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Gender differences in outcomes following aortic valve replacement surgery

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ABSTRACT

Objective: The objective of this study was to assess outcome differences in aortic valve replacement based on gender.

Methods: A study from a ten-year hospitalization cohort with prospective data collection was conducted. Included in the study were patients undergoing aortic valve replacement surgery between March 1997 and July 2003 ($N = 406$). There were 223 males and 183 females included in the study. The study examined 41 potential confounding risk factors and 16 outcome variables.

Results: Univariate analysis on potential confounding risk factors revealed a significant difference between males and females on 12 factors. Co-morbid disease, hypertension, current vascular disease, aortic insufficiency, body surface area, blood added on pump, and annulus size significantly correlated with age. The correlation resulted in five confounding risk factors: age, tobacco history, obesity, left ventricular hypertrophy, and creatinine level. Logistic regression analysis found that after controlling for age, tobacco history, obesity, left ventricular hypertrophy, and creatinine level, there is no difference between males and females on outcomes following aortic valve replacement. Additionally, choice of vascular prosthesis had no impact on post-operative outcomes.

Conclusion: After controlling for confounding variables, similar outcomes were observed for males and females undergoing aortic valve replacement.

1. Introduction

Women undergoing coronary artery bypass grafting (CABG) are reported to be at increased risk for post-operative morbidity and mortality.[1,2] Aortic valve replacement (AVR) can be performed either in isolation or in conjunction with CABG. In aortic valve surgeries combined with CABG, female gender has been found to be an independent risk factor for morbidity and mortality.[1–4] This increased risk in women is partially related to gender differences in preoperative risk profiles.[5,6] Men and women with similar degrees of aortic stenosis and clinical status without coronary disease have different adaptations. Women more frequently have a greater degree of ventricular hypertrophy, smaller end systolic and end diastolic chamber size, higher relative wall thickness, greater fractional shortening and higher ejection fractions.[7] In the case of aortic regurgitation, women are more likely to have aortic valve surgery for class III and IV symptoms and men for severe left ventricular dysfunction.[3,8] Previous literature has been inconsistent regarding the effect of gender on outcomes following isolated aortic valve surgery. Some authors have determined that the operative morbidity and mortality were similar in men and women for isolated AVR.[8–10] However, other authors have found that female gender is associated with a 2.5 fold increase risk in post-operative cardiac morbidity and mortality after AVR surgery.[5] The present study examined gender as a risk factor for morbidity and mortality after isolated AVR.

2. Methods

A ten-year hospitalization cohort ($N = 11{,}398$) with prospective data collection was conducted after receiving institutional review board approval. Nurses, physicians, and perfusionists collected data on 225 variables during admission. Data were grouped into demographics, medical history, postoperative, perfusion, and procedure sections. Using a series of cross-checking questions, two

Abbreviations: AVR, Aortic valve replacement; BSA, Body surface area; CABG, Coronary artery bypass graft; COPD, Chronic obstructive pulmonary disease; IABP, Intra-aortic balloon pump; ICU, Intensive care unit; LVH, Left ventricular hypertrophy; LOH, Length of hospitalization; NYHA, New York Heart Association.

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individuals audited all data forms for completeness and consistency. To further ensure accuracy and consistency, a physician audited at random 10% of patient forms. Data were then entered into an interactive multi-institutional database (Patient Analysis and Tracking System, Axis Clinical Systems, Portland, OR).

Included in the study were patients aged 18 and older undergoing AVR surgery between March 1997 and July 2003 ($N = 406$). Patients who underwent any surgery other than AVR or in combination with AVR were excluded. There were 223 males and 183 females included in the study.

The study examined 41 potential confounding risk factors. The dichotomous potential confounding risk factors included race, tobacco history, diabetes, hypertension and obesity. Additional risk factors included other systemic disorders, significant associative disorders, chronic obstructive pulmonary disorder (COPD) and neurological history. Current vascular disease, previous cardiac surgery, cor sinus CP site, urgent surgical procedure, New York Heart Association (NYHA) functional class were also considered as risk factors. Cardiac pathology risk factors included aortic stenosis, aortic insufficiency, mitral valve stenosis, mitral insufficiency and aortic aneurysm. Aortic disease, transesophageal color flow, left ventricular hypertrophy (LVH), left ventricular ejection fraction estimate, and echo result were additional risk factors. Procedural risk factors included a prosthetic and ross mix/root. Etiological risk factors were: atherosclerosis, congential, rheumatic, degenerative, Marfan syndrome, infection, and trauma. The continuous potential confounding risk factors included age, body surface area (BSA), creatinine level, pump time, cross-clamp time, volume of blood added on pump, and annulus size. Table 1 lists the definitions for the potential confounding risk factors.

