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The Influence of Gender on In-Hospital Clinical Outcome Following Isolated Mitral or Aortic Heart Valve Surgery☆

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ABSTRACT

Background: With the expected growth in the elderly segment of the U.S. population particularly in women, the prevalence of valvular heart disease is bound to increase in the coming years. We sought to delineate the impact of gender on in-hospital clinical outcomes in Medicare-age patients undergoing isolated left-side heart valve surgery.
Methods: Using the National Inpatient Sample files from 2003 to 2014, we compared the in-hospital major adverse cardiac and cerebral events (MACCE: all-cause mortality, stroke, or myocardial infarction) and composite complications (MACCE, permanent pacemaker implantation, bleeding requiring transfusion, iatrogenic vascular complications, acute respiratory failure, acute kidney injury requiring hemodialysis, sepsis and prolonged hospital stay) following isolated mitral or aortic surgery between genders with 1:1 propensity score analysis. Further, we examined gender-specific temporal trends of in-hospital clinical outcomes over the study period.
Results: There were 336,506 isolated left-side heart valve surgeries over the study period. Following propensity score matching, 24,637 unweighted pairs were identified for gender-specific comparison. Female gender was independently associated with a higher in-hospital MACCE (9.4% vs. 8.3%; OR = 1.14, 95% CI = 1.07–1.21, P < 0.0001) driven mostly by all-cause mortality (5.2% vs. 4.3%; OR = 1.33, 95% CI = 1.12–1.33, P < 0.0001). The composite complication rate (37.9% vs. 35.3%; OR = 1.12, 95% CI-1.08–1.16, P < 0.0001) was also higher in women. Significant reduction in both in-hospital MACCE and all-cause mortality was observed over time regardless of gender.
Conclusions: Following isolated left-side heart valve surgery, women experienced higher in-hospital MACCE including all-cause mortality compared to men. Continued temporal improvements in in-hospital clinical outcomes were observed in both genders.
Summary for the annotated table of contents: The influence of gender on surgical aortic or mitral valve replacement/repair outcome is unclear. The current study showed that women fared worse than men including all-cause mortality following isolated left-side valve surgery and significant temporal improvements have been made in in-hospital clinical outcomes in both genders during the 12-year study period. Further research in gender-specific approach in management of valve disease is warranted.

1. Introduction

Valvular heart disease is one of the leading causes of morbidity and mortality in the U.S. In the 2017 American Heart Association heart disease and stroke statistic update stated that 1.8% of the population have at least moderate valvular heart disease and its prevalence increases with age. About 17% of the U.S. adult population in the year 2000 had at least moderate mitral regurgitation and the incidence increased from 0.5% in 8 to 44 years old group to 93% in the ≥75 age group while prevalence of at least moderate aortic stenosis and aortic regurgitation was 28% and 20% respectively [1,2]. Coffey et al. demonstrated that the annual heart valve-related deaths increased by 2.8% per year from 15,054 in 1979 to 26,663 in 2009 in the U.S. and the heart valve-related mortality is projected to double over the next 25 years due to growing elderly population [3].

As the baby boomers begin to turn 65, the share of the population in this age group is projected to increase from 56 million to 74 million, reaching 18% by 2030 and survival rates are predicted to be higher for females than for males [4]. Therefore, with the anticipated increase in the U.S. population age and particularly in the proportion of female gender in the coming years, the incidence of valvular disease is likely to continue to rise. The two major objectives of the current study are

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1) to assess the impact of gender on the in-hospital clinical outcomes following isolated left-side heart valve surgery and 2) to compare the temporal trends of in-hospital clinical outcomes following isolated left-side heart valve surgery in men and woman by using a large real-world database.

2. Methods

2.1. Data source: the NIS database

The National Inpatient Sample (NIS) is part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS is a 20% stratified sample of all nonfederal US hospitals. The latest 2014 NIS sampling database involved 44 States and the District of Columbia representing >96% of the U.S. population and >94% of U.S. hospitals discharges. Data for the current study were obtained from HCUP-NIS files from January 1, 2003, through December 31, 2014 [5]. Weill Cornell Medical College determined that institutional review board approval and informed consent were not required for the current study since uses a deidentified administrative database. Each discharge record in the NIS includes information on patient diagnosis and procedures performed during the hospitalization that are based on International Classification of Diseases-Ninth Revision-Clinical Modification (ICD-9-CM) codes. In addition, Clinical Classification Software (CCS) codes that group multiple ICD-9-CM codes to facilitate statistical analyses are available. We identified patient comorbidities and in-hospital complications using ICD-9-CM and CCS codes.

