Original Article

Dynamic statistical analysis of TCM symptoms on coronary heart disease angina pectoris

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Abstract: The effects of Traditional Chinese Medicine (TCM) for the treatment of coronary heart disease angina pectoris require accurate assessment. However, the TCM symptoms of this disease are numerous and complicated. To evaluate TCM treatment based on TCM symptoms, in this study, we applied descriptive statistical methods to 73 symptoms in the attack period, and after three-months of TCM treatment, the same group of patients, now in the remission period, underwent the same analysis again. Using two-way contingency table analysis, we compared the dynamic changes of all 73 TCM symptoms between the above-mentioned attack and remission periods. Furthermore, we chose symptoms that arise in more than 10% of patients (high-incidence symptoms) and investigated the dynamic changes between the attack period and the remission period. Finally, we found that almost all symptoms (except blackish complexion (*P* value equals 0.93)) were significantly different between the two periods. The number of patients with high-incidence symptoms (except tinnitus) decreased. The percentage of patients with tinnitus increased 6.72% from the attack period to the remission period. Therefore, we concluded that three-months of TCM treatment significantly improved patients' performance in coronary heart disease angina pectoris TCM symptoms. Based on the survey data and dynamic statistical analysis, this study provides references for doctors, experts, and patients to evaluate the effects of TCM treatment in a more efficient and statistical manner.

Keywords: Coronary heart disease angina pectoris, symptoms, traditional Chinese medicine

Introduction

Traditional Chinese Medicine (TCM) is an ancient and important medical system that provides a deep understanding of the laws and patterns of nature. With a history of more than five thousand years, TCM has resulted in immense knowledge of medical science, theory, diagnostic methods, prescriptions, and cures, which is completely different from Western medicine [1]. Based on ancient Chinese philosophical theories, the TCM theory includes the following: (1) Yin and Yang theory: The philosophical basis of TCM. (2) Five elements theory: Wood, fire, earth, metal, and water. (3) Jing-Qi: Vital energy. (4) Diagnosis methods: Observation, auscultation, and olfaction, interrogation, pulse taking, and palpation.

Coronary heart disease angina pectoris is a key contributor to the morbidity and mortality from noncommunicable diseases [2]. The incidence and mortality of this disease significantly increased especially in young patients. In developing countries, coronary heart disease angina pectoris is one of the main causes leading to death [2, 3]. To positively control the risk factors of coronary heart disease angina pectoris, experts in Chinese and Western medicine have been committed to many researches. As one of the existing treatments for coronary heart disease angina pectoris [4, 5], percutaneous coronary intervention (PCI) plays an important role, and has good treatment outcomes, fast recovery, minor injuries, and reduced perioperative complications [6]. However, PCI is also associated with high risks.

Most patients face negative emotions and psychological stress, which induces stress responses [7-9]. Compared with PCI, Chinese medicine has major advantages in many aspects, including drug safety. However, due to the complexity of TCM theories, effective evaluation of coronary heart disease angina pectoris is quite a challenge.

In recent studies, Chinese medicine symptoms or syndromes of coronary heart disease angina pectoris were investigated [10-16]. However, few studies focused on the dynamic changes in the symptoms of coronary heart disease angina pectoris after TCM treatment. The analysis of dynamic changes was carried out in phenotypic groups in patients with stable angina pectoris after treatment with *xinxuekang* capsule (a type of Chinese patent medicine) through a randomized controlled trial [17]. Different from existing studies, we investigated the dynamic changes of TCM symptoms on coronary heart disease angina pectoris based on 595 patients from the attack period to the remission period.

