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Does Aortic Valve Replacement Restore Normal Life Expectancy? A Twenty-Year Relative Survival Study

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Abstract

Background
This 20-year relative survival study investigates life expectancy in defined age cohorts and evaluates the role of patient, procedural and peri-operative variables on absolute survival after aortic valve replacement.

Methods
Absolute long-term survival variance was calculated using Cox regression analysis in 585 consecutive aortic valve replacement patients. Relative survival curves in defined age groups were constructed using age- and gender-matched controls.

Results
There were 12 peri-operative deaths (2.1%), and 11 further deaths (1.9%) during the first year. 154 patients (26.3%) died subsequently and 408 patients (69.7%) were alive after 20 years. Relative survival increased with age: in patients over 68 survival was equivalent to an age- and gender-matched population. Patient risk indicators for decreased absolute survival included age, Parsonnet score, additive and logistic EuroSCORE, and for increased absolute survival included weight, body surface area, and stroke volume. Procedural risk indicators for decreased absolute survival included bypass time, use of a tissue valve, and prosthesis-patient mismatch with size 19 valves, and for an increased absolute survival included use of a mechanical valve. Post-operative risk indicators for decreased absolute survival included ITU stay, ventilation time, transfusion, haemorrhage volume and new-onset atrial fibrillation/flutter. Strong risk indicators included intra-aortic balloon pump use, and dialysis.

Conclusions
Patients over 68 years discharged from hospital after aortic valve replacement had a similar 10-year survival as an age- and gender-matched population. In this age cohort surgery restored the patient's normal life expectancy.

Key words: aortic valve replacement; absolute survival predictors; relative survival

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Introduction

The debate regarding surgery on asymptomatic or mildly symptomatic patients with aortic valve disease (AVD) is long-standing.[1,2] Brock recommended invasive investigation and intervention before the advent of heart failure.[3] The median time to death with stenosis (AS) is 4.5 years after chest pain, 2.6 years after syncope and 1 year after heart failure, with a 5-year survival of less than 20%.[4] In untreated aortic regurgitation, long-term survival is curtailed, especially in patients with reduced functional class and elevated end-systolic dimensions.[5] Surgery improves outcomes even in the setting of left ventricular dysfunction.[6]
The increasing incidence of AVD in the elderly population renders this condition a significant public-health problem. It is against this control group, with up to 12% incidence in the over 75's, that the impact of surgery should be evaluated.[7]
When patients die within 30 days of surgery, death is attributed to the procedure. However the cause of late death is often undetermined because of inaccurate information. The effect of surgery on long-term survival may be evaluated in a relative survival model.[8] This long-term study compares survival after aortic valve replacement (AVR) with local age- and gender-matched controls, providing an estimate of predicted post-operative life expectancy.
Patients understand that operative risk is offset by a predicted significant survival enhancement with AVR. They also wish to know whether surgery can restore normal life expectancy.

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Long-term survival is determined by post-operative survival, the lasting effects of surgery, and continuing medical therapy. Survival prediction is meaningful when taken in context with local relative survival analysis, incorporating data from national life expectancy tables and local post-operative outcome data.[9] The inclusion of variables other than age and gender may further enhance risk-benefit assessment.[10] Such analysis aids decision making regarding surgery, particularly in elderly patients, when individual risk scores are of limited value.[9]

Methods

Study design

The Ethical Committee of the University of Malta granted approval for this study.
585 consecutive patients undergoing AVR, with or without concomitant coronary revascularization, between January 1995 and December 2014, in a single-surgeon practice, were entered into the study. Patients requiring combined procedures on the mitral valve or the ascending aorta were excluded.

Patients and protocols

All procedures were performed on normothermic cardiopulmonary bypass with a membrane oxygenator. Myocardial protection was with antegrade St Thomas' cardioplegia prior to May 2006 and subsequently with blood cardioplegia. Patients under 70 received a mechanical prosthesis, while older patients generally received a xenograft unless there were confounding factors. All mechanical valve patients were anticoagulated, whereas patients with xenografts received aspirin in the absence of a separate indication for anticoagulation. Prior to 2002 CarboMedics R-Series® Sorin was used for sizes 19 and 21 and the Standard valve for sizes 23 and 25. Subsequently CarboMedics Top Hat® Sorin was used for sizes 19, 21 and 23 while CarboMedics Standard® Sorin was used for size 25. Xenografts implanted prior to 2002 were all Carpentier-Edwards Perimount® except for 11 Toronto SPV valves. Subsequently Sorin Mitroflow® valve was used for sizes 19 and 21 and Perimount for sizes 23 and 25. Eleven Perceval® Sorin valves were implanted in 2014.