The 16 outcome variables were hours on ventilator, intensive care unit (ICU) length of stay, total length of hospitalization (LOH), arrhythmias requiring treatment, positive cultures, renal complications, sternal wound complications, neurologic complications, pulmonary complications, gastrointestinal complications, low cardiac output, intra-aortic balloon pump (IABP), return to ICU, pulmonary hypertension, intra-operative complications, and mortality. Table 2 lists the definitions for each of the outcome variables.

To generate the unadjusted risks of each potential confounding risk factor, Chi-square and *t*-tests comparing males and females with each of the 41 variables were performed. Correlation coefficients were computed among the significant confounding risk factors. Chi-square and *t*-tests were conducted comparing males and females with each of the 16 outcomes. Logistic regression analysis was then used to investigate the adjusted risk between cases and controls with each of the significant outcome variables, while controlling for the significant risk factors. SPSS (SPSS Corporation, Chicago, Illinois) statistical software was used to perform the analyses.

Table 1
Definitions of potential confounding risk factors.

Variables	Definition of variables
Race	Caucasian, other
Significant associative disorder	no, yes (dialysis, gout, ch steroids, phsch hx, CA, chr afib, int afib, VT/VF, prior mediastinal radiation)
Other systemic diseases	no, yes (syphilis, lupus, marfan's, rheum heart disease, ETOH, rheum arthritis, drug abuse, HIV+, AIDS)
COPD	no, yes
Diabetes	no, yes (diet, oral meds, insulin dependent)
Hypertension	no, yes (diastolic blood pressure > 90 mmHg)
Tobacco history	no, yes
Neurological history	no, yes (seizures, encephalopathy or dementia, neuromuscular, tumor, intracranial hemorrhage, aneurysm, other)
Current vascular disease	No, yes (carotid, vertebral, innominate, subclavian, thoracic aorta, abdominal aorta, visceral/renal, upper extremity, lower extremity)
Obesity	no, yes (>1.5 times ideal weight)
Cor sinus CP site	no, yes
Urgency of Procedure	elective, non-elective (urgent, emergent, desperate)
NYHA Functional Class	Class I, Class II, Class III, Class IV
Cardiac pathology – aortic stenosis	no, yes
Cardiac pathology – aortic insufficiency	no, yes
Cardiac pathology – mitral stenosis	no, yes
Cardiac pathology mitral insufficiency	no, yes
Cardiac pathology – aortic aneurysm	no, yes
Aortic disease	no, yes (atherosclerotic, dilated, dissection, calcified, severe, thin, soft, aneurysm, thick wall, old graft, aneurysmal origin of vein graft)
Transesophageal color flow	no, yes
Abnormal LVH	normal, abnormal (mild, moderate, or severe)
LV ejection fraction	no, yes (39 or less)
Procedure – prosthetic	no, yes
Procedure – conduit	no, yes
Procedure – ross mi/root	no, yes
Etiology - atheroscl	no, yes
Echo result	Satisfactory, unsatisfactory
Age	Years
Creatinine level	mg%
Pump time	Minutes
Cross-clamp time	Minutes
Blood added on pump	ml
Annulus size	mm
Body surface area	m^2

3. Results

Univariate analysis on potential confounding risk factors revealed a significant difference between males and females on 12 factors (Table 3). Males had significantly higher creatinine level ($p = 0.020$), larger BSA ($p < 0.001$), and larger annulus size ($p < 0.001$). Males also had more tobacco history ($p = 0.003$), aortic insufficiency ($p = 0.013$), and LVH ($p = 0.026$). Females were significantly older ($p < 0.001$) and required more blood added on pump ($p < 0.001$). Females also had more significant associative disorders ($p = 0.008$), hypertension ($p = 0.007$), current vascular disease ($p = 0.017$), and obesity ($p < 0.001$).

Correlation coefficients were calculated for the 12 significant confounding risk factors. Seven of the 12 risk factors significantly correlated with age. These factors include associative disorder, hypertension, current vascular disease, aortic insufficiency, BSA, blood added on pump, and annulus size. The correlation resulted in five confounding risk factors: age, tobacco history, obesity, LVH, and creatinine level.

There was a significant difference between males and females following AVR on one outcome variable: greater number of females (65%) experienced low cardiac output following AVR ($p = 0.016$). There was no significant difference between males and females for the remaining 15 outcome variables.

Logistic regression analysis showed that after controlling for age, tobacco history, obesity, LVH, and creatinine level, there is no difference between males and females on low cardiac output (OR 1.5, CI 0.95–2.5, $p = 0.077$). No significant difference in outcomes was found between males and females following AVR.

4. Discussion

Previously CABG has been examined for gender related outcomes, and unadjusted mortality and morbidity rates have been