# Correlation Between Thyroid Autoantibodies and Cardiovascular Disease in Patients With Stages 3-5 Chronic Kidney Disease

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# Abstract

Background: Chronic kidney disease (CKD) interacts with thyroid disease and cardiovascular disease (CVD). Our research aimed to analyze the correlation between echocardiographic parameters E / A, E / E ', E' / A ', LVEF and thyroid autoantibodies, and evaluate the role of thyroid autoimmunity in the development of CVD in patients with stages 3-5 CKD.

Methods: The patients who were diagnosed as stages 3-5 CKD in our department from January 2015 to May 2019 were recruited. We collected the routine medical history, general clinical data, and laboratory test index of patients. Echocardiography is performed by a trained echocardiographer to measure mitral valve blood flow velocity (E) in early diastole and Mitral valve flow velocity (A), E / A ratio, mitral annulus velocity (E ') in early diastole, mitral annulus velocity (A') in end-diastole, E / E 'ratio, and E' / A ' ratio. The SPSS 22.0 statistical software was used to analyze the data.

Results: A total of 1164 patients with stages 3-5 CKD were included. Thyroglobulin antibody (TGAb) was negatively correlated with eGFR (r = -0.287, P <0.05). Thyrotropin receptor antibody (TRAb) was significantly positively correlated with CRP (r = 0.206, P <0.001). The titers of TPOAb and TGAb in male diabetic patients were higher (r = 0.137, P = 0.023; r = 0.159, P = 0.011). In female patients, both TPOAb and TGAb are significantly negatively correlated with HGB (r = -0.213, P = 0.018; r = -0.188, P = 0.019). The E / E' of patients with TPOAb positive was higher (r = 0.181, P  0.001). The LVEF in patients with TPOAb positive were higher (r = 0.159, P = 0.007). In addition, LVEF was significantly negatively correlated with TRAb (r = -0.112, P = 0.026).

Conclusion: The prevalence of AITD in stages 3-5 CKD gradually increases with the decline of renal function, and the titers of TPOAb and TGAb also gradually increase. In patients with stages 3-5 CKD, AITD may accelerate the incidence of CVD in CKD patients by affecting TG levels, accelerating the occurrence of anemia, and promoting the micro-inflammation. Female patients with high titers of TPOAb and TGAb should be paid more attention. The average E/E' of patients with stage 5 CKD was 16. Women with low FT3 and TPOAb positive maybe more likely to develop diastolic heart failure.


# Introduction

Chronic kidney disease (CKD) has been recognized as a growing public health problem and affects 10-15% of the population worldwide [1]. It is well established that Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in all patients with CKD, accounting for nearly half of all deaths [2-3]. Targeting modifiable factors has been frequently recommended as a first-line strategy for cutting the dangers of kidney disease progression and cardiovascular disease in patients with CKD. Although some studies have suggested an increased risk of coronary heart disease in autoimmune thyroiditis, the presence of thyroid autoantibodies does not appear to correlate with CVD risk in patients with subclinical hypothyroidism [4-5]. So far, little is known about the association of thyroid autoantibodies with renal function or cardiac function in patients with CKD. The purpose of this study was to investigate the relationship between thyroid autoimmunity and cardiac function of patients with stages 3-5 CKD.

# Method

### Study Population

We recruited a total of 1477 patients with stages 3-5 CKD, at least 18 years of age, who visited the Department of Nephrology at the Third Affiliated Hospital of Southern Medical University from January 2015 to May 2019 in this study. Exclusion criteria are as follows: 1) patients with overt hypothyroidism (TSH> 4.20uIU/L) or overt hyperthyroidism (TSH < 0.27uIU/L); 2) patients lacking TPOAb and echocardiography data; 3) patients whose thyroid function was altered due to previous use of thyroid medications or drugs. Finally, 1164 patients (598 men and 566 women, mean age of 64.95±14.84 years) were enrolled in this study. The study was approved by the ethics committee of the Third Affiliated Hospital of Southern Medical University and conducted following the Declaration of Helsinki. All participants provided informed consent in writing.

