

Original Article

A New Method to get the LVEF Reference Values of the Healthy Adult Male by Heart Rate and Geographical Environment Factors

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SUMMARY

Background: Finding a new method to get the Chinese healthy adult male LVEF reference values with heart rate & geo graphical environment factors. It is more accurate and simpler while considering different areas and individual differences.**Methods:** Collecting 3502 cases from more than 44 cities healthy adult male LVEF reference values and heart rate reference values (X_1) within 10 years published articles in CNKI. A correlation analysis and ridge regression were employed to extract dependent geographical environment factors and predict the reference values of LVEF. The Kriging interpolation of geostatistical analysis were developed to reveal the spatial distribution characteristics of the LVEF values.**Results:** It has a correlation between LVEF and heart rate (X_1)& geographical environment factors. The ridge regression equation of LVEF reference values and geographical environment factors is formula(1). The equation of LVEF reference values with heart rate and geographical environment factors is formula(2).**Conclusion:** The Chinese healthy adult male LVEF distribution showed a downward trend from south to north. Some geographical environment factors have impact on LVEF reference values including latitude, annual precipitation amount and mean air temperature distribution. LVEF is negative correlation with heart rate. When geographical environment factors and individual's heart rate are known, the local and individual's LVEF reference values can be derived from the formulas.Copyright © 2018, Taiwan Society of Geriatric Emergency & Critical Care Medicine. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Left ventricular ejection fraction (LVEF) is the stroke volume (SV) divided by the left ventricular end-diastolic volume (LVEDV) mathematically. It is a most popular clinical index in evaluating left ventricular function. It has very important significance on clinical treatment, observation of drugs and operation efficacy, determination of prognosis and the prevention of heart diseases. The more severe the systolic dysfunction, the more the LVEF is reduced from normal and, generally, the greater the end-diastolic and end-systolic volumes. In patients with reduced contraction and emptying of the left ventricle (i.e. systolic dysfunction), stroke

volume is maintained by an increase in end-diastolic volume (because the left ventricle dilates), i.e. the heart ejects a smaller fraction of a larger volume.¹ Generally, the severe the systolic dysfunction, the LVEF is reduced, the greater the end-diastolic and end-systolic volumes. It have many factors affect LVEF. In this study, we focus on heart rate and geographical environment factors. Heart rate is the main factor of myocardial oxygen consumption, the faster the heart rate, the more oxygen the myocardium. Heart rate slows down may increase myocardial ischemia threshold and improve myocardial work.² Some research said, the faster the heart rate, the lower the LVEF.³ As we all know, human live in geographical environment, LVEF reference values of healthy human are closely related with geographical environment. Then how to quantify LVEF reference values with these factors?

At present, imaging methods can be used to determine the LVEF including line left cardiac imaging, cardiac magnetic resonance imaging, radionuclide gated cardiac blood pool imaging and cardiac ultrasound and so on. As it is noninvasive, accurate, safe and

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inexpensive, cardiac ultrasound is the preferred method by clinical doctors and patients. Although, measuring left ventricular function by cardiac ultrasound is keep improving in ways from M-mode ultrasonography single-blind scan to B-mode ultrasound real-time two-dimensional visual measurement and the recent three-dimensional imaging, its accuracy has been improved, the measurement methods tend to complex.^{4,5} Some studies have shown that the differences in cardiac function LVEF of healthy adult male after acute high altitude suggest that different environment do have different influence on cardiac function LVEF,^{6–8} but seldom do research on the relationship between geographical environment and LVEF specifically. Here is a proposed quantitative study on the relationship between healthy adult male LVEF reference values, heart rate and geographical environment factors. The study is more accurate and simpler while consider different areas and individual differences.

