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Study to Evaluate Coronary Artery Disease Prevalence and Risk Factors in Heart Failure Patients with Reduced Ejection Fraction

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ABSTRACT

Introduction: Even though heart failure (HF) is a major global health problem, studies on the prevalence and etiology of HF in Nepal are scant. This study aimed to assess the prevalence and risk factors of coronary artery disease (CAD) in HF with reduced ejection fraction (HFrEF) using invasive coronary angiography (CAG).

Methods: This was a prospective, cross-sectional, descriptive observational study conducted from July 2020 to September 2021. All consecutive patients with HFrEF who met the inclusion criteria underwent CAG at Manipal Teaching Hospital were evaluated and analyzed using various statistical tools.

Results: A total of 108 patients with a male to female ratio of 2.02:1 were assessed. The mean age of patients was 63±6.08 years. The prevalence of CAD was 72% of which 42% were having significant CAD (stenosis >50%) with 45% (20), 32% (14), and 23% (11) having triple (TVD), double (DVD), and single-vessel disease (SVD) respectively. Smoking was the commonest risk factor (61%) followed by hypertension (52%), dyslipidemia (27%), and diabetes (22%). The prevalence of CAD increased with an increase in the number of risk factors. There was a significant association of smoking (OR: 11.5, P: 0.005), hypertension (OR: 8.5, P: 0.002), and diabetes (OR: 10, P: 0.001) for the occurrence of significant CAD.

Conclusion: In our study, otherwise unexplained HFrEF showed overall 72% of CAD with 42% having significant CAD (stenosis >50%). Conventional risk factors like smoking, hypertension, and diabetes were significantly associated with the development of CAD.

Keywords: *Coronary Artery Disease; Heart Failure; Risk Factors*

INTRODUCTION

Heart failure is considered a major health problem worldwide.[1] It is classified into heart failure with preserved ejection fraction

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(HFpEF) and heart failure with reduced ejection fraction (HFrEF). HFpEF is considered when the left ventricular ejection fraction is (LVEF) ≥50%. If LVEF is ≤40% then it is considered as HFrEF. There is a third category considering the LVEF 40-50% as heart failure with mid-range ejection fraction (HFmEF).[1,2]

More than half or two-thirds of symptomatic heart failure patients fall under HFrEF. Coronary artery disease (CAD) is considered as a major cause of HFrEF and coronary angiography (CAG) is considered as class 1 recommendation as investigation.[1,2] Other causes like hypertension, myocarditis, toxin-induced cardiomyopathies, valvular heart diseases, tachyarrhythmias, peripartum, etc also should be evaluated. A recent study done in central Nepal for otherwise unexplained HFrEF showed 33% significant CAD.[3] Studies done outside show CAD accounting for about two-thirds of cases of heart failure with reduced ejection fraction (HFrEF).[4] Demonstration of underlying etiology is the cornerstone of HF diagnosis and virtually all patients with unexplained HF should be evaluated for the presence of CAD. Most patients with HF due to ischemic cardiomyopathy have known coronary heart disease. [5]

Data regarding the prevalence of heart disease in Nepal are sparse. Shrestha et al. had described the profile of HF in the western regions and reported CAD as etiology in 29% while a study from Bharatpur reported 36.5% CAD as the etiology of HF.[6,7] In both studies, the commonest cause of HF was CAD. The main aim of this study was to evaluate the prevalence of CAD using the angiographic approach in patients with HFrEF in this part of the world.

METHODS

A prospective, cross-sectional, descriptive an observational study was conducted in Manipal Teaching Hospital, Pokhara Nepal from June 2020 to September 2021. All consecutive patients aged more than 18 years with HFrEF (Patients with LVEF ≤ 40% by trans-thoracic echocardiography) were included in the study. Patients with eGFR <60ml/min/ 1.73m^2 or with serum creatinine ≥1.5mg/dl**,** history of contrast allergy**,** very frail patients (age≥85yrs) with severe symptoms (NYHA III/IV), and patients not giving consent were excluded.

