Impact of Type 2 Diabetes Mellitus on Prognosis in Patients with Dilated Cardiomyopathy: Post-print

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Date: 2022-10-28T00:00:00+00:00

Abstract

Background Type 2 diabetes mellitus increases the risk of premature cardiovascular disease in patients, representing a major health threat. Elucidating the impact of type 2 diabetes mellitus on the prognosis of patients with dilated cardiomyopathy can guide clinical management.

Objective To investigate the effect of type 2 diabetes mellitus on the prognosis of patients with dilated cardiomyopathy.

Methods A retrospective analysis was performed on 313 patients with dilated cardiomyopathy admitted to the First Affiliated Hospital of Guangxi Medical University from January 2015 to May 2020. Patients were divided into a diabetes group (66 cases) and a non-diabetes group (247 cases), and landmark analysis was used to compare all-cause mortality between the two groups. To balance confounding factors, propensity score matching was implemented. A multivariate COX regression model was established to analyze the prognostic value of type 2 diabetes mellitus in patients with dilated cardiomyopathy.

Results There was no statistically significant difference in 1-year survival rates between the diabetes and non-diabetes groups in patients with dilated cardiomyopathy (87.9% vs. 81.4%, ^{2}=1.520, P=0.218). After 1 year, the survival rate of patients with dilated cardiomyopathy in the diabetes group was lower than that in the non-diabetes group (66.0% vs. 76.6%, ^{2}=4.414, P=0.036). After propensity score matching, the difference in survival rates between the diabetes and non-diabetes groups in patients with dilated cardiomyopathy was similar to the results before matching (within 1 year: 83.3% vs. 78.6%, ^{2}=0.288, P=0.592; after 1 year: 62.5% vs. 83.9%, ^{2}=4.206, P=0.040). In the multivariate COX regression model constructed using piecewise fitting, type 2 diabetes mellitus was not associated with prognosis in patients with dilated cardiomyopathy within 1 year; after 1 year, patients with dilated cardiomyopathy complicated by type 2

diabetes mellitus had a higher risk of all-cause mortality (P=0.046, RR=1.756, 95% CI 1.011-3.050).

Conclusion Type 2 diabetes mellitus is closely associated with adverse outcomes after 1 year in patients with dilated cardiomyopathy.

Full Text

The Effect of Type 2 Diabetes Mellitus on the Prognosis of Patients with Dilated Cardiomyopathy

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Abstract

Background: Type 2 diabetes mellitus poses a significant health threat by increasing the risk of premature cardiovascular disease. Elucidating the effect of type 2 diabetes on the prognosis of patients with dilated cardiomyopathy is crucial for guiding clinical management. **Objective:** To investigate the impact of type 2 diabetes mellitus on the prognosis of patients with dilated cardiomyopathy. **Methods:** We retrospectively analyzed 313 patients with dilated cardiomyopathy admitted to the First Affiliated Hospital of Guangxi Medical University between January 2015 and May 2020. Patients were divided into a diabetic group (66 cases) and a non-diabetic group (247 cases), with all-cause mortality compared between the two groups using landmark analysis. To balance confounding factors, propensity score matching was performed. A multivariate Cox regression model was constructed to analyze the prognostic significance of type 2 diabetes in dilated cardiomyopathy patients. **Results:** No significant difference in one-year survival rate was observed between the diabetic and non-diabetic groups (87.9% vs. 81.4%, ^{2}=1.520, P=0.218). However, after one year, the survival rate in the diabetic group was significantly lower than in the non-diabetic group (66.0% vs. 76.6%, ^{2}=4.414, P=0.036). After propensity score matching, the survival difference between groups remained consistent with the pre-matching results (within one year: 83.3% vs. 78.6%, ^{2}=0.288, P=0.592; after one year: 62.5% vs. 83.9%, ^{2}=4.206, P=0.040). In the multivariate Cox regression model constructed using piecewise fitting, type 2 diabetes was not associated with prognosis within one year, but became an independent risk factor for all-cause mortality after one year (P=0.046, RR=1.756, 95% CI 1.011-3.050).