Data collection

Data was collected by the surgeon and entered into an electronic database. Patient risk assessment was calculated at the preoperative visit, operative parameters were entered at the termination of surgery, and in-hospital clinical course was completed at the patient's discharge. Parsonnet risk stratification was used from the outset of the study whilst additive and logistic EuroSCORE were also used from 2000 and 2006 respectively. The logistic EuroSCORE for patients entered between 2000 and 2006 was calculated retrospectively. Data collected prospectively was combined with patient data pertaining to survival or date of death derived from the Patient Administration System while general population survival data was derived from the National Statistics Office database.

Endpoints

Absolute survival after AVR is presented as Kaplan-Meier survival curves for four subgroups of the surgical population. Hazard ratios were calculated for certain demographic, operative and post-operative clinical parameters. Relative survival curves relate the post-operative absolute survival curves with those of an age- and gender-matched population for the matched follow-up year, derived from the National Statistics Office database.

Risk variables

Variables selected for evaluation were categorized according to patient characteristics, the procedure, and the in-hospital post-operative course. The date of death was recorded but the cause not specified. Patient-related variables included age, gender, height, weight, body surface area (BSA), body mass index (BMI), diabetes, hypertension, Parsonnet score, additive and logistic EuroSCORE, and cardiac indices (ejection fraction EF, end-diastolic volume EDV, end-systolic volume ESV and stroke volume SV). Procedural variables included urgency, repeat procedure, ischaemic time, bypass time, mechanical valve, tissue valve, concomitant revascularization (+CABG), valve stenosis, mixed disease or pure regurgitation, and indexed Effective Orifice Area (iEOA). Post-operative variables included intensive care (ITU), high dependency (HDU) and step-down ward stay, ventilation time, haemorrhage volume, blood transfusion, atrial fibrillation or flutter, stroke (CVA) and transient ischaemic attack (TIA), and post-operative intra-aortic balloon pump (IABP) and dialysis usage.

Relative survival

Relative survival is the ratio of the observed survival to the expected survival patients would experience had they been exposed only to the survival probabilities of the general population (background mortality). The relative survival curves compare the absolute survival with an age- and gender-matched population derived from the National Statistics Office database. Differences in mortality vary considerably in the later years of life and so life tables truncated at 85+ and 90+ years were extended into single year tables up to 100 years of age. In the absence of reliable data for Malta, life tables derived from England and Wales from 1998 to 2000 were extended and smoothed using the Ewbank four parameter method for each table by year and gender separately.[11] Goodness of fit of the derived life tables was assessed by plotting the smoothed mortality rates and survivor function in each table against the observed mortality rates. Life expectancy as published by the Office for National Statistics in Malta is 79.6 for males and 84 for females (78.7 and 82.6 respectively in England and Wales). Analysis was conducted in STATA version 11.

Statistical Methods

Means and standard deviations were used to measure central tendency and dispersion for continuous variables and frequency tables and crosstabs were used to describe categorical variables. Statistical inference was carried out using the One-Way ANOVA and Chi square tests. The One-Way ANOVA test compares means of patient-related, procedural and post-operative continuous variables between independent age groups (15-59, 60-67, 68-73 and >74 years). The Chi squared test assesses the association between patient-related, procedural and post-operative categorical variables and age groups. Survival probabilities for the study cohort (total population and age specific groups) and the age- and gender-matched population were computed using the Kaplan-Meier estimate. Cox regression analysis was used to relate survival times (follow-up duration) to a number of patient-related, procedural and post-operative predictors, where the patients who were still alive at the end of the investigation period were right censored. The hazard ratios and their 95% confidence intervals were computed for each of these risk/protective variables.

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Table 1. Peri-operative and late deaths

age group	n	F%	peri-op	death 30dy-1yr	> 1yr	follow-up (yr) mean±SD	max	ADR%
A 15-59	149	24.8	1	3	19	11.3±5.2	20.0	1.31%
B 60-67	147	34.0	2	2	39	8.4±5.6	19.0	3.32%
C 68-73	152	42.8	5⁺	3	49	7.2±5.2	18.8	4.75%
D >74	137	52.6	4*	3	47	4.5±3.9	16.8	8.11%

Legend: ADR%: annualised percentage death rate
F%: percentage female ⁺includes one in-hospital death at 30 days *includes one in-hospital death at 117 days