2. Methods

2.1. Data selection

By CNKI database retrieval, we have access to nearly 10 years published in the CNKI magazine included more than 44 cities and regions 184 units 3502 cases of Chinese healthy adult male (age range 18–83) with LVEF reference values and heart rate reference values (X_1). Some research reported that they anticipate a CVD incidence of nearly 8% in the men and 3–5% in the women population, defined as fatal or nonfatal myocardial infarction, angina pectoris and stroke over a 5-year follow up period.⁹ In China, a recent study has reported that the rates of CVD mortality in Beijing increased by >50% in men and >27% in women from 1984 to 1999.¹⁰ It can be seen that men are more likely to suffer from heart disease than women. So we only study on healthy adult male. Western cities have less data than the eastern ones. There are 107 cities from eastern regions, 35 cities from middle regions and 42 cities from western regions. However, Hong Kong Special Administrative Region, Macao Special Administrative Region and Taiwan province were not involved in this study. In addition, *t*-test was employed to test the disparities of LVEF reference values among different regions, and the result is $P = 0.001 < 0.05$, which indicate there is a significant difference of LVEF reference values among different regions (Table 1).

The subjects were apparently healthy, with no abnormal cohorts. The inclusion criteria were normal weight and height (body mass index >18.5 but <25.0, in Kg/m^2), normal blood pressure, normal blood glucose and 8 h fasting before testing blood. The primary exclusion criteria were hepatobiliary and kidney diseases (fatty liver, liver cirrhosis, hepatitis, nephritis, kidney stone, etc.), blood diseases (hemangioma, disturbance of blood circulation, other blood abnormalities and so on) and hepatobiliary ultrasound abnormalities. The cardiac healthy adult male we selected according to the standard¹¹: (1) Confirmed the normal size of the left ventricular cavity and no myocardial dysmotility; (2) Ventricular arrhythmia and non-pacing rhythm, no tachycardia and bradycardia; (3) Left ventricular myocardium without myocardial infarction or segmental ischemia; (4) Left ventricular outflow tract without abnormal structure; (5) Left heart valve no obvious morphological and functional abnormalities (no obvious stenosis and regurgitation); (6) No heart shunt. Data sources are in line with ethical review of human and biomedical research.

Table 1
Medical data & T-test.

Group	Total	Male	Age	BMI	LVEF	HR	P
Healthy people	3502	3502	18–81	18.5–25.0	50.45–75	60–88	0.001

The distribution of sampling points shows in Fig. 1.

Image acquisition using GE Vivid 7 ultrasonic diagnostic apparatus, M5S probe, probe frequency of 1.7–3.4 MHz, frame rate (45 ± 10) frames/s. Image processing using Echo PAC workstations. Collecting images at the end of one breath with the left lateral decubitus position and synchronous recording ECG. Using a full set of two-dimensional and Doppler ultrasound images, collecting three continuous cardiac cycles, stored images in order to off-line analysis. Obtaining Left ventricular septal diameter and left ventricular end diastolic diameter from left ventricular long axis section besides sternum. Obtaining diastolic compartment upper thickness, left ventricular wall thickness, left ventricular posterior wall thickness from left ventricular short axis section besides sternum. LVEF obtained by Simpson method from the apical four-chamber view.¹²

2.2. Geographical environment factors

It shows a complex relationship between body homeostasis and geographical environment. The Huangdi Neijing, a classic medical text in ancient China, indicated the heart plays a crucial role in the body and it is deeply influenced by geographical environment.¹³ Ancient Chinese try to recover heart disease during summer; if failed, it will become worse in winter. Till the spring of the next year, the patients' condition are stable. With time goes by, it might be get better in summer.¹⁴ According to the former researches, there is a significant impact between cardiac function and geographical environment. In conclusion, the paper selected nine geographical environment factors including longitude (X_2), latitude (X_3), altitude (X_4), annual duration of sunshine (X_5), annual mean air temperature (X_6), annual mean relative humidity (X_7), annual precipitation amount (X_8), annual air temperature range (X_9) and annual mean wind speed (X_{10}). The longitude, latitude, altitude data derive from relevant geographical works and dictionaries,^{15,16} while the other meteorological indexes come from The Annual Surface Climate Normals of China (1971–2000), offered by the China Meteorological Data Sharing Service System (<http://old-cdc.cma.gov.cn/>).

There are 10 independent variables include heart rate and nine geographical environment factors (Table 2).

