Factors Associated with Reversal of Cardiac Structure and Function in Patients with Primary and Secondary Dilated Cardiomyopathy: Postprint

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Abstract

Objective: To investigate the incidence and predictive factors of reverse remodeling of cardiac structure and function in patients with primary and secondary dilated cardiomyopathy. Methods A retrospective study design was employed. A total of 462 patients with dilated cardiomyopathy (DCM) hospitalized in the Department of Cardiology between January 2012 and June 2016 were enrolled. Through dynamic monitoring of echocardiographic results, left ventricular reverse remodeling (LVRR) was defined as an absolute increase in left ventricular ejection fraction (LVEF) of 100%, or an absolute LVEF value 45%, combined with an absolute decrease in left ventricular end-diastolic diameter (LVEDD) of 10 mm, or an absolute LVEDD value 55 mm (in males) and 50 mm (in females). Based on the occurrence of LVRR, patients were divided into LVRR and non-LVRR groups. Clinical characteristics at first admission (baseline) were collected, and predictive factors for LVRR were analyzed. Results A total of 462 patients were included in this study, with a follow-up duration of (24.13±15.60) months. In patients with primary dilated cardiomyopathy, compared with the non-LVRR group, the LVRR group showed a significant decrease in LVEDD (P<0.01), a significant increase in LVEF (P<0.01), and a significant increase in mean exercise tolerance during follow-up (P<0.01). Multivariate logistic regression analysis indicated that a short baseline history of heart failure (OR=0.913, P<0.01), high systolic blood pressure (OR=1.062, P<0.01), absence of electrolyte disturbances (OR=0.347, P<0.01), low red cell distribution width (OR=0.205, P<0.01), small LVEDD (OR=0.799, P<0.01), and high LVEF (OR=1.142, P<0.01) were associated with LVRR occurrence. In patients with secondary DCM, compared with the non-LVRR group, the LVRR group showed a significant decrease in LVEDD (P<0.01), a significant increase in LVEF (P<0.01), and a significant increase in mean exercise tolerance dur-

ing follow-up (P<0.01). A short baseline history of heart failure (OR=0.954, P<0.01), low red cell distribution width (OR=1.011, P<0.01), and whether etiological intervention was performed during hospitalization (OR=1.073, P<0.01) were associated with LVRR occurrence. Conclusion In some patients with primary and secondary dilated cardiomyopathy, exercise tolerance improves and cardiac structure and function can reverse after treatment with standard anti-heart failure medications and etiological intervention.

Full Text

Predictive Factors of Left Ventricular Reverse Remodeling in Patients with Idiopathic or Secondary Dilated Cardiomyopathy

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Abstract

Objective: To investigate the occurrence of left ventricular reverse remodeling (LVRR) and its predictive factors in patients with idiopathic or secondary dilated cardiomyopathy (DCM).

Methods: A consecutive cohort of 462 patients with DCM admitted to our department between January 2012 and June 2016 was enrolled. Based on dynamic echocardiographic monitoring, LVRR was defined as an absolute increase in left ventricular ejection fraction (LVEF) by 10% or LVEF reaching 45%, combined with an absolute decrease in left ventricular end-diastolic diameter (LVEDD) by 10 mm or LVEDD reaching 50 mm (in women) or 55 mm (in men). Patients were divided into LVRR and non-LVRR groups. Clinical characteristics at initial admission (baseline) were collected to analyze predictive factors for LVRR.

Results: Among 462 patients followed for (24.13±15.60) months, 17.06% of patients with idiopathic DCM achieved LVRR. Compared with the non-LVRR group, the LVRR group showed significant reductions in LVEDD (P<0.01), significant improvements in LVEF (P<0.01), and significantly increased mean exercise tolerance during follow-up (P<0.01). Multivariate logistic regression analysis identified shorter heart failure history (OR=0.913, P<0.01), higher systolic blood pressure (OR=1.062, P<0.01), absence of electrolyte imbalance (OR=0.347, P<0.01), lower red cell distribution width (RDW) (OR=0.205, P<0.01), smaller LVEDD (OR=0.799, P<0.01), and higher LVEF (OR=1.142, P<0.01) as independent predictors of LVRR in idiopathic DCM.

In secondary DCM, 43.81% of patients achieved LVRR. The LVRR group also demonstrated significant reductions in LVEDD (P<0.01), improvements in LVEF (P<0.01), and increased exercise tolerance (P<0.01) compared to the non-LVRR group. Multivariate analysis revealed shorter heart failure history (OR=0.954, P<0.01), lower RDW (OR=1.011, P<0.01), and etiological intervention during hospitalization (OR=1.073, P<0.01) as independent predictors.

Conclusion: In a subset of patients with idiopathic or secondary DCM, standard heart failure therapy combined with etiological intervention can reverse cardiac structure and function while improving exercise tolerance.

Keywords: dilated cardiomyopathy; left ventricular reverse remodeling; predictors

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Introduction

According to the 2007 Chinese guidelines for diagnosis and treatment of cardiomyopathy, dilated cardiomyopathy (DCM) is a complex myocardial disease with both genetic and non-genetic etiologies, characterized by left ventricular or biventricular enlargement with impaired systolic and/or diastolic function, with or without congestive heart failure. Traditionally, these patients often experience recurrent exacerbations despite standard heart failure therapy, progressively developing end-stage refractory heart failure that ultimately requires cardiac transplantation.

