Is Waist-To-Height Ratio The Best Predictive Indicator of Cardiovascular Disease Incidence in Hypertensive Adults? A Cohort Study

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Research Article

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Abstract

Background

Cardiovascular disease (CVD) brings high mortality and economic burden to patients, especially in rural areas. Simple, low-cost abdominal adiposity measures may help identify individuals with increased CVD risk. It is unclear that which obesity indice is the best to predict CVD in hypertensive people.

Methods

NCRCHS is a prospective cohort study in a general population in Northeast China. The study examined the cardiovascular health from 2013–2015, and follow-up captured the CVD incidence in 2018. Baseline waist-to-height ratio (WHtR), body mass index (BMI),waist-to-hip(WHR)and waist circumference (WC) were calculated and analyzed in relation to the CVD incidence.

Results

A total of 4244 hypertensive adults without pre-existing CVD at baseline were included in this analysis (age 35–92 years; 2108 men). Over a median follow-up of 4.66 years, a total of 290 CVD cases (6.83%) were documented during the follow-up. Baseline WHtR showed a significant positive association with CVD incidence, even after adjusting for age, sex, diabetes, drinking, smoking, SBP, DBP, Triglyceride, HDL-C, LDL-C, and TC (Hazard Ratios per SD of WHtR ranging from 1.03 to 1.31, $p = 0.017$). Reclassification and discrimination analyses indicated WHtR addition could improve the conventional model for predicting adverse outcomes within 4 years. Moreover, WHtR predicted the CVD incidence better than other obesity indices (BMI, WC, WHR).

Conclusion

These findings support a positive association between WHtR and CVD incidence in CVD-free hypertensive adults. WHtR may be useful in predicting CVD incidence in hypertensive adults.

Background

Cardiovascular disease (CVD), has becoming a public health challenge caused by an aging global population [1–3]. In China, CVD is the leading cause of death. It accounts for 45.01% of total deaths in rural areas in 2015,while the proportion of urban areas is relatively lower than rural areas. The number of CVD patients is on the rise and predicted to increase substantially over the next 10 years. In particular, the mortality of the CVD increased from 150/100,000 in 1990 to 298/100,000 in 2015 in rural areas in China [4].

Obesity, particularly abdominal, is a key risk factor of cardiovascular disease (CVD) [5–7]. Using anthropometric indices to categorize obesity such as body mass index (BMI), the waist-to-height ratio (WHtR), the waist-to hip ratio (WHR), and waist circumference (WC)[8] are the simplest and the most cost-effective methods recommended in clinical practice and epidemiological research, especially in developing countries. Some studies demonstrated that WHtR was better for predicting CVD risk, but it is unclear in the hypertensive adults [9–10].

Hypertension (HTN) is regarded as a serious public health problem [11–13]. The prevalence of HTN has been increasing all over the world [14–16]. However, it is not known that which anthropometric indice is the best to predict CVD in people with hypertension. Thus, elucidation of the best predictive indicator of cardiovascular disease incidence in hypertension adults is of great significance.

In the present study, we aimed to determine the role of WHtR as a predictor of CVD incidence in the NCRCHS (the Northeast China Rural Cardiovascular Health Study) cohort of hypertensive adults without previous CVD, and compare its discriminating ability against other commonly anthropometric indices of central obesity (i.e., WC, WHR and BMI).

Methods

Study population

Northeast China Rural Cardiovascular Health Study (NCRCHS) is a cohort study in a general population. The methods of the study, including design, personnel recruitment, and laboratory techniques, have been described in previous publications [16-17]. Between January 2013 and August 2013, 11956 subjects aged ≥35 years were recruited from rural areas of Liaoning province. Subsequently, subjects were invited to attend follow-up visits in 2015 and 2018, and 6017 hypertensive participants were consented and eligible for the follow-up study. A total of 5249 participants of hypertension completed at least one follow-up visit. In the present study, we excluded baseline history of coronary heart disease (n=355) and stroke (n=590), and missing data (n=60). Eventually, data from 4244 participants were available for analysis. The Ethics Committee of the First Hospital of China Medical University (Shenyang, China) approved the study. Written informed consent was obtained from all participants.

Data collection

Data was collected during a single clinic visit by cardiologists and trained nurses using a standard questionnaire by face-to-face interview. During data collection, our inspectors had further instructions and support.

