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*Original Article*

# Relationship between serum uric acid and ventricular diastolic dysfunction in type 2 diabetes mellitus patients

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**Abstract:** Objective: To investigate the correlation of serum uric acid (SUA) levels with ventricular diastolic dysfunction (DD) in the diabetic population. Methods: Clinical data from 702 patients with type 2 diabetes mellitus (T2DM), including 394 males and 308 females, were retrospectively analyzed in this study. The data included demographic characteristics, biochemical test results, and echocardiography findings. Univariate and multivariate logistic regression analyses were performed to assess the association between SUA and DD. Additionally, the diagnostic efficacies of SUA and the multivariate logistic regression model (Logit P) for DD were evaluated using receiver operating characteristic (ROC) curves. Results: Compared to T2DM patients with normal diastolic function, those with DD had a higher prevalence of hypertension, older age, longer diabetes duration, elevated levels of low-density lipoprotein cholesterol (LDL-c), total cholesterol (TC), blood urea nitrogen (BUN), SUA, and hemoglobin A1c (HbA1c), as well as lower levels of 1,5-anhydroglucitol (1,5-AG) and estimated glomerular filtration rate (eGFR) ($P<0.05$). As indicated by the Logistic regression analysis, gender, age, and SUA were independent risk factors for DD ($P<0.05$). Women had a 47.8% lower risk of DD compared to men [95% CI (0.318-0.718)]. The risk of DD increased by 6.8% for each one-year rise in age [OR 1.068, 95% CI (1.051-1.085)] and by 0.5% for each 1 mmol/L increase in SUA [OR 1.005, 95% CI (1.003-1.007)]. The regression model incorporating sex, age, and SUA exhibited an area under the curve (AUC) of 0.753 (95% CI 0.712-0.794) for diagnosing DD, with a sensitivity of 65.65% and specificity of 78.65%. Conclusions: Gender, age, and SUA were independent factors influencing the development of DD in T2DM patients. Among them, SUA is the only modifiable factor. Early and long-term control of SUA levels is essential to reduce the risk of DD in T2DM patients.

**Keywords:** Cardiac diastolic dysfunction, type 2 diabetes, serum uric acid, logistic regression

## Introduction

Worldwide, diabetes mellitus (DM) is a significant public health challenge. The prevalence of type 2 DM (T2DM) in China is rising annually, accounting for 11.2% of the global diabetic population [1]. As DM becomes more prevalent, cardiovascular complications secondary to DM have emerged as the leading cause of DM-related mortality, imposing a substantial social and economic burden [2, 3]. Among these complications, diabetic cardiomyopathy (DCM) is one of the most common complications, occurring independently of coronary artery disease (CAD) and hypertension. DCM initially manifests as diastolic cardiac dysfunction and can progress to systolic dysfunction in later stages [4]. Studies indicate that the prevalence of ventricular diastolic dysfunction (DD) in T2DM patients ranges from 40 to 60% [5, 6].

Ventricular DD is characterized by impaired ventricular diastolic functioning and decreased ventricular compliance, resulting in increased ventricular filling pressure. It represents an early clinical manifestation of cardiac insufficiency and is associated with adverse cardiovascular outcome [7]. DD has been identified as a potent predictor of cardiovascular adverse events and sudden heart failure (HF) among older adults [4, 8]. If left untreated, DD can eventually progress to HF with preserved ejection fraction or evolve into HF with reduced left ventricular ejection fraction. Disturbed glucose metabolism contributes to structural and functional alterations in the heart. Early risk stratification and timely management of DD in T2DM

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patients are crucial for impeding the progression of diastolic HF and other complications.

