ATS/2010/249094

Changing Outcome Characteristics of Multiple Valve Surgery in North America: A 15-Year Perspective and Comparison to Single Valve Procedures

by

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from

Society of Thoracic Surgeons Adult Cardiac Surgical Database
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Running Head: Multiple Valve Surgery

Keywords: Cardiac Valve Surgery; Statistical Risk Analysis; Outcome Assessment

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Article Word Count = 4938
Tables + Figures = 10

Abstract

Purpose: While results in valvular heart surgery seem to be improving, too few multiple valve cases are available in most centers to appreciate changes in outcome. This study examined trends in national results for multiple valve procedures over the past 15 years, within the context of overall valve surgery.

Methods: From 1994 through 2007, 623,039 valve procedures were divided into three 5-year periods and grouped into single aortic (A), mitral (M) and tricuspid (T) operations, along with AM, MT, AT and AMT +/- coronary artery bypass grafting. Pulmonary valve surgery was excluded. Trends in baseline characteristics were documented, and logistic regression analysis adjusted for differences in preoperative patient profiles. Outcomes were expressed as unadjusted operative mortality (UOM), adjusted odds ratios for mortality (AORM) and a composite of mortality and major complications (AORC).

Results: Multiple valve procedures comprised 11% of valve surgery. As compared to single valves, age, non-elective status, and most baseline characteristics were little different for multiple valves. However, UOM and AORM were higher for multiple valve cases, but all mortalities fell significantly over the 15 years ($p<0.001$). The relative importance of the various preoperative risk factors on operative mortality differed little across single and multiple valve categories. Cardiac etiology accounted for 54% of deaths, and pulmonary and/or infectious etiologies for 16%. Overall, cardiac etiology of death fell by 16% over time, but pulmonary death and complications increased by 71% and 39%, respectively. Primarily as a consequence of increasing pulmonary events, AORC remained relatively unchanged over the 15 years.

Conclusions: Preoperative risk profiles for multiple valve patients generally were similar to single valve cohorts. Risk-adjusted operative mortalities fell over the past 15 years for all valve surgery, but remained higher for multiple valves. The relative importance of mortality risk factors appeared similar for most valve categories. The finding of increasing pulmonary deaths and complications suggests that enhanced peri-operative pulmonary management could be a focus for quality improvement in this population.

Abstract Word Count = 321

Introduction

Multiple valve procedures comprise only a small percentage of adult cardiac surgery, representing approximately 10% of valve operations in North America (1). This small sample makes it difficult to identify and compare outcome changes based on single-institutional data. Although a few slightly larger series exist (2), the majority of reports are limited to less than 500 patients (3-6), and reviews of triple valve procedures are even more limited (7). Even in the larger centers, the time required to complete a multiple valve series usually exceeds a decade, making trends in multiple valve operations difficult to assess (8, 9).

Overall, outcomes in cardiac surgery are improving. While patients having coronary bypass are more complex and high-risk, risk-adjusted mortalities have declined over the past 15 years (10), especially in critically ill groups (11). Mortalities also have fallen for patients undergoing isolated valve surgery, such as aortic valve replacement (1, 12), again primarily in patients with more advanced risk profiles and age (13, 14). Declining mortality is a prominent feature of patients undergoing mitral valve surgery (15) and may be due in part to increased application of early mitral valve repair (16, 17). While trends appear positive (1, 18, 19), however, recent quantitative data are not available, especially for multiple valve subgroups. The goals of this analysis were to compare baseline and outcome characteristics of multiple valve patients to those undergoing single valve operations and to assess trends in results over time.

Methods

Data source

The STS national database was established in 1989 by North American heart surgeons to collect and analyze cardiac surgical results in a consistent manner (20, 21). The STS currently records more than 80% of adult cardiac surgery in North America with well-developed variable sets and certified software systems. Detailed definitions for preoperative risk factors, as well as postoperative complications have been established by the STS and can be viewed online (http://www.sts.org). Data from individual centers

are harvested semiannually and sent to the STS data warehouse and analysis center at the Duke Clinical Research Institute. A series of data quality checks are performed before data are aggregated into the national sample. Audits are obtained for randomly selected centers annually. Since 1993, the variables entered and definitions used have been fairly consistent and have changed only in minor ways. The accuracy and comparability of STS results have been confirmed by comparison with other mandatory and audited cardiac databases (22), and a more complete description of the data set is given elsewhere (1).

Patient Population

The population for this study included 623,039 patients undergoing valve surgery with or without concomitant CABG. Patients were divided into three 5-year time periods 1 (1994-1998), 2 (1999-2002), and 3 (2003-2007) and grouped by type of valve operation: aortic (A) n=338,143, mitral (M) n=211,167, tricuspid (T) n= 5,803, AM n=39,260, AT n=2,236, MT n=21,056 or AMT n=5,374. Patient undergoing pulmonary valve operations were excluded from analysis, as were patients having other major concomitant procedures, such as left ventricular aneurysm repair. Patients with atrial fibrillation undergoing various ablation procedures were included.

Analysis Techniques

The valve surgery population was grouped according to the seven procedures: (A, M, T, AM, AT, MT, AMT), and demographic and outcome variables were compared over the three 5-year time intervals for all seven procedures. Raw mortality data were expressed as unadjusted operative mortality (UOM). Using standard approaches (1), seven separate multivariable logistic regression analyses were performed, one for each type of procedure. Operative mortalities adjusted for differences in patient baseline characteristics were expressed as adjusted odds ratios for mortality (AORM), and were compared for the seven procedures over the 3 time intervals, as were the relative importance and ranking of risk factors for mortality in each procedural regression analysis. Operative mortality predicted from the model for a given patient's risk profile was expressed as "predicted" or "expected" mortality. Observed to expected (O/E) ratios for risk-adjusted mortality were calculated for all procedures, with the mid-year of the study (2000) as the reference. Finally, causes of postoperative death were assessed over time, along with major

postoperative morbidities (re-operation, neurologic defect, various pulmonary and infectious complications, and renal/multiorgan failure). A risk-adjusted odds ratio for the composite of mortality and major morbidity (AORC) was developed and evaluated over the 15 years for all procedures. A list of standard STS covariates used in the regression model and more detailed descriptions of the methodology are given elsewhere (1). Valve repair versus replacement was not included in the analysis for reasons of complexity.

Results

Trends in Overall Patient Demographics

Over the 15 years of the series, interesting changes occurred in the demographics of valve surgery patients (Table 1). Although mean patient age remained around 67 years, the age distribution changed, with increasing percentages of patients in younger (50 to 60 years) and older (over 80 years) groups. Nearly 17% of valve surgery currently is performed in patients over 80 years of age. At present, 12% of valve patients have a Body Mass Index above 35, and this incidence has doubled over the last decade. Diabetes has increased by 6 % and hypertension by more than 20%. Preoperatively, valve patients now are more likely to have renal failure (8%), severe lung disease (22%), and cerebrovascular disease (15%). They are more likely to have had prior coronary artery bypass grafting (9%), but less likely to have had prior valve surgery (6.5%). They are less likely to have congestive heart failure (44%) and have higher ejection fractions (median EF=0.55) overall. However, the percentage of patients with extremely low ejection fractions continues to increase. Recently, patients with ejection fractions lower than 0.35 account for 12.5% of the population. The type of valve disease also appears to be changing: aortic stenosis is increasing, and mitral stenosis is decreasing. Aortic insufficiency, mitral insufficiency and tricuspid insufficiency all are on the rise. With regard to procedural status over the last 15 years, elective surgical referral continues to fall (as described previously [1]), non-elective urgent operations continue to increase (30% at present), but emergency and salvage operations now are less common.