2.3. Correlation analysis

Correlation analysis finished by the Statistical Package for Social Science (SPSS, Chicago, IL), version 22.0 for Windows. By using correlation analysis, single correlation coefficients can be calculated with the normal reference values of Chinese adult male LVEF and heart rate & nine geographical environmental factors.

2.4. Ridge regression

Ridge regression analysis is a biased estimator regression method which aims to solve multicollinearity data.¹⁷ Essentially it is an improved least squares estimation method. By abandoning the unbiasedness of the least squares method, the regression method with more realistic and reliable regression coefficient could be obtained at the cost of losing some part of the information and reducing the accuracy. By allowing small deviations in exchange for higher calculation accuracy than unbiased estimator, the calculated result is more likely to be close to true values. It is beneficial to analyze the effect of each variable and the relationship among variables by using ridge regression.

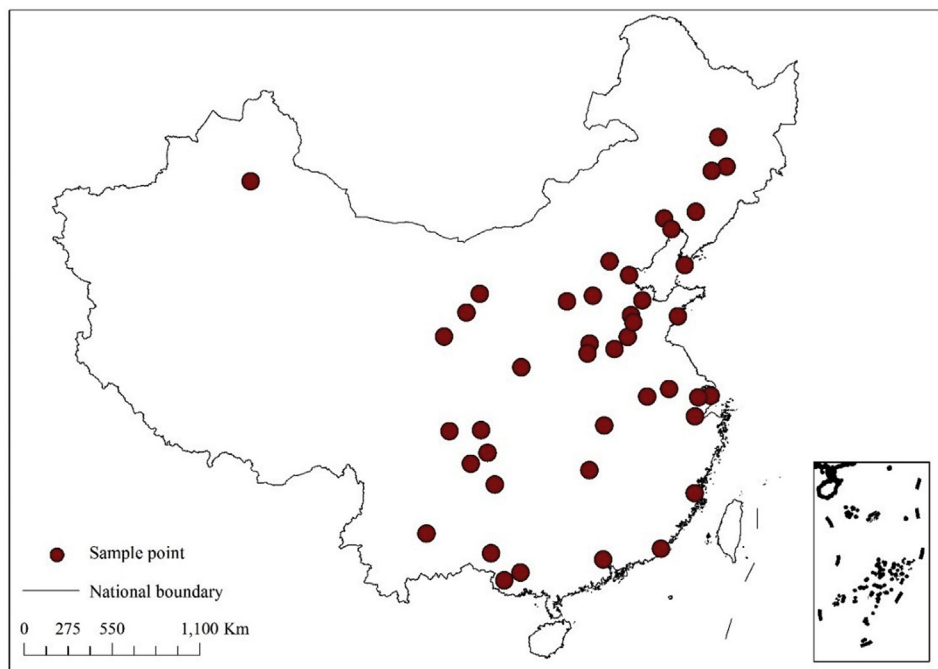


Fig. 1. Distribution of sample points.

Table 2
Independent variables.

X_n	Independent variable
X_1	heart rate
X_2	longitude
X_3	latitude
X_4	altitude
X_5	annual duration of sunshine
X_6	annual mean air temperature
X_7	annual mean relative humidity
X_8	annual precipitation amount
X_9	annual air temperature range
X_{10}	annual mean wind speed

2.5. Spatial distribution

In order to reveal the distribution law of LVEF reference values of Chinese adults male, 2322 cities in China were selected as the observation points, and the predicted values of LVEF were calculated. The Kriging interpolation was performed by using the spatial analysis module of ArcGIS software and the spatial distribution map was output.^{18,19}

3. Results

3.1. Correlation analysis

The correlations between LVEF and heart rate of Chinese subjects and nine geographical environment factors are shown in Table 3. It can be seen that the LVEF and heart rate are significantly correlated with nine geographical environment factors in China. Apparently, the LVEF has a negative correlation with heart rate (X_1), latitude (X_3) and annual air temperature range (X_9), but has a positive correlation with annual mean air temperature (X_6), annual mean relative humidity (X_7) and annual precipitation amount (X_8).