### Clinical and laboratory examinations

Fasting (> 8 hours) blood samples were obtained to measure biochemical parameters. Levels of hemoglobin (HGB), C-reactive protein (CRP), serum creatinine (SCr), blood urea nitrogen (BUN), uric acid (UA), serum albumin (ALB), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), triglycerides (TG), creatine kinase (CK), creatine kinase isoenzyme (CK-MB), α-hydroxybutyrate dehydrogenase (HBDH), troponin T (cTnT), myoglobin (Mb), type B natriuresis Peptide precursor (pro-BNP), thyroid-stimulating hormone (TSH), thyroid peroxidase antibody (TPOAb), thyroglobulin antibody ( TGAb), thyrotropin receptor antibody (TRAb) were measured. Roche cobas6000 and Roche's reagents were used to measure blood glucose, HDL, TG, and SCr by colorimetry, and BUN were measured by rate method; LDL cholesterol was calculated indirectly. Roche cobas6000 and Orion's reagents were used to determine CRP by immune transmission nephelometry. Levels of serum thyroid-stimulating hormone (TSH, reference interval: 0.27–4.20 mIU/L), TGAb (reference interval: 0–115 IU/mL), TPOAb (reference interval: 0–34 IU/mL), and TRAb (reference interval: <1.58 U/L) were measured by Beckman's automatic chemiluminescence immunoassay analyzer and original supporting reagents.

The estimated GFR (eGFR) was calculated using the Modification of Diet in Renal Disease equation [6]:

$$eGFR[ml \cdot min^{-1} \cdot (1.73\mathrm{m}^2)^{-1}] = 175 * \mathrm{SCr}^{-1.234} * \mathrm{age}^{-0.179} * (0.79,\ if\ female)$$

We define the non-thyroidal illness syndrome (NTIS) as patients with normal serum TSH. Autoimmune thyroid diseases (AITD) can be diagnosed when a patient has one or more thyroid autoantibodies that are positive and imaging evidence of abnormal thyroid function and/or imaging evidence of thyroid injury.

### Echocardiographic Measurements

All patients were performed two-dimensional, M-mode, pulsed, and color flow Doppler echocardiographic examinations (EPIQ 7 Ultrasound system for cardiology, Philips) in a left lateral position. Echocardiography was performed by a trained cardiac sonographer, who was blinded to the clinical status of the subjects. Standard 2DE Values for all 2DE parameters were obtained as average values of 3 consecutive cardiac cycles. Echocardiographic measurements were carried out following the "Recommendations on Quantitative Methods of Adult Echocardiography Heart Cavity" published by the American Society of Echocardiography (ASE) in 2015 [7]. The following measurements regarding diastolic dysfunction were assessed in all patients and controls: early diastolic trans-mitral flow velocity (E), late diastolic trans-mitral flow velocity (A), E/A ratio, early diastolic mitral annular velocity (E'), late diastolic mitral annular velocity (A'), E/E' ratio, and E'/A' ratio. The LV ejection fraction (LVEF) was estimated by using the biplane method. Left ventricular diastolic function was measured concerning the 2016 ASE/EACVI Recommendations on Echocardiographic Assessment of Left Ventricular Diastolic Function [8].

### Statistical Methods

All statistical analyses were carried out using SPSS 20.0 for Windows (Chicago, IL, USA). Variables with a normal distribution were expressed as the mean ± standard deviation (SD) and those with an abnormal distribution were expressed as the median (interquartile range). The categorical variables were expressed as proportions. Differences in clinical and laboratory values between patients with stages 3-5 CKD were assessed by a Pearson chi-square test, Wilcoxon test, or ANOVA. Significant factors from univariate analysis were included in multiple linear regression analyses to assess the association between thyroid status and echocardiographic parameters. Statistical correlations between factors in each group were analyzed using Pearson correlation analysis. The statistical tests were two-sided, and a P value less than 0.05 was considered statistically significant.

## Results

### Clinical and biochemical characteristics of the study subjects

A total of 1164 patients with stages 3-5 CKD were enrolled, including 566 women and 598 men. There were 340 patients in stage 3 CKD, 366 in stage 4 CKD and 458 in stage 5 CKD. Baseline data are shown in table 1. The mean age of all stages was over 60 years, among which stage 3 was 65.06 years old, stage 4 was 66.47 years old, and stage 5 was 63.45 years old. There was no statistical difference in age among patients of different stages. (P = 0.137). There was no statistically significant difference in the gender distribution of each period (P = 0.909). The prevalence of hypertension in patients with stage 5 CKD was significantly higher than that in patients with stage 3 or 4 (P <0.001), while the prevalence of diabetes was the opposite (P = 0.007). All patients with stages 3-5 CKD suffer from anemia, and with the loss of kidney function, anemia becomes more severe (P <0.001). Patients at all stages had hypertriglyceridemia, and there were statistically significant differences in each stage. The prevalence of AITD was statistically different among all stages (P = 0.001). The prevalence of AITD in stages 3-5 CKD was 11.8%, 14.2%, and 21.4% respectively. Interestingly, there was no statistically significant difference in thyroid autoantibodies titers among patients with different stages. However, the positive rate of TPOAb in patients with stage 5 CKD was significantly higher than that in stage 3 or stage 4 CKD. (P = 0.004). There were statistically significant differences in CRP and pro-BNP among patients with different stages (P <0.001, P = 0.021 respectively), and both gradually increased with the deterioration of renal function. There was no significant difference in cTnT between patients with different stages (P> 0.05). As for echocardiography parameters, there was no significant difference in E/A among patients with different stages (P = 0.087), but multiple comparisons showed that the E/ A of patients with stage 5 CKD were higher than that in stage 4 CKD (P <0.05). There were statistically significant differences in E/E' among patients of different stages (P <0.001). But multiple comparisons only showed that the E / E' value of patients with stage 5 CKD were higher than that in stage 3 and stage 4 CKD, while no significant difference between stage 3 and stage 4 CKD. To some extent, E'/A' is statistically different among each stage (P = 0.053). Although multiple comparisons only showed a significant difference in E'/A' between stages 4 and 5 CKD (P <0.05). The average left ventricular ejection fraction (LVEF) of the included patients was greater than 50%, and no significant systolic dysfunction was found. But it can be found that as the disease progresses, LVEF decreases. Multiple comparisons suggested that LVEF was slightly lower in patients with stage 5 CKD than in patients with stage 3 CKD (P <0.05).

### Correlation between renal function and thyroid autoantibodies

As shown in table 2, the titer of TPOAb is positively correlated with SCr and BUN (r = 0.259, r = 0.311, P <0.05) and negatively correlated with eGFR (r = -0.289, P <0.05). There was a negative correlation between TGAb and eGFR (r = -0.287, P <0.05), but there was no significant correlation with SCr and BUN (P> 0.05). While TRAb was not significantly associated with SCr, BUN and eGFR (P > 0.05).

### Correlation of thyroid autoantibodies with risk factors for CVD

As shown in table 3, we used multiple linear regression to analyze the correlation between risk factors for CVD and thyroid autoantibodies. After adjusting for age and gender, TPOAb and TGAb were not significantly related to HGB, CRP, TG, TC, HDL-C, LDL-C. And TRAb only observed a significant positive correlation with CRP (r = 0.206, P <0.001).

As shown in table 4, the titer and positive rate of TPOAb and TGAb were statistically different in male and female patients. The correlations between diabetes mellitus, hypertension, HGB, CRP, TG, TC, HDL-C, and LDL-C levels and TPOAb and TGAb were statistically analyzed between different genders.

As shown in table 5 and 6, men with diabetes had higher TPOAb and TGAb titers (r = 0.137, P = 0.023; r = 0.159, P = 0.011). While there was no significant correlation between TPOAb and TGAb with hypertension, HGB, CRP, TG, TC, HDL-C, and LDL-C (P> 0.05).

And in female patients, TPOAb and TGAb were significantly negatively correlated with HGB (r = -0.213, P = 0.018; r = -0.188, P = 0.019). And there was no significant correlation between TPOAb and TGAb with hypertension, diabetes mellitus, CRP, TG, TC, HDL-C, LDL-C (P> 0.05).

### Correlation of thyroid autoantibodies with markers of cardiac function

As shown in Table 7, after adjusting for age and gender, there was no significant correlation between TPOAb and TGAb and CK, CK-MB, HBDH, cTnT, Mb, pro-BNP. However, TRAb was significantly negatively correlated with Mb (r = -0.178, P = 0.038), and positively correlated with pro-BNP (r = 0.213, P <0.001). Breaking the data down by gender, we found that TRAb was only associated with Mb and pro-BNP in women (r = -0.190, P = 0.015; r = 0.313, P <0.001). There was still no significant correlation between TPOAb and TGAb with CK, CK-MB, HBDH, cTnT, Mb, pro-BNP in different genders, as shown in Table 8.

### Correlation of thyroid autoantibodies with echocardiographic parameters

We used multiple linear regression to analyze the correlation between thyroid autoantibodies and E / A, E / E ', E' / A ', LVEF. After adjusting for age and sex, E/A was not associated with thyroid autoantibodies (P> 0.05). Patients with TPOAb positive had higher E / E' values (r = 0.181, P <0.001), while there was no significant correlation between E/E 'and TPOAb, TGAb, TRAb, and TGAb positive (P> 0.05). Interestingly, patients with TPOAb positive had higher LVEF (r = 0.159, P = 0.007). In addition, LVEF was significantly negatively correlated with TRAb (r = -0.112, P = 0.026). There was no significant correlation between E'/A' and TPOAb, TGAb, TRAb, TPOAb and TGAb positive (P> 0.05), as shown in Table 9.

## Discussion

The prevalence and mortality of CKD is increasing worldwide. Despite rising medical standards and an increase in the average survival time of patients, CKD will eventually lead to ESRD, which poses a great challenge to clinical work. There is a close connection between the thyroid and kidneys. Thyroid autoantibodies and their antigens may be deposited in the glomeruli and cause kidney damage. In addition, immune abnormalities in AITD patients may lead to secondary renal disease. Compared with the normal population, the prevalence of thyroid dysfunction is higher in patients with CKD. Patients with CKD are complicated with CVD in the early stage, and CVD is the leading cause of death in patients with CKD.

A total of 1164 patients with stages 3-5 CKD were enrolled in our study, including 566 women and 598 men. There were 340 patients in stage 3 CKD, 366 in stage 4 CKD and 458 in stage 5 CKD. We found that the prevalence of AITD gradually increased with the deterioration of renal function, and pro-BNP and CRP and the titers of TPOAb and TGAb gradually increased. Patients with stage 5 CKD have higher TPOAb positive rate and E/A, E/E ' and E'/A'. The TG of patients in each stage was high, and the increase of TG in stage 5 CKD was more obvious. The prevalence of AITD was statistically different in each stage, and the prevalence was 11.8%, 14.2%, and 21.4% respectively. In patients with stage 3-5 CKD, TRAb was significantly positively correlated with CRP, and negatively correlated with Mb and while only positively correlated with pro-BNP in female patients. At the same time, there was big gender differences between TPOAb and TGAb. Among males, patients with diabetes have higher levels of TPOAb and TGAb. Among female patients, TPOAb and TGAb are significantly negatively correlated with HGB. The TPOAb positive patients had higher E/E' and LVEF, while patients with higher TRAb titers had lower LVEF.

