Int J Clin Exp Med 2019;12(9):11851-11858
www.ijcem.com /ISSN:1940-5901/IJCEM0097061

Original Article

Correlation between traditional Chinese medicine syndrome elements and relevant factors of essential hypertension

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Received May 15, 2019; Accepted July 24, 2019; Epub September 15, 2019; Published September 30, 2019

Abstract: Objective: Analyze the correlation between distribution law of Syndrome Elements (SEs) and relevant factors in patients with Essential Hypertension (EH), provide reference for objective and standardized research on Traditional Chinese Medicine (TCM) diagnosis of EH. Methods: During a clinical cross-sectional survey, four diagnostic information and laboratory indexes of EH patients were collected. Binary logistic regression analysis was used for correlation analysis. Results: In this study 12 SEs were involved in 1192 EH patients. There were four SEs of disease location: kidney, liver, heart, spleen, four excess SEs: dampness, hyperactivity of *Yang*, phlegm, fire (heat), four deficiency SEs: *Qi* deficiency, *Yin* deficiency, deficiency of kidney essence, blood deficiency. The female EH patients are related to kidney, heart, and *Qi*, blood or kidney essence deficiency; while male patients to spleen, phlegm, dampness and fire (heat). The age is related to liver and kidney; illness course to kidney, deficiency of kidney essence and hyperactivity of *Yang*; hypertension degree to *Yin* deficiency; BMI and CREA to dampness; GLU to kidney; HDL to *Qi* deficiency; HDL/TC to hyperactivity of *Yang*; combined with coronary heart disease to kidney, heart, phlegm and deficiency of kidney essence; combined with arrhythmia to heart; combined with hyperlipemia to spleen. Conclusion: Most elderly EH patients are mainly revealed as having deficiency of both liver and kidney, *Qi* and *Yin*, and the excess of *Yang*, lumbago with damp-phlegm, or hyperactivity of fire. The diagnosis of SEs is related to the gender, age, IBM, illness course, GLU, CREA, dyslipidemia, combined with coronary heart disease, arrhythmia, diabetes, and hyperlipemia.

Keywords: Essential hypertension, traditional chinese medicine, syndrome elements, relevant factors

Introduction

Essential Hypertension (EH) is a kind of cardiovascular and cerebrovascular disease with high incidence. There are close correlations between EH and major organ diseases, such as stroke, congestive heart failure, coronary heart disease, and renal dysfunction, etc. In recent years, a nationwide survey showed that the prevalence of hypertension in the Chinese population, over 18 years old, was significantly higher than that of ten years ago [1]. Traditional Chinese Medicine (TCM) has unique advantages in treating hypertension, not only to depress blood pressure, but also to improve symptoms and quality of life, prevent and treat target organ damage, and to reduce complications, etc [2]. Syndrome elements (SEs) differentiation can simply show the complexity [3], and more accurately, flexibly and clearly reflect the nature of the disease, and also be more convenient for clinical diagnosis. In this study, we collected clinical data of four diagnostic methods and laboratory indexes, obtained in an epidemiological survey of 1192 EH patients; we analyzed the correlation between distribution law of SEs and relevant factors, as well as provided reference for objective and standardization research on TCM diagnosis of EH.

Methods

Inclusion criteria

(a) Patients conformed to the standard for diagnosing EH in both Western Medicine and TCM.

In Western Medicine, EH patients conformed to the "Guidelines for Prevention and Treatment of Hypertension in China (Revised Edition) [4]" issued by the Ministry of Health of PRC, in 2013. The standard for diagnosing EH in TCM was from the teaching materials of "Traditional Chinese Internal Medicine (6th edition) [5]", referring to vertigo, headache, and chest tightness, etc. (b) The diagnostic criteria of SEs was from "Differentiation of Syndrome Elements [6]", Zhu Wenfeng editor in chief, published in 2008.

Exclusion criteria

(a) Patients with secondary hypertension. (b) Patients with unclear ESs diagnosis. (c) The cases, that did not meet the diagnosis and inclusion criteria, were excluded.