Single vs. Multiple Valves

Surprisingly, baseline characteristics of patients undergoing the various valve procedures were relatively similar, both among single valves, and for multiple valve operations (Table 2). However, small differences did exist: Patients undergoing isolated A surgery tended to be older, and T younger than other valve categories (Table 6). Women underwent T procedures more often than men: MT (65% female), AMT (61%), AT (56%), and T (56%). Hypertension and dyslipidemia were more common in A (66% and 49% respectively), and A patients tended to be more obese, with 11.5% having a BMI > 35. Renal failure was present in over 15% of T and AT patients, significantly higher than in other groups, and isolated T and AT patients more often had endocarditis (20% and 15% respectively). This finding likely represents dialysis-related endocarditis in the renal failure subset. Re-operations more commonly involved the tricuspid valve, and as in other analyses, T patients tended to be somewhat unique. Patients with A were the least likely to have congestive heart failure (37%) and less frequently had cardiogenic shock (1%). Patients undergoing M or A were most likely to have a concomitant coronary artery bypass (44% and 50%, respectively), whereas multiple valve patients had less coronary disease and more reoperations.

Trends in Mortality

Overall, average UOM for all types of valve surgery declined over time and is now 5.6% (Table 3). In particular, mortality decreased for isolated aortic and mitral valves, and for all combinations of multiple valves. UOM after T was the highest of single valves but also fell slightly, although the change was not statistically significant. UOM for multiple valve procedures, while falling over the 15 years, remained over twice as high as for single valves (Figure 1A; Table 3). The results of the 7 logistic regression analyses are shown in Table 4. After adjustment for differences in patient baseline characteristics, AORM declined over time for all single and multiple valve procedures (Figure 1B; Table 4), and AORM for multiple valves fell faster than for single valves. Multivariable analysis within each model produced a ranking of importance of preoperative risk factors according to independent odds ratios (Table 4). A surprisingly consistent ranking of risk factors was observed across all valve procedures, both

in terms of order and individual odds ratios (Figure 2), except again, procedures involving T valves produced more variability. As reported previously (1), non-elective procedural status, renal failure, preoperative shock, and reoperation were the most important risk factors. It should be emphasized that the mortality data in this paper represent all patients, including all high-risk categories (such as emergency/salvage, endocarditis, etc.). Variations in preoperative patient characteristics had a profound effect on mortality across all categories of procedures (Table 5). In the last 5-year period, elective heart valve surgery in North America was very safe, with a 0.5% UOM in all ***elective*** single and multiple valve patients with ***normal EF*** and less than ***55 years*** of age. However, just the addition of 3 risk factors (age > 65 years, EF < 0.4, and urgent status) increased the overall UOM twenty-fold, to 10% (Table 5). The addition of more risk factors or comorbidities would have an even greater effect.

The majority of deaths were initiated by cardiac factors for all procedures and over time (Table 6). However, a reduction in cardiac causes of mortality occurred for all valve surgery over the past 15 years, decreasing from 61% of deaths in the first period to 51% in the last. The full gamut of causes of death for all procedures over time is given in Table 6. Of significant interest, an increase in mortality from pulmonary and infectious etiologies was evident, increasing from 11% in the first period to 20% in the last, and consistently comprising the second most common cause of death.

Morbidity over Time

Morbidity from pulmonary and infectious causes with resultant multiorgan failure increased over the period (Table 7A). This was largely due to increases in prolonged ventilation, pneumonia, and multi-system organ failure. As a result, the composite of unadjusted mortality and major morbidity steadily increased overtime for each valve procedure (Figure 3A); and even after adjustment for worsening risk factors, AORC for each procedure remained close to 1 or rose slightly (Figure 3B). Patients undergoing multiple valve surgeries also were more likely to experience complications (Table 7B). For the recent period, unadjusted composite of morbidity and mortality ranged from 17% for isolated aortic valves to over 40% for triple valves, and unadjusted composite outcome has continued to worsen over time. In the last year of the analysis, 2007, the observed composite morbidity and mortality was: A 20%, M 24%, T

32%, AM 36%, AT 39%, MT 35% and AMT 46%. This seems to be occurring despite falling mortality, and largely because of increasing pulmonary/infectious complications.

Discussion

The STS database has the advantage of excellent sample size, but studies can be limited by the detail of variables collected. Recently, the valve data set has been expanded, but many important aspects of patient characteristics and peri-operative care are not available in the present analysis. Additionally, the data are viewed from quite a distance from each patient, and undefined confounding variables or treatment selection biases can complicate the interpretation of results. Thus, like most database studies, the findings of this paper should be interpreted within the context of observational design. However, one strength of this type of database is the ability to define longitudinal trends over time in patient care and outcomes for an entire population, and for the purposes of this study, observational limitations are less important.

Demographic profiles of valve patients in North America are changing (Table 1). Patients are increasingly more complex, and in general, sicker and higher risk, reflecting societal trends in diabetes, hyperlipidemia, hypertension, and coronary disease (24-29). While comorbidities such as renal failure and pulmonary disease increased, overall age at operation was relatively constant - although changes were evident at both ends of the spectrum. Patients greater than 80 years were treated surgically more often, but also, surgery was more frequent in the younger population. Patients with extremely low ejection fractions were being operated more, but median ejection fraction was actually increasing. Thus, even though patients were sicker and higher risk overall, a growing population of low risk patients was evident. This finding may have been due in part to an increase in earlier surgery for mitral and other types of severe valve disease (1, 23). Similarly, reoperation after prior coronary surgery was more common. Previous studies have suggested that cardiac reoperations can be performed very safely in valve patients (30, 31), but in this large data set, reoperation was a relatively important risk factor (ranking similarly to renal failure and cardiogenic shock); and a fairly uniform effect was observed across all

procedural types. This finding is at odds with several smaller analyses, and suggests that future surgical strategies should attempt to minimize probabilities for reoperation.

Demographics of the various valve groups were similar, but some differences were evident (Table 2). In particular, isolated tricuspid patients were younger, and had more advanced cardiac and systemic disease, renal dysfunction, endocarditis, and prior cardiac surgery, seeming somewhat unique in the valve population. Aortic valve patients were older and had more coronary disease. Multiple valve patients had more comorbidities, heart failure, and reoperation - but less coronary disease. The overall incidence of reoperation after previous valve surgery was falling, perhaps due to improved stability of newer valve types and/or possibly lower reoperation rates with valve repair (33).

