Research Article

THE DISTINCTION BETWEEN ISCHEMIC AND NON-ISCHEMIC CARDIOMYOPATHY BY CAROTID ULTRASOUND IN YEMENI POPULATION

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Abstract

Background: Differential diagnosis between ischemic (IDCM) and the non-ischemic cardiomyopathy (NIDCM) constitutes a challenge in the daily medical practice. Coronary artery disease (CAD) is a major cause of heart failure associated with left ventricular systolic dysfunction (LVSD). The prognosis of LVSD is significantly influenced by the etiology of heart failure and therefore differentiation of significant CAD from other etiologies is important. Carotid intima-media thickness (IMT), carotid plaque and carotid stenosis >50% are useful predictors for cardiovascular events, including CAD and stroke. Objectives: To assess the usefulness of carotid ultrasonography in differentiating between ischemic and non-ischemic dilated cardiomyopathy. Methods: We retrospectively studied 75 subjects with dilated cardiomyopathy (DCMP) of uncertain origin who underwent echocardiography and coronary angiography between February 1, 2021, and august 30, 2022. They have been applied for carotid ultrasonography. Results: Carotid atherosclerosis was found to be very common in ischemic and rare in non-ischemic cardiomyopathy. CAD was found in 47 patients (62.6%, IDCM group) on coronary angiography. Carotid IMT> 1.0% (85.1% vs 21.4%, p<0,001) was significantly higher in the IDCM group. Carotid plaque (63.8% vs 3.6%, p<0.001) was significantly higher in the IDCM group and Carotid stenosis > 50% (27.7% vs 0.0%, p<0.001) was also, higher in the IDCM group. Conclusion: Carotid intima-media thickness (IMT), carotid plaque and carotid stenosis > 50% are useful predictors for IDCM in DCMP of unknown origin.

Keywords: Ischemic cardiomyopathy, non-ischemic cardiomyopathy, plaque, intima-media thickness, coronary artery disease

INTRODUCTION

Differentiating ischemic from non-ischemic causes of left ventricular (LV) systolic dysfunction has profound clinical and therapeutic implications in patients with chronic heart failure (HF). Coronary artery disease (CAD) is one of the most important causes of left ventricle systolic dysfunction (LVSD) and it is found in approximately 68% of patients with LVSD[1]. The definition of cardiomyopathies was given by 2013 World Heart Federation classification[2]. The ischemic etiology of cardiomyopathy (IDCM) was given by Felker et al[3], and that of non-ischemic cardiomyopathy (NIDCM) was given by Packer et al[4]. The differentiation between ICMP and NIDCM is of paramount importance because revascularization has a mortality benefit in ICMP, whereas for patients NIDCM, there is no need for either high dose antiplatelet therapy, hypolipidemic drugs or expeditious revascularization[5]. Although ischemic cardiomyopathy bears a worse prognosis than non-ischemic cardiomyopathy[6,7], patients with proven hibernation may show an improved outcome after myocardial revascularization[8,9]. Appropriate differentiation is achieved by coronary angiography, since it still remains the gold standard. Many non-invasive techniques have been tested in this distinction with variable accuracy [10,11]. However, there are some limitations in interpretation and availability of these tests which often involves expensive equipment, radiation exposure, needs medication and contrast administration [12], while inconsistent findings have been reported. Carotid scanning is efficient, relatively inexpensive, highly reproducible and does not expose patients to contrast dye and radiation. Extracranial carotid artery disease has been associated with increased prevalence of significant coronary atherosclerosis and acute coronary events [13,14] and vice versa [15,16]. Furthermore, both coronary and carotid arterial trees share many risk factors that contribute to the atherosclerotic process [17,18]. Ultrasonic scanning is a reliable and feasible technique to detect carotid disease. In our study we examined the value of carotid atherosclerosis in the prediction of coronary artery disease as the underlying cause of diffuse left ventricle dilatation and dysfunction in cases of undetermined etiology.