2.2. Patient population and clinical variables

All patients who underwent surgical mitral valve replacement, mitral valve repair or aortic valve replacement were identified using ICD-9-CM procedure codes and included in the study (Supplemental Table 1). Of note, those who received concomitant aortic and mitral valve surgeries were also included. Patients were excluded if any of the following concomitant cardiac surgeries were performed: coronary artery bypass grafting, heart transplantation, ventricular/atrial repair, congenital heart defect repair, ventricular restoration procedures, transmyocardial revascularization, infundibulectomy, creation of septal defect, endocardial cushion defect repair, endovascular implantation of graft in thoracic aorta and any other concomitant valve surgeries. Also, patients with age < 65 years and missing mortality or gender data were excluded from the study. NIS variables were used to identify patient's age and gender. The Deyo modification of the Charlson Comorbidity Index was used to define overall severity of comorbidities [6,7]. Comorbidities included in the study were defined using ICD-9-CM diagnosis codes.

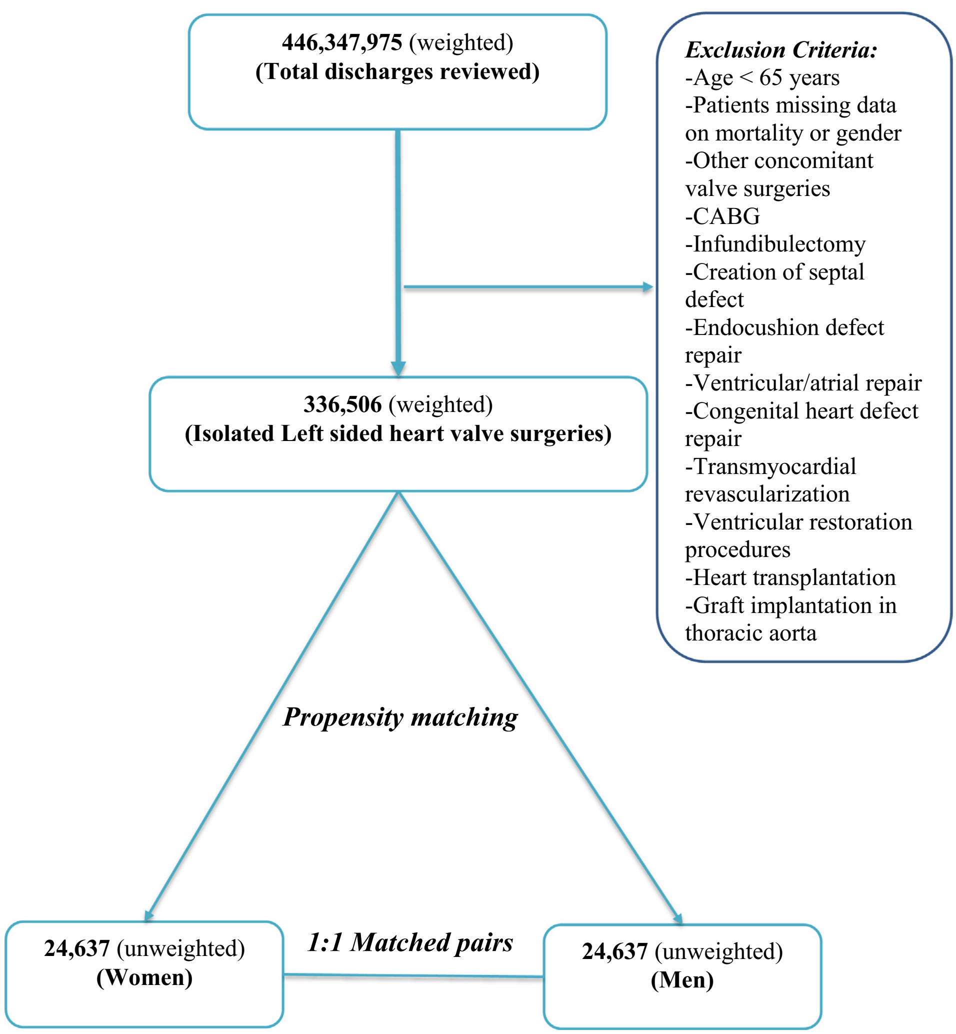

Fig. 1. Patient consort flow chart.