With worsening risk profiles, it is striking that UOM decreased over time for every valve category (Figure 1A). This finding suggests real outcome improvement despite worsening risk. When risk-adjusted mortality (AORM) was assessed, major independent improvements in adjusted mortality were evident over the 15 years and across all valve categories (Figure 1B). Overall UOM for A procedures now averages 4.4 %, and UOM for M operations has fallen to 5.8% across all levels of risk (including emergencies, elderly patients, etc.). Although this analysis did not separate mitral replacement from mitral valve repair, it has been shown that AORM for mitral repair is approximately half of that for replacement, so transition to repair is one likely explanation for improved results (23). Unadjusted mortalities for T procedures were the highest of single valves (currently 9.6%), as noted previously (1), but also were falling. Multiple valve UOM ranged from 9-13%, lowest for MT and highest for triple valves. It was not clear why multiple valve mortality should be higher than single valves, since patient demographics and risk factors were not that different. Perhaps the longer cardiopulmonary bypass and aortic cross-clamp times required for multiple valve procedures resulted in more patient injury, or other factors may have been operative. This subject would be of interest for future investigation, but the exact cause of higher multiple valve risk is not evident from this analysis.

In the 7 multivariable regressions, risk factors for mortality seemed surprisingly consistent across all procedural categories (Table 4, Figure 2). No matter the operation, non-elective

presentation had the highest odds ratio, followed by renal failure, reoperation, preoperative hemodynamic derangement, etc. Age per year had a low odds ratio, but accumulated advanced age (>65 years) has been shown to be the second most important variable following non-elective presentation (1). The consistency of risk factors across valve categories again would argue for some other variable, such as longer bypass times, as being the factor responsible for higher multiple valve mortality. The similarity of risk factors also would suggest that one large risk model, with valve procedure as a single covariate, could be appropriate for assessing multivariable risk for all valve surgery (1).

It should be emphasized that worsening baseline risk influences outcome in a major way. Elective surgical therapy in a low-risk patient is now extremely safe across all valve procedural types, with an overall UOM of 0.5% (Table 5). However, allowing patients to develop severe ventricular dysfunction, serious symptoms requiring urgent surgery, or other adverse factors markedly increases mortality (20-fold or more), again emphasizing the importance of elective surgical referral of patients with severe valve disease. Since advanced age itself multiplies risk, perhaps higher risk patients should be referred earlier, rather than waiting until no other option exists. This message may be becoming accepted, to some extent, as evidenced by the increase in younger low-risk subsets in recent years. However, earlier referral of high-risk patients continues to be a major outcome improvement opportunity (1).

The variable "cause of death" in the STS database refers to the single cause initiating the series of complications that led to the fatal event. Over the 15 years of this series, cardiac etiology always has been the most important cause, but a decline in cardiac etiology has occurred over time. This may be due to improvements in myocardial protection, better arrhythmia management, advances in critical care, earlier mechanical support, or a combination of these and other factors. Moreover, it is likely that still further improvements in cardiac management are possible (33). The most striking finding in the cause of death analysis was the dramatic increase in pulmonary and infectious mortalities. This observation may reflect national trends of worsening antibiotic-resistant gram negative pneumonia across all of medicine (34). In the US population before 1936, pneumonia was the leading cause of death, and Osler called pneumonia "The captain of the men of death". Given the recent rise in resistant pneumonia rates

internationally, “the captain may be back”. Based on the results of the present study, an effective campaign to prevent and treat pulmonary complications after valve surgery seems to be the primary candidate for outcome improvement in the near future (35). Little emphasis has been placed on this topic in recent cardiac surgical literature, but from clinical practice and this analysis, a serious examination seems to be in order.

When unadjusted composite of mortality and major morbidity was assessed (Figure 3A), recent gains in mortality seem to have been offset by increases in pulmonary and infectious complications (Tables 7A and B). This increase in morbidity may be due in part to sicker patients at baseline, but the phenomenon was evident even after adjusting for longitudinal increases in baseline risk using AORC (Figure 3B). It seems that surgical care systems have become better in producing survival of patients with major postoperative morbidity, but the ideal approach would be to prevent or more effectively treat these problems before major complications occur, including direct management of post-cardiopulmonary bypass immune dysfunction (34, 35). Even in 2007, more than one in three patients having a multiple valve procedure had a major morbid or fatal event. Over the next 5 years, this might be an area of significant focus.

Another quality improvement candidate would be enhanced preoperative management of the sicker patients. Intensive preoperative pulmonary, renal, arrhythmia, or hemodynamic interventions can improve patient profiles appreciably and thereby augment outcomes. Increasing emphasis on preoperative care may be evident in the current data already, with fewer patients now having operation in emergency or salvage status, but possibly being converted to an urgent (and lower risk) category preoperatively. Finally, extremely high risk profiles do exist that have little chance of recovery. Endocarditis in the sickest dialysis patients is an example in which better patient selection and avoidance of surgical intervention may be appropriate (36). With current technology, very few patients should be turned down for surgery. However, appropriate selection is important and could reduce individual institutional and national mortality appreciably without worsening overall survival benefit.

In conclusion, valve surgery patients in North America have increasingly adverse baseline risk profiles. Despite this finding, operative mortalities are progressively falling, whether assessed as raw values or risk adjusted data. Multiple valve surgery is associated with twice the risk of single valves and is an area for potential outcome improvement. Increasing use of valve repair, earlier surgical referral, and reducing pulmonary complications are good quality improvement candidates. However, the most significant aspect of this review is the steadily improving results being obtained by North American heart surgeons in all valve surgery categories. Because continuous quality improvement has been part of the fabric of cardiac surgery from the beginning, this phenomenon likely will continue. Hopefully, the next 15 years will witness even greater progress in the surgical treatment of valvular heart disease.

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Table 1: Trends in pre-operative characteristics of patients undergoing valve surgery.

Variable		Total N (623,039)	Overall (%)	N (136,071)	1993-1997 (%)	N (194,425)	1998-2002 (%)	N (292,543)	2003-2007 (%)	P-value+
DEMOGRAPHICS										
Age	Median	623,039	70.00	136,071	69.00	194,425	70.00	292,543	70.00	<.0001
	Mean	623,039	66.91	136,071	66.07	194,425	67.06	292,543	67.19	<.0001
	≥80	93,118	14.95	14,894	10.95	28,746	14.79	49,478	16.91	<.0001
	≥50 and <60	89,730	14.40	18,469	13.57	26,996	13.89	44,265	15.13	<.0001
RISK FACTORS										
Body Mass Index	Mean	606,004	27.70	125,652	26.66	189,493	27.57	290,859	28.24	<.0001
	≥40	21,955	3.52	2,813	2.07	6,245	3.21	12,897	4.41	<.0001
Diabetes/Treatment	Diabetes	143,405	23.02	24,903	18.30	42,128	21.67	76,374	26.11	<.0001
Hypertension	Yes	391,156	62.78	67,376	49.52	117,500	60.43	206,280	70.51	<.0001
Dyslipidemia	Yes	282,570	45.35	38,898	28.59	75,168	38.66	168,504	57.60	<.0001
Renal Failure/Dialysis	Renal Failure with Dialysis	13,849	2.22	1,956	1.44	4,017	2.07	7,876	2.69	<.0001
	Renal Failure without Dialysis	33,723	5.41	6,660	4.89	10,566	5.43	16,497	5.64	<.0001
Chronic Lung Disease	Yes	103,673	16.64	9,439	6.93	28,826	14.82	65,408	22.36	<.0001
Immunosuppressive Treatment	Yes	17,594	2.82	2,774	2.04	5,536	2.85	9,284	3.17	<.0001
Cerebrovascular Disease	Yes	81,985	13.16	12,140	8.92	25,159	12.94	44,686	15.28	<.0001
PREVIOUS CV INTERVENTIONS										
Previous Coronary Artery Bypass Surgery	Yes	55,198	8.86	10,575	7.77	17,155	8.82	27,468	9.39	<.0001
Previous Valve Surgery	Yes	47,839	7.68	14,050	10.33	14,603	7.51	19,186	6.56	<.0001
PRE OPERATIVE CARDIAC STATUS										
Congestive Heart Failure	Yes	282,410	45.33	62,411	45.87	91,237	46.93	128,762	44.01	<.0001
Ejection Fraction	Median	544,878	55.00	101,805	50.00	169,410	51.00	273,663	55.00	<.0001
	<35	72,773	11.68	13,597	9.99	22,568	11.61	36,608	12.51	<.0001
Aortic Stenosis	Yes	304,134	48.81	63,902	46.96	93,900	48.30	146,332	50.02	<.0001
Mitral Stenosis	Yes	64,012	10.27	18,178	13.36	23,053	11.86	22,781	7.79	<.0001
Aortic Insufficiency	Yes	249,254	40.01	43,483	31.96	76,567	39.38	129,204	44.17	<.0001
Mitral Insufficiency	Yes	338,388	54.31	51,343	37.73	97,215	50.00	189,830	64.89	<.0001
Tricuspid Insuffuciency	Yes	139,395	22.37	10,125	7.44	30,624	15.76	98,646	33.72	<.0001
OPERATIVE										
Status of the Procedure	Emergent Salvage	2,431	0.39	1,194	0.88	676	0.35	561	0.19	<.0001
	Emergent	13,975	2.24	4,136	3.04	4,271	2.20	5,568	1.90	<.0001
	Urgent	156,228	25.08	24,759	18.20	44,831	23.06	86,638	29.62	<.0001
	Elective	447,241	71.78	104,065	76.48	143,790	73.96	199,386	68.16	<.0001

