Original Article

ANATOLIAN CURRENT MEDICAL

DOI: 10.38053/acmj.1501933

Anatolian Curr Med J. 2024;6(4):286-291

Predictors of ejection fraction recovery and baseline differences in patients with peripartum cardiomyopathy and dilated cardiomyopathy

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Cite this article as: İnan D, Demirtola Mammadli Aİ. Predictors of ejection fraction recovery and baseline differences in patients with peripartum cardiomyopathy and dilated cardiomyopathy. *Anatolian Curr Med J.* 2024;6(4):286-292.

Received:15.06.2024 ◆ **Accepted**: 16.07.2024 ◆ **Published**: 29.07.2024

ABSTRACT

Aims: Dilated cardiomyopathy (DCM) and peripartum cardiomyopathy (PPCM) are heart failure conditions with similar clinical, morphological and pathophysiological features but different underlying pathways. In PPCM and DCM patients, improvement in left ventricular ejection fraction (LVEF) varies depending on a number of factors. In this study, we aimed to determine the main differences between DCM and PPCM patients and the predictors of LVEF recovery in these patients.

Methods: This cross-sectional, observational study included 33 consecutive female patients, 10 with PPCM and 23 with DCM, attending a tertiary cardiac center between March 2020 and April 2023. We performed a retrospective analysis of some clinical data and LVEF measurements. The main outcome was accepted as EF improvement at a follow-up of at least 12 months. Binary logistic analysis was conducted to assess predictive factors linked to LVEF recovery. This involved using binary logistic regression analysis to figure out odds ratio (OR) and 95% confidence interval (CI).

Results: The PPCM group had a higher mean follow-up LVEF and LVEF value increase (p<0.001). A total of 10 patients (30%), 4 (17%) in the DCM group, and 6 (60%) in the PPCM group revealed evidence of LVEF recovery. Left atrium anteroposterior (LA-AP) diameter emerged as an independent predictor of EF recovery in the multivariate analysis (OR:0.566, 95 CI%; 0.322-0.995, p=0.048). Furthermore, the receiver operating characteristic (ROC) curve analysis identified a cutoff value of <37.5 mm for LA-AP diameter as the optimal threshold for predicting EF recovery, with 80% sensitivity and 78% specificity.

Conclusion: LA-AP diameter was a significant indicator of LVEF recovery in patients with DCM and PPCM.

Key words: Dilated cardiomyopathy, ejection fraction recovery, peripartum cardiomyopathy

INTROUCTION

Dilated cardiomyopathy (DCM) is a heart muscle disease characterized by a decrease in systolic function, dilation in the heart chambers, and arrhythmia.[1] Various causes are implicated in the a etiology of dilated cardiomyopathy, including viral infections, genetic factors, systemic diseases, and toxic agents (alcohol or chemotherapy).[1-3] A large number of DCM patients referred to as idiopathic DCM, do not have an identifiable a etiological cause.[1,4] Furthermore, patients with coronary artery disease, valvular diseases, congenital heart diseases, hypertension, and abnormal loading conditions are excluded from this characterization, and therefore, in some sources, are also referred to as non-ischemic DCM.[1,4]

Peripartum cardiomyopathy (PPCM) is a clinical condition that reveals in late pregnancy or early postnatal period in the absence of a known pre-existing cardiac dysfunction, has a diverse clinical presentation and shares similar morphological findings with DCM, including ventricular dilatation and impaired systolic function.[1,5,6] Data on the pathophysiology of PPCM are limited and underlying risk factors include advanced age, history of pre-eclampsia, malnutrition, smoking, African ethnicity, diabetes, multiparity and teenage pregnancy.[1,5,6,7]

Due to the similar clinical, morphological and pathophysiological features of DCM and PPCM, it has been assumed that PPCM is DCM with a pregnancy-onset.[5,6,8] Nonetheless, fundamental variations in underlying pathways highlight significant differences between the two cardiomyopathies.[6-8] PPCM is diagnosed in the absence of other a etiological causes of DCM.[5,7] There are currently limited data

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regarding prognosis, response to medical care, and variations in both diseases' morphological and clinical features. More than half of PPCM patients have an improvement in left ventricular ejection fraction (LVEF) within the first 6 months, whereas this rate varies in DCM patients depending on a number of factors such as age, gender and baseline EF.[1,3,5-7] The main objectives of this study were to identify the key distinctions between DCM and PPCM patients and the predictors of LVEF recovery in these patients.

