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J Tradit Chin Med 2013 April 15; 33(2): 194-199 ISSN 0255-2922 © 2013 JTCM. All rights reserved.

CLINICAL STUDY

Traditional Chinese Medicine syndrome patterns and *Qi*-regulating, chest-relaxing and blood-activating therapy on cardiac syndrome X

Yingfei Bi, Jingyuan Mao, Xianliang Wang, Yongbin Ge, Henghe Wang, Zhenpeng Zhang

Yingfei Bi, Jingyuan Mao, Xianliang Wang, Yongbin Ge, Henghe Wang, Department of Cardiovascular, the First Teaching Hospital of Tianjin University of Chinese Medicine, Tianjin 300193, China

Zhenpeng Zhang, Department of Cardiovascular, Guang'anmen Hospital of China Academy of Chinese Medical Sciences, Beijing 100053, China

Supported by Special Project of National Clinical Research Base of TCM (No. JDZX2012140), Innovation Team Development Plan of the Ministry of Education (No. IRT1276)

Correspondence to: Prof. Jingyuan Mao, the First Teaching Hospital of Tianjin University of Chinese Medicine, Tianjin 300193, China. jymao@126.com

Telephone: +86-22-27432325 **Accepted:** February 16, 2012

Abstract

OBJECTIVE: To master the syndrome patterns characteristics and explore the effective therapy methods of Traditional Chinese Medicine (TCM) for cardiac syndrome X (CSX).

METHODS: The TCM syndrome characteristics were mastered and the TCM intervention programs were determined by clinical investigations for TCM syndrome patterns characteristics of CSX patients. Then, the clinical efficacy studies on TCM intervention for CSX were carried out through randomized controlled trials.

RESULTS: CSX is a clinical syndrome with the main manifestations of chest pain and chest stuffiness, and *Qi* stagnation, phlegm retention and blood stasis are the basic symptoms of CSX. As a result, the *Qi*-regulating, chest-relaxing and blood-activating

therapy integrated with some Western Medicines was adopted for treatment. The effect of *Qi*-regulating, chest-relaxing and blood-activating therapy can reduce the frequency and degree of angina, improve the symptoms and exercise the tolerance of patients, inhibit the inflammatory response of vascular walls and protect the function of vascular endothelial cells, which is better than that of the simple and conventional Western Medicine alone.

CONCLUSION: A good effect was achieved in the integration of Chinese and Western Medicines for CSX. The therapy is worthy to be applied further in clinical practice. On the other hand, more long-term and randomised controlled studies with large samples are still required to further determine the clinical efficacy and safety of the therapy.

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Key words: Microvascular angina; *Qi* stagnation; Phlegm retention; Blood stasis; Regulating *Qi*-flowing for removing blood stasis; Relieving stuffiness of the chest-diaphragm

INTRODUCTION

Cardiac syndrome X (CSX) is a kind of clinical syndrome with typical symptoms of angina, positive results of electrocardiograph (ECG) and/or treadmill exercise test, negative results of coronary angiography (CAG) and absence of coronary artery spasm, which is also known as microvascular angina. Likoff *et al* ¹ were the first to report such case, referring to it as angina pectoris with normal coronary arteries. Kemp *et al* ² called it the X syndrome. CXS may be induced by vari-

ous factors, such as the reduction of the reserve capacity of coronary artery,³ impaired endothelial function,⁴ estrogen deficiency,⁵ abnormal pain perception,⁶ emotional factors⁷ and so on.

Recent studies on CSX have been increasing with the development of percutaneous coronary intervention. However, they focused more on a few standardised and no exact concept such as CSX in Traditional Chinese Medicine (TCM) has been developed. Most studies consider that CSM belongs to the category of chest impediment and chest pain. Based on the TCM theory, we analysed the syndrome characteristics of CSX and used the *Qi*-regulating, chest-relaxing and blood-activating therapy integrated with Western Medicine for treatment.

METHODS

Analysis of the TCM syndrome patterns of CSX

A total of 12 CSX patients consisting of 5 men and 7 women aged 46 to 66 years were enrolled and investigated for the TCM syndrome patterns in study I. All patients were admitted to the Cardiovascular Department of the First Teaching Hospital of Tianjin University of Chinese Medicine from March 2003 to July 2004.

The study I systematically explains the TCM pathogenesis characteristics of CSX. However, its analysis of the TCM syndrome patterns of CSX was not sufficiently clear and detailed, and the number of samples was small. Based on these shortcomings, we summarised the distribution characteristics of the TCM syndrome patterns in 51 CSX patients in study II. The 51 CSX patients consisted of 11 men and 40 women aged 35 to 71 years. All patients were admitted to the Cardiovascular Department of the First Teaching Hospital of Tianjin University of Chinese Medicine from March 2003 to January 2006.