Design of experiment

The experiment was a clinical cross-sectional survey. 1192 cases of EH were collected in Longhua Hospital, Shanghai Putuo Distuict Central Hospital and Wang Gang Community Hospital of Shanghai from April 2014 to October 2015. All data obtained by the hospital were from patients with informed consent and was used only in this medical research. The patient's personal information was strictly confidential.

The investigation table was designed under the guidance of TCM experts, according to the purpose and content of information collection. The basic information, symptoms and signs, laboratory indexes and the common diseases of the EH patients were involved. The basic information included the patient's name, age, height, weight, waist circumference, hip circumference, blood pressure value, illness course, combined diseases, and dates, etc. The symptoms and signs contained head and body symptoms, chills and fever, urine and stool, diet and drink, sleep, sweat, tongue quality and fur, pulse, etc. Glucose, blood lipid, renal function and so on, were included in laboratory indexes. The combined diseases including diabetes, fatty liver, hyperlipidemia, coronary heart disease and arrhythmia. Information collection staff were trained under the guidance of experts. The standards were uniform to ensure the accuracy of the data collection. Three TCM experts differentiated the SEs independently, each with senior titles and rich clinical experience.

Clinical data

There were 478 males (40.10%) and 714 females (59.90%) among the 1192 EH patients, aged 36-95 years, (68.11 ± 10.27) years on average. There were 269 cases (22.57%) under the age of 61, 456 cases (38.26%) were 61-70 years, 304 cases (25.50%) were 71-80 years, 163 cases (13.67%) were over 80 years. Illness course was 0-50 years, with an average of (9.74 ± 8.41) years. The blood pressure value was divided into I, II, III level, 864 cases (72.48%) as I level, 208 cases (17.45%) as II level, 120 cases (10.07%) as III level.

Statistic method

Epidata 3.1 was used to input data. SPSS 21.0 statistics software was used to build a database. We used frequency, constituent ratio and rate to express enumeration data. The measurement data of different detection sources were translated into grade data, according to the diagnostic criteria. Binary logistic regression analysis was used for correlation analysis (Forward: Wald). Zero or 1 was used to express binary enumeration data and frequency was counted. $P < 0.05$ was considered a statistical difference.

Results

Distribution of SEs in EH patients

Based on the statistical analysis, 12 SEs were involved in 1192 EH patients. There were four SEs of disease location: kidney, liver, heart, spleen. Eight SEs on nature of disease were involved, including four excess SEs: dampness, hyperactivity of *Yang*, phlegm, fire (heat), and four deficiency SEs: *Qi* deficiency, *Yin* deficiency, kidney essence deficiency, blood deficiency. 1617 cases had excess SEs, and 1530 cases had deficiency SEs. The cases distribution with different SEs is shown in **Table 1**.

Logistic regressive analysis between SEs and EH factors

In this study, binary logistic regression analysis was used to explore the correlation between the 12 common SEs and the influence factors of EH. The influence factors were divided into three categories: general factors, laboratory indexes and combined diseases. The general factors included gender, age, body mass index

Table 1. Distribution of SEs in 1192 EH patients

SE	*n*	Percentage (%)	SE	*n*	Percentage (%)
Kidney	668	56.04	Spleen	410	34.40
Liver	599	50.25	Hyperactivity of *Yang*	387	32.47
Heart	573	48.07	Phlegm	334	28.02
Qi Deficiency	545	45.72	Deficiency of Kidney Essence	263	22.06
Yin Deficiency	481	40.35	Fire (Heat)	220	18.46
Dampness	461	38.67	Blood Deficiency	163	13.67

Note: SEs: syndrome elements.

(BMI), Waist-to-Hip (WHR) ratio, the degree of hypertension and illness course. Laboratory indexes included glucose (GLU), triglyceride (TG), total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), high density lipoprotein/total cholesterol (HDL/TC), blood urea nitrogen (BUN), uric acid (UA) and creatinine (CREA). The combined diseases included coronary heart disease, arrhythmia, fatty liver, hyperlipidemia and diabetes. SEs were taken as the dependent variables, influence factors as independent variables. All measurement indicators were divided into 2 or 3 levels, from low to high. Dummy variables were set when the dependent variable was ranked data. When the regression coefficient was positive, this indicated that the factor is positively related to the diagnosis of SEs. The greater Exp (B) value indicated a stronger correlation, and the greater the contribution of diagnosis factor to SEs [7].