METHODS

The study was carried out with the permission of Ethical Committe of Faculty of Başakşehir Çam Sakura City Hospital Research Ethics (Date: 24.04.2024, Decision No: 272). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In the study by Zhang et al.[9] analyzing ejection fraction (EF) recovery, EF recovery rate was found to be 24.5%. The minimum sample size was determined to be 31 individuals in a power analysis (logistic regression model) with an OR of 0.099 obtained from this study, an α=0.1, and a power of 95%.[10] Based on this result, our cross-sectional, observational study included 33 consecutive female patients, 10 with PPCM and 23 with DCM, admitted to a tertiary cardiac center between March 2020 and April 2023. Exclusion criteria were as follows: baseline EF > 40%, male gender, ischemic cardiomyopathy, acute myocarditis, infiltrative myocardial disease, neuromuscular disease, moderate or severe primary valvular stenosis and regurgitation, congenital heart disease, general systemic disease, and stage III-V renal failure. Laboratory and clinical data, as well as demographic data, were gathered utilizing the hospital's medical database. Additionally, phone interviews were used to gather follow-up data. The study population was divided into two groups to compare peripartum and dilated cardiomyopathy patients. Informed consent was obtained from the patients. Artificial intelligence-enabled technologies including chatbots, image generators, and large language models weren't implemented in this study.

The main outcome was LVEF improvement at a follow-up of at least 12 months. DCM and PPCM were defined on the basis of the current European and American guidelines on heart failure (HF), cardiomyopathy and cardiac diseases in pregnant women as mentioned above.[1,3,5,6] According to the expert panel's recommendations, the improvement in ejection fraction was determined on the basis of documented LVEF, <40% at baseline, ≥10% absolute improvement in LVEF, and a second LVEF measurement >40%.[11] Blood samples were obtained from all patients upon admission to the hospital, in order to measure the complete blood count (using the Beckman Coulter LH 750 in Fullerton, California, USA) and various biochemical variables, such as N- terminal pro-brain natriuretic peptide (NT-proBNP), glucose, creatinine, lipid profile, albumin, and others, using the Cobas Integra 800 Roche Diagnostic Basel, Switzerland. The patient's baseline EF and supplementary echocardiographic parameters were measured at the time of the patient's initial diagnosis of cardiomyopathy. The 12-month follow-up EF was determined as the highest value in repeated measurements. The New York Heart Association (NYHA) classification, Kansas City Cardiomyopathy Questionnaire and six minute walk test were used to assess the patients' social, functional, and physical capacity.[2,3] According to the American Society of Echocardiography recommendations, licensed physicians at the study clinic performed echocardiographic evaluations.[12] A Philips ultrasound cardiovascular system, Affiniti CVx, United States of America (USA) was used with a X51 transducer. LVEF was measured by modified bi-plane Simpson method in the apical 4-chamber and 2-chamber view.

Statistical Analysis

The statistical analysis was conducted using the SPSS 22.0 Statistical Package Program for Windows (SPSS Inc., Chicago, IL, USA). The normality of the distribution was evaluated using the kolmogorov–smirnov test. Quantitative variables with a normal distribution were previewed as mean±standard deviation, while variables with non-normal distribution were represented as median (interquartile range). Categorical variables were expressed as percentages. The Independent Samples t-test was utilized to match quantitative variable groups, while the chi-square test was handled for categorical variables. In addition to the variables that were statistically significant between the groups, we created a model by analyzing parameters that could be predictive in preliminary studies and our clinical experience. Binary logistic analysis was conducted to assess predictive factors linked to LVEF recovery. This involved using binary logistic regression analysis to figure out OR and 95% confidence interval (CI). Potential confounding factors were assessed using univariate regression analysis, and any confounders with a p-value less than 0.25 were included in the multivariate analysis. The Hosmer-Lemeshow goodness-of-fit test was applied to this multivariate logistic regression model. An analysis using the receiver operating characteristic (ROC) curve was performed to determine the area under the curve for predicting improvement in ejection fraction. The Youden index was utilized to identify the ideal threshold and sensitivity and specificity values for the significant parameters in the ROC analysis. A p-value less than 0.05 was accepted statistically significant. Moreover, post hoc power analysis was also performed to evaluate the statistical power of our study. The power of the study was calculated as 85% with an α=0.1 and a sample size of 33. This analysis supports that our study results were statistically significant and reliable.

