DIAGNOSTIC VALUE OF SERUM SST2 IN ELDERLY HYPERTENSION WITH LEFT VENTRICULAR HYPERTROPHY AND ASSESSMENT OF LEFT VENTRICULAR HYPERTROPHY SEVERITY

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ABSTRACT

Objective*: To analyze the value of serum soluble ST2 (sST2) in the diagnosis of hypertension (HP) complicated with left ventricular hypertrophy (LVH) and to evaluate the severity of left ventricular hypertrophy in the elderly.*

Methods: *Two hundred and four elderly patients with hypertension treated in our hospital from January 2019 to January 2020 were collected, and the patients were divided into the LVH group (n=68), the early LVH group (n=73), and the early HP group (63). The levels of left ventricular end-diastolic diameter (LVDD), left ventricular posterior wall thickness (LVPWTD), and end-diastolic ventricular septal thickness (IVSTD) were measured by echocardiography. Four ml of fasting venous blood were collected from each group, then serum levels of sST2, Galectin-3, and transforming growth factor β1(TGF-β1) were detected by enzyme linked immunosorbent assay. Serum indexes of patients in each group were compared. Pearson's linear correlation analysis was used to analyze the correlation between sST2, Galectin-3, and TGF- 1 and LVMI. Moreover, ROC curve was used to examine the value of sST2, Galectin-3, and TGF- 1 in the diagnosis of hypertensive patients with left ventricular hypertrophy.*

Results: *The levels of LVDD, LVPWTD, and IVSTD in the LVH group were significantly higher than those in the early LVH group and the simple HP group. Additionally, IVSTD levels in the early LVH group were considerably higher than those in the simple HP group, with statistically significant differences (P<0.05). There was no significant difference in LVDD or LVPWTD between the early LVH group and the simple HP group (P>0.05). The serum levels of sST2, Galectin-3, and TGF- 1 in the LVH group and the early LVH group were notably higher than those in the HP group alone. Furthermore, the serum levels of sST2, Galectin-3, and TGF-1 in the LVH group were significantly higher than those in the early LVH group, with statistically significant differences (P<0.05). Pearson linear correlation analysis showed that LVMI was positively correlated with sST2, Galectin-3, and TGF- 1 (R=0.335, 0.156 and 0.286, P<0.05 or <0.01, respectively). ROC curve analysis showed that the AUC, sensitivity, and specificity of sST2 in diagnosing left ventricular hypertrophy in elderly patients with hypertension were 0.859, 86.37%, and 82.17%, respectively. The AUC, sensitivity, and specificity of GALectin-3 in diagnosing left ventricular hypertrophy in elderly patients with hypertension were 0.712, 75.34%, and 71.04%, respectively. The AUC, sensitivity, and specificity of TGF- 1 in diagnosing left ventricular hypertrophy in elderly patients with hypertension were 0.723, 69.58%, and 70.24%, respectively.*

Conclusion: *The levels of sST2, Galectin-3, and TGF- 1 were significantly higher in elderly patients with HP combined with LVH and increased with the aggravation of the severity of LVH. The three levels were positively correlated with LVMI and had a particular value in the diagnosis of HP combined with LVH in the elderly. Furthermore, sST2 had the highest diagnostic value and could be widely used in clinical practice.*

Keywords: *sST2, diagnosis, hypertension, left ventricular hypertrophy, severity, value.*

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Introduction

Hypertension (EH) is a cardiovascular disease characterized by high blood pressure and is the most common in the clinic[1]. In recent years, the incidence of hypertension in China is increasing year by year. Long-term hypertension can lead to serious injury of the heart, brain, kidney, and other essential target organs, seriously threatening human health[2]. Left ventricular hypertrophy (LVH) is a compensatory left ventricular hypertrophy caused by the combined effects of sustained hypertension, cardiac overload, and other blood factors[3]. HP combined LVH, myocardial weight increase, ventricular remodeling, and increased myocardial ischemic events lead to acute myocardial infarction, congestive heart failure,

and the occurrence of ventricular arrhythmia. This is the cause of heart, cerebrovascular disease, and renal dysfunction independent risk factors, which seriously affect patients' quality of life and even mortality[4]. Therefore, the early assessment of elderly patients with HP combined with LVH plays a vital role in the early treatment and improvement of patients' quality of life. Soluble ST2 (sST2), a member of the interleukin-1 receptor family, was highly expressed in myocytes or fibroblasts and sST2, which was the decoy receptor for IL-33[5-7].

