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Original Article

Prevalence and trends of occult coronary artery disease in patients with dilated cardiomyopathy

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Abstract: Background: Many patients with dilated cardiomyopathy (DCMP), presenting with only dyspnea, have hidden ischemic etiology. In low-income countries, logistic and financial restraints lead to reduced identification of this ischemic burden. We aimed to assess the role of coronary angiography in patients with cardiomyopathy presenting predominantly dyspnea. Methods: This was a single-center, prospective, observational study conducted at a tertiary-care center in North India over the period of one year. The study population consisted of patients with dyspnea (NYHA II and III) and left ventricular dysfunction [i.e., left ventricular ejection fraction (< 40%)] without a prior documented coronary artery disease (CAD). All patients underwent invasive coronary angiography to detect underlying occult CAD. Results: A total of 209 patients with global left ventricular hypokinesia (LVEF) were enrolled. Almost half of the study population belonged to the 51-60-year-old group. Diabetes mellitus and smoking were most prevalent risk factors observed in 93 (44.5%) and 92 (44.1%) patients, respectively. Abnormal coronaries were detected in 75 (35.9%) patients; 44 (58.7%) and 29 (38.7%) patients had significant and insignificant CAD, respectively. Single-, double-, and triple-vessel disease was observed in 18 (40.9%), 14 (31.8%), and 12 (27.3%) patients, respectively. The mean age (54.08 ± 6.02 years), LVEF (39.83 ± 3.27%), SYNTAX score (17.14 ± 2.21), and left ventricular internal dimensions (4.93 ± 0.44 cm) were all statistically insignificant. Conclusion: Patients with DCMP presenting predominantly with dyspnea and having silent underlying significant CAD may benefit from revascularization if CAD is detected by angiography on time.

Keywords: Coronary angiography, dilated cardiomyopathy, ischaemic cardiomyopathy

Introduction

Dilated cardiomyopathy (DCMP) is the most common cause of heart failure, and it may have fatal consequences only a few years after symptomatic onset. When diagnosing dilated cardiomyopathy, it is important to first rule out secondary causes of heart failure such as coronary artery disease (CAD) and valvular heart disease [1]. Ischemic cardiomyopathy (ICMP) is usually defined as left ventricular dysfunction, i.e., left ventricular ejection fraction (LVEF) of less than 40% owing to CAD. This type of cardiomyopathy can be identified using readily available diagnostic modalities such as electrocardiography and coronary angiography. However, the need for patients with dilated cardiomyopathy to undergo coronary angiography considerably decreases the number of eligible patients owing to the disease risk factor bias [2]. Furthermore, ischemic cardiomyopathy patients frequently do not complain of angina but display dyspnea as the only primary presenting feature. Such patients are usually managed without any revascularization procedures [3, 4]. It is highly likely that LVEF can improve if timely angiography followed by revascularization is performed in such patients [5]. Surgical Treatment for Ischemic Heart Failure (STICH) trial evidenced improved cardiovascular outcomes in patients under revascularization who had a viable myocardium and CAD [6].

Many studies have observed beneficial cardiovascular outcomes when hibernating myocardium is partially responsible for a decrease in LVEF [4, 7, 8]. This is one of the largest studies conducted to evaluate the role of coronary angi-

ography in such patients. In this study, we aimed to perform coronary angiography to define coronary anatomy in patients presenting with dyspnea with left ventricular dysfunction. This study will help to identify patients with significant CAD and DCMP despite an absent history of angina or chest pain.

Materials and methods

Study design and patient population

This was a prospective, observational study, which enrolled 209 consecutive patients during a one-year study duration. The study group consisted of patients with left ventricular dysfunction without prior documented CAD. The inclusion criteria were patients with: (i) dyspnea functional New York Heart Association (NYHA) class II or III; (ii) left ventricular dysfunction with global hypokinesia of left ventricle; or (iii) LVEF ≤ 40%, as assessed by Simpson's method. The exclusion criteria were patients with: (i) history of angina; (ii) dyspnea at rest (NYHA class IV); (iii) history of CAD; (iv) electrocardiographic (ECG) evidence of old myocardial infarction or ischemia; (v) regional wall motion abnormality (RWMA) identified by 2D-echocardiography; (vi) glomerular filtration rate (GFR) (< 30 ml/min); or (vii) refusal to provide consent to undergo study procedure. The study procedure was approved by the Institutional Ethics Committee prior to study commencement. All enrolled patients provided informed consent for the procedure and subsequent data collection and analysis for the research purposes.