METHODS

This retrospective study included 75patients more than 30 years of age who were presented to our cardiac center with signs and symptoms of heart failure between February 1, 2021, and august 30, 2022. The study was approved by the local scientific ethics committee, the included individuals were informed about the study and asked for their participation, taking the consent of those who agreed to be included in this study. The following were excluded: Those with known coronary artery disease; those with a history and findings of primary valvular, congenital, pericardial disease, or myocarditis, peripartum cardiomyopathy; or those with post-anthracyclines, other antineoplastic drug exposure or cervical irradiation therapy. Individuals with anterior Q waves on the electrocardiogram or angina were eligible in the absence of aclear history of myocardial infarction, as both can also be present in dilated cardiomyopathy [19]. Patients whose history, clinical evaluation and echocardiography failed to define the cause of left ventricular dysfunction, were eligible for the study. Cardiac catheterization and coronary angiography were indicated in all those who were stabilized. They all underwent carotid ultrasonic imaging as well. Three electrocardiographic parameters (rhythm, presence of left bundle branch block,

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anterior Q waves) and the major risk factors for coronary artery diseases were also assessed. Arterial hypertension was defined by history of repeated blood pressure readings >140/90 mmHg. Hypercholesterolemia by a total cholesterol level >220 mg.dl-1 or medication dependence, diabetes mellitus by a fasting blood glucose level >120 mg.dl-1 or use of insulin or oral hypoglycemic, and obesity by a body mass index >27 kg.m². Both current smokers and those who had stoppedsmoking <6 months before were included. The family history was regarded as positive when first-degree relatives had documented coronary artery disease into their sixth decade.

Echocardiography

Each patient underwent echocardiography independently by an experienced cardiologist with transthoracic M-mode, two-dimensional (2D), and Doppler imaging using a commercially available Hewlett-Packard Sonos 7500 system equipped with a 2.5/2.0 MHz phased array transducers, before coronary angiography was performed. The echocardiography was done as per the American College of Cardiology/American Heart Association 2015 guidelines of chamber quantification[20]. The left ventricle(LV) end-diastolic volume, LV end-systolic volume, and left ventricle ejection fraction (LVEF) were assessed on apical two-chamber and four-chamber views using the modified Simpson's rule.

Carotid ultrasonic examination

Carotid scanning was performed by the same Hewlett-Packard system using a 7.5/5.5 MHz linear array transducer, according to the methods previously described[21]. Bilateral B-mode and colour Doppler images of the entire common carotid artery, the carotid bifurcation, the proximal internal and external carotid arteries were taken in anterolateral, lateral, and posterolateral directions in both transverse and longitudinal planes. Pulse-wave Doppler tracings were obtained with a sonication angle of 60ºat any site with colour-flow disturbance. Intima-media thickness was calculated electronically by means of calipers from frozen longitudinal 2-D images, with the R wave on the electrocardiogram. The far wall of the distal 2 cm of the common carotid artery was magnified with care to be horizontally displayed across the screen. Measurements were made from the leading edge of the luminal echo to the leading edge of the media/adventitia line in each of all three planes (Fig. 1).
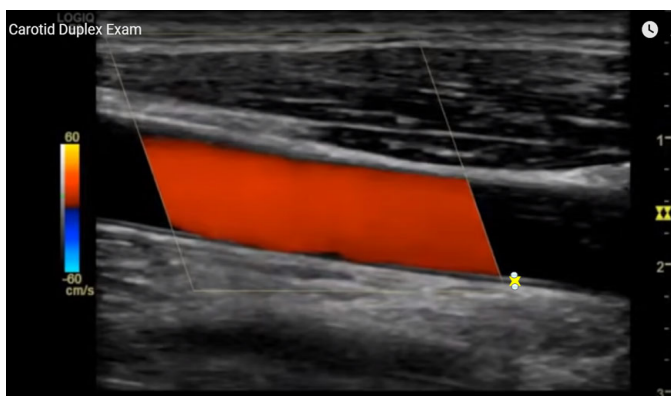

Figure 1. Measurement of the intima-media complex from 2-D tracing. The far wall of the distal 2 cm of common carotid artery has been magnified and values are derived at late diastole with the R wave on electrocardiogram

