ORIGINAL ARTICLE
OBSTRUCTIVE CORONARY ARTERY DISEASE IN PATIENTS UNDERGOING RHEUMATIC VALVULAR HEART SURGERY

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Objectives: The presence of concomitant obstructive coronary artery disease (CAD) in patients with valvular heart disease (VHD) carries significant prognostic implications. Therefore, the objective of this study was to determine the frequency and severity of obstructive CAD in patients undergoing valvular heart surgery for rheumatic heart disease (RHD) at a tertiary care hospital in Karachi, Pakistan.

Methodology: This descriptive study included patients of either gender, between 40 to 70 years of age, diagnosed with RHD on transthoracic echocardiography, and undergone valvular heart surgery. As a routine, pre-operative diagnostic coronary angiography was performed and the presence and severity of obstructive CAD were recorded.

Results: Among 126 patients, 73% (92) were male, and the mean age was 48.3 ± 7.1 years. Smoking was the most common risk factor with a frequency of 22.2%, followed by hypertension (7.1%) and diabetes (4.8%). Obstructive CAD was observed in 24.6% with 19.4% single-vessel disease, 16.1% with two-vessel disease, and 64.5% with three-vessel disease. The presence of obstructive CAD was found to be positively associated with older age (p=0.040) and type of RHD (p=0.048).

Conclusion: The obstructive concomitant CAD is prevalent in around 1/4th of patients, most of them with multi-vessel diseases, undergoing valvular heart surgery for rheumatic heart disease. It has been further observed that older age and the type of RHD are positively associated with the incidence of concomitant CAD in these patients.

Keywords: rheumatic heart disease, valvular heart disease, coronary artery diseases, Pakistan

INTRODUCTION

Valvular heart disease (VHD) is among the major contributors to the substantial loss of quality of life, functional capacity, and longevity of life around the globe with significantly varying epidemiology in relation to the economic plight of the region.[1] The rheumatic etiology of VHD is predominant in middle- to low-income countries, while calcific or degenerative VHD is more common in high-income countries.[1] Considering the global population share, rheumatic VHD remains the leading manifestation of VHD which afflicted around 41 million people, followed by degenerative VHD with 24 million, and calcific aortic stenosis with 9 million people worldwide.[1] In a typical clinical observation, VHD is less common than ischemic heart disease, heart failure, or hypertension but owing to its correlation with deterioration of heart functional capacity, it carries high rates of fatal outcomes, especially in the older population.[2]

Among various other factors, the presence of concomitant obstructive coronary artery disease (CAD) in patients with rheumatic VHD is found to be associated with an increased risk of adverse clinical outcomes and complications.[3-7] CAD is more common among patients with degenerative or calcific valvular lesions due to shared pathophysiological risk factors such as hypertension, smoking, lipid deposition, inflammatory processes, and aging.[8-11] The reported prevalence of concomitant CAD varies from the smallest of 9% to as high as 41% depending on the size of the sample, type of the VHD, and definition of CAD used by these studies.[5, 12, 13] One of the largest studies conducted in the United States of America included 5,360 patients of VHD without a known history of CAD, the prevalence of concomitant CAD was reported in around 19.3% in coronary CT/ diagnostic coronary angiography.[14]

Considering the growing prevalence and prognostic implications of concomitant CAD in patients undergoing surgical procedures for VHD, a coronary angiographic assessment is recommended by the "American Heart Association / American College of Cardiology (AHA/ACC) guidelines", especially for the patients above 40 years of age.[15] Systematic and robust evidence regarding the prevalence of concomitant VHD and CAD are available for high-income countries, however, there is a dearth of reliable estimates for developing and under-developing countries such as Pakistan, where VHD of rheumatic etiology is more common.[13] It is of paramount importance to know the true prevalence of concomitant VHD and CAD for optimal management of the diseases. Additionally, an accurate assessment of burden of concomitant CAD in VHD patients can help in optimal utilization of hospital resources, surgical supplies, and services, especially high volume public sector hospitals like ours. Therefore, the aim of this study was to determine the frequency and severity of obstructive CAD in patients undergoing valvular heart surgery for rheumatic heart disease (RHD) at a tertiary care hospital in Karachi, Pakistan.

METHODOLOGY

This descriptive study was conducted as part of the fellowship in cardiac surgery from the College of Physicians and Surgeons Pakistan (CPSP). This study was approved by the CPSP and it was conducted at the "National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan" between 1st July 2020 and 31st December 2020. The verbal consent for participation was taken by the principal investigator prior to the inclusion in the study purpose, benefits, and processes involved in the study were explained to all the participants in accordance with the Declaration of Helsinki. Participation in the study was voluntary and we included patients in the study a through non-probability consecutive sampling technique.

