

Big Data Study on Thyroid Dysfunction in Patients with Chronic Nephropathy

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Keywords: Patients with chronic kidney disease; Thyroid gland; Abnormal function; Big data

Abstract: The prevalence and incidence of CKD(Chronic Kidney Disease) are increasing all over the world. In the disease progression of CKD patients, most patients are accompanied by abnormal synthesis, secretion, metabolism and degradation of TH(Thyroxine). This paper studies the big data of thyroid dysfunction in CKD patients. Studies have shown that renal tubular reabsorption in CKD patients is decreased, and the reabsorption of thyroid hormone-binding globulin complex binding T3 and T4 is reduced, resulting in a large number of T3 and T4 lost with urine. Especially in nephrotic syndrome, due to the damage of glomerular filtration barrier, a large amount of protein is lost from urine, including thyroid hormone binding globulin, which hinders the synthesis of TH and eventually leads to the decrease of TH level in the body. At the same time, it affects the metabolism of hypothalamus-pituitary-thyroid axis and T4 in peripheral tissues, reduces the levels of thyroid binding protein and thyroid pre-binding protein, and changes the intake and storage of iodide in thyroid. Low T3 syndrome is the most common change of TH in these patients.

1. Introduction

Chronic kidney disease is considered as a global public health problem, which is more common among the elderly and related to many diseases. Thyroid gland is one of the most important glands in human body to regulate physiological functions. The prevalence and incidence of CKD are increasing all over the world. In the disease progression of CKD patients, most patients are accompanied by abnormalities in TH synthesis, secretion, metabolism and degradation. Previous studies have shown that thyroid diseases are related to creatinine, estimated glomerular filtration rate, measured glomerular filtration rate and cysteine protease inhibitor [1]. Thyroid hormone plays a very important role in regulating metabolism, development, protein synthesis and influencing the function of other hormones. Since 2011, the primary kidney disease spectrum of hospitalized patients in China has evolved from nephritis to kidney damage related to common chronic diseases such as diabetes and hypertension, which is also the main type of kidney disease in western countries [2]. The kidney mainly promotes iodide clearance through glomerular filtration. Therefore, in patients with progressive renal failure, with the decrease of glomerular filtration rate, iodide excretion decreases, inorganic iodine content in plasma increases, and iodine uptake by thyroid increases. The increase of iodine pool in thyroid gland of uremia patients can lead to the decrease of thyroid uptake of radioactive iodine; The increase of total inorganic iodine in the body may block the synthesis of thyroid hormone. This change can explain the slightly higher incidence of mild goiter and hypothyroidism in patients with chronic renal failure. The high-risk population of CKD accounts for a high proportion in the community population, so it is of great significance to carry out effective early screening and prevention of CKD in the community to improve the prognosis of patients and reduce the burden of disease. This paper attempts to study the big data of thyroid dysfunction in CKD patients. Kidney plays an important role in the production, secretion and degradation of thyroid hormone. Therefore, renal injury will lead to thyroid physiological dysfunction, and any level of hypothalamus-pituitary-thyroid axis may be affected, causing changes in hormone production, secretion and distribution [3-4]. Patients with uremia often need thyroid function test to know whether there is abnormal thyroid function. The reasons why the prevalence rate of CKD is high and increasing year by year are as follows: with the improvement of material

living standard and working conditions, some nutrients such as carbohydrates, fat and salt are eaten too much and exercise is too little; Excessive work pressure, high mental stress, serious lack of sleep, as well as smoking, alcoholism, various environmental pollution and other factors, make metabolic diseases such as hyperglycemia, hypertension, lipid metabolism disorder, hyperuricemia, obesity and so on, and the prevalence of CKD secondary to these metabolic diseases is increasing day by day. Coupled with the complexity of medical information data itself, it is very difficult to obtain accurate data of large-scale and multi-center community medical institutions in China at this stage [5].