All participants were asked about the current status of smoking, drinking and the history of diseases. Base on the recommendations of the Working Group on Obesity in China, participants were stratified according to the BMI levels as underweight group (BMI$<$18.5 kg/m^2), normal weight group (18.5 kg/m^2≤BMI$<$24 kg/m^2), overweight (24 kg/m^2≤BMI$<$30 kg/m^2), or obesity (BMI≥30 kg/m^2). WHtR was calculated as WC divided by height. According to the reports from Ashwell, we categorized WHtR as WHtR <0.40, $0.40 \leq$ WHtR ≤ 0.50, $0.50<$ WHtR ≤ 0.60, WHtR >0.60. The group with $0.40 \leq$ WHtR ≤ 0.50 was used as the reference group [18-20].

According to American Heart Association protocol, blood pressure was measured three times at 2-min intervals after at least 5 min of rest using a standardized automatic electronic sphygmomanometer (HEM-907; Omron). The mean of three blood pressure measures was calculated and used in all analyses. Hypertension was defined as a mean SBP $\geq$ 140 mmHg and/or a mean DBP $\geq$ 90 mmHg, and/or use of antihypertensive medication in the previous 2 weeks [21-22]. Diabetes mellitus was defined as FBG$\geq$ 7.0 mmol/l and/or self-reported physician-confirmed diagnosis [23]. Fasting blood samples were collected after at least 10 h of fasting. Blood samples were taken from an antecubital vein into BD Vacutainer tubes containing ethylenediaminetetraacetic acid. Serum was subsequently isolated from the whole blood, and all serum samples were frozen at -80°C for testing at a central, certified laboratory. We used the Olympus AU640 auto-analyzer (Olympus, Kobe, Japan) for analyzing blood biochemical indexes. All blinded duplicate samples were used for these analyses.

Judgment and definition of clinical outcomes

We collected all available clinical information about possible diagnoses or mortality, including data from medical records and death certificates. CVD was defined as stroke or Coronary heart disease (CHD). Stroke were diagnosed by neurologists following the examination of computed tomography and magnetic resonance imaging data in accordance with World Health Organization (WHO) criteria [24]. CHD was defined as a diagnosis of angina requiring hospitalization, myocardial infarction (MI), revascularization procedure and CHD-related mortality [25].

Statistical analysis

Continuous variables were presented as means and SDs and categorical variables were reported as frequencies and percentages in each group. Differences between categories were evaluated using the t test, or the x2 test. Kaplan–Meier method was used to calculate the cumulative incidence for adverse events, and log-rank test was used to compare differences. To evaluate the improvement in risk prediction for adverse outcomes by adding WHtR to the conventional model (including age, sex, current smoking, current drinking, SBP, DBP, TC, HDL-C, LDL-C, triglyceride, and diabetes), net reclassification improvement (NRI) and integrated discrimination improvement (IDI) was calculated for CVD prediction models respectively (conventional model vs. conventional model+ WHtR). The calculation method is IDI=(Pnew, events-Pold, events)-(Pnew, non-events-Pold, non-events). With the larger value of IDI, the new model has the better prediction ability.

Statistical analyses were performed using SPSS software version 22.0 (SPSS Inc., Chicago, Illinois, USA) and statistical software packages R (http://www. R-project.org, The R Foundation). P values<0.05 were considered to be statistically significant.

Results

1. Baseline characteristics of the study sample according to CVD incidence

In this study, there are 6017 hypertensive participants consented and eligible for the follow-up study. A total of 5249 participants of hypertension completed at least one follow-up visit. In the current study, we excluded baseline history of coronary heart disease (n = 355) and stroke (n = 590), and missing physical indicators (n = 60). Presents the baseline characteristics of participants according to the CVD incidence. 4244 participants (2108 men and 2136 women, mean age 56.26 ± 10.15 years) were included in this cohort study (Supplemental figure S1). During a median follow-up of 4.66 years, 290 participants (6.83%) incident stroke or CHD (crude incidence rate, 14.66 incident stroke or CHD per 1000 person-years).

The group of participants who developed CVD during the study follow-up consisted mainly of older men and exhibited higher anthropometric indices/ratios of total and central obesity (BMI, WC, WHR, WHtR), compared to those who remained CVD-free. Furthermore, this group had higher baseline DBP, SBP levels and lipids (TC and LDL-C) (all p-values < 0.05; Table 1). The mean WHtR value at baseline was 2% higher in the group of participants who developed a CVD event than in those who remained CVD-free ($p < 0.05$, Table 1).

Table 1
Baseline characteristics of the study sample.