RESULTS

The study population consisted of total 33 female patients with a mean age of 44.39 ±13.69 years. Patients were categorized as PPCM (n=10) and DCM (n=23) group. PPCM patients were younger (p<0.001). Other demographic characteristics and comorbidities were comparable between the groups (Table 1). Cardiac resynchronization therapy (CRT-D) and implantable cardioverter defibrillator (ICD) were implanted in 3 and 5 patients, respectively, all of whom were in the DCM group. Metoprolol was the most commonly prescribed beta-blocker in PPCM patients, whereas carvedilol was more common in DCM patients (p=0.014). Sixty-one per cent of DCM patients were receiving sodium-glucose cotransporter -2 inhibitor therapy (p=0.003). Prescription of other medical treatments

was similar in both groups. The total number of patients under the guideline-recommended quadruple therapy for HF with reduced LVEF was 15 (45%). Functional, social and physical capacity assessments of both groups were similar (Table 1).

Table 1. Demographic and clinical characteristics of patients with PPCM and DCM

Parameter	DCM (n: 23)	PPCM (n: 10)	Total (n: 33)	p value
Demographic features				
Age, years	50.08 (± 11.37)	31.30 (± 8.76)	44.39 (± 13.69)	<0.001
DM, n(%)	7 (30%)	1 (10%)	8 (24%)	0.203
HT, n(%)	11 (48%)	2 (20%)	13 (39%)	0.133
COPD, n(%)	3 (13%)	1 (10%)	4 (12%)	0.806
Smoking, n(%)	7 (30 %)	0 (0%)	7 (30%)	0.145
Alcohol, n(%)	1 (4%)	0 (0%)	1 (3%)	0.503
Hyperlipidemia, n(%)	1 (4%)	0 (0%)	1 (3%)	0.503
Hypothyroidism, n(%)	2 (9%)	1 (10%)	3 (9%)	0.905
Weight, kg	74.64 (± 15.79)	73.30 (± 14.15)	74.23 (± 15.10)	0.818
SBP, mmHg	124.95 (± 22.24)	119.50 (± 18.02)	123.30 (± 20.92)	0.500
DBP, mmHg	73.74 (± 14.77)	76.10 (± 7.59)	74.45 (± 12.94)	0.638
CRT-D, n(%)	3 (13%)	0 (0%)	3 (9%)	0.231
ICD, n(%)	5 (22%)	0 (0%)	5 (15%)	0.109
Medical treatment				
Beta-blocker				0.014
Metoprolol, n(%)	6 (26%)	8 (80%)	14 (42%)	
Carvedilol, n(%)	13 (57%)	2 (20%)	15 (45%)	
Bisoprolol, n(%)	4 (17%)	0 (0%)	4 (12%)	
ACE-I	0 (0%)	0 (0%)	0 (0%)	0.266
Ramipril, n(%)	10 (43%)	8 (80%)	18 (55%)	
Enalapril, n(%)	1 (4%)	0 (0%)	1 (3%)	
Perindopril, n(%)	4 (17%)	1 (10%)	5 (15%)	
ARB	0 (0%)	0 (0%)	0 (0%)	0.633
Valsartan, n(%)	1 (4%)	1 (10%)	2 (6%)	
Candesartan, n(%)	2 (9%)	0 (0%)	2 (6%)	
Losartan, n(%)	1 (4%)	0 (0%)	1 (3%)	
ARNI, n(%)	3 (13%)	0 (0%)	3 (9%)	0.231
MRA, n(%)	18 (78%)	7 (70%)	25 (85%)	0.673
Furosemide, n(%)	20 (86%)	8 (80%)	28(0%)	0.578
HCT, n(%)	3 (13%)	1 (10%)	4 (12%)	0.806
SGLT-2 inhibitor, n(%)	14 (61%)	1 (10%)	15 (45%)	0.003
Digoxin, n(%)	1 (4%)	0 (0%)	1 (3%)	0.503
Ivabradine, n(%)	6 (26%)	2 (20%)	8 (24%)	0.708
Warfarin, n(%)	4 (17%)	0 (0%)	4 (12%)	0.159
NOAC, n(%)	3 (13%)	0 (0%)	3 (9%)	0.231
ASA, n(%)	11 (48%)	2 (20%)	13 (39%)	0.133
P2Y12 inhibitor, n(%)	2 (9%)	0 (0%)	2 (6%)	0.336
Functional, social and physical capacity				
NYHA class, n(%)				0.799
I	5 (22%)	3 (30%)	8 (24%)	
II	14 (61%)	6 (60%)	20 (61%)	
III	4 (17%)	1 (10%)	5 (15%)	
6 MWT, m	326.26 ± 104.81	393.40 ± 50.67	346.60 ± 96.21	0.064
Kansas Score (Summary)	68.38 ± 18.18	74.17± 17.07	70.14 ± 17.79	0.399