Serum uric acid (SUA), a weak organic acid and the end product of purine metabolism in the human body, is closely associated with cardiovascular risk and events, including hypertension, CAD, and HF [9]. With changess in lifestyle, the prevalence of hyperuricemia has been increasing annually, affecting approximately 8.4%-13.3% of Chinese adults [10, 11]. Persistent high SUA levels can cause cardiac and vascular injuries, inducing hypertension, coronary heart disease, and other cardiovascular diseases (CVD) [12-14]. In addition, clinical and animal studies have shown that reducing SUA levels through xanthine oxidase (XO) inhibitors improves cardiovascular outcomes [15]. Elevated SUA has been associated with structural and functional heart disease in CVD [16], and hyperuricemia is recognized as an independent risk factor for HF, possibly influencing certain stages of HF [17]. Echocardiographic investigations have demonstrated a positive association between SUA levels and measures of left ventricular diastolic dysfunction (LVDD) [18, 19]. Many researchers believe that LVDD is a primary manifestation of heart remodeling in diabetic patients [20]. DM and HF exhibit a bidirectional relationship, influencing each other in both causation and outcomes [21]. Reports indicate that 19% of HF patients have T2DM; conversely, the presence of T2DM elevates the risk of HF by two to eight times [22]. However, few studies have reported a relationship between SUA on cardiac DD in T2DM patients, which is the aim of the current study.

## Research design and methods

### *Study population*

This retrospective study included T2DM patients admitted to the Endocrinology and Cardiology departments of our hospital from March 2020 to September 2021, diagnosed according to the 1999 World Health Organization criteria for diabetes mellitus [10]. Exclusion criteria: long-term glucocorticoid use, treatment with Sodium-glucose cotransporter 2 (SGLT2) inhibitors, ejection fraction less than 50%, organic heart disease, estimated glomerular filtration rate (eGFR) less than 30 ml/min/1.73 $m^2$, mental disorders and pregnancy. Finally, 702 T2DM patients were screened. The experiment was approved by the Ethics Committee of Southeast University (2017ZDSYLL006-P), and all procedures were conducted in accordance with the principles of the Declaration of Helsinki.

### *Data acquisition*

All participants completed a questionnaire providing basic information, including age, history of hypertension, history of CAD, duration of DM, smoking status, and alcohol consumption. A trained professional performed three measurements of each participant's height, weight, systolic (SBP) and diastolic blood pressure (DBP), as well as heart rate (HR), recording the mean values. Hypertension was defined as a history of hypertension, ongoing medication treatment, or SBP ≥140 mmHg and DBP ≥90 mmHg.

On the morning after admission, fasting blood samples (minimum 8-hour fast) were collected to assess the following: fasting blood glucose (FBG), hemoglobin A1c (HbA1c), 1,5-anhydroglucitol (1,5-AG), total cholesterol (TC), triglyceride (TG), low- (LDL-c) and high-density lipoprotein cholesterol (HDL-c), blood urea nitrogen (BUN), serum creatinine (Scr), SUA, free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH). Among these, HbA1c was measured by high-performance liquid chromatography (D-10 Analyzer, Bio-Rad, USA). The 1,5-AG level was determined using an enzymatic method (GlycoMark, Tomen-America, New York, USA), and eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation [11].

A Philips EPIQ5 color Doppler ultrasound system was employed, using a cardiac ultrasound probe frequency of 2 MHz-5 MHz. During the examination, participants were instructed to maintain smooth breathing and lie on their left side. Echocardiography measurements included early diastolic mitral inflow velocity (E), late diastolic mitral inflow velocity (A), early diastolic mitral annular velocity (E'), left ventricular ejection fraction (LVEF), left ventricular end diastolic diameter (LVID), end diastolic septal thickness (IVST), and left ventricular posterior wall thickness (LVPW).

### *Diagnostic criteria*

The diagnostic criteria of cardiac DD were referred to the 2016 American Society of