The inclusion criteria for the study was; patients of either gender, between 40 to 70 years of age, diagnosed with RHD and undergoing valvular heart surgery. While patients with a history of prior cardiac related surgery or who refused to give consent were excluded. The spectrum of RHD included confirmed diagnosis of severe mitral stenosis (MS), severe aortic stenosis (AS), severe aortic regurgitation (AR), or severe mitral regurgitation (MR), or multi/mixed valvular heart disease on Transthoracic Echocardiogram (TTE). Parameterization and diagnosis of valvular pathologies were made as per the recommendations of the American Society of Echocardiography (ASE).[16, 17]

Demographic and clinical characteristics of the patients were recorded at the time of presentation such as age (years), gender, smoking status, diabetic mellitus (taken anti-hyperglycemic treatment for at least 6 months), obesity (body mass index $\geq 30 \ kg/m^2$), and hypertension (taken anti-hypertensive treatment for at least 6-months). Based on TTE evidence valvular pathology was recorded as severe MS, severe AS, severe MR, or severe AR. As a routine, pre-operative diagnostic coronary angiography was performed in all the patients, and the presence and severity of obstructive CAD were recorded as either more than 70% stenosis in any one of the major coronary arteries, i.e. "left anterior descending artery (LAD), the left circumflex artery (LCX), the right coronary artery (RCA)", or more than 50% obstruction in the left main artery. The severity of obstruction was further categorized as a single-vessel disease (SVD), two-vessel disease (2VD), or three-vessel disease (3VD). The surgical management of valvular pathologies and revascularization (coronary artery bypass grafting) strategies were decided and adopted as per the institutional protocols and status of the patient.

Sample size for this study was calculated to be 126 with an expected 20% frequency of concomitant VHD and obstructive CAD, [12] at a 95% confidence level, and a 7% error margin. Data were analyzed with IBM SPSS (version 19), mean ± standard deviation (SD) was calculated for the age (in years) of the patients, while, all other categorical variables including co-morbid, valvular pathologies, obstruction of CAD were expressed as frequencies and percentages. Effect modifiers like age, gender, co-morbid conditions (obesity, smoking status, diabetic mellitus, hypertension), and valvular pathology were controlled through stratification as their association with the incidence of concomitant obstructive CAD was assessed with the help of appropriate Chi-square test or fisher exact test with the level of significance of p-value ≤ 0.05.

RESULTS

Among 126 patients, 73% (92) were male and mean age was 48.3 ± 7.1 years with 4.8% (6) above 60 years of age. Smoking was the most common risk factor with a frequency of 22.2%, followed by hypertension (7.1%) and diabetes (4.8%). Obesity was observed in 4% of the patients. Both sever mitral stenosis and regurgitation were the commonly found isolated valvular pathology with a frequency of 33.3% (42) and 33.3% (42). Multi-valvular disease was observed in 31.7% (40) of the patients and two patients (1.6%) had isolated severe aortic stenosis. Obstructive CAD was

observed in 24.6% with 19.4% single-vessel disease, 16.1% two-vessel disease, and 64.5% with three-vessel disease (Table 1).

Table 1: Distribution of demographic and clinical characteristics, valvular pathology, and coronary artery disease

	Total
Total (N)	126
Gender	
Male	92 (73%)
Female	34 (27%)
Age (years)	48.3 ± 7.1
40 to 50 years	86 (68.3%)
51 to 60 years	34 (27%)
> 60 years	6 (4.8%)
Body mass index (kg/m²)	22.8 ± 2.9
Type of rheumatic heart disease	
Severe mitral stenosis	42 (33.3%)
Severe mitral regurgitation	42 (33.3%)
Severe aortic stenosis	2 (1.6%)
Multi-valvular disease	40 (31.7%)
Co-morbid conditions	
Smoking	28 (22.2%)
Diabetes mellitus	6 (4.8%)
Hypertension	9 (7.1%)
Obesity	5 (4%)
Obstructive CAD	31 (24.6%)
Single vessel disease	6 (19.4%)
Two vessel disease	5 (16.1%)
Three vessel disease	20 (64.5%)

CAD=coronary artery disease

The presence of obstructive CAD in patients with VHD was found to be positively associated with older age (p<0.001) and with the type of RHD, as presented in Table 2.

Table 2: The incidence of obstructive coronary artery diseases stratified by demographic and clinical characteristics and valvular pathology

	Obstructive CAD		P-value
	No	Yes	
Total (N)	95 (75.4%)	31 (24.6%)	-
Gender			
Male	70 (73.7%)	22 (71%)	0.767
Female	25 (26.3%)	9 (29%)	
Age (years)	46 ± 5.7	49 ± 7.4	0.040
Body mass index (kg/m²)	22.6 ± 2.8	23.5 ± 3.2	0.150
Type of RHD			
Severe mitral stenosis	29 (30.5%)	13 (41.9%)	0.048
Severe mitral regurgitation	33 (34.7%)	9 (29%)	
Severe aortic stenosis	0 (0%)	2 (6.5%)	
Multi-valvular disease	33 (34.7%)	7 (22.6%)	
Smoking			
No	76 (80%)	22 (71%)	0.294
Yes	19 (20%)	9 (29%)	

Diabetes mellitus			
No	90 (94.7%)	30 (96.8%)	>0.999
Yes	5 (5.3%)	1 (3.2%)	
Hypertension			
No	90 (94.7%)	27 (87.1%)	0.222
Yes	5 (5.3%)	4 (12.9%)	
Obesity			
No	93 (97.9%)	28 (90.3%)	0.095
Yes	2 (2.1%)	3 (9.7%)	