Conclusion: Type 2 diabetes mellitus is closely associated with adverse outcomes in dilated cardiomyopathy patients after one year of follow-up.

Keywords: dilated cardiomyopathy; type 2 diabetes mellitus; prognosis; short-term; long-term

Introduction

Diabetes mellitus and its complications represent a major global health threat, substantially increasing the worldwide burden of mortality and disability. Cardiovascular disease occurs at a significantly earlier age in patients with type 2 diabetes and with greater severity. In China, the prevalence of diabetes among adults has been rising annually, currently reaching 11.9%, with type 2 diabetes being the predominant form and a higher prevalence observed in men than women (12.1% vs. 10.3%). Early detection, diagnosis, and treatment of type 2 diabetes are essential for reducing the cardiovascular disease burden.

Dilated cardiomyopathy (DCM) is a common form of cardiomyopathy. Population-based surveys in China have reported a prevalence of 19 per 100,000 among the general population, while a later study by Li Shi' e et al. in northern China found a prevalence of 12 per 100,000. A 2014 report from Fuwai Hospital documented a mortality rate as high as 42.24% during a median follow-up period of 52 months. Although left ventricular ejection fraction (LVEF) <35%, New York Heart Association (NYHA) class III-IV, right ventricular involvement, myocardial fibrosis, and ventricular dyssynchrony are recognized as important prognostic factors for DCM, managing these patients remains challenging. Notably, research on the impact of comorbidities on prognosis is insufficient. Previous studies have been limited by small sample sizes and short follow-up durations, leaving the effect of type 2 diabetes on DCM prognosis unclear. This study addresses this gap by examining a larger cohort with extended follow-up to reveal the impact of type 2 diabetes on outcomes in DCM patients.

Methods

Study Subjects We included patients with DCM admitted to the First Affiliated Hospital of Guangxi Medical University between January 2015 and May 2020. DCM was defined as left ventricular end-diastolic dimension (LVEDD) >55 mm in men or >50 mm in women, with LVEF <45% and left ventricular fractional shortening <25%, while excluding ventricular dilation caused by volume or pressure overload at disease onset. Inclusion criteria were: (1) first admission, (2) age $ $18 years, (3) NYHA class III-IV, and (4) complete data on blood glucose, biochemical parameters, and echocardiography. Exclusion criteria included: (1) history of myocardial infarction, (2) coronary revascularization,

(3) congenital heart disease, (4) heart transplantation, (5) valvular heart disease, (6) ischemic cardiomyopathy, (7) in-hospital death, (8) loss to follow-up, and (9) impaired fasting glucose or glucose intolerance. Type 2 diabetes was diagnosed if any of the following were met: (1) previously established diagnosis, (2) diabetic symptoms with oral glucose tolerance test 2-hour glucose $ $11.1 mmol/L, fasting glucose $ $7 mmol/L, or random glucose $ $11.1 mmol/L.

Analysis Indicators and Grouping Clinical data were collected from electronic medical records, including age, sex, blood pressure, weight, height, medical history, personal habits, glucose levels, blood counts, biochemistry, electrocardiography, echocardiographic parameters, and medication use. Follow-up was completed through hospital electronic record systems and telephone interviews, with a loss to follow-up rate of 8.21%. Patients were divided into diabetic and non-diabetic groups, with all-cause death serving as the primary endpoint.

Statistical Analysis Data were processed using SPSS 23.0 and R 4.2.0. Normally distributed continuous variables were expressed as mean ± standard deviation and compared using independent samples t-tests. Skewed continuous variables were presented as median (interquartile range) and compared using rank-sum tests. Categorical variables were described as counts (percentages) and compared using chi-square tests or Fisher' s exact test. Because the risk associated with type 2 diabetes differs between time periods after discharge (within one year versus after one year), we used one year as a cutoff point and applied landmark analysis to compare survival curves between groups. To balance differences in clinical characteristics, 1:1 propensity score matching was performed with a caliper value of 0.01, matching for age, sex, smoking, alcohol consumption, body mass index, hypertension, and triglycerides. Variables showing statistical significance in univariate Cox regression were included in a multivariate Cox regression model using stepwise forward selection with piecewise fitting to analyze the effect of type 2 diabetes on the primary endpoint. The significance level was set at α=0.05 for two-sided tests.