Table 2. Pathology and risk stratification

	n	+CABG (%)	urgent %	AS/M%	Parsonnet	Euro SCORE* additive	Logistic
A 15-59	149	35 (23.5)	9.4	83.3	8.87 ± 3.60	2.99 ± 1.32	2.47 ± 1.90
B 60-67	147	53 (36.1)	7.5	91.1	9.71 ± 4.17	4.34 ± 1.32	3.21 ± 1.92
C 68-73	152	58 (38.2)	8.6	92.5	14.52 ± 4.81	5.78 ± 1.31	5.20 ± 4.04
D >74	137	48 (35.0)	24.1	96.5	23.12 ± 5.20	7.33 ± 1.33	8.08 ± 3.82

Legend: +CABG: concomitant revascularisation AS/M: pure aortic stenosis or mixed aortic valve disease *calculated from 2000 onwards, n=453

Results

Study cohort

585 patients were divided into four age ranges of comparable size (groups A-D), as determined by the closest whole year integer (table 1). 224 (38.3%) were female, and incidence increased with age. All in-hospital deaths (2.1%) were classified as peri-operative deaths, even if they occurred after 30 days from surgery. Survivors were defined as patients who were discharged from hospital and survived surgery beyond 30 days. Amongst survivors the mean and maximum follow-up for each group is shown in table 1. The mean follow-up was shorter with increasing age, reflecting a trend for more surgery in the elderly in recent years. The annualized percentage death rate (ADR%) was derived by dividing the number of deaths other than peri-operative deaths (expressed as a percentage of the group) by the mean follow-up in years.
93% (322/348) patients under 70 received a mechanical valve, whereas 95% (226/237) patients over 70 received a tissue valve. Concomitant revascularization was highest in group C whilst the requirement for urgent surgery was highest in group D (table 2). The valve lesion was classified as stenosis, mixed (stenosis and regurgitation) or pure regurgitation. The incidence of combined stenosis and mixed valve disease increased with age, whereas pure regurgitation was rare (<4%) in group D. Risk stratification score increased with age, with a significant increment in Parsonnet in the over 70's and a similar increment in the EuroSCORE in the over 60's, in-keeping with the weighting design of these systems.

Absolute survival

The mean follow-up in survivors was 8.2 years (median 7.6 years). The follow-up period was 20 years and during this time 407 patients were censored and 178 patients died. There were 12 peri-operative deaths (2.1%), 4 deaths in the valve replacement only group (1.0%, n=386) and 8 in the valve replacement + CABG group (4.0%, n=199). The predicted mortality for the whole group was 5.2% by additive EuroSCORE and 4.9% by logistic EuroSCORE. Another 11 patients (1.9%) died within the first year after surgery and a further 154 (26.3%) died beyond the first year. 408 patients (69.7%) were alive at the end of the 20-year follow-up period. The absolute survival Kaplan-Meier curves for the entire study group as well as for the age-defined sub-groups are presented in figure 1.

The risk indicators for the sub-groups A to D are presented in table 3. A hazard ratio (HR) above 1.0 ascribes an increased propensity for an event in the presence of certain variables, categorized as patient variables, procedure variables and post-operative variables, while a hazard ratio below 1.0 ascribes a protective factor (tables 4 and 5).

Patient variables

Four patient risk indicators for a decreased absolute survival included age (HR 1.077, 95% CI 1.058-1.096, $p<0.001$), Parsonnet score (HR 1.084, 95% CI 1.064-1.104, $p<0.001$), additive EuroSCORE (HR 1.244, 95% CI 1.152-1.343, $p<0.001$), and logistic EuroSCORE (HR 1.046, 95% CI 1.017-1.077, $p=0.002$). Three patient protective variables for absolute survival included weight (HR 0.979, 95% CI 0.964-0.994, $p=0.008$), BSA (HR 0.290, 95% CI 0.104-0.810, $p=0.018$), and SV (HR 0.992, 95% CI 0.983-0.999, $p=0.041$).

Procedural variables

Four procedural risk indicators for a decreased absolute survival included bypass time (HR 1.018, 95% CI 1.008-1.028, $p=0.001$), the use of a tissue valve (HR 2.648, 95% CI 1.931-3.630, $p<0.001$), combined tissue valve and CABG (HR 2.150, 95% CI 1.508-3.064, $p<0.001$) and prosthesis-patient mismatch for size 19 valves (HR 1.127, 95% CI 1.034-1.228, $p=0.006$). A strong procedural protective variable for absolute survival included the use of a mechanical valve (HR 0.302, 95% CI 0.210-0.433, $p<0.001$) and combined mechanical valve and CABG (HR 0.284, 95% CI 0.209-0.385, $p<0.001$).