Variable	Without CVD (N = 3954)	With CVD (N = 290)	P value
Age (years)	55.85(± 10.10)	61.85(± 9.26)	< 0.001
Male [n (%)]	1945(50.8%)	163(56.2%)	0.021
Current smoking [n (%)]	1406(35.6%)	118(40.8%)	0.090
Current drinking [n (%)]	1065(26.9%)	87(30.0%)	0.287
Body mass index (kg/m^2)	25.55(± 3.58)	25.79(± 3.54)	0.268
Waist circumference (cm)	84.39(± 9.52)	85.80(± 10.49)	0.016
Waist-to-hip ratio	0.87(± 0.07)	0.89(± 0.10)	< 0.001
Waist-to-height ratio	0.53(± 0.06)	0.54(± 0.06)	0.001
SBP (mmHg)	157.90(± 18.18)	168. 47(± 23.21)	< 0.001
DBP (mmHg)	88.69(± 10.78)	91.47(± 14.12)	0.001
TC (mmol/L)	5.40(± 1.09)	5.55(± 1.11)	0.023
LDL-C (mmol/L)	3.08(± 0.85)	3.22(± 0.91)	0.017
HDL-C (mmol/L)	1.45(± 0.41)	1.45(± 0.45)	0.909
Triglyceride (mmol/L)	1.76(± 1.65)	1.77(± 1.53)	0.978
Diabetes [n (%)]	192(4.9%)	19(6.6%)	0.253

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; CVD, cardiovascular disease.
Note: Date are presented as mean ± standard deviation, or n (%), as appropriate

2. Baseline WHtR in relationship to the CVD incidence

The Kaplan-Meier survival curves for the four groups according to the values of WHtR were showed in Fig. 1. The curves showed that the cumulative CVD incidence in the group with WHtR > 0.60 was highest among four groups and was significantly higher than that in the group with 0.4 ≤ WHtR < 0.5. (p for Log-rank test = 0.003, $p < 0.05$)

The association between baseline WHtR and the CVD incidence was further evaluated through multivariate Cox proportional hazards models (Table 2). Univariate analysis showed that the HR of CVD for participants with for a 1-SD Increase in WHtR by 1.21-fold ($p = 0.001$). After adjustment for age, sex, current smoking, current drinking, TC, HDL-C, LDL-C, triglyceride, diabetes, SBP and DBP, the HR (95% CI) for a 1-SD increase in WHtR was 1.16 (95% CI: 1.03–1.31) for CVD.

Table 2
Hazard Ratios and 95% Confidence Intervals of CVD for a 1-SD Increase in Anthropometric Indicator.

All participants	**Unadjusted HR (95%CI)**	**P value**	**Adjusted HR (95%CI)**	**P value**
Continuous (Per SD increase)				
WHtR	1.21(1.08–1.35)	0.001	1.16(1.03–1.31)	0.017
BMI	1.06(0.95–1.19)	0.298	1.15(1.03–1.29)	0.016
WC	1.16 (1.03–1.29)	0.013	1.13(0.99–1.28)	0.053
WHR	1.20(1.10–1.30)	< 0.001	1.15(1.04–1.27)	0.005
Adjusted for age, sex, current smoking, current drinking, TC, HDL-C, LDL-C ,triglyceride, diabetes, SBP and DBP.				

Table 3 shows the HRs for CVD according to the levels of four abdominal adiposity indices. Univariated HR of CVD for participants with WHtR 0.60 increased by 1.98-fold ($P < 0.001$), compared with the reference group. After adjustment for age, sex, current smoking, current drinking, TC, HDL-C, LDL-C, triglyceride, diabetes, SBP and DBP, the HR (95% CI) for participants with WHtR 0.60 increased was 1.87 (95% CI: 1.23–2.83) for CVD. ($P = 0.003$). Moreover, the participants with $0.50 \leq$ WHtR < 0.60 still had a significant difference comparing with the reference group. The multivariate-adjusted HR (95% CI) for $0.50 \leq$ WHtR < 0.60 was 1.45 (95% CI: 1.09–1.94) for CVD. However, the other three abdominal adiposity indices didn't show the such significant results.

Table 3
Associations between risks of adverse outcomes and different values of WHtR, BMI, WC and WHR.