Recent studies have increasingly demonstrated that effective treatment can reverse cardiac structure and function in some patients with idiopathic and secondary DCM, a phenomenon termed left ventricular reverse remodeling (LVRR). However, reported LVRR incidence varies substantially across centers, primarily due to inconsistent classification of idiopathic versus secondary DCM, incomplete etiological identification or intervention in secondary cases, and heterogeneous LVRR criteria. Therefore, this study employed strict inclusion/exclusion criteria and standardized LVRR evaluation to separately analyze idiopathic and secondary DCM, investigating predictive factors for cardiac structural and functional reversal to provide novel insights for managing refractory heart failure and DCM.

Methods

1.1 Study Population We retrospectively collected data from 462 patients diagnosed with DCM at the First Affiliated Hospital of Fujian Medical University between January 2012 and June 2016.

1.2 Inclusion and Exclusion Criteria for Idiopathic DCM Inclusion Criteria:
(1) Met 2007 Chinese diagnostic criteria for DCM: (a) Cardiac enlargement with LVEDD >5.0 cm (women) or >5.5 cm (men); (b) LVEF <45%.
(2) Underwent follow-up laboratory testing and echocardiography.

Exclusion Criteria:
(1) Secondary DCM including ischemic cardiomyopathy, hypertensive heart disease, infectious/immune-mediated DCM, toxic DCM, and peripartum cardiomyopathy.
(2) Chronic kidney disease with glomerular filtration rate <60%.
(3) Loss to follow-up or all-cause mortality.

1.3 Inclusion and Exclusion Criteria for Secondary DCM Inclusion Criteria:
(1) Met the same DCM diagnostic criteria as above.
(2) Completed follow-up testing.
(3) Identified etiology:
- Ischemic cardiomyopathy: Confirmed by rest/stress gated myocardial perfusion imaging; if percutaneous coronary intervention (PCI) was performed, all target vessels achieved TIMI grade 3 flow; atrial fibrillation/flutter excluded if tachyarrhythmia coexisted.
- Tachycardia-induced cardiomyopathy: Documented recurrent tachyarrhythmias on multiple ECGs or Holter monitoring; all patients underwent radiofrequency ablation; coronary artery disease, hypertension, and diabetes excluded.
- Obesity cardiomyopathy: BMI 32 kg/m² with disease duration 10 years.
- Alcoholic cardiomyopathy: Heavy alcohol consumption (ethanol 125 mL/day) for 10 years; if hypertension or diabetes coexisted, disease duration 5 years.
(4) Etiological intervention performed (PCI, radiofrequency ablation, or lifestyle modification).

Exclusion Criteria:
(1) Chronic kidney disease (GFR <60%).
(2) Loss to follow-up or all-cause mortality.
(3) Autoimmune, metabolic, endocrine, or genetic diseases that may cause DCM.

1.4 Data Collection Baseline and follow-up data included:
(1) Demographics: age, sex, smoking/alcohol history, height, weight, family history of cardiomyopathy.
(2) Clinical features: symptoms, signs, blood pressure, heart rate, NYHA functional class.
(3) Laboratory tests: complete blood count, biochemistry, echocardiographic parameters (LVEDD, LVEF), NT-proBNP, troponin I.
(4) Follow-up exercise tolerance (METs) and medication use.
(5) Etiological interventions (PCI, radiofrequency ablation, lifestyle modification).

(6) Patients were categorized into LVRR and non-LVRR groups based on outcomes.

1.5 LVRR Evaluation Criteria LVRR was defined as:
- LVEF increase 10% (absolute) or LVEF reaching 45%, **AND**
- LVEDD decrease 10 mm or LVEDD reaching 50 mm (women) or 55 mm (men).

1.6 Statistical Analysis Data were analyzed using SPSS 19.0. Continuous variables are expressed as mean±standard deviation; intergroup comparisons used independent samples t-tests, while intragroup comparisons used paired t-tests. Categorical variables are presented as numbers/percentages and compared using ^{2} tests. Multivariate logistic regression identified predictors of cardiac structural/functional reversal. $P<0.05$ was considered statistically significant.

Results

2.1 Baseline Characteristics The study included 252 patients with idiopathic DCM and 210 with secondary DCM. In the idiopathic group, 193 (76.6%) were male, mean age was (44.11±15.60) years, heart failure duration was (23.80±19.53) months, and NYHA class distribution was 7.54% (Class I), 25.79% (Class II), 40.48% (Class III), and 26.19% (Class IV). Baseline systolic blood pressure was (118.24±16.92) mmHg. At discharge, 81.35% were on ACEI/ARB, 77.78% on -blockers, and 88.49% on spironolactone.