Study of Qi-regulating, chest-relaxing and blood-activating therapy of TCM for CSX

The above studies suggest that chest pain and chest stuffiness are the main manifestations of CSX, and Qi stagnation, phlegm retention and blood stasis are the most common TCM syndrome patterns. Based on the pathogenesis characteristics of CSX, the Qi-regulating, chest-relaxing and blood-activating therapy was determined as the main treatment method. We treated the patients with the Qi-regulating, chest-relaxing and blood-activating therapy integrated with some Western Medicines and evaluated its clinical efficacy through randomised controlled trials in study III and study IV. The TCM syndrome patterns of 51 CSX patients were analysed. In study III, the selected cases were assigned to the control group (19 patients) and the treated group (32 patients). No statistically significant differences in gender, age, main complications and distribution of risk factors were observed among the two groups. The control group was treated with conventional treatment, such as nitroglycerin injection of 5-10 mg, which is diluted by 500 mL of 5% glucose for intravenous dripping, regulated at 20 drops/min to 30 drops/min and given once daily. When necessary, Betaloc of 6.25-25 mg, given twice daily, and/or diltiazem hydrochloride of 30 mg, given trice daily, were administered. The treated group was treated similar to the control group aside from the herbal decoction of the Qi-regulating, chest-relaxing and blood-activating therapy composed of Chaihu (Radix Bupleuri) 10 g, Zhiqiao (Fructus Aurantii) 12 g, Chuanxiong (Rhizoma Chuanxiong) 10 g, Danggui (Radix Angelicae Sinensis) 12 g, Gualoupi (Pericarpium Trichosanthis) 15 g, Xiebai (Bulbus Aallii Macrostemi) 10 g, Danshen (Radix Salviae Miltiorrhizae) 15 g, Yunling (Yunnan Poria) 12 g, Chuanxiong (Rhizoma Atractylodis Macrocephalae) 12 g, Chenpi (Pericarpium Citri Reticulatae) 12 g, Honghua (Carthamus Tinctorius) 15 g, and Yanhusuo (Rhizoma Corydalis) 15 g. The decoction was prepared by decocting crude drugs with water and was boiled down to about 300 mL and administered at 150 mL once or twice daily. The treatment course was for 14 days.

In study IV, a total of 55 CSX patients consisting of 8 men and 47 women aged 18 to 74 years were enrolled for the study. All patients were admitted to the Cardiovascular Department of the First Teaching Hospital of Tianjin University of Chinese Medicine from July 2006 to August 2007.

The selected cases were assigned to the control group (27 patients) and the treated group (28 patients) by the random number table method. No statistically significant differences in gender, age, major complications and distribution of risk factors were observed between the two groups. The control group was treated with conventional treatment, such as nitroglycerin injection of 5-10 mg, which was diluted by 500 mL of 5% glucose for intravenous dripping, regulated at 20 drops/ min to 30 drops/min and given once daily. When necessary, Betaloc of 6.25-12.5 mg, given twice daily, and/ or diltiazem hydrochloride of 30 mg, given thrice daily, were administered. The treated group was treated similar to the control group aside from the herbal decoction of the Qi-regulating, chest-relaxing and blood-activating therapy composed of Chaihu (Radix Bupleuri) 10 g, Zhiqiao (Fructus Aurantii) 12 g, Gualoupi (Pericarpium Trichosanthis) 15 g, Chuanxiong (Rhizoma Chuanxiong) 10 g, Danggui (Radix Angelicae Sinensis) 12 g, Xiebai (Bulbus Allii Macrostemi) 10 g, Danshen (Radix Salviae Miltiorrhizae) 15 g, Yunling (Yunnan Poria) 12 g, Chenpi (Pericarpium Citri Reticulatae) 12 g, Baizhu (Rhizoma Atractylodis Macrocephalae) 12 g, Yanhusuo (Rhzoma Corydalis) 15 g and Honghua (Carthamus Tinctorius) 15 g. The decoction was prepared by decocting crude drugs with water and boiled down to about 300 mL. It was administered at 150 mL once or twice daily. The treatment course was 14 days.

RESULTS

Study I

Analysis of TCM symptoms: the main manifestations observed in the 12 CSX patients include serious chest pain that worsens with activity, chest stuffiness, shortness of breath, palpitations, swollen and dark purple tongue with stasis spots, stringy-taut and thready pulse, fatigue, inactive talking, irritability and red or teeth-printed tongue in 5 patients.

