Original Article Persistent reduction in the age adjusted mortality rate from aortic valve surgery in the United State with elimination of gender gap in recent years

Mohammad Reza Movahed^{1,2}, Sara Etemad³, Mehrnoosh Hashemzadeh¹, Mehrtash Hashemzadeh⁴

¹Department of Medicine, University of Arizona, Tucson, AZ, USA; ²CareMore, Tucson, AZ, USA; ³Hoag Medical Group, USA; ⁴Long Beach VA Health Care System, USA

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Abstract: Background: Advancement in the surgical techniques should translate into better outcome. The goal of this study was to evaluate mortality trends from aortic valve surgery in the United State using large inpatient database. Method: The Nationwide Inpatient Sample (NIS) database was used to calculate the age-adjusted mortality rate from aortic valve surgery from 1988 to 2011 in the United State using ICD-9 coding for aortic valve surgery. Results: We found that age adjusted mortality rate from aortic valve surgery gradually decreased from 1988 until end of study in 2011 to the lowest level with elimination of gender gap that was seen in the early years. For men, age adjusted mortality rate from aortic valve surgery in 1988 was 438 per 100,000 with steady reduction to the lowest level of 214 per 100,000 in 2011 which remained unchanged from 2007. For women, age adjusted mortality from aortic valve surgery was 620 per 100,000 in 1988 with steady reduction to the lowest level of 235 per 100,000 in 2011 which also remained unchanged since 2007. Conclusion: Age adjusted mortality from aortic valve surgery has been gradually decreasing in the last decade and remained stable at the lowest rates in recent years suggesting improvement in surgical technics and post-surgical care.

Keywords: Aortic valve disease, aortic valve replacement surgery, surgical techniques, epidemiology, incidence, prevalence, cardiac surgery

Introduction

Aortic valve disease can be caused by a number of conditions such as aortic stenosis, aortic regurgitation or a combination of the two [1]. Aortic stenosis has become the most frequent type of valvular heart disease in the United State [2]. It usually presents as calcified aortic stenosis in adults of advanced age representing roughly 2-7% of the population over the age of 65 [2, 3]. Additionally, 2% of the population has bicuspid aortic valves with higher risk for stenosis [4]. Echocardiography is the key diagnostic tool for confirming the presence of aortic valvular disease.

The first human heart valve surgery was a digital valvotomy of a stenotic aortic valve performed by Tuffier in 1914. The first aortic valve replacement surgery was performed by Harken and Braunwald. This sparked the concurrent development of mechanical prostheses and tissue valves. Aortic valve replacement has been the definitive therapy for severe aortic stenosis until the introduction of percutaneous aortic valve implantation. It remains the standard of practice for aortic regurgitation [2].

The standard operative technique includes a median sternotomy and extracorporal circulation [5]. Cardiac arrest is then induced by infusion of blood cardioplegia directly into the coronary ostia [5]. The operative mortality is approximately 1-3% for aortic valve replacement without coronary bypass surgery (CABG) [2]. However, in-hospital (short-term) mortality rate has been demonstrated to be 4-8% [6]. Some of the clinical predictors of poor outcomes among the asymptomatic patients include older age and presence of atherosclerotic risk factors [3]. Once symptoms occur, the prognosis becomes dismal [2]. There are several

Table 1. Summary of data

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AV surgery total of 258,506 patients	Male: 159,346
	Female: 99,160
Age adjusted mortality rate of AVR in male	In 1988: 438/100,000
	In 2011: 214/100,000
Age adjusted mortality rate of AVR in female	In 1988: 620/100,000
	In 2011: 235 per 100,000

risk factors that can increase operative mortality [2]. These risk factors include elderly, women, symptom severity, ejection fraction, and urgency [2]. Advancement in surgical techniques and perioperative care should translate into better outcome. The aim of this study was to assess the age adjusted mortality rate for aortic valve surgery using a large nationwide inpatient sample database from 1988-2011 in the United States.

Methods

Data source

The National Inpatient sample (NIS) is a product of Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project. This data base is publicly available and has been used by policymakers and researchers. NIS data base represents nearly 20% sample of all short-term, general, and specialty hospitals including non-federal serving adults in the United States and making the data anonymous. NIS also detains information on primary and secondary diagnoses and procedures, discharge vital status, and demographics. Association of discharge data in NIS data set can be made available by a unique hospital identifier.