ASA; acetylsalicylic acid, ACEI: angiotensin-converting enzyme inhibitör, ARB; angiotensin receptor blocker, ARNI; angiotensin receptor/neprilysin inhibitör, DBP; diastolic blood pressure, DCM; dilated cardiomyopathy, DM; diabetes mellitus, HCT; hydrochlorothiazide, HT; hypertension, COPD; chronic obstructive pulmonary disease, CRT; cardiac resynchronization therapy, MRA; mineralocorticoid receptor antagonist, NOAC; non–vitamin K antagonist oral anticoagulant, NYHA; New York Heart Association, ICD; implantable cardioverter defibrillator, MRA: Mineralocorticoid Receptor Antagonist, PPCM; peripartum cardiomyopathy, SBP; systolic blood pressure, SGLT-2: sodium-glucose cotransporter -2, 6 MWT; six minute walking test

Left bundle branch block (LBBB) was detected in 5 patients and atrial fibrillation in 4 patients. Baseline electrocardiographic findings were comparable between the groups. Left atrium anteroposterior (LA-AP) diameter, right atrium area (RAA), basal right ventricular end-diastolic diameter (RVEDD) were larger and estimated systolic pulmonary artery pressure was higher in DCM patients. Other echocardiographic findings were similar in both groups (Table 2).

Table 2. ECG, echocardiography and follow up features of the study population

Parameter	DCM (n: 23)	PPCM (n: 10)	Total (n: 33)	p value
ECG features				
AF, n(%)	4 (17%)	0 (0%)	4 (12%)	0.159
LBBB, n(%)	4 (17%)	1 (10%)	5 (15%)	0.586
RBBB, n(%)	2 (9%)	0 (0%)	2 (6%)	0.336
QRS Width, ms	111.78 ± 25.10	103.00 ± 22.67	109.12 ± 24.38	0.350
Heart Rate, bpm	70.60 ± 10.24	71.40 ± 11.64	70.84 ± 10.50	0.846
Echocardiographic measurements				
LVDD, mm	57.52 ± 4.64	53.80 ± 9.35	56.39 ± 6.51	0.134
LVSD, mm	46.04 ± 6.13	44.50 ± 6.67	45.57 ± 6.23	0.522
EF,%	28.52 ± 5.30	31.97 ± 4.63	29.57 ± 5.28	0.085
LA-AP diameter, mm	40.87 ± 6.34	36.30 ± 3.62	39.48 ± 5.99	0.042
LA-SI diameter, mm	51.00 ± 7.60	46.20 ± 5.65	49.54 ± 7.33	0.084
RAA, cm^2	14.73 ± 4.82	10.75 ± 2.84	13.52 ± 4.66	0.022
TAPSE, mm	20.40 ± 6.41	21.65 ± 3.00	20.78 ± 5.57	0.564
RV S',cm/s	10.76 ± 2.99	12.91 ± 2.60	11.41 ± 3.01	0.059
sPAP, mmHg	32.65 ± 12.90	22.900± 5.89	29.69 ± 12.03	0.030
RVEDD (basal), mm	36.78 ± 6.45	31.70 ± 5.98	35.24 ± 6.65	0.042
Mitral regurgitation				0.792
Grade 1, n(%)	14 (61%)	7 (70%)	21 (64%)	
Grade 2, n(%)	5 (22%)	1 (10%)	6 (18%)	
Grade 3, n(%)	3 (13%)	1 (10%)	4 (12%)	
Tricuspid regurgitation				0.146
Grade 1, n(%)	14 (61%)	10 (100%)	24 (73%)	
Grade 2, n(%)	4 (17%)	0 (0%)	4 (12%)	
Grade 3, n(%)	3 (13%)	0 (0%)	3 (9%)	
Grade 4, n(%)	2 (9%)	0 (0%)	2 (6%)	
Aortic regurgitation				0.696
Grade 1, n(%)	8 (35%)	2 (20%)	10 (30%)	
Grade 2, n(%)	2 (9%)	1 (10%)	3 (9%)	
Follow up				
Follow-up Time, months	23.09 ± 16.92	23.70 ± 11.43	23.27 ± 15.28	0.918
Re-hospitalization, n(%)	9 (39%)	2 (20%)	11 (33%)	0.284
Follow-up EF, %	33.92 ± 8.55	48.300 ± 7.50	38.28 ± 10.54	<0.001
Increase in EF value, Median+IQR	0 (0-10)	15.5 (13.7-20.6)	8 (0-16.5)	0.010

