

**Normal Reference Values in Han Adults of Extremity**

**Arterial Structure and hemodynamics by High-frequency**

**Ultrasound: a Multi-center Study in China**

**(NOVAEA-HFUS Study)**

**2023.05.28**

**Dear Madam / Sir:**

We sincerely invite you to participate in the Normal Reference Values in Han Adults of Extremity Arterial Structure and hemodynamics by High-frequency Ultrasound: a Multi-center Study in China (NOVAEA-HFUS Study). The study will be carried out in nine hospitals across the country, with an estimated 540 volunteers. This study has been approved by the Medical Science Research Ethics Committee of the First Affiliated Hospital of China Medical University. Before you decide whether to participate, please read the following carefully to help you understand the program. If you have any questions, please do not hesitate to ask and your doctor will answer them for you. If you wish, you can also discuss with your relatives and friends to help you make a decision. The following is the introduction of the research project:

**[Research Background]**

The extremity artery is the peripheral blood vessel of the whole body, and it is often involved early in the diseases that are easy to damage the small vessels, such as atherosclerosis and connective tissue diseases. Early lower limb atherosclerosis mainly occurs in the dorsal foot artery, which is commonly seen in people with diabetes and long-term smoking. Connective tissue diseases such as systemic sclerosis and systemic lupus erythematosus also mainly involve small blood vessels, and vascular lesions may appear earlier than those of other specific organs such as heart and lung. Because of its shallow location, the extremity artery can be better used as a screening site for vascular diseases, and it is the window for early reaction of vascular diseases. However, the early stage of extremity artery disease is easy to be ignored, and patients often have pain and numbness of the affected limb. When the disease is severe, it can lead to ulcer not healing, and even limb gangrene and amputation, which greatly affects the quality of life and brings huge troubles and economic pressure to the patients. Therefore, early diagnosis of extremity arterial lesions is of great significance for early diagnosis of microvascular injury diseases such as atherosclerosis and connective tissue diseases, reducing the incidence of complications, and reducing the rate of

amputation and mortality.

Ultrasound is a non-invasive imaging technique widely used in clinic. In recent years, with the development of ultrasound technology, the frequency of ultrasonic probes has been increasing. Because of its higher resolution, high-frequency ultrasound can clearly display the superficial vascular structure and blood flow, detect vascular lesions early, and accurately quantify the degree of stenosis, providing a new and beneficial tool for clinical observation of the structure and blood flow of the extremity artery. The purpose of this multi-center clinical study was to establish the normal value of high frequency ultrasound for the structure and blood flow of the extremities of Chinese Han adults, and to explore its influencing factors, so as to provide a quantitative reference for the early diagnosis, degree evaluation and curative effect observation of the structure and blood flow of the extremities.

#### **[Research Objective]**

1. To establish the normal values of the structure and hemodynamic parameters of the extremity artery in Chinese Han adults by high-frequency ultrasound;
2. Identify the factors affecting the structure and hemodynamic parameters of the extremity artery.

#### **[Inclusion and exclusion criteria]**

##### **1. Inclusion criteria:**

Each volunteer must meet the following criteria to be included in the study:

- (1) Han nationality;
- (2) Ages 18-79;
- (3) Normal blood pressure (139-90/89-60mmHg);
- (4) Body mass index < 30 kg/m<sup>2</sup>;
- (5) Blood routine, fasting blood glucose, blood lipid, liver and kidney function, electrocardiogram were normal;
- (6) No history of cyanosis of hands and feet, cold stimulation without

discomfort, no Raynaud phenomenon has occurred in all parts of the body;

(7) No cardiovascular disease, diabetes, rheumatic connective tissue disease, serious liver and kidney dysfunction;

(8) No history of drug use affecting cardiovascular system.

## **2. Exclusion criteria:**

(1) Patients with hypertension, diabetes, hyperthyroidism, arrhythmia and other diseases;

(2) Patients with systemic lupus erythematosus, polymyositis, rheumatoid arthritis and other connective tissue diseases;

(3) A history of related blood diseases;

(4) Have taken vasoconstrictor drugs in the past 1 month;

(5) Gangrene of fingers and toes or history of trauma or surgery;

(6) Have a history of handicraft, hammering, digging and other related work;

(7) Have a long history of smoking and drinking;

(8) Peripheral vascular disease, arterial occlusion can not detect blood flow signal;

(9) Unable to cooperate with the examiner.

## **[Research content and procedure]**

This is a prospective multicenter clinical study conducted in the People's Republic of China. The multi-center clinical study method was adopted.

The study will start in August 2023 and last for 18 months. Nine different medical institutions across the country participated in this study, a total of 540 people were included, 60 of whom will participate in this study in the cooperation center.

(1) Subject selection: Subjects are screened strictly according to clinical manifestations, blood pressure, blood biochemistry and electrocardiogram. Subjects are required to meet all criteria for inclusion and there are no exclusions.

(2) Sign informed consent.

(3) Fill in the questionnaire to measure height, weight, blood pressure and

heart rate.

(4) To perform vascular ultrasound examination, the ultrasonic instrument used in the study is the ultrasonic diagnostic instrument currently used in hospitals, and no drugs or procedures are prohibited.

**[What aspects of your cooperation are needed in the research]**

To participate in this study, you will receive an extremity artery ultrasound examination, and your doctor will inform you of the examination time. No special preparation and precautions are required before and after participating in the study. During the study, please cooperate to reveal the blood vessels of the feet and fingers.

**[Possible risks]**

This study is a non-invasive ultrasound, and the placement of the probe during the examination may cause you slight discomfort, which will not be harmful to you.

**[Study Fee]**

You do not have to pay any fee to participate in this study. If you join the study, you will not receive any financial compensation.

**[Rights and benefits]**

If you meet the inclusion criteria and do not have the exclusion criteria and are willing to participate in the study, you may benefit from:

1. Free access to your current extremity arterial structure and blood flow parameters without financial compensation.
2. During the study period, a doctor will provide you with relevant knowledge.

**[Voluntary study participation/withdrawal]**

Participation in this study is voluntary. You may refuse to participate or withdraw from the study at any time, and you will not be subject to discrimination, unfair treatment or retaliation, and your medical treatment and rights will not be affected in any way.

### **[Privacy of Personal Information]**

All information collected during the study will be confidential and kept by the investigator. Researchers, ethics committee members and relevant administrative authorities have the right to review your information records to the extent permitted by law. In any research reports and publications related to this project, your personal information will not be independently disclosed.

### **[Contact information]**

You can ask any questions about this study at any time. You can contact your doctor, contact: Ma Chunyan Tel: 024-83282129. If you have any complaints about participating in the program, please contact the Ethics Committee (tel: 024-83282837).

### **Declaration of consent**

1. I have carefully read the above introduction to this study and have had the opportunity to discuss it with doctors and ask questions about it. All my questions were answered satisfactorily.

2. I know that participation in the study is voluntary, I confirm that I have had sufficient time to consider it, and I understand that:

1) I have understood the potential risks of participating in the trial and the treatment after the risk occurs;

2) I have understood the relevant alternative treatment plan of this trial;

3) I can always consult my doctor for more information;

4) I can withdraw from the study at any time without discrimination and retaliation, and my medical treatment and rights will not be affected;