3.2. Ridge regression

By programming algorithm with the help of SAS software (Fig. 2), with the LVEF dependent variable and five geographic environment factors as independent variables from the result of correlation analysis, then the Ridge trace figure was constructed (Fig. 3):

From the analysis result, when the ridge parameter k is 0.3, the ridge regression equation of Chinese healthy adult male LVEF reference values and geographical environment factors was built as follow:

$$Y = 68.464 - 0.0949X_3 - 0.0619X_6 - 0.00128X_7 + 0.00069X_8 - 0.0199X_9 \pm 3.329 \tag{1}$$

By plugging the geographical environment data of a certain region into above-mentioned regression equation, the local healthy male LVEF reference value could be obtained.

Using the SAS software and programming algorithm, we input the independent variables LVEF and heart rate & five Geographic environment factors dependent variables by the correlation

Table 3
Correlation between LVEF and heart rate of Chinese adult males and nine geographical environment factors.

	r -value	P -value
X_1	-0.149 ^a	0.043
X_2	-0.010	0.893
X_3	-0.242 ^b	0.001
X_4	0.058	0.435
X_5	-0.137	0.065
X_6	0.154 ^a	0.037
X_7	0.164 ^a	0.026
X_8	0.208 ^b	0.005
X_9	-0.190 ^b	0.010
X_{10}	-0.136	0.065

^a Correlation is significant at the 0.05 level (2-tailed).

^b Correlation is significant at the 0.01 level (2-tailed).