The results showed that the diagnosis of liver is related to age; the kidney to female, age, illness course, GLU, combined with coronary heart disease or diabetes; the heart to female, combined with coronary heart disease or arrhythmia; the spleen to male, and combined with hyperlipidemia; the phlegm to male and combined with coronary heart disease; the dampness to male, BMI and CREA; the hyperactivity of *Yang* to illness course and HDL/TC; the fire (heat) to male and HDL/TC; the *Qi* deficiency to female and HDL; the blood deficiency to female; the *Yin* deficiency to hypertension degree and combined with diabetes; the deficiency of kidney essence to female, illness course combined with coronary heart disease. The results are shown in **Tables 2**-**4**.

Discussion

Hypertension is a multifactorial disease, caused by various factors, including age, gender, overweight, smoking, dyslipidemia, disorders of glucose metabolism and target organ damage, etc., which are strongly related to the formation, development, prognosis and treatment of hypertension. SEs summarize the cause, nature, focus, and situation of a disease at some stage reflecting the innate character of the disease and act as the basis of its clinical treatment [8]. In this study, we explored the correlation between the factors of EH and the SEs.

The characteristics of pathogenesis of patients with EH

EH is a cardiovascular disease, but its onset is unknown. A lot of patients in addition to the high blood pressure in physical examination, show no other obvious discomfort. All cases were in middle aged or older people, that were collected in this study. Such people often present debilitated constitution and deficiency of viscera essence. The results show that the frequency of kidney and liver, disease location of SEs, in patients with EH were high, as well as the SEs on disease natures of *Qi* deficiency and *Yin* deficiency. So we know that the fundamental deficiency, performance as deficiency of both *Qi* and *Yin,* is the main pathogenesis of EH. This study also found that the types of excess SEs in EH were slightly more of the deficiency SEs. So from the total number of cases, we show that more patients with EH have complex excess SEs on the basis of deficiency in origin. The nature of the disease in most elderly patients were deficiencies in origin and excess in superficiality. The deficiency in origin mainly revealed in both liver and kidney, or in *Qi* and *Yin*. The excess in superficiality mainly revealed in hyperactivity of *Yang*, blockade with damp-phlegm or hyperactivity of fire, etc.

The correlation between the general factors and the SEs of EH

The results of regression analysis showed that gender, age, illness course, BMI and hypertension level were related to the diagnosis of SEs in EH. The female patients were more likely to suffer from kidney, heart, *Qi* deficiency, blood deficiency and deficiency of kidney essence.

Table 2. Results of logistic regression analysis of single SEs and general factors

