Prevalence, Referral Patterns, Testing, and Surgery in Aortic Valve Disease: Leaving Women and Elderly Patients Behind?

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Background and aim of the study: **The prevalence of aortic valve disease is not well defined, and it is not known to what degree gender and age affect testing and surgery for this condition. The study aim was to describe the prevalence of aortic valve disease in the United States population by extrapolating from administrative claims databases; and to investigate differences associated with gender and age in referral, diagnostic testing, and aortic valve replacement (AVR).**

Methods: **A claims database of approximately five million privately insured beneficiaries and a 5% sample of Medicare beneficiaries were queried for patients with aortic valve disease. Prevalence was calculated by age group and gender, and extrapolated to the 2005 US population. The proportion of patients with a cardiologist or cardiovascular surgeon visit, performance of echocardiography or stress testing, and AVR within a year of diagnosis was determined.**

Results: **The extrapolated prevalence of aortic valve disease in the US in 2005 was 1.8% (~5.2 million people); in persons aged ≥65 years, prevalence was 10.7%. Women were seen by a specialist, underwent diagnostic tests and underwent AVR at rates significantly lower than men, as did patients aged ≥80 years compared to those aged 65-79 years. AVR was performed at approximately half the rate in women (1.4%) compared to men (2.7%, p <0.001), and in patients aged ≥80 years (1.1%) compared to those aged 65-79 years (2.5%, p <0.001).**

Conclusion: **In 2005, approximately 5.2 million adults in the US were estimated to have a diagnosis of aortic valve disease. Advanced age and female gender were associated with lower rates of specialist visits, diagnostic testing, and AVR.**

The Journal of Heart Valve Disease 2007;16:362-369

Valvular heart disease in general - and diseases of the aortic valve in particular - are common among the US adult population (1-4) and responsible for substantial morbidity and mortality. Estimates made by The American Heart Association suggest that, in 2002, aortic valve disease was responsible for 19,989 deaths in the United States, and was a contributing or underlying cause in more than 26,000 deaths (5). The prevalence of aortic valve disease increases dramatically with age (1-4). In a random, population-based study of the elderly conducted between 1990 and 1991 in Helsinki, Finland, at least moderate aortic stenosis was present in 4.8% of people aged 75 to 86 years, and increased in prevalence from 2.5% to 8.1% among people aged 75 to 76 years and 85 to 86 years, respectively (1). A similar population-based survey based on the Framingham Heart Study found that moderate or greater aortic regurgitation increased in prevalence from 0.5% in men and 0.2% in women ages 50 to 59 years to 2.2% in men and 2.3% in women aged 70 to 83 years (2). Finally, a recent survey combining epidemiological studies which included 11,911 adults found that at least moderate-to-severe aortic stenosis increased in prevalence from 0.2% among people aged 55 to 64 years to 2.8% among those aged over 75 years; and at least moderate-to-severe aortic regurgitation increased in prevalence from 0.7% to 2.0% in the same age groups (4).

Aortic valve disease usually is treated conservatively in the absence of symptoms (6,7), although diagnostic testing is important for the assessment of disease severity and risk (8,9). In its severe, symptomatic form, aortic valve disease has a very poor prognosis; aortic

Presented in part at the 2006 Annual Scientific Sessions of the American Heart Association, 14th November 2006, Chicago, Illinois, USA

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valve replacement (AVR) remains the only proven, effective treatment for severe, symptomatic aortic valve disease (9).

Despite aortic valve disease being closely associated with age, and despite the demonstrated benefit of intervention regardless of age (9), there are ample data available that suggest AVR to be under-utilized in the elderly population, and especially in patients aged ≥80 years (10-14). In addition, multiple studies conducted over the past two decades have identified discrepancies in the rates of utilization of diagnostic testing and therapy among women compared to men with known or suspected coronary artery disease (15-19). Similar studies addressing diagnostic testing and therapy in patients with valvular heart disease have not been performed. Finally, despite dramatic reductions in mortality associated with cardiovascular diseases over the past 25 years, improvement in mortality has been relatively less among elderly patients, among women, and in association with cardiovascular diseases other than coronary heart disease (20). It is not known whether discrepancies in rates of testing and intervention contribute to different outcomes in women and in elderly patients with valvular heart disease.