Analysis of TCM pathogenesis: chest pain and stuffiness, likely to be caused or aggravated when angry or depressed, are manifestations of Qi stagnation. A dark purple tongue with stasis spots and a stringy-taut and thready pulse are the manifestations of blood stasis. Based on these symptoms, the main TCM pathogenesis of CSX is Qi stagnation and blood stasis. Moreover, the additional symptoms in 5 patients are manifestations of Qi and Yin deficiencies, such as mental and physical fatigue, inactive talking, irritability and red or teeth-printed tongue.

Study II

Analysis of TCM symptom frequency: among the 51 CSX patients, 46 had chest pain (90.2%), which is the most common clinical manifestation of CSX. Moreover, chest stuffiness (86.3%), abdominal distention (70.6%), emotional depression (60.8%), mental and physical fatigue (41.2%), spontaneous perspiration (21.6%), inactive talking (19.6%) and looking without lustre (11.8%) were also observed (Table 1).

Analysis of tongue and pulse manifestations: among the 51 CSX patients, 25 (49%) had dark purple tongue or tongue with stasis spot, 20 (39.2%) had greasy coating, 19 (37.3%) had a stringy-taut pulse, 9 (17.6%) had a rapid pulse and 7 (13.7%) had a weak pulse. The analysis clearly shows that Qi stagnation, phlegm retention and blood stasis are the primary TCM pathogenesis of CSX.

Analysis of TCM syndrome pattern distribution: chest pain, chest stuffiness and abdominal distention were observed to be the most common manifestations of CSX. Emotional depression and irritability were also observed as main manifestations. The results suggest that Qi stagnation, phlegm retention and blood stasis are the primary TCM syndrome patterns. As the disease progresses, Qi and Yin deficiencies in CSX can be observed. As shown in Table 1, 34 cases (66.7%) had three syndrome patterns (i.e., Qi stagnation, phlegm retention and blood stasis) at the same time and belonged to simple excess syndrome. Moreover, 17 cases (33.3%) also had three syndrome patterns and additional deficient syndromes, such as Qi deficiency, Yin deficiency and both Qi and Yin deficiencies, and belonged to integrated deficient and excess syndrome.

Study III

Clinical efficacy on angina pectoris: in the treated

Table 1 Analysis of TCM symptor	m frequer	псу
Symptom	n	Frequency (%)
Chest pain	46	90.2
Chest stuffiness	44	86.3
Abdominal distention	36	70.6
Emotional depression	31	60.8
Sticky feeling in the mouth	26	51.0
Mental and physical fatigue	21	41.2
Shortness of breath	20	39.2
Palpitations	19	37.3
Dizziness	18	35.3
Irritability	13	25.5
Anorexia	13	25.5
Fat body	12	23.5
Spontaneous perspiration	11	21.6
Inactive talking	10	19.6
Dry stool	8	15.7
Looking without lustre	6	11.8
Insomnia, dreaming and disturbed sleep	6	11.8
Thin stool	4	7.8
Tinnitus	4	7.8
Dry mouth	3	5.9
Night sweating	2	3.9
Aversion to cold	1	2.0
Tidal fever	1	2.0
Forgetfulness	1	2.0

Note: TCM: Traditional Chinese Medicine.

group, the clinical efficacy on angina pectoris was evaluated as markedly effective in 19 cases and effective in 8 cases. The total effective rate was 81.2%. In the control group, the clinical efficacy on angina pectoris was evaluated as markedly effective in 7 cases and effective in 3 cases. The total effective rate was 52.6%. The total effective rate in the former was clearly better than that in the latter (P<0.05).

Effect on the main symptoms: as shown in Table 2, the effect on chest pain, chest stuffiness, abdominal distention, fidgetiness and palpitation in the treated group was significantly better than that before treatment (P< 0.05 or P<0.01), whereas the improvement was only observed in chest pain, chest stuffiness and fidgetiness in the control group (P<0.05). The comparison between the two groups shows that the effect on chest pain, chest stuffiness and palpitation in the treated group is significantly better than that in the control group (P<0.05), whereas the effect on abdominal distention and fidgetiness is insignificantly different between the two groups (P>0.05).

Effect on the TCM syndrome: according to the guiding principles for clinical study on new Chinese medicines, the TCM syndrome score that decreases greater than 70% is identified as markedly effective, 30% to 70% is effective, less than 30% is ineffective and less than 0 is aggravated. In the treated group, 15 cases proved to be markedly effective and 12 cases were effective. The total effective rate was 84.4%. In the control group, 6 cases proved to be markedly effective, and 5 cases were effective. The total effective rate was 57.9%. The total effective rate in the treated group is clearly better than that in the control group (P<0.05).

Effect on the treadmill exercise test: a treadmill exercise test was carried out in 51 patients before treatment and repeated after treatment in 35 patients (22 in the treated group and 13 in the control group). The results are listed in detail in Table 3.

The result of the treadmill exercise test shows that the maximal metabolic equivalent (Max MET) and the time of angina onset and ST segment depression by 0.1 mV clearly improved after treatment in both groups. However, the improvement in the treated group was better than that in the control group (P<0.05).

Adverse reactions and drug safety: in the course of treatment, one patient of the control group became flustered after the sublingual administration of nitroglycerin, but the symptom disappeared 1 min later. Among the treated group, 32 patients had no obvious adverse reactions. The function tests of blood, urine, liver and kidneys of the two groups showed no abnormal changes before and after treatment.

Study IV

Clinical efficacy on angina pectoris: according to the guiding principles for clinical study on new Chinese medicines, in the treated group, the clinical efficacy on angina pectoris in 17 cases was evaluated as markedly effective and 6 cases as effective. The total effective rate was 82.14%. In the control group, 12 cases were evaluated as markedly effective and 3 cases as effective. The total effective rate was 55.56%. The total effective rate in the former is obviously better than that in the latter (P<0.05).

Effect on the TCM syndrome: in the treated group, the effect on TCM syndrome in 13 cases was markedly effective and that in 11 cases was effective. The total effective rate was 82.14%. In the control group, 8 cases were markedly effective and 7 cases were effective. The total effective rate was 55.56%. The total effective rate in the treated group is obviously better than that in the control group (P<0.05).

Effect on electrocardiogram: according to the guiding principles for clinical study on new Chinese medicines, in the treated group, the effect on electrocardiogram in 7 cases was markedly effective and that in 8 cases was effective. The total effective rate was 53.57%. In the control group, 5 cases proved to be markedly effective, and 8 cases were effective. The total effective rate was 48.15%. No significant difference in the total effective rate was observed between the treated and control groups (P>0.05).

Effect on the treadmill exercise test: a treadmill exercise test was carried out in 55 patients before treatment and

Table 2 Effect on main symptoms ($ar{x}\pm s$)						
Symptom	Control gro	Control group (n=19)		Treated group (n=32)		
	Before treatment	After treatment	Before treatment	After treatment		
Chest pain	2.31±0.01	1.72±0.54 ^a	2.42±0.01	1.21±0.58 ^{bc}		
Chest stuffiness	2.02±0.69	1.54±0.61 ^a	2.22±0.67	$1.04\pm0.65^{\rm bc}$		
Abdominal distention	1.84±0.52	1.63±0.69	1.94±0.61	1.45±0.62ª		
Fidgetiness	1.92±0.83	1.43±0.82°	2.14±0.75	1.67±0.55ª		
Palpitation	1.93±0.64	1.63±0.66	1.74±0.68	$0.68 \pm 0.76^{\rm bc}$		

Notes: control group was treated with conventional treatment; treated group was treated similar to the control group aside from the herbal decoction of the Qi-regulating, chest-relaxing and blood-activating therapy. ${}^{a}P$ <0.05, ${}^{b}P$ <0.01, compared with before treatment; ${}^{c}P$ <0.05, compared with the control group after treatment.

Table 3 Effect on the treadmill exercise test ($\bar{x} \pm s$)					
	Control group		Treated group		
Item	Before treatment (<i>n</i> =19)	After treatment (<i>n</i> =13)	Before treatment (<i>n</i> =32)	After treatment (<i>n</i> =22)	
Maximal metabolic equivalent (Mets)	5.3±1.1	6.0±0.8 ^a	5.6±2.1	$7.3\pm1.0^{\mathrm{bc}}$	
Time of angina onset and ST segment depression by 0.1 mV (s)	222.5±99.6	285.9±76.5ª	245.3±60.9	360.7±64.8 ^{bc}	

Notes: control group was treated with conventional treatment; treated group was treated similar to the control group aside from the herbal decoction of the Qi-regulating, chest-relaxing and blood-activating therapy. ${}^{a}P$ <0.05, ${}^{b}P$ <0.01, compared with before treatment; ${}^{c}P$ <0.05, compared with the control group after treatment.

repeated in 40 patients after treatment (18 in the treated group and 22 in the control group). The results are listed in detail in Table 4.

The result of treadmill exercise test shows that the Max MET, exercise duration and ST segment depression after exercise obviously improved after treatment in both groups (P<0.05). However, the improvement in the treated group was greater than that in the control group (P<0.05). The result implies that the herbal decoction of Qi-regulating, chest-relaxing and blood-activating therapy could improve the exercise tolerance of patients.