Sample selection

The Nationwide Inpatient Sample (NIS) database was used to calculate the age-adjusted mortality rate from aortic valve surgery. ICD-9-CM codes for Aortic valve surgery from 1988 to 2011 in the United State were available. Records with ICD-9-CM as primary procedure code signifying aortic valve surgery (V43.3) was utilized for our statistic. Furthermore, we stratified our data based on gender.

Statistical analysis

The average age adjusted mortality rates from aortic valve surer were calculated by multiply-

ing age specific mortality rates with age specific weights for available data. We used each age-specific rate weighted by the proportion of people in that age group in the U.S. 2000 standard population. The weighted rates were summed across age groups to calculate the age adjusted rate for each

year from 1988 to 2011. We used ANOVA trend analysis for our study. The Statistical Package for Social Sciences (SPSS) software was used for this study and data analysis. A pvalue of less than 0.05 was accepted as statistically significant.

Results

AV surgery were done in 258,506 patients from which 159,346 were male and 99,160 were female. We found that age adjusted mortality rate from aortic valve surgery gradually decreased from 1988 until 2007 to the lowest level and remained stable until end of study in 2011 with elimination of gender gap that was seen in the early years. For men, age adjusted mortality rate from aortic valve surgery in 1988 was 438 per 100,000 with steady reduction to the lowest level of 214 per 100,000 in 2011 which remained unchanged from 2007. For women, age adjusted mortality from aortic valve surgery was 620 per 100,000 in 1988 with steady reduction to the lowest level of 235 per 100,000 in 2011 with stable rate since 2007 Table 1 and Figure 1.

Discussion

As life expectancy increases and the US population ages, there will be a greater number of patients with aortic stenosis and increasing need for aortic valve replacement or procedures. Based on our results, age-adjusted mortality rates from aortic valve surgery have been gradually decreasing in the last decade and remaining stable since 2007 suggesting that improvements in surgical techniques and postsurgical care have led to a better outcome. A systematic review of predictors of mortality after aortic valve replacement found strong evidence to support that mortality is increased by emergency surgery [7] while the risk of late mortality is increased with older age and preoperative atrial fibrillation [7]. Some other risk factors that reduce survival are elderly, abnorMortality Age-Adjusted Rate per 100,000



Figure 1. Age adjusted mortality rate from aortic valve replacement based on gender using ANOVA trend analysis seen since 1988 with steady reduction in mortality.

mal ventricular function, aortic regurgitation, infection, end stage renal disease and bypass time [7]. Consistent with our results, a study performed in North America looked at isolated aortic valve replacements and found that mortality decreased more than 30% between 1997 and 2006 in the presence of diabetes, nonurgent cases and renal failure among all adults [4].

Decreased mortality rates despite increasing age and co-morbidities may be due to successful risk stratification. A prospective study looked at 652 patients from January 1999 and June 2007 using the EuroSCORE and the STS-PROM to compare predicted mortality rates of patients who were undergoing isolated AVR surgery [8]. The EuroSCORE, European system for cardiac operative risk evaluation has been thought to overestimate mortality rates [8].

The STS-PROM (Society of Thoracic Surgeons predicted risk of mortality) score is one the most accurate score to predict complications of AVR [9-11]. The EuroSCORE clearly overestimates the risk of mortality, especially in very high-risk patients [8-10]. Investigators argued that the EuroSCORE is still based on a 1995 mortality rate across all cardiac surgeries and has not been updated or recalibrated [8]. This study concluded that the results of conventional AVR are excellent even in high-risk patients and the most current scores systematically overestimate the risk. The current scores are inadequate in identifying patients who are truly not suitable for conventional AVR because of a high risk [8]. Out of the current available scoring systems for predicting rates of mortality, the STS score appears to be the most accurate one [8, 9]. In spite of the sharply increasing number of AVRs being performed each year, the risk profile of patients has worsened over time [12]. Despite the fact that patients are now older with increasing prevalence of comorbid conditions, the risk of perioperative death has decreased significantly [11, 12]. These studies are also suggesting that reduction in perioperative deaths amongst an increasing elderly population

with co-morbidities signify improvements in surgical techniques [11, 12].