**Table 1.** Comparison of baseline data between disease and control groups

| | Total (n=702) | Disease group (n=524) | Control group (n=178) | $\chi^2$/t | *P* value |
|---|---|---|---|---|---|
| Gender (male), N (%) | 394 | 274 | 120 | 12.341 | <0.001 |
| Age, years | 64 (55, 71) | 66 (58, 74) | 56 (46, 66) | 9.483 | <0.001 |
| Diabetes duration, years | 6.00 (0.02, 14.00) | 6.5 (0.00, 15.00) | 5 (0.50, 10.00) | 3.593 | <0.001 |
| Smoking, N (%) | 186 (26.50%) | 122 (23.28%) | 64 (35.96%) | 10.961 | 0.001 |
| Alcohol consumption, N (%) | 86 (12.25%) | 54 (10.31%) | 32 (17.98%) | 7.275 | 0.007 |
| Hypertension, N (%) | 486 (69.23%) | 380 (72.52%) | 106 (59.55%) | 10.491 | 0.001 |
| CAD, N (%) | 284 (40.46%) | 228 (43.51%) | 56 (31.46%) | 8.010 | 0.005 |
| Family history of DD | 120 (17.09%) | 82 (15.65%) | 38 (21.35%) | 3.045 | 0.081 |
| BMI, kg/m$^2$ | 25.04 (22.78, 27.64) | 24.98 (22.86, 27.73) | 25.39 (22.70, 26.93) | 0.834 | 0.404 |
| SBP, mmHg | 138 (124, 154) | 139 (126, 156) | 127 (119, 146) | 0.605 | 0.545 |
| DBP, mmHg | 77 (71, 86) | 76 (70, 86) | 77 (74, 87) | 1.339 | 0.181 |
| HR, bpm | 80 (73, 89) | 80 (72, 89) | 80 (76, 92) | 2.617 | 0.009 |
| FT3, pmol/L | 4.33 (3.91, 4.74) | 4.28 (3.92, 4.73) | 4.39 (3.89, 4.77) | 0.353 | 0.724 |
| FT4, pmol/L | 17.00 (15.20, 18.70) | 16.8 (15.2, 18.7) | 17.50 (15.43, 18.83) | 0.504 | 0.614 |
| TSH, ulU/ml | 2.01 (1.27, 3.07) | 2.01 (1.30, 3.17) | 2.02 (1.18, 2.76) | 1.088 | 0.277 |

Notes: Data are presented as either number of cases (percentages) or medians (interquartile ranges). CAD: coronary artery disease; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; FT3: free triiodothyronine; FT4: free thyroxine; TSH: thyroid-stimulating hormone.

Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) Recommendations for the Assessment of Left Ventricular Diastolic Function by Echocardiography [10] and the 2016 Guidelines for Measurement of Echocardiographic Examination in Chinese Adults. Dual parallel entry checking was performed to ensure data quality.

*Statistical methods*

For sample size calculation, both δ and α were set to 0.05 for a two-tailed test. The calculation indicated that a minimum of 402 participants was required (as determined using PASS Sample Size Software 15.0, NCSS LLC, Kaysville, Utah, USA). Database establishment was realized using Excel (2010). Data were processed with SPSS 26.0. Non-normally distributed quantitative data were described as medians (interquartile ranges), with inter-group differences determined by non-parametric rank sum tests. For normally distributed data, t-tests were used for inter-group comparisons. Counted data, expressed as percentages or rates, were compared using either $\chi^2$ tests or Fisher's test as appropriate. Spearman's correlation was used for correlation analysis. Multivariate logistic regression was performed to assess the correlation of SUA with DD, and the diagnostic efficacy of SUA for DD was evaluated using the receiver operating characteristic (ROC) curve. A two-sided test was used, with a significance level set at P<0.05.

## Results

*Clinical characteristics of patients*

A total of 702 diabetic patients were enrolled in the study, including 394 men and 308 women, with an average age of 64 years. Of these, 74.6% (524/702) developed DD, comprising the disease group. The other 178 non-DD patients were assigned to the control group. Compared to controls, the disease group had a higher prevalence of hypertension, older age, and longer DM duration, as shown in **Table 1**.

*Echocardiographic parameters*

The disease group had significantly higher IVST and LVPW but significantly lower E/A and E/E' ratios compared to the control group (P<0.01), as shown in **Table 2**.

*Glycolipid metabolism indicators*

T2DM patients with DD exhibited higher LDL-c and TC and lower 1,5-AG compared to those with normal diastolic function (all P<0.05). No

**Table 2.** Comparison of echocardiographic measures between the disease and control groups

| | Total (n=702) | Disease (n=524) | Control (n=178) | t | *P* value |
|---|---|---|---|---|---|
| IVST (mm) | 10.70 (9.80, 11.70) | 11.00 (10.20, 11.90) | 9.60 (8.80, 10.38) | 12.260 | <0.001 |
| LVPW (mm) | 10.80 (9.70, 11.80) | 11.10 (10.10, 12.00) | 9.70 (8.90, 10.50) | 11.580 | <0.001 |
| LVID (mm) | 46.20 (43.50,49.30) | 46.20 (43.50, 49.23) | 46.05 (43.63, 49.60) | 0.073 | 0.942 |
| LVEF (%) | 55.00 (51.50, 58.20) | 54.70 (51.38, 58.00) | 55.95 (51.63, 59.05) | 1.846 | 0.065 |
| E/A | 0.90 (0.80, 1.00) | 0.80 (0.70, 0.90) | 1.20 (1.10, 1.40) | 34.060 | <0.001 |
| E/E' | 7.70 (6.80, 8.60) | 7.40 (6.60, 8.20) | 8.90 (7.90, 10.40) | 14.600 | <0.001 |