Effect on the endothelin-1 (ET-l), nitrogen monoxide (NO) and hs-CRP levels: The tests of ET-l, NO and high-sensitivity C-reactive protein(hs-CRP) levels were carried out in 55 patients before treatment and repeated in 46 patients after treatment (25 in the treated group and 21 in the control group). The results are listed in detail in Table 5.

The test results show that the ET-l, NO and hs-CRP levels obviously improved after treatment in both groups (P<0.05). However, the improvement in the treated group was greater than that in the control group (P<0.05). The results imply that the herbal decoction of Qi-regulating, chest-relaxing and blood-activating therapy could inhibit the inflammatory response of vascular walls and protect the function of vascular endothelial cells.

Security analysis: in the course of the treatment, both groups had no obvious adverse reactions. The function tests of blood, urine, liver, and kidneys of both groups showed no abnormal changes before and after treatment.

DISCUSSION

The studies (I-IV) show that CSX is a clinical syndrome with the main manifestations of chest pain and chest stuffiness. The enrolled CSX cases (i.e., 19 men and 87 women) were distributed in multiple age groups, from 18 to 74 years old. Women are more likely to be susceptible than men. Based on the TCM, the etiology location of CSX is in the liver, the diseased part is in the heart, and spleen dysfunction is also related. Qi stagnation, phlegm retention and blood stasis are considered the basic pathogenesis, and the heart meridian blocking is the pathological result. The manifested Qi stagnation, phlegm retention and blood stasis are the basic symptoms of CSX throughout the whole course of the disease. As a result, the Qi-regulating, chest-relaxing and blood-activating therapy integrated with some Western Medicine was adopted for treatment. The results show that the effect of Qi-regulating, chest-relaxing and blood-activating therapy is better than that of the simple and conventional Western Medicine alone. This therapy serves to reduce the frequency and degree of angina, improve the symptoms, and exercise the tolerance of patients. Moreover, it can inhibit the inflammatory response of vascular walls and protect the function of vascular endothelial cells.

A good effect was achieved in the integration of Chinese and Western Medicine for CSX. The therapy is worthy to be applied further in clinical practice. However, the modification of the prescription should be applied according to the individual conditions of the patients when using the *Qi*-regulating, chest-relaxing and blood-activating decoction. Moreover, long-term and

Table 4 Effect on the treadmill exercise test ($\bar{x} \pm s$)				
Item	Control group		Treated group	
	Before treatment (<i>n</i> =27)	After treatment (<i>n</i> =22)	Before treatment (<i>n</i> =28)	After treatment (<i>n</i> =18)
Maximal metabolic equivalent (Mets)	5.6±1.2	6.2±0.7ª	5.9±1.8	7.2±0.9 ^{ab}
Exercise duration (s)	243.1±78.8	295.3±65.7 ^a	247.8±80.8	347.0 ± 71.7^{ab}
ST segment depression after exercise (mm)	7.5±2.1	6.2±1.8°	7.9±2.4	$5.3\!\pm\!1.8^{ab}$

Notes: control group was treated with conventional treatment; treated group was treated similar to the control group aside from the herbal decoction of the *Qi*-regulating, chest-relaxing and blood-activating therapy. ${}^{a}P$ <0.05, compared with the control group before treatment; ${}^{b}P$ <0.05, compared with the control group after treatment.

Table 5 Effect on ET-I, NO and hs-CRP levels ($ar{x}\pm s$)					
Item	Contro	Control group		Treated group	
	Before treatment (<i>n</i> =27)	After treatment (n=22)	Before treatment (n=28)	After treatment (n=18)	
ET-1 (ng/L)	99.64±12.61	64.06±15.45°	94.97±10.24	50.01±13.20 ^{ab}	
NO (μmol/L)	45.41±5.91	54.69±4.62 ^a	46.07±5.83	62.34±5.60 ^{ab}	
hs-CRP (mg/L)	3.47±0.24	2.31±0.28 ^a	3.48±0.25	1.80 ± 0.17^{ab}	

Notes: control group was treated with conventional treatment; treated group was treated similar to the control group aside from the herbal decoction of the *Qi*-regulating, chest-relaxing and blood-activating therapy. ET-l: endothelin-1; NO: nitrogen monoxide; hs-CRP: high-sensitivity C-reactive protein. **P*<0.05, compared with the control group before treatment; **P*<0.05, compared with the control group after treatment.

randomised controlled studies with large samples are still required to further determine the clinical efficacy and safety of the *Qi*-regulating, chest-relaxing and blood-activating therapy.

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