Prevalence of metabolic syndrome risk factors and their relationships with renal function in Chinese centenarians

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As the first time, this study was to investigate the prevalence of metabolic syndrome (MetS) risk factors and explore their relationships with renal function in Chinese centenarians. China Hainan Centenarian Cohort Study was performed in 18 cities and counties of Hainan Province. Home interview, physical examination and blood analysis were performed in 874 centenarians following standard procedures. Prevalence of MetS was 15.6% (136 centenarians). There were 229 centenarians with abdominal obesity (26.2%), 645 centenarians (73.8%) with hypertension, 349 centenarians with dyslipidemia (39.9%) and 92 centenarians with diabetes mellitus (10.5%). In multivariate linear regression, age, smoking, waist circumstance (WC), systolic blood pressure (SBP) and triglyceride levels were inversely and diastolic blood pressure (DBP) levels were positively associated with glomerular filtration rate levels (P < 0.05 for all). This study reported low prevalence of MetS risk factors and demonstrated that age, smoking, abdominal obesity (WC), hypertension (SBP and DBP) and triglyceride levels were independently associated with renal function in Chinese centenarians. This study provided reliable data about Chinese centenarians, analyzed significant relationships between Mets risk factors and renal function, and explained possible reason (low prevalence of MetS and its risk factors) and mechanism (interrelationship of age, Mets risk factors with renal function) of longevity.

During the last few decades, metabolic syndrome (MetS) and renal function decline (RFD) continue to grow in prevalence all over the world, and this trend is particularly obvious in developing countries. MetS refers to a clustering of risk factors: abdominal obesity, hypertension, dyslipidemia and diabetes mellitus (DM), all which contribute to the development of cardiovascular disorders and events. Meanwhile, RFD plays a significant role in the progression of cardiovascular disorders, and has close association with cardiovascular events. More importantly, both MetS and RFD have obvious effects on mortality, and accelerate the occurrence of adverse outcome. Previous studies have observed the prevalence of MetS and analyzed their relationships with renal function, but drawn controversial conclusions. Meanwhile, most of these studies were performed in the general population of developed countries, and there may be obviously different conclusions in the centenarians in China. Moreover, different conclusions may also derive from race, and thus it is very essential to perform this study in Chinese.

The centenarians have been suggested to have a delayed or escaped onset and interaction of age-related illnesses, such as MetS and RFD. Some centenarians may experience a delayed onset of age-related illnesses (delayers), while others may do not succumb to any age-related illnesses (escapers). Thus, the centenarians may represent a prototype of successful aging. However, it is still under scientific debate. More importantly, what is this model of successful aging? Studies analyzing this model in the centenarians could provide valuable information for early promoting successful aging and preventing age-related diseases. As a possible part of this...
model, whether the interaction between MetS and RFD exists in the aging process of centenarians is still unclear and needs further studies.

Prevalence of MetS increases with age, reaching 42.0% in U.S. adults 70 years or older\(^{15}\). However, prevalence of MetS and its risk factors are still unclear in Chinese centenarians\(^{16}\). Moreover, its relationship with renal function still has significant debate in the elderly, not to say the centenarians\(^{17}\). Considering the specificity of centenarians, previous studies in the general population cannot accurately represent the centenarians\(^{18}\). Meanwhile, in order to understand the reasons and mechanisms of longevity, it is very valuable to perform the studies in Chinese centenarians. Hainan is a longevity area with the highest population density of centenarians in China, and China Hainan Centenarian Cohort Study (CHCCS) with a considerable sample size provides a significantly population-based sample of Chinese centenarians. As the first time all over the world, this study was designed to investigate the prevalence of MetS risk factors and explore their relationships with renal function in a representative sample of Chinese centenarians.