Notes: Data are presented as median (interquartile range). IVST: end diastolic ventricular septal thickness; LVPW: left ventricular posterior wall thickness; LVID: left ventricular end diastolic diameter; LVEF: left ventricular ejection fraction; E: early diastolic mitral valve orifice blood flow velocity; A: late diastolic mitral flow velocity; E': early diastolic bicuspid velocity of lobe ring motion.

**Table 3.** Comparison of glucose and lipid metabolism indicators between the disease and control groups

| | Total (n=702) | Disease (n=524) | Control (n=178) | t | *P* value |
|---|---|---|---|---|---|
| HDL-c, mmol/L | 1.23 (1.03, 1.41) | 1.21 (1.02, 1.40) | 1.25 (1.08, 1.42) | 0.526 | 0.599 |
| LDL-c, mmol/L | 2.43 (1.79, 2.91) | 2.51 (1.83, 3.05) | 2.37 (1.74, 2.91) | 2.304 | 0.022 |
| TC, mmol/L | 4.24 (3.38, 5.11) | 4.38 (3.40, 5.13) | 4.17 (3.38, 5.11) | 2.320 | 0.021 |
| TG, mmol/L | 1.40 (0.95, 2.17) | 1.34 (0.95, 2.18) | 1.42 (0.95, 2.14) | 0.789 | 0.430 |
| FBG, mmol/L | 7.19 (5.65, 9.93) | 7.45 (5.84, 10.98) | 7.00 (5.45, 9.84) | 1.837 | 0.063 |
| 1,5-AG, ug/mL | 3.50 (1.40, 13.80) | 2.90 (1.40, 7.90) | 3.70 (1.50, 14.30) | 2.971 | 0.003 |
| HbA1c, % | 8.00 (6.12, 9.70) | 8.14 (6.38, 9.93) | 7.70 (6.06, 9.59) | 1.426 | 0.154 |

Notes: Data are presented as median (interquartile range). HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; TC: total cholesterol; TG: triglyceride; FPG: fasting plasma glucose; 1,5-AG: 1,5-anhydroglucitol; HbA1c: hemoglobin A1c.

significant inter-group differences were noted in HDL-c, TG, FBG, or HbA1c (P>0.05), as shown in **Table 3**.

*Renal function-related indices*

Compared to T2DM patients with normal diastolic function, those with DD had significantly higher Scr, BUN, and SUA and lower eGFR values (all P<0.05), as shown in **Table 4**.

*Correlation of SUA level with echocardiographic measures*

The SUA level showed a positive correlation with IVST and LVPW and an inverse association with E/A and E/E' (P<0.01), as shown in **Figure 1**.

*Univariate and multivariate logistic regression analyses of cardiac DD*

Univariate logistic regression analysis was performed using the occurrence of DD as the dependent variable, and gender, age, smoking, alcohol consumption, duration of DM, hypertension, CAD, BMI, SBP, DBP, HDL-c, LDL-c, TC, TG, FBG, 1,5-AG, and HbAlc as independent variables. The results showed that gender, age, duration of DM, FBG, and SUA were significant factors influencing cardiac DD (P<0.05). These factors were assigned values (**Table 5**) and further incorporated into the multivariate regression analysis. Considering previous studies and clinical experience, BMI [23] and 1,5-AG [24] were also included. As shown in **Table 6**, gender, age, and SUA were independently associated with the development of cardiac DD in T2DM patients (P<0.05). Compared to men, women had a 47.8% reduced risk of developing DD. Age [OR 1.068, 95% CI (1.051-1.085)] and SUA [OR 1.005, 95% CI (1.003-1.007)] were identified as risk factors, with the DD risk elevated by 6.8% for each one-year rise in age and by 0.5% for each 1 mmol/L rise in SUA.