Methods

Notation

The data is supported by the Affiliated Hospital of Changchun University of Chinese Medicine in China. The sample size of this study was 595, and mainly consisted of 7 vital sign variables and 73 TCM symptom variables. Vital sign variables included body temperature (T), respiration (R), pulse (P), diastolic blood pressure (DBP), systolic blood pressure (SBP), heart rate (HR), and body mass index (BMI), respectively. All 73 TCM symptom variables were reflected in 13 dimensions: Complexion (Dimension 1), lip color (Dimension 2), nails (Dimension 3), morphology (Dimension 4), cold and heat (Dimension 5), sweating (Dimension 6), head, body, chest and abdomen (Dimension 7), thirsty (Dimension 8), taste (Dimension 9), diet (Dimension 10), stool (Dimension 11), urine (Dimension 12), and sleep (Dimension 13). All TCM symptom variables were 0-1 binary variables. The indicators and their symbols are presented in Table 1.

Data were obtained through two surveys from the same 595 subjects. The two surveys were held 3 months apart, during the attack period (A) and remission period (R), throughout which patients received TCM treatment only.

Descriptive statistical methods

To compare the vital signs of 595 patients between the attack period and remission period, the mean values, standard deviations, minimum values, maximum values, and 95% confidence intervals were calculated. Next, we calculated the frequency percentages of high-incidence symptoms (more than 10% of the patients show these symptoms) and investigated their changes between the two periods.

The mean value of a variable (denoted as \overline{V}) was calculated as the sum of all values (denoted as v_1 , v_2 , ..., v_n) divided by the number of observations (denoted as n). The formula to calculate the mean value was as follows:

$$\overline{V} = \sum_{1}^{n} v_i / n$$

The standard deviation (denoted as δ) is the square root of the variance. The variance is the average of the squares of the deviations between the observations and the mean values. The formula to calculate the standard deviation was as follows:

$$\sigma = \sqrt{\sum_{1}^{n} (v_i - \overline{v})^2 / n}$$

The minimum value (denoted as *Min*) and maximum value (denoted as *Max*) of a variable are the least and largest value of all values, respectively. The formulas to calculate the minimum value and maximum value were as follows:

$$Min = minmum (v_1, v_2, ..., v_p)$$

$$Max = maxmum (v_1, v_2, ..., v_n)$$

The 95% confidence interval (denoted as $Cl_{95\%}$) is an interval computed from sample data by a method that has a probability of 95% of producing an interval containing the true value of the mean value. The formula to calculate the 95% confidence interval was as follows:

$$CI_{95\%} = (\overline{V} - 1.96 * \sigma / \sqrt{n}, \overline{V} + 1.96 * \sigma / \sqrt{n})$$

The frequency percentage (denoted as FP) of a symptom (say the kth symptom, k = 1, ..., K) is calculated as the number of observations with this symptom (denoted as $Count_k$), divided by the total number of observations (denoted as

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Table 1. Indicators and their symbols

Indicators	Symbols	Indicators	Symbols
pale complexion	V1	heart vexation	V38
sallow complexion	V2	belching	V39
red complexion	V3	decreased appetite 1	V40
flushed cheeks	V4	abdominal distention	V41
dim complexion	V5	gastric lump	V42
blackish complexion	V6	acid reflux	V43
lusterless complexion	V7	nausea and vomit	V44
puffy face	V8	frequent sighing	V45
pale lips	V9	impatient and irritable	V46
dark reddish lips	V10	distending of hypochondria	V47
cyanotic lips	V11	emotional depression	V48
black lips	V12	soreness and weakness of waist and knees	V49
blue nails	V13	headache	V50
dark nails	V14	dizziness	V51
cyanotic nails	V15	deafness	V52
fat	V16	tinnitus	V53
thin	V17	others in head, body, chest and abdomen	V54
edema of face	V18	thirst or not	V55
swelling limbs	V19	thirst without liking for drink	V56
heavy cumbersome limbs	V20	thirst without liking for a drink	V57
numbness limbs	V21	thirst with liking hot drinks	V58
joint pain	V22	bland taste in mouth	V59
cold limbs	V23	bitter taste in mouth	V60
withered hair	V24	foul breath	V61
dry scaly skin	V25	sticky sensation in mouth	V62
withered skin	V26	decreased appetite 2	V63
grayish skin	V27	rapid digestion with polyphagia	V64
fearing wind	V28	constipation	V65
fearing cold	V29	loose stool	V66
tidal fever	V30	scanty urine	V67
feverish sensation over palm, sole and heart	V31	frequent urination	V68
limbs lacking warmth	V32	nocturnal polyuria	V69
spontaneous sweating	V33	difficult and painful urination	V70
night sweating	V34	clear and profuse urine	V71
chest oppression	V35	scanty reddish urine	V72
painful chest	V36	insomnia	V73
palpitation	V37	-	-