Echocardiography was done to evaluate the left ventricular ejection fraction (LVEF) by an expert cardiologist and confirmed by another cardiologist available in the department. Following this, the patient underwent CAG for evaluation of possible CAD. CAG of the right and left coronary arteries were performed and the best projection, representing stenosis of the lesion with progression, were selected and examined for percentage diameter stenosis by quantitative CAG analysis using cardiovascular measurement system (Seimen's Artis zee floor). The CAG was further reviewed by one independent observer experienced in angiographic interpretation. The degree of coronary artery obstruction was expressed as the percent diameter stenosis, by comparing the diameter of the site of narrowest to an adjacent segment assumed to be free of disease. The lesion in an epicardial coronary artery was considered significant in ≥ 50% stenosis of the examined vessel. Lesion severity shall also classified as: Minimal / minor CAD: <50% stenosis; Moderate: 50-70% stenosis; Obstructive: ≥ 70% stenosis whereas >50% are considered as significant.[5]

Conventional risk factors assessment was done by taking smoking history, lipid profile, fasting blood sugar, HbA1C levels, etc. Dyslipidemia was defined as the presence of any of the following: patients on lipid-lowering drugs or total cholesterol >200 mg/dl, triglycerides (TG) >150 mg/dl, low-density lipoprotein >100 mg/dl, and high-density lipoproteins (HDL) <40mg/dl in male.[8] Diabetes mellitus was defined as a fasting blood sugar level of 126 mg/ dl (7.0 mmol/L) or HbA1C level > 6.5% or if the

patient was on oral hypoglycemic agents.[9] Hypertension was defined as systolic blood pressure >140 and/or diastolic >90 mmHg and/or on anti-hypertensive treatment.[10] The data was collected in a preformed proforma and was analyzed using SPSS software version 21. Percentage, mean value, and odds ratios were calculated wherever required and p-values were considered significant at a predetermined alpha level of 5%.

RESULT

The total number of cases undergone coronary angiography in the study period was 497 out of which 108 were having ejection fraction of 40% or less. Out of 108 patients, 73 were male while 35 patients were female with a male to female ratio of 2.02:1. The age range of the patients was from 27years to 89years with a mean age of 63±6.08 years (Table 1).

Table 1: Age group analysis

Age group	Number of patients undergone CAG	Mean ± Standard deviation
<45 years	12	63 ± 6.08 years
45-65 years	70	
>65yrs	26	

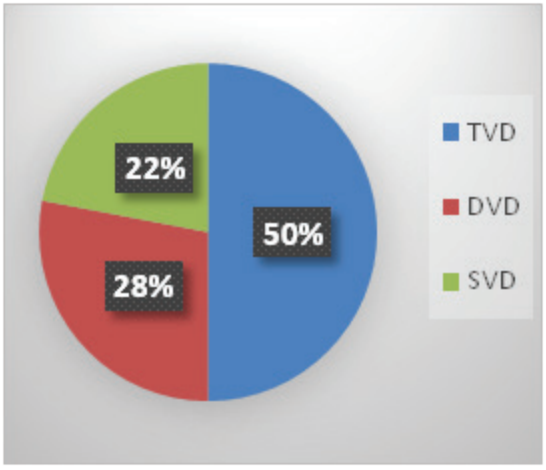
Obstructive CAD/ significant was present in 27% of patients while non-obstructive (mild and moderate) CAD was present in 45% of cases. Twenty-eight percent of patients with heart failure and reduced ejection fraction had normal coronaries (Table 2).

On further analysis, of patients with significant CAD (CAD> 50%) it was found that almost 20 (45%) had triple vessel disease (TVD), 14 (32%) had double vessel disease and 11 (23%) had single vessel disease as shown in Figure 1. Individual assessment of coronary vessels showed involvement of the Left anterior descending (LAD) in 25 (55.5%), the Right coronary artery (RCA) in 12 (26.6%), and the Left circumflex artery (LCX) in 8 (17.8%) cases. (Figure 2)