*ROC curve analysis*

A binary logistic regression model was constructed using the occurrence of cardiac DD as

**Table 4.** Comparison of renal function related parameters between the disease and control groups

| | Total (n=702) | Disease group (n=524) | Control group (n=178) | t | *P* value |
|---|---|---|---|---|---|
| Scr, mmol/L | 65.00 (55.00, 78.00) | 67.00 (56.00, 80.00) | 61.00 (53.00, 74.00) | 2.418 | 0.016 |
| eGFR, % | 95.72 (79.30, 114.36) | 93.10 (76.65, 111.11) | 109.91 (93.81, 128.70) | 5.695 | <0.001 |
| BUN, mmol/L | 6.00 (4.90, 7.10) | 6.10 (5.10, 7.20) | 5.40 (4.68, 6.70) | 2.273 | 0.023 |
| SUA, mmol/L | 315 (251, 387) | 320 (252, 396) | 286 (249.25, 368) | 2.925 | 0.004 |

Notes: Data are presented as median (interquartile range). Scr: serum creatinine; eGFR: estimated glomerular filtration rate; BUN: blood urea nitrogen; SUA: serum uric acid.

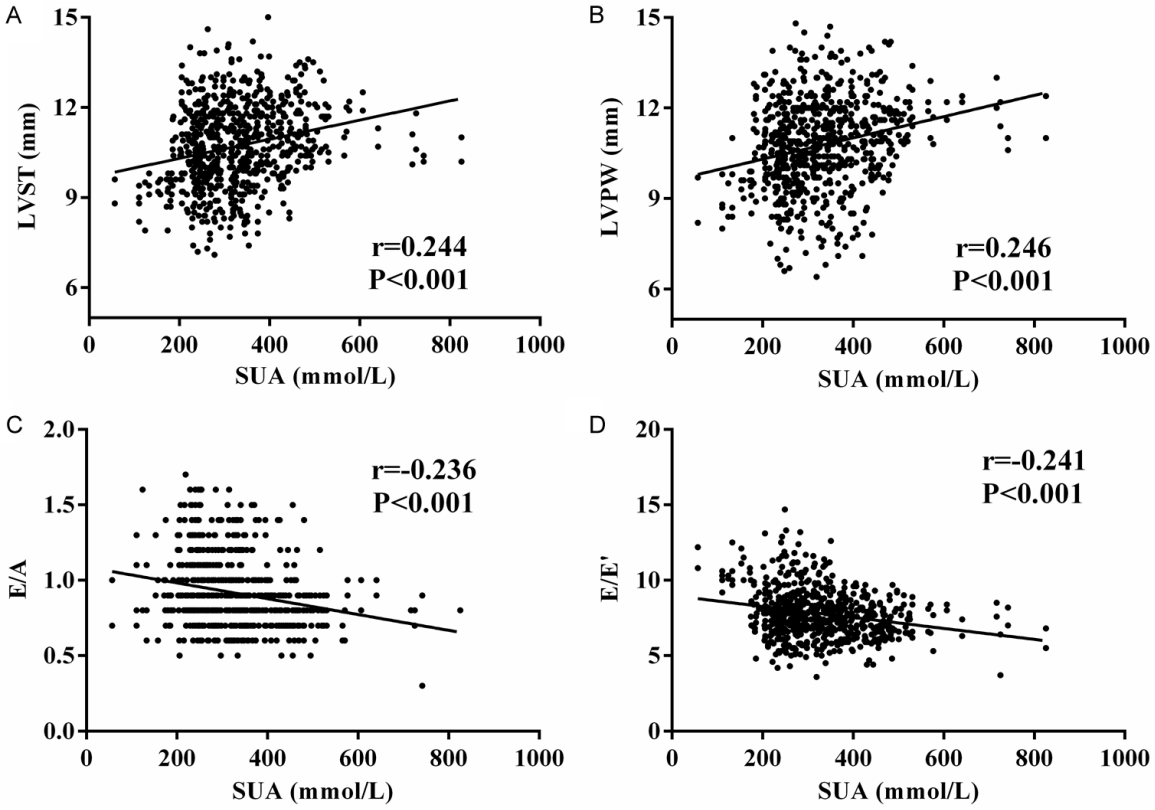


**Figure 1.** Correlation of SUA with echocardiographic parameters. A: Correlation between SUA and LVST; B: Correlation of SUA with LVPW; C: Correlation between SUA and E/A; D: Correlation of SUA with E/E'; SUA: serum uric acid; IVST: end diastolic ventricular septal thickness; LVPW: left ventricular posterior wall thickness; E: early diastolic mitral valve orifice blood flow velocity; A: late diastolic mitral flow velocity; E': early diastolic bicuspid velocity of lobe ring motion.