Data collection and study procedure

All patients underwent routine laboratory investigations, which included a hemogram and blood sugar evaluation (fasting and post-prandial). GFR was calculated before and after coronary angiography. All patients underwent a 12-lead electrocardiogram (ECG) test. 2D echocardiography was performed using a GE (VIVID-7) machine. All measures to minimize contrast-induced nephropathy (CIN) were taken. Transradial access was preferred over femoral access. The femoral route was used as an alternative whenever radial access could not be taken owing to severe radial spasm, negative Allen's test, or local loops of radial artery. A 5 Fr Tiger diagnostic catheter (Terumo Medical Corporation, Japan) was used for coronary angiography. The significance of stenosis was assessed by eye balling; the quantitative assessment of coronary angiogram was performed along with SYNTAX score calculation. In 5 patients, viability testing was performed by dobutamine stress echocardiography (DSE) before coronary artery revascularization. The patients underwent coronary artery bypass grafting (CABG) or PCI as per decision after viability assessment.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 16. Categorical variables were expressed as percentages; continuous variables were expressed as the mean ± standard deviation, median, range, and ratio. Univariate analysis was performed. For univariate analysis, categorical variables (e.g., gender, hypertension, diabetes, smoking, alcohol, and hypothyroidism) were compared using the chi-square test or Fisher exact test, as applicable; continuous variables (e.g., age and LVEF) were compared using Student's t-test. ANOVA was used to compare the mean of normal, single-, double-, and triple-vessel disease corresponding to age, LVEF, SYNTAX score, and left ventricular diameter. All *p*-values of < 0.05 were considered to be statistically significant.

Results

Demographics of the overall study population

A total of 209 consecutive patients who fulfilled the inclusion and exclusion criteria were enrolled in this prospective study and underwent coronary angiography during the study period. The overall mean age in this study was 54.08 ± 6.02 years. Males constituted 175 (83.73%) patients of the study population. Almost half of the study population belonged to the 51-60-year-old group. Risk factors such as diabetes mellitus, smoking, and obesity were prevalent in 93 (44.5%), 92 (44.0%), and 32 (15.3%) patients, respectively. The demographic characteristics of the study population are shown in **Table 1**.

Prevalence and severity of coronary artery disease among the study population

Lesion severity was estimated by eyeballing; quantitative coronary angiography (QCA) was performed when needed. On coronary angiog-

Table 1. Demographic characteristics of overall study population

Variables	Total n = 209
Mean age, years (mean ± SD)	54.08 ± 6.02
< 40 years, n (%)	2 (1.0%)
41-50 years, n (%)	76 (36.4%)
51-60 years, n (%)	104 (49.8%)
> 60 years, n (%)	27 (12.9%)
Males, n (%)	175 (83.73%)
Diabetes mellitus, n (%)	93 (44.5%)
Smoker, n (%)	92 (44.0%)
Obesity, n (%)	32 (15.3%)
Hyperthyroidism, n (%)	6 (2.9%)
Radial, n (%)	179 (85.6%)
Femoral, n (%)	30 (14.4%)

raphy, normal coronaries were found in 134 (64.1%) patients, while 75 (35.9%) of enrolled patients had abnormal coronaries. Out of these 75 patients with abnormal coronaries, 44 (58.7%) patients had significant CAD, and 29 (38.7%) had insignificant CAD. Single-vessel disease (SVD) was the most commonly observed in 18 (40.9%) patients, followed by double-vessel disease (DVD) observed in 14 (31.8%) patients and triple-vessel disease (TVD) observed in 12 (27.3%) patients. Disease severity among patients with CAD is illustrated shown in **Figure 1**.

Prevalence of CAD

DVD was present in 14 (6.7%) patients. LAD non-significant stenosis (50-70%) lesion was present in 1 (0.5%) patient. LAD, left circumflex artery (LCx) and right coronary artery (RCA) plaquing was observed in 21 (10.0%), 4 (1.9%), and 5 (2.4%) patients, respectively. SVD was present in 13 (6.2%) patients; TVD was present in 12 (5.7%) patients. A total of 10 (4.8%) patients had deferred revascularization, as determined by DSE. CABG was performed in 2 (1.0%) patients. PCI was performed in both LAD and RCA (4 in LAD and 1 in RCA). The prevalence of CAD among the overall study population and according to gender and age is outlined shown in **Tables 2**-**4**, respectively.