AF; atrial fibrillation, QTc; corrected QT interval, DCM; dilated cardiomyopathy, EF; ejection fraction, LA- AP; left atrium anterior-posterior, LA-SI; left atrium superior-inferior, LBBB; left bundle branch block, LVDD; left ventricle diastolic diameter, LVSD; left ventricle systolic diameter, PPCM; peripartum cardiomyopathy, RAA; right atrium area, RBBB; right bundle branch block, RVEDD; right ventricle end-diastolic diameter, RV S'; right ventricle S', sPAP; systolic pulmonary pressure, TAPSE; Tricuspid annular plane systolic excursion.

The PPCM group had higher mean follow-up LVEF (p<0.001) and LVEF value increase (p=0.010). A total of 10 patients (30%), 4 (17%) in the DCM group, and 6(60%) in the PPCM group revealed evidence of LVEF recovery. During a follow-up of 23.27± 15.28 months, no deaths occurred, 11(33%) patients were re-hospitalized. In the DCM group, mean potassium level was higher and glomerular filtration rate was lower. Serum iron, ferritin and thyroxine levels were lower and total iron binding capacity was higher in PPCM patients (Table 3). A total of 24 (72%) patients, including all PPCM patients, were diagnosed with iron deficiency.

Table 3. Laboratory parameters of the study population

Parameter	DCM (n: 23)	PPCM (n: 10)	Total (n: 33)	p value
Laboratory measurements				
Glucose, mg/dl	102.73 ± 16.61	98.30 ± 18.40	101.39 ± 17.00	0.499
Creatinine, mg/dl	0.84 ± 0.27	0.66 ± 0.16	0.79 ± 0.25	0.056
GFR, mL/min/1.73m²	85.08 ± 25.35	114.50 ± 19.50	94.00 ± 27.15	0.003
Sodium, mEq/L	139.08 ± 2.69	138.70 ± 1.33	138.97 ± 2.35	0.671
Potassium, mEq/L	4.51 ± 0.43	4.18 ± 0.27	4.41 ± 0.42	0.038
Calcium, mg/dl	9.08 ± 0.49	9.19± 0.64	9.11 ± 0.53	0.577
AST, U/L	20.52 ± 14.28	14.90 ± 4.70	18.81 ± 12.38	0.237
ALT, U/L	16.73 ± 8.02	14.70 ± 9.11	16.12 ± 8.27	0.524
LDH, U/L	207.43 ± 47.08	162.00 ± 20.02	193.66 ± 45.67	0.007
Total Cholesterol, mg/dl	176.26 ± 60.33	172.60 ± 23.20	175.15 ± 51.54	0.855
LDL –C, mg/dl	110.95 ± 54.80	103.80 ± 22.93	108.78 ± 47.15	0.695
HDL –C, mg/dl	43.78 ± 11.41	47.70 ± 8.16	44.97 ± 10.56	0.336
Triglycerides, mg/dl	110.17 ± 40.29	105.80 ± 52.02	108.84 ± 43.37	0.795
TSH, µIU/mL	3.15 ± 6.46	6.54 ± 13.83	4.17 ± 9.22	0.339
Thyroxine, µg/dl	1.35 ± 0.29	1.06 ± 0.31	1.26 ± 0.32	0.018
Serum Iron, µg/dl	71.47 ± 26.76	48.40 ± 29.29	64.48 ± 29.15	0.034
TIBC, µg/dl	328.34 ± 44.57	364.60 ± 43.54	339.33 ± 46.75	0.039
Ferritin, ng/ml	137.39 ± 118.65	35.30 ± 26.94	106.45 ± 110.24	0.012
Folate, ng/mL	10.73 ± 7.81	5.89 ± 4.01	9.26 ± 7.18	0.074
Vitamin B12, pg/ml	344.91 ± 107.17	268.80 ± 116.19	321.8 ± 113.82	0.077
Lowest NT-pro BNP, pmol/L	770.4 ± 1715.3	177.1 ± 302.6	590.7 ± 1457.8	0.290
Highest NT-pro BNP, pmol/L	4332.5 ± 5324.4	6465.4 ± 11300.6	4978.8 ± 7509.8	0.462
CRP, mg/L	5.13 ± 4.32	6.31 ± 10.36	5.48 ± 6.58	0.644
Total Protein, g/dl	56.55 ± 27.24	64.70 ± 10.06	59.02 ± 23.52	0.369
Albumin, g/dl	39.29 ± 11.52	43.60 ± 6.78	40.59 ± 10.40	0.281
Hemoglobin, g/dl	13.17 ± 1.81	12.45 ± 1.55	12.95 ± 1.74	0.284
Hematocrit (%)	39.23 ± 5.15	37.85 ± 4.72	38.81 ± 4.99	0.474
Platelets, 109/L	254.34 ± 76.36	318.20 ± 66.91	273.69 ± 78.46	0.029

