Analysis of Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) in healthy young Chinese adults

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Currently, the prevalence of cardio-cerebral vascular diseases (CCVD) and cancer is increasing in developed and developing countries.[1] These diseases have become major sections of public health problems. On the other hand, metabolic syndrome (MS) consisted of a cluster of risk factors causing CCVD. As we know, insulin resistance (IR) was a common pathophysiology of MS and many CCVD, and closely related with some cancers; therefore, many studies focused on researching IR. However, limited research reports the reference interval of the homeostasis model assessment-insulin resistance (HOMA-IR), which was a good index to quantify IR. The objective of this study was to establish the normal reference value of the HOMA-IR in young Chinese adults without MS.

The study was approved by the Ethical Committee of the Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China. From March to December 2008, 10,513 young adults visited our center for a health checkup. Subjects came from different cities and districts in the Zhejiang province. According to the following conditions, finally 811 young adults (women: 437, men: 374; age range: 19-44 years) were enrolled in the study. The conditions were: 1) The results of the health checkup did not include any point of definition of MS according to the International Diabetes Federation (IDF);[2] 2) Both fatty liver in any subject and polycystic ovary in any female subject were not detected by ultrasound sonography (US). There were no history of acanthosis in any female individual; 3) The values of C reactive protein (CRP), uric acid (UA), white blood cell count (WBC) and fasting insulin (FINS) were also within normal ranges. The normal reference ranges were: CRP: 0-10mg/L, UA: ≤6mg/dL in women (≤7mg/dL in men), WBC: 4-10 x 10^9/L, and FINS: 2.6-24.9 uIU/ml. Venous blood samples were drawn and abdominal US was performed after an overnight fast: (1) the results of abdominal US were reported by immovable physicians (machines: LOGIQ7 [GE health care, USA] and SIEMENS VF-105, [Siemens, Germany). Qualified technicians measured blood pressure, height, weight, and waist circumference; (2) The FINS concentration was measured by the antibody sandwich ELISA method, using DPC IMMULITE automatic immunoanalyzer (DPC, USA). The blood triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and CRP concentrations were measured by the terminal method, using an OLYMPUS AU machine (Olympus, Japan). Fasting blood glucose (FBG) concentration was measured by the hexokinase method, using OLYMPUS AU machine (Olympus, Japan). Plasma UA concentration was measured by the uricase peroxidase method, using OLYMPUS AU machine (Olympus, Japan). The WBC was measured by the principle of electrical impedance, using LH-750 machine; (Beckman Coulter Inc, USA.). 3) The HOMA-IR was calculated according to the following formula: HOMA-IR = [FINS (uIU/ml) x FBG (mmol/L)]/22.5.

The Statistical Package for Social Sciences (SPSS Inc, Chicago, IL, USA), version 11.5 was used for the statistical analysis, and $p<0.05$ was considered statistically significant. The normal distribution data were expressed as the mean ± standard deviation (SD). Skewed distribution data were expressed as the median with 25th and 75th percentiles (P25~P75). The independent sample t test was used to compare the normal-distribution data in different gender groups. If the data were transformed into the normal distribution by taking a natural logarithm (Ln) of it, the independent sample t test was used to compare with the transformed data. If there was still a skewed distribution by taking a Ln of the data, the non-parametric rank sum test was used to compare with the original data in different genders. The 95% confidence interval (CI) of normal reference value of the HOMA-IR was estimated by the bootstrap method in Stata 10 (StataCorp LP, Texas, USA).