SE	Factors	B	S.E.	Wald	Sig.	Exp (B)
Liver	Age (≤ 60)			8.118	0.044	
	Age (71~)	0.414	0.168	6.063	0.014	1.514
	Age (81~)	0.426	0.200	4.549	0.033	1.531
	Constant	-0.216	0.123	3.114	0.078	0.805
Kidney	Female	0.502	0.122	16.803	0.000	1.652
	Age (≤ 60)			16.104	0.001	
	Age (61~)	0.343	0.159	4.653	0.031	1.409
	Age (71~)	0.466	0.174	7.148	0.008	1.593
	Age (81~)	0.826	0.214	14.948	0.000	2.285
	Illness course (0~5 years)			7.878	0.019	
	Illness course (6~10 years)	0.077	0.136	0.325	0.568	1.080
	Illness course (10 years~)	0.442	0.162	7.412	0.006	1.556
	Constant	-0.545	0.162	11.259	0.001	0.580
Heart	Female	0.591	0.120	24.218	0.000	1.805
	Constant	-0.433	0.094	21.428	0.000	0.648
Spleen	Female	-0.271	0.124	4.778	0.029	0.763
	Constant	-0.486	0.094	26.659	0.000	0.615
Deficiency of Kidney Essence	Female	0.322	0.147	4.833	0.028	1.381
	Illness course (0~5 years)			10.294	0.006	
	Illness course (10 years~)	0.579	0.181	10.247	0.001	1.785
	Constant	-1.702	0.156	119.759	0.000	0.182
Qi Deficiency	Female	0.534	0.120	19.705	0.000	1.707
	Constant	-0.495	0.094	27.582	0.000	0.609
Blood Deficiency	Female	0.509	0.182	7.806	0.005	1.663
	Constant	-2.170	0.151	207.014	0.000	0.114
Yin Deficiency	BMI (Normal)			7.593	0.022	
	BMI (Overweight)	-0.378	0.137	7.587	0.006	0.685
	Hypertension (I)			27.167	0.000	
	Hypertension (III)	1.056	0.203	27.162	0.000	2.875
	Constant	-0.305	0.106	8.254	0.004	0.737
Hyperactivity of *Yang*	BMI (Normal)			9.944	0.007	
	BMI (Overweight)	-0.444	0.142	9.833	0.002	0.641
	Illness course (0~5 years)			12.122	0.002	
	Illness course (10 years~)	0.562	0.162	12.089	0.001	1.754
	Constant	-0.699	0.131	28.400	0.000	0.497
Phlegm	Female	-0.856	0.131	42.392	0.000	0.425
	Constant	-0.469	0.094	24.856	0.000	0.626
Dampness	Female	-0.754	0.123	37.720	0.000	0.471
	BMI (Normal)			9.218	0.010	
	BMI (Overweight)	0.341	0.141	5.868	0.015	1.406
	BMI (Obesity)	0.472	0.169	7.808	0.005	1.602
	Constant	-0.283	0.129	4.831	0.028	0.753
Fire (Heat)	Female	-0.631	0.150	17.589	0.000	0.532
	Constant	-1.138	0.107	113.780	0.000	0.320

Notes: BMI: Body Mass Index; B: regression coefficient β value; S.E.: standard error; Sig.: significance; Exp (B): odds ratio.

While the male patients were prone to spleen, phlegm, dampness and fire (heat). Women with weak constitution are often worrying and anxious, consuming much more *Qi* and blood. For

Table 3. Results of logistic regression analysis of single SEs and laboratory indexes

SE	Factors	B	S.E.	Wald	Sig.	Exp (B)
Kidney	LDL (High)	-0.952	0.256	13.845	0.000	0.386
	GLU (High)	0.364	0.147	6.147	0.013	1.439
	Constant	0.420	0.200	4.381	0.036	1.521
Yin Deficiency	LDL (High)	-0.456	0.185	6.052	0.014	0.634
	Constant	-0.563	0.077	53.200	0.000	0.569
Hyperactivity of *Yang*	HDL/TC (High)	0.344	0.171	4.035	0.045	1.411
	Constant	-0.875	0.100	77.092	0.000	0.417
Phlegm	HDL (Grade 1)			11.959	0.003	
	HDL (Grade 3)	-0.791	0.295	7.178	0.007	0.453
	HDL/TC (High)	-0.594	0.171	12.108	0.001	0.552
	Constant	-0.330	0.276	1.423	0.233	0.719
Dampness	CREA (Grade 1)			14.213	0.001	
	CREA (Grade 3)	0.610	0.170	12.889	0.000	1.841
	Constant	-0.659	0.112	34.373	0.000	0.517
Fire (Heat)	HDL/TC (High)	-0.647	0.220	8.632	0.003	0.524
	Constant	-1.612	0.122	174.811	0.000	0.199

Notes: GLU: Glucose; TG: Triglyceride; TC: Total Cholesterol; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; CREA: Creatinine; B: regression coefficient β value; S.E.: standard error; Sig.: significance; Exp (B): odds ratio.

women "the blood is the base of life". So female patients are prone to suffer from deficiency of kidney essence, *Qi* and blood, and disease location in the heart and kidney. While the men prefer eating more fat, smoking and drinking, so the male EH patients are prone to excess SEs of phlegm-damp, and disease located in the spleen.

