Prevalence of Coronary Artery Lesion(S) in Patients Aged 40-50 Years Undergoing Rheumatic Valvular Surgery

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Abstract

Objective: To determine the prevalence of coronary artery disease in patients undergoing valve surgery for rheumatic heart disease between age 40-50 years, usefulness, and indication of pre-operative coronary angiography. **Methods:** This is an observational prospective study that took place in 2 hospitals (National Heart Institute and Nasser Institute) within the period starting from January 2013 to January 2015. We included 454 rheumatic patients that were admitted for elective primary mitral, aortic or double valve surgery, and that had a coronary angiogram in their regular pre-operative workup. All coronary angiographies were performed by injecting right and left coronaries by using 80-100 ml of iodinated contrast to obtain the standard views of both right and left coronaries using Philips or Siemens machines in both hospitals. Coronary artery disease (CAD) of 50% is considered to be a positive finding. **Results:** There was no correlation between rheumatic heart disease in this age group and CAD as only 1.76% had the significant stenosis. Male gender, family history of CAD, age above 45yrs, hypertension, and smoking showed significant correlation with the CAD in this study. **Conclusion:** Our results suggest that the overall prevalence of coronary artery disease in patients undergoing rheumatic valve surgery in our population is not comparable with the prevalence reported in international data. So, multicenter studies are needed in developing countries to set their own guidelines. Therefore, our study can be the nucleus for these guidelines in our country.

Keywords: Prevalence, Coronary Artery, Rheumatic, Valvular

Introduction

Valvular heart disease is a growing problem, particularly in developing countries. It is important to consider that the spectrum of valve disease in the developing world is different from that of developed countries. The predominant pathology of valve disease in our patients is rheumatic, whereas degenerative valve disease is the predominant one in the west. Rheumatic heart disease is a major health issue in developing countries with an incidence of over 1 per 1000 people (David, 1995). In children and young adults, it is the commonest form of valvular disease that requires surgery (Markus et al., 1994).

Guidelines of the American College of Cardiology (ACC)/American Heart Association (AHA) recommended that a coronary angiography should be performed before valve surgery in men aged >35 years, women aged >35 years with coronary risk factors, and in post-menopausal women (Bonow et al., 2008). However, these guidelines may not be applicable to all our patients as coronary artery disease is not the prevalent heart problem in developing countries.

The aim of our study is to determine an overall prevalence of CAD in patients undergoing rheumatic valve surgery between ages 40-50 years and to what extent pre-operative coronary artery angiography as an invasive diagnostic form is needed.

Patients and Method

454 consecutive preoperative patients aged from 40- 50 years, who had rheumatic valvular heart disease at National Heart Institute and Nasser Institute from January 2013 to January 2015, were prospectively studied to see the incidence of significant coronary artery disease-among them by performing preoperative elective coronary angiography as per SCC/ AHA guidelines (Bonow et al., 2008).

Patients who need emergent valve replacement surgeries were not delayed for assessment of coronary anatomy. Also, they were excluded from the study as per hospital protocol; similarly, patients with a history of prior revascularization were also excluded.

All coronary angiographies are performed by injecting right and left coronaries by using 80 -100 ml of iodinated contrast to obtain the standard views of both right and left coronaries (AP (0) caudal (30), AP (0) cranial (30), LAO (50) cranial (30), LAO (50) caudal (30), RAO (20) caudal (20), RAO shallow cranial, left lateral view for left coronary system, and LAO 30, RAO 30, PA cranial for right coronary artery) using Philips (DICOM viewer

software) or Siemens (Artis one, Sango Angio package software) machines in both hospitals. Coronary artery disease (CAD) of 50% is considered to be a positive finding. All coronary angiograms were performed and reported by well trained and experienced cardiologists. Concomitant coronary artery bypass surgery was added to the valvular surgery on the basis of coronary anatomy.

In this study, diabetes mellitus is defined as fasting glucose >126 mg/dl, hyperlipidemia as cholesterol > 200 mg/dl or on treatment, hypertension as blood pressure >140/90 mmHg. On the other hand, due to treatment, family history of coronary artery disease such as any first degree that is relative had received anti-ischaemic drug, history of chest pain, previous catheterization or stenting for coronaries, or ICU admission for myocardial infarction and obesity as BMI> 30. An echocardiogram was performed routinely to diagnose the affected valve and justify the need for surgery.