Legend: Demographic characteristics of the overall valve surgery population for three time intervals: 1993-1997, 1998-2002, and 2003-2007.

Table 2: Pre-operative patient characteristics by individual valve procedure.

Variable		Total N (623,039)	Overall (%)	N (338,143)	Single Valve - A (%)	N (211,167)	Single Valve - M (%)	N (5,803)	Single Valve - T (%)	N (39,260)	Double Valve - AM (%)	N (2,236)	Double Valve - AT (%)	N (21,056)	Double Valve - MT (%)	N (5,374)	Triple Valve - AMT (%)	P-value+
DEMOGRAPHICS																		
Age	Median	623,039	70.00	338,143	72.00	211,167	66.00	5,803	58.00	39,260	69.00	2,236	70.00	21,056	69.00	5,374	69.00	<.0001
	Mean	623,039	66.91	338,143	69.00	211,167	64.13	5,803	56.09	39,260	65.95	2,236	66.50	21,056	66.13	5,374	66.06	<.0001
	≥80	93,118	14.95	65,352	19.33	18,740	8.87	280	4.83	5,159	13.14	416	18.60	2,461	11.69	710	13.21	<.0001
	≥50 and <60	89,730	14.40	39,298	11.62	39,235	18.58	967	16.66	5,986	15.25	296	13.24	3,166	15.04	782	14.55	<.0001
	<50	69,233	11.11	28,196	8.34	30,298	14.35	2,079	35.83	5,114	13.03	334	14.94	2,509	11.92	703	13.08	<.0001
Gender	Female	267,345	42.91	125,478	37.11	101,506	48.07	3,272	56.38	18,851	48.02	1,241	55.50	13,697	65.05	3,300	61.41	<.0001
RISK FACTORS																		
Body Mass Index	Median	606,004	26.82	328,638	27.45	205,432	26.10	5,636	26.03	38,217	26.22	2,191	26.29	20,630	25.88	5,260	25.81	<.0001
	≥40	21,955	3.52	13,879	4.10	5,553	2.63	211	3.64	1,209	3.08	108	4.83	838	3.98	157	2.92	<.0001
	≥35 and <40	40,231	6.46	25,079	7.42	10,782	5.11	351	6.05	2,288	5.83	137	6.13	1,299	6.17	295	5.49	<.0001
Smoker Status	Current Smoker	86,139	13.83	43,724	12.93	32,057	15.18	1,083	18.66	5,986	15.25	295	13.19	2,362	11.22	632	11.76	<.0001
Diabetes / Treatment	Yes	143,405	23.02	83,435	24.68	43,690	20.69	1,213	20.91	8,447	21.51	542	24.24	4,854	23.05	1,224	22.77	<.0001
Hypertension	Yes	391,156	62.78	224,789	66.48	122,650	58.08	2,733	47.10	23,458	59.75	1,370	61.27	13,008	61.78	3,148	58.58	<.0001
Dyslipidemia	Yes	282,570	45.35	164,904	48.77	88,859	42.08	1,733	29.86	16,079	40.96	855	38.24	8,186	38.88	1,954	36.36	<.0001
Last Creatinine Level Preop	≥2.5	19,695	3.16	8,679	2.57	7,306	3.46	378	6.51	1,847	4.70	169	7.56	1,014	4.82	302	5.62	<.0001
	≥2 and <2.5	12,727	2.04	5,967	1.76	4,544	2.15	242	4.17	1,035	2.64	83	3.71	668	3.17	188	3.50	<.0001
Renal Failure / Dialysis	Renal Failure with Dialysis	13,849	2.22	6,105	1.81	4,949	2.34	250	4.31	1,440	3.67	143	6.40	710	3.37	252	4.69	<.0001
	Renal Failure without Dialysis	33,723	5.41	15,793	4.67	12,153	5.76	674	11.61	2,582	6.58	239	10.69	1,809	8.59	473	8.80	<.0001
Infectious Endocarditis / Type	Endocarditis / Active	15,444	2.48	5,714	1.69	5,837	2.76	724	12.48	2,295	5.85	195	8.72	461	2.19	218	4.06	<.0001
Chronic Lung Disease	Yes	103,673	16.64	54,094	16.00	35,166	16.65	1,004	17.30	7,531	19.19	454	20.30	4,350	20.66	1,074	19.98	<.0001
PREVIOUS CV INTERVENTIONS																		
Previous Coronary Artery Bypass Surgery	Yes	55,198	8.86	29,987	8.87	17,658	8.36	596	10.27	3,491	8.89	301	13.46	2,584	12.27	581	10.81	<.0001
Previous Valve Surgery	Yes	47,839	7.68	16,817	4.97	18,799	8.90	1,313	22.63	4,883	12.44	666	29.79	4,121	19.57	1,240	23.07	<.0001
PRE OPERATIVE CARDIAC STATUS																		
Congective Heart Failure	Yes	282,410	45.33	126,585	37.44	109,967	52.08	2,981	51.37	23,425	59.67	1,434	64.13	14,227	67.57	3,791	70.54	<.0001
Cardiogenic Shock	Yes	14,214	2.28	3,957	1.17	8,475	4.01	184	3.17	890	2.27	58	2.59	533	2.53	117	2.18	<.0001
NYHA Classification	IV	119,245	19.14	54,487	16.11	46,581	22.06	1,328	22.88	9,455	24.08	595	26.61	5,271	25.03	1,528	28.43	<.0001
	III	245,560	39.41	134,280	39.71	80,319	38.04	2,119	36.52	16,417	41.82	945	42.26	9,136	43.39	2,344	43.62	<.0001
Ejection Fraction	Median	544,878	55.00	291,179	55.00	188,315	50.00	4,810	55.00	34,648	50.00	1,984	50.00	19,085	50.00	4,857	50.00	<.0001
	≥50	353,055	56.67	198,716	58.77	114,819	54.37	3,408	58.73	20,586	52.44	1,147	51.30	11,464	54.45	2,915	54.24	<.0001
OPERATIVE																		
Status of the Procedure	Emergent Salvage	2,431	0.39	773	0.23	1,394	0.66	31	0.53	143	0.36	8	0.36	63	0.30	19	0.35	<.0001
	Emergent	13,975	2.24	5,122	1.51	7,318	3.47	160	2.76	851	2.17	62	2.77	367	1.74	95	1.77	<.0001
	Urgent	156,228	25.08	79,079	23.39	55,674	26.36	1,793	30.90	11,223	28.59	780	34.88	6,050	28.73	1,629	30.31	<.0001
	Elective	447,241	71.78	251,305	74.32	14,579	69.04	3,785	65.22	26,861	68.42	1,376	61.54	14,509	68.91	3,611	67.19	<.0001
Concominant procedure - CABG	Yes	286,202	45.94	167,502	49.54	93,522	44.29	1,336	23.02	15,289	38.94	671	30.01	6,340	30.11	1,542	28.69	<.0001
Pre-op IABP	Yes	19,637	3.15	4,342	1.28	13,428	6.36	160	2.76	775	1.97	41	1.83	795	3.78	96	1.79	<.0001

