

**Official Title of the study:** The diagnostic value of acupoint sensitization based on stable angina pectoris

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**Reasons for the updated protocol:** In the detection of acupoint sensitization, due to the special spelling of 3 acupoints in the Traditional Chinese medicine, including Jueyinshu, Xinshu, Dushu. In our previous version protocol in October, 2017, we made some spelling mistakes about this very 3 acupoints, Now, we need to correct it.

# The diagnostic value of acupoint sensitization based on stable angina pectoris: a study protocol

## **Abstract :**

**Backgrounds:** this study, as the second part, aims to detect the correlation between the coronary artery stenosis, Canadian Cardiovascular Society(CCS) angina pectoris classification and the differential functional status of acupoints in distinguishing the severity of chronic stable angina.

**Methods:** We apply the cross-sectional study design to carry out the exemplary research in the aspects of disease diagnosis, in order to confirm the hypothesis "acupoint sensitization is associated with the severity of angina pectoris, and can contribute to the diagnosis of stable angina pectoris ".

**Discussion:** This project will enrich the basic theory of TCM with a clear point of different functional acupoint status in the diagnosis of stable angina, which will offer important examples for the clinical application in disease diagnosis.

**Keywords:** Study protocol, diagnostic trial, stable angina pectoris

## **1. Background**

Stable angina pectoris (AP) is the result of myocardial ischemia, typified by the clinical symptoms discomfort in the chest, jaw, shoulder, back, or arms, typically provoked by physical exertion or emotional stress and relieved by rest or nitroglycerin[1]. Despite the multiple medical and interventional technologies that have been developed to reduce myocardial ischemia, the ischemic heart disease was still be the top causes of death according to the released World Health Organization (WHO) report in 2004 and the updated data published in *the New England journal medicine* 2013[2-4].

Compared to the traditional Chinese medicine (TCM) syndrome, the invasive coronary angiography(ICA) is considered the “gold standard” by providing a more accurate assessment of lesion severity than visual assessment in patients with suspected coronary artery disease (CAD), especially with high prevalent baseline cardiac risk factors[5]. A few studies have proved that there were relationships between TCM and coronary artery lesion. Historically, acupoint is described and understood with the state according to the core viewpoint and theory of The Inner Canon of Huangdi or Yellow Emperor's Inner Canon. When the human body has disease, acupoints on the body surface may be sensitized with various types of sensitization, and acupoint heat-sensitization is a type of acupoint sensitization. This sensitized acupoint can not only reflect the pathological phenomenon of the diseases but also can distinguish the severity of the disease effectively.

But, there was no study to explore the correlation between the coronary artery stenosis and the acupoint sensitization. Thus, our study is designed to explore the correlation between the coronary artery lesions, Canadian Cardiovascular

Society(CCS) angina pectoris classification and the acupoint sensitization, which can ensure the degree of acupoint sensitization in distinguishing the severity of the disease.

## **2. Methods**

This part adopts the "single entry" cross-sectional study design. After the eligible patients recruited in group, the coronary artery stenosis will be evaluated through coronary angiography and the Canadian Cardiovascular Society(CCS) angina pectoris classification will also be evaluated at the same time. The degree of acupoint sensitization will be tested by the electronic Von Frey instrument by one professional acupuncturist .

### **2.1 Study population**

Eligible stable angina pectoris patients should match the inclusion criteria and the exclusion criteria. Inclusion criteria: participants will be included if they fulfill the following criteria:1)patients meet the diagnostic criteria of ACC/AHA angina pectoris of coronary heart disease ; 2) $35 \leq \text{age} \leq 80$  years, male or female; 3) the onset of

angina pectoris  $\geq 3$  months and the frequency of angina attack  $\geq$  twice a week; 4)

patients agree to do coronary angiography examination and signed the informed consent. Exclusion criteria: patients with any of the following conditions will be excluded:1)People with mental disabilities and intelligent obstacle;2) Patients who can't accomplish the detection of acupoint sensitization;3)Patients with allergic condition, especially the contrast media;4) Patients with acute myocardial infarction, unstable angina, during arrhythmia and serious diseases which can affect the blood supply of myocardial;5) Skin or peripheral nerve paresthesia, pain or the detect area of skin ulcerate ;6) pregnant or lactating women;7) Patients who undergoing other clinical trials.

### **2.2 Detection of acupoint sensitization**

Theoretically, the higher readings of the Von Frey electronic measuring instrument, the higher the degree of acupoint sensitization. First of all, in order to ensure the privacy of the participants, an independent sensitizing detection room will be set. Meanwhile, there must be a nurse or other medical staff when the female subjects in sensitization detection operation. Secondly, the participants pose the right position, double lower limbs stretch the knee, testers press each region with finger and proper strength in total 12 acupoints, including Shenmen, Yinxu, Shaohao, Jiquan, Neiguan, Ximen, Quze, Danzhong, Jueque, Jueyinshu, Xinsu, Dushu. Researchers detect the sensitization of acupoints by using Von Frey electronic measuring pain instrument. Every acupoint will be tested for 2 times, and if the mean value is higher than 15, the third test will be conducted.