Table 3. Risk indicators for age groups

	149 patients 15-59 years n(%)/m(SD)	147 patients 60-67 years n(%)/m(SD)	152 patients 68-73 years n(%)/m(SD)	137 patients >74 years n(%)/m(SD)	p value
Patient Characteristics					
age	49.6 (8.99)	63.5 (2.32)	70.3 (1.72)	77.7 (3.02)	<0.001
gender(female)	37 (24.8%)	50 (34.0%)	65 (42.8%)	72 (52.6%)	<0.001
outcome (died)	22 (14.8%)	43 (29.3%)	57 (37.5%)	54 (39.4%)	<0.001
operative death	1 (0.7%)	2 (1.4%)	5 (3.3%)	4 (2.9%)	0.329
time to death (yr)	7.1 (4.90)	7.8 (4.72)	7.5 (4.83)	6.6 (4.36)	0.605
height(m)	1.63 (0.10)	1.60 (0.09)	1.55 (0.21)	1.55 (0.10)	<0.001
weight(kg)	79.4 (15.9)	78.9 (14.2)	73.0 (12.8)	70.8 (13.3)	<0.001
BSA(m2)	1.96 (1.40)	1.82 (0.19)	1.74 (0.18)	1.70 (0.19)	0.017
BMI(kg/m2)	29.8 (5.49)	30.7 (5.06)	29.3 (4.30)	29.4 (5.06)	0.097
diabetes	12 (8.1%)	23 (15.6%)	30 (19.7%)	34 (24.8%)	0.130
hypertension	26 (17.4%)	50 (34.0%)	54 (35.5%)	67 (48.9%)	0.014
Parsonnet	8.9 (3.60)	9.7 (4.17)	14.5 (4.81)	23.1 (5.20)	<0.001
EuroSCORE(add)	3.0 (1.32)	4.3 (1.32)	5.8 (1.31)	7.3 (1.33)	<0.001
EuroSCORE(log)	2.5 (1.90)	3.2 (1.92)	5.2 (4.04)	8.1 (3.82)	<0.001
EF(%)	66.6 (14.9)	69.1 (13.6)	72.1 (15.0)	71.7 (12.6)	0.390
EDV(ml)	135.6 (32.4)	143.4 (61.9)	148.8 (51.1)	141.8 (49.9)	0.783
ESV(ml)	45.3 (22.3)	44.3 (36.2)	41.5 (29.4)	40.2 (29.9)	0.902
SV(ml)	90.3 (31.1)	99.1 (34.4)	107.3 (43.3)	101.6 (27.7)	0.370
Procedural Variables					
urgent/emergency	16 (10.7%)	12 (8.2%)	14 (9.2%)	35 (25.5%)	<0.001
redo	7 (4.7%)	3 (2.0%)	3 (2.0%)	2 (1.5%)	0.289
ischaemia(min)	56.8 (14.6)	57.9 (14.1)	57.5 (11.1)	58.1 (12.4)	0.903
bypass(min)	69.5 (20.7)	71.5 (19.0)	72.5 (17.8)	71.8 (16.9)	0.679
mech±CABG	148 (99.3%)	137 (93.2%)	46 (30.3%)	3 (2.2%)	<0.001
mechanical	113 (75.8%)	83 (56.5%)	24 (15.8%)	2 (1.5%)	<0.001
mech+CABG	35 (23.5%)	54 (36.7%)	22 (14.5%)	1 (0.7%)	<0.001
tissue±CABG	1 (0.7%)	10 (6.8%)	106 (69.7%)	134 (97.8%)	<0.001
tissue	1 (0.7%)	8 (5.4%)	68 (41.4%)	87 (63.5%)	<0.001
tissue+CABG	0 (0.0%)	2 (1.4%)	38 (25.0%)	47 (34.3%)	<0.001
stenosis/ mixed	121 (81.3%)	133 (90.7%)	140 (92.2%)	131 (95.6%)	0.002
regurgitation	28 (18.7%)	14 (9.3%)	12 (7.8%)	6 (4.4%)	0.002
Indexed EOA					
19	0.63 (0.06)	0.66 (0.05)	0.72 (0.12)	0.78 (0.05)	<0.001
21	0.87 (0.09)	0.85 (0.09)	0.84 (0.10)	0.82 (0.09)	0.141
23	1.04 (0.10)	1.06 (0.10)	1.03 (0.12)	0.97 (0.12)	0.003
25	1.05 (0.12)	1.05 (0.12)	1.02 (0.11)	0.95 (0.21)	0.045
all sizes	0.98 (0.16)	0.97 (0.15)	0.93 (0.15)	0.88 (0.14)	<0.001
Post-operative Variables					
ITU(dy)	1.18 (1.40)	1.07 (0.52)	1.36 (1.94)	1.96 (9.86)	0.445
HDU(dy)	1.71 (3.02)	1.48 (2.09)	1.54 (1.72)	2.53 (4.12)	0.030
ward(dy)	3.42 (3.10)	3.57 (2.40)	3.76 (2.77)	5.34 (5.71)	<0.001
ventilation(hr)	12.2 (40.1)	9.4 (8.6)	12.8 (35.8)	16.2 (51.9)	0.617
transfusion(unit)	0.92 (2.56)	0.86 (1.60)	1.14 (1.89)	1.77 (2.92)	0.026
haemorrhage(ml)	412.8 (301.1)	437.8 (345.7)	498.4 (316.8)	480.9 (321.2)	0.181
IABP	6 (4.0%)	4 (2.7%)	8 (5.3%)	4 (2.9%)	0.641
atrial fib/flutter	19 (12.8%)	39 (26.5%)	36 (23.7%)	51 (37.2%)	<0.001
dialysis	3 (2.0%)	4 (2.7%)	5 (3.3%)	12 (8.8%)	0.009
CVA/TIA	2 (1.3%)	4 (2.7%)	3 (2.0%)	2 (1.5%)	0.817