Results

A total of 454 patients were enrolled prospectively in this study. The demographic criteria of them are shown in Table 1. The mean age was 45.152 years. 254 (55.9%) were females while 200 (44.1%) were males. 109 (24%) patients had aortic valve surgery for aortic stenosis, while 35 (7.7%) patients had aortic valve surgery for aortic regurgitation. 297 (65.4%) patients with mitral stenosis had mitral valve surgery, while 100 (22%) patients with mitral regurgitation had mitral valve surgery. It was noted that 87 (19.2%) of these patients had double valve disease, 23 (5.1%) of these patients had diabetes mellitus, 24 (5.3%) were hypertensive, 19 (4.2%) were smokers, 36 (7.9%) were obese, 4 (0.9%) had hyperlipidemia, and 9 (2%) had a positive family history of coronary artery disease (CAD) (see Figure 2).

Table 1. Demographic criteria of the study group

Table 1			
	n	%	*P*
40-45 years	1	12.5	0.023
46-50 years	7	87.5	
Female	0	0	0.001
Male	8	100	
Diabetes Mellitus	1	12.5	0.333
Hypertension	2	25	0.012
Smoking	2	25	0.003
Obesity	1	12.5	0.629
Hyperlipidemia	0	0	0.788
Family History of CAD	2	25	0

n: number; %: percentage; *p*: predictive value

The results showed that from the 454 patients, 8 (1.76%) had >50% coronary stenosis (see Figure 1). 1 (12.5% of all CAD) (0.2% of whole sample) patient were aged 40 – 45 years, while 7 (87.5% of all CAD) (1.5% of whole sample) patients were aged 46 – 50 years (*p = 0.023*). 8 (100% of all CAD) (1.76% of whole sample) were males, while none (0%) were females (*p = 0.001*). 1 (12.5% of all CAD) (0.23% of whole sample) had diabetes mellitus (*p = 0.333*). 2 (25% of all CAD) (0.46% of whole sample) were hypertensive (p = 0.012). 2 (25% of all CAD) (0.46% of whole sample) were smokers (*p = 0.003*). 1 (12.5% of all CAD) (0.23% of whole sample) was obese (*p = 0.629*). None (0%) of the patient had hyperlipidemia (*p = 0.788*). 2 (25% of all CAD) (0.46% of whole sample) had a positive family history of CAD (*p = 0.12*) (*see Table 1*). Distribution of coronary artery disease among different rheumatic lesions is shown in Table 2. 5 (62.5% of all CAD) (1.1% of whole sample) patients had mitral stenosis (*p = 0.861*), while 1 (12.5% of all CAD) (0.23% of whole sample) patient had mitral regurgitation (*p = 0.521*). 4 (50% of all CAD) (0.88% of whole sample) patients had aortic stenosis (*p = 0.082*), while none (0%) had aortic regurgitation (*p = 0.410*). 6 (75% of all CAD) (1.3% of whole sample) patients had single valve disease, while 2 (25% of all CAD) (0.46% of whole sample) patients had double valve disease (*p = 0.965*) (*see Table 2*).

Table 2. Distribution of coronary artery disease among different rheumatic lesions

Table 2

	n	%	*P*
SVD	6	75	0.965
DVD	2	25	
MS	5	62.5	0.861
MR	1	12.5	0.521
AS	4	50	0.082
AR	0	0	0.410

n: number; %: percentage; p: predictive value; SVD: single valve disease; DVD: double valve disease; MS: mitral stenosis; MR: mitral regurgitation; AS: aortic stenosis; AR: aortic regurgitation

However, the outcome of the previous results showed no correlation between rheumatic heart disease in this age group and significant coronary artery stenosis. Thus, only 1.76 % had coronary stenosis. Male gender, family history of CAD, age above 45 years, hypertension, and smoking showed significant correlation with the coronary artery stenosis in this study as shown in Figure 2.