A retrospective study looked at patients over 80 years old undergoing AVR using the data from the Department of Veteran Affairs Continuous Improvement in Cardiac Surgery Program between 1991 and 2007 [12]. The patients were matched by risk profile. Their results demonstrated similar mortality rates (5.2% vs 3.3%; P=.19) for both groups, but higher morbidity rates (21.1% vs 15.5%; P < 0.03) for the old patient group aged greater than 80 years compared to the younger patients [12]. Similar findings were described in a study performed in Austria [13]. These findings again illustrate that advancements in surgical techniques, improved myocardial protection strategies, and better perioperative care have led to safer aortic valve replacements for the adult populations [12, 13]. Improvement in surgical techniques include the use of retrograde coronary sinus perfusion with warm oxygenated blood which provides myocardial protection and can improve right ventricular protection during retrograde cardioplegia [14]. Surgical advancements have led to an alternative to the cardioplegic arrest technique which is the on-pump beating heart aortic valve replacement with retrograde coronary sinus warm blood perfusion. It has the advantage of maintaining physiologic conditions of the heart throughout the procedure and thereby reducing the risk of myocardial ischemia [14, 15]. Long cardiopulmonary bypass time has been shown to be an independent risk factor in short term mortality rates for elderly patients undergoing primary isolated aortic valve replacement [16]. Improvements in CPB time and technique may explain the reduction in early mortality rates for patients. Additionally, meticulous perioperative care with early mobilization is another explanation for the decline in mortality rates [17].

The rate of surgical AVR for elderly Medicare patients between 1999 and 2011 increased by 19% and found that women and black patients have less procedure but higher mortality rates [18]. Additionally, there was a decreased use of mechanical prosthetic implants. It has been shown that the type of valve used during valve surgery does not significantly affect mortality rates [11]. The independent factors that predicted the length of stay included procedural urgency, age, renal impairment, cerebrovascular disease, diabetes, respiratory disease and NYHA class [7, 11]. The frequency of perioperative death following tissue AVR was not significant (3.1% compared with 2.5% following mechanical AVR) [11]. These results conclude that the type of AVR should not influence the rate of perioperative death nor the postoperative length of stay. However, valve prosthesispatient mismatch has been shown to be a strong and independent risk factor for shortterm mortality rates among patients undergoing aortic valve surgery [19]. Greater experience with prosthesis-patient matching may be a contributing factor in the declining mortality rates after aortic valve surgery.

An analysis of 41,227 patients undergoing aortic valve surgery from 2004 to 2009, found an increased annual volume of aortic valve replacements [20]. The increased volume was concluded to be a result of an increasing life expectancy with an increasing elderly population with aortic stenosis [20]. This study found the mortality rate for octogenarians to be 8.1%, and an even greater 11.1% for high-risk patients. This mortality rate compares with an overall mortality rate of 4.5% and a rate of 9.8% for high-risk younger patients. This study also found a 26% increase in the number of patients undergoing aortic valve surgery with a 70% increase in the octogenarians [20].

Although it has been demonstrated that aortic valve surgery has been denied based on older age and LV dysfunction [21] surgery should not be withheld based on age. Not only have mortality rates progressively declined for aortic

valve replacements in the last decade, but patients appear to be at a greater mortality risk and risk of poorer quality of life if refusing to have surgery [22]. A study in the UK demonstrated a > 12-fold increase in mortality risk for elderly patients with aortic stenosis refusing the operation when they were otherwise fit for surgery [21]. AVR or percutaneous aortic valve implantation should be strongly considered in all patients with severe aortic stenosis irrespective of age [22]. Performing an AVR before severe LV hypertrophy and dysfunction occurs has been shown to optimize survival [22]. For younger patients, implanting the largest possible prosthesis will help to minimize residual gradient. For elderly patients, avoidance of complex operations to insert larger prostheses can improve survival [22].

Gender has been found to be an independent risk for mortality after mechanical aortic valve surgery [23]. Additional CABG and redo surgery in females predicts survival whereas severely impaired LVEF independently predicts survival in males [23]. Although age affects survival in both sexes independently, gender significantly influenced freedom from cardiac death with females showing inferior results. We found a significant decrease in aortic valve surgery related to in-hospital mortality as well as a disappearing gender gap, with the lowest level reached in 2007-2011 across the United States. There are several reasons as to why there was a previously greater gender gap in the age-adjusted mortality rates from 1994-2002. Reports of the efficacy of appetite suppressant drugs appeared in 1992 [24]. By 1997 a high incidence of cardiac valve regurgitation was reported in patients who had taken the fenfluramine-phentermine combination for an average of 11 months [24]. This may have contributed to a steady gender gap in mortality rates. Additionally, a population-based study revealed that women are less often diagnosed than men, which could indicate an important imbalance in regard to the associated lower survival of women [25]. Improvements in diagnosis and access to aortic valve surgery sooner for females can explain the progressively narrowed gender gap in mortality rates. More recently, high volume surgical centers appear to play a factor in mortality rates for high-risk patients undergoing AVR surgery. This study concluded that all hospitals beyond the hinge-point