Table 1
Baseline characteristics in women and men with isolated left heart valve surgeries before matching (NIS 2003–2014).

	Overall	Women	Men	P value	SD[b]
Number of discharges, weighted	336,506	162,820 (48.4%)	173,686 (51.6%)		
Age, mean ± SE[a]	75.1 ± 0.1	75.5 ± 0.1	74.7 ± 0.1	<0.0001	12.2
Valvular heart diseases[c]					
Aortic valve disorder[d]	57.6	54.0	60.9	<0.0001	14.0
Rheumatic aortic stenosis	0.5	0.6	0.4	0.001	2.5
Congenital aortic stenosis	0.2	0.2	0.2	0.24	0.9
Rheumatic aortic regurgitation	0.1	0.1	0.1	0.33	0.7
Congenital aortic regurgitation	4.4	3.4	5.2	<0.0001	8.6
Mitral stenosis	0.9	1.5	0.3	<0.0001	12.4
Mitral regurgitation	20.6	22.0	19.2	<0.0001	7.0
Mitral stenosis + regurgitation	1.0	1.7	0.4	<0.0001	13.4
Infective endocarditis	1.2	1.0	1.5	<0.0001	4.9
Comorbidities					
Smoking	4.3	3.7	5.0	<0.0001	6.4
Hypertension	68.2	68.8	67.6	0.001	2.6
Pulmonary hypertension	15.9	18.4	13.5	<0.0001	13.3
Hyperlipidemia	47.7	45.9	49.4	<0.0001	6.8
CAD	37.0	30.2	43.4	<0.0001	27.5
Atrial fibrillation	51.3	52.0	50.7	0.001	2.6
Diabetes mellitus	23.5	23.2	23.7	0.14	1.0
CHF	42.5	45.0	40.1	<0.0001	9.9
PVD	11.7	9.4	13.8	<0.0001	14.0
Chronic pulmonary disease	15.5	14.2	16.8	<0.0001	7.4
Renal disease	12.9	10.8	14.9	<0.0001	12.3
Dialysis status	0.4	0.4	0.4	0.31	0.7
Malignancy	8.7	10.1	7.3	<0.0001	10.0
Liver disease	0.7	0.7	0.8	0.43	0.5
Any anemia	19.2	20.2	18.3	<0.0001	4.7
Coagulopathy	25.9	25.1	26.7	<0.0001	3.5
Depression	5.4	7.0	3.8	<0.0001	14.1
Obesity	12.0	14.3	9.9	<0.0001	13.4
Previous PCI	6.2	4.7	7.7	<0.0001	12.1
Previous CABG	7.8	4.1	11.3	<0.0001	27.6
Elective surgery	71.3	70.4	72.2	<0.0001	4.1
Charlson comorbidity score, mean ± SE[a] (median)	1.6 ± 0.01 (0.8)	1.6 ± 0.01 (0.8)	1.6 ± 0.01 (0.8)	0.10	3.2
Surgery type					
AV replacement	76.3	72.8	79.6	<0.0001	16.1
MV replacement	18.7	23.1	14.6	<0.0001	21.7
MV repair	11.5	11.2	11.9	0.01	2.1
AV replacement + MV replacement	4.3	5.0	3.6	<0.0001	6.9
AV replacement + MV repair	2.1	1.9	2.4	<0.0001	3.4

[a] SE: standard error.
[b] SD: standardized difference, all <10% after matching indicates successful matching.
[c] Percentages do not add up to 100% because of incomplete coding for the valvular disease etiologies in NIS data.
[d] Aortic valve disorder: Aortic stenosis or aortic regurgitation of unspecified cause.

2.3. Study endpoints

Primary safety endpoint of the study was the incidence of in-hospital major adverse cardiac and cerebral event (MACCE) rate defined as in-hospital all-cause mortality, stroke, or myocardial infarction. In addition, we also delineated and compared gender differences in the incidence of in-hospital serious adverse events [composite complication] which included all non-hierarchical peri-procedural complications in addition to MACCE by using a combination of ICD-9-CM and CCS codes as defined in Supplemental Table 2: permanent pacemaker implantation, bleeding requiring transfusion, iatrogenic vascular complications, acute respiratory failure, acute kidney injury (AKI) requiring hemodialysis, sepsis as well as prolonged hospital stay which was defined as greater than the upper 75th percentile of length of stay [8].