### Thyroid immune disorder and CKD

Similar immune complex deposits were observed in thyroid follicular epithelium and glomerular basement membrane in patients with glomerulonephritis associated with Hashimoto's thyroiditis (HT). And the same circulating immune complex can be involved in both diseases [9]. W Hasnain et al. found deposition of TPOAb in renal of patients with membranous nephropathy complicated with Graves' disease (GD), suggesting that TPOAb may be involved in the occurrence of membranous nephropathy [10]. Therefore, some autoimmune-mediated glomerulonephritis and AITD may have similar pathogenesis.

Our study found that the prevalence of AITD gradually increased in patients with stage 3-5 CKD. The positive rate of TPOAb in patients with stage 5 CKD was significantly higher than that in stage 3 and stage 4 CKD. With the decrease of eGFR, titers of TPOAb and TGAb gradually increased, suggesting that there may be some interaction between AITD and CKD. There may be antigenic cross-reactions between AITD and CKD, but these hypotheses require further research to confirm. It has been reported

that patients with hyperthyroidism developed membranous nephropathy after treatment with prothiouracil, and $^{131}$I treatment led to ANCA positive crescent nephritis [18,23]. And the pathogenesis remains to be further investigated.

**Correlation between thyroid immune disorder and echocardiographic parameters**

Echocardiography has the advantages of accurate, objective, reproducible, and safe operation in evaluating cardiac function. It can display patients' ventricular systolic and diastolic processes, cardiac cavity structure, and blood flow. Pro-BNP may be used to diagnose and evaluate the prognosis of heart failure, but it is not used to distinguish the types of heart failure. Echocardiography can not only be used to evaluate the cardiac function and prognosis of patients, but also can be used to classify the types of heart failure. Studies have shown that the sensitivity and specificity of various echocardiographic parameters in evaluating ejection fraction-retaining heart failure are high, 95% and 100%, respectively [11]. Echocardiography plays an important role in ejection fraction-retaining heart failure. Echocardiography can evaluate the left ventricular diastolic function by measuring the E peak, A peak, E/A, E peak deceleration time, A 'and E/E', and so on. Kasner et al. [12] found that TDI combined with PW examination of E/E' can better assess left ventricular diastolic function. Similarly, studies have shown that E/E' is significant in evaluating left ventricular filling pressure [13] and can well predict the occurrence of adverse events during ESRD [14]. Sutter et al pointed out that E '/A' decreases and E/ E 'increases with age [15]. These results are consistent with the results of our study.

Our study found that the E/E' increased significantly in patients with stage 5 CKD, with an average value of 16.89, which was higher than that in stage 3 and stage 4. Patients with stage 5 CKD have already had ejection fraction-preserving heart failure. The E/E' of patients with TPOAb positive is higher, suggesting that patients with TPOAb positive may be more prone to diastolic dysfunction, and early intervention should be given. For the E'/A', only patients with stage 5 CKD were found to be higher, but there was no statistical difference in the analysis of E'/A' in patients with stages 3-5 CKD. E'/A' was also not found to be significantly related to thyroid autoantibodies, which is consistent with guidelines that do not recommend the use of E'/A' to assess cardiac function. Besides, patients with TPOAb positive have higher LVEF values, while TPOAb has a negative correlation with HGB in female patients, and anemia may increase LVEF. The specific mechanism needs further study. Patients with higher TRAb have lower LVEF values, and TRAb is significantly positively correlated with CRP. CRP can promote the formation of AS, can also cause coronary spasm, trigger myocardial ischemia, and cause LVEF to decrease. For E/A, E/E', E'/A', and LVEF, no significant difference was found between stage 3 and stage 4 CKD. Only the disease progressed to stage 5 CKD, heart dysfunction that may be detected by echocardiography may occur.

# Conclusion

The prevalence of AITD in patients with stages 3-5 CKD was 11.8%, 14.2%, and 21.4%, respectively. With the decline of renal function, the prevalence of AITD increased gradually, and the titers of TPOAb and TGAb gradually increased. The average E/E' of patients with stage 5 CKD was 16. Women with TPOAb positive may be more prone to diastolic heart failure. TRAb may reduce LVEF by promoting inflammation or triggering coronary spasm.