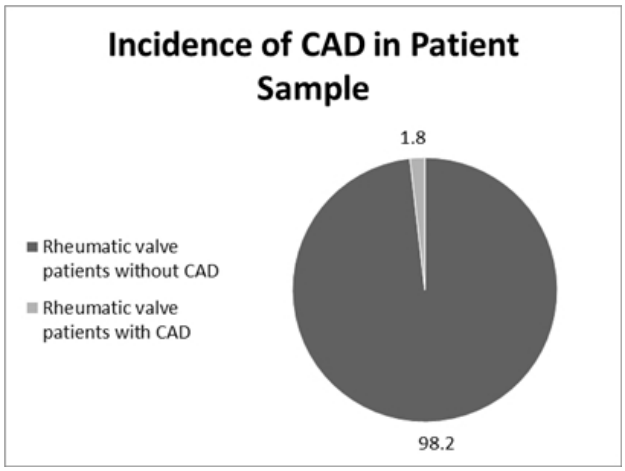

Figure 1. Incidence of CAD in patients' sample

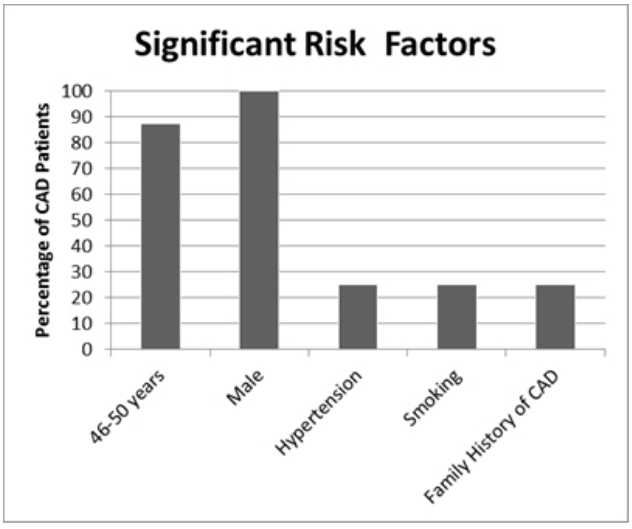

Figure 2. Incidence of significant risk factors in rheumatic patients with CAD

Statistical Methods

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as the mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage. The following tests were done: Paired sample t-test of significance was used when comparing between the related sample; Chi-square (X^2) test of significance was used in order to compare proportions between two qualitative parameters; the confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as follows: Probability value (P-value) $\leq$0.05 was considered significant, P-value $\leq$0.001 was considered to be highly significant, and P-value >0.05 was considered insignificant.

Comment

Guidelines for preoperative CA in patients with VHD undergoing valvular surgery are primarily based on studies where the majority of the patients had degenerative VHD (Bonow et al., 2008). There is no distinction between rheumatic valvular heart disease and degenerative valvular heart disease in this matter. Moreover, the incidence of CAD in patients undergoing valve surgery had been shown to vary widely from 9% to 41 % (Sonmez et al., 2002). In addition, we should strongly consider the fact that the majority of these patients are elderly, and they have degenerative valve disease and multiple coronary risk factors. However, in Egypt and other developing countries where the major aetiology of VHD is rheumatic, the prevalence of coexistent CAD is much lower as compared to western patients (Jose et al., 2004; Kruczan et al., 2008).

In this series, the overall prevalence of CAD in all rheumatic groups was 1.76%, which is much lower than that of the western population (16% to 50%) according to some authors (Bonow et al., 2006; Silaruks et al., 2001; Li et al., 2007; Shaikh et al., 2011). It is also much lower from studies done in so many developing countries. Only one study from Spain done by Rangel *et al*. showed the prevalence of 8%. In South East Asian countries like China, the prevalence was found to be 11% (Bozbaş et al., 2004), but in Pakistan, it was on higher side 31.3% (Rangel et al., 1996). In some Indian studies, the prevalence was found between 7% and 12% (Paradis et al., 2013; Atalar et al., 2012; Lim et al., 2003). Saharia and Devi (2016) analyzed CA of 100 patients with rheumatic valvular disease and reported the prevalence of significant CAD to be 14%. Shaikh et al. (2011) reviewed medical records of 144 patients and found CAD in 25% patients of RHD. Two studies from India by Jose et al. (2004) and Narang et al. (2009) have reported the prevalence of CAD to be 12.2% and 11% respectively in patients with RHD undergoing valve surgery. Kruczan et al. (2006) in their study of 294 patients with rheumatic and non-rheumatic VHD reported that patients with rheumatic VHD had a lower prevalence of CAD (4%) when compared to those with non-rheumatic VHD (33.61%).