At the side, at the plane and at the site where the maximum value was found, five more measurements were averaged and used as the intima-media thickness. Sites of plaques were excluded from measurements. Increased intima-media thickness was taken to be > 1.0 mm. which is the higher median value in the general population that has been reported[22]. Plaques were regarded as discrete thickenings that extended more than 50% beyond the surrounding wall, within any segment of extracranial carotid system and/or localized irregular thickenings of at least 1.3 mm (Fig. 2). Continuous, not localized thickening less than 1.3 mm was not considered as plaque. Carotid stenosis was considered significantwhen there was a greater than 50% diameter stenosis (Fig. 3).
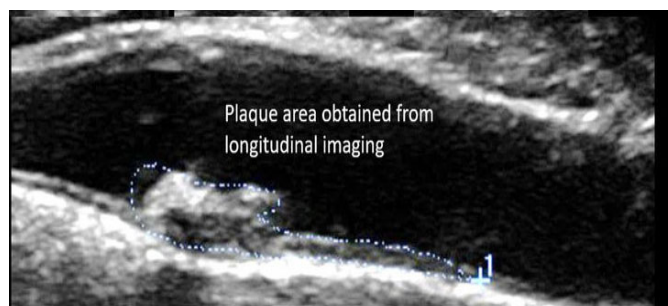
Figure 2. Plaque in common carotid artery
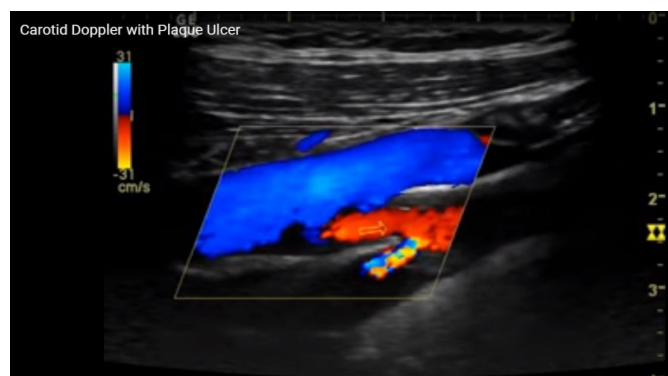
Figure 3. Significant stenosis in ostial segment of internal carotid artery

Coronary angiography

Coronary artery disease (CAD) is a pathological process characterized by atherosclerotic plaque accumulation in the epicardial arteries, whether obstructive or nonobstructive. Obstructive CAD was defined as at least 50% stenosis of luminal diameter of the left main coronary artery (LMCA) or at least 70% stenosis of luminal diameter of at least one of the major epicardial coronary arteries. Nonsignificant lesion was defined as <30% stenosis of luminal diameter of any epicardial artery. Intermediate lesion was defined as 30%-50% stenosis of luminal diameter of LMCA, OR 30%-70% stenosis of luminal diameter of one of the major epicardial arteries[23]. The ICMP was diagnosed for patients with ≥50% luminal diameter stenosis of the left main or ≥70% proximal left descending anterior coronary artery, or ≥2 major epicardial coronary arteries; otherwise, patients were diagnosed as having NICMP[23].

Statistical analyses

Values are expressed as mean ± one standard deviation and frequencies are expressed as percentages. The differences

between measurements were tested using t-test for continuous variables and Chi-square test for categorical variables. Comparisons of continuous variables between groups were examined with analysis of variance (ANOVA). Logistic regression analysis was employed in order to detect possible significant association between a dichotomous dependent variables (non-ischemic or ischemic cardiomyopathy) and a number of independent ones. A probability value of $p < 0.05$ was considered statistically significant. Data were analyzed by using SPSS version 17.0 for Windows (SPSS, Inc., Chicago, IL, USA).