the dependent variable and incorporating gender, age, and SUA as independent variables. The model demonstrated an area under the curve (AUC) of 0.753 (95% CI 0.712-0.794) in predicting diastolic cardiac insufficiency, with sensitivity and specificity being 65.65% and 78.65%, respectively. The AUC of SUA in predicting cardiac diastolic insufficiency was 0.566 (95% CI 0.518-0.614), with sensitivity of 60.69% and specificity of 57.30%, as shown in **Figure 2** and **Table 7**.

## Discussion

Although many studies have explored the influencing factors for ventricular DD, few have specifically examined the exact role of SUA in the T2DM population. Herein, we identified key risk factors for the development of DD in the T2DM patients, with gender, age, and SUA emerging as independent influences on the onset of cardiac diastolic insufficiency. These findings can help clinicians identify high-risk diabetic indi-

**Table 5.** Univariate logistic regression analysis of factors associated with cardiac DD

| | OR | 95% CI | *P* value |
|---|---|---|---|
| Gender (male), N (%) | 0.442 | 0.266-0.735 | 0.002 |
| Age, years | 1.069 | 1.046-1.092 | 0.000 |
| Diabetes duration, years | 1.033 | 1.002-1.065 | 0.035 |
| Smoking, N (%) | 0.918 | 0.546-1.544 | 0.747 |
| Drinking, N (%) | 0.727 | 0.386-1.368 | 0.323 |
| Hypertension, N (%) | 1.267 | 0.814-1.972 | 0.295 |
| CAD, N (%) | 0.910 | 0.577-1.436 | 0.685 |
| BMI, kg/m$^2$ | 1.040 | 0.983-1.100 | 0.175 |
| SBP, mmHg | 0.999 | 0.995-1.002 | 0.443 |
| DBP, mmHg | 1.014 | 0.995-1.034 | 0.150 |
| HR, bpm | 0.992 | 0.974-1.010 | 0.372 |
| HDL-c, mmol/L | 1.353 | 0.629-2.909 | 0.439 |
| LDL-c, mmol/L | 1.434 | 0.671-3.067 | 0.353 |
| TC, mmol/L | 0.747 | 0.418-1.335 | 0.325 |
| TG, mmol/L | 1.108 | 0.883-1.389 | 0.376 |
| FT3, pmol/L | 1.203 | 0.884-1.636 | 0.239 |
| FT4, pmol/L | 0.994 | 0.926-1.067 | 0.867 |
| TSH, uIU/ml | 0.999 | 0.952-1.048 | 0.969 |
| FBG, mmol/L | 0.928 | 0.884-0.973 | 0.002 |
| 1,5-AG, ug/mL | 1.030 | 0.995-1.066 | 0.097 |
| HbA1c, % | 1.120 | 0.991-1.266 | 0.069 |
| Scr, mmol/L | 1.006 | 0.998-1.015 | 0.146 |
| eGFR, % | 0.998 | 0.994-1.003 | 0.396 |
| BUN, mmol/L | 0.917 | 0.802-1.049 | 0.208 |
| SUA, mmol/L | 1.003 | 1.001-1.006 | 0.009 |

Notes: DD: diastolic dysfunction; CAD: coronary artery disease; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; TC: total cholesterol; TG: triglyceride; FT3: free triiodothyronine; FT4: free thyroxine; TSH: thyroid-stimulating hormone; FPG: fasting plasma glucose; 1,5-AG: 1,5-anhydroglucitol; HbA1c: hemoglobin A1c; BUN: blood urea nitrogen; Scr: serum creatinine; eGFR: estimated glomerular filtration rate; SUA: serum uric acid.

viduals early and facilitate effective prevention and management of cardiac complications.