Obesity is one important cause of elevated blood pressure. Central obesity, with the typical feature of abdominal fat accumulation, will further increase the risk of hypertension. This study found that the higher a patients' BMI, the greater the possibility to go through dampness, the less possibility to undergo *Yin* deficiency and *Yang* hyperactivity. Some studies have shown that the BMI in EH patients with internal exuberance of phlegm-damp were higher than the persons with flaring up of liver fire [9], which conform to the theory of TCM about "Fat people are vulnerable to phlegm-dampness, while the thin people are prone to hyperactivity of fire due to *Yin* deficiency".

As people's physiological and visceral functions gradually decline, *Qi* and blood disorder, *Yin* and *Yang* unbalance, increase with age. The consumption on the body of the disease and the performance of deficiency syndrome increase gradually with the extension of the illness course. Therefore, the older EH patients are more likely to suffer from liver, kidney, essence of kidney and *Yin* deficiency with age. Chronic diseases transform to collaterals, *Yin* deficiency cause *Yang* hyperactivity, so the EH patients with higher age and longer duration are prone to undergo syndromes, such as hyperactivity of *Yang*, phlegm disturbance, stroke, etc. EH patients' with more serious conditions and higher blood pressure levels aggravate *Yin* deficiency and *Yang* hyperactive, and should be aware of the danger of wind caused by hyperactive *Yang*.

The correlation between the dyslipidemia and the SEs of EH

This study found that the lower level of HDL and HDL/TC in EH patients aggravated the phlegm, dampness and fire (heat). As we know, the HDL is an anti-atherogenic lipoprotein in plasma, which has a negative correlation with arterial stiffness in EH patients. The HDL decrease may aggravate the arterial stiffness [10]. LDL is a carrier of cholesterol into the peripheral tissue cells of the lipoprotein particles. Vascular endothelial cells are prone to autolysis and exfoliation as LDL increases. Repeated injury can lead to platelet adhesion and aggregation, lipid deposition, monocyte infiltration and smooth muscle cell proliferation, eventually forming atherosclerotic plaque. There is a significant positive correlation between LDL level and coronary artery disease [11]. From the perspective of TCM, the main cause of hyperlipidemia and coronary heart disease were that the phlegm, dampness and static blood blocked the blood vessels [12]. A study on the correlation between

Table 4. Results of logistic regression analysis of single SEs and combined diseases

SE	Factors	B	S.E.	Wald	Sig.	Exp (B)
Kidney	Coronary Heart Disease	0.394	0.163	5.843	0.016	1.482
	Diabetes	0.392	0.154	6.500	0.011	1.480
	Constant	0.109	0.069	2.461	0.117	1.115
Heart	Coronary Heart Disease	1.171	0.175	44.730	0.000	3.224
	Arrhythmia	0.824	0.133	38.096	0.000	2.279
	Constant	-0.500	0.075	44.077	0.000	0.607
Spleen	Hyperlipemia	0.301	0.125	5.820	0.016	1.351
	Diabetes	-0.501	0.167	8.963	0.003	0.606
	Constant	-0.726	0.095	58.082	0.000	0.484
Deficiency of Kidney Essence	Coronary Heart Disease	0.376	0.178	4.453	0.035	1.456
	Constant	-1.328	0.078	291.589	0.000	0.265
Qi Deficiency	Diabetes	-0.337	0.152	4.948	0.026	0.714
	Constant	-0.110	0.064	2.896	0.089	0.896
Yin Deficiency	Diabetes	0.450	0.149	9.097	0.003	1.569
	Constant	-0.477	0.066	52.179	0.000	0.620
Phlegm	Coronary Heart Disease	0.396	0.167	5.633	0.018	1.485
	Constant	-1.012	0.072	199.925	0.000	0.363

Notes: B: regression coefficient β value; S.E.: standard error; Sig.: significance; Exp (B): odds ratio.