All participants	Unadjusted HR (95%CI)	P value	Adjusted HR (95%CI)	P value
WHtR				
WHtR < 0.4	0.83(0.20–3.37)	0.790	0.98(0.24–3.99)	0.973
0.4 ≤ WHtR < 0.5	1	-	1	-
0.5 ≤ WHtR < 0.6	1.42(1.08–1.87)	0.013	1.45(1.09–1.94)	0.012
WHtR > 0.6	1.98(1.35–2.89)	< 0.001	1.87(1.23–2.83)	0.003
BMI				
BMI < 18.5	1.42(0.33–2.40)	0.496	1.03(0.38–2.82)	0.954
18.5 ≤ BMI < 24	1	-	1	-
24 ≤ BMI < 30	1.07(0.83–1.38)	0.601	1.12(0.86–1.47)	0.399
BMI > 30	1.42(0.96–2.10)	0.083	1.52(0.99–2.33)	0.055
WC				
1st quartile	1	-	1	-
2nd quartile	1.38(0.98–1.95)	0.063	1.36(0.96–1.92)	0.081
3rd quartile	1.34(0.96–1.88)	0.086	1.28(0.90–1.81)	0.170
4th quartile	1.45(1.03–2.05)	0.033	1.33(0.92–1.92)	0.133
WHR				
1st quartile	1	-	1	-
2nd quartile	1.58(1.12–2.23)	0.009	1.47(1.04–2.08)	0.031
3rd quartile	1.62(1.13–2.32)	0.009	1.43(0.99–2.07)	0.059
4th quartile	1.85(1.31–2.62)	< 0.001	1.41(0.98–2.03)	0.064
Adjusted for age, sex, current smoking, current drinking, TC, HDL-C, LDL-C ,triglyceride, diabetes, SBP and DBP.				

3. Predictive value of WHtR on the CVD risk against other common anthropometric indices of obesity

Furthermore, we evaluated whether adding WHtR to the conventional model could improve prediction perfor-mance. Fortunately, the IDI value and NRI value suggested that the model after addition of WHtR led to a significant improvement in predicting incident stroke or CHD within 4 years (Table 4).

Table 4
Reclassification and discrimination statistics for adverse outcomes within 4 years by WHtR,BMI, WC and WHR.

	NRI(95% CI)	IDI	P
WHtR	0.05(-0.01-0.12)	0.0026	0.01
BMI	-0.01(-0.05-0.03)	0.0009	0.09
WC	-0.01(-0.05-0.02)	0.0007	0.14
WHR	-0.01(-0.05-0.04)	0.0013	0.04
Conventional model: age, sex, current smoking, current drinking, TC, HDL-C, LDL-C ,triglyceride, diabetes, SBP and DBP.			

The result showed that the NRI value of WHtR was 0.05(more than 0 indicating improvement). The IDI value of WHtR was 0.0026(p = 0.01). Based on these models, WHtR exhibited better predictive value for the CVD incidence as revealed through the IDI value and NRI value (the higher the better), than other common anthropometric indices. Similarly, baseline WHtR was also a better predictor of the CVD than BMI, WHR and WC.

Discussion

In this prospective cohort study, WHtR was associated with risk of the CVD in people with hypertension. Notably, this positive association remained significant even after adjusting for various CVD risk factors. Moreover, in the performed comparisons of the predictive value of WHtR on the CVD incidence, WHtR was better than other common anthropometric indices of obesity (BMI, WHR and WC). WHtR exhibited better predictive value for the CVD incidence than the others.

CVD is a public health challenge. The number and mortality of CVD patients is on the rise. The incidence rate of CVD was higher in rural areas than the national average level in China. Therefore, the results of our study will have important clinical predictive significance. Especially the rural population, their income is generally low, WHtR without cost is the simplest and effective method in clinical practice.

WHtR, as a rapid screening tool, can help to predict CVD risk, and then reduce the CVD incidence. Our results also indicated that addition of WHtR could improve the conventional model for predicting adverse outcomes within 4 years. In addition, our results appear to be stable because the value of WHtR for predicting adverse events remained constant. It is the best indicator of obesity that predicts CVD risk in the population with hypertension.

Recently, there are some studies that reveal the relationship between WHtR and CVD [26–28]. A study by Gelber showed that WHtR had the strongest association with CVD in men [29]. Moreover, the superiority of WHtR for detecting CVD risk has been reported among children and adolescents [30]. Therefore, WHtR may be considered as a good screening tool for CVD. Some studies demonstrated that WHtR was better for predicting CVD risk [31–33]. However, the result is from mostly cross-sectional studies, and the study population is not hypertensive.

The strength of current study is that it is a large prospective cohort study. It is the first study to examine the association between WHtR and CVD in hypertensive people. Moreover, confounding factors were adequately adjusted and the results were still stable. Nevertheless, our study also has limitations. Our study is a Chinese cohort, which limits the generalizability of our findings to other ethnic groups.

Conclusion

The present study emerges evidence suggesting that WHtR may constitute a simple and accurate prognostic marker of CVD risk as compared to other obesity-related indices in hypertensive people. Indeed, the present findings offer new prospective data suggesting that WHtR exhibits a positive association with the CVD incidence in Asiatic adults from the hypertensive population without pre-existing CVD. WHtR appears to be a better predictor of CVD risk than the other anthropometric indices of total and central obesity. Future studies are still required to further evaluate the association between WHtR and CVD in different ethnic and patient populations.