# Declarations

- **Ethics approval and consent to participate:** The study was approved by the ethics committee of the Third Affiliated Hospital of Southern Medical University and all participants provided informed consent in writing.
- **Consent for publication:** Manuscript is approved by all authors for publication.
- **Availability of data and materials:** The raw/processed data required to reproduce these findings cannot be shared at this time as the data also forms part of an ongoing study.
- **Competing interests:** No conflict of interest exits in the submission of this manuscript.
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- **Authors' contributions:** Yongqiang Li conceived the idea for this study. Weicheng Xu, Ge qian, Yuxiang Huang, Chijian Li and Shiyi Liang participated in the collection and collation of clinical data, and Weicheng Xu analyzed the collected data. Yongqiang Li and Yunfang Zhang proofread the results. The manuscript was drafted by Weicheng Xu. All authors critically reviewed and approved the final manuscript.
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# Tables

Table 1: Characteristics of subjects in terms of the stage of CKD`x±s`

| Characteristics | Total (n=1164) | Stage 3 (n=340) | Stage 4 (n=366) | Stage 5 (n=458) | P-Value |
|---|---|---|---|---|---|
| Age (years) | 64.95±14.84 | 65.96±16.86 | 66.47±14.41 | 63.45±13.51 | 0.137 |
| Male, n (%) | 598 (51.4%) | 178(52.4%) | 186(50.8%) | 234(51.1%) | 0.909 |
| Diabetes mellitus, n (%) | 384(33.0%) | 112(32.9%) | 142(38.8%) * | 130(28.4%) *# | 0.007 |
| Hypertension, n (%) | 652(56.0%) | 174(51.2%) | 183(50.0%) | 295(64.4%) *# | 0.001 |
| HGB (g/L) | 96.29±24.74 | 112.84±25.09 | 91.50±17.96 * | 88.16±22.51 * | 0.001 |
| CRP (mg/L) | 34.35±40.37 | 21.98±38.37 | 32.97±48.14* | 42.95±34.81*# | 0.001 |
| eGFR(ml/min/1.73m2) | 21.46±16.43 | 43.2±8.39 | 21.62±4.24* | 6.74±2.94*# | 0.001 |
| SCr (μmol/L) | 471.16±384.14 | 143.68±28.19 | 261.16±58.46* | 808.7±340.43*# | 0.001 |
| BUN (mmol/L) | 16.85±9.71 | 9.71±5.39 | 15.01±6.68* | 22.69±9.79*# | 0.001 |
| UA (μmol/L) | 432.85±142.52 | 425.16±152.76 | 441.5±141.87 | 433.01±136.50 | 0.672 |
| TG (mmol/L) | 2.62±1.41 | 1.72±1.01 | 1.63±1.04 | 3.70±0.94*# | 0.001 |
| TC (mmol/L) | 4.29±1.21 | 4.32±1.43 | 4.41±1.15 | 4.21±1.07 | 0.342 |
| HDL-C (mmol/L) | 1.15±0.32 | 1.17±0.33 | 1.17±0.3 | 1.13±0.32 | 0.485 |
| LDL-C (mmol/L) | 1.69±1.11 | 1.88±1.14 | 1.62±1.15 | 1.61±1.06* | 0.065 |
| VLDL-C (mmol/L) | 0.77±0.45 | 0.79±0.47 | 0.74±0.47 | 0.78±0.43 | 0.741 |
| CK (IU/L) | 155.35±364.39 | 145.38±498.88 | 125.31±138.6 | 176.55±355.99 | 0.467 |
| CK-MB (IU/L) | 18.40±22.41 | 20.28±39.96 | 16.89±6.96 | 18.13±11.19 | 0.511 |
| HBDH (IU/L) | 181.30±83.70 | 169.52±111.19 | 187.83±77.22 | 184.48±67.26 | 0.196 |
| cTnT (ng/mL) | 0.09±0.18 | 0.07±0.22 | 0.09±0.1 | 0.11±0.17 | 0.283 |
| Mb (ng/mL) | 193.76±206.74 | 146.65±283.91 | 167.56±167.61 | 234.12±162.44*# | 0.001 |
| pro-BNP (pg/ml) | 8983.17±11005.72 | 6947.26±8490.39 | 8483.26±10856.85 | 10321.04±12478.78* | 0.021 |
| TSH (uIU/mL) | 1.91±0.85 | 1.94±0.83 | 1.78±0.77 | 1.95±0.90 | 0.236 |
| TGAb (IU/ml) | 135.18±573.61 | 57.84±168.25 | 153.39±557.03 | 170.98±711.61 | 0.145 |
| TRAb (IU/L) | 0.39±0.16 | 0.40±0.10 | 0.42±0.18 | 0.38±0.23# | 0.115 |
| TPOAb (U/mL) | 26.50±62.80 | 19.19±21.89 | 30.84±62.71 | 29.02±79.14 | 0.249 |
| TPOAb positive | 156(13.4%) | 32(9.4%) | 40(10.9%) | 77(16.8%) *# | 0.004 |
| TGAb positive | 83(7.1%) | 17(5.0%) | 29(7.9%) | 37(8.1%) | 0.192 |
| AITD | 190(16.3%) | 40(11.8%) | 52(14.2%) | 98(21.4%) *# | 0.001 |
| E/A | 0.99±0.55 | 0.98±0.56 | 0.9±0.29 | 1.05±0.63# | 0.087 |