Legend: Preoperative demographics of individual valve procedures over the entire 15 years.

Table 3: Trends in unadjusted mortality by procedure over 15 years for the 3 time periods.

Variable	Total Patients	Total Mortality	Mortality (%)	Total Patients	Total Mortality	Mortality (%)	Total Patients	Total Mortality	Mortality (%)	Total Patients	Total Mortality	Mortality (%)	P-value+
	Overall			1993-1997			1998-2002			2003-2007			
Overall	623,039	38,996	6.26	136,071	9,779	7.19	194,425	12,804	6.59	292,543	16,413	5.61	<.0001
A	338,143	16,663	4.93	76,018	4,285	5.64	105,852	5,502	5.20	156,273	6,876	4.40	<.0001
M	211,167	14,458	6.85	46,000	3,831	8.33	67,572	4,943	7.32	97,595	5,684	5.82	<.0001
T	5,803	582	10.03	1,000	112	11.20	1,652	168	10.17	3,151	302	9.58	0.3253
AM	39,260	4,200	10.70	8,469	919	10.85	12,089	1,365	11.29	18,702	1,916	10.24	0.0130
AT	2,236	294	13.15	316	60	18.99	517	69	13.35	1,403	165	11.76	0.0027
MT	21,056	2,049	9.73	3,328	408	12.26	5,316	564	10.61	12,412	1,077	8.68	<.0001
AMT	5,374	750	13.96	940	164	17.45	1,427	193	13.52	3,007	393	13.07	<.0001

Legend: See text for valve abbreviations.

Table 4: Risk factors for mortality and AORM by procedure type.

	Adjusted Odds Ratios for Mortality per Procedure						
Preoperative Risk Factor	**A**	**M**	**T**	**AM**	**MT**	**AT**	**AMT**
Emergent/Salvage Status	3.59	3.12	5.68	3.01	3.12	3.02	4.36
Renal Failure with Dialysis	3.27	3.84	3.21	3.51	3.28	2.46	2.92
Second Reoperation	2.52	2.14	2.30	2.12	2.05	1.30	1.44
Renal Failure w/o Dialysis	2.05	2.06	2.28	1.86	2.26	2.45	2.28
Cardiogenic Shock	2.00	1.84	1.96	1.71	1.97	2.57	3.44
First Reoperation	1.93	1.75	1.61	1.56	1.56	1.43	1.67
Preop IABP	1.64	1.42	1.42	1.65	1.42	3.23	1.01
Insulin-Dependent Diabetes	1.59	1.60	1.17	1.54	1.60	1.07	1.74
Concomitant CABG	1.50	1.56	1.46	1.45	1.31	1.97	1.48
Endocarditis	1.49	1.64	1.09	1.55	1.18	1.12	1.10
Urgent Status	1.47	1.48	1.69	1.37	1.70	1.48	1.48
Arrhythmia	1.34	1.04	1.21	0.99	0.91	1.03	0.83
CVA	1.24	1.28	1.08	1.04	1.23	0.77	1.00
Age	1.03	1.04	1.03	1.04	1.03	1.03	1.03
Years '98-'02 (vs '93-'97)	0.85	0.83	0.87	0.90	0.75	0.56	0.67
Years '03-'07 (vs '93-'97)	0.72	0.67	0.81	0.74	0.59	0.53	0.63

Legend: Both "Status" variables are referenced to elective presentation; Second reoperation includes 2+ procedures; IABP = Intra-aortic balloon pump; CABG = coronary artery bypass grafts; CVA = history of cerebral vascular accident.

Table 5: Effects of adverse risk factors on predicted and observed mortality by procedure.

Low Risk Patients (Elective, EF>0.4, Age<55 years)

Surgery	Single Valves			Multiple Valves			All Valve Surgery		
Year	n	POM%	UOM%	n	POM%	UOM%	n	POM%	UOM%
2003	1285	1.02	0.39	66	2.91	1.52	1351	1.11	0.44
2004	1371	1.03	0.36	75	3.01	0	1446	1.13	0.35
2005	1795	1.01	0.50	102	2.85	1.96	1897	1.12	0.58
2006	1955	1.04	0.61	120	2.77	0	2075	1.14	0.58
2007	1894	1.04	0.48	102	2.89	0.98	1996	1.13	0.50
2003-07	8,301	1.03	0.48	465	2.87	0.86	8,765	1.13	0.50

High Risk Patients (Urgent, EF<0.4, Age>65 years)

Surgery	Single Valves			Multiple Valves			All Valve Surgery		
Year	n	POM	UOM	n	POM	UOM	n	POM	UOM
2003	3370	11.41	13.32	526	18.33	18.82	3896	12.34	14.07
2004	3597	10.72	11.34	556	17.35	16.55	4153	11.61	12.04
2005	3915	10.67	9.91	676	17.23	15.98	4591	11.63	10.80
2006	4174	10.52	10.21	702	17.57	18.38	4876	11.54	11.38
2007	3934	10.55	9.35	715	16.79	13.43	4649	11.51	9.98
2003-07	19,010	10.74	10.73	3,175	17.42	16.47	22,165	11.71	11.56

Legend: The effects of adding 3 risk factors on "Predicted" Operative Mortality (POM) (derived from the multivariable model) and "Observed" Unadjusted Operative Mortality (UOM). Observed mortality increased twenty-fold with addition of 3 risk factors.

Table 6: Trends in causes of death after valve operations over time.