2.4. Statistical analysis

Baseline imbalances of patient and hospital characteristics between genders that might influence postoperative outcomes were controlled by propensity score matching method. Each patient's propensity score of being female gender was determined by a nonparsimonious multivariate logistic regression model that examined the impact of 48 variables. Patients with similar propensity scores in each gender group were matched by 1:1 scheme using 8 to 1 digit match without replacement. Standardized differences were used to assess covariate balance between two matched groups and <10% was used as an indicator of successful matching [9]. For comparison of matched groups, paired *t*-test was used for continuous variables and McNemar test and conditional logistic regression were used for categorical variables. All tests were 2-sided with P values < 0.05 indicating statistical significance and SAS software, version 9.4 (SAS institute, Cary, NC) was used for all analyses.

3. Results

3.1. Patient cohort (Fig. 1)

We reviewed a total of 446,347,975 weighted discharges over the 12-year study period from January 1st 2003 to December 31st 2014 and identified patient records representing 336,506 isolated left-side heart valve surgeries that conformed to all enrollment criteria for analysis in the study. Following 1:1 propensity score matching, 24,637 unweighted gender pairs were identified for the gender-matched comparison.

3.2. Patient characteristics (Tables 1 and 2)

Of the 336,506 isolated left-side heart valve surgery discharges, 48.4% of patients were female. Women were slightly older, had a lower prevalence of aortic valve disorder but more mitral valve pathology.

Table 2
Baseline characteristics in women and men with isolated left heart valve surgeries after 1:1 propensity score matching (NIS 2003–2014).

	Overall	Women	Men	P value	SD[b]
Number of discharges, unweighted	49,274	24,637 (48.4%)	24,637 (51.6%)		
Age, mean ± SD[a]	75.2 ± 6.4	75.2 ± 6.4	75.2 ± 6.4	0.25	1.0
Valvular heart diseases[c]					
Aortic valve disorder[d]	57.8	57.7	57.8	0.84	0.2
Rheumatic aortic stenosis	0.5	0.5	0.5	0.84	0.2
Congenital aortic stenosis	0.2	0.2	0.2	0.85	0.2
Rheumatic aortic regurgitation	0.1	0.1	0.1	0.59	0.5
Congenital aortic regurgitation	4.0	4.0	4.0	0.87	0.1
Mitral stenosis	0.5	0.5	0.5	0.64	0.4
Mitral regurgitation	21.2	21.2	21.1	0.68	0.4
Mitral stenosis + regurgitation	0.5	0.5	0.5	0.84	0.2
Infective endocarditis	1.1	1.1	1.1	0.86	0.2
Comorbidities					
Smoking	4.3	4.1	4.5	0.04	1.9
Hypertension	67.6	67.7	67.5	0.69	0.4
Pulmonary hypertension	15.3	15.4	15.3	0.77	0.3
Hyperlipidemia	46.3	46.3	46.3	0.99	0
CAD	34.1	34.1	34.1	0.98	0
Atrial fibrillation	51.0	50.1	51.9	<0.0001	3.7
Diabetes mellitus	22.9	23.0	22.9	0.77	0.3
CHF	42.3	42.4	42.2	0.68	0.4
PVD	11.0	11.0	11.0	0.84	0.2
Chronic pulmonary disease	15.2	15.2	15.3	0.74	0.3
Renal disease	11.9	11.9	12.0	0.62	0.4
Dialysis status	0.4	0.4	0.4	0.63	0.4
Malignancy	8.2	8.3	8.2	0.70	0.3
Liver disease	0.7	0.7	0.6	0.58	0.5
Any anemia	19.0	18.9	19.1	0.57	0.5
Coagulopathy	25.3	25.4	25.3	0.68	0.4
Depression	4.8	4.8	4.7	0.74	0.3
Obesity	11.5	11.5	11.4	0.82	0.2
Previous PCI	5.5	5.5	5.5	0.90	0.1
Previous CABG	5.3	5.2	5.4	0.28	0.8
Elective surgery	71.3	70.7	71.9	0.003	2.7
Charlson comorbidity score, mean ± SD[a] (median)	1.6 ± 1.5 (0.7)	1.6 ± 1.5 (0.7)	1.6 ± 1.5 (0.7)	0.58	0.5
Surgery type					
AV replacement	76.7	76.6	76.8	0.59	0.5
MV replacement	18.0	18.1	17.9	0.51	0.6
MV repair	12.1	12.0	12.1	0.60	0.5
AV replacement + MV replacement	4.4	4.4	4.4	0.84	0.2
AV replacement + MV repair	2.2	2.1	2.2	0.23	1.1