Percutaneous coronary intervention based on viability testing

DSE was performed in 17 (8.13%) patients. Based on the stress test results of these 17 patients, 7 (41.17%) patients showed a significant viable myocardium and underwent PCI/CABG, as per coronary anatomy and SYNTAX score. Of these 7 patients, 2 patients were sent for CABG and 5 patients for PCI.

Association between gender and left ventricular variables

The mean LVEF, SYNTAX score, and left ventricular internal dimension (LVID) were statistically non-significant in males and females. The mean LVEF was 39.83 ± 3.27%; the mean SYNTAX score was 17.14 ± 2.21; mean LVID was 4.93 ± 0.44 cm. The association between gender and left ventricular variables is detailed shown in **Table 5**.

Association between CAD and left ventricular variables

Mean LVEF was 39.80 ± 3.32%, 42.06 ± 2.48%, 38.21 ± 3.26%, 38.50 ± 3.03%, and 39.95 ± 2.96% (P = 0.007) for normal coronaries, SVD, DVD, TVD, and other disease, respectively. The SYNTAX score was 16.84 ± 1.96, 17.06 ± 2.58, 18.85 ± 2.07, 18.50 ± 3.06, and 17.12 ± 2.29 (P = 0.003) for normal coronaries, SVD, DVD, TVD, and other disease, respectively. The association between CAD and left ventricular variables is indicated shown in **Table 6**.

Discussion

The mean age of our study population was 54.08 ± 6.02 years, which is similar to that of other Indian studies that revealed mean ages of 41.7 ± 16.5 years [9] and 54.4 ± 16.2 years [10]. This study assessed dilated cardiomyopathy patients presenting predominantly with dyspnea, which frequently was the most common clinical presentation [10, 11]. In this study, the 51-60-year-old group was the most common age group, which is comparable to another Indian study by Das et al. [9], which determined the 31-40-year-old group to be the most common age group. Cardiovascular risk factors were also assessed. Hypertension has been reported to be present in 32.4% of an American population [2] compared to 44.5% in this study. Diabetics, smokers, and obese patients comprised 11.1%, 7.4%, and 16.7% of Sub-Saharan population compared to 44.5%, 44.0%, and 15.3%, respectively, in this study [12]. Low mean age, earlier onset of heart disease, and

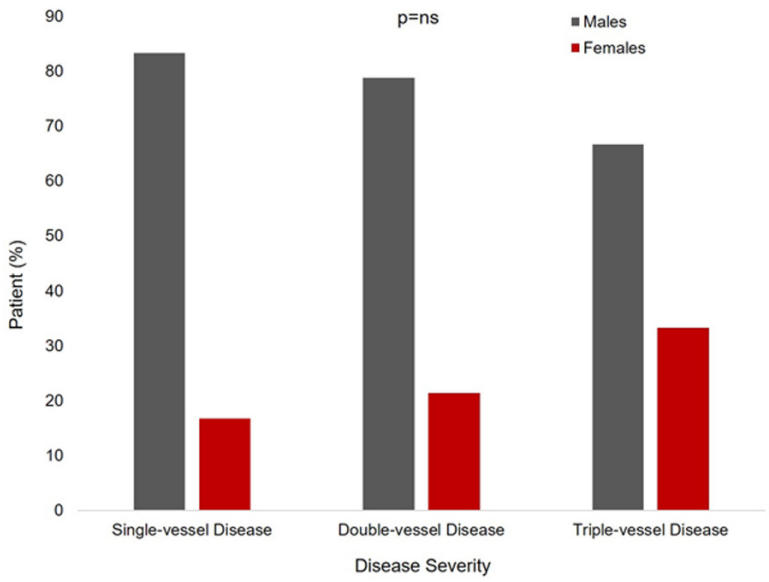

Figure 1. Disease severity among patients with significant coronary artery disease.

Table 2. Prevalence of coronary artery disease among overall study population

Disease	Patients n = 209
DVD, (n = 14)	14 (6.7%)
LAD (50-70% lesion) (n = 1)	1 (0.5%)
LAD plaquing, (n = 21)	21 (10.0%)
LCx plaquing, (n = 4)	4 (1.9%)
RCA plaquing, (n = 5)	5 (2.4%)
Significant SVD, (n = 13)	13 (6.2%)
SVD (PCI done), (n = 21)	5 (2.4%)
TVD (revascularization not possible) (n = 10)	10 (4.8%)
TVD (CABG done), (n = 2)	2 (1.0%)
Normal coronaries, (n = 134)	134 (64.1%)

All data are expressed as numbers (percentage). LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; SVD, single-vessel disease; DVD, double-vessel disease; TVD, triple-vessel disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

elevated rates of cardiovascular risk factors indicate the greater prevalence of premature CAD in an Indian population. Although the exact prevalence of DCM in the general population is unknown, it usually varies with age of an individual and geographical location [13, 14].

