ORIGINAL ARTICLE

CORONARY ARTERIAL DISEASE IN PATIENTS OF AORTIC STENOSIS AND ASSOCIATED IN-HOSPITAL COMPLICATIONS AFTER SURGICAL MANAGEMENT

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Objectives: This study aimed to determine the frequency of coronary artery disease (CAD) and its complications following surgical management in patients with aortic stenosis (AS).

Methodology: This descriptive case series included 113 patients, both male and female, aged between 40 and 80 years, diagnosed with severe AS. All patients underwent coronary angiography prior to surgical management to assess the presence of CAD. Postoperatively, patients were monitored during their hospital stay for up to 72 hours, and complications such as major bleeding, acute kidney injury (AKI), stroke, and mortality were recorded.

Results: The study included 113 patients with a mean age of 55.4±12.4 years, of whom 63 (55.8%) were male. Positive family history of CAD was found in 24 (21.2%) patients. CAD was observed in 65 (56.6%) patients. In-hospital complications were as follows: major bleeding occurred in 7 (6.2%) patients, AKI in 13 (11.5%), stroke in 10 (8.8%), and mortality in 3 (2.7%) patients. Mortality rates were 4.7% vs. 0% (p=0.125), stroke rates were 14.1% vs. 2% (p=0.026), and AKI rates were 17.2% vs. 4.1% (p=0.023) for patients with and without CAD, respectively.

Conclusion: The prevalence of CAD was found to be high in more than half of the patients with severe AS. The presence of CAD was associated with an increased risk of mortality and complications such as stroke and AKI. It is crucial to identify the underlying risk factors for CAD in this patient population in order to effectively address the burden of the disease and optimize management strategies accordingly.

Keywords: aortic stenosis, coronary artery disease, complications, prognosis

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INTRODUCTION

Aortic valve stenosis, generally known as aortic stenosis (AS), is the most common form of valvular heart disease in elderly patients. It frequently occurs in conjunction with coronary artery disease (CAD). The standard options are aortic valve replacement and coronary artery bypass grafting (CABG) surgical treatment for patients with AS and CAD.[1] The CAD is reported to present in as high as 60% of the patients undergoing surgical aortic valve replacement (SAVR) and 65% of patients undergoing transcatheter aortic valve replacement (TAVR). A number of pathophysiological processes influence the association between AS and CAD, including "low-density lipoprotein–mediated inflammatory response," resulting in enhanced atherosclerotic process and sharing similar risk factors, including age, smoking, hypertension, and hyperlipidemia.[2] Severe AS pathophysiology includes endothelial dysfunction, calcification, and genetic factors. Recent studies have determined that increased plasma homocysteine concentration is an independent risk factor for CAD. It facilitates atherosclerotic vascular diseases and thrombus formation in the venous system by causing atherosclerosis through various mechanisms.[3] However, the prevalence of obstructive CAD has shown significant variability, from 10% to 50%.[4,5]

The similarity in pathophysiological aspects has led to treating AS with statins and angiotensin-converting enzyme inhibitors, however, no significant results have been obtained.[6] Previously published studies showed that CABG at the time of SAVR for treating patients of severe AS with

concomitant CAD is a safe strategy. However, there was a belief that the operative risk significantly increased with the addition of CABG to the treatment plan. Hence the pre-operative history should include any current symptoms, a complete inventory of comorbidities, including cardiac risk factors, and entire family history.[1,2,7-8]

Local data are scarcely addressing CAD frequency and its prognostic implications in patients with severe AS undergoing surgical management. With an imbalance risk profile and lifestyle variations, we expected to observe different results in our population compared to other regions. Therefore, this study was designed to assess the burden of CAD and its associated outcomes in severe AS patients.

METHODOLOGY

This descriptive case series was conducted in the Department of Adult Cardiology at the "National Institute of Cardiovascular Diseases (NICVD)" in Karachi, Pakistan, from December 2019 to June 2020. Verbal consent was obtained from all patients before their participation in the study, and the research protocol was approved by the Research and Evaluation Department of the "College of Physicians and Surgeons Pakistan (CPSP)" as part of the fellowship program in adult cardiology.