List Of Abbreviations

WHtR, waist-to-height ratio

BMI, body mass index

WHR, waist-to-hip

WC, waist circumference

CVD, cardiovascular disease

NCRCHS, Northeast China Rural Cardiovascular Health Study

TC, total cholesterol

CHD, coronary heart disease

NRI, net reclassification improvement

IDI, integrated discrimination improvement

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of China Medical University (Shenyang, China) (2018194). Written informed consent was obtained from all participants. Our protocol was performed in accordance with the relevant guidelines and Helsinki's declaration.

Consent for publication

Not applicable.

Availability of Data and Materials

The datasets supporting the conclusions of this article are included within the article.

Competing interests

None declared.

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Author's contribution

ZS participated in wrote the manuscript. DZ conducted statistical analyses. XFG and GZS assisted with critical revision of manuscript for intellectual content. LZ, ZY, YHM, YSS coordinated data collection and subjects' follow-up. FX and ZS was responsible for the study concept and design. All authors have read and approved the final manuscript.

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value. Nutr Res Rev 2010;23(2):247e69.

Figures

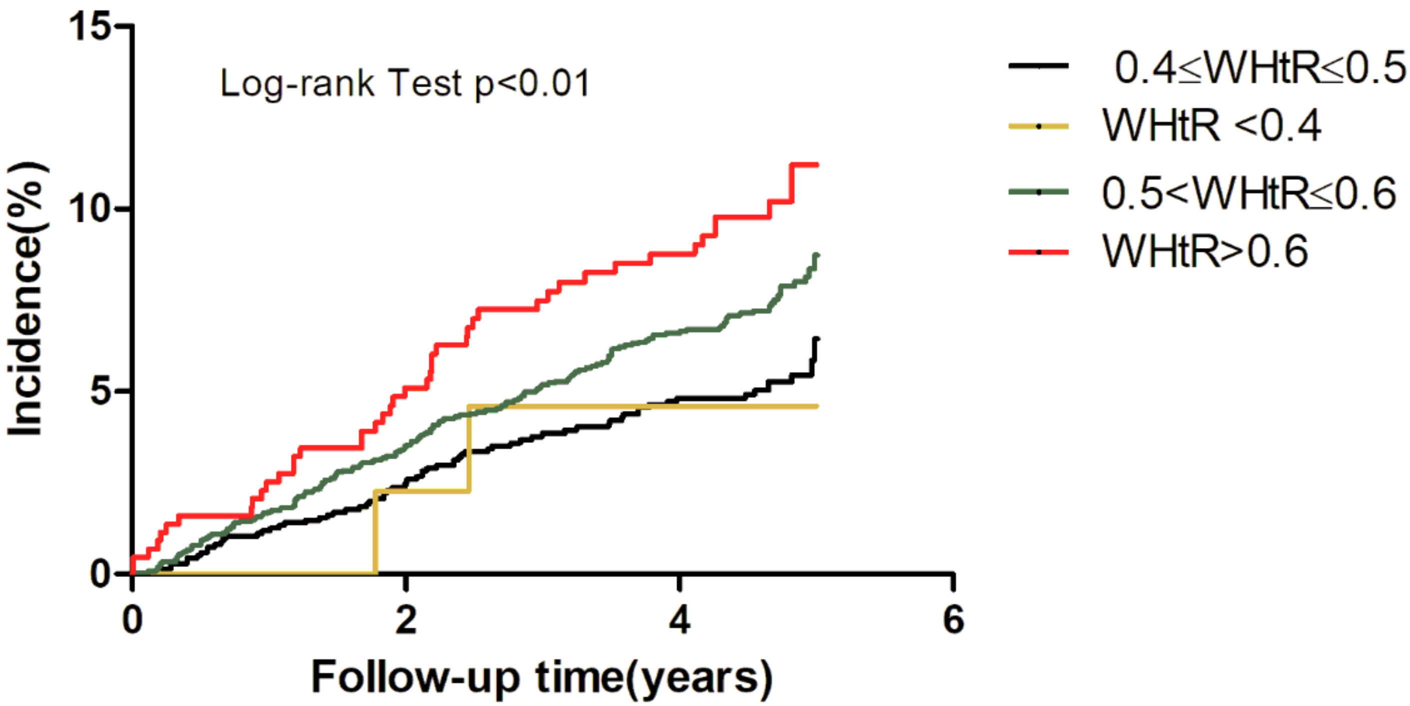

Figure 1

Unadjusted Kaplan–Meier curves for incident adverse events stratified by WHtR.

Supplementary Files

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