The study aim was two-fold: first, to estimate the prevalence of aortic valve disease in the United States using a privately insured employer claims database and Medicare claims data and extrapolating those data to the US population in general; and second, to evaluate for differences associated with gender and advanced age in specialty referral, diagnostic testing, and AVR among patients with aortic valve disease.

Materials and methods

Data sources

Data were derived from two de-identified, administrative claims databases: an employer claims database of privately insured persons aged <65 years; and a Medicare claims database for persons aged ≥65 years. Estimates of the US population were based on Census Bureau data by age and gender in 2005 (21). Both claims databases contained similar information but were relevant for different demographic groups. Because Medicare data apply only to people aged 65 years and over, private insurance data were used to estimate disease prevalence in people aged under 65 years.

The employer database contained medical and demographic information on privately insured employees, retirees, and their spouses and dependents from 31 large self-insured companies in the US. The claims covered services provided during the period between January 1999 and December 2004. The 31 companies had national operations, spanned a broad array of industries and occupations, and covered approximately five million lives. The database included medical and prescription drug claims for all enrollees, including spouses and dependents. Data on the monthly eligibility of enrollees were available, as well as enrollee demographic information such as age, gender, geographic region of residence, and employee status of the primary beneficiary.

The Medicare claims database contained encrypted claims data for a 5% random sample of Medicare beneficiaries (approximately 2.7 million lives), covering services provided between 1999 and 2004. Data elements included in-patient and out-patient medical claims with diagnosis and procedure codes, as well as payment, date (quarter only), and other typical claims file variables. Data on socioeconomic status were not available.

All data were de-identified and Health Insurance Portability and Accountability Act (HIPAA)-compliant.

Study design

Prevalence of aortic valve disease in the 2005 US population

Prevalence rates in 2004 were estimated using the employer database for patients aged <65 years and using the Medicare claims database for patients aged ≥65 years. The aortic valve disease prevelence rate in 2004 was defined as the proportion of patients eligible for coverage in 2004 with a new diagnosis of aortic valve disease in 2004 (ICD-9-CM codes: 093.22, 359.0, 395.2, 395.9, 396, 396.2, 396.8, 424.1, 746.3) or a diagnosis of aortic valve disease in any previous year since 1999 when the person was eligible for coverage.

The gender- and age group-specific aortic valve disease prevalence rates in 2004 were then applied to the 2005 US population in the corresponding gender and age group. Because age group and gender distributions in the employer and Medicare databases differ from those in the US population, a direct standardization approach was used to estimate the US aortic valve disease prevalence rates overall and among people aged ≥65 years. Specifically, for each age group, a weighted average of the claims-based prevalence estimates were calculated for both men and women in that age group, where the weights were the proportion of men and women in that age group in the US population. For example, for people aged 65-79 years, the claims-based estimates for aortic valve disease are 8.51% for men and 7.58% for women. In 2005, the proportion in the population of men and women aged 65-79 years was 44.71% and 55.29%, respectively; in this age group, the US prevalence estimate is calculated as ([0.4471×0.0851] + [0.5529×0.0758]) = 0.0800. Overall aortic valve disease prevalence in the US population

was calculated using weighted averages of age- and gender-specific claims-based prevalence estimates and population estimates for each age group.

Treatment pattern analyses

The treatment pattern analysis sample included patients aged ≥65 years from the Medicare claims database with at least one aortic valve disease diagnosis and 12 months' continuous health coverage before and after the initial diagnosis. In addition, patients who had a symptom diagnosis of angina (ICD-9-CM: 413.xx (codes beginning with 413), heart failure (ICD-9-CM: 428.xx (codes beginning with 428)), dyspnea (ICD-9-CM: 786.0), or syncope (ICD-9-CM: 780.2) within a year from aortic valve disease diagnosis were also required to have 12 months of continuous eligibility after their symptom diagnosis. The index date for the treatment pattern analysis was defined as the date of the initial aortic valve disease diagnosis for patients without symptom diagnoses, and for patients with symptom diagnoses predating the first aortic valve disease diagnosis. For patients with a first symptom diagnosis within a year after their initial aortic valve disease diagnosis, the index date was defined as the date of the first symptom diagnosis.