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Table 4. Cox regression (Univariate Analysis)

	n(%)/ m(SD)	Hazard Ratio	(95%) CI of HR	p value
patient characteristics				
age	65.1 (11.4)	1.077	1.058 – 1.096	<0.001
gender(female)	224 (38.3%)	1.068	0.789 – 1.445	0.671
height(m)	1.59 (0.10)	0.191	0.025 – 1.474	0.112
weight(kg)	76.1 (15.1)	0.979	0.964 – 0.994	0.008
BSA(m2)	1.82 (0.83)	0.290	0.104 – 0.810	0.018
BMI(kg/m2)	30.0 (5.20)	0.968	0.929 – 1.009	0.129
diabetes	99 (16.9%)	1.318	0.714 – 2.433	0.377
hypertension	197 (33.7%)	1.546	0.791 – 3.021	0.203
Parsonnet	13.9 (7.13)	1.084	1.064 – 1.104	<0.001
EuroSCORE(add)	5.23 (2.09)	1.244	1.152 – 1.343	<0.001
EuroSCORE(log)	4.91 (3.85)	1.046	1.017 – 1.077	0.002
EF (%)	69.9 (13.8)	0.988	0.971 – 1.005	0.166
EDV(ml)	142.4 (51.6)	0.996	0.990 – 1.001	0.093
ESV(ml)	42.9 (30.7)	1.002	0.994 – 1.009	0.675
SV(ml)	99.6 (36.9)	0.992	0.983 – 0.999	0.041
procedural variables				
urgent/emergency	77 (13.2%)	1.384	0.918 – 2.087	0.120
redo	15 (2.6%)	1.018	0.451 – 2.300	0.965
ischaemia(min)	57.6 (13.0)	1.012	0.997 – 1.026	0.108
bypass(min)	71.4 (18.6)	1.018	1.008 – 1.028	0.001
mech±CABG	334 (57.1%)	0.284	0.209 – 0.385	<0.001
mechanical	222 (37.9%)	0.302	0.210 – 0.433	<0.001
mech+CABG	112 (19.1%)	0.831	0.576 – 1.199	0.321
tissue±CABG	251 (42.9%)	3.437	2.532 – 4.664	<0.001
tissue	164 (28.0%)	2.648	1.931 – 3.630	<0.001
tissue+CABG	87 (14.9%)	2.150	1.508 – 3.064	<0.001
stenosis/ mixed	283 (48.4%)	0.872	0.721 – 1.056	0.161
regurgitation	46 (7.9%)	0.704	0.372 – 1.331	0.280
indexed EOA				
19	0.72 (0.10)	1.127	1.034 – 1.228	0.006
21	0.84 (0.09)	1.011	0.987 – 1.036	0.365
23	1.03 (0.11)	0.987	0.965 – 1.010	0.268
25	1.02 (0.14)	0.988	0.973 – 1.004	0.148
all sizes	0.94 (0.16)	0.999	0.990 – 1.008	0.827
post-operative variables				
ITU(dy)	1.38 (4.95)	1.039	1.024 – 1.053	<0.001
HDU(dy)	1.83 (2.92)	1.046	0.984 – 1.111	0.150
ward(dy)	4.00 (3.76)	1.071	1.042 – 1.101	0.150
ventilation(hr)	12.8 (38.3)	1.010	1.007 – 1.013	<0.001
transfusion(unit)	1.21 (2.34)	1.213	1.155 – 1.273	<0.001
haemorrhage(ml)	459.8 (322.2)	1.001	1.000 – 1.002	0.002
IABP	22 (3.8%)	4.567	2.458 – 8.483	<0.001
atrial fib/flutter	145 (24.8%)	1.618	1.147 – 2.281	0.006
dialysis	24 (4.1%)	8.737	4.942 – 15.45	<0.001
CVA/TIA	11 (1.9%)	1.120	0.357 – 3.507	0.846