### Results

For all centenarians, median age was 102 (100–115) years, and males account for 18.9%. Prevalence of MetS was 15.6% (136 centenarians). For MetS risk factors, there were 229 centenarians with abdominal obesity (26.2%), 645 centenarians (73.8%) with hypertension, 349 centenarians with dyslipidemia (39.9%) and 92 centenarians with DM (10.5%). There were 371 centenarians with GFR \(< 60 \text{ ml/min/1.73 m}^2\) (42.4%). As shown in Table 1, the prevalence of MetS in centenarians with GFR \(< 60 \text{ ml/min/1.73 m}^2\) was 15.6% (136 centenarians). For MetS risk factors, there were 229 centenarians with abdominal obesity (26.2%), 157 centenarians with hypertension (18.8%), 371 centenarians with dyslipidemia (42.4%) and 92 centenarians with DM (10.5%). Table 1 shows the prevalence of MetS risk factors and description of other characteristics in centenarians.

### Discussion

Studies about the centenarians can help us understand the reasons and mechanisms of longevity. In previous studies, Mets has a prevalence more than 20% in the general population and a higher prevalence in the elderly\(^{19–21}\). In U.S. adults, prevalence of MetS increases with age, reaching 42.0% in those 70 years or older\(^{15}\). This study reported that there was obviously low prevalence of Mets (15.6%) and its risk factors in Chinese centenarians. Georgia Centenarian Study has concluded that major barriers to reaching centenarians come from several incident chronic age-related disorders, especially cardiovascular disorders\(^{16}\). Meanwhile, Mets and its risk factors...
play significant roles in the development of cardiovascular and other chronic age-related disorders. Moreover, longevity data from Framingham Study have supported that MetS risk factors, such as blood pressure, glucose and lipids, are significant contributors to morbidity and mortality. Thus, low prevalence of Mets and its risk factors found in this study was a possible reason of longevity in Chinese centenarians.
Both MetS and RFD have been underlined to be independently associated with cardiovascular incidence, events and mortality. Previous studies have shown significant relationship between MetS and renal function, but drawn controversial conclusions. Meanwhile, most of these studies about the centenarians are performed in the general population of developed countries, with little information available on the centenarians in China. Additionally, the data on ethnic Chinese are limited, and the relationship between MetS and renal function is still unknown in ethnic Chinese. This study realized a possible mechanism of longevity in Chinese centenarians that not only age, but also Mets and its risk factors had significant relationships with renal function. On the one hand, Mets and its risk factors may impair the renal function, aggravate the cardiovascular disorders and reduce the life expectancy. The hypothesized mechanism is that as age increases, the clustering of MetS risk factors may result in oxidative stress and endothelial dysfunction, which consequently cause the atherosclerosis-related RFD. In turn, RFD may gradually affect the blood pressure, glucose and lipids, and also aggravate the metabolic disturbance and promote the development of MetS. On the other hand, the relationships between age, Mets and renal function also remind us that Mets and RFD may result from a common cause linked to the aging phenomenon. Either one of MetS and RFD may enforce the effects of other one on cardiovascular disorders and their incidence, and the interrelationship between MetS and RFD may worsen further cardiovascular events and mortality.

Abdominal obesity is a fundamental pathology of MetS, and contributes to the development of other MetS risk factors, such as hypertension, dyslipidemia and DM. Abdominal obesity is significantly associated with high mortality risk, and there is an obviously increased prevalence of abdominal obesity in many developed and developing countries. There have been inconsistent study results on the relationship between abdominal obesity and renal function. Several studies have realized that abdominal obesity is significantly associated with renal function in the general population. But other study has not verified significant association between abdominal obesity and renal function in the elderly. This study observed that with a prevalence of 26.2%, abdominal obesity was independently associated with renal function in Chinese centenarians.

