2004. National Vital Statistics Reports from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System 2007;56:1-39.
- Ellison P. Survival analysis using the SAS system 1995. Cary, NC: The SAS Institute.
- Ghali WA, Quan H, Brant R, et al. Comparison of 2 methods for calculating adjusted survival curves from proportional hazards models. *JAMA* 2001;286:1494-7.

## INVITED COMMENTARY

Of the four left-sided valvular lesions treated with valve replacement, aortic valve replacement for severe aortic stenosis yields the best early and late results. After removal of the obstruction to the left ventricular outflow, the heart is almost immediately better, in part because the ventricle has been preconditioned to generate higher pressures. Thus, there are few contraindications to valve replacement for severe aortic stenosis.

Hannan and colleagues [1], using the New York State cardiac surgery database, identified risk factors that impact mortality and generated survival statistics for

those with and without the important risk factors and compared those results with the general population. None of the risk factors identified and compared (including advanced age, recent acute myocardial infarction, congestive heart failure, diminished ejection fraction, and hemodynamic instability) are actually surprising, although the degree of their impact is more clearly defined.

This study, sufficiently powered with 6,369 patients, substantiates the risk associated with concomitant myocardial revascularization. For decades cardiac surgeons have