Table 2: Percentage of patients with CAD

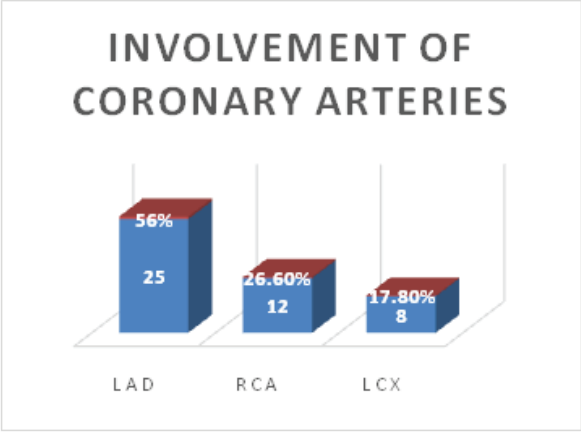
Total patients who underwent CAG for HFrEF (EF of 40% or less): 108	
Obstructive CAD (Stenosis >70%)	29 (27%)
Moderate CAD (stenosis >50% but <70%)	16 (15%)
Minor CAD (stenosis <50%)	33 (30%)
Normal coronaries	30 (28%)

CAG: Coronary angiography; CAD: Coronary artery disease



TVD: Triple vessel disease; DVD: Double vessel disease; SVD: Single vessel disease

Figure 1: Coronary angiography findings



LAD: Left anterior descending; RCA:Right coronary artery ; LCX: Left circumflex artery

Figure 2: Involvement of coronary arteries

The most common risk factor in patients with HFrEF was smoking (61%) followed by hypertension (52%), dyslipidemia (27%), and

diabetes (22%).The prevalence of coronary artery disease increased with an increase in risk factors (22% in patients with risk factors two or less and 73% in patients with risk factors of tree or more) as shown in the following Figure 3.

Table 3: A risk factor analysis in case of HFrEF (Total number: 108)

Risk Factors	Number of patients	% of patients
Smoking	66	61
Hypertension	56	52.5
Dyslipidemia	29	27
Diabetes Mellitus	24	22.2

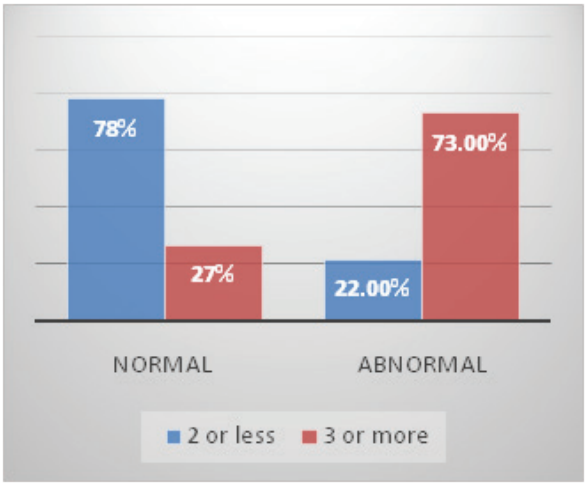


Figure 3: Risk factors and prevalence of CAD

DISCUSSION

Heart failure is the ultimate disease to be established in all the diseases affecting the heart. It is a common final pathway for all the risk factors or any structural or electrical abnormalities within the heart. According to LVEF, HF is broadly classified as HFrEF when the LVEF ≤40%, Heart failure with preserved ejection fraction (HFpEF) when the LVEF ≥50%, and heart failure with mid-range ejection fraction (HFmEF) when the LVEF lies between 40 and 50%. There is evidence recommending the evaluation of CAD by CAG in patients with HFrEF as a substantial percentage of patients do have established CADs. As previously demonstrated the use of angiography during the index hospitalization after admission for HF would allow CAD identification in a higher proportion of patients than after discharge.[11]

