PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Association between mid-upper arm circumference and cardiometabolic risk in Chinese population: a cross-sectional study
AUTHORS	Hou, Yanan; Jia, Xu; Xuan, Liping; Zhu, Wen; Deng, Chanjuan; Wang, Long; Zhao, Zhiyun; Li, Mian; Lu, Jieli; Xu, Yu; Chen, Yuhong; Wang, Weiqing; Bi, Yufang; Xu, Min; Wang, Tiange

VERSION 1 – REVIEW

REVIEWER	Prof. Dr. Wajid Aziz Loun 1.University of Azad Jammu & Kashmir, Muzaffaranad, (AJK), Pakistan 2. University of Jeddah, Kingdom of Saudi Arabia
REVIEW RETURNED	01-Feb-2019

GENERAL COMMENTS	Reviewer Comments The authors investigated the associations of mid-upper arm circumference (MUAC) with the cardiometabolic risk factors or biomarkers and subclinical atherosclerosis by conduction a cross-sectional study. The study is meaningful and show authors effort. However, the following issues should be addressed: 1. Improve the introduction section by including more related literature. 2. Provide more details about the need of the study. 3. In detail explain the sampling procedure and how sample size in taken. 4. The multivariate regression analysis is conducted to study the association of MUAC with a wide spectrum of cardiometabolic risk factors. If MUAC is the only dependent variable, then multiple regression analysis is applicable in this case (Multivariate regression is used where there are more than one dependent variables while multiple regression is used where there is one dependent and more than one independent variables). 5. Further highlight the outcomes the study in discussion section. 6. Table 1: It is mentioned that “Data are presented as means ± standard deviation (SD), or medians (inter-quartile ranges) for skewed variables, or number (proportions) for categorical variables”. It could not find results present in the format means ± standard deviation (SD).

REVIEWER	MD, PhD Suárez-Llanos, José Pablo Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain
REVIEW RETURNED	04-Feb-2019

GENERAL COMMENTS	MUAC is not only representative of the composition of the upper body, but of the whole body, evidenced in numerous works (including this one) by its direct relationship to the BMI. The authors stated that MUAC measurement was performed on the left arm, though it should be determined on the non-dominant arm. In a large sample like this, one would expect to find many left-handers. This should be pointed out. In addition to proposing MUAC as a CVR marker, would not it be interesting to suggest a threshold for a higher CV risk as well as for subclinical atheromatosis? The latter would have to be specific to women and men. MUAC is not only applied to children and adolescents, but essentially to adults, where it is an important marker rather for malnutrition in this population. Please, correct on line 48.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Prof. Dr. Wajid Aziz Loun
Institution and Country: 1. University of Azad Jammu & Kashmir, Muzaffaranad, (AJK), Pakistan
2. University of Jeddah, Kingdom of Saudi Arabia
Please state any competing interests or state 'None declared': None
Please leave your comments for the authors below
The authors investigated the associations of mid-upper arm circumference (MUAC) with the cardiometabolic risk factors or biomarkers and subclinical atherosclerosis by conduction a cross-sectional study. The study is meaningful and show authors effort. However, the following issues should be addressed:
1. Improve the introduction section by including more related literature.

Response: We greatly appreciate the Reviewer's positive comments and thoughtful suggestions. In the revised manuscript, we have added two important literatures in the Introduction section: " In a prospective cohort of 1061 European elderly participants with a follow-up of approximately 6 years, a larger MUAC was associated with elevated risks of all-cause and cardiovascular diseases mortality.[12] In contrast, in the Canada Fitness Survey of 10638 adults, a larger MUAC was independently associated with a lower risk of all-cause mortality [13]" (Page 5-6, Lines 94-98).

2. Provide more details about the need of the study.

Response: We greatly appreciate the constructive suggestion provided by the Reviewer. In the revised manuscript, we have added more details about the need of the study in the Introduction section, "Most of these previous studies were conducted in European population; so far, comprehensive data on the associations between MUAC and cardiovascular risk profiles in Chinese population are limited. Chinese population tend to have a higher percentage of body fat, a weaker willingness on body build, and less muscle mass as well as connective tissue,[15] as compared with their European counterparts. And these different features may translate into varying susceptibilities to adiposity related cardiometabolic disorders. Therefore, this study aimed to investigate the association between MUAC and cardiometabolic disorders as well as subclinical atherosclerosis in Chinese population (Page 6, Lines 102-110)."

3. In detail explain the sampling procedure and how sample size in taken.

Response: We thank the Reviewer for the useful suggestion. In the Method section, we have explained the sample size and sampling procedure in detail as follows: “This is a cross-sectional analysis based on one of the follow-up circles of our established community-based cohort.16,17 Eligible participants aged 40 years or above were identified from the local residence registration records. There was no restriction on ethnicity or gender. Each eligible participant was recruited by trained community staff and local health workers using a door-to-door invitation method. Participants who consented for the study and signed informed consent were scheduled for health examinations. In brief, a total of 6570 participants aged 40 years or above were enrolled from Jiading district, Shanghai, China, from August 2014 to May 2015. All participants received anthropometric measurements (including height, weight, WC, and MUAC), a standard 75-g oral glucose tolerance test (OGTT), and a standard questionnaire to acquire information regarding lifestyle factors (including smoking and alcohol drinking habits, and physical activity), education, social demographic information, and history of diseases and medicines. Blood samples were collected for biochemical measurements. In the present study, 283 participants were excluded due to missing data on MUAC or CIMT. Thus, a total of 6287 participants were included in the final analysis. This study was approved by the Institutional Review Board of Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. Written informed consent was obtained from all study participants (Page 6-7, Lines 114-131)”.

4. The multivariate regression analysis is conducted to study the association of MUAC with a wide spectrum of cardiometabolic risk factors. If MUAC is the only dependent variable, then multiple regression analysis is applicable in this case (Multivariate regression is used where there are more than one dependent variables while multiple regression is used where there is one dependent and more than one independent variables).

Response: Thank you so much for pointing out this very important question. In this study, we treated MUAC as an independent variable and cardiometabolic risk factors as dependent variables. Models were fitted with multivariable linear regression or multivariable logistic regression, where only one of the cardiometabolic risk factors was included in the model at a time. Then we repeated this analysis for other cardiometabolic risk factors. These analyses aimed to explore the associations of MUAC with cardiometabolic risk factors or biomarkers. We greatly appreciate your thoughtful corrections. In the revised manuscript, we have corrected the methods to multivariable regressions (Page 10, Line 198), and have carefully edited the languages throughout the manuscript, primarily to assist in the interpretation of the data in the manuscript.

5. Further highlight the outcomes of the study in discussion section.
Response: We appreciate the suggestions provided by the Reviewer. Our present study has extended the existing evidence by demonstrating that MUAC increment was associated with an increased risk of a series of cardiometabolic disorders including central obesity, hypertension, low HDL cholesterol, and subclinical atherosclerosis in Chinese population, particularly among women. In the Discussion section, we further highlighted the outcomes of the study. “Central obesity, hypertension, low HDL cholesterol, and subclinical atherosclerosis have been robustly associated with increased risks of CVD. Detecting more effective risk factors for these cardiometabolic disorders is critical to the prevention of CVD. Our findings suggest that paying more attention to women with higher MUAC would be useful in the early identification and prevention of cardiometabolic disorders (Page 13, Lines 286-291)”.

6. Table 1: It is mentioned that “Data are presented as means ± standard deviation (SD), or medians (inter-quartile ranges) for skewed variables, or number (proportions) for categorical variables”. It could not find results present in the format means ± standard deviation (SD).

Response: We sincerely appreciate for your careful reading and corrections. In the original version of the manuscript, we presented means and SDs as means (SDs). We have carefully changed the presentations of means and SDs as means ± SDs in the revised manuscript (Page 21-22, Table 1).

Reviewer: 2
Reviewer Name: MD, PhD Suárez-Llanos, José Pablo
Institution and Country: Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
1. MUAC is not only representative of the composition of the upper body, but of the whole body, evidenced in numerous works (including this one) by its direct relationship to the BMI.

Response: We greatly appreciate the insightful comments provided by the Reviewer. We totally agree with you that MUAC is not only representative of the composition of the upper body, but of the whole body. We have justified the need to use MUAC as a complementary measure to BMI in the Discussion section in the revised manuscript. One previous study has demonstrated that MUAC may play a complementary role to BMI in predicting prognosis in patients with heart failure. Evaluating body composition by combined BMI with fat mass or lean mass plays a critical role in predicting cardiovascular diseases (Kentaro Kamiya, JACC Heart Fail. 2016; 4(4):265-73). Also, in the revised manuscript, we have acknowledged this point as an important limitation as: "although our finding supported that it can be a reliable surrogate of upper body adiposity, MUAC is a measure comprised of both adipose and lean tissue rather than a direct indicator for adiposity (Page 14, Lines 316-318)."
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2. The authors stated that MUAC measurement was performed on the left arm, though it should be determined on the non-dominant arm. In a large sample like this, one would expect to find many left-handers. This should be pointed out.