ALT; alanine transaminase, AST; aspartate transaminase, CRP; C-reactive protein, DCM; dilated cardiomyopathy, HDL-C; high- density lipoprotein cholesterol LDH; lactate dehydrogenase, LDL-C; low-density lipoprotein cholesterol, PPCM; peripartum cardiomyopathy, TIBC; total iron binding capacity, TSH; thyroid-stimulating hormone

Table 4. Univariate and multivariate logistic regression analysis for predicting EF recovery

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Age, years	0.936	(0.880-0.997)	0.039	1.049	(0.930-1.184)	0.435
Beta blocker treatment	0.730	(0.234-2.273)	0.578			
SGLT-2 inhibitor treatment	0.388	(0.086-1.748)	0.218	0.425	(0.024-7.618)	0.561
LVDD, mm	0.887	(0.769-1.023)	0.100	1.067	(0.881-1.293)	0.508
Basline EF, %	1.098	(0.944-1.277)	0.226			0.354
Follow-up EF, %	4.956	(0.139-176.22)	0.380			
LA-AP diameter, mm	0.700	(0.539-0.909)	0.007	0.656	(0.449-0.959)	0.029
RAA, cm2	0.685	(0.505-0.930)	0.015	1.144	(0.571-2.293)	0.704
RVEDD, mm	0.826	(0.699-0.975)	0.024	0.828	(0.609-1.126)	0.229
sPAP, mmHg	0.878	(0.763-1.010)	0.068	1.012	(0.843-1.215)	0.896
Highest BNP, pmol/L	1.000	(1.000-1.000)	0.883			
CMP type	7.125	(1.352-37.558)	0.021	6.126	(0.104-362.960)	0.384

Hosmer-Lemeshow Goodness-of-Fit Test: $\chi^2 = 9.238$, df = 8, p = 0.323. CMP; cardiomyopathy, EF; ejection fraction , LA-AP; left atrium anterior-posterior, LVDD; left ventricle diastolic diameter, RAA; right atrium area, RVEDD; right ventricle end-diastolic diameter, SGLT-2: sodium-glucose cotransporter -2, sPAP; systolic pulmonary pressure.

The statistical examination utilized multivariable logistic regression to establish a predictive model. Within this analytical framework, LA-AP diameter emerged as an independent predictor of EF recovery, exhibiting an OR:0.566, 95 CI%; 0.322-0.995, p=0.048 in the multivariate analysis (Table 4). The prognostic performance of LA-AP diameter for LVEF recovery was assessed through ROC curve analysis. The calculated area under the curve (AUC) for LA-AP diameter was 0.863 (95 CI%; 0.734-0.992, p-value=0.001), indicating statistical significance. Furthermore, the ROC curve analysis identified a cutoff value of <37.5 mm for LA-AP diameter as the optimal threshold for predicting LVEF recovery, with 80% sensitivity and 78% specificity (Figure). In contrast, when evaluating PPCM as a determinant of LVEF recovery, its significance was solely evident in univariate analysis and did not maintain significance in multivariate analysis. ROC curve analysis also revealed no statistically significant difference in terms of predicting LVEF recovery (AUC:0.713, 95 CI%;0.508-0.919, p=0.055).