We performed a study analyzing the prevalence of CAD in patients with HFrEF undergoing CAG at our institute. Despite excluding patients with a history or evidence of previous coronary events, the prevalence of CAD was 72% (total) of which 42% were having significant CAD (stenosis >50%). This is almost similar to the overall CAD prevalence where about two-thirds of cases of HFrEF have CAD.[12] Upon comparison with studies of CAD prevalence including cohorts with unexplained heart failure, our prevalence figures are similar16. The guideline as above used coronary stenosis of ≥ 50% to define significant CAD, hence showing higher prevalence than in another study where significant CAD was considered when stenosis was more than 70%.[13] If taken that also our prevalence of CAD having stenosis >70% was 27% that closely matches with the descriptive studies from Nepal suggesting almost one-third of HFrEF are likely due to obstructive CAD (ischemic).[3,6,7] We further analyzed the forty-five cases with significant CAD (i.e stenosis >50%) for the involvement of coronary arteries where 20 (45%) were having triple vessel disease (TVD), 14 (32%) were having double vessel disease and 11 (23%) were having single vessel disease as shown in Figure 1. Individual assessment of coronary vessels showed involvement of LAD in 25 (55.5%), RCA in 12 (26.6%), and LCX in 8 (17.8%) cases (as in Figure 2). Similar findings were seen in patients in the studies one within and outside the country.[7,14,15] One study from central Nepal had shown significant CAD in only 33% of patients.[3] This is because the investigator had taken stenosis >70% as significant. In our study, only 27% of patients had obstructive CAD (stenosis >70%) which

is slightly lower than the study done above.

Also, we analyzed the conventional risk factors for potential causes for significant CAD and found smoking as the most common risk factor in patients with HFrEF (61%) followed by hypertension (52%), dyslipidemia (27%), and diabetes (22%). The prevalence of coronary artery disease increased with an increase in risk factors (22% in patients with risk factors 2 or less

Table 4: Impact of risk factors on the possibility of Heart Failure With a reduced ejection fraction and significant CAD

Risk Factors No		Significant CAD (stenosis >50%): N=45		Odds ratio	95% Confidence interval	p- value
		Yes				
Smoking	Yes	09	26	11.55	2.05-64.85	0.005
	No	08	02			
Hypertension	Yes	08	17	8.5	2.13- 33.81	0.002
	No	16	04			
Dyslipidemia	Yes	04	08	2.4	0.60-9.55	0.214
	No	18	15			
Diabetes Mellitus	Yes	04	20	10.0	2.45-40.77	0.001
	No	14	07			

and 73% in patients with risk factors of 3 or more) as shown in Figure 3. These findings are similar to a few other studies even in patients with young acute coronary syndromes where smoking was found to be the major risk factor along with hypertension, diabetes, and dyslipidemia.[16-19] There was a significant association between smoking (OR: 11.5, p:0.005), hypertension (OR:8.5, p: 0.002), and diabetes (OR: 10, p: 0.001). Similar results are seen in other studies too and there are studies where smoking and diabetes are commonly associated with multivessel diseases.[3,12,17] Use of statins primarily also has been proven beneficial in these patients.[20] In clinical practice, systematic CAG is not always possible in all patients admitted for HF, but the potential survival benefit of revascularization justifies the aggressive management of heart failure even in elderly patients with significant VHD like aortic stenosis.[14, 21-23]

Further studies are needed to evaluate systematic angiography in HFmEF/HFpEF, and whether this approach is cost-effective and revascularization improves morbidity or mortality.

The sample size was relatively small and patients were enrolled from a single center in this study which may be subjected to referral bias. However, the current prospective design with coronary angiography is merit. We enrolled only the patients with HFrEF and excluded patients with HFmEF / HFpEF where we could compare the findings. Larger studies are required to enroll all groups of patients with heart failure and a comparative study may be done accordingly.

CONCLUSION

We determined the prevalence and characteristics of CAD in patients with HFrEF in a prospective study using a systematic coronary angiography approach in our part of the world. In our study, otherwise unexplained HFrEF showed overall 72% of CAD with 42% having significant CAD (stenosis >50%) and 27% having obstructive CAD (stenosis >70%). Conventional risk factors like smoking, hypertension, and diabetes were significantly associated with the development of CAD and the cause for HFrEF. We recommend all patients undergo an evaluation for possible CAD in all cases of HFrEF as the cause.

CONFLICT OF INTEREST
None

SOURCES OF FUNDING
None

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