CAD=coronary artery disease

DISCUSSION

The concomitant obstructive CAD in patients undergoing valvular heart surgery carries a significant prognostic implication, hence, pre-operative diagnostic angiography remains a common and recommended clinical practice for adult (≥ 40 years) patients undergoing valvular heart surgery. Therefore, this study was conducted to evaluate the frequency of concomitant obstructive CAD in patients undergoing rheumatic valvular heart surgery at the largest cardiac care center in Pakistan. It has been observed that around 1/4th of patients undergoing valvular heart surgery also have concomitant obstructive CAD. The incidence of obstructive CAD has a strong association with the aging of patients as the mean age of patients with obstructive CAD was significantly higher as compared to their counterparts (49 ± 7.4 years vs. 46 ± 5.7; p<0.001) with a difference of around 3 years in absolute terms. Due to low prevalence, the association between the presences of conventional risk factors of CAD as co-morbid conditions to the RHD could not be established with concomitant obstructive CAD. Such as, the presence of diabetes and hypertension were found only in 4.8% and 7.1% of the patients. As expected, smoking was found to be the commonest risk factor with 22.2% prevalence, however, there was no statistically significant association between the incidence of concomitant obstructive CAD and smoking with an incidence rate of 22.4% vs. 32.1%; p=0.294 among smokers and non-smokers, respectively.

Findings in our population were more or less similar to the data from western countries, for instance, a study conducted by Lappé JM et al.[14] reported obstructive CAD 19.3% in a pool of 5,360 referred for VHD and age (odds ratio (OR) 2.41 [95% confidence interval (CI); 2.17-2.68]) was reported to be an independent predictor of obstructive CAD. Contrary to our findings, male gender (OR 1.94 [95% CI; 1.64-2.3]), diabetes (OR 2.07 [95% CI; 1.7-2.52]), family history of premature CAD (OR 1.34 [95% CI; 1.02-1.76]), hyperlipidemia (OR 1.47 [95% CI; 1.02-2.1]),

and renal dysfunction (OR 1.47 [95% CI; 1.21-1.78]) were also reported to be independent predictors of obstructive CAD on multivariable analysis.[14] A study of 1308 patients with severe VHD by Matta A et al.[18] detected CAD in 27.75% of the patients with highest prevalence of 41.66% among patients with severe AS. In a study by Cazelli JG et al.[12] from Brazil, obstructive CAD was reported in 20% of the 2898 valvular patients, on multivariable analysis age, family history, and chest pain were reported to be independent predictors of obstructive CAD with OR of 1.06 [95% CI; 1.04-1.09], 2.42 [95% CI; 1.46-3.99], and 3.83 [95% CI; 2.44-6.01], respectively. A study by Ahmad M et al.[13] in our local population reported obstructive CAD in 29.3% out of the study sample of 140 cases of VHD. Study further reported the incidence of obstructive CAD was 22.4% in patients with VHD of rheumatic etiology, close to over observation of 24.6%. Other global estimated for the incidence of significant CAD in VHD of rheumatic etiology are; 11.1% by Atalar E et al.,[19] 22.6% by Sahi R et al.,[20] and 11% by Narang R et al.,[21] in comparison to these estimated, a higher prevalence of concomitant obstructive CAD in our population is alarming and required immediate attention.

The prognostic role of VHD with concomitant obstructive CAD is well established. It has been reported that the concomitant CAD is associated with an increased risk of cardiovascular mortality and ischemic events at one year follow-up of patients undergoing transcatheter aortic valve implantation (TAVI).[3] Similarly, in another study of octogenarians patients by Wang TK et al.,[4] prolonged ventilation and 30-day mortality were significantly higher for patients undergoing aortic valve replacement (AVR) with concurrent coronary artery bypass grafting (CABG) compared to isolated AVR. The concomitant CAD are also found to have a detrimental effects on kidney function after valvular heart surgery and moderate to severe CAD remained an independent predictors of acute kidney injury after valvular heart surgery.[5] Similarly, a registry based study of 896 patients who underwent TAVI by Huczek Z et al.[6] reported negative impact of obstructive CAD on short-term prognosis and an improvement in survival was noted with revascularization prior to TAVI.[6] Similar, data reported by Millan-Iturbe O et al.[22] also supported the selective pre-TAVR revascularization strategy.

Even though, the concomitant obstructive CAD is more common in patients of degenerative VHD due to aging factor, in our part of the world it is more of less equally prevalent in patients with rheumatic VHD may be due to delay in diagnosis and lake of timely screening.

Small sample size, single-center experience, and predominantly urban population are the key limitation of our study, thus, the results might not be generalizable.

CONCLUSION

The obstructive concomitant CAD is prevalent in around 1/4th of patients, most of them with multi-vessel diseases, undergoing valvular heart surgery for rheumatic heart disease. It has been further observed that older age and type of VHD are positively associated with the incidence of concomitant CAD in these patients.

AUTHORS' CONTRIBUTION

SU and AK: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. NNM, RK, WK, ARM, and SAK: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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