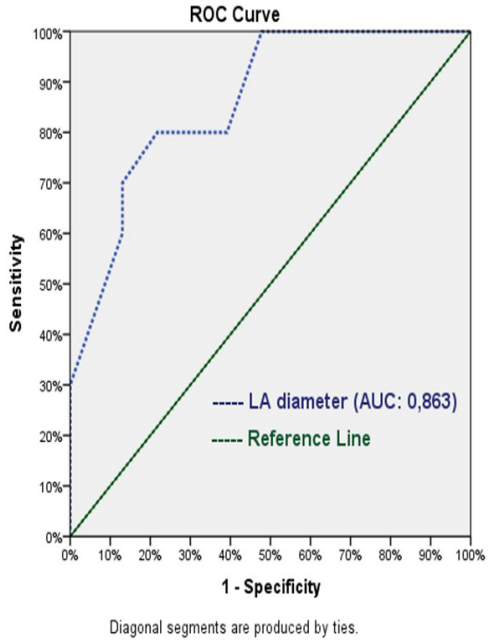

Figure. ROC analysis of LA diameter as a predictor of EF improvement. (AUC:0.863, 80% sensitivity, 78% specificity, with a cut- off 37.5 mm)

DISCUSSION

The main findings of this study were as follows: i) LA-AP diameter was a reliable predictor of LVEF recovery, ii) In PPCM patients, LVEF value increase at follow-up and mean LVEF at follow-up were higher than in DCM patients, iii) Iron deficiency was more common in PPCM patients than in DCM patients, iv) Only about half of the patients received the quadruple medical therapy recommended by the guidelines, and a significant proportion of these individuals had DCM.

PPCM is an uncommon and idiopathic form of systolic HF, and its incidence varies widely around the world, ranging from a high of 1 in 96 births in parts of Nigeria to a low of 1 in 20,000 births in Japan.[6,13-15] Although the precise cause of PPCM is uncertain, theories include pregnancy-related alterations in hormones and hemodynamics, autoimmune diseases, ççk, classic symptoms and signs of HF.[5-6] However, in pregnancy, the diagnosis of PPCM is rather challenging and often misdiagnosed, as some of these symptoms are associated with physiological changes experienced during pregnancy

and other a etiological causes.[5-7] Approximately 50% to 80% of patients reveal improvement in systolic function, mostly in the first 6 months.[6,7,15,21] PPCM is also associated with serious conditions such as cardiogenic shock, arrhythmias and thromboembolism, and in some women cardiac function never fully recovers.[5-7,15,21] Moreover, even if complete recovery occurs in some patients, relapse may occur in subsequent pregnancies.[5-6] In this study, recovery of systolic function was observed in 6(60%) of 10 PPCM patients. There were no serious complications and no relapse during follow-up.

Although the precise underlying pathways are different, patients with DCM and PPCM experience comparable pathophysiological processes, including as impaired microvasculature and sarcomere integrity, increased oxidative stress, and underlying genetic abnormalities.[1,3,4,7] Cardiac remodeling is observed as a part of these processes in both patient groups.[1,3,5] In DCM patients, as well as in PPCM patients, improvement in LVEF has been reported, ranging from approximately 7.3% to 70%, although the definition of LVEF recovery has led to differences in reported rates.[9,11,22-25] In a study by Cho et al.,[27] LVEF recovery was defined as LVEF > 50% on follow-up echocardiography, with an improvement rate of 30.9%. However, when LVEF recovery was defined as an increase in LVEF > 10%, the improvement rate increased to 70%.[26] In another study focusing on changes in left ventricle (LV) diameter and fractional shortening, an improvement rate of 37% in systolic functions was reported. In this study, while the LVEF recovery was 17% in isolated DCM patients, it was 30% in the entire group. Furthermore, although LVEF improvement in PPCM patients was relatively higher than in DCM patients, LV systolic function improved markedly in both DCM and PPCM groups.

