

Research name:

The tongue features associated with chronic kidney disease(CKD)

Principal Investigator(s): Jia-Ming Chen

Institution: CHANGHUA CHRISTIAN HOSPITAL, TAIWAN

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Continuing review: The protocol extends for one year

Informed consent · Informed page

Dear patients:

It is our pleasure to invite you to participate in a clinical research entitled ‘The effect of acupuncture on dialysis patients with restless legs syndrome(RLS)’.

Please read the following contents carefully, which will help you understand the details of the study. If you wish, you can discuss it with your relatives and friends, or ask your doctor to give an explanation to help you make a decision.

1. Research introduction

Chronic kidney disease (CKD) is an important global public health problem. According to related literatures, the prevalence of CKD is about 11% .(1) CKD is a progressive disease. If it progresses to end-stage renal disease (ESRD), renal replacement therapy: dialysis and renal transplantation, is required to maintain life(2). The growing prevalence and progression of chronic kidney disease (CKD) raises concerns about our capacity to manage its economic burden to patients, caregivers, and society. The societal direct and indirect costs of CKD and end-stage renal disease are substantial and increase throughout disease progression. There is significant variability in the evidence about direct and indirect costs attributable to CKD and end-stage renal disease, with the most complete evidence concentrated on direct health care costs of patients with advanced to end-stage CKD.(2)

CKD, also called chronic kidney failure, is described as a sustained reduction in glomerular filtration rate or evidence of structural or functional kidney abnormalities.(3) Chronic kidney disease (CKD) refers to all five stages of kidney damage, from very mild damage in stage 1 to complete kidney failure in stage 5. CKD symptoms include pain, itch(pruritus), peripheral numbness, sleep disturbances, depression, fatigue, nausea and vomiting. Factors that contribute to these symptoms include anaemia, uraemic toxins, reduced renal capacity, chronic disease-related inflammation, and psychological stress associated with long-term illness.(4)

If it progresses to end-stage renal disease (ESRD), renal replacement therapy, including hemodialysis, peritoneal dialysis and kidney transplantation, is required to maintain life. Therefore, it is essential to find effective and conservative treatment methods to delay the progression of CKD.

Diagnosis in traditional Chinese medicine (TCM) is based on four procedures, observation, smelling or listening, inquiry, and palpation. Tongue diagnosis, serving as a vital non-invasive tool to provide useful clinical information, plays a pivotal role in TCM. The tongue is considered to reflect the physiological and pathological condition of the body, as well as the degree and progression of disease, through the meridians that connect the tongue to the internal organs. By observing tongue features, TCM practitioners can probe qi-blood, yin-yang disorders which are important in treatment selection and prognosis.[18,19] Clinically, practitioners observe tongue characteristics, such as tongue color and shape, fur color and thickness, and the amount of saliva, to help deduce the primary pattern of a patient. However, tongue diagnosis is often biased by subjective judgment, which originates from personal experience,

knowledge, diagnostic skills, thinking patterns, and color perception/interpretation. The inconsistency of subjective diagnosis can be improved by using the development of validated instruments. The automatic tongue diagnosis system (ATDS) has shown high consistency and can provide objective and reliable information and analysis of tongue features, facilitating doctors in making effective observations and diagnoses of specific diseases. [10] [18] Previous studies have been conducted on exploring the association between tongue characteristics and specific diseases, including rheumatoid arthritis,[11] breastcancer,[12,13] type 2 diabetes,[14] metabolic syndrome,[15] eczema,[16] dysmenorrhea,[17] and functional dyspepsia,[22] gastroesophageal reflux disease(). However, to the best of our knowledge, no study has yet been performed on the comprehensive scrutiny of tongue features in patients with CKD using ATDS.

2. Research objectives

The objectives of this protocol are to apply the noninvasive ATDS to evaluate tongue manifestations in patients with CKD, and to provide valuable information for clinical doctors, which can be used to facilitate the early detection and diagnosis of CKD, to analyze the current status of patients, and to dynamically schedule treatment plans.

3. What should I do if I participant in this study?

If you meets the inclusion criteria and agree to participant in the study, the ATDS was developed to capture tongue images and reliably analyze tongue features. The system has3 major functions: image capturing and color calibration, tongue area segmentation, and tongue feature extraction.

To reduce the influence of background surroundings, the ATDS is placed in a set location and the operator and the patientsit on fixed seats. To start, the well-trained operator adjusts thechin support horizontally and vertically in order to capture the whole tongue. Then, the patient protrudes their tongue and holds it relaxed and stable for about 10 seconds, allowing the operator to capture a tongue image.

The ATDS can automatically correct any lighting and color deviation caused by changes in background lighting using a color bar attached beside the chin support. After capturing, the tongue images are prepared by isolating the tongue region to eliminate any irrelevant sections of the image including the teeth, lower facial portions, or background surrounding the tongue. After this, feature identification and extraction can be carried out.