In their study, Saharia and Devi (2016) stated that coronary angiography was performed in patients over the age of 50 years, those having angina or ECG signs of ischemia, which can explain the higher prevalence. However, in the study of Shaikh et al. (2011), the relatively high incidence of CAD (25% patients of RHD) can be attributed to a very high incidence of DM, hypertension, and dyslipidemia in their study population and the elderly as well. Consequently, the range of age for patients with regards to CAD risk factors was not specified in the study of Narang et al. (2009) as well as the symptoms.

Kruczan et al. (2006), in their study of 294 patients with rheumatic and non-rheumatic VHD, reported that patients with rheumatic VHD had a lower prevalence of CAD (4%) when compared to those with non-rheumatic VHD (33.61%). The prevalence of CAD (4%) in this study is still higher than our study (1.76%). In addition, this higher incidence can be attributed to a higher frequency of male sex and older age.

The hypothesis of rheumatic fever that can cause arteritis in intramyocardial coronaries is yet to be proven. Even more, the actual prevalence of CAD in RHD patients is not more than that of the general population (Manjunath et al., 2014). However, there are so many factors that can play a significant role in the variation of the incidence of CAD in rheumatic populations and between different countries. For example, the higher age group in the Western countries and different sample sizes. It also entails the demographic, clinical, and environmental characteristics of the different populations such as race, dietary habits, and physical activity.

In regards to the male to female ratio, it is given as 1.27:1 in our study, and it is matched with 1.86:1 of Choudary study in 2016 (Choudhary et al., 2016). Also, some other studies showed ratio between 1.6:1 and 2.6:1 (Sonmez et al., 2002; Li et al., 2007; Rangel et al., 1996). Furthermore, only one study from China done by Li *et al*. showed a ratio of 3:1 (Li et al., 2007). The mean age of RHD patients who had CAD was 52.8 ± 8.6 years (52.3 ± 8.9 for males and 53.6 ± 8 for females) in Choudary study (Choudary et al., 2016). In Nikhil study (Nikhil et al., 2016), it was 55.2±8.65 years. The mean age of CAD in RHD patients was around 55–60 years in Western and Chinese studies (Li et al., 2007; Bozbaş et al., 2004; Paradis et al., 2013) when compared to other Indian studies (Jose et al., 2004; Narang et al., 2009; Gupta et al., 1990) and a study from Pakistan (Shaikh et al., 2011). In our study, we investigated one age group of 40-50 years and, probably, this is one of the reasons why we had a low overall incidence of CAD in our cohort.

The SVD and DVD were found in 6 patients (75% of all CAD) (1.3% of the whole sample). 2 patients (25% of all CAD) (0.46% of whole sample) had double valve disease respectively ($p = 0.965$) opposite to 55.1% of CAD and 29% of CAD in Nikhil study respectively (Nikhil et al., 2016). Moreover, Left anterior descending was the most common vessel involved (overall 63.7% and 30.4% in isolated cases) followed by LCX (51%) and RCA (35.7%) in Nikhil's study. Rangel et al. (1996) and Li et al. (2007) also found that LAD was the most commonly involved artery followed by RCA and LCX. Also, we did not report frequency and distribution of the involved coronaries or their occurrence with individual rheumatic valve disease because we believe that their occurrence with them is causal and has no specific relation.

Furthermore, there are modifiable and non-modifiable risk factors for CAD. The most important of which is Hypertension, smoking, DM, family

history of CAD, post-menopausal females, and old age. Most authors who investigated this matter looked at these factors thoroughly. A prospective study using multimarker strategy showed a higher predictivity of CAD risk factors in rheumatic valve patients (Narang R, 2009). Another study reported a higher incidence of HTN, smoking, DM, and dyslipidemia in RHD patients having CAD than those without CAD (Gupta et al., 1990). Same risk factors were found to be strong predictors of CAD in some studies (Lin et al., 2001; Silaruks et al., 2001). Lin et al. (2003) and Lim et al. (2001) found that the incidence of CAD in the two models was 19.3% and 36% respectively. This, however, means a low incidence of CAD in rheumatic patients. Therefore, the strength of prediction and the respective relationship between predictors derived in previous analyses might be lost. Unfortunately, we did not report patients symptomatology as such, but most authors reported a strong association between angina as a predictor and CAD in rheumatics (Kruczan et al., 2008; Paradis et al., 2013; Silaruks et al., 2001).