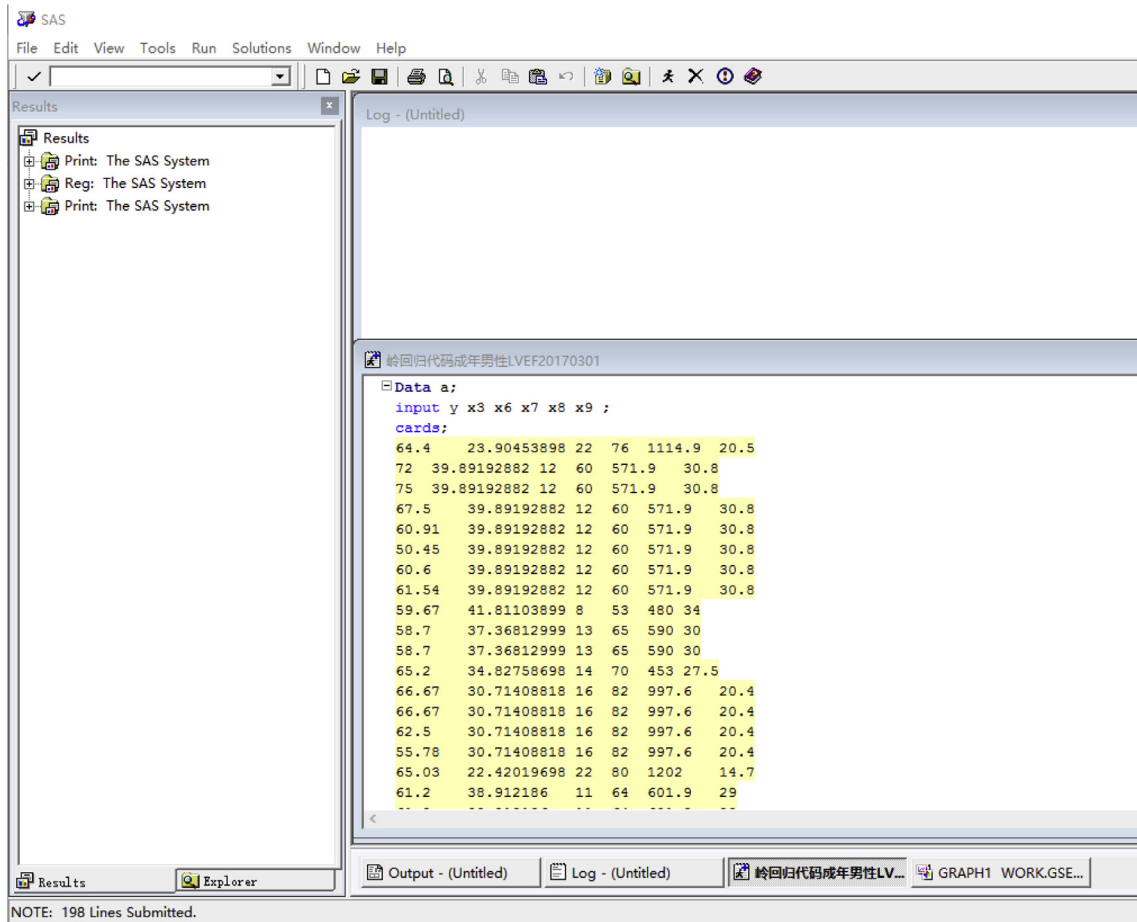


Fig. 2. Program algorithm of adults male LVEF reference values.

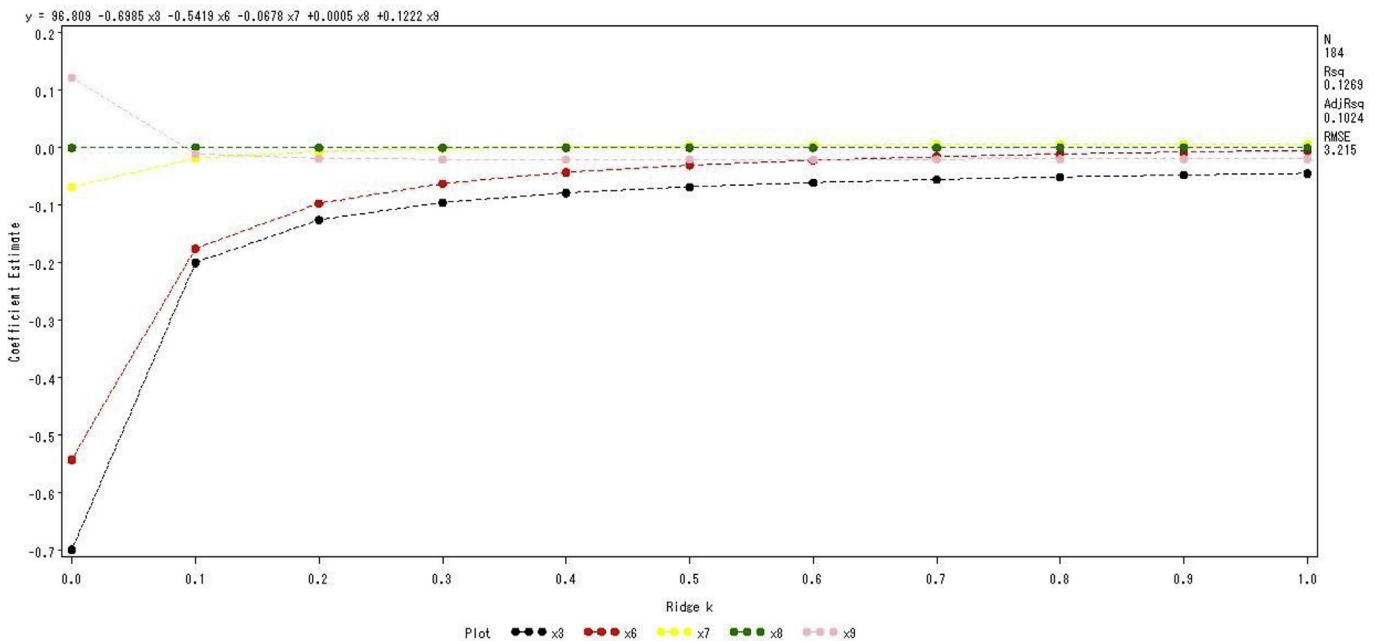


Fig. 3. Ridge trace figure of adults male LVEF reference values.

analysis results, then output Chinese healthy adult male LVEF reference values Ridge trace figure (Fig. 4):

From the analysis result, when the ridge parameter k is 0.3, the ridge regression equation of Chinese healthy adult male LVEF reference values by heart rate and geographical environment factors was built as follow:

$$Y = 75.9230.1035X_1 - 0.0958X_3 - 0.0741X_6 + 0.00094X_7 + 0.00081X_8 - 0.0211X_9 \pm 3.288 \quad (2)$$

By substituting individual heart rate and the local geographical environment factors indicators data available for healthy male personal LVEF reference values.

3.3. Spatial distribution

In order to clearly and accurately show the geographical distribution law of the LVEF of Chinese healthy adult male, with the help of geostatistics module in ArcGIS software, 2322 Chinese cities were located in Chinese map, after analyzing, screening and transforming the data which were predicted by the optimal predictive model, the Kriging interpolation was conducted and the spatial tendency chart of the reference values for LVEF of Chinese healthy adult males was output (Fig. 5).

It can be seen from Fig 5, the distribution of LVEF of Chinese healthy adult male shows a downward trend from south to north. LVEF is negatively correlated with latitude (X₃) and annual air temperature range (X₉); while positively correlated with annual mean air temperature (X₆), annual mean relative humidity (X₇), annual precipitation amount (X₈). The trend in Fig 5 is consistent with distribution law of annual precipitation amount and in contrary to annual air temperature range distribution of China (Fig. 6).

With the increase of latitude and annual precipitation amount the reference values of LVEF of Chinese healthy adult men increased. With the increase of annual air temperature range, the reference values of LVEF decreased in Chinese healthy adult male. This shows that Chinese healthy adults LVEF and geographical environment factors have a correlation in spatial distribution.

4. Discussion

Geographical environment factors form the physical bases in which human beings live. Our environment is an organic whole consisting of essential elements such as air, water, soil, living things and minerals. Living organism absorbs nutritious substances from the environment and excretes useless materials into it. This process of metabolism, along with the exchange of energy, forming the dynamic balance of physical exchange between human beings and environment. Therefore, normal reference values of LVEF will be different in different geographic regions. It has a dependent relationship between the normal reference values of LVEF and geographical environment factors.

Human activities, physiological and pathological phenomena are limited by the laws of nature and constraints factors, while meteorological conditions is the most significant one. The view that natural climate conditions affecting human health can be traced back to the Hippocrates era, and his book "Translation of Hippocrates'Air, Water and Places" influenced the view of natural conditions and human health.²⁰ In ancient China, the earliest medical masterpiece "Yellow Emperor" had discussed many issues about medical geography.²¹ It means that people live in different geographical environment will cause different physiological conditions of the human body.

This study shows that geographical environment factors have a greater influence on Chinese healthy adult LVEF including latitude (X₃), annual precipitation amount (X₈), annual air temperature range (X₉), annual mean air temperature (X₆), annual mean relative humidity (X₇).

Through analyzing of the reasons, it might be an increase in negative ions in the air when precipitation occurs, and air negative ions could make blood vessels expand and remove arterial spasm. At the same time it can also increase blood oxygen content, and improve cardiac function and myocardial nutritional status.²²

A study in North America shows that every daily mean temperature increases 4.7° could cause the rate of cardiovascular disease mortality increases 2.6%.²³ At present, the main reason of seasonal fluctuations in blood pressure is the temperature. Its

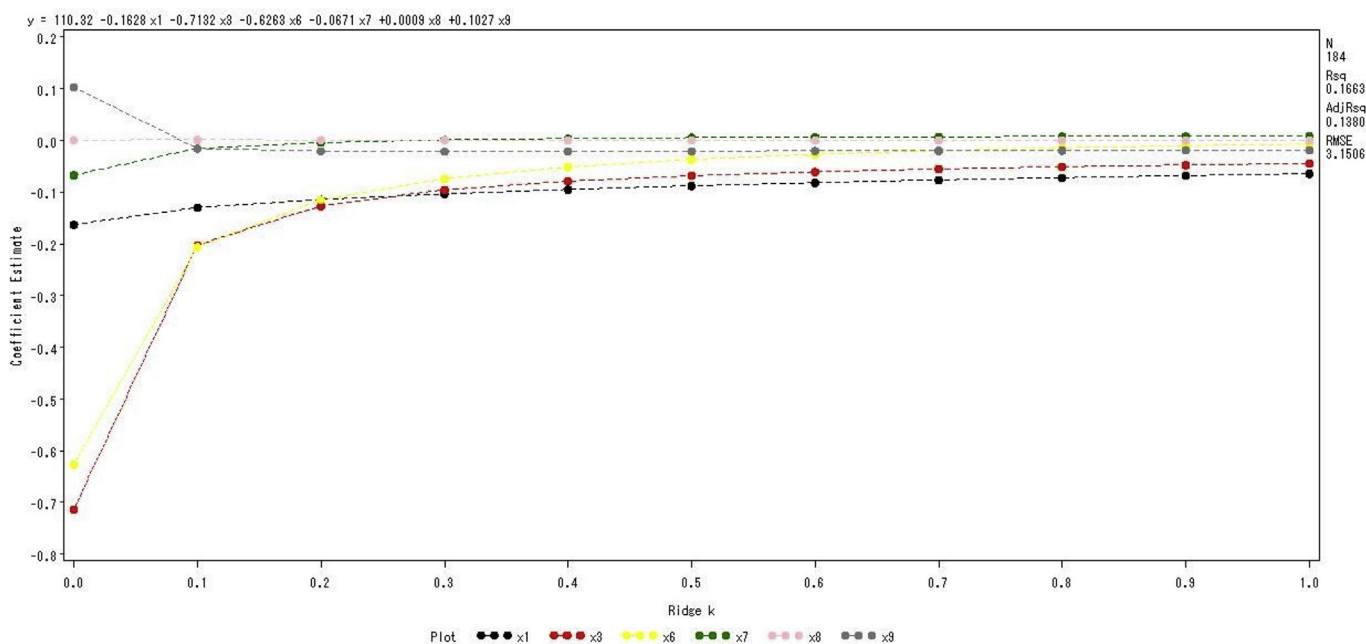


Fig. 4. Ridge trace figure of adults male LVEF reference values with heart rate.

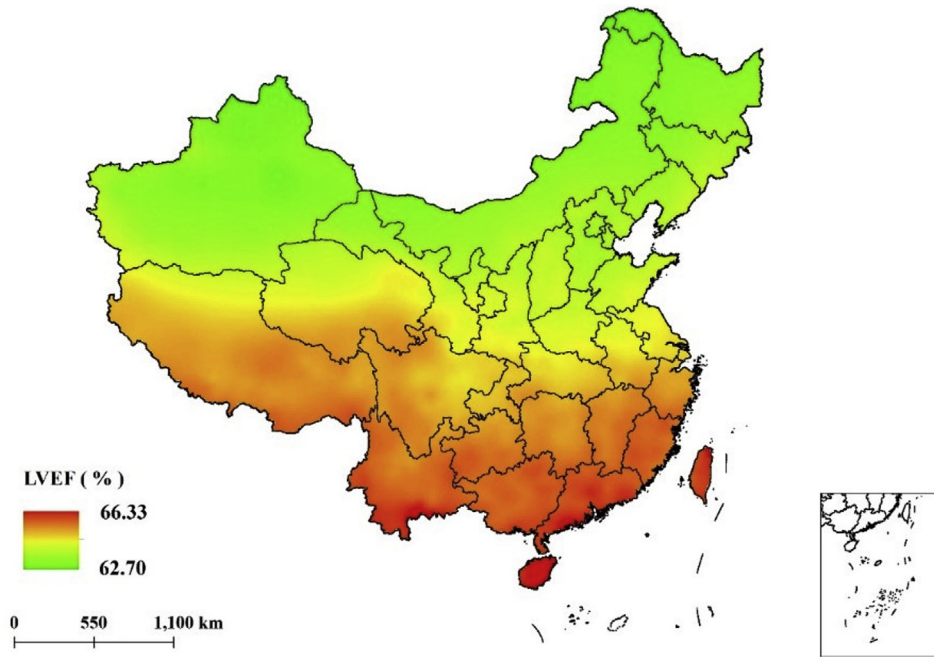


Fig. 5. Spatial tendency chart of the reference values for LVEF of Chinese healthy adult males.

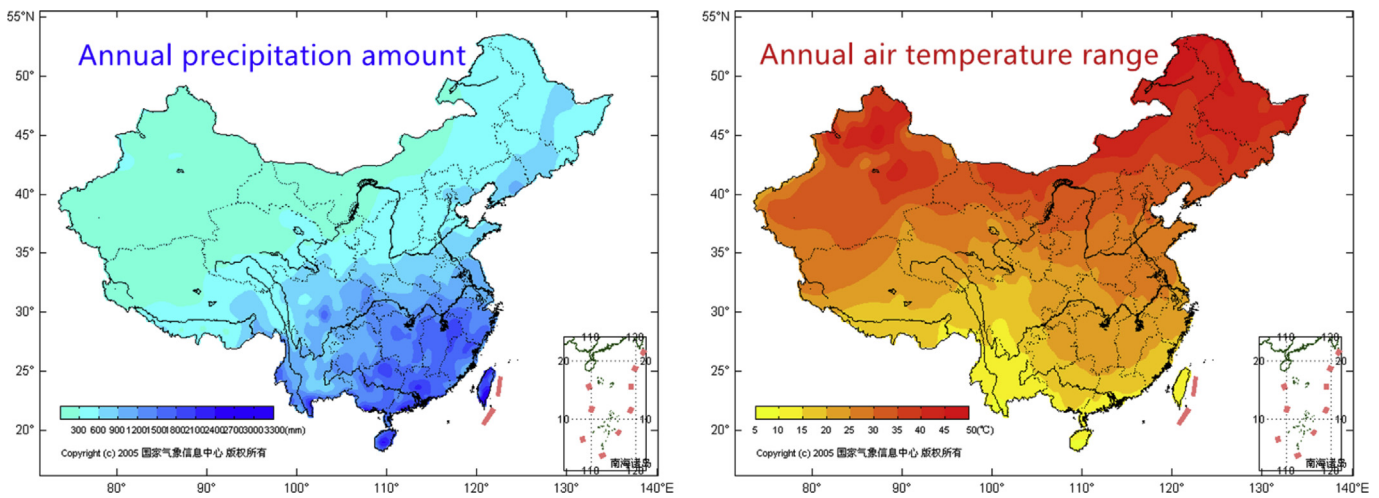


Fig. 6. Annual precipitation amount and Annual air temperature range map of China (1971–2000).

mechanism might be the sympathetic nervous system was activated when the temperature becoming lower, then increasing the catecholamine release. At last it leads to heart rate increased.²⁴

In the normal range, the increase of normal peoples' heart rate could cause the heart output increased. Because of the cardiac systolic become shorted, so SV decreased.²⁵ Due to the shorting of diastole the volume of blood back to the heart also reduced. During this short time, LVEDV changes a little.²⁶ So the values of LVEF would be reduced. And vice versa.

5. Conclusions

The present research, through studying and exploring, provides a new view and insight in medical geography science. We have probed the relationship between reference values of LVEF of healthy adults and geographical factors. This study also explored the spatial distribution characteristics of LVEF reference values for

clinical practice and future study. It shows the laws of the distribution of Chinese healthy adult male LVEF reference values. The country generally shows the overall trend that a downward trend from south to north.

There are some geographical environment factors effected Chinese healthy adult male LVEF reference values. Latitude and annual mean air temperature are main effected factors. So the spatial distribution of Chinese healthy adult male LVEF reference values is consistent with latitude, annual precipitation amount, annual air temperature range and annual mean air temperature distribution.

LVEF is negative correlation with heart rate. Chinese healthy adult male heart rate increases, LVEF decreases.

When geographical environment factors are known, the local LVEF reference values can be derived from [formula \(1\)](#). According to the individual's heart rate and local geographical environment factors value, it can be calculated the individual's LVEF reference values by [formula \(2\)](#) more accurate.

Conflicts of interest

None of the authors have any financial or other potential conflict of interest for this study.

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