	Other	Unknown	Valvular	Pulmonary	Infection	Vascular	Renal	Neurologic	Cardiac	Missing
Primary Cause of Death										
Total N (623,039)	3,694	431	380	3,865	2,560	578	1,238	2,714	20,871	2,665
Overall	9.47	1.11	0.97	9.91	6.56	1.48	3.17	6.96	53.52	6.83
N (136,071)	588	0	109	516	576	107	299	656	5940	988
1993-1997	6.01	0.00	1.11	5.28	5.89	1.09	3.06	6.71	60.74	10.10
N (194,425)	1,264	0	122	1,259	787	176	418	909	6,570	1,299
1998-2002	9.87	0.00	0.95	9.83	6.15	1.37	3.26	7.10	51.31	10.15
N (292,543)	1,842	431	149	2,090	1,197	295	521	1,149	8,361	378
2003-2007	11.22	2.63	0.91	12.73	7.29	1.80	3.17	7.00	50.94	2.30
P-value+	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Operative Mortality - A										
Total N (623039)	1,558	198	135	1,816	978	309	546	1,224	8,695	1,204
Overall	9.35	1.19	0.81	10.90	5.87	1.85	3.28	7.35	52.18	7.23
N (136071)	261	0	41	240	235	62	140	297	2,541	468
1993-1997	6.09	0.00	0.96	5.60	5.48	1.45	3.27	6.93	59.30	10.92
N (194425)	531	0	44	595	303	94	188	424	2,754	569
1998-2002	9.65	0.00	0.80	10.81	5.51	1.71	3.42	7.71	50.05	10.34
N (292543)	766	198	50	981	440	153	218	503	3,400	167
2003-2007	11.14	2.88	0.73	14.27	6.40	2.23	3.17	7.32	49.45	2.43
P-value+	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Operative Mortality - M										
Total N (623,039)	1,267	147	143	1,301	970	189	428	1,028	8,003	982
Overall	8.76	1.02	0.99	9.00	6.71	1.31	2.96	7.11	55.35	6.79
N (136,071)	219	0	43	198	232	36	100	263	2,385	355
1993-1997	5.72	0.00	1.12	5.17	6.06	0.94	2.61	6.87	62.26	9.27
N (194,425)	463	0	49	446	316	55	143	358	2,622	491
1998-2002	9.37	0.00	0.99	9.02	6.39	1.11	2.89	7.24	53.04	9.93
N (292,543)	585	147	51	657	422	98	185	407	2,996	136
2003-2007	10.29	2.59	0.90	11.56	7.42	1.72	3.25	7.16	52.71	2.39
P-value+	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Operative Mortality - T										
Total N (623,039)	64	7	2	68	66	3	16	25	294	37
Overall	11.00	1.20	0.34	11.68	11.34	0.52	2.75	4.30	50.52	6.36
N (136,071)	6	0	1	4	11	0	3	6	68	13
1993-1997	5.36	0.00	0.89	3.57	9.82	0.00	2.68	5.36	60.71	11.61
N (194,425)	16	0	1	21	12	3	7	4	84	20
1998-2002	9.52	0.00	0.60	12.50	7.14	1.79	4.17	2.38	50.00	11.90
N (292,543)	42	7	0	43	43	0	6	15	142	4
2003-2007	13.91	2.32	0.00	14.24	14.24	0.00	1.99	4.97	47.02	1.32
P-value+	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005

Table 6 (cont'd)

	Other	Unknown	Valvular	Pulmonary	Infection	Vascular	Renal	Neurologic	Cardiac	Missing
Operative Mortality - AM										
Total N (623,039)	435	37	59	361	335	55	137	261	2,253	267
Overall	10.36	0.88	1.40	8.60	7.98	1.31	3.26	6.21	53.64	6.36
N (136,071)	64	0	17	43	60	7	30	62	549	87
1993-1997	6.96	0.00	1.85	4.68	6.53	0.76	3.26	6.75	59.74	9.47
N (194,425)	151	0	19	109	117	19	53	73	675	149
1998-2002	11.06	0.00	1.39	7.99	8.57	1.39	3.88	5.35	49.45	10.92
N (292,543)	220	37	23	209	158	29	54	126	1,029	31
2003-2007	11.48	1.93	1.20	10.91	8.25	1.51	2.82	6.58	53.71	1.62
P-value+	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Operative Mortality - AT										
Total N (623,039)	30	N/A	4	45	20	1	15	13	149	17
Overall	10.20	N/A	1.36	15.31	6.80	0.34	5.10	4.42	50.68	5.78
N (136,071)	4	N/A	0	6	3	0	2	2	37	6
1993-1997	6.67	N/A	0.00	10.00	5.00	0.00	3.33	3.33	61.67	10.00
N (194,425)	6	N/A	1	12	4	1	4	2	30	9
1998-2002	8.70	N/A	1.45	17.39	5.80	1.45	5.80	2.90	43.48	13.04
N (292,543)	20	N/A	3	27	13	0	9	9	82	2
2003-2007	12.12	N/A	1.82	16.36	7.88	0.00	5.45	5.45	49.70	1.21
P-value+	0.6845	N/A	0.6845	0.6845	0.6845	0.6845	0.6845	0.6845	0.6845	0.6845
Operative Mortality - MT										
Total N (623,039)	254	34	21	206	132	14	63	121	1,095	109
Overall	12.40	1.66	1.02	10.05	6.44	0.68	3.07	5.91	53.44	5.32
N (136,071)	26	0	4	22	22	1	16	20	254	43
1993-1997	6.37	0.00	0.98	5.39	5.39	0.25	3.92	4.90	62.25	10.54
N (194,425)	80	0	5	57	25	3	16	34	303	41
1998-2002	14.18	0.00	0.89	10.11	4.43	0.53	2.84	6.03	53.72	7.27
N (292,543)	148	34	12	127	85	10	31	67	538	25
2003-2007	13.74	3.16	1.11	11.79	7.89	0.93	2.88	6.22	49.95	2.32
P-value+	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Operative Mortality - AMT										
Total N (623,039)	86	8	16	68	59	7	33	42	382	49
Overall	11.47	1.07	2.13	9.07	7.87	0.93	4.40	5.60	50.93	6.53
N (136,071)	8	0	3	3	13	1	8	6	106	16
1993-1997	4.88	0.00	1.83	1.83	7.93	0.61	4.88	3.66	64.63	9.76
N (194,425)	17	0	3	19	10	1	7	14	102	20
1998-2002	8.81	0.00	1.55	9.84	5.18	0.52	3.63	7.25	52.85	10.36
N (292,543)	61	8	10	46	36	5	18	22	174	13
2003-2007	15.52	2.04	2.54	11.70	9.16	1.27	4.58	5.60	44.27	3.31
P-value+	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001

Legend: Cause of death after valve surgery, overall and by procedure type. Cardiac deaths decreased over each of the five year periods for every procedure, but pulmonary and infectious deaths increased.