In line with other studies (Jose et al., 2004; Kruczan et al., 2008; Guray et al., 2004), our study reports a low incidence of CAD (1.75%) in the rheumatic patients. Nikhil et al. (2016) stated that antibiotic prophylaxis, with its proposed anti-inflammatory effect against coronary atherosclerosis, is a remote explanation for the low incidence of CAD because his patients rarely had this prophylaxis. Kruczan et al. (2008), on the other hand, concluded that the low prevalence could be due to the demographic and clinical characteristics. Again, we believe that the main reason why our incidence of CAD is low is that the age group that we elected to investigate is only 40-50 years and the incidence of CAD in older rheumatics may be higher. Moreover, we accept the theory of different demographic, clinical, and environmental characteristics as well as dietary, smoking habits, and race as a reason for the variable incidence of CAD in rheumatic population.

In our series, Mitral valve was involved in 75% of RHD patients with CAD, aortic valve in 50% of them, and DVD was involved in only 25% of them. This perfectly matches with what had been found by some authors (Nikhil et al., 2016) (66.1% mitral, 7.3% aortic and both valves in 26.6%). In agreement with our findings, Shaikh et al. (2011), just like us, also reported a higher incidence of mitral valve involvement than the aortic and double valve involvement in RHD patients with CAD. This can be attributed to the high prevalence of mitral valve disease in RHD patients.

In our cohort, the incidence of CAD in regurgitation lesions was very low (one patient only 12.5% who had MR) in comparison with stenotic lesions (100% of the sample almost half by half MS and AS). This is in concordant with the study of Nikhil et al. (2016) that showed a significant inverse association between MR and prevalence of CAD ($P = 0.005$) based on univariate analysis. On the other hand, Narang *et al.* (2009) showed a

significant inverse association between AR and CAD, and there was no significant association between MR and CAD. Other authors found the same association of stenotic lesions and CAD (Sonmez et al., 2002; Narang et al., 2009). Therefore, we can conclude that the stenotic lesions of both mitral and aortic rheumatic valves are more likely to be associated with CAD than the regurgitation lesions. The reason for this can be a more prolonged and ongoing inflammatory process responsible for stenotic lesion, leading to microvascular changes and endothelial dysfunction (Nikhil et al., 2016). Though it is not a solid conclusion, we need more studies to prove or disprove it.

Finally, it is interesting to state that only rheumatic males had significant CAD in our cohort as compared to females. Also, CAD was found only in patients with major coronary risk factors namely: age >45 years, hypertension, family history, and smoking. Thus, it can be inferred that in this subset of patients, preoperative coronary angiography can be considered only in the presence of multiple coronary risk factors or symptoms suggestive of CAD, or if there is a high clinical likelihood of CAD.

Conclusion

In this age group, the rheumatic valvular disease shows no correlation with coronary artery disease. All of the coronary artery disease patients were males, with CAD risk factors of family history, hypertension, and smoking. Thus, any female below the age of 45 with no risk factor should not undergo a routine preoperative coronary angiography. Moreover, our results suggest that the overall prevalence of coronary artery disease in patients undergoing rheumatic valve surgery in our population is not comparable with the prevalence reported in international data. As a result, multicenter studies are needed in developing countries to set their own guidelines, and our study can be the nucleus for these guidelines in our country.

List of abbreviations

CAD: Coronary Artery disease; RHD: Rheumatic Heart Disease; LAD: Left Anterior Descending; LCx: Left Circumflex; RCA: Right Coronary Artery; CA: coronary angiography; AP: antero-posterior; LAO: left anterior oblique; RAO: right anterior oblique; DM: diabetes mellitus; ICU: intensive care unit; CABG: coronary artery bypass grafting; BMI; body mass index; SVD: single valve disease; DVD: double valve disease; VHD: valvular heart disease; MS: mitral stenosis; MR: mitral regurgitation; AS: aortic stenosis; AR: aortic regurgitation.

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