for volume, > 390 cases over the 4-year study period, had O/E mortality ratios less than 1 [25]. However, it was noted that this volumeoutcome relationship identified seemed only applicable to high-risk patients and existed for hospital volume but not for surgeon volume after AVR [25]. There have been various factors that can explain the progressive decline in mortality rates after aortic valve surgery. These would include earlier diagnosis and access to surgery, improvements in risk stratification and prosthesis-patient matching, advancements in surgical techniques, increase in high volume surgical centers, and meticulous perioperative care with early mobilization. Improvement in surgical technic such as minimal invasive approach is promising with some data suggesting improvement in outcome [26]. Despite improvement in surgical techniques, women have higher mortality during any cardiac surgery due to age and having more comorbidities [27].

Conclusion

Age adjusted mortality from aortic valve surgery has been gradually decreasing in the last decade suggesting improvement in surgical technics and post-surgical care.

Limitations

This study was based on ICD 9 coding with inherent limitation of ICD-9 coding. Our study evaluated in-hospital mortality and not longterm mortality. We did not evaluate the effect of different techniques on outcome such as on or off pump surgical approach.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Mohammad Reza Movahed, Clinical Professor of Medicine, CareMore, 7901 E Speedway, Tucson, AZ 85710, USA. Tel: 949-400-0091; E-mail: rmova@aol.com

References

- Nishimura RA. Cardiology patient pages. Aortic valve disease. Circulation 2002; 106: 770-772.
- [2] Vahanian A, Baumgartner H and Bax J. Guidelines on the management of valvular heart disease: the task force on the management of valvular heart disease of the European society of cardiology. Eur Heart J 2007; 28: 230-268.

- Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, [3] Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Soliman EZ, Sorlie PD, Sotoodehnia N, Turan TN, Virani SS, Wong ND, Woo D and Turner MB: American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2012 update a report from the American heart association. Circulation 2012; 125: e2-e220.
- [4] Brown JM, O'Brien SM, Wu C, Sikora JA, Griffith BP and Gammie JS. Isolated aortic valve replacement in North America comprising 108,687 patients in 10 years: changes in risks, valve types, and outcomes in the Society of Thoracic Surgeons National Database. J Thorac Cardiovasc Surg 2009; 137: 82-90.
- [5] Langer F, Aicher D, Kissinger A, Wendler O, Lausberg H, Fries R and Schäfers HJ. Aortic valve repair using a differentiated surgical strategy. Circulation 2004; 110 Suppl 1: II67-II73.
- [6] Ambler G, Omar RZ, Royston P, Kinsman R, Keogh BE and Taylor KM. Generic, simple risk stratification model for heart valve surgery. Circulation 2005; 112: 224-231.
- [7] Tjang YS, van Hees Y, Körfer R, Grobbee DE and van der Heijden GJ. Predictors of mortality after aortic valve replacement. Eur J Cardiothorac Surg 2007; 32: 469-474.
- [8] Wendt D, Osswald BR, Kayser K, Thielmann M, Tossios P, Massoudy P, Kamler M and Jakob H. Society of thoracic surgeons score is superior to the EuroSCORE determining mortality in high risk patients undergoing isolated aortic valve replacement. Ann Thorac Surg 2009; 88: 468-475.
- [9] Dewey TM, Brown D, Ryan WH, Herbert MA, Prince SL and Mack MJ. Reliability of risk algorithms in predicting early and late operative outcomes in high-risk patients undergoing aortic valve replacement. J Thorac Cardiovasc Surg 2008; 135: 180-187.
- [10] Grossi EA, Schwartz CF and Yu PJ. High-risk aortic valve replacement: are the outcomes as bad as predicted? Ann Thorac Surg 2008; 85: 102-107.
- [11] McLean RC, Briggs AH and Slack R. Perioperative and long-term outcomes following aortic valve replacement: a population cohort study of 4124 consecutive patients. Eur J Cardiothorac Surg 2011; 40: 1508-1514.
- [12] Bakaeen FG, Chu D, Huh J and Carabello BA. Is an age of 80 years or greater an important predictor of short-term outcomes of isolated aor-

tic valve replacement in veterans? Ann Thorac Surg 2010; 90: 769-774.