Additionally, transforming growth factor-1 (TGF-β1) is a member of the TGF-β superfamily, while galectin-3 is a member of the galectin-glycoside lectin family. However, both were abnormally expressed in elderly hypertensive patients with left ventricular hypertrophy[8]. In this study, 204 elderly patients with hypertension treated in our hospital from January 2019 to January 2020 were selected as observation subjects to analyze the value of serum factors, such as sST2, in diagnosing elderly patients with HP and LVH and assessing the severity of left ventricular hypertrophic levels.

Materials and methods

General information

A total of 204 elderly patients with hypertension treated in our hospital from January 2019 to January 2020 were collected.

Inclusion criteria:

• All patients met the diagnostic criteria of HP in the Guidelines for Hypertension Prevention and Treatment in China[9];

• Systolic pressure (SBP) ≥140mmHg or diastolic pressure (DBP) ≥90mmHg;

• All patients were between 60-79 years old;

• Patients and their family members signed the informed consent form.

Exclusion criteria:

• Patients with secondary hypertension;

• The patient's heart, liver, kidney, and other critical organs have serious functional disorders;

• The patient was hospitalized due to acute myocardial infarction, unstable angina pectoris, or acute exacerbation of chronic heart failure over the past six months;

• Patients with malignant tumors;

• Dilated cardiomyopathy, hypertrophic cardiomyopathy, rheumatic heart disease, etc.;

• Patients rejected during the study or terminated from the study for other reasons.

Patients were divided into HP combined with the LVH group (n=68), early HP combined with the LVH group (n=73), and a control group (n=63), according to the "Expert Consensus on Diagnosis and Treatment of Asian Hypertension Combined with Left Ventricular Hypertrophy." Among them, patients ≥95g/m^2 (female) and LVMI≥115 g/m^2 (male) were grouped into HP combined with LVH.

IVST or LVPWT≥10mm (female) or ≥11mm (male) but did not meet the diagnostic criteria for left ventricular hypertrophy were deemed early HP combined with LVH, while the remaining patients were HP non-LVH.

There were 68 patients in the HP combined LVH group, including 35 males and 33 females, with an average age of (65.06±4.78) years old and an average BMI of (20.05±0.98) Kg/m^2. There were 73 patients in the early HP combined LVH group, including 38 males and 35 females, with an average age of (65.06±3.76) years old and an average BMI of (20.03±1.05) Kg/m^2.

There were 63 patients in the HP group, 32 males and 31 females, with an average age of (65.25±4.31) years old and an average BMI of (20.11±0.78) Kg/m^2. There were no statistically significant differences in age, sex, and BMI between the groups ($P > 0.05$).

Observation index

Serum detection

Four ml of fasting venous blood of each group was collected in the early morning, placed at room temperature for 20 min, centrifuged at 3000R/min for 10 min, while the serum was carefully separated and stored at -70°C to avoid repeated freezing-thawing. Serum sST2, Galectin-3, and TGF- β1 levels were measured by enzyme-linked immunosorbent assay.

Echocardiography detection

The instrument is a heart colored ultrasound instrument provided by the Jiangsu Jiahua Electronic Equipment Co., LTD., with a frequency of 1.7-3.4mhz. All patients rested for about 15 min before their examination to ensure stable breathing. The patient was then placed in the supine position, while the room temperature was 20-25°C. Measurement of cardiac color Doppler echocardiography was then taken, including the vertical distance between the left ventricle and the right ventricle from the diastolic thickness of the interventricular septum (IVSTD), the vertical distance between the endocardial surface of the posterior wall of the left ventricle, and the epicardial surface from the diastolic thickness of the left

ventricular posterior wall (LVPWTD), as well as the ventricular septal surface of the left ventricle and the left ventricular posterior wall of the endocardial surface of the vertical distance between the left ventricular end-diastolic diameter (LVDD). Thus, the Left Ventricular Mass Index (g/m^2) =LVM (g) /BSA (m^2).