All the collected data will be documented in the case report form(CRF). At the same time, the data will be saved in the computer folder which established beforehand.

### **2.3 CCS angina pectoris classification**

Based on the following standard and combined with our concept of design, all

the eligible patients will be evaluated referring to the following standards by two researchers.

Classifications	Detailed contents
Class I:	Ordinary physical activity does not cause angina, such as walking, climbing stairs. Angina (occurs) with strenuous, rapid or prolonged exertion at work or recreation
Class II	Slight limitation of ordinary activity. Angina occurs on walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, in wind, or under emotional stress, or only during the few hours after awakening. Angina occurs on walking more than 2 blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal condition.
Class III	Marked limitations of ordinary physical activity. Angina occurs on walking one to two blocks on the level and climbing one flight of stairs in normal condition and at a normal pace.
Class IV	Inability to carry on any physical activity without discomfort anginal symptoms may be present at rest

## 2.4 Coronary angiography

All the included patients will undergo the coronary angiography to observe and record stenosis in coronary artery branches, including left main artery, left anterior descending artery, diagonal branches, left circumflex artery, obtuse marginal branch, acute marginal artery, right coronary artery and posterior descending artery.

All the collected data will be documented in the CRF. At the same time, the data will be saved in the computer folder which established beforehand.

## 2.5 Recruitment procedures

The following scheme will be used to recruit participants with angina pectoris. Patients visiting the outpatient clinics and inpatient department in the department of Cardiology of the West China Hospital in Sichuan university will be informed by the cardiologist of the present trial. Research assistants will continue the enrollment process by screening eligible participants according to the inclusion/exclusion criteria. Participants will be included only if they meet the inclusion criteria and provide written informed consent indicating that they agree to every procedure of the trial and join in the trial willingly.

## 2.6 Sample size calculation

According to the diagnostic test sample size, ensuring the accuracy in the prediction, sensitivity is set 80% and specificity is 60%,  $\alpha = 0.05$ , the difference between the samples and the overall is  $\delta = 0.10$ . Considering a 15% dropout, 183 participants will be included in this trial finally.

$$n = Z_{\alpha}^2 \times p \times (1 - p) / \delta^2, (\alpha = 0.05, \delta = 0.1)$$

## 2.7 Practitioners training

All researchers involved in this trial, all clinical physicians who enroll participants

and all assessors who collect data must attend training classes to make sure all practices in the hospital are generalized and standardized.

## **2.8 Benefits and risks**

This study is a single entry, cross-sectional and diagnostic studies. During this research, patients did not receive any therapeutic interventions, but stick to the original angina treatment plan. The main detection of acupoint sensitization concerned with stable angina pectoris by the VonFrey electronic measuring instrument: just put the instrument probe at the acupoint sensitization on the surface of the skin and record the data displayed in the instrument. In the process of operation, the sponsor will shoulder the economic burden caused by the occurrence of adverse events related to this study. Besides, the cost in the following examination may reduce considerably. In order to protect patient privacy, all the data are shrouded in secrecy, all relevant researchers must sign a confidentiality agreement before access to the data.

## **2.9 Safety and adverse event**

For the sake of patient safety, prevention measures and emergency medical plans will include well-equipped treatment rooms, emergency department, cardiovascular specialist and first-line clinical physicians. All adverse events(AEs) associated with detection would be recorded in detail; these AEs concerning the short transient local skin discomfort include redness, itching and subcutaneous bleeding. On the other hand, the anti-anginal drugs (basic therapy) will be documented as well. Serious adverse events (SAE) are defined as death or life threatening events, which may require inpatient hospitalization, cause prolongation of existing hospitalization, or even result in persistent or significant disability/incapacity and need intervention to prevent permanent impairment or damage. If participants suffer any AE/SAE, researchers must immediately take measures to protect the safety of the patients, all details will be documented, and then report to the principal investigator and the ethics committee within 24 hours so that they can decide whether the patient should withdraw from the trial. The sponsor will ensure that meet the requirements of all laws and regulations of reporting procedures.

## **3. Statistical analysis**

Analysis were conducted to explore relationships between the degree of acupoint sensitization, the degree of coronary artery stenosis and CCS angina pectoris classification by SPSS20.0 software. For the collected data, the mechanical pain threshold of acupoint sensitization collected by Von Frey electronic measuring instrument and the degree of coronary angiography are continuous quantitative data. The grade of Canadian angina is qualitative data and specific correlation analysis method will be choose based on the type and distribution of collected data. Diagnostic value will be further analyzed in the final step.

## **Trial status**

This trial hasn't recruited any patients yet.

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