 Σ_k^{κ} Count_k). The formula to calculate the frequency percentage was as follows:

 $FP = Count_k / \sum_{k=1}^{K} Count_k$

Contingency table analysis

To investigate the dynamic changes of 73 TCM symptoms from the attack period to the remis-

sion period, two-way contingency table analysis was used. Two-way contingency table analysis is based on a 2×2 table, which arises by crossclassifying two binary variables on a sample. When V1 is taken as an example, the hypothesis of interest is the independence of X and Y. Let n_{ij} , i=j=1, 2 as the observed cell frequency at cell (i,j). The table form can be displayed as shown in **Table 2**.

Table 2. Contingency table analysis for V1 and V2

	A: Yes	A: No
R: Yes	n ₁₁	n ₁₂
R: No	n ₂₁	n ₂₂

A, attack period; R, remission period.

Based on **Table 2**, we used the chi-square X^2 test to determine if significant differences were observed in the same symptoms between the attack period (A) and the remission period (R).

Results

Basic statistical characteristics analysis

The data consisted of 595 patients with coronary heart disease angina pectoris, including 278 males and 317 females. The average age was 62 years (range 31-93). The average height of patients was about 165 cm (range 142-192). From the attack period to the remission period, the average weight remained at 66 kg. **Table 3** displays statistical characteristics of the patients' vital signs (including T, R, P, DBP, SBP, HR, and BMI) in the two periods. As shown in **Table 3**, none of the vital signs changed much, indicating that no significant changes in vital signs occurred between the attack period and the remission period.

Dynamic changes of symptoms

Through contingency table analysis, all 73 TCM symptom variables were investigated and the results are shown in **Table 4**. The data show that nearly all *P* values of the chi-square tests were less than 0.0001, except for blackish complexion (V6) with a *P* value of 0.93. These data indicated significant differences between the attack period and the remission period for all TCM symptom indicators, except for blackish complexion (V6).

The dynamic changes of symptoms from the attack period to the remission period can be concluded as follows. (1) Complexion. Red complexion (V3) and flushed cheeks (V4) disappeared, dim complexion (V5) decreased and sallow complexion (V2) increased. Both blackish complexion (V6) and pale complexion (V1) occurred in the remission period, and do not appear in the attack period. (2) Lip color. Cyanotic lips (V11) disappeared, dark reddish

lips (V10) and black lips (V12) occurred in the remission period. (3) Nails. Cyanotic nails (V15) decreased, blue nails (V13) and dark nails (V14) occurred in the remission period. (4) Morphology. Swelling limbs (V19) and withered hair (V24) disappeared, fat (V16), heavy cumbersome limbs (V20) and cold limbs (V23) decreased, numbness limbs (V21) increased, joint pain (V22) occurred in the remission period. (5) Cold and heat. Fearing wind (V28) and feverish sensation over palm, sole and heart (V31) disappeared, limbs lacking warmth (V32) increased. (6) Head, body, chest and abdomen. Abdominal distention (V41), impatient and irritable (V46), emotional depression (V48) and headache (V50) disappeared, some other symptoms like painful chest (V36), palpitation (V37), decreased appetite 1 (V40), gastric lump (V42), soreness and weakness of waist and knees (V49), deafness (V52), tinnitus (V53), heart vexation (V38) and belching (V39) increased, chest oppression (V35) occurred in the remission period. (7) Stool and urine. Loose stool (V66) and scanty reddish urine (V72) disappeared, constipation (V65) decreased, frequent urination (V68) and nocturnal polyuria (V69) occurred in the remission period.