A total of 113 consecutive patients, aged between 40 to 80 years and diagnosed with severe aortic stenosis (AS), were included in the study. Patients who did not provide consent, those with a prior history of cardiac-related surgery, and those with chronic kidney disease (CKD) were excluded from the study.

Severe AS was defined based on transthoracic echocardiogram (TTE) parameters, including an aortic jet velocity (m/s) >4.0, mean gradient >50 mmHg, aortic valve area (AVA) <1 cm2, and velocity ratio <0.25. Pre-operative coronary angiography was performed on all patients by an experienced cardiologist with a minimum of 5 years of experience to assess the presence of coronary artery disease (CAD). CAD was defined as more than 70% stenosis in one or more of the major coronary arteries (left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA)). The severity of CAD was classified into three categories: single-vessel disease (SVD), two-vessel disease (2VD), and three-vessel disease (3VD), based on the number of vessels involved.

Patients with concomitant CAD underwent surgical aortic valve replacement (SAVR) plus coronary artery bypass grafting (CABG), while patients with severe AS without CAD underwent SAVR alone. All surgical procedures were performed by surgeons with a minimum of five years of experience. Post-operative complications, including major bleeding, acute kidney injury, stroke, and mortality, were recorded during the patients' hospital stay for up to 72 hours post-surgery. Major bleeding was defined as a decrease in hemoglobin >5g/dL or a reduction in hematocrit >15% from baseline at 72 hours. Acute kidney injury was determined by a post-operative serum creatinine level greater than 1.4mg/dL. Stroke was defined as any impairment of motor, sensory, or cognitive function persisting for >24 hours during the hospital stay. Mortality was defined as death from any cause within 72 hours of hospital admission.

Demographic data and other clinical factors, such as hypercholesterolemia, arterial hypertension, diabetes mellitus, smoking, and low HDL levels, were also recorded. Hypercholesterolemia was defined as a total serum cholesterol level >200 mg/dL or the use of statins at the time of angiography. Arterial hypertension was identified based on a previous diagnosis or the use of antihypertensive medications at the time of angiography. Diabetes mellitus was considered if there was a previous diagnosis or fasting glycemia >110 mg/dL. Smoking was defined as tobacco consumption at the time of AS diagnosis, and low HDL levels were characterized by a serum value <25 mg/dL at the time of angiography.

The sample size for the study was calculated using an expected frequency of CAD in severe AS patients as 25%.[9] The confidence interval was set at 95% with a desired precision of 8%, resulting in a calculated sample size of 113 using the WHO sample size calculator version 2.0. The collected data were analyzed using IBM SPSS version 21. Summary statistics, including mean ± standard deviation (SD) and frequency (%), were calculated. The patients were stratified into two groups based on the presence of CAD and clinical data, and outcomes were compared between the two groups using appropriate statistical tests such as the Chi-square or Fisher's exact test at a significance level of 5%.

RESULTS

In the study sample of 113 patients, the mean age was 55.4 ± 12.4, with 76 (67.3%) patients being older than 50 years. The mean body mass index (BMI) was 25.7 ± 5.3 kg/m2. Among the patients, 41 (36.3%) were classified as obese, while 72 (63.7%) were non-obese. Out of the total participants, 50 (44.2%) were female. A positive family history of coronary artery disease (CAD) was observed in 24 (21.2%) patients. Among the study participants, 50 (44.2%) were smokers, 66 (58.4%) had hypertension, and 44 (38.9%) were diagnosed with diabetes.

Coronary artery disease was found in 64 (56.6%) patients, with the classification of single-vessel disease (SVD) in 29 (45.3%) patients, two-vessel disease (2VD) in 12 (18.8%) patients, and three-vessel disease (3VD) in 23 (35.9%) patients. In-hospital complications were reported as follows: major bleeding in 7 (6.2%) patients, acute kidney injury in 13 (11.5%) patients, stroke in 10 (8.8%) patients, and mortality in 3 (2.7%) patients, as presented in Table 1.