| | | | | | |
|---|---|---|---|---|---|
| E/E' | 11.46±10.24 | 5.58±7.65 | 7.61±7.57 | 16.89±10.39*# | 0.001 |
| E'/A' | 0.68±0.34 | 0.68±0.24 | 0.61±0.22 | 0.71±0.43# | 0.053 |
| LVEF% | 65.32±8.21 | 67.38±7.03 | 65.42±6.83 | 64.03±9.27* | 0.001 |

*Significantly different (P<0.05) from the patients with stage 3 of CKD; #significantly different (P<0.05) from the patients with stage 4 of CKD.

Table 2: Relationship between renal function and thyroid hormone and antibody levels

| r | TPOAb | TGAb | TRAb |
|---|---|---|---|
| SCr | 0.259¥ | 0.259 | -0.011 |
| BUN | 0.311¥ | 0.258 | -0.118 |
| eGFR | -0.289¥ | -0.287¥ | 0.202 |

¥ Significant correlation at the 0.05 level (both sides).

Table 3: Multiple linear regression of thyroid-associated antibody and CVD risk factors

| | TPOAb | | TGAb | | TRAb | |
|---|---|---|---|---|---|---|
| | r | P | r | P | r | P |
| Hypertension | -0.004 | 0.935 | 0.056 | 0.257 | -0.064 | 0.184 |
| Diabetes mellitus | 0.045 | 0.341 | 0.038 | 0.437 | 0.001 | 0.986 |
| HGB | -0.073 | 0.127 | -0.075 | 0.126 | 0.014 | 0.772 |
| CRP | -0.027 | 0.567 | -0.028 | 0.564 | 0.206 | **0.001** |
| TG | 0.012 | 0.803 | 0.046 | 0.347 | -0.078 | 0.110 |
| TC | 0.043 | 0.370 | 0.041 | 0.403 | 0.038 | 0.436 |
| HDL | 0.059 | 0.226 | 0.005 | 0.922 | 0.042 | 0.392 |
| LDL | 0.016 | 0.735 | -0.031 | 0.531 | -0.002 | 0.973 |

Table 4: Gender differences in thyroid autoantibodies（$\bar{x}$±s）

| | male | female | P |
|---|---|---|---|
| TPOAb | 19.45±40.31 | 38.64±87.98 | 0.001 |
| TGAb | 68.57±341.44 | 256.06±815.96 | 0.002 |
| TRAb | 0.40±0.16 | 0.40±0.18 | 0.780 |
| TPOAb(+), n(%) | 58(9.1%) | 102(19.4%) | 0.001 |
| TGAb(+), n(%) | 17(2.7%) | 78(14.8%) | 0.001 |