2. Materials and methods

2.1 Research object

This study selected CKD5-8 patients diagnosed from January 2022 to June 2023 at 7 hospitals affiliated with a Jiao Tong University School of Medicine, including Renji Hospital, Ruijin Hospital, Longhua Hospital, Shuguang Hospital, Ninth People's Hospital, Dongfang Hospital, and Tenth People's Hospital, regardless of gender or ethnicity, Provide a detailed explanation of the research objectives and methods to the patients participating in this study, and obtain their informed consent [6]. Exclusion criteria: 1. Patients undergoing hemodialysis, peritoneal dialysis, and previous history of thyroid disease; 2. Clinical hypothyroidism and hyperthyroidism; 3. Taking drugs that affect thyroid function, such as glucocorticoids, amiodarone, antiepileptic drugs, tyrosine kinase inhibitors, etc. The non CKD population who underwent routine physical examination at the health examination center of the hospital will be used as the control group, excluding those with a history of thyroid diseases [7]. All research subjects have signed an informed consent form and obtained the consent of the Ethics Committee of Linyi Central Hospital. Referring to the 2022 edition of the Guiding Principles for Clinical Research of Traditional Chinese Medicine New Drugs issued by the National Drug Administration, the various syndromes of this deficiency are divided into spleen kidney qi deficiency, spleen kidney yang deficiency, spleen kidney qi yin deficiency, liver kidney yin deficiency, and yin yang deficiency. The various syndromes of pathogenic excess are divided into dampness turbidity syndrome, dampness heat syndrome, blood stasis syndrome, and dampness toxin syndrome [8].

2.2 Survey methods

In this experiment, the gender, age, onset time, related medical history [hypertension, diabetes, hepatitis, systemic lupus erythematosus (SLE)] and related laboratory examination indexes [including blood calcium, blood phosphorus, alkaline phosphatase (ALP), albumin (Al-bumin, ALB), alanine aminotransferase (AST), aspartate aminotransferase (ALT), blood sugar, serum parathyroid hormone (PTH), thyrotropin (TSH), TH (Thyroxine T4, T4), and TH. The "Collection Form of TCM Symptoms and Conditions of CKD Patients" was made. According to the patients' chief complaints, symptoms, signs, tongue picture and pulse condition, nephrologists or specially trained questionnaire investigators conducted questionnaire survey and four diagnostic observations on all the observed objects to judge TCM syndromes. All participants were asked whether they had hypertension, diabetes, cardiovascular disease history and drug treatment and recorded them [9-10].

2.2.1 Hypertension

The measurement of blood pressure adopts indirect measurement method, referring to the standard method recommended by JNC VII. Each subject measures twice, with a 5-minute interval between each measurement. The average of the two results is taken as the blood pressure measurement result. If the two readings differ by 10mm Hg, the third measurement is taken, and the average of the two readings that are similar is taken as the blood pressure measurement result. All participants should rest for at least 5 minutes before measuring their blood pressure (blood pressure monitor model Omron U30). The blood pressure should be measured in 3 times, with a 5-minute interval between each measurement. The average of the 3 measurements should be calculated. If the

difference between the two measurements is greater than 10mm Hg, the average value should be calculated using the two measurements with the smallest difference. Hypertension is a clinical syndrome characterized by elevated systemic arterial pressure.

2.2.2 Diabetes

Oral glucose tolerance test (OGTT) was performed on all personnel. OGTT test method: 1. Participants can drink water on an empty stomach for at least 8 hours before the test. 2. Participants are not allowed to smoke during OGTT. 3. After obtaining the fasting blood sample, drink about 250ml of water containing 75g glucose. 4. Glucose water must be drunk within 5 minutes. 5. Blood samples were taken at 0.5 hour, 1.5 hour and 2 hours after taking sugar.

2.2.3 Other

Blood lipid, uric acid, high density lipoprotein (HDL), low density lipoprotein (LDL) and other biochemical indicators were detected by automatic biochemical analyzer (Olympus AU5400 automatic biochemical analyzer).

3. Result

3.1 Thyroid function in CKD patients

As shown in Table 1, there were 35 cases (13.7%) with abnormal thyroid function, including 24 cases (66.2%) with decreased serum T3, 5 cases (16.3%) with decreased serum T3 and T4, 4 cases (5.6%) with increased serum TSH and 8 cases (13.7%) with decreased serum T4. CKD stage 1 ~ 2 group was lower than CKD stage 3 ~ 4 group, and the difference was statistically significant ($P < 0.05$).

Table 1 Comparison of related indexes of patients in CKD staging groups

Group	ALT	AST	ALP	T3	T4	TSH
CKD Phase 1 ~ 2	15.2±6.1	16.5±6.6	52.4±19.7	2.1±0.7	1.3±0.3	1.7±0.9
CKD Phase 3 ~ 4	17.2±11.9	18.8±12.4	69.4±28.1	2.5±0.5	1.3±0.5	2.7±2.4

3.2 Relationship between TCM dialectical classification of CKD patients and T4 abnormality

As shown in Table 2, 35 cases of CKD patients with abnormal thyroid function were diagnosed as hypothyroidism and abnormal thyroid function syndrome: among them, T3 decreased only, and T4 and TSH were normal (group A), with 14 cases of spleen-kidney yang deficiency (70%) and 6 cases of spleen-kidney qi deficiency (30%); In group B, T3 and T4 all decreased, with or without TSH increasing, mainly showing deficiency of both yin and yang in 5 cases (62.5%), deficiency of both qi and yin in 3 cases (37.5%) and deficiency of spleen and kidney in 1 case (12.5%).