RESULTS

Among the 75 patients of dilated cardiomyopathy who underwent coronary angiography, 47 of them (62.7%) show significant coronary artery stenosis. The remaining 28 patients (37.3%) had angiographically normal coronaries. Of patients with ischemic cardiomyopathy, triple-vessel disease was found in 37 (78.7%), two-vessel disease in 10 (21.3%) and five patients had additional significant left main stem involvement. In Table 1, patients with ischemic cardiomyopathy were most likely to be smokers, hypertensives, diabetics, and to have significantly more coronary risk factors than those with non-ischemic cardiomyopathy. Thirty two out of the 47 (68.1%) ischemic-cardiomyopathy patients, had at least two risk factors. From 28non-ischemic patients, ten(35.7%) had no risk factors at all, 13 had one (46.4%) and 5 (17.9%) had two risk factors.

Table 1. Demographic characteristics and clinical data of the study population

Item	IDCM N=47 (62.7%)	NIDCM N=28 (37.3%)	P. value
Age (range)	60.02±5.30 (40-73)	58.3 ±7.9 (40-80)	0.312
Male Gander (%)	34 (72.3%)	18 (64.3%)	0.481
Height	171.3±4.1 (160-178)	171.6±5.1 (160-180)	0.744
Weight	69.3±6.2 (52-81)	68.6±6.4 (50-77)	0.649
BMI	23.7±2.5 (17-29.3)	23.3 ±1.8 (19.5-28.3)	0.448
NYHA class 3 or 4 (%)	43 (91.5%)	25 (89.3%)	0.679
Angina (%)	44 (93.6%)	3 (10.7%)	0.001
Obesity (%)	11 (23.4%)	8 (28.6%)	0.624
Diabetes Mellitus (%)	25 (53.2%)	5 (17.9%)	0.001
High cholesterol (%)	41 (87.2%)	12 (42.9%)	0.001
Smoking (%)	27 (57.4%)	5 (17.9%)	0.001
Hypertension (%)	29 (61.7%)	7 (25%)	0.001
Heredity (%)	24 (51.1%)	3 (10.7%)	0.001
Number of RF for CAD	2.7±0.9	1.3±0.9	0.002

Atrial fibrillation and left bundle branch block and other parameters in Table 2, show no significant difference between the two groups but anterior Q-wave show significant difference as in Table 2

Table 2. Electrocardiographic and echocardiographic data

Item	IDCM N=47 (62.7%)	NIDCM N=28 (37.3%)	P. value
Atrial fibrillation	6 (12.8%)	4 (14.3%)	0.854
Left bundle branch block	9 (19.1%)	8(28.6%)	0.353
Anterior Q wave	26 (55.3%)	6 (21.4%)	0.002
LVEDD (mm range)	66.1±5.1 (58-80)	65.0±6.7 (59-77)	0.340
%LVEF (range)	35.9 ± 4.7(28-41)	32.9 ± 3.7(23-40)	0.326
LA in mm (Range)	41.5 ±3.5 (39-44)	43.2 ±2.7 (36-51)	0.341

Carotid atherosclerosis was very frequent in ischemic, but rare in non-ischemic patients as in Table 3. Fourty ischemic patients (85.1%) had an intima-media thickness >1.0 mm. 30 patients (63.8%) had plaques and 13 patients (27.7%) had carotid stenosis of internal carotid artery, and only seven (14.9%) ischemic patients had a normal carotid scan. Only six

(21.4%) non-ischemic patients had an intima-media thickness >1.0 mm. Five of them were older than 65 years of age and had more than two risk factors, while the sixth had an additional plaque but no one had a significant stenosis.

Table 3. Carotid ultrasonic data in IDCM vs NIDCM

| Item	IDCM N=47 (62.7%)	NIDCM N=28 (37.3%)	P. value
IMT in mm (Range)	1.3±0.2 (0.8-1.8)	0.9±0.1 (0.7-1.2)	0.001
IMT >1.0(%)	40 (85.1%)	6 (21.4%)	0.001
Carotid plaque%	30 (63.8%)	1 (3.6%)	0.001
Carotid stenosis>50%	13 (27.7)	0 (0)	0.001
Any single carotid parameter	40 (85.1%)	6 (21.4%)	0.001

The diagnostic ability of all parameters that were significantly different between the two groups was subsequently analysed. Their respective sensitivity, specificity, positive and negative predictive values were assessed in the identification of patients with ischemic cardiomyopathy (Table 4).A cut-off value of intima-media thickness > 1 mm showed a sensitivity of 85.1%, specificity of 78.6%, 86.9% positive predictive value and 75.9% negative predictive value. Carotid plaque had sensitivity of 63.8%, specificity of 96.4%, positive predictive value of 96.8% and negative predictive value of 61.4%. Carotid stenosis > 50% had sensitivity of 27.7 %, but specificity of 100%, 100% positive predictive value with 45.2% negative predictive value.