Statistical methods

All data were analyzed by an SPSS20.0 software package, while all measurements were compared to (x±s), with a comparison between groups using a t-test. All counts were expressed as percentages, and an χ^2 test was used to compare between groups. Pearson linear correlation analysis sST2, Galectin-3, and the correlation between TGF-β1 and LVMI were used. The value of sST2, Galectin-3, and TGF-β1 in the diagnosis of hypertension with left ventricular hypertrophy was analyzed by ROC curve. Furthermore, P<0.05 was statistically significant.

Results

Comparison of echocardiography indexes between the groups

The IVSTD levels of patients in the LVH group were significantly higher than those in the early LVH group and the simple HP group.

In comparison, the IVSTD levels in the early LVH group were considerably higher than those in the simple HP group, with statistically significant differences (P<0.05).

There was no noticeable difference in LVDD or LVPWTD between the early LVH group and the simple HP group (P>0.05). See Table 1.

Group	n	LVDD (mm)	LVPWTD (mm)	IVSTD (mm)
LVH group	68	50.26±4.28[ab]	9.36±0.87[ab]	12.82±1.34[ab]
Early LVH group	73	46.32±3.48	8.78±0.74	11.49±1.28[a]
Simple HP group	63	46.37±3.01	8.65±0.72	9.15±0.81

Table 1: Comparison of echocardiography indicators in each group ($\bar{x}$±s).
Note: a represents [a]P<0.05 compared with HP alone; b was compared with the early LVH group, [b]P<0.05.

Comparison of serum sST2, Galectin-3, and TGF-β1 levels in each group

The serum levels of sST2, Galectin-3, and TGF-β1 in the LVH group and the early LVH group were significantly higher than those in the HP group alone. In comparison, the serum levels of sST2, Galectin-3, and TGF-β1 in the LVH group were considerably higher than those in the early LVH group, with statistically notable differences (P<0.05). These results are shown in Table 2.

Group	n	sST2 (ng/ml)	Galectin-3 (ng/ml)	TGF-β1 (ng/ml)
LVH group	68	28.73±7.25[ab]	8.06±4.15[ab]	17.598.59[ab]
Early LVH group	73	23.15±5.38[a]	5.96±1.58[a]	13.64±5.14[a]
Simple HP group	63	22.01±4.37	5.16±2.05	12.45±4.42

Table 2: Comparison of serum sST2, GALectin-3, and TGF-β1 levels in each group ($\bar{x}$±s).
Note: a represents [a]P<0.05 compared with HP alone; b was compared with the early LVH group, [b]P<0.05.

Correlation analysis of sST2, Galectin-3, and TGF-β1 with echocardiography indexes

Pearson linear correlation analysis showed that LVMI was positively correlated with sST2, Galectin-3, and TGF-β1 (R = 0.335, 0.156, and 0.286, P<0.05 or <0.01, respectively). See Table 3.

Index	LVMI	
	r	*P*
sST2	0.335	0.001
Galectin-3	0.156	0.046
TGF-β1	0.286	0.012

Table 3: Correlation analysis between sST2, Galectin-3, and TGF-β1 and echocardiography indexes.

Value analysis of sST2, Galectin-3, and TGF-β1 in diagnosing left ventricular hypertrophy in elderly patients with hypertension

ROC curve analysis showed that the AUC, sensitivity, and specificity of sST2 in diagnosing left ventricular hypertrophy in elderly patients with hypertension were 0.859, 86.37%, and 82.17%, respectively. The AUC, sensitivity, and specificity of Galectin-3 in diagnosing left ventricular hypertrophy in elderly patients with hypertension were 0.712, 75.34%, and 71.04%, respectively. The AUC, sensitivity, and specificity of TGF-β1 in diagnosing left ventricular hypertrophy in elderly patients with hypertension were 0.723, 69.58%, and 70.24%, respectively. See Table 4.

Index	AUC	95%CI	Sensitivity	Specificity
sST2	0.859	0.804-0.902	86.37%	82.17%
Galectin-3	0.712	0.659-0.764	75.34%	71.04%
TGF-β1	0.723	0.679-0.784	69.58%	70.24%

Table 4: Value analysis of sST2, Galectin-3, and TGF-β1 in diagnosing left ventricular hypertrophy in elderly patients with hypertension.