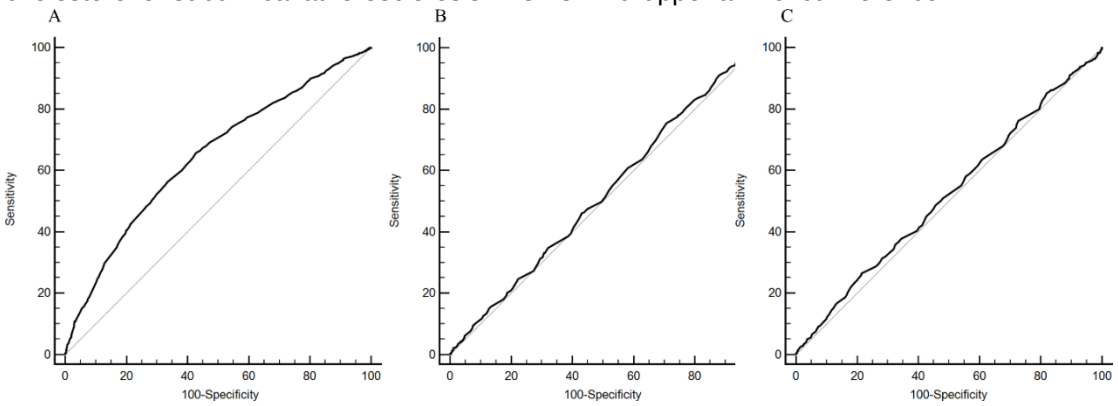
Response: We thank the Reviewer for the helpful comment. We agree with the Reviewer that MUAC measurement should be determined on the non-dominant arm rather than on the left arm. Thus, we listed it as one limitation of the present study in the Discussion section (Page 14-15, Lines 320-322) as follows: "MUAC measurement was performed on the left arm, though it should be determined on the non-dominant arm. Given the fact that the majority of Chinese population were right-handers, measurement protocol employed in our study for MUAC was acceptable."

3. In addition to proposing MUAC as a CVR marker, would not it be interesting to suggest a threshold for a higher CV risk as well as for subclinical atheromatosis? The latter would have to be specific to women and men.

Response: We greatly appreciate the Reviewer's insightful suggestions. According to your suggestion, we have performed receiver operating characteristics curves to examine the best cutoff points of MUAC in relation to high cardiometabolic risk as well as subclinical atherosclerosis. As shown in the Figure below, the area under ROC curve (AUC) was 0.63 (95% CI 0.62-0.64 ; $P < 0.001$) for the association between MUAC and cardiometabolic risk. MUAC ≥ 29.0 cm was the best cutoff point for determining subjects with cardiometabolic risk in total samples (Figure 1A). Besides, the ACU was 0.52 (95% CI 0.50-0.54; $P = 0.07$) for the association between MUAC and subclinical atherosclerosis in women; and 0.52 (95% CI 0.49-0.54; $P = 0.10$) for the association between MUAC and subclinical atherosclerosis in men (Figure 1B, Figure 1C). MUAC ≥ 27.0 cm for women and MUAC ≤ 27.9 cm was the threshold for detecting subclinical atherosclerosis (Figure 1B, Figure 1C).

However, the AUCs were not significant to indicate appropriate cutoff point for these outcomes. Besides, due to the cross-sectional nature of this study, we could not conclude a “predictive” relationship between MUAC and these outcomes. Therefore, we did not include these results in the main manuscript.

Figure 1. Receiver operating characteristics curves of MUAC value in relation to cardiometabolic risk as well as subclinical atherosclerosis. ROC curve for MUAC and cardiometabolic risk (A); subclinical atherosclerosis in women (B); subclinical atherosclerosis in men (C). In this analysis, cardiometabolic risk refers to subjects with central obesity, diabetes, hypertension, hypertriglyceridemia, low HDL cholesterol or subclinical atherosclerosis. MUAC: mid-upper arm circumference.



4. MUAC is not only applied to children and adolescents, but essentially to adults, where it is an important marker rather for malnutrition in this population. Please, correct on line 48.

Response: We appreciate the brilliant comments provided by the Reviewer. In the revised version of the manuscript, we have carefully revised the statement according to your comments (Page 13, Lines 274-275).

VERSION 2 – REVIEW

REVIEWER	Prof. Dr. Wajid Aziz Loun University of Jeddah, Saudi Arabia
REVIEW RETURNED	09-Jun-2019

GENERAL COMMENTS	Research ethics (e.g. participant consent, ethics approval) should be addressed appropriately.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Prof. Dr. Wajid Aziz Loun

Institution and Country: University of Jeddah, Saudi Arabia

1. Please state any competing interests or state ‘None declared’: None

2. Please leave your comments for the authors below

Research ethics (e.g. participant consent, ethics approval) should be addressed appropriately.

Response: We appreciate the Reviewer's thoughtful suggestions. We have stated that "This study was approved by the Institutional Review Board of Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. Written informed consent was obtained from all study participants" in the main text (page 6), and have added the relative information in "Patient consent for publication" and "Ethics approval" sections (page 15-16).