[a] SD: standard deviation.
[b] SD: standardized difference, all <10% after matching indicates successful matching.
[c] Percentages do not add up to 100% because of incomplete coding for the valvular disease etiologies in NIS data.
[d] Aortic valve disorder: Aortic stenosis or aortic regurgitation of unspecified cause.

Infective endocarditis was more frequent in men. Female patients had a higher frequency of hypertension, pulmonary hypertension, atrial fibrillation, congestive heart failure, malignancy, anemia, depression, and obesity while men were more likely to have history of smoking, hyperlipidemia, coronary artery disease, peripheral vascular disease, chronic pulmonary disease, renal dysfunction, coagulopathy, prior percutaneous and surgical revascularizations and underwent elective valve surgeries. Women underwent less frequent aortic valve replacement (72.8% vs. 79.6%, $P < 0.0001$) but more double-valve replacements (5.0% vs. 3.6%, $P < 0.0001$) than men. In patients undergoing mitral valve surgery, both men and women underwent more replacement than repair (18.7% vs. 11.5%, $P < 0.0001$). However, mitral repair was performed less frequently in women than in men (11.2% vs. 11.9%, $P = 0.01$) and so was mitral repair combined with aortic valve

Table 3A
In-hospital outcomes in women and men following isolated left heart valve surgeries before matching (NIS 2003–2014).

Isolated left heart valve surgeries complications	Overall (n = 336,506)	Women (n = 162,820)	Men (n = 173,686)	P value
Composite complications	36.5	38.0	35.0	<0.0001
MACCE[a]	8.7	9.3	8.1	<0.0001
In hospital death	4.6	5.1	4.0	<0.0001
Post op stroke	3.3	3.5	3.2	0.05
Myocardial infarction	1.7	1.7	1.7	0.67
Permanent pacemaker	6.3	6.8	5.9	<0.0001
Bleeding requiring transfusion	14.7	15.3	14.2	<0.0001
Iatrogenic vascular complications	5.2	5.3	5.2	0.86
Acute respiratory failure	11.2	12.2	10.3	<0.0001
AKI requiring hemodialysis	1.8	1.8	1.8	0.54
Sepsis	4.0	3.6	4.4	<0.0001
Prolonged hospital stay[b]	25.5	27.7	23.4	<0.0001

[a] MACCE: Composite outcome of postoperative in-hospital death, stroke or myocardial infarction.
[b] Prolonged hospital stay: Hospital stay ≥ 13 days (3rd quartile).

Table 3B
In-hospital outcomes in women and men following isolated left heart valve surgeries after propensity score matching (NIS 2003–2014).

Isolated left heart valve surgeries complications	Overall (n = 49,274)	Women (n = 24,637)	Men (n = 24,637)	Odds ratio (95% CI)	P value
Composite complications	36.6	37.9	35.3	1.12 (1.08–1.16)	<0.0001
MACCE[a]	8.9	9.4	8.3	1.14 (1.07–1.21)	<0.0001
In hospital death	4.7	5.2	4.3	1.22 (1.12–1.33)	<0.0001
Post op stroke	3.3	3.5	3.2	1.09 (0.99–1.21)	0.08
Myocardial infarction	1.7	1.7	1.7	1.00 (0.87–1.14)	0.94
Permanent Pacemaker	6.3	6.4	6.3	1.03 (0.96–1.11)	0.39
Bleeding requiring transfusion	14.4	15.1	13.7	1.12 (1.07–1.18)	<0.0001
Iatrogenic vascular complications	5.3	5.5	5.0	1.11 (1.03–1.20)	0.01
Acute respiratory failure	11.5	12.1	10.9	1.14 (1.07–1.20)	<0.0001
AKI requiring hemodialysis	1.8	1.8	1.9	0.94 (0.83–1.07)	0.37
Sepsis	4.1	3.7	4.6	0.81 (0.74–0.88)	<0.0001
Prolonged hospital stay[b]	25.5	26.9	24.2	1.15 (1.10–1.20)	<0.0001

[a] MACCE: Composite outcome of postoperative in-hospital death, stroke or myocardial infarction.
[b] Prolonged hospital stay: Hospital stay ≥ 13 days (3rd quartile).

replacement (1.9% vs. 2.4, P < 0.0001). Following 1:1 propensity score matching, patient profile in each of the gender group was well balanced with similar patient characteristic and procedure types and the standardized differences were well under 10% in all categories.