Table 5. Cox regression (Multivariate Analysis)

	m(SD)	Hazard Ratio	95%) CI of HR	*p* value
patient characteristics				
Parsonnet	13.9 (7.13)	1.057	1.019 – 1.097	0.003
post-operative variables				
ITU(dy)	1.38 (4.95)	1.364	1.218 – 1.527	<0.001
ward(dy)	4.00 (3.76)	1.129	1.069 – 1.193	<0.001
haemorrhage(ml)	459.8 (322.2)	1.001	1.000 – 1.002	0.031

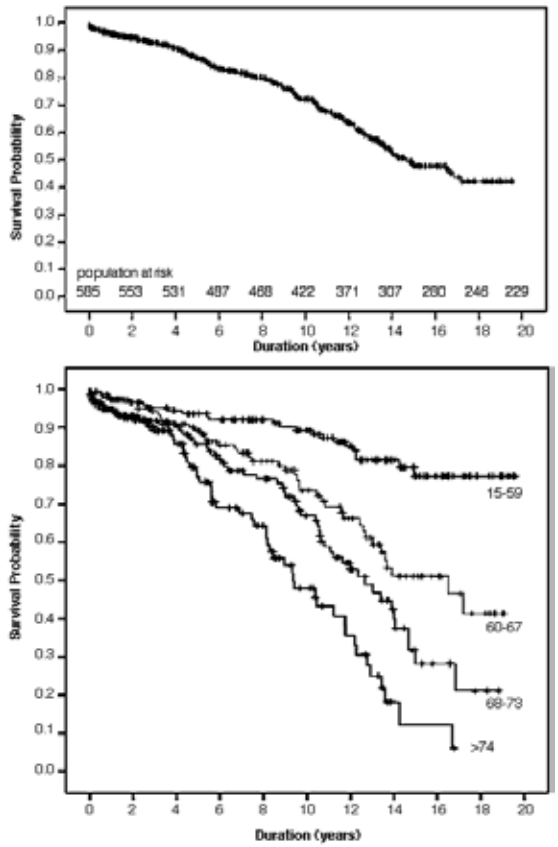

Figure 1. Kalpan-Meier absolute survival curves for whole study population and for four age cohorts. For univariate analysis, the Cox regression model identified the following strong predictors of survival times:

Post-operative variables

Post-operative risk indicators for a decreased absolute survival included ITU length of stay (HR 1.039, 95% CI 1.024-1.053, $p<0.001$), ventilation time (HR 1.010, 95% CI 1.007-1.013, $p<0.001$), blood transfusion (HR 1.213, 95% CI 1.155-1.273, $p<0.001$), haemorrhage volume (HR 1.001, 95% CI 1.000-1.002, $p=0.002$) and new-onset atrial fibrillation or flutter (HR 1.618, 95% CI 1.147-2.281, $p=0.006$). Very strong risk indicators included the use of IABP (HR 4.567, 95% CI 2.458-8.483, $p<0.001$), and of dialysis (HR 8.737, 95% CI 4.942-15.45, $p<0.001$). When these predictors were analyzed collectively (multivariate analysis), the Cox regression model identified four significant predictors for a decreased absolute survival: Parsonnet score, ITU stay, ward stay and haemorrhage volume (table 5).

Relative survival

Patients included in this analysis (n=524) underwent surgery up to 2013 to allow for a minimum follow-up of a year. Relative survival curves were plotted by age groups and follow-up time was truncated at the point where less than 50 patients remained at risk.

Figure 2 shows the survival curve with 95% confidence intervals for the total population. The one-year relative survival probability (98.2%, 95% CI 96.0-99.6) was slightly lower in the first year than the survival expected in age- and gender-matched counter parts. However the 5-year (99.3%, 95% CI 95.5-102.4) and 10 year survival probability (98.1%, 95% CI 91.7-104.5) show similar survival. Relative survival hazard was significantly lower in groups B, C and D when compared with group A (figure 3). Analysis by age groups was performed for the four age groups and also for two amalgamated age groups (15-67 and 68+) to allow for more robust analysis (figure 2). Survival in the15-67 age group remains lower than the age- and gender-matched general population over the 10 years of follow up (upper CI does not surpass 1). For those aged 68+ no difference in survival was noted for age- and gender-matched counterparts except at the fourth year of follow up where patients showed a higher survival probability (106%, 95% CI 100.6-110.3). In spite of wider confidence intervals with increasing follow-up, the data suggests that survival in the 68+ group is better than that in the younger age group.