The incidence of cardiac DD in diabetics ranges from 23% to 75%, increasing significantly with age [25-27]. As the disease progresses, systolic dysfunction can also occur, manifested by ventricular hypertrophy and worsening of HF [28]. This was confirmed by a median age of 64 years and a DD prevalence as high as 74.6% in our study, suggesting a high risk of cardiac disorders among middle-aged and elderly DM patients. Age was identified as an independent risk factor for cardiac insufficiency, with aging contributing to structural and functional changes in the heart, such as increased ventricular arterial stiffness, oxidative stress, and mitochondrial damage, leading to myocardial cell death and impaired endothelium-dependent vasodilation, which are key contributors to diastolic heart failure [27, 29, 30]. Even in patients with well-controlled blood pressure, aging increases left ventricular stiffness and decreases cardiac compliance [31].

In this study, we found that compared to men, the risk of DD in women was lower by 47.8%. However, previous studies had suggested that hyperuricemia exerts a more significant detrimental effect on females with cardiac disorders, possibly attributed to the influence of estrogen levels [32, 33]. Diabetic women have also been shown to be more prone to develop DCM than diabetic men [34]. This difference may be due to the bias introduced by the limited samples included, which require further investigation. In our study, there were 250 female DD patients and 274 male DD patients, with a lower prevalence of DD in women than in men. Moreover, a meta-analysis [18] demonstrated that hyperuricemia predicted an increase in left ventricular mass index in women but not in men. However, unlike in men, hyperuricemia in the female population was associated with age, BMI, and elevated systolic blood pressure. As such, our findings do not support an independent role for SUA in left ventricular remodeling in women. Moreover, we did not classify and compare SUA levels in women before and after menopause. Some researchers have suggested that the estrogen-related increase in renal clearance of urate in premenopausal women may explain the lower SUA levels in women compared to men [35]. Thus, caution should still be exercised, as elevated blood uric acid levels may increase the risk of heart disease in men.

Hyperuricemia is an important component of metabolic disorders and is often associated with obesity and hypertension. Hyperlipidemia may be present concomitantly. The relationship between SUA and CVD mortality has been reported in the general population. The mechanisms underlying this association include: 1) Elevated SUA levels can cause oxidative stress,

**Table 6.** Multivariate logistic regression analysis of independent factors influencing the development of cardiac DD

| Factor | β | SE | Wald $X^2$ | *P*-value | OR (95% CI) |
|---|---|---|---|---|---|
| Gender (male) | -0.739 | 0.208 | 12.661 | <0.001 | 0.478 (0.318, 0.718) |
| Age, years | 0.066 | 0.008 | 67.692 | <0.001 | 1.068 (1.051, 1.085) |
| SUA, mmol/L | 0.005 | 0.001 | 21.030 | <0.001 | 1.005 (1.003, 1.007) |
| Constant | -4.050 | 0.635 | 40.630 | <0.001 | 0.017 |

Notes: DD: diastolic dysfunction; SUA: serum uric acid.

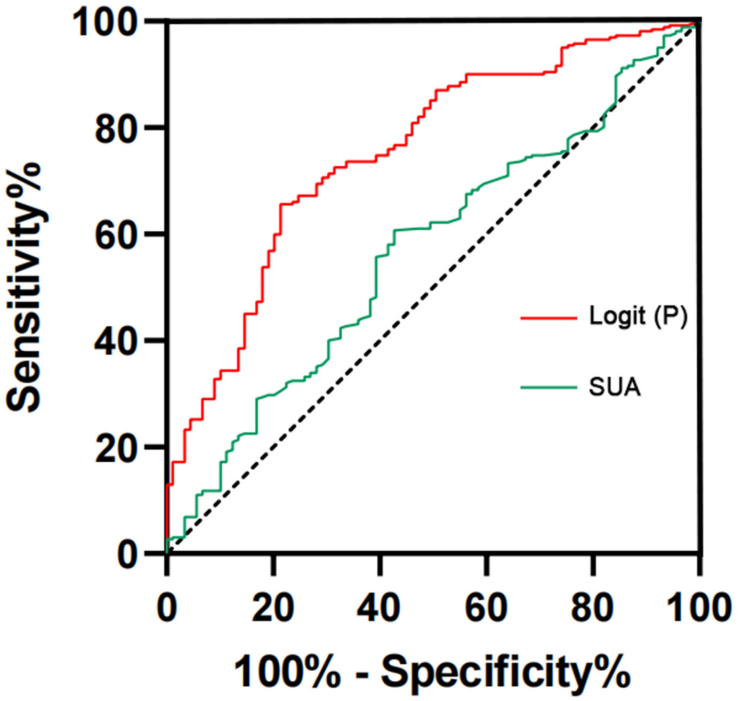


**Figure 2.** Predictive significance of serum uric acid and regression model for cardiac DD in type 2 diabetes patients using ROC curve analysis. Note: ROC: receiver operating characteristic; DD: diastolic dysfunction.