Table 2 Relationship between thyroid dysfunction and TCM syndrome differentiation in CKD patients

Group	Yang deficiency of spleen and kidney	Spleen and kidney qi deficiency type	Yin deficiency of liver and kidney	Deficiency of both qi and yin	Deficiency of yin and yang
Group a	10(46.2)	8(40.5)a	4(11.4)	2(3,7)	0(0)
Group b	3(27.2)	0(0)	0(0)	3(26.1)	3(45.2)

4. Discuss

Kidney is an endocrine organ that produces hormones, and has the function of degrading and excreting many hormones, including thyroid hormones. Therefore, renal injury will lead to thyroid dysfunction, and any level of hypothalamus-pituitary-thyroid axis may be affected, thus causing changes in hormone synthesis, secretion and distribution. CKD can affect

hypothalamus-pituitary-thyroid axis, and then lead to thyroid physiological dysfunction. Epidemiological data show that non-dialysis patients with chronic renal insufficiency are at greater risk of hypothyroidism. Patients with CKD usually show normal thyroid dysfunction syndrome, that is, in patients with chronic non-thyroid diseases, the serum T4 level is decreased and the TSH level is normal, and there is no clinical hypothyroidism. Thyroid hormone plays a vital role in the metabolic activities of adults, affecting almost all organ systems. Some patients with chronic renal failure have a large amount of proteinuria for a long time, combined with chronic consumption, resulting in obvious hypoproteinemia, which reduces the affinity between thyroid hormone-binding globulin and thyroxine-binding prealbumin, resulting in a decrease in T3 and T4. The early stage of CKD is related to thyroid dysfunction. Hypothyroidism may be related to the moderate increase of plasma total cholesterol, low-density lipoprotein cholesterol and triglyceride, and may lead to atherogenic changes in lipoprotein metabolism and function. In CKD patients, the renal tubular reabsorption function decreased, and the reabsorption of thyroid hormone-binding globulin complex binding T3 and T4 decreased, resulting in a large number of T3 and T4 lost with urine. Especially in nephrotic syndrome, due to the damage of glomerular filtration barrier, a large amount of protein is lost from urine, including thyroid hormone binding globulin, which hinders the synthesis of TH and eventually leads to the decrease of TH level in the body. During the disease development of CKD patients, many links affect the thyroid function, such as lowering the circulating T4 level, and affecting the metabolism of hypothalamus-pituitary-thyroid axis and T4 in peripheral tissues, lowering the levels of thyroid binding protein and thyroid pre-binding protein, and changing the intake and storage of iodide in thyroid. Low T3 syndrome is the most common change of TH in these patients.

5. Conclusions

There is currently no consensus on whether CKD patients require TH replacement therapy. Due to the complex pathophysiological relationship between the kidneys and TH, there is very little clinical research on whether TH replacement therapy is necessary for CKD complicated with non thyroid disease syndrome. CKD is closely related to thyroid diseases. By studying the relevant factors of SCH in CKD patients, guidance can be provided for future clinical work, early clinical intervention can be carried out to improve the quality of life and prognosis of CKD patients. The renal tubular reabsorption function of CKD patients decreases, and the reabsorption of thyroid hormone binding globulin complexes binding T3 and T4 decreases, resulting in a large loss of T3 and T4 in urine. Especially in nephrotic syndrome, due to the damage of the glomerular filtration barrier, a large amount of proteins, including thyroid hormone binding globulin, are lost from urine, resulting in a blockage of TH synthesis and ultimately a decrease in TH levels in the body. The course of CKD is long, and it may merge with various other acute and chronic diseases during the development of the disease. If the symptoms of these combined extrarenal diseases are confused with them, it will inevitably affect the understanding of CKD symptoms, pathogenesis, and evolution rules. Only "disease diagnosis and syndrome differentiation" can eliminate interference with CKD diagnosis and treatment, and achieve the best therapeutic effect by referring to the traditional principles of traditional Chinese medicine.

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