Patients aged ≥65 years were evaluated by age group (65-79 years versus ≥80 years) and gender for a visit to a specialist (a cardiologist or a cardiovascular surgeon), echocardiography (CPT codes: 93320-93350, 93662, 93318, 93303-93317, 76825, 76826, 76827, 76828), stress test (CPT codes: 93015-93018) or aortic valve replacement (ICD-9-CM procedure code: 35.2; CPT codes: 33405, 33406, 33410-33412) within a year from the patient index date.

The Charlson Comorbidity Index (CCI) was used to adjust for patient comorbidities that could have affected referral for testing and intervention. The index was calculated using claims data in the year before the index date as the weighted sum of comorbidities, using comorbidity weights based on adjusted risk of one-year mortality (22). ICD-9-CM diagnosis codes were used to identify the 17 included comorbidities (23).

Statistical analysis

Descriptive comparisons of the proportion of patients with a specialist visit, echocardiography, stress test, and AVR by gender and age group were performed using chi-squared tests. As a sensitivity analysis, logistic multivariate models were used to evaluate the impact of age group and gender on specialist visit, echocardiogram, stress test and AVR within a year from index date, adjusting for the symptom diagnoses of angina, syncope, dyspnea and heart failure, and the CCI score. Statistical significance was evaluated at the 0.05 level. All analyses were performed using SAS Version 9.1 (SAS Institute, Cary, NC, USA).

Results

Aortic valve disease prevalence

Prevalence rates of aortic valve disease among the employer and Medicare databases were extrapolated by age and gender to the 2005 US population (Table I), yielding an estimate of approximately 5.2 million persons (95% confidence interval (CI): 5.16 to 5.32 million) or 1.8% of the US population in 2005 with aortic valve disease. The prevalence of aortic valve disease increased with age. Disease prevalence in people aged ≥65 years (10.7%) was much higher than in the general population, and increased from 8.0% in people aged 65-79 years to 15.9% in people aged 80-84 years and 19.1% in people aged ≥85 years. In all age groups, aortic valve disease prevalence tended to be higher in men than in women.

Table I: Extrapolated aortic valve (AV) disease prevalence in 2005 US population.

Age group (years)	Male persons	Female persons	All persons	95% CI	
				Lower	Upper
All AV disease	2,404,319 (1.65)	2,835,776 (1.89)	5,240,094 (1.77)	1.74	1.79
0-17	44,980 (0.12)	24,231 (0.07)	69,211 (0.09)	0.08	0.10
18-64	662,128 (0.71)	556,635 (0.60)	1,218,763 (0.65)	0.64	0.67
65-79	991,228 (8.51)	1,092,248 (7.58)	2,083,475 (8.00)	7.93	8.06
80-84	374,775 (17.34)	522,491 (15.01)	897,266 (15.90)	15.71	16.10
≥ 85	331,208 (20.65)	640,171 (18.33)	971,379 (19.06)	18.84	19.29
≥ 65	1,697,211 (11.01)	2,254,910 (10.55)	3,952,121 (10.74)	10.63	10.85

Values in parentheses are percentages.
CI: Confidence interval.

Table II: Characteristics of treatment pattern analysis sample in all diagnosed patients aged ≥65 years (n = 128,224).

Parameter	Value
Symptomatic status (%)	
Asymptomatic	25
Symptomatic	75
Angina	59
Heart failure	41
Dyspnea	34
Syncope	50
Gender (%)	
Male	43
Female	57
Overall age (years)*	77.3 ± 7.2
65-79 (%)	62
80-84 (%)	21
≥85 (%)	17
Charlson Comorbidity Index*	2.46 ± 2.15

*Values are mean ± SD.

Treatment pattern analyses

In the Medicare claims database there were 128,224 patients aged ≥65 years with at least one diagnosis of aortic valve disease, and at least 12 months of continuous eligibility before and after the treatment pattern analysis index date. The majority of patients had at least one symptom diagnosis of angina, heart failure, dyspnea or syncope within a year before or after aortic valve disease diagnosis (Table II). Most patients in the treatment pattern analyses were female and aged 65-79 years.

For this Medicare claims sample, comparisons by age and gender of rates of specialist visit, diagnostic testing and AVR are listed in Table III. A lower proportion of women than men had a specialist visit, underwent echocardiographic imaging or stress testing, or underwent AVR within one year of the index date. Women were significantly less likely than men to see a specialist, to undergo stress testing, or to undergo AVR both the 65-79-year and ≥80-year age groups (Table IV). Among patients aged ≥80 years, women were also less likely than men to undergo echocardiographic imaging.