Dynamic changes of high-incidence symptoms

In this subsection, we performed a comparative analysis of the high-incidence symptoms (more than 10% of the patients showed these symptoms). Therefore, 19 high-incidence symptoms were selected in the attack period and 14 symptoms in the remission period. We found that all high-incidence symptoms in the remission period belonged to the attack period. The 5 symptoms that disappeared in the remission period were as follows: constipation (V65), gastric lump (V42), belching (V39), feverish sensation over palm, sole and heart (V31) and lusterless complexion (V7). Thus, 14 high-incidence symptoms in the remission period were dim complexion (V5), cyanotic lips (V11), fat (V16), heavy cumbersome limbs (V20), spontaneous sweating (V33), chest oppression (V35), painful chest (V36), palpitation (V37), heart vexation (V38), frequent sighing (V45), tinnitus (V53), thirst or not (V55), thirst without liking for a drink (V57), and insomnia (V73).

Table 5 displays the dynamic changes of high-incidence symptoms from the attack period to the remission period. There are 16 high-inci-

Table 3. Statistical characteristics of vital signs based on two surveys

Vital Sign	Survey	Mean	SD	Min	Max	95% LCI	95% UCI
T	Α	36.34	0.23	35.30	37.20	36.32	36.35
	R	36.36	0.22	35.20	37.20	35.94	36.79
R	Α	18.37	2.44	12.00	68.00	18.18	18.57
	R	18.22	2.35	12.00	68.00	18.03	18.40
Р	Α	70.82	11.28	44.00	180.00	69.92	71.73
	R	69.92	8.39	48.00	100.00	53.48	86.37
DBP	Α	132.02	16.41	90.00	220.00	130.70	133.34
	R	130.95	14.46	90.00	190.00	102.61	159.29
SBP	Α	79.89	9.93	60.00	130.00	79.09	80.69
	R	78.95	8.90	80.00	130.00	61.52	96.39
HR	Α	71.04	11.73	44.00	180.00	70.10	71.99
	R	70.24	8.78	48.00	100.00	53.02	87.02
BMI	Α	24.31	3.10	13.67	36.51	24.06	24.56
	R	24.34	3.06	16.02	36.51	18.34	30.34

SD, Standard Deviation; Temperature, T; Respiration, R; Pulse, P; Diastolic Blood Pressure, DBP; Systolic Blood Pressure, SBP; Heart Rate, HR; Body Mass Index, BMI; A, attack period; R, remission period.

dence symptoms with reduced frequencies in the remission period when compared with the corresponding results in the attack period (variations in frequency are displayed in parentheses). These include chest oppression (V35, 97), painful chest (V36, 86), cyanotic lips (V11, 71), insomnia (V73, 61), palpitation (V37, 45), thirst or not (V55, 38), dim complexion (V5, 33), heart vexation (V38, 29), cyanotic nails (V15, 22), and loose stool (V66, 22). Together, these findings indicate that some symptoms relieved after three-months of TCM treatment. However, from the attack period to the remission period, there were still several symptoms that showed increased frequencies. These include tinnitus (V53, 40), sallow complexion (V2, 3), nausea and vomiting (V44, 3), dark reddish lips (V10, 2), thin (V17, 2), dark nails (V14, 1), edema of face (V18, 1) and thirst without liking for a drink (V57, 1). Blackish complexion (V6), grayish skin (V27), difficult and painful urination (V70), and clear and profuse urine (V71), and showed the same frequencies from the attack period to the remission period.