Table 4. Sensitivity, Specificity, positive (PPV) and negative (NPV) predictive value of the parameters that were significantly associated with ischemic cardiomyopathy

| Item	Sensitivity	Specificity	PPV	NPV
Angina	93.6%	89.3%	93.6%	89.3%
Diabetes Mellitus (%)	53.2%	82.1%	83.3%	51.1%
High cholesterol (%)	87.2%	57.1%	77.4%	72.7%
Smoking (%)	57.5%	82.1%	84.4%	53.5%
Heredity (%)	51.1%	89.3%	88.9%	52.1%
> 2 risk factors for CAD	68.1%	82.1%	86.5%	60.5%
Anterior Q wave	55.3%	78.6%	81.3%	51.2%
IMT >1.0(%)	85.1%	78.6%	86.9%	75.9%
Carotid plaque%	63.8%	96.4%	96.8%	61.4%
Carotid stenosis>50%	27.7%	100%	100%	45.2%

Table 3 show, at least one of the abnormal findings of the carotid scan (any single carotid parameter) was present in 6 (21.4%) non-ischemic patients, and in 40 (85.1%) of those with ischemic cardiomyopathy (p<0.001). Thus, carotid scanning distinguished patients with coronary artery disease with a sensitivity of 85.1% and specificity of 78.6% (Table 4). In a logistic regression model with carotid findings, age, gender, diabetes mellitus, cigarette smoking, high cholesterol, and number of coronary risk factors included as covariates, abnormal carotid findings were still significantly and independently associated with ischemic cardiomyopathy (p=0.001).
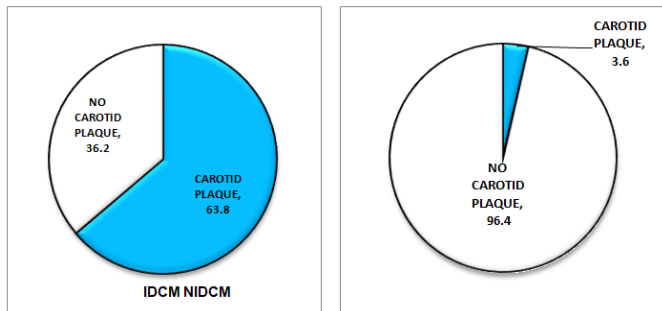
Carotid IMT > 1mm in IDCM VS NIDCM
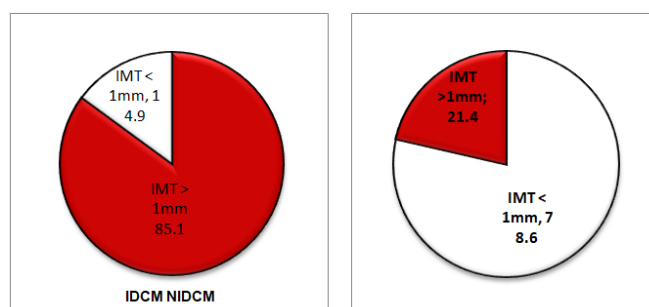
Carotid stenosis > 50% in IDCM VS NIDCM
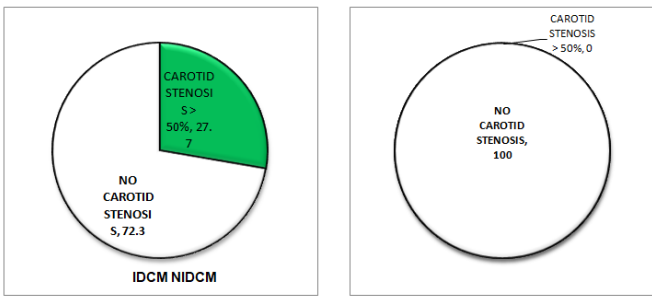
Carotid Plaque in IDCM VS NIDCM