- [13] Mächler H, Salaymeh L, Zirngast B, Anelli-Monti M, Oberwalder P, Yates A, Knez I, Huber St, Streinu Ch, Ovcina I, Malliga D, Keeling I, Beran E, Mircic A, Meszaros K, Hetterle R, Rieger K, Curcic P, Vötsch A, Marte W, Toller W, Quehenberger F and Dacar D. There is no significant difference in the operative risk between octogenarians compared with patients younger than 60 years in cardiac surgery. Eur Surg 2011; 43: 338-341.
- [14] Gersak B. A technique for aortic valve replacement on the beating heart with continuous retrograde coronary sinus perfusion with warm oxygenated blood. Ann Thorac Surg 2003; 76: 1312-1314
- [15] Cicekcioglu F, Tutun U, Babaroglu S, Aksoyek A, Parlar Al, Mungan U, Tosya A, Tuncel C, Demirtas E and Katircioglu SF. Aortic valve replacement with on-pump beating heart technique. J Card Surg 2007; 22: 211-214.
- [16] Bloomstein LZ, Gielchinsky I, Bernstein AD, Parsonnet V, Saunders C, Karanam R and Graves B. Aortic valve replacement in geriatric patients: determinants of in-hospital mortality. Ann Thorac Surg 2001; 71: 597-600.
- [17] Thourani VH, Ailawadi G, Szeto WY, Dewey TM, Guyton RA, Mack MJ, Kron IL, Kilgo P and Bavaria JE. Outcomes of surgical aortic valve replacement in high-risk patients: a multiinstitutional study. Ann Thorac Surg 2011; 91: 49-56.
- [18] Barreto-Filho JA, Wang Y, Dodson JA, Desai MM, Sugeng L, Geirsson A and Krumholz HM. Trends in aortic valve replacement for elderly patients in the United States, 1999-2011. JAMA 2013; 310: 2078-2085.
- [19] Blais C, Dumesnil JG, Baillot R, Simard S, Doyle D and Pibarot P. Impact of valve prosthesispatient mismatch on short-term mortality after aortic valve replacement. Circulation 2003; 108: 983-988.
- [20] Dunning J, Gao H, Chambers J, Moat N, Murphy G, Pagano D, Ray S, Roxburgh J and Bridgewater B. Aortic valve surgery: marked increases in volume and significant decreases in mechanical valve use-an analysis of 41,227 patients over 5 years from the Society for Cardiothoracic Surgery in Great Britain and Ireland National database. J Thorac Cardiovasc Surg 2011; 142: 776-782, e3.

- [21] Kojodjojo P, Gohil N, Barker D, Youssefi P, Salukhe TV, Choong A, Koa-Wing M, Bayliss J, Hackett DR and Khan MA. Outcomes of elderly patients aged 80 and over with symptomatic, severe aortic stenosis: impact of patient's choice of refusing aortic valve replacement on survival. QJM 2008; 101: 567-573.
- [22] Mihaljevic T, Nowicki ER, Rajeswaran J, Blackstone EH, Lagazzi L, Thomas J, Lytle BW and Cosgrove DM. Survival after valve replacement for aortic stenosis: implications for decision making. J Thorac Cardiovasc Surg 2008; 135: 1270-1279.
- [23] Roedler S, Neuhauser J, Sodeck G, Dziodzio T, Juraszek A, Zimpfer D, Gottardi R, Holfeld J, Dunkler D, Dumfarth J, Rosenhek R, Laufer G, Grimm M and Czerny M. Gender-related differences in patients undergoing mechanical aortic valve replacement with the CarboMedics valve. J Thorac Cardiovasc Surg 2011; 52: 887.
- [24] Soler-Soler J and Galve E. Worldwide perspective of valve disease. Heart 2000; 83: 721-725.
- [25] Patel HJ, Herbert MA, Drake DH, Hanson EC, Theurer PF, Bell GF and Prager RL. Aortic valve replacement: using a statewide cardiac surgical database identifies a procedural volume hinge point. Ann Thorac Surg 2013; 96: 1560-5.
- [26] Elghannam M, Aljabery Y, Naraghi H, Moustafine V, Bechte M, Strauch J and Haldenwang P. Minimally invasive aortic root surgery: midterm results in a 2-year follow-up. J Card Surg 2020; 35: 1484-1491.
- [27] Bechtel AJ and Huffmyer JL. Gender differences in postoperative outcomes after cardiac surgery. Anesthesiol Clin 2020; 38: 403-415.