Discussion

In this study, descriptive statistical methods and two-way contingency table analysis were used to investigate the changes between the attack period and the remission period. As expected, no big differences were observed in

patients' temperature, respiration, pulse, diastolic blood pressure, systolic blood pressure, heart rate, and body mass index during the past three months. Based on the results of contingency table analysis and frequency percentages of high-incidence, we found that blackish complexion was the only symptom that was not significantly different between the two periods. We found that all 14 high-incidence symptoms in the remission period belonged to the attack period. Other 5 high-incidence symptoms in the attack period included constipation, gastric lump, belching, feverish sensation over palm, sole and heart, and lusterless complexion. The frequencies of 16 highincidence symptoms in the re-

mission period were obviously lower compared to those in the attack period. Blackish complexion, grayish skin, difficult and painful urination, and clear and profuse urine did not change in frequency. The frequency of tinnitus, sallow complexion, nausea and vomit, dark reddish lips, thin, dark nails, edema of face, and thirst with liking for drink increased.

From the perspective of dimensions that symptoms belong to, we drew the following conclusions: (1) Complexion. Dim complexion decreased and sallow complexion increased. Both blackish complexion and pale complexion occurred. (2) Lip color. Dark reddish lips and black lips occurred in the remission period. (3) Nails. Blue nails and dark nails occurred. (4) Morphology. Fat, heavy cumbersome limbs and cold limbs decreased numbness of limbs increased, joint pain occurred. (5) Cold and heat. Limbs lacking warmth increased. (6) Head, body, chest and abdomen. Painful chest, palpitation, decreased appetite 1, gastric lump, soreness and weakness of waist and knees, deafness, tinnitus, heart vexation and belching increased, chest oppression occurred. (7) Stool and urine. Frequent urination and nocturnal polyuria occurred.

In the future, we will apply more network-based methods, including social network analysis, to

Table 4. Contingency table analysis on all 73 TCM symptom indicators

Ind.	χ^2	Р									
V1	132.43	<0.0001	V20	336.14	<0.0001	V39	208.29	<0.0001	V58	172.70	<0.0001
V2	218.93	<0.0001	V21	207.97	<0.0001	V40	157.90	<0.0001	V59	346.84	<0.0001
V3	164.70	<0.0001	V22	221.79	<0.0001	V41	239.40	<0.0001	V60	374.20	<0.0001
V4	205.10	<0.0001	V23	295.70	<0.0001	V42	237.06	<0.0001	V61	426.69	<0.0001
V5	253.89	<0.0001	V24	236.80	<0.0001	V43	194.92	<0.0001	V62	226.93	<0.0001
V6	0.01	0.93	V25	445.50	<0.0001	V44	40.05	<0.0001	V63	145.94	<0.0001
V7	270.77	<0.0001	V26	220.86	<0.0001	V45	196.32	<0.0001	V64	108.55	<0.0001
V8	355.79	<0.0001	V27	595.00	<0.0001	V46	176.12	<0.0001	V65	278.33	<0.0001
V9	312.37	<0.0001	V28	244.89	<0.0001	V47	216.26	<0.0001	V66	14.64	<0.0001
V10	157.53	<0.0001	V29	70.71	<0.0001	V48	278.24	<0.0001	V67	197.00	<0.0001
V11	165.72	<0.0001	V30	342.34	<0.0001	V49	151.73	<0.0001	V68	135.26	<0.0001
V12	293.96	<0.0001	V31	260.82	<0.0001	V50	192.50	<0.0001	V69	112.54	<0.0001
V13	269.98	<0.0001	V32	182.72	<0.0001	V51	269.78	<0.0001	V70	595.00	<0.0001
V14	185.72	<0.0001	V33	298.18	<0.0001	V52	345.27	<0.0001	V71	422.55	<0.0001
V15	150.66	<0.0001	V34	226.06	<0.0001	V53	206.11	<0.0001	V72	140.34	<0.0001
V16	362.35	<0.0001	V35	104.03	<0.0001	V54	429.03	<0.0001	V73	182.97	<0.0001
V17	354.73	<0.0001	V36	203.24	<0.0001	V55	237.51	<0.0001	-	-	-
V18	351.88	<0.0001	V37	299.03	<0.0001	V56	380.51	<0.0001	-	-	-
V19	327.84	<0.0001	V38	289.30	<0.0001	V57	241.61	<0.0001	-	-	-