Comparison of the data between male and female groups, body mass index (BMI), WC, BP, LDL-C, HDL-C, TG, UA, FINS and WBC were all statistically significant, but not in comparison of age, FBG, and CRP (data not shown). The data of the HOMA-IR showed a skewed distribution in both men and women. The HOMA-IR value was higher in women than in men ($p=0.008$). The one-sided upper border of normal 95% reference value of the HOMA-IR was 2.31 in women and 2.23 in men (**Table 1**). Results indicated that P5, P50 and P95 95% CI of the HOMA-IR values were 0.56-0.61, 1.04-1.17, and 2.08-2.54 in women, and 0.54-0.60, 0.95-1.07, and 1.91-2.49 in men by Bootstrap in Stata 10 (data not shown). The data of the HOMA-IR were transformed into normal distribution by taking Ln of it. The mean±SD of the Ln (HOMA-IR) was 0.125±0.440 (95% CI: 0.083-0.166) in women and 0.043±0.396 (95% CI: 0.003-0.083) in men. The Ln (HOMA-IR) value was higher in women than in men ($p=0.005$). The one-sided upper

Table 1 - Analysis of the HOMA-IR in healthy young Chinese adults.

Variables	HOMA-IR			Ln (HOMA-IR)		
	Median (P$_{25}$-P$_{75}$)	One sided upper border of normal 95% references value	Mean±SD	One sided upper border of normal 95% reference value	Mean 95% CI	
					Lower	Upper
Women (n=437)	1.10 (0.81-1.57)	2.31	0.125 ± 0.440	0.851	0.083	0.166
Men (n=374)	1.01 (0.77-1.34)	2.23	0.043 ± 0.396	0.696	0.003	0.083
z value (*p*-value)	-2.638 (0.008)					
t value (*p*-value)			-2.789 (0.005)			

CI - confidence interval, HOMA-IR: Homeostasis Model Assessment-Insulin Resistance. z value - comparison of the HOMA-IR between women and men by rank sum test. t value - comparison of the Ln (HOMA-IR) between women and men by independent sample t test.

border of the normal 95% reference value of the Ln (HOMA-IR) was 0.851 in women and 0.696 in men (**Table 1**). Presently, the hyperinsulinemic-euglycemic clamp is considered the golden standard in diagnosing IR. The "clamp" technique was complicated and expensive, so it was rarely performed in clinical practice and public healthcare. However, the HOMA-IR value was calculated easily, which only needed the results of FINS and FBG. Moreover, a previous study[3] showed that the HOMA-IR showed a good correlation with the hyperinsulinemic-euglycemic clamp. In reality, the HOMA-IR has been used extensively to evaluate IR;[4] nevertheless, few studies reported the normal reference value of the HOMA-IR in large samples. Due to increasing prevalence of cardiovascular disease, diabetes mellitus, and metabolic disorders in young adults, it is crucial to prevent these diseases in the young. Because of the close correlation between IR and these diseases, it is necessary to establish the normal reference value of HOMA-IR in young adults. Establishing the normal reference value in young adults will be useful in clinical care and future research.

This study analyzed the data of the HOMA-IR in 811 healthy young subjects. The results showed that the HOMA-IR value was statistically significant in comparison between different gender groups; therefore, the different normal reference value of the HOMA-IR was established in young men and women. The gender differences in the HOMA-IR values could be due to body fat distribution.[5] However, a recent study[6] showed that healthy young women were as insulin sensitive as men. This remains to be further studied. Because the HOMA-IR data showed a skewed distribution and was transformed into a normal distribution by taking the a Ln of it, it is recommended that the Ln (HOMA-IR) is used in research. The one-sided upper border of the normal 95% reference value of the Ln (HOMA-IR) was 0.851 in young women and 0.696 in young men. On the other hand, it is better that the HOMA-IR value

itself be used in clinical practice and public healthcare for the simple calculation method. The one-sided upper border of normal 95% reference value of the HOMA-IR was 2.31 (95% CI: 2.08-2.54) in young women and 2.23 (95% CI: 1.91-2.49) in young men.

In conclusion, the IR should be considered if the HOMA-IR value is higher than the relevant normal reference value. Establishing the normal reference value of the HOMA-IR in healthy young adults will be useful in future research and public healthcare.

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