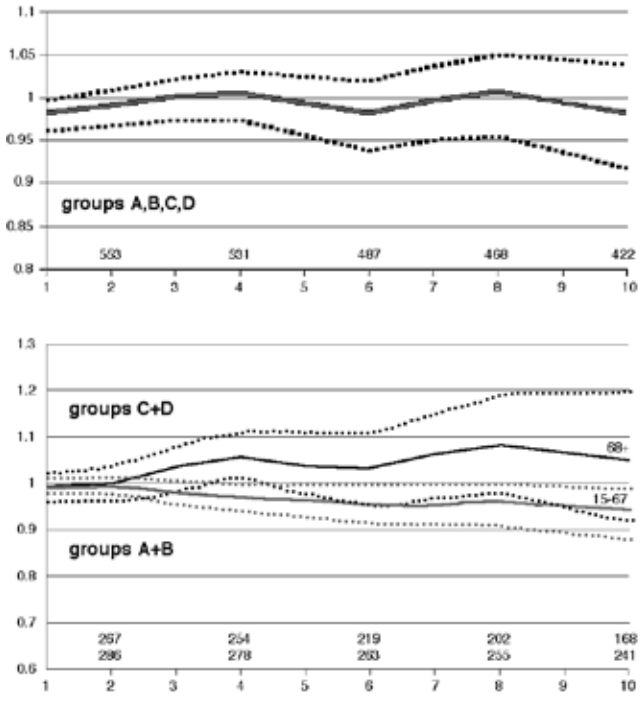

Figure 2. Relative survival curves for whole study population and for two amalgamated age cohorts. Population at risk: upper figures groups C+D, lower figures groups A+B.

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Discussion

Findings and Data interpretation

A higher risk stratification score predicted an increased propensity for reduced long-term survival. Although the additive and logistic EuroSCORE have superseded the older Parsonnet system, the latter remained the strongest indicator for long-term survival when subjected to multivariate analysis. Parsonnet score is a reliable predictor of intensive care stay and of complications including intra-aortic balloon pump use and renal replacement therapy, variables that strongly predicted long-term outcome in our study.[12] Despite its shortcomings in over-predicting operative mortality, Parsonnet remains a simple and useful predictor of long-term survival after AVR.

Despite the guarded prognosis associated with pure aortic regurgitation reported in previous studies, our results do not support this variable as a significant risk predictor of decreased long-term survival.[2,13] Confounding factors in our study include a preserved EF of 65.1±15.8% (75% had an EF >55%) in spite of a significantly increased left ventricular end-systolic volume of 66.5±41.1ml as calculated at ventriculography, suggesting that surgery was performed expeditiously. The small numbers in the elderly subgroup may pose a further study limitation.
The effect of prosthesis-patient mismatch (PPM) on long-term survival was evaluated by using the indexed Effective Orifice Area (EOA) for each size category and for the entire group. An indexed EOA of ≤ 0.85cm^2/m^2 defined moderate PPM and ≤ 0.65cm^2/m^2 defined severe PPM. The EOA's for the valves were obtained from independent researchers and derived from in vivo studies.[14,15] Data was available on 565 patients and their valves, of which 71% had no PPM. There were 10 cases of severe PPM, all in patients receiving size 19 valves and 156 cases of mild PPM (33 in size 19, 111 in size 21, 8 in size 23 and 4 in size 25). Ninety-three cases of moderate PPM occurred in patients over 70 receiving a xenograft, in whom a presumed relatively curtailed activity would reduce the impact of trans-valvular flow on trans-valvular pressure gradient. Our incidence of mismatch is lower than that quoted in other series using the same criteria.[16,17] For size 19 valves, mismatch impacted negatively on long-term survival, with mortality increasing by 12.7% when compared with the other sizes, suggesting that valve size was a more important predictor than valve type or model. Mismatch in larger sizes had no significant impact on long-term survival.