Patients aged ≥80 years similarly were less likely than those aged 65-79 years to see a specialist, to undergo diagnostic testing, or have AVR (see Table III). When comparing treatment patterns by age group for men and women separately (Table V), both men and women aged ≥80 years were less likely to have stress testing and AVR than were men and women aged 65-79 years. Women aged ≥80 years also were less likely than women aged 65-79 years to see a specialist or to have an echocardiogram. The rate of AVR in women was approximately half that of men in both age groups.

The results of multivariate analysis, when adjusted for patient characteristics, were similar to those in the descriptive analyses (Table VI). Women were significantly less likely than men to have a specialist visit, undergo echocardiography, stress testing, or AVR within a year. Similarly, patients aged ≥80 years were significantly less likely than were patients aged 65-79 years to have a specialist visit, echocardiogram, stress test, or AVR. Patients with angina or dyspnea were significantly more likely than those without to undergo each of the variables studied. Patients with heart failure were significantly more likely than those without to have a specialist visit, echocardiography, and AVR within a year, and also less likely to have a stress test. A higher CCI score was associated with a significantly higher likelihood of seeing a specialist within a year. However, it was also associated with a lower likelihood of undergoing echocardiography, stress testing, or AVR within a year.

Table III: Treatment pattern analyses by gender and age group.

Treatment	Female gender	Male gender	p-value	Age (years)		p-value
				65-79	≥80	
Diagnosed patients (age ≥65)	73,674	54,550		79,616	48,608	
Specialist visit (%)	85.4	88.0	<0.001	86.9	85.9	<0.001
Echocardiogram (%)	84.3	84.8	0.01	85.0	83.7	<0.001
Stress test (%)	25.1	33.0	<0.001	34.1	19.3	<0.001
AVR	1.4	2.7	<0.001	2.5	1.1	<0.001

AVR: Aortic valve replacement.

J Heart Valve Dis
Vol. 16. No. 4
July 2007

Discussion

Prevalence of aortic valve disease

The findings of the present study suggests a high prevalence (1.8%) of aortic valve disease in the US population. As has been noted by others (1,2,4), disease prevalence increased dramatically with age. Comparing age-based disease prevalence observed in the present study with that in earlier published reports is confounded by three factors: (i) age ranges in other reports are varied and exactly match neither each other nor those in the present study; (ii) the present study reported aortic valve disease (including both aortic stenosis and regurgitation) whereas previously published studies reported only regurgitation (2), age-based data only for stenosis (1), or the two lesions separately (4); and (iii) the present study relied on diagnoses recorded in administrative claims data rather than echocardiographic findings.

Despite these limitations, some comparisons are possible. First, the prevalence of aortic valve disease appeared substantially higher in the present study than

Table IV: Treatment pattern analyses by gender within age group.

Treatment	Age 65-79 years			Age ≥80 years		
	Female gender	Male gender	p-value	Female gender	Male gender	p-value
Diagnosed patients (age ≥65)	42,316	37,300		31,358	17,250	
Specialist visit (%)	85.9	88.0	<0.001	84.8	87.7	<0.001
Echocardiogram (%)	85.2	84.7	0.06	83.0	84.9	<0.001
Stress test (%)	31.3	37.3	<0.001	16.9	23.6	<0.001
AVR (%)	1.9	3.2	<0.001	0.8	1.6	<0.001

AVR: Aortic valve replacement.

Table V: Treatment pattern analyses by age group among females and males.

Treatment	Female gender			Male gender		
	Age 65-79 years	Age ≥80 years	p-value	Age 65-79 years	Age ≥80 years	p-value
Diagnosed patients (age ≥65)	42,316	31,358		37,300	17,250	
Specialist visit (%)	85.9	84.8	<0.001	88.0	87.7	0.32
Echocardiogram (%)	85.2	83.0	<0.001	84.7	84.9	0.62
Stress test (%)	31.3	16.9	<0.001	37.3	23.6	<0.001
AVR (%)	1.9	0.8	<0.001	3.2	1.6	<0.001

AVR: Aortic valve replacement.

Table VI: Multivariate logistic models for the association of gender and age group with treatment of aortic valve disease.