3.3. In-Hospital procedural outcome (Tables 3A and 3B)

Women experienced more frequent in-hospital adverse events (Table 3A). The composite complication rate was higher in women (38.0 vs. 35.0, P < 0.0001). Specifically, more frequent complication rates in women than men were observed in component outcomes of all-cause mortality, permanent pacemaker implantation, bleeding requiring transfusion, acute respiratory failure and sepsis as well as prolonged hospital stay. After adjusting for differences in patient- and hospital-level characteristics between genders using propensity score matching, female gender remained independently associated with the majority of outcomes (Table 3B). Composite complication rate was higher in women (37.9% vs. 35.3%; OR = 1.12, 95% CI-1.08–1.16, P < 0.0001). MACCE was significantly higher (9.4% vs. 8.3%; OR = 1.14, 95% CI = 1.07–1.21, P < 0.0001) in female patients driven mostly by all-cause mortality (5.2% vs. 4.3%; OR = 1.33, 95% CI = 1.12–1.33, P < 0.0001) and marginally by stroke. Permanent pacemaker implantation rate was no longer significantly different between genders. Women had a higher incidence of bleeding requiring transfusion (15.1% vs. 13.7%; OR = 1.12, 95% CI = 1.07–1.18, P < 0.0001), vascular complications (5.5% vs. 5.0%; OR = 1.11, 95% CI = 1.03–1.20, P = 0.01), acute respiratory failure (12.1% vs.10.9%, OR = 1.14, 95% CI = 1.07–1.20, P < 0.0001) while sepsis was noted more frequently in men (3.7% vs. 4.6%; OR = 0.81, 95% = 0.74–0.88, P < 0.0001).

3.4. Temporal trends in clinical outcomes post left-side heart valve surgery

Over the 12-year study period, there were continuous improvements in the clinical outcomes in patients following left-side heart valve surgery. There was a significant overall reduction in both MACCE (Fig. 2A) and in-hospital all-cause mortality rates (Fig. 2B) over time regardless of gender. Specifically, the MACCE rate decreased by 37.6% and 32.8% while the mortality rate declined by 56.1% and 45.9% in men and women, respectively. However, the annual mortality rates for women had reached a plateau in 2009 and then stabilized with P for trend of 0.30. A similar significant temporal reduction in rates of MACCE and in-hospital mortality was observed in both men and women when analyzed separately for each left-side heart valve surgery except for mitral valve repair surgery where MACCE remained stable in women over time (Supplemental Figs. 1–2).

4. Discussion

With the aging of the U.S. population, particularly in females, in the coming years and the associated increasing number of patients with valvular disease requiring treatment, it is important to understand the contemporary gender-specific differences in treatment approaches and clinical outcomes following valvular surgeries which may help shape future management strategies in valvular heart disease.

Due to a number of innate gender differences in cardiovascular physiology; women have 5–10% higher cardiac output, 10–15% lower body mass adjusted maximal aerobic capacity and a greater capacity to perform isotonic exercise than men [10]. In addition, women also have lower hemoglobin level and body surface area, as well as smaller