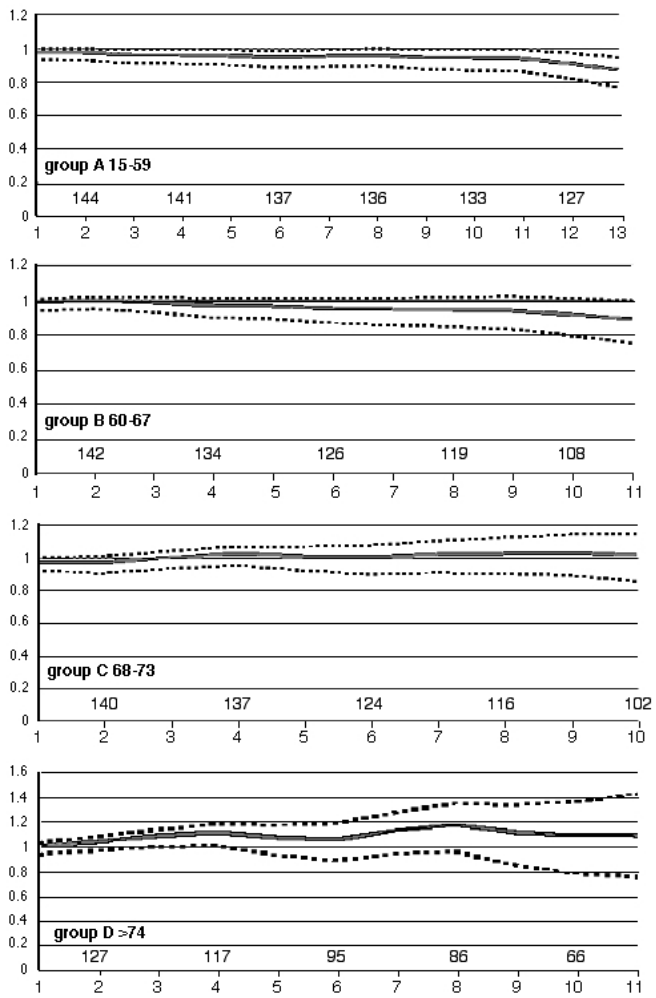

Figure 3. Relative survival curves for four age cohorts, including population at risk.

Peri-operative transfusion has been shown independently to double 5-year mortality after cardiac surgery. We demonstrated a similar trend after AVR. Blood was administered more frequently in older and smaller patients, variables associated with a decreased long-term survival in our study.[18,19]
New-onset atrial fibrillation or flutter increased with age and was a significant predictor of reduced long-term survival (HR 1.618). This is in keeping with a similar study by Filardo et al, citing an HR of 1.48.[20]

The strongest post-operative indicator for a poor long-term outcome was renal dialysis (HR 8.737), also reported in a previous study,[10] followed by IABP usage (HR 4.567), which has been reported to affect both early and late mortality after AVR.[21] Other significant variables, reported in previous studies, were not analysed in our study due to a very low incidence. Thus Lassnigg et al reported an HR of 1.8 for resternotomy, which occurred in 9.36% of cases (173/1848 patients) whilst our incidence was significantly less at 2.05% (p<0.0001). Similarly our incidence of reoperation was 2.56%, compared with Lassnigg's 9.90%.[10]

The newer alternative therapy of transcatheter aortic valve implantation (TAVI) may significantly impact the long-term survival of patients with aortic valve disease.[22] Although patients were increasingly treated by this method in Malta since 2010, these were not included in this study.

Clinical implications

This study demonstrates multiple variables that impacted absolute long-term survival. Size 19 valves reduced long-term survival, as did blood transfusion, highlighting the importance of strategies that reduce its requirement. We have shown that in patients aged over 68 years, relative survival was comparable to age- and gender-matched controls. Other investigators have emphasized the importance of additional clinical features including severe valve calcification,[23] a jet velocity of >4m/s,[24] and of a positive stress test[25] in helping the surgeon reach a decision regarding surgery. All patients in our study had symptomatic aortic valve disease. Previous series that also included asymptomatic patients with severe AS demonstrated a lower operative mortality and a long-term survival similar to that in symptomatic patients and comparable to an age- and gender-matched control population.[26] This data is important when making a decision regarding AVR, especially in the absence of symptoms. Our results and those of other groups would favor a policy of considering all patients with severe AS for surgery, irrespective of symptoms.

Limitations

Since variables included in this retrospective study where those that were collected after 1995, other, possibly relevant, confounding factors may have been omitted. Our cardiac unit is the only one serving the local population and protocols and methods may be at variance with other foreign units, limiting its value with regard to generalizations. This study analysed overall survival and non-cardiac causes of mortality may have obscured the results, especially in older cohorts. Nevertheless the model of relative survival is designed to take this factor into account and to yield valuable data predicting life expectancy. A possible limitation from reliance on foreign life tables in the absence of reliable local data pertaining to differences in mortality in the very elderly was mitigated by goodness of fit analysis.

Conclusions

Certain risk predictors affect absolute long-term survival after AVR. Although absolute survival is shorter in older patients, increasing age had an incrementally smaller negative impact on relative survival such that patients over 68 years enjoyed a normal life expectancy after surgery. These findings provide important additional data when weighing up the risks and benefits of surgery for AVD.

Declarations of Interest

The authors declare no conflicts of interest

Acknowledgements

The authors state that they abide by the statement of ethical publishing of the International Cardiovascular Forum Journal.[27]

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