Variable	Specialist visit		Echocardiogram		Stress test		AVR	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Female	0.74 (0.72-0.76)	<0.001	0.93 (0.9-0.96)	<0.001	0.68 (0.66-0.7)	<0.001	0.5 (0.46-0.54)	<0.001
Age ≥80 years	0.83 (0.81-0.86)	<0.001	0.82 (0.8-0.85)	<0.001	0.48 (0.47-0.49)	<0.001	0.39 (0.36-0.43)	<0.001
Angina	2.37 (2.3-2.44)	<0.001	1.45 (1.4-1.49)	<0.001	3.57 (3.46-3.67)	<0.001	1.86 (1.69-2.04)	<0.001
Heart failure	1.77 (1.72-1.83)	<0.001	1.55 (1.49-1.61)	<0.001	0.7 (0.68-0.72)	<0.001	3.3 (3.02-3.62)	<0.001
Syncope	1.4 (1.36-1.45)	<0.001	1.37 (1.32-1.42)	<0.001	1.02 (0.99-1.05)	0.21	0.95 (0.87-1.04)	0.28
Dyspnea	1.56 (1.52-1.61)	<0.001	1.58 (1.52-1.63)	<0.001	1.31 (1.28-1.35)	<0.001	2.17 (1.98-2.39)	<0.001
CCI	1.04 (1.03-1.04)	<0.001	0.97 (0.96-0.97)	<0.001	0.97 (0.96-0.97)	<0.001	0.71 (0.7-0.73)	<0.001

AVR: Aortic valve replacement: CCI: Charlson Comorbidity Index; CI: Confidence interval; OR: Odds ratio.

in the most recent survey based on pooled epidemiological studies (4). Data from that survey suggested that combined aortic stenosis and regurgitation were present in approximately 0.9% of people aged 55-64 years (compared to 0.7% of people aged 18-64 years in the present study); in approximately 2.3% of people aged 65-74 years (compared to 8.0% of people aged 65-79 years in the present study); and in approximately 4.8% of people aged at least 75 years (compared to 15.9% of people aged 80-84 years and 19.0% of those aged ≥85 years in the present study). Similarly, the extrapolated estimate of aortic valve disease prevalence of 0.9% in the year 2000 US population (4) was substantially lower than the present estimate of 1.8% in 2005 (over five million cases of aortic valve disease in a population of 296 million). In the Cardiovascular Health Study (from which the epidemiology data were in part derived), only 2% of people aged ≥65 years had any degree of aortic stenosis, a figure which was well below the present estimate of aortic valve disease prevalence, even if aortic regurgitation were taken into account (24). However, differences were not as great when comparing present data to the population survey performed 1990 to 1991 in Helsinki (1). Assuming that the prevalence of aortic stenosis and aortic regurgitation were roughly equal, then doubling the observed prevalence of stenosis yields an aortic valve disease prevalence of 5.0% among people aged 75-76 years, of 7.8% in those aged 80-81 years, and of 16.2% in those aged 85-86 years.

Justifying these differences in observed disease prevalence is not straightforward. Aside from possible cross-country differences, data from the present study relied on diagnostic testing performed through 2004, potentially taking advantage of better echocardiographic imaging than was available for the epidemiological surveys conducted between the late 1980s and mid-1990s (4,25-27). In addition, the epidemiological surveys were predominantly performed for the assessment of ischemic heart disease (4,25,26), whereas the Helsinki Aging Study (1) was performed to evaluate specifically for valvular heart disease. In contrast, the present study drew on data reflective of clinical diagnoses, likely without bias toward or away from detecting any one particular pathology.

Concordant with most previous reports, the present study found higher prevalences of aortic valve disease in men compared with women. However, because aortic valve disease prevalence increases dramatically with age, and because there are more elderly women in the US than elderly men, there are substantially more women than men with aortic valve disease in the US. The greater number of women with disease underscores the potential importance of apparently lower rates among women of referral, diagnostic testing and intervention.