Table 1: Descriptive summary of demographics and clinical characteristics, and angiographic findings of the patients included in the study

	Summary
Total (N)	**113**
Gender	
Male	63 (55.8%)
Female	50 (44.2%)
Age (years)	55.4 ± 12.4
40-50 Years	37 (32.7%)
>50 Years	76 (67.3%)
Body mass index (kg/m^2)	25.7 ± 5.3
Obesity	
Obese	41 (36.3%)
Non-obese	72 (63.7%)
Family history of ischemic heart diseases	
Positive	24 (21.2%)
Negative	89 (78.8%)
Smoking status	
Smoker	50 (44.2%)
Non-smoker	63 (55.8%)
Diabetes mellitus	
Diabetic	44 (38.9%)
Non-diabetic	69 (61.1%)
Hypertension	
Hypertensive	66 (58.4%)
Non-hypertensive	47 (41.6%)
Angiographic findings	
Coronary artery disease (CAD)	
CAD	64 (56.6%)
Non-CAD	49 (43.4%)
The severity of coronary artery disease	
Single vessel disease	29 (45.3%)
Two vessel disease	12 (18.8%)
Three vessel disease	23 (35.9%)

Table 2 demonstrates that the presence of CAD is associated with an increased risk of mortality (4.7% vs. 0%, p=0.125) as well as complications such as stroke (14.1% vs. 2%, p=0.026) and acute kidney injury (17.2% vs. 4.1%, p=0.023) compared to patients without CAD.

Table 2: Comparison of in-hospital complications and outcomes for severe aortic stenosis patients with and without coronary artery disease

	Total	**Coronary Artery Disease**		**P-value**
		Absent	**Present**	
Total (N)	**113**	**49**	**64**	
Major bleeding				
Yes	7 (6.2%)	2 (4.1%)	5 (7.8%)	0.415
No	106 (93.8%)	47 (95.9%)	59 (92.2%)	
Acute kidney injury (AKI)				
Yes	13 (11.5%)	2 (4.1%)	11 (17.2%)	0.030
No	100 (88.5%)	47 (95.9%)	53 (82.8%)	
Stroke				
Yes	10 (8.8%)	1 (2%)	9 (14.1%)	0.026
No	103 (91.2%)	48 (98%)	55 (85.9%)	
Mortality				
Yes	3 (2.7%)	0 (0%)	3 (4.7%)	0.125
No	110 (97.3%)	49 (100%)	61 (95.3%)	

DISCUSSION

Coronary artery diseases (CAD) are a significant cause of morbidity and mortality. The economic burden of society not only increases morbidity but also increases mortality.[10] CABG and Aortic valve operations play an important role in cardiac surgery at various cardiac centers worldwide.[11] The most prevalent type of valvular heart disease affecting older people is aortic valve stenosis, which frequently coexists with coronary artery disease (CAD). Adult patients in Pakistan estimated one in five middle-aged might have had CAD.

Inadequate data addresses the implications of coronary artery disease in patients with severe aortic

stenosis undergoing surgical management among our population. The primary study endpoint was all-cause in-hospital (within 72 hours) death and its complications, including those diagnosed with severe aortic stenosis (AS) who underwent coronary angiography at the largest cardiac care center in Pakistan.

The mortality rate in this study was 3.2%, consistent with the study by Ahmed, OF et al. and others around the world.[1,7,8,11,12] The mortality rate for isolated valve surgery is 2.7%, and for combined CABG and valve surgery, it is 4.7%.[2] Overall surgical mortality in Gunay R et al.[13] study was 10%, whereas Ahmed OF et al.[11] mortality rate of 14% has been reported. Over the decade, surgical mortality for AVR-CABG surgeries has ranged from 5.5% to 7.5%. The Society of Thoracic Surgeons National Cardiac Database found that operative mortality in patients undergoing AVR with CABG 4.5%) was slightly higher than in patients undergoing isolated AVR (3%) over the past decade.[14] Zorbozan O et al.[4] reported in-hospital mortality in 15 (9%) patients. Grossi EA et al.[7] that all-cause mortality after isolated aortic valve replacement ranged from 2% to 4%, rising to approximately 8% in high-risk patients. Similarly, the current study also showed that CAD increased mortality risk (42.3% vs. 11.8%, p=0.007).