Discussion

Among all target organ injuries induced by HP, LVH is regarded as one of the most common injuries in HP patients. Thus, the occurrence and development of LVH seriously affects the prognosis of HP patients[10]. At present, electrocardiogram (ECG) and echocardiography are commonly used to diagnose LVH. An electrocardiogram has the advantages of being simple, easily operational, and having a low price. However, it is less sensitive to LVH in the early stages and commonly misses a diagnosis. The sensitivity of echocardiography is high, but the location and examination method of ultrasound may affect the timely diagnosis and early recognition. Therefore, it is of great significance to find a sensitive and easy to operate method for early diagnosis of elderly patients with HP complicated with LVH.

Thus, the sST2 is a vital biomarker of heart disease, and the specific binding of ST2L and IL-33 ligand play a specific protective role in myocardial cells. However, sST2 can bind to IL-33 receptors, blocking the ST2L/IL-33 pathway that has a protective effect on myocardium[11]. Studies suggest that sST2 can predict the prognosis of patients with acute heart failure as well as the mortality of patients with acute coronary syndrome[12]. TGF-β1 is primarily expressed in vascular smooth muscle cells, macrophages, endothelial cells, and hematopoietic cells, regulating cell proliferation, angiogenesis, fibrosis, lipid metabolism, and immune regulation[13]. Studies have found that TGF-β1 can promote the generation of fibrosis and regulate cardiac hypertrophy, while increased myocardial pressure load in HP patients can lead to the activation of serum TGF-β1. This encourages the expression of contractility protein, leading to left ventricular cardiac hypertrophy[14]. Galectin-3 plays a role in regulating cell growth and apoptosis, mediating inflammatory response, and cell adhesion. Foreign studies have found that Galectin-3 is associated with the degree of myocardial fibrosis in mice[15].

In this study, the levels of sST2, Galectin-3, and TGF-β1 in the LVH group and the early LVH group were significantly higher than those in the HP group alone. Furthermore, the levels of sST2, Galectin-3, and TGF-β1 in the LVH group were significantly higher than those in the early LVH group, with statistically significant differences ($P<0.05$). These results indicate that the levels of sST2, Galectin-3, and TGF-β1 were considerably higher in elderly patients with HP combined with LVH and changed with the severity of LVH. Thus, this finding may provide strong support for the diagnosis of HP combined with LVH in the elderly.

To further analyze the value of sST2 combined with LVH in the elderly, Pearson linear correlation analysis was used in this study to determine that LVMI was significantly positively correlated with sST2, Galectin-3, and TGF- 1 ($R = 0.335, 0.156$, and 0.286, respectively, $P<0.05$ or <0.01). ROC curve analysis demonstrated that the AUC, sensitivity, and specificity of sST2 in diagnosing left ventricular hypertrophy in elderly patients with hypertension were 0.859, 86.37%, and 82.17%, respectively. The AUC, sensitivity, and specificity of GALectin-3 in diagnosing left ventricular hypertrophy in elderly patients with hypertension were 0.712, 75.34%, and 71.04%, respectively. The AUC, sensitivity, and specificity of TGF-β1 in diagnosing left ventricular hypertrophy in elderly patients with hypertension were 0.723, 69.58%, and 70.24%, respectively. These findings suggest that sST2, Galectin-3, and TGF -β1 on the diagnosis of senile HP combined with LVH have good predictive value. Moreover, the sST2 detection compared with the other two indicators for diagnosis of senile HP combined with LVH have a better predictive value, as well as helping doctors diagnose elderly HP combined with LVH and taking corresponding measures. These have a paramount important significance in patients with effective treatment.

To sum up, the levels of sST2, Galectin-3, and TGF-β1 were significantly higher in elderly patients with HP combined with LVH and increased with the aggravation of the severity of LVH. These three levels were positively correlated with LVMI and had particular value in diagnosing of elderly patients with HP combined with LVH, among which sST2 had the highest diagnostic value and could be widely used in clinical practices.

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