Differences based on gender and age

The results of the present study suggested that women and patients aged ≥80 years had lower rates of referral to a specialist, diagnostic testing, and AVR compared to men and to patients aged 65-79 years. However, several limitations of the data should be noted. The data reflect billed tests, visits and procedures, but not referrals; it is also possible that some patients may have been referred for tests or treatment that they did not undergo. In addition, disease severity was not known, and it is possible that lower rates of testing and intervention could have been associated with less-severe disease. Studies have noted, however, that women are referred less often for diagnostic testing compared to men with known or suspected coronary artery disease (15-19); in addition, elderly patients undergo clinically indicated AVR less often than younger patients, despite findings that the benefits of AVR in the elderly significantly outweigh the risks (3,10-14). Recently, Charlson and colleagues showed that patients aged <80 years with aortic stenosis are significantly more likely to be operated on than older patients (10), while an analysis of AVR in the elderly from the European Heart Study found that age was independently associated with a decision not to operate (14). However, current and past guidelines suggest that, owing to absence of an effective alternative therapy, age should not be considered a contraindication to AVR (9).

The results of the present study also revealed different rates of AVR between men and women aged ≥65 years, with the rate in women only half that in men. Female gender may be associated with a somewhat higher operative mortality at the time of AVR (28). However, anticipated operative risks alone do not appear sufficient to explain the two-fold discrepancy in rates of AVR between men and women. As with advanced age, in the absence of an effective alternative therapy, female gender should not preclude consideration for AVR.

Arguably, lower rates of AVR in women and elderly patients may have been due to excessive operative risks that would preclude safe intervention. The CCI attempts to account for comorbid conditions that could affect therapies and outcomes (22), and has been successfully adapted to studies addressing outcomes using administrative databases (23). In multivariate analysis, a higher CCI score was associated with a lower likelihood of AVR. However, echocardiography also was performed less often, which suggested that disease severity also was less rigorously investigated. Without additional detail, this appears justified only in fairly extreme circumstances of comorbidity.

Notably, despite statistical significance of the differences, the absolute rates of some measured outcomes

were only slightly different between men and women, and between age groups. However, the rate of AVR was about two-fold higher in men than in women, and in patients aged 65-79 years than in those aged ≥80 years. These data suggest that, as a patient progresses through the medical process of referral, diagnostic testing and therapy, relatively small differences in rates of individual factors appear to have a large cumulative effect on ultimate therapeutic intervention.

Study advantages and limitations

The use of administrative insurance claims and Medicare beneficiary claims data provide access to a much larger population sample than is feasible with medical records review. Prevalence and treatment rates for 2005 were extrapolated to the US population based on the claims samples for approximately eight million lives. Although privately insured beneficiaries might not be fully representative of the population as a whole, the size and diversity of the sample should minimize potential bias. The reliance on US census data for population estimates of aortic valve disease precluded treatment of age as a continuous variable. Patients who became eligible for coverage in 2004 may not have been covered for long enough to have a recorded diagnosis of aortic valve disease, which would (potentially) result in an underestimation of disease prevalence. In addition, patients who were diagnosed with aortic valve disease prior to 1999 but did not receive a subsequent diagnosis by the end of 2004 would not have been captured in the present study, and similarly could contribute to an underestimation of disease prevalence. In contrast, some patients captured by the study may have previously undergone AVR; the absence of native aortic valve disease was not taken into consideration, thereby introducing a potential for prevalence overestimation.

The present study was based on analyses of administrative claims data, and not of medical treatment. The causal relationship between aortic valve disease-related claims and performed procedures is not known. Specifically, without review of individual medical records, symptoms could not be causally linked with diagnosis; neither was it feasible to determine why patients were or were not referred for testing, specialty evaluation or intervention. Furthermore, because the ICD-9-CM codes identifying aortic stenosis and regurgitation are the same, it was not possible to distinguish between aortic stenosis and aortic regurgitation. Additionally, mitigating factors affecting referral, testing, and treatment were not known. Neither the severity of aortic valve disease nor related indications or contraindications for AVR could be established in each individual case. A lack of follow up data precludes the drawing of conclusions with regards to the effects of the revealed differences in treatment on long-term survival in the groups studied.

In conclusion, in 2005 approximately 5.2 million US adults - or approximately 1.8% of the entire population - received a diagnosis related to aortic valve disease. The prevalence of aortic valve disease was 10.7% in people aged ≥65 years. Advanced age and female gender were associated with lower rates of specialty referral, diagnostic testing, and AVR. AVR was performed at approximately half the rate in women (1.4%) compared to men (2.7%, $p < 0.001$), and in patients aged ≥80 years (1.1%) compared to those aged 65-79 years (2.5%, $p < 0.001$).

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