Results

Overall Characteristics A total of 313 DCM patients were included, comprising 235 men (75.1%) with a median age of 55.0 (47.0-64.0) years. The median follow-up duration was 24.0 (12.8-45.8) months. Sixty-six patients (21.1%) had type 2 diabetes, while 247 (78.9%) did not. The primary endpoint occurred in 116 patients (37.1%).

Clinical Data Comparison No significant differences were observed between diabetic and non-diabetic DCM patients in age, sex distribution, smoking and alcohol history, blood pressure, body mass index, comorbidities (coronary artery disease, atrial fibrillation, chronic kidney disease, chronic obstructive pulmonary

disease), NYHA class, QRS duration, echocardiographic parameters, or medical and device therapy. However, the diabetic group had higher proportions of hypertension, fasting glucose, glycated hemoglobin, and triglycerides. No significant differences were found in other laboratory indicators between the two groups (Table 1). After 1:1 propensity score matching, no significant differences in clinical characteristics remained between groups except for fasting glucose and glycated hemoglobin (Table 2). Among diabetic DCM patients, α-glucosidase inhibitors were the most commonly used hypoglycemic agents, followed by insulin, while sodium-glucose cotransporter 2 inhibitors had the lowest usage rate (Table 3).

Survival Analysis Within one year, no significant difference in survival rates was observed between diabetic and non-diabetic DCM patients (87.9% vs. 81.4%, ^{2}=1.520, P=0.218) [Figure 1: see original paper]. After one year, survival rates were significantly lower in the diabetic group compared to the non-diabetic group (66.0% vs. 76.6%, ^{2}=4.414, P=0.036). Following propensity score matching, the survival difference between groups remained similar to pre-matching results (within one year: 83.3% vs. 78.6%, ^{2}=0.288, P=0.592; after one year: 62.5% vs. 83.9%, ^{2}=4.206, P=0.040) [Figure 2: see original paper].

Cox Regression Analysis Factors potentially affecting prognosis identified through literature review were included in univariate Cox regression analysis, followed by stepwise forward selection for the multivariate model with piecewise fitting (Table 4). Within one year, type 2 diabetes was not a prognostic risk factor for DCM patients after adjusting for other covariates. After one year, type 2 diabetes became an independent risk factor for all-cause mortality (P=0.046, RR=1.756, 95% CI 1.011-3.050). Compared with the non-diabetic group, diabetic DCM patients had a 0.756-fold higher risk of all-cause death (Table 5).

Discussion

This study uniquely focuses on the effect of type 2 diabetes on survival prognosis specifically in a DCM population, examining both short-term and long-term all-cause mortality risks in Chinese patients. During the first year of follow-up, the presence of type 2 diabetes did not affect prognosis in DCM patients. However, after one year, diabetic patients exhibited worse outcomes compared with non-diabetic patients, demonstrating that the prognostic impact of type 2 diabetes varies over time.

The male predominance (75.1%) in our cohort may be explained by sex differences in fundamental physiological, immune, and fibrotic responses to mutations and environmental factors. Male patients may have greater susceptibility, though the underlying mechanisms require further clinical and basic research.

DCM patients at admission are typically in the acute phase of disease with increased energy demands and cardiac burden. The diabetic group had higher fasting glucose and triglyceride levels, which are important energy substrates. We hypothesize that diabetic DCM patients may have better myocardial energy supply, which mitigates the short-term negative effects of diabetes. Previous studies have confirmed protective effects of triglycerides in peritoneal dialysis and breast cancer patients, though specific mechanisms remain unclear.