Approximately 30-50% of cases have a familial component, and to date, numerous genes have been identified that can lead to DCMP [15]. DCMP may also have secondary to multiple etiologies such as ischemic, valvular, and congenital heart disease as well as hypertension. The 5 year survival after diagnosis of DCMP is low, i.e., approximately half of these patients develop progressive CHF and fatal complications such as thromboembolism and arrhythmias. Many patients with ICMP may have history of CAD along with supportive evidence in ECG, RWMA, and biomarker elevation [16]. Felker et al. [17, 18] have determined that the prevalence of ICMP in 1,230 unexplained cases of global hypokinesia of left ventricle was approximately 7%. In this study, the prevalence was much higher (i.e., 35.89%) compared to the Western world. In low-income countries, owing to lack of medical insurance support, most patients have to pay out of pocket for their medical expenditures [19]. Thus, the phenomenon of underdiagnosis of the underlying ischemic heart disease is expected because coronary angiography may not be performed frequently owing to logistics and financial reasons.

Many patients diagnosed with diabetes mellitus or chronic kidney disease or of elderly age may have a defective anginal warning system [20-22]; thus, ICMP patients may present with only dyspnea. Limited activities in older population, owing to good family support, may be one of the reasons of not having angina. There are studies that assessed the burden of silent underlying significant CAD, e.g., a study by Repetto et al. [23]. In this study, coronary anatomy was assessed in hearts excised during cardiac transplantation from 55 idiopathic dilated cardiomyopathy (IDCM) patients. It was determined that one-quarter of the patients with end-stage IDCM excised hearts during cardiac transplantation (who had normal coronary arteries during initial

Table 3. Prevalence of coronary artery disease according to gender

Disease	Males	Females	*p* value
DVD, (n = 14)	11 (78.6%)	3 (21.4%)	0.244
LAD (50-70% lesion) (n = 1)	1 (100.0%)	-	0.178
LAD plaquing, (n = 21)	19 (90.5%)	2 (9.5%)	0.406
LCx plaquing, (n = 4)	2 (50.0%)	2 (50.0%)	0.353
RCA plaquing, (n = 5)	5 (100.0%)	-	0.125
Significant SVD, (n = 13)	13 (100.0%)	-	0.796
SVD (PCI done), (n = 21)	2 (1.1%)	3 (8.8%)	0.312
TVD (revascularization not possible) (n = 10)	6 (60.0%)	4 (40.0%)	0.847
TVD (CABG done), (n = 2)	2 (100.0%)	-	0.455
Normal coronaries, (n = 134)	114 (85.1%)	20 (14.9%)	0.623

All data are expressed as numbers (percentage). *p*-value < 0.05 were considered statistically significant. LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; SVD, single-vessel disease; DVD, double-vessel disease; TVD, triple-vessel disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

Table 4. Prevalence of coronary artery disease according to age

Disease	< 40	41-50	51-60	> 60	*p* value
DVD, (n = 14)	-	6 (42.9%)	6 (42.9%)	2 (14.3%)	0.263
LAD (70%-90% lesion), (n = 1)	-	-	1 (100.0%)	-	0.677
LAD plaquing, (n = 21)	-	5 (23.8%)	13 (61.9%)	3 (14.2%)	0.858
LCx plaquing, (n = 4)	-	2 (50.0%)	0 (0.0%)	2 (50.0%)	0.342
RCA plaquing, (n = 5)	-	-	3 (60.0%)	2 (40.0%)	0.403
Significant SVD, (n = 13)	-	6 (46.2%)	6 (46.2%)	1 (7.7%)	
SVD (PCI done), (n = 5)	-	4 (80.0%)	1 (20.0%)	-	0.274
TVD (revascularization not possible), (n = 10)	-	4 (40.0%)	4 (40.0%)	2 (20.0%)	0.574
TVD (CABG done), (n = 2)	-	-	2 (100.0%)	-	0.632
Normal coronaries, (n = 134)	2 (1.5%)	49 (23.4%)	68 (32.5%)	15 (7.2%)	0.116