As prevalence of hypertension is rapidly increasing all over the world, the relationship between blood pressure and renal function has drawn considerable attention. Previous studies have shown that hypertension was significantly associated with renal function. However, other study has also found that blood pressure has no significant association with renal function. This study showed that with a prevalence of 73.8%, hypertension was inversely associated with renal function. More interestingly, SBP was inversely associated with renal function, but DBP was positively associated with renal function in this study. One the one hand, elevated SBP may induce the glomerulosclerosis and lower GFR, while reduced DBP may cause the renal hypoperfusion and lower GFR. On the other hand, RFD may affect the sodium and water retention, activate the renin-angiotensin-aldosterone system and induce the abnormality of SBP and DBP.

It is a significant issue to analyze the relationships between different types of dyslipidemia and renal function, especially in the elderly, and there has been a controversial relationship between TG levels and renal function. Previous studies have proved that TG levels were significantly associated with renal function. Triglyceride-rich apolipoprotein B-containing lipoproteins may promote the progression of RFD. However, Helsinki Heart Study has provided an evidence that there is no significant association between TG levels and renal function. This study confirmed that TG levels were significantly associated with renal function in Chinese centenarians, and lowering TG therapy may play a role in preserving renal function in addition to preventing cardiovascular disorders.

Smoking is a significant public health problem all over the world, and has been considered to be harmful to renal function in previous studies. Meanwhile, there has been a concern for many countries about the relationship between DM and renal function, and previous large-scale survey in the US general population has concluded that DM was not associated with renal function. Consistent with previous studies, this study demonstrated that with a prevalence of 3.3%, smoking exerted harmful effects on renal function. And with a prevalence of 10.5%, DM had no significant association with renal function in Chinese centenarians.

The current study had one limitation. Smoking was assessed by asking each centenarian whether he or she was a current smoker. Although ex-smoker does not seem to be counted as smoker, it should be considered to be one limitation.

Conclusion
As the first time all over the world, this study reported low prevalence of MetS and its risk factors, and demonstrated that age, smoking, abdominal obesity (or WC), hypertension (or SBP and DBP) and TG levels were independently associated with renal function in Chinese centenarians. Low prevalence of MetS and its risk factors was a possible reason of longevity, and the interrelationship of age, Mets and its risk factors with renal function was a possible mechanism of longevity in Chinese centenarians. Based on CHCCS, this study not only provided reliable data about Chinese centenarians and analyzed significant relationships between Mets risk factors and renal function, but also explained possible reason and mechanism of longevity.

Methods
Study population. CHCCS was performed in population-based individuals aged 100 or above from July 2014 to December 2016 in 18 cities and counties of Hainan Province, China. Its cohort profile has been described previously. Based on National Civil Registry, a total of 1,002 centenarians were identified by Hainan Civil Affairs Bureau and enrolled in this study. Age was ascertained from national identification cards. The following inclusion criteria were used to recruit study participants: (1) was 100 years or older; (2) volunteered to participate in the study and provided written informed consent; and (3) was conscious and could cooperate to complete the home interview, physical examination and blood analysis. The following were participant exclusion criteria: (1) personal identity information was not complete or identification cards showed an age of less than 100 years; (2) refused to comply with the requirements of the study, including the collection of physical or blood samples. There were 874 centenarians included in the final analysis. This study followed the approval from Ethics
Committee of Hainan branch of Chinese People’s Liberation Army General Hospital (Sanya, Hainan; Number: 301hn11201601). Written informed consent was obtained from all centenarians in this study. All methods were performed in accordance with the relevant guidelines and regulations.

**Standard procedures.** Home interview, physical examination and blood analysis were performed following standard procedures35. The research team included internists, geriatricians, cardiologists, endocrinologists, nephrologists and nurses. Smoking was assessed by asking each centenarian whether he or she was a current smoker36. Waist circumference (WC) was measured with a soft tape midway between the lowest rib and the iliac crest. Consistent with current recommendations, systolic and diastolic blood pressures (SBP and DBP) were measured with the right arm of centenarians two times consecutively, with at least 1 minute between measurements, and the reported blood pressures were the average of these two measurements. Samples of venous blood were obtained from the centenarians and transported in chilled bio-transport container (4°C) to our Central Laboratory within 4 hours. Serum concentrations of fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and creatinine were measured using the enzymatic assays (Roche Products Ltd, Basel, Switzerland) on a fully automatic biochemical autoanalyzer (Cobas c702; Roche Products Ltd, Basel, Switzerland). All assays were performed by qualified technicians without knowledge of clinical data.