The differential impact of type 2 diabetes on short-term versus long-term mortality likely reflects the chronic pathophysiological processes of diabetes. Diabetes-induced cardiac injury progresses slowly, often causing diastolic dysfunction, reduced compliance, and impaired contractility even without significant epicardial coronary disease. Underlying mechanisms include mitochondrial damage, impaired calcium handling, upregulated inflammatory signaling, and cardiac remodeling, ultimately leading to structural and functional abnormalities that worsen prognosis. Diabetes increases heart failure risk and complicates disease course, resulting in poorer outcomes. Notably, fasting glucose and glycated hemoglobin did not show prognostic value in univariate analysis, possibly due to non-linear relationships with the primary endpoint when analyzed as continuous variables. Diabetes management is a long-term process; although early cardiac damage may be subtle and undetectable, clinicians should remain vigilant for myocardial injury when diabetes-related complications emerge.

A previous small study limited to NYHA class I-II patients found that diabetes was associated with worsened DCM prognosis, a finding supported by Hidekazu Tanaka et al. Our study, with a larger sample size and focusing primarily on NYHA class III-IV patients, provides valuable complementary evidence. Although Tanaka' s study included some NYHA III-IV patients (20%), it predominantly comprised class I-II patients, representing a significant difference from our cohort. These divergent results suggest that diabetes management strategies may need to be tailored differently for DCM patients according to NYHA class and disease stage. For patients with lower NYHA classes, stricter diabetes control may be warranted, while for those with advanced heart failure, short-term priority should be given to improving cardiac function with long-term diabetes management. Additionally, Christine Meindl et al.' s large registry study found that heart failure patients with both diabetes and DCM had significantly higher one-year mortality (15.2%) than those with DCM alone (6.5%). However, their study targeted chronic heart failure patients with reduced ejection fraction, had shorter follow-up, and included older patients with >50% having ischemic heart disease and coronary revascularization—characteristics distinctly different from our population.

Current research on diabetes and cardiovascular prognosis has focused primarily on ischemic cardiomyopathy, myocardial infarction, and heart failure, with fewer studies examining DCM specifically. Multi-center randomized controlled trials are needed. Interestingly, previous studies found lower 30-day mortality in diabetic heart failure patients, but this relationship reversed by one year, with

diabetes predicting higher mortality. However, this short-term survival advantage requires cautious interpretation, as non-diabetic patients in these studies may have had more severe disease affecting prognosis. Giovanni Targher et al. demonstrated that diabetes independently increased in-hospital mortality, one-year all-cause death, and one-year heart failure readmission in acute heart failure patients, while Enrique Fairman' s one-year observational study found no prognostic impact of diabetes in elderly decompensated heart failure patients. These conflicting findings highlight the ongoing controversy regarding diabetes' role in cardiovascular disease, particularly in DCM populations, necessitating further investigation.

In our study, systolic blood pressure and NT-proBNP demonstrated strong short-term prognostic value, suggesting these parameters reflect not only hemodynamic and cardiac congestion changes but also the severity of functional impairment and disease stage. In contrast, the prognostic significance of type 2 diabetes and LVEDD emerged only in the long term. This indicates that hemodynamic changes significantly impact short-term outcomes in DCM patients, while structural cardiac changes require longer timeframes to manifest their prognostic effects.

Limitations This study's retrospective design precludes establishing causality between type 2 diabetes and adverse outcomes in DCM patients. Additionally, we did not account for diabetes duration or medication changes during follow-up, which may influence prognosis. Finally, although sodium-glucose cotransporter 2 inhibitors have established cardiovascular benefits and prevent heart failure onset, their usage was extremely low in our cohort due to cost and limited availability, precluding their inclusion in the final model.

Author Contributions WANG Haiyan contributed to study conception and design, data collection and management, statistical analysis, and drafting of the manuscript. HUANG Yuan participated in data collection and management. GUI Chun contributed to study conception and design, quality control, and critical revision of the manuscript, taking overall responsibility for the work. All authors approved the final version of the manuscript.

Conflict of Interest: The authors declare no conflicts of interest.

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