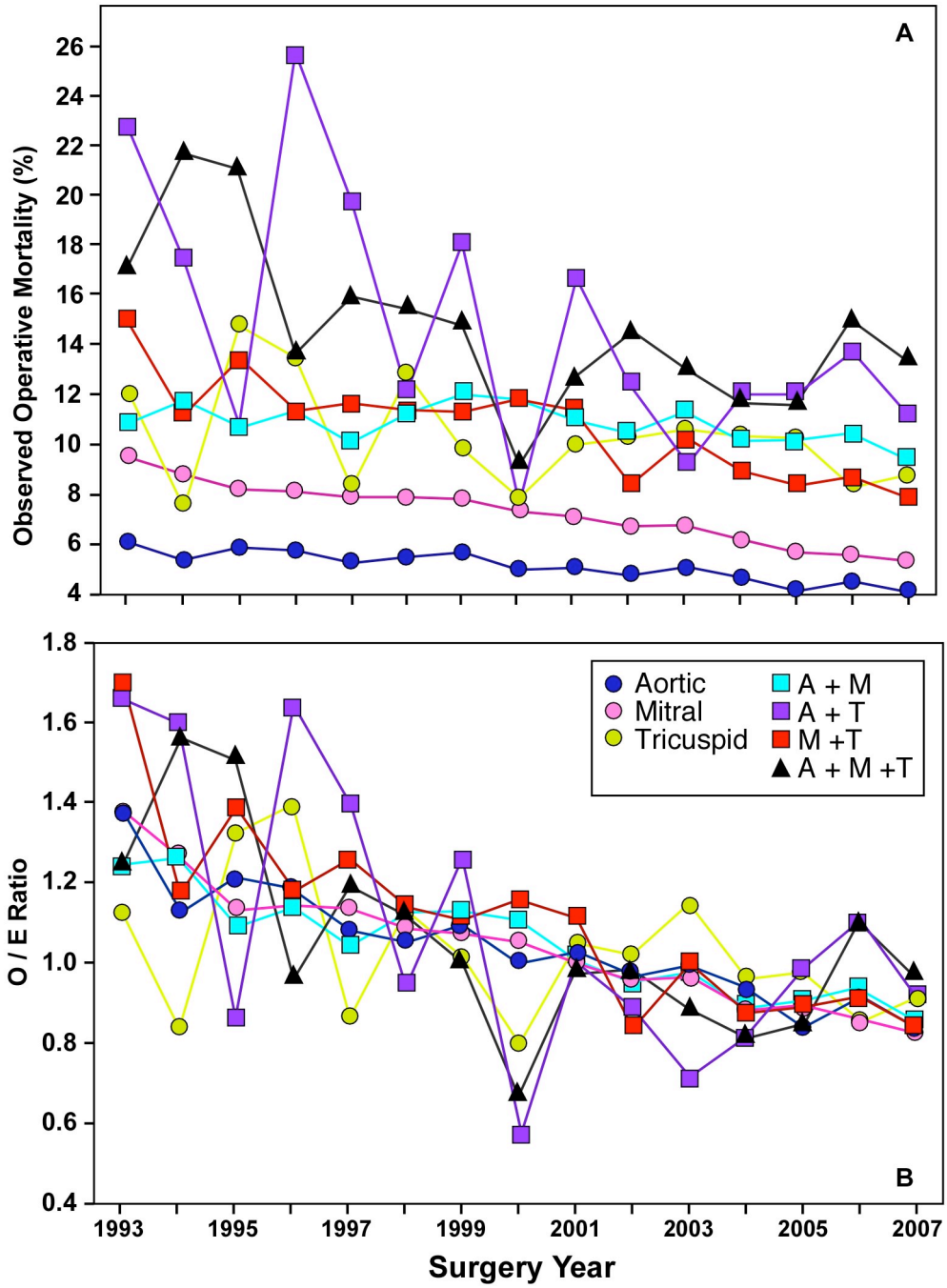
Table 7A: Major morbidity after valve surgery over the three 5-year periods.

Variable	Total N (623,039)	Overall (%)	N (136,071)	1993–1997 (%)	N (194,425)	1998–2002 (%)	N (292,543)	2003–2007 (%)	P-value+
COMPLICATIONS - NEUROLOGICAL									
Any neurological complications	27,566	4.42	6,290	4.62	9,939	5.11	11,337	3.88	<.0001
COMPLICATIONS - PULMONARY									
Prolonged Ventilation	90,410	14.51	16,243	11.94	25,942	13.34	48,225	16.48	<.0001
Pneumonia	27,936	4.48	4,715	3.47	8,781	4.52	14,440	4.94	<.0001
COMPLICATIONS - OTHER									
Multi-System Failure	12,858	2.06	2,504	1.84	4,090	2.10	6,264	2.14	0.0178
COMPOSITE OF OP MORTALITY AND MAJOR COMPLICATIONS	127,952	20.54	25,685	18.88	38,664	19.89	63,603	21.74	<.0001

Table 7B: Major morbidity after valve surgery for all 7 procedures.

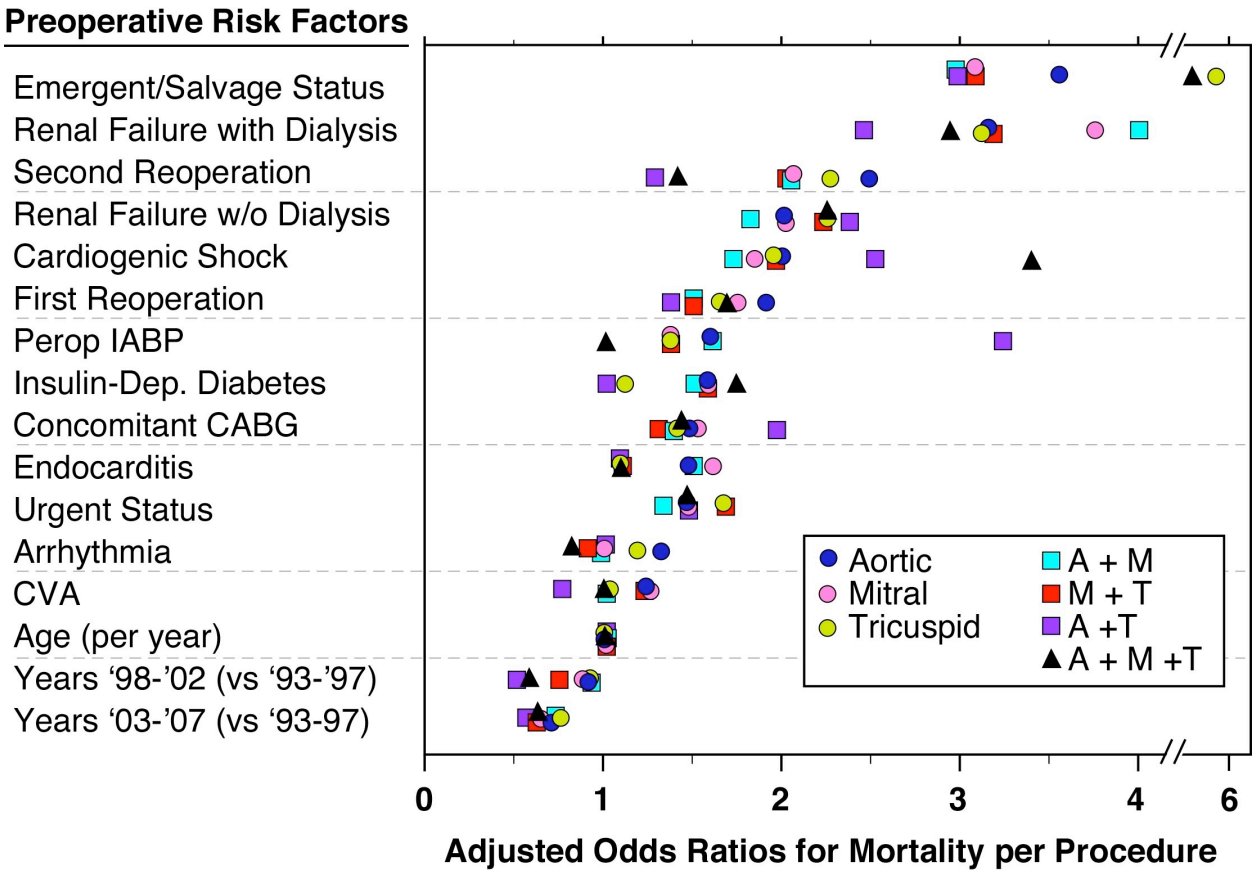
Variable	Total N (623,039)	Overall (%)	N (338,143)	Single Valve - A (%)	N (211,167)	Single Valve - M (%)	N (5,803)	Single Valve - T (%)	N (39,260)	Double Valve - AM (%)	N (2,236)	Double Valve - AT (%)	N (21,056)	Double Valve - MT (%)	N (5,374)	Triple Valve - AMT (%)	P-value+
OPERATIVE MORTALITY	38,996	6.26	16,663	4.93	14,458	6.85	582	10.03	4,200	10.70	294	13.15	2,049	9.73	750	13.96	<.0001
COMPLICATIONS - NEUROLOGICAL																	
Any neurologic complications	27,566	4.42	13,922	4.12	9,788	4.64	211	3.64	2,205	5.62	123	5.50	1,017	4.83	300	5.58	<.0001
COMPLICATIONS - RENAL																	
Post-op Renal Failure with Dialysis	10,318	1.66	3,994	1.18	3,711	1.76	212	3.65	1,173	2.99	116	5.19	823	3.91	289	5.38	<.0001
COMPLICATIONS - PULMONARY																	
Prolonged Ventilation	90,410	14.51	38,787	11.47	34,450	16.31	1,159	19.97	8,710	22.19	624	27.91	5,024	23.86	1,656	30.82	<.0001
Pneumonia	27,936	4.48	12,703	3.76	10,210	4.84	393	6.77	2,418	6.16	205	9.17	1,535	7.29	472	8.78	<.0001
COMPLICATIONS - OTHER																	
Multi-System Failure	12,858	2.06	4,973	1.47	5,011	2.37	235	4.05	1,418	3.61	105	4.70	813	3.86	303	5.64	<.0001
COMPOSITE OF OP MORTALITY AND MAJOR COMPLICATIONS	127,952	20.54	57,889	17.12	47,335	22.42	1,555	26.80	11,747	29.92	822	36.76	6,474	30.75	2,130	39.64	<.0001