**Variable definitions.** Based on the worldwide consensus on the definition of MetS recommended by International Diabetes Federation, MetS was defined as abdominal obesity plus any two of four additional factors: SBP ≥ 130 mmHg or DBP ≥ 85 mmHg (or previously diagnosed hypertension); FBG ≥ 5.6 mmol/L (or previously diagnosed DM); and TG ≥ 1.7 mmol/L (or previously diagnosed dyslipidemia)37. Based on Chinese guidelines on prevention and control of obesity, abdominal obesity was defined as WC ≥ 85 cm for men and ≥ 80 cm for women38. Hypertension was defined as SBP ≥ 140 mmHg, DBP ≥ 90 mmHg or taking antihypertensive drugs39. DM was defined as FBG ≥ 7.0 mmol/L or taking hypoglycemic drugs/insulin40. Dyslipidemia was defined as TG ≥ 1.7 mmol/L, LDL-C ≥ 3.37 mmol/L, HDL-C ≥ 1.04 mmol/L or taking lipid-regulating drugs41. Estimated glomerular filtration rate (GFR) was calculated using a modified version of Modification of Diet in Renal Disease (MDRD) equation based on the data from Chinese patients as follows: 175 × serum creatinine (mg/dL)−1.234 × age (year) − 0.189 × 0.79 (if female)42.

**Statistical analyses.** Continuous variables were described as the mean and standard deviation for variables with normal distribution and the median and interquartile range for variables with skewed distribution. Categorical variables were described as the number and percentage. Continuous variables were compared with Student’s t-test (normal distribution) and Mann–Whitney U test (skewed distribution). Categorical variables were compared with Chi-square test. Pearson's (continuous variables with normal distribution) and Spearman’s (continuous variables with skewed distribution and categorical variables) correlations were used to assess the simple relationships between MetS risk factors and renal function. In order to assess the independent relationships between MetS risk factors and renal function, multivariate linear regression analyses were adjusted by age, sex, smoking, WC, SBP, DBP, TC, TG, LDL-C and FBG, and multivariate logistic regression analyses were adjusted by age, sex, smoking, abdominal obesity, hypertension, dyslipidemia and DM. Statistical significance was accepted at the two-sided 0.05 level, and confidence interval (CI) was computed at the 95% level. Statistical analyses were performed with Statistic Package for Social Science (SPSS) version 17 (SPSS Inc., Chicago, IL, U.S.).

**Availability of data and materials.** In attempt to preserve privacy of patients, clinical data of patients will not be shared; data can be available from authors upon request.