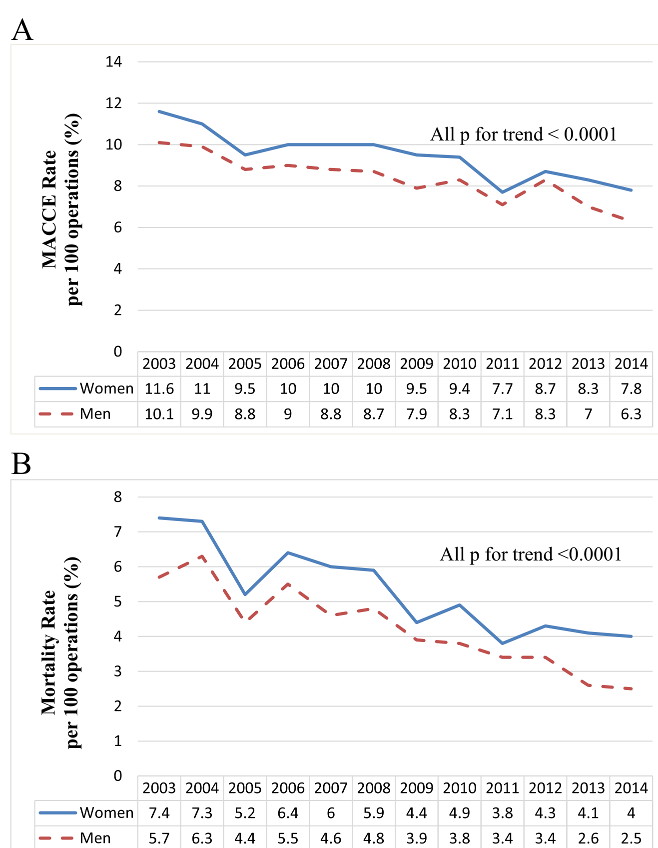

Fig. 2. A. Temporal trends of MACCE rate by gender following left heart valve surgery. B. Temporal trends of mortality rate by gender following left heart valve surgery.

left ventricular and atrial dimensions than men. These differences in physiology, disease pathology, presentation and management may contribute to gender-specific differences in clinical outcomes following valve surgery [10].

4.1. Previous studies

While the negative influence of female gender on CABG has long been recognized [11], how women fared after isolated left-side valve surgery without other concomitant procedures is less clear.

4.1.1. In combined CABG and valve surgery

In a retrospective analysis of 717 patients undergoing aortic valve surgery and 54% with concomitant CABG, Aranki SF et al. noted that female gender was a predictor of in-hospital mortality in those with simultaneous CABG but not in patients undergoing isolated aortic valve replacement [12]. Christakis and his co-workers from University of Toronto retrospectively analyzed clinical outcomes of 2488 patients with valvular surgery (1098 aortic, 1107 mitral, and 283 double valves) between 1982 and 1986 and concluded that gender did not independently impact on operative mortality [13]. Similarly, using the Massachusetts Cardiac Surgery Database from 2002 to 2008, Stamou et al. assessed the impact of gender and ethnicity on clinical outcomes in 6809 patients following aortic valve replacement with and without concurrent CABG. They reported that the 30-day mortality between the female and male patients was similar [14]. More recently, Trienekens and co-workers retrospectively evaluated the influence of gender on cardiac surgery on 4030 patients undergoing cardiac surgery; 3075 underwent isolated CABG and 955 had aortic valve replacements with or without simultaneous CABG. Gender was not an independent risk factor for in-hospital or early mortality [15]. Additionally, Ibrahim MF et al. studied 1570 consecutive patients (68% men and 32% women) undergoing combined valve (62% aortic, 31% mitral and 7% double or triple valves) and CABG but failed to identify female gender as an independent risk factor for in-hospital morbidity and mortality [16].

4.1.2. Gender difference in surgical outcome in different valves

Saxena A et al. used data from the Australasian Society of Cardiac and Thoracic Surgeons Cardiac Surgery from 6/2001 to 12/2009 to evaluate the impact of gender on early and late mortality after isolated surgical AVR in 2790 patients. There was no difference in the incidence of early complications or in long-term survival between men and women [17]. However, Rankin JS et al. demonstrated female gender as an independent predictor of operative mortality in the Society of Thoracic Surgeons database involving 409,904 valve procedures between 1994 and 2003 [18]. Interestingly, Nowicki ER et al. analyzed the Northern New England Cardiovascular Disease Study Group registry which involved 8943 heart valve surgery patients (5793 AVR and 3150 mitral valve repair or replacement) and demonstrated that female gender was an independent predictor of in-hospital mortality following mitral but not aortic valve surgery [19]. More recently, Onorati F et al. reported on the role of gender on clinical outcomes following surgical versus transcatheter AVR in the OBSERVANT registry involving 2108 patients. Female gender was identified as an independent predictor in the AVR population for risk-adjusted 30-day mortality but not in TAVR [20].