Figure 1



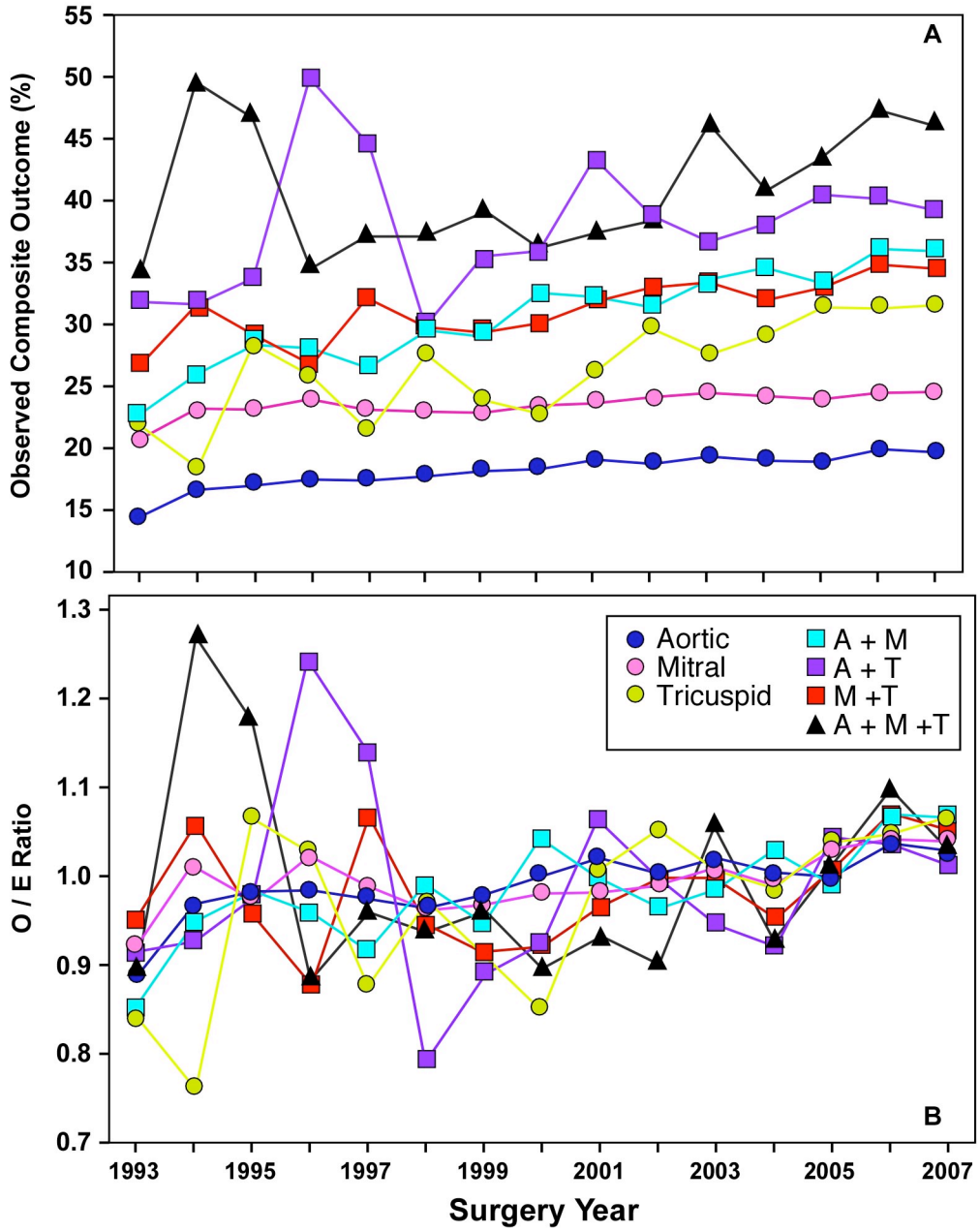
Legend: Unadjusted mortalities (Panel A) and observed to expected (O/E) adjusted mortality ratios (Panel B) for 7 single and multiple valve procedures over 15 years. The mid-year of the study (2000) was used as the reference for the O/E ratios. See text for valve abbreviations.

Figure 2



Legend: Adjusted odds ratios for relevant preoperative risk factors for 7 single and multiple valve procedures over 15 years. See text for valve abbreviations. IABP=intra-aortic balloon pump, CABG=coronary artery bypass grafting, and CVA=cerebrovascular accident.

Figure 3



Legend: Panel A is unadjusted composite of mortality and major morbidity for the 7 procedures over 15 years, and panel B is the observed to expected (O/E) adjusted mortality ratio for the same procedures and time with the year 2000 as the reference. See text for valve abbreviations.