TCM syndromes and blood lipid level in patients with coronary heart disease (CHD) showed that the cardiac blood stasis syndrome and phlegm blocking heart vessel syndrome were common in elderly CHD patients. Among the syndrome of phlegm blocking heart vessel, abnormal blood lipid is the most significant [13].

In this study, it was found that the EH patients combined with hyperlipidemia were prone to spleen disfunction. The phlegm-dampness was created from the dysfunction of spleen in transportation. The lower the level of HDL and HDL/TC, the higher degree of arteriosclerosis, the stronger extent of blockade of phlegm, dampness and static blood. The phlegm-dampness pent-up for a long time would breed fire (heat), so the fire (heat) increased. The level of HDL/TC aggravates *Yin* deficiency and *Yang* hyperactivity, while LDL and TG are on the contrary. In conclusion, the EH patients with worse dyslipidemia are more likely to suffer from phlegm, dampness and fire (heat) than *Yin* deficiency and *Yang* hyperactivity.

The correlation between blood glucose and the SEs of EH

Diabetes is similar to the "Consumptive Thirst" in TCM, whose basic pathogenesis is *Yin* fluid depleted and dryness-heat excess, and the lung, stomach and kidney are the disease location. Diabetic nephropathy is one of the most serious and common chronic complications of diabetes, about 30%-40% patients with diabetes ultimately developed into this disease [14]. This research found that the EH patients combined with diabetes were more likely to be prone to kidney and *Yin* deficiency. This study also found that the possibility of occurrence in kidney rose with the level of GLU. The EH patients without diabetes were more likely to suffer from spleen and *Qi* deficiency.

The correlation between combined cardiovascular disease and the SEs of EH

Coronary heart disease and arrhythmia belongs to "Oppression in Chest", "Chest Discomfort", "Palpitation" and "Severe Palpitation" in TCM, mainly caused by deficiency, stagnation, phlegm and blood stasis [15]. Some research has analyzed the syndrome characteristics of coronary heart disease, and found that heart and kidney were the disease location [16]. Regression analysis found that heart appears to be 3.224 times in EH patients combined with coronary heart disease, and 2.279 times in patients combined with arrhythmias, compared to the ones didn't combine. The EH patients combined with coronary heart disease are more

likely to have kidney issues. Elderly patients worn with age, loss of kidney essence, have imbalance of *Yin* and *Yang*, deficiency of heart *Qi*, dysfunction of *Qi* and blood, coupled with internal damage and exogenous diseases, results in stagnation of *Qi* and blood stasis, internal exuberance of phlegm-damping, stagnation of the heart meridian, performance as oppression in chest, palpitation, and so on. This study also found that EH patients combined with coronary heart disease or cardiac arrhythmia were prone to phlegm, dampness and deficiency of kidney essence.

The correlation between creatinine and the SEs of EH

It was found that dampness was positively correlated to CREA levels. The higher level of CREA indicates a worse renal function in EH patients. TCM considers that kidney governs water metabolism, so deficiency of kidney essence causes the dysfunction and accumulation of water metabolism transport, leading to internal exuberance of phlegm-dampness. Therefore, the higher level of CREA, the greater possibility of dampness. Another study also found that damp-turbidity accumulated in the interior was the main syndrome for nephropathy patients in renal failure stage, and the syndrome was highly correlated to CREA [17].

Overall, this study analyzed the clinical distribution of TCM SEs in EH patients from the point of SEs differentiation, using logistic regression analysis method to explore the correlation between the SEs of EH and the influence factors, such as gender, age, BMI, hypertension degree, illness course, laboratory indexes and diseases combination; revealing the sensitivity and specificity indexes and relevant factors for diagnosis of EH. This study provides a basis for the research on objective and standardized diagnosis of TCM syndrome on EH, which is based on SEs as the core.

Acknowledgements

National Science & Technology Pillar Program during the 12th Five-year Plan Period (No. 2012BAI25B05); Shanghai Medical Excellent Discipline Leader Program (No. XBR2011070).

Disclosure of conflict of interest

None.

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