In the secondary DCM group, 159 (75.71%) were male, mean age was (49.27±18.76) years, heart failure duration was (23.49±19.34) months, and NYHA class distribution was 9.52% (Class I), 21.90% (Class II), 37.62% (Class III), and 30.95% (Class IV). Baseline systolic blood pressure was (119±20.75) mmHg. At discharge, 75.71% were on ACEI/ARB, 74.76% on -blockers, and 90.95% on spironolactone [Figure 1: see original paper].

2.2 Follow-up Outcomes During (24.13±15.60) months of follow-up, 17.06% of idiopathic DCM patients achieved LVRR. In this group, LVEF increased from (33.80±10.37)% to (50.41±9.88)% ($P<0.01$), while LVEDD decreased from (63.22±6.01) mm to (46.18±5.90) mm ($P<0.01$).

In secondary DCM, 43.81% achieved LVRR, with LVEF increasing from (32.38±7.47)% to (48.13±7.36)% ($P<0.01$) and LVEDD decreasing from (61.77±4.85) mm to (48.73±6.89) mm ($P<0.01$) [Figure 2: see original paper][Figure 3: see original paper].

2.3 Multivariate Logistic Regression Analysis In idiopathic DCM, multivariate analysis identified the following independent predictors of LVRR: shorter heart failure history (OR=0.913, $P<0.01$), higher baseline systolic blood

pressure (OR=1.062, P<0.01), absence of electrolyte imbalance (OR=0.347, P<0.01), lower RDW (OR=0.205, P<0.01), smaller LVEDD (OR=0.799, P<0.01), and higher LVEF (OR=1.142, P<0.01) .

For secondary DCM, independent predictors were: shorter heart failure history (OR=0.954, P<0.01), lower RDW (OR=1.011, P<0.01), and etiological intervention during hospitalization (OR=1.073, P<0.01) .

Discussion

Traditionally, DCM has been considered poorly responsive to pharmacological therapy alone, with disease progression requiring advanced interventions such as cardiac resynchronization therapy, stem cell transplantation, or heart transplantation. However, recent guidelines emphasize the importance of etiological treatment and intensive follow-up management (including pharmacotherapy, lifestyle modification, and cardiac rehabilitation) in improving prognosis, with particular attention to pharmacological reversal of ventricular remodeling. Well-established therapies include ACEI/ARB, -blockers, and spironolactone.

Previous multicenter studies have reported that 26-48% of DCM patients show LVEF improvement with standard heart failure therapy, with some achieving normalization of both LVEF and LVEDD. However, most studies focused exclusively on idiopathic DCM or single-etiology secondary DCM, with no comparative analysis of treatment priorities between idiopathic and secondary forms.

Our study found that 17.06% of idiopathic DCM patients achieved LVRR with standard therapy, while 43.33% of secondary DCM patients achieved LVRR when etiological intervention was added to standard therapy. The lower LVRR rate in idiopathic DCM may be attributed to: (1) our retrospective design with strict classification, where the idiopathic cohort had fewer patients with common causes of cardiac enlargement (hypertension, diabetes, tachyarrhythmias); (2) exclusion of chronic kidney disease and all-cause mortality, which often involve multiple comorbidities introducing bias; and (3) more stringent LVRR criteria.

We confirmed previous findings regarding predictors such as heart failure history, systolic blood pressure, QRS duration, baseline LVEDD/LVEF, serum sodium, and QT dispersion. Notably, we identified RDW as a novel predictor for both idiopathic and secondary DCM. RDW, a parameter of erythrocyte heterogeneity, is used in anemia differential diagnosis and correlates with malignancy, inflammatory bowel disease, liver disease, and malnutrition. Over the past decade, RDW has emerged as a prognostic marker in cardiovascular diseases including heart failure, coronary artery disease, atrial fibrillation, and pulmonary hypertension, though its role in DCM remains underexplored. Potential mechanisms for elevated RDW in DCM include: (1) neurohormonal activation in severe heart failure (more prevalent in the non-LVRR group) stimulating erythropoietin secretion and bone marrow production; and (2) chronic cardiac enlargement

causing coronary microcirculatory ischemia and reduced flow reserve, conditions associated with increased RDW.

Furthermore, LVRR patients in both groups demonstrated significantly higher exercise tolerance during follow-up. Exercise capacity is a powerful prognostic indicator in cardiovascular disease, with each 1-MET increase reducing all-cause mortality risk by 12%. Mechanisms involve improved peak oxygen uptake, endothelial function, and serum nitrate concentration. While metabolic agents like trimetazidine enhance exercise tolerance by 1.1-1.5 METs in coronary artery disease, data on exercise tolerance in DCM remain limited. Our study highlights the significant improvement in exercise capacity among DCM patients achieving LVRR, though baseline exercise data were insufficient to determine whether increasing exercise tolerance directly promotes cardiac recovery.

In conclusion, this study provides robust evidence that standard heart failure therapy can reverse cardiac structure and function in some idiopathic DCM patients, while etiological intervention achieves similar effects in secondary DCM. We identified RDW as a novel predictor of LVRR in both DCM types. Limitations include the single-center design, modest sample size, incomplete follow-up data, and relatively short follow-up duration. Future research should address long-term prognosis of LVRR patients, recurrence rates, and other clinically relevant outcomes.

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Note: Figure translations are in progress. See original paper for figures.