Table 5: Multiple linear regression analysis of TPOAb and risk factors for CVD in different genders

| | Male | | Female | |
|---|---|---|---|---|
| | r | P | r | P |
| Hypertension | -0.018 | 0.656 | 0.002 | 0.983 |
| Diabetes mellitus | 0.137 | 0.023 | -0.029 | 0.707 |
| HGB | 0.041 | 0.495 | -0.213 | 0.018 |
| CRP | -0.026 | 0.666 | -0.043 | 0.580 |
| TG | -0.021 | 0.729 | 0.042 | 0.587 |
| TC | -0.012 | 0.843 | 0.112 | 0.155 |
| HDL | -0.048 | 0.423 | 0.166 | 0.034 |
| LDL | 0.032 | 0.591 | 0.037 | 0.642 |

Table 6: Multiple linear regression analysis of TGAb and risk factors for CVD in different genders

| | Male | | Female | |
|---|---|---|---|---|
| | r | P | r | P |
| Hypertension | 0.041 | 0.504 | 0.067 | 0.401 |
| Diabetes mellitus | 0.159 | 0.011 | -0.047 | 0.551 |
| HGB | 0.045 | 0.464 | -0.188 | 0.019 |
| CRP | -0.040 | 0.518 | -0.034 | 0.669 |
| TG | -0.022 | 0.721 | 0.102 | 0.200 |
| TC | 0.005 | 0.933 | 0.093 | 0.247 |
| HDL | -0.060 | 0.335 | 0.066 | 0.410 |
| LDL | 0.072 | 0.249 | -0.065 | 0.420 |

Table 7: Multiple linear regression of thyroid hormones and cardiac function markers

| | TPOAb | | TGAb | | TRAb | |
|---|---|---|---|---|---|---|
| | r | P | r | P | r | P |
| CK | -0.037 | 0.671 | -0.003 | 0.973 | -0.051 | 0.559 |
| CK-MB | 0.041 | 0.640 | -0.039 | 0.686 | 0.141 | 0.107 |
| HBDH | 0.037 | 0.576 | 0.040 | 0.594 | -0.051 | 0.434 |
| cTnT | -0.029 | 0.607 | -0.014 | 0.814 | -0.055 | 0.322 |
| Mb | -0.053 | 0.540 | -0.001 | 0.990 | -0.178 | 0.038 |
| Pro-BNP | -0.039 | 0.514 | -0.051 | 0.417 | 0.213 | 0.001 |

Table 8: Multiple linear regression of TRAb and Mb and pro-BNP in female

| | TRAb | |
|---|---|---|
| | r | P |
| Mb | -0.190 | 0.015 |
| Pro-BNP | 0.313 | 0.001 |

Table 9: Multiple linear regression analysis of thyroid hormones and related antibodies and echocardiographic parameters

| | E/A | | E/E’ | | E’/A’ | | LVEF | |
|---|---|---|---|---|---|---|---|---|
| | r | P | r | P | r | P | r | P |
| TPOAb | -0.029 | 0.563 | 0.106 | 0.105 | 0.006 | 0.900 | -0.054 | 0.407 |
| TGAb | -0.045 | 0.369 | 0.099 | 0.129 | 0.008 | 0.869 | -0.069 | 0.291 |
| TRAb | 0.068 | 0.175 | 0.029 | 0.561 | 0.031 | 0.539 | -0.112 | 0.026 |
| TPOAb(+) | -0.054 | 0.284 | 0.181 | 0.001 | 0.031 | 0.534 | 0.159 | 0.007 |
| TGAb(+) | -0.063 | 0.208 | -0.069 | 0.179 | -0.041 | 0.426 | -0.057 | 0.338 |