**References**

1. Aguilar, M. et al. Prevalence of the metabolic syndrome in the United States, 2003–2012. JAMA. 2015, 313(19) (1973).
2. Samson, S. L. & Garber, A. J. Metabolic syndrome. Endocrinol Metab Clin North Am. 43(1), 1e23 (2014).
3. Sattar, N. et al. Can metabolic syndrome usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies. Lancet. 371(9628), 1927–1935 (2008).
4. Gami, A. S. et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J Am Coll Cardiol. 49(4), 403e14 (2007).
5. Ronco, C. et al. Cardio-renal syndromes: report from the consensus conference of the Acute Dialysis Quality Initiative. Eur Heart J. 31(46), 703–711 (2010).
6. Rifkin, D. E. et al. Rapid renal function decline and mortality risk in older adults. Arch Intern Med. 168(20), 2212–8 (2008).
7. Gomez, P. et al. Prevalence of renal insufficiency in individuals with hypertension and obesity/overweight: the FATH study. J Am Soc Nephrol. 17(B3), S194–200 (2006).
8. Chien, K. L., Hsu, H. C., Lee, Y. T. & Chen, M. F. Renal function and metabolic syndrome components on cardiovascular and all-cause mortality. Atherosclerosis. 197(2), 860–7 (2008).
9. Li, Y. et al. Metabolic syndrome, but not insulin resistance, is associated with an increased risk of renal function decline. Clin Nutr. 34(2), 269–75 (2015).
10. Peralta, C. A. et al. Racial and ethnic differences in renal function decline among persons without chronic renal disease. J Am Soc Nephrol. 22(7), 1327–34 (2011).
11. Ebert, J., Lawler, E., Bogan, H. & Perls, T. Morbidity profiles of centenarians: survivors, delayers, and escapers. J Gerontol A Biol Sci Med Sci. 58(3), 232–237 (2003).
12. Ismail, K. et al. Compression of Morbidity Is Observed Across Cohorts with Exceptional Longevity. J Am Geriatr Soc. 64(8), 1583–91 (2016).
13. Motta, M. et al. Successful aging in centenarians: myths and reality. Arch Gerontol Geriatr. 40(3), 241–51 (2005).
14. Jopp, D. S., Park, M. K., Lehrfeld, J. & Paggi, M. E. Physical, cognitive, social and mental health in near-centenarians and centenarians living in New York City: findings from the Fordham Centenarian Study. BMC Geriatr. 16, 1 (2016).
15. Ford, E. S., Giles, W. H. & Dietz, W. H. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA. 287(3), 356–359 (2002).
16. Cheng, H. T. et al. Metabolic syndrome and insulin resistance as risk factors for development of chronic kidney disease and rapid decline in renal function in elderly. J Clin Endocrinol Metab. 97(4), 1268–76 (2012).
17. Tanaka, H., Shiohira, Y., Uezu, Y., Higa, A. & Iseki, K. Metabolic syndrome and chronic kidney disease in Okinawa, Japan. Kidney Int. 69(2), 369–374 (2006).
18. O’Hare, A. M. et al. Age affects outcomes in chronic kidney disease. J Am Soc Nephrol. 18(10), 2758–2765 (2007).
19. Moumndzad, A. & Liguori, G. Persistent Increase of Prevalence of Metabolic Syndrome Among USA: Adults: NHANES III to NHANES 1999–2006. Diabetes Care. 34(1), 216 (2011).
20. van Vlet-Ospatichouk, J. V. et al. The prevalence of metabolic syndrome and metabolically healthy obesity in Europe: a collaborative analysis of ten large cohort studies. BMC Endocr Disord. 14, 9 (2014).
21. Fu, S., Ping, P., Luo, L. & Ye, P. Deep analyses of the associations of a series of biomarkers with insulin resistance, metabolic syndrome, and diabetes risk in non-diabetic middle-aged and elderly individuals: results from a Chinese community-based study. Clin Interv Aging. 11, 1531–1538 (2016).
22. Willcox, D. C., Willcox, B. J. & Poon, L. W. Centenarian studies: important contributors to our understanding of the aging process and longevity. Curr Gerontol Geriatr Res. 2010, 484529 (2010).
23. Hostetter, T. H., Remmke, H. G. & Brenner, B. M. The case for intrarenal hypertension in the initiation and progression of diabetic and other glomerulopathies. Am J Med. 72(3), 375–380 (1982).