Ind., Indicator; χ^2 , chi-square statistics; P, *P* value; V1, pale complexion; V2, sallow complexion; V3, red complexion; V4, flushed cheeks; V5, dim complexion; V6, blackish complexion; V7, lusterless complexion; V8, puffy face; V9, pale lips; V10, dark reddish lips; V11, cyanotic lips; V12, black lips; V13, blue nails; V14, dark nails; V15, cyanotic nails; V16, fat; V17, thin; V18, edema of face; V19, swelling limbs; V20, heavy cumbersome limbs; V21, numbness limbs; V22, joint pain; V23, cold limbs; V24, withered hair; V25, dry scaly skin; V26, withered skin; V27, grayish skin; V28, fearing wind; V29, fearing cold; V30, tidal fever; V31, feverish sensation over palm, sole and heart; V32, limbs lacking warmth; V33, spontaneous sweating; V34, night sweating; V35, chest oppression; V36, painful chest; V37, palpitation; V38, heart vexation; V39, belching; V40, decreased appetite 1; V41, abdominal distention; V42, gastric lump; V43, acid reflux; V44, nausea and vomit; V45, frequent sighing; V46, impatient and irritable; V47, distending of hypochondria; V48, emotional depression; V49, soreness and weakness of waist and knees; V50, headache; V51, dizziness; V52, deafness; V53, tinnitus; V54, others in head, body, chest and abdomen; V55, thirst or not; V56, thirst without liking for drink; V57, thirst without liking for a drink; V58, thirst with liking hot drinks; V59, bland taste in mouth; V60, bitter taste in mouth; V61, foul breath; V62, sticky sensation in mouth; V63, decreased appetite 2; V64, rapid digestion with polyphagia; V65, constipation; V66, loose stool; V67, scanty urine; V68, frequent urination; V69, nocturnal polyuria; V70, difficult and painful urination; V71, clear and profuse urine; V72, scanty reddish urine; V73, insomnia.

investigate dynamic changes on Coronary Heart Disease Angina Pectoris TCM Symptoms [18-20]. Based on these results, we will further investigate syndromes before and after three months TCM treatment. Moreover, theoretical innovation in algorithms or methods is needed in future investigations.

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Disclosure of conflict of interest

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Table 5. Dynamic changes of high-incidence symptom indicators

Ind.	Α	R	Percentage (%)	Change (%)
V5	123	90	20.67→15.13	-5.54
V7	72	56	12.10→9.41	-2.69
V11	179	108	30.08→18.15	-11.93
V16	102	100	17.14→16.81	-0.33
V20	82	72	13.78→12.10	-1.68
V31	65	56	10.92→9.41	-1.51
V33	119	100	20.00→16.81	-3.19
V35	513	416	86.22→69.92	-16.30
V36	374	288	62.86→48.40	-14.46
V37	297	252	49.92→42.35	-7.57
V38	144	115	24.20→19.33	-4.87
V39	61	48	10.25→8.07	-2.18
V42	64	56	10.76→9.41	-1.35
V45	65	61	10.92→10.25	-0.67
V53	118	158	19.83→26.55	6.72
V55	118	80	19.83→13.45	-6.38
V56	217	208	36.47→34.96	-1.51
V65	62	46	10.42→7.73	-2.69
V73	129	68	21.68→11.43	-10.25

A, attack period; R, remission period; V5, dim complexion; V7, lusterless complexion; V11, cyanotic lips; V16, fat; V20, heavy cumbersome limbs; V31, feverish sensation over palm, sole and heart; V33, spontaneous sweating; V35, chest oppression; V36, painful chest; V37, palpitation; V38, heart vexation; V39, belching; V42, gastric lump; V45, frequent sighing; V53, tinnitus; V55, thirst or not; V56, thirst without liking for drink; V65, constipation; V73, insomnia.

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