In the current study found coronary artery disease in 64 (56.6%) patients, of whom 29 (45.3%) were classified as SVD, 12 (18.8%) as 2VD, and 23 (35.9%) as 3VD. A similar study reported that CAD was present in 40% of patients.[5] Many studies have reported the prevalence of primary CAD in AS patients ranging from 25% to 50%. A large prospective Swedish study reported an overall 39% prevalence of CAD.[3,6] Similar studies observed a 56% prevalence rate of coronary artery disease (CAD) in patients with aortic stenosis.[9-15] Results from our study showed 15 SVD (45.5% of cases), 6 (18.2%) 2VD, and 12 (36.4%) 3VD. Osnabrugge RL et al. observed a similar finding in the literature.[12] Another recent study reported similar results: Obstructive CAD was observed in 24.6%, with 19.4% of single-vessel disease, 16.1% of two-vessel disease, and 64.5% of three-vessel disease.[16] Another study conducted by Ahmed OF et al. found that 24 patients (38.7%) had single grafts, 26 cases (41.9%) had two grafts, and 12 (19.3%) had three grafts.[11] The ESC/EACTS guidelines reported significantly lower mortality when SAVR was combined with CABG compared to CABG alone (42 vs. 78% at a median follow-up of approximately six years. There was no survival benefit from combined surgery in patients with mild AS.[17]

In this study, surgical management with AVR included 64 (56.6%) patients, while the remaining 49 (43.4%) patients had managed with AVR+CABG. Bonow RA et al.[18] reported the prevalence of AVR+CABG in 50% of the patients. Baumbach H, et al.[19] noted that 464 patients (74.1%) underwent AVR+CABG. The current study found coronary artery disease in 33 (29.2%). According to the Ibrahim KS et al.[8] Heart Survey, 23% of all valve surgeries (33% for AS and 32% for MR) are associated with CABG. A similar result was reported in this study. A study of 1308 patients with severe VHD by Matta A et al.[1] detected CAD in 27.75%, with the highest prevalence of 41.66% among patients with severe AS.

In the present study, in-hospital complications were major bleeding, were reported in 7 (6.2%) patients, acute kidney disease in 13 (11.5%), and stroke was documented in 10 (8.8%) patients. Gouda M et al.[20] reported hospital mortality in 19 (8.8%) patients. Stroke 2 (3.2%) and bleeding 3 (4.8%) were the commonest complication reported by Ahmed OF et al.[11] In 157 asymptomatic patients with severe AS and normal LV function, a randomized trial of early SAVR versus conservative management demonstrated improvement in the composite endpoint of death, myocardial infarction, stroke, and hospitalization for heart failure with early SAVR over a median follow-up of 32 months.[21] An earlier observational study also suggested that AVR improved outcomes and complications in patients with asymptomatic very severe AS.[22] A recent study conducted a meta-analysis found that women had a higher risk of mortality and stroke after heart surgery than men with AS.[23] Findings from numerous observational international datasets provide credence to this assertion.[24] A national-scale study in Sweden concluded that additional risk factors and complications such as stroke and bleeding cause technically more difficult coronary surgery.[25]

The present study suffers from some limitations. The case series design does not precisely assess tobacco exposure as a risk factor for coronary heart disease, which could have led to misclassification errors in exposure. It was not designed with enough power to analyze interactions between different coronary heart disease risk factors, which could have made the coefficients for known coronary heart disease risk factors insignificant, so these should be interpreted cautiously.

CONCLUSION

In conclusion, this study reveals that coronary artery disease (CAD) is prevalent in more than one-fourth of patients with severe aortic stenosis (AS). The presence

of CAD is associated with a higher risk of mortality and complications such as stroke and acute kidney injury. These findings emphasize the importance of identifying and addressing the underlying risk factors for CAD in patients with severe AS. It is crucial to develop comprehensive management strategies that focus on optimizing patient care and reducing the burden of disease. By effectively managing CAD in these patients, healthcare professionals can improve outcomes and enhance the overall quality of care.

AUTHORS' CONTRIBUTION

SA and MNK: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. NAS, KN, SR, and HM: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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