All data are expressed as numbers (percentage). *p*-value < 0.05 were considered statistically significant. LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; SVD, single-vessel disease; DVD, double-vessel disease; TVD, triple-vessel disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

Table 5. Association between gender and left ventricular variables

Variables	Males (n = 175)	Females (n = 34)	Patients (n = 209)
Age, years	54.65 ± 6.01	51.17 ± 3.26	54.08 ± 6.02
Left ventricular ejection fraction, %	39.72 ± 3.26	40.41 ± 3.54	39.83 ± 3.27
SYNTAX score	17.09 ± 2.22	17.35 ± 2.17	17.14 ± 2.21
Left ventricle internal diameter, cm	4.9 ± 0.43	4.91 ± 0.47	4.93 ± 0.44
p value	0.01	0.05	0.05

All data are expressed as the mean ± standard deviation.

diagnosis) had underlying significant CAD. Non-invasive imaging to detect myocardial ischemia and viability is a reasonable option in patients with known CAD when angina is absent [24]. In this study, myocardial viability assessment was performed using DSE. In this study, in 17 cases with DCMP, we performed a viability study; a total of 10 patients underwent deferred revascularization based on DSE, and 2 patients were advised grafts.

Revascularization is beneficial for patients with positive viability testing. Many prior studies have observed improvement in surrogate parameters (e.g., exercise capacity or LVEF ejection); however, survival benefits have also been doc-

Table 6. Association between coronary artery disease and left ventricular variables

Disease	Age	Left ventricular ejection fraction	SYNTAX score	Left ventricular internal diameter
Normal coronaries (n = 134)	53.94 ± 6.04	39.80 ± 3.32	16.84 ± 1.96	4.92 ± 0.47
Single-vessel disease (n = 18)	52.50 ± 4.86	42.06 ± 2.48	17.06 ± 2.58	4.71 ± 0.29
Double-vessel disease (n = 14)	53.72 ± 6.14	38.21 ± 3.26	18.85 ± 2.07	5.05 ± 0.45
Triple-vessel disease (n = 12)	56.08 ± 6.21	38.50 ± 3.03	18.50 ± 3.06	5.05 ± 0.33
Other (n = 31)	55.06 ± 6.49	39.95 ± 2.96	17.12 ± 2.29	4.99 ± 0.38
ANOVA	F = 0.88	F = 3.61	F = 4.24	F = 1.765
	P = 0.47	P = 0.007	P = 0.003	P = 0.137
	NS	SIG	SIG	NS

All data are expressed as the mean ± standard deviation.

umented [13]. In this study, the majority of patients were male and belonged to the 51-60-year-old group. In most cases, radial route was chosen for coronary angiography because it was more comfortable for patients and allowed same day discharge. In this study, it was determined that patients with DCMP (LV global hypokinesia) had normal coronaries in 64.1% of cases, and abnormal results were present in 35.9% of cases; these results were in line with those in other studies [25]. In our study, the mean EF was 39.83 ± 3.27%, SYNTAX score was 17.14 ± 2.21, LVID was 4.93 ± 0.44 cm. Except for age, which was determined to be higher in males, no significant gender-related differences were observed between EF, SYNTAX score, and LVID.

In this study, the coronary angiographic results revealed normal epicardial coronaries in 64.1%, LAD plaquing in 10.0%, DVD in 6.7%, and SVD in 6.2%. SVD, for which PCI was performed, accounted for 2.4%. CABG was performed in 2 patients (1.0%) with TVD. Significant CAD was determined to present in 44 (58.7%) patients. SVD, DVD, and TVD were observed in 18 (40.9%), 14 (31.8%), and 12 (27.3%) patients, respectively. There were no major complications or mortality during this study.

Study limitation

This study has some limitations because it is a single-center study. Although the number of DCMP subjects undergoing coronary angiography in this study was sufficient (209), a much larger study may provide a more accurate prevalence of occult CAD. Thus, further large studies conducted at multiple centers may provide better distribution of occult CAD. Furthermore, long-term follow up results of study patients are not available.

Conclusion

This study is allowed to infer that all DCMP patients should undergo physiological stress testing or invasive coronary angiography to rule out ischemic etiology even when angina is absent. Dyspnea can be the sole presenting complaint even in ICMP patients. A large proportion of DCMP patients (i.e., up to 20%) may have significant CAD; if timely intervened with revascularization based on coronary anatomical and physiological assessment, it can be considerably improved.

Disclosure of conflict of interest

None.

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