**Table 7.** Predictive value of SUA and regression model for cardiac DD in type 2 diabetes mellitus patients

| Indicator | AUC | Optimal cut-off | Specificity | Sensitivity | Youden Index |
|---|---|---|---|---|---|
| SUA, mmol/L | 0.566 | 293.50 | 57.30 | 60.69 | 117.99 |
| Age | 0.724 | 57.50 | 57.30 | 80.20 | 0.375 |
| Gender | 0.576 | - | 47.70 | 67.40 | 0.151 |
| Regression model | 0.753 | 0.77 | 78.65 | 65.65 | 144.30 |

Notes: DD: diastolic dysfunction; AUC: area under the curve; SUA: serum uric acid.

increase the generation of oxygen free radicals, and cause vascular endothelial injury, platelet activation, and subsequent endothelial dysfunction [36]; 2) Hyperuricemia can damage mitochondria and lysosomes, leading to cardiomyocyte apoptosis through activation of the renin-angiotensin system, reduction of nitric oxide production, vascular smooth muscle cell remodeling, promotion of inflammatory responses, and related metabolic dysfunction [37, 38]. Hyperuricemia is often linked to enhanced XO activity in purine metabolism, which may promote excessive production of reactive oxygen species (ROS), reduce nitric oxide bioavailability, contributing to inflammatory states, endothelial dysfunction, myocardial fibrosis, and ultimately LVDD [39]. The present study identified SUA as an independent risk factor for DD in T2DM population. For every 1 mmol/L increase in SUA, the prevalence of DD increased by 0.5%. Notably, compared with other independent risk factors, SUA was the only controllable factor. Stepwise multiple regression analysis showed that HbA1c, SBP, DBP and other common risk factors for DD were not statistically significant. This may be because our study participants, most of whom were inpatients on long-term use of hypoglycemic and antihypertensive medications, had less variability in blood pressure and glucose levels. This would cause a lack of significant differences between the disease and control groups. However, in daily clinical work, patients' awareness of hyperuricemia and the management of uric acid levels often fall short of recommended standards. This highlights the importance of monitoring SUA levels in T2DM patients, alongside blood glucose and blood pressure, and emphasizes the need for better education and management strategies for hyperuricemia.

Regardless of the presence of typical risk factors such as aging, metabolic syndrome, and high uric acid levels, DM itself can significantly distort diastolic function, triggering cascade of events that may lead to severe cardiac complications, such as HF. People with T2DM may develop underlying CVD without experiencing obvious symptoms, often until the condition has progressed too far. Recent advances have highlighted the importance of early screening in asymptomatic diabetics [40, 41]. For example, the concept of "unrecognized diabetic cardiac damage" includes not only atypical and asymptomatic manifestations visible on the rest electrocardiogram but also LVDD [42]. If not identified early, LVDD may progress to HF with preserved ejection fraction, posing significant risk to patient survival. These findings underscore the need for early detection measures, which recent guidelines suggest may become a routine part of clinical practice [43]. Early screening of DM patients for subclinical manifestations holds clinical significance, since the long-term benefits of timely intervention outweigh concerns about the cost-effectiveness of such programs.

Despite these valuable insights, this study has several limitations. First, it was a cross-sectional, observational, single-center study, and long-term follow-up is needed to evaluate the impact of SUA levels on patient outcomes. Second, the effect of treatment modalities was not considered. Finally, the selection of hospitalized patients and the relatively small sample size may have introduced selection bias, affecting the statistical validity of the findings.

## Conclusions

Diabetic patients are at a higher risk of developing ventricular diastolic dysfunction (DD), with gender, age and SUA identified as independent risk factors. Among these, SUA is the only controllable factor. Therefore, SUA represents an important therapeutic target for alleviating diastolic insufficiency in patients with T2DM. In clinical practice, early control of SUA levels is essential to reduce the risk of diastolic dysfunction in T2DM patients.

## Disclosure of conflict of interest

None.

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