Using the Cardiovascular Research Database of the Bluhm Cardiovascular Institute at Northwestern Memorial Hospital, Andrei A et al. performed a retrospective propensity score matching analysis in 628 consecutive patients with bicuspid aortic valve undergoing AVR and noted that women experienced a higher risk for in-hospital mortality before matching. However, the operative, 30-day and overall survival were similar between men and woman following 1:1 propensity score matching [21]. In contrast, using the Center for Medicare and Medicaid Services data involving 183,792 patients undergoing mitral valve surgery from 2000 to 2009, Vassileva CM et al. reported a higher operative mortality and a lower long-term survival following mitral valve surgery in women. Importantly, mitral valve repair seemed to restore normal life expectancy for men but not for women [22].

4.2. Current study

Our study represents the largest matched cohort analysis to date on the influence of gender on clinical outcomes following isolated left heart surgery not compounded by other concurrent coronary bypass surgical procedures. This study revealed that among left-side heart valve surgeries, mitral valve replacement was more frequently performed than mitral repair regardless of gender. Although data on valvular disease etiology is incomplete, this finding reflects the potential gap between real-world practice pattern and U.S. guideline that recommends mitral valve repair whenever possible [23]. Female gender was an independent predictor of in-hospital complications including all-cause mortality following isolated left heart valve surgery in the current study. Women also tend to experience more frequent vascular complications, bleeding requiring transfusion, acute respiratory failure and, not surprisingly, prolonged hospital stay. Importantly, although it is gratifying to demonstrate a significant overall improvement in clinical outcomes over the 12-year study period regardless of gender, the mortality rate reduction in women was not as substantial as in men, and the temporal trend of mortality rate had stabilized since 2009. In addition, MACCE rate in women after mitral valve repair remained stable while men experienced a significant reduction of the rate during the study period. Our findings highlight that much work remains to be done to improve left-valve postoperative outcomes in women and eventually overcome discrepancies of surgical outcomes between genders.

The difference in cardiovascular physiology, disease etiologies and valve type between the genders all contributed to the differences observed in the clinical outcomes following left-side heart valve surgery in the current study. With the baby boomers coming of age, there will be a higher prevalence of women needing valve surgeries in the coming years. Hopefully, the awareness of these discrepancies will enable clinicians to be more cognizant of gender specific difference in heart valve disease states and its clinical management approaches.

4.3. Limitations

The NIS file is a comprehensive real world all-comers US registry and the current study analyzed all isolated left heart valve surgeries from 2003 to 2014. However, events in the NIS database were self-reported and not adjudicated or audited and only 20% of the available data were sampled. There is no uniform protocol for repair versus replacement in mitral valve surgery or the choice of mechanical versus bioprosthesis. No information on the cause of mortality, precise timing of in-hospital stroke and permanent pacemaker implant or sepsis was captured. For example, whether the higher prevalence of sepsis in male was due to urosepsis as a result of Foley catheter placement is unknown. There is also no uniform definition of myocardial infarction post valve surgery, severity of bleeding, acute kidney injury or severity of stroke. Relevant procedural variables including detailed hemodynamic data, anesthesia time, procedural time, time to extubation, and volume of chest tube drainage were not collected. Post-op management is likely different from institution to institution which may affect the length of stay. Furthermore, no long-term clinical outcomes data were available. Although the matched cohorts had a similar Charlson comorbidity index which had been shown to provide reasonable prognostic information in patients with aortic stenosis undergoing surgical AVR [24], the STS scores were not available. Finally, unknown confounders that may affect gender-specific outcome such as body mass index cannot be adjusted in the model. Despite all the aforementioned limitations, the HCUP- NIS represents one of the largest datasets capturing real world practice data on of cardiac surgery in the US. Hopefully, with the introduction of ICD 10 codes in the upcoming NIS files will provide more granularity on specific patient, disease and procedure related factors which may help enhance our capacity to be more precise in correlating these factors to in-hospital adverse events in future studies.

5. Conclusions

Our study demonstrated an increase in in-hospital complications including all-cause mortality in women undergoing isolated left heart valve surgery and continued temporal improvements in in-hospital clinical outcomes in patients undergoing isolated left heart valve surgery in both genders. The influence of gender on long-term clinical outcomes and differential impact of gender, if any, on specific valve pathology or surgical valve repair versus replacement warrant further study.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2018.08.004.

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