24. Egan, R. M., Greene, E. L. & Goodfriend, T. L. Insulin resistance and cardiovascular disease. Am J Hypertens. 14(6 Pt 2), 1165–1255 (2001).
25. Liu, X., Chen, Y., Boucher, N. L. & Rotherberg, A. F. Prevalence and change of central obesity among US Asian adults: NHANES 2011–2014. BMC Public Health. 17(1), 678 (2017).
26. Sahakyan, K. R. et al. Normal-Weight Central Obesity: Implications for Total and Cardiovascular Mortality. Ann Intern Med. 163(11), 827–35 (2015).
27. Wang, F., Ye, P., Luo, L., Xiao, W. & Wu, H. Association of risk factors for cardiovascular disease and glomerular filtration rate: a community-based study of 4925 adults in Beijing. Nephrol Dial Transplant. 25(12), 3924–3931 (2010).
28. Kuo, H. W., Tsai, S. S., Tiao, M. M. & Yang, C. Y. Epidemiological features of CKD in Taiwan. Am J Kidney Dis. 49(1), 46–55 (2007).
29. McCullough, P. A. Why is chronic kidney disease the “spoiler” for cardiovascular outcomes? J Am Coll Cardiol. 41(5), 725–8 (2003).
30. Samuelsson et al. Complex apolipoprotein B-containing lipoprotein particles are associated with a higher rate of progression of human chronic renal insufficiency. J Am Soc Nephrol. 9(8), 1482–8 (1998).
31. Manninen, V. et al. Joint effects of serum triglyceride and LDL cholesterol and HDL cholesterol concentrations on coronary heart disease risk in the Helsinki Heart Study. Implications for treatment. Circulation. 85(1), 37–45 (1992).
32. Khali, M. A. M. et al. Cigarette Smoking and Its Hazards in Kidney Transplantation. Adv Med. 2017, 6213814 (2017).
33. Chen, J. et al. The metabolic syndrome and chronic kidney disease in U.S. adults. Ann Intern Med. 140(3), 167–74 (2004).
34. He Y., et al. Cohort Profile: The China Hainan Centenarian Cohort Study (CHCCS). Int J Epidemiol. https://doi.org/10.1093/ije/dyox017 (2018 Feb 28).
35. Yang, S. H., Dou, K. F. & Song, W. J. Prevalence of diabetes among men and women in China. N Engl J Med. 362(25), 2425–2426 (2010).
36. Wang, F. et al. Lipid-lowering therapy and lipid goal attainment in patients with metabolic syndrome in China: subgroup analysis of the Dyslipidemia International Study-China (DYSIS-China). Atherosclerosis. 237(1), 99–105 (2014).
37. Alberti, K. G., Zimmet, P. & Shaw, J. IDF Epidemiology Task Force Consensus Group. The metabolic syndrome: a new worldwide definition. Lancet. 366(9491), 1059–1062 (2005).
38. Chen, C. & Lu, F. Department of Disease Control Ministry of Health. PR China. The guidelines for prevention and control of overweight and obesity in Chinese adults. Biomed Environ Sci. 17(Suppl), 1–36 (2004).
39. Committee of Cardio-Cerebro-Vascular Diseases of Gerontological Society of China; Chinese College of Cardiovascular Physicians of Chinese Medical Doctor Association. Chinese expert consensus on the diagnosis and treatment of hypertension in the elderly. Zhonghua Nei Ke Za Zhi. 56(11), 885–893 (2017).
40. Tong, Y. Z. et al. Consensus on the Prevention of Type 2 Diabetes in Chinese Adults. Chin Med J (Engl). 130(5), 600–606 (2017).
41. Joint Committee for Developing Chinese guidelines on Prevention and Treatment of Dyslipidemia in Adults. Chinese guidelines on prevention and treatment of dyslipidemia in adults. Zhonghua Xin Xue Guan Bing Za Zhi. 35(5), 390–419 (2007).
42. Ma, Y. C., Zuo, L. & Chen, J. H. Modified Glomerular Filtration Rate Estimating Equation for Chinese Patients with Chronic Kidney Disease. J Am Soc Nephrol. 17(10), 2937–2944 (2006).

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Author Contributions

FS., Y.Y., L.F., Z.Y.: contributed to the study design, performed the data collection and analyses, and drafted the paper.

Additional Information

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