Several studies have identified certain demographic, clinical, and echocardiographic features contribute to LVEF recovery.[23-29] Young age, female gender, shorter duration of HF symptoms, absence of LBBB, basal LVEF, basal LVDD, LA diameter, NT-pro BNP, and troponin levels constituted a significant portion of major predictors of LVEF recovery.[3,11,22-29] Interestingly, while LBBB was a strong predictor of LVEF improvement after CRT implantation, it did not maintain this value in patients receiving only medical treatment.[25,30] In this study, age, LA-AP diameter, RAA, basal RVEDD and presence of PPCM were found to be good predictors for LVEF recovery in univariate analysis, with LA-AP diameter being identified as a major predictor in multivariate analysis. Additionally, the relatively young age of the study population has been considered as a reason for the lack of significant age as a predictor, unlike other studies.

Until recently, the role of the LA in the development of HF was not clearly understood. Traditionally, focus was on impaired LV function and remodeling in HF patients, and the role of the LA was overlooked. Classically, the LA in HF patients was thought to modulate LV filling and cardiac output.[31,32] Recent research has revealed that the LA also has endocrine and regulatory roles in HF patients, in addition to mechanical function.[31-34] In response to elevated LV filling pressures in HF patients, the LA undergoes remodeling, which involves myosin isoform expression, collagen matrix transformation, reduced intrinsic contractility, necrosis, fibrosis, and apoptosis.[31,32] This process manifests as more eccentric LA remodeling in patients with DCM and increased LA stiffness in patients with HF and preserved EF.[31-33] In the early stages of HF, the LA acts as an effective pump, maintaining LV filling and contractile function through the Frank-Starling mechanism.[31] However, in the later stages, structural and functional changes render this effect inadequate.[31-33] It has been reported that LA diameters are larger in patients with chronic HF and atrial AF.[28,33,34] Furthermore, LA dilation has been identified as a prognostic marker in HF patients, indicating mortality and the need for heart transplantation.[26-28,33,34] In our study, we found that patients with smaller LA-AP diameters showed greater improvements in LV function.

In patients with HF, a diagnosis of iron deficiency was made in the presence of low transferrin saturation (<20%) or low serum ferritin concentration (<100 µg/L) criteria.[2,3] Based on these diagnostic criteria, the prevalence of iron deficiency in HF patients varies between 55% and 80% depending on the HF presentation.[35] According to recent studies, intravenous iron supplementation is suggested by current guidelines to reduce HF symptoms, improve quality of life, and reduce hospitalization risk in patients with low LVEF or mildly reduced LVEF and iron deficiency.[2,3,35-38] In this study, iron deficiency was present in approximately 72% of patients and was observed in all PPCM patients. The greater likelihood of iron deficiency in PPCM patients was explained by the physiological changes of pregnancy and the postpartum period, together with HF. These facts highlight the importance of careful evaluation for the diagnosis and treatment of iron deficiency in PPCM patients.

Some limitations of this study existed. Firstly, this study was an observational evaluation of a single, tertiary referral center record with relatively small numbers. Furthermore, the likelihood of doing accurate and reliable multivariate analyses was hampered by the very low number of clinical events that were discovered during follow-up. Secondly, considering the retrospective nature of the study, selection bias was inevitable. Thirdly, given that the study required the inclusion of patients who had two transthoracic echocardiography at least 6 months apart and the initial echocardiography obtained might not have been the first evaluation for HF diagnosis, we could not exclude potential temporal bias. The inclusion of only patients with LVEF <40% was another limitation of the study. Fourthly, due to limitations in echocardiographic data, volumetric measurements were not included to evaluate improvement in LVEF. Nevertheless, since the study group consisted of DCM and PPCM patients with global LV dysfunction, the calculated LVEF and diameter indices represented a rough estimate of systolic function. Finally, the lack of genetic analysis and cardiac magnetic resonance imaging findings of the patients were other limitations.

CONCLUSION

DCM and PPCM patients were similar to each other with many clinical and morphological features. In both patient groups, there was a possibility of improvement in cardiac function. LA-AP diameter was a significant indicator of improved heart function in these individuals.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Faculty of Başakşehir Çam and Sakura City Hospital Research Ethics Committe (Date: 24.04.2024, Decision No: 272).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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