DISCUSSION

In daily medical practice, it remains a challenge to distinguish between ischemic and non-ischemic cardiomyopathy. Ischemic etiology has been shown to be independently associated with worse long-term outcome in patients with left ventricle systolic dysfunction as mentioned previously in Felker et al. The etiology of cardiomyopathy also influences the decision to pursue revascularization and the choice of pharmacologic intervention[24]. Dilated cardiomyopathy, defined as left ventricle dysfunction with chamber dilatation, represents a final common pathway for many pathologic processes. However, in certain patients, determination of etiology may be difficult because patients with heart failure without coronary artery disease (CAD) may present with typical angina or regional wall motion abnormalities on echocardiography, whereas patients with severe CAD may present without symptom of angina or history of myocardial ischemia/infarction[25] Accurate distinction of ischemic from non-ischemic cardiomyopathy is fundamentally achieved by coronary angiography, which also delineates the coronary anatomy before considered revascularization. several techniques have been utilized for non-invasive differentiation. radioisotope Perfusion imaging and stress echocardiography have been acceptable and feasible methods[26]. However,overlaps and dissimilar findingshave been described, especially in low ejection fractions and severe wall motion abnormalities. Positron emission tomography is extremely useful in assessing myocardial viability and also precisely differentiates between ischemic and dilated cardiomyopathy[27]. However, it is problematic in diabetic patients and its application is limited because of unavailability and high cost. Carotid IMT is a well-established surrogate marker of coronary atherosclerosis[28], and is associated with cardiovascular events[29]. It is efficient, relatively inexpensive and highly reproducible and dose not expose patients to contrast dye or radiation. Previous studies demonstrated the relationship between carotid IMT, carotid plaque and carotid stenosis with the extent and severity of coronary stenosis[30]. Therefore, it can be postulated that carotid IMT, carotid plaque

and carotid stenosis provide diagnostic clue for ischemic etiology in severe left ventricle dysfunction patients. Atherosclerosis is a systemic disease and, as such, increasing carotid IMT, carotid plaque and carotid stenosis >50% are correlated with CAD. However, this association remains debatable[31]. Our study demonstrated that carotid IMT> 1 mmis higher in the IDCM group (Table 3), and showed a sensitivity of 85.1% and specificity of 78.6%. Carotid plaque exhibited high specificity (96.4%) and high positive predictive value (96.8%), Carotid stenosis showed high specificity (100%) and high positive predictive value (100%) but low sensitivity for the diagnosis of IDCM (Table 4). In contrast, carotid disease was infrequent in non-ischemic cardiomyopathy group. Therefore, we weighted on carotid IMT>1mm, carotid plaque or carotid stenosis > 50% can be used as tools to support the presence of ischemic etiology in severe LVSD patients and normal carotid scan support the non-ischemic etiology of severe LVSD patients.Our findings are similar to other studies[32,33]. Based in our findings, carotid ultraonography with its different parameters can be useful tools for the prediction of CAD in severe LVSD patients with unknown etiology.

Limitations

This study is limited by the small sample size and its retrospective nature.In a logistic regression model with age, gender and abnormal carotid findings included as covariates, only the later were significantly and independently associated with ischemic heart disease. The cut-off point for increased intima-media thickness > 1mm although arbitrarily chosen (being the upper median value of the general population), provided the best diagnosis in the ROC curve analysis. The definition of plaque as localized thickening > 1.3 mm was chosen as the intermediate value from that used in the literature, i,e from > 1.0 mm to 1.5 mm 1[34,35].

Conclusion

Carotid IMT> 1 mm, carotid plaque and carotid stenosis>50%, was higher with ischemic cardiomyopathy group and showed high specificity, positive predictive value and good sensitivity for IDCM. In patients with dilated cardiomyopathy, carotid ultrasonography can be useful additional tools for the prediction and/or exclusion for CAD.

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