4. What is the inclusion and exclusion criteria?

4.1 Inclusion criteria & 4.2Exclusion criteria

All individuals were recruited were informed of the study purpose, procedures, potential risks and benefits, and then the consent form were signed. Subjects will be eligible if they satisfy the following criteria: age over 20 years old; with CKD stage 3-5 including dialysis patients , or who without symptoms and visit clinic for health examination; volunteered to join this research and signed the institutional review board agreement. Both men and women will be enrolled. Subjects with any of the following conditions will be excluded: cancer; acute infection; unable to protrude the tongue stably; risk of

temporomandibular joint dislocation..

5. What are the benefits if I participate in the study?

The aim of this protocol is to apply a noninvasive ATDS to evaluate tongue manifestations of patients with CKD and examine its efficacy as a diagnostic tool.

6. What is the risk if I participant in this study?

Acupuncture is generally considered to be safe when done by a trained professional. The most common side effects of acupuncture include bleeding, soreness, or bruising at the site of needle insertion. Other risks of acupuncture include dizziness, fainting, local internal bleeding, convulsions, hepatitis B, dermatitis, nerve damage, increased pain, and very rarely injury to an internal organ. The number of complications reported to the FDA is relatively low, given that millions of people receive acupuncture treatment each year.

7. Will my medical expenses increase if I participate in this study?

No. We do not charge any fees in this study. All examinations on the biological characteristics of meridian phenomenon are free.

8. What is the compensation if I participant in the study?

We will offer you NTD100 each time as traffic expenses at your each visit.

9. What is the compensation if I suffer from serious adverse events during the study?

If you suffer from any serious adverse events due to this study, the researchers will compensate you according to relevant laws and regulations of Taiwan.

10. Is personal information confidential ?

Your personal information will be kept in the study record and case report forms. All test results (including your personal information, laboratory test report, etc.) will be kept completely confidential. Your name will not appear directly in the case report form or published papers, instead, only the abbreviation of your name and the assigned code will appear.

If necessary, members from the drug administration department, ethics committee, or the funding authority of the study will have access to your research material according to relevant regulations. However, without permission, they don't have the right to use the data of your personal information for other purpose or disclose it to other organizations.

11. How to obtain more information ?

You can submit any questions about this study at any time and consult Dr. Jia-Ming Chen. His mobile number is 86-47238595. During the study, the researchers will inform you of any new information promptly that may affect your willingness to continue participating in the study.

12. Will I be forced to take part in the study?

It is your own right to decide whether you want to participate in the study. You could refuse to participate in this study for any reason.

13. Could I quit the study at anytime during the study?

You have the right to withdraw from this study at any time during the research, which will not affect your rights and you will not be discriminated or retaliated against. If you choose to participate in this study, we hope that you will be able to complete the entire research process.

For your best interest and benefits, a physician or researcher may suspend your participation in the study at any time during the study.

If you withdraw from the study due to any reasons, you may be asked relevant information. If the physician thinks it is necessary, you may also be asked to carry out a laboratory examination and physical examination. You may also refuse the request and you will not be discriminated or retaliated against.

14. What should I do now?

Whether to participate in this study is decided by yourself. You can also discuss it with your family or friends before making a final decision. Before you make your decision, please ask your doctor about more details so that you could completely understand the study.

15. How to contact the ethics committee?

If you have any problems or complaints during the study, please contact the Institutional Review Board Committee A Changhua Christian Hospital, Taiwan.

Address: 135 Nanxiao St., Changhua City, Changhua County 500, Taiwan (R.O.C.)

Tel: 886-4-723-8595

Officers: ShihLi Su, Ph.D

Thank you for reading the informed consent form. If you decide to participate in this study, please tell the researchers, they will arrange all the matters for you. Please keep this informed consent form by yourself.

Informed consent · Signature page

Patient's statement

1. I have read this informed consent form, and the doctor has explained the purpose, contents, risks and benefits of this experiment to me in details.
2. I have discussed and asked relevant questions about this study and I am satisfied with the answers.
3. Plenty of time is offered to me for making a decision on whether I should participate in this study.
4. I participate in this clinical study on my own decision.
5. If I withdraw from the trial due to the reasons related to the study, I will inform the doctors of the change of my health condition in time.
6. If I receive any additional treatments due to the change of my health condition, I will seek for the doctor's advice in advance or tell the doctors afterwards.
7. I allow members from the drug administration department, ethics committee, or the funding authority of the study to have access to my research materials.
8. I will receive a copy of the signed informed consent with the date written on it. Finally, I have decided to participate in this study.

Patient' signature:

Date:

Contact number:

Doctor's statement

I confirm that the details of the trial have been explained to the patients, including its right, possible benefits and risks. A copy of the informed consent has been signed to the patient.

Researcher's signature: Date:

Contact number: