Introduction: Body mass index (BMI), despite being widely used as a marker of obesity, fails to fully capture cardiovascular risks as it is an insufficient biomarker of abdominal adiposity, unlike waist circumference (WC). We aimed to characterize associations between BMI and WC with cardiovascular structure and function in older adults.

Methods: Among an observational cohort study of a community of older adults, transthoracic echocardiography determined cardiovascular structure and function, while aerobic capacity was determined by peak oxygen uptake (VO\textsubscript{2}) metrics. The cutoffs for obesity were 27.5 kg/m\textsuperscript{2} for BMI, and >90 cm for males and >80 cm for females for WC.

Results: Of 970 older adults without cardiovascular disease (mean age 73 ± 4 years, 432 [44%] males), 124 (12.8%) were obese by BMI definition while 347 (35.7%) were obese by WC definition. Interdefinitional agreement was fair (Cohen’s κ = 0.345). Unlike the BMI definition, participants defined as obese by WC were more likely to be women (65% vs. 50%, \(p<0.001\)), older (65 ± 11 vs. 63 ± 14 years, \(p=0.007\)), and had lower handgrip strength (24 ± 0.6 vs. 26 ± 0.4 kg, \(p=0.022\)). Across BMI categories, high WC was associated with more impaired myocardial relaxation (E/A), and VO\textsubscript{2} measurements (all \(p<0.05\)). Among those with low BMI, high WC was associated with larger left atrial (LA) volumes (\(p=0.003\)). WC, but not BMI, was independently associated with E/A (β = −0.114, SE −0.114 ± 0.024, \(p<0.001\)) in regression analysis.

Conclusion: WC identified a higher prevalence of obesity, possibly related to central adiposity. Across BMI categories, WC identified more adverse measurements in E/A, aerobic capacity, and LA structure. Trial Registration: ClinicalTrials.gov Identifier: NCT02791139.

Introduction

Obesity and ageing are major health challenges of the 21st century. Obesity increases the risk of death from any cause and from cardiovascular disease in adults, while age is a well-established cardiovascular risk factor. Although the body of evidence indicates that obese older subjects are prone to cardiovascular morbidity [1, 2], younger adults have higher relative risks associated with obesity.
than older adults, based on body weight definitions of obesity [3]. This may lead to reduced emphasis on obesity as a risk factor among older adults [4]. However, body weight among older adults reflects a combination of overall health status and processes of aging-induced weight loss, such as sarcopenia [5]. This may explain lower relative risks associated with body mass index (BMI) definition of obesity among older adults, compared to younger adults. Therefore, the assessment of obesity based on BMI in older adults may inadequately identify older adults at risk of obesity-related cardiovascular disease.

Given the cardiometabolic effects of obesity on cardiovascular risks, waist circumference (WC) on the other hand, may enhance assessments of obesity among older adults. As a marker of central adiposity, measurement of WC is not influenced by limb sarcopenia, which is relevant among older adults with age-related sarcopenia. In addition, older adults with obesity have been recognized as a distinct metabolic phenotype (compared to older adults without obesity) that is associated with higher risks of cardiovascular disease [6]. Hypothetically, WC may have added value in identifying older adults with more adverse phenotypic alterations in cardiovascular structure and function, compared to BMI. Accordingly, we aimed to compare the relative prevalence and factors associated with obesity defined by WC vis-à-vis BMI, and to characterize their associations with cardiovascular structure and function in older adults without cardiovascular disease.

**Methods**

**Study Population**

The subjects were recruited from the Cardiac Ageing Study (CAS) [7], a prospective study initiated in 2014 that examines characteristics and determinants of cardiovascular function in elderly adults. CAS participants were recruited from the prospective, population-based cohort, the Singapore Chinese Health Study [8] and directly from the local community. The current study sample consisted of men and women who participated in the baseline CAS 2014–2017 examination who had no self-reported history of physician-diagnosed cardiovascular disease (such as coronary heart disease, atrial fibrillation), stroke, or cancer. Written informed consent was obtained from participants upon enrolment. The SingHealth Centralised Institutional Review Board (CIRC/2014/628/C) had approved the study protocol.

**Data Acquisition**

All participants were examined and interviewed on one study visit by trained study coordinators. Participants completed a standardized questionnaire that included medical history and coronary risk factors. Hypertension was defined by current use of antihypertensive drugs or physician-diagnosed hypertension. Diabetes mellitus was defined by the current use of antidiabetic agents or physician-diagnosed diabetes mellitus. Dyslipidemia was defined by the current use of lipid-lowering agents or physician-diagnosed dyslipidemia. Smoking history was defined as ever smokers (former or current smokers) or never smokers. BMI was calculated as weight in kilograms divided by the square of height in meters. Sinus rhythm status was ascertained by resting electrocardiogram. Clinical data were obtained on the same day as assessment of echocardiography and serum collection. WC was obtained 2.5 cm above the umbilicus, an anatomical landmark associated with abdominal fat mass measured by dual-energy X-ray absorptiometry [9].

We compared two definitions of obesity, namely: (1) BMI cut-off of 27.5 kg/m² as recommended by the World Health Organization for Asian populations [10] and (2) WC cut-offs of >90 cm for males and >80 cm for females, as recommended by the International Diabetes Federation Consensus Worldwide Definition of the Metabolic Syndrome [11]. Handgrip strength was measured from each participant using the Takei hand grip dynamometer (Model TKKS401 Grip D) and following standard protocols. Participants were instructed to stand upright with their arms let down naturally. The handgrip dynamometer was held with the indicator facing outwards, and the grip width was adjusted so that the second joint of the pointing finger made a right angle at the dynamometer. Participants were then instructed to clasp the grip with full force. Measurements obtained were recorded to the nearest 0.1 kg. Two trials were performed for each hand, starting with the right hand. Only the highest value obtained from each hand was used. Overall handgrip strength was calculated as the mean of the maximum left-hand and right-hand grip strength measurements.

Echocardiography was performed using ALOKA α10 with a 3.5-MHz probe. In each subject, standard echocardiography, which included 2-D, M-mode, pulse Doppler and tissue Doppler imaging, was performed in the standard parasternal and apical (apical 4-chamber, apical 2-chamber, and apical long) views, and three cardiac cycles were recorded. Left ventricular ejection fraction, left atrial (LA) volume, and LA volume index (LAVI) were measured. The trans-mitral flow E and A waves with the sample volume position at the tip of the mitral valve leaflets from the apical 4-chamber view were recorded by Doppler echocardiography. Myocardial relaxation (E/A) ratio was computed as a ratio of peak velocity flow in early diastole E (MV E) (m/s) to peak velocity flow in late diastole by atrial contraction A (MV A) (m/s). Pulsed wave tissue Doppler imaging was performed with the sample volume at the septal and lateral annulus from the apical 4-chamber view. The frame rate was between 80 and 100 frames per second. The tissue velocity patterns

**Table 1. Prevalence of obesity based on BMI versus WC**

| Definition                  | Subjects, n (%) |   |
|-----------------------------|----------------|---|
| Nonobese BMI ≥27.5 kg/m²    | 846 (87.2)     | 124 (12.8) |
| Obese BMI ≥27.5 kg/m²       |                |   |
| WC >90 cm in males          | 623 (64.3)     | 347 (35.7) |
| >80 cm in females           |                |   |

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were recorded and expressed as E′, and A′. All measurements were measured by the same operator and the measurements were averaged over three cardiac cycles and adjusted by the RR interval. The specific cardiovascular function of interest in this cohort of older adults was E/A properties, for which impairments in E/A, would suggest myocardial ageing [12]. E/A was defined by ratio of peak velocity flow in MV E to peak velocity flow in late diastole by MV A, also referred to as the E/A ratio. MV E refers to the peak velocity of blood flow during early diastole from the left atrium into the left ventricle, where blood flows passively into the left ventricle during relaxation. MV A refers to the peak velocity of blood flow into the left ventricle in late diastole due to contraction of the left atrium. The echocardiography readers were blinded to the obesity status of the participants. We used a validated non-exercise prediction model comprising of physical activity questionnaire to estimate peak oxygen uptake (VO₂) milliliter/kilogram/minute (mL/kg/min) [13, 14], also previously used in this cohort [15].

**Statistics**

Clinical characteristics are presented as means and standard deviations for continuous data and frequency and percentage for categorical data. We determined agreement between BMI and WC definitions using Cohen’s kappa. We compared demographics, clinical characteristics, and echocardiographic characteristics between nonobese and obese subjects based on either BMI or WC definitions. The Student’s t test was used for continuous data and the χ² test was used for categorical data. Multiple linear regression analysis was subsequently performed to ascertain the relationship of cardiovascular structure and function to BMI and WC definitions, respectively. Variability of cardiovascular structure and function across BMI group and WC group were displayed in the error bar charts with standard error.

All statistical analyses were performed using STATA 15 (College Station, TX, USA). For all analyses, a two-tailed p value of <0.05 was considered statistically significant.

**Results**

**Obesity Definitions**

Among 970 participants, 124 (12.8%) were defined as obese by the BMI definition, while 347 (35.7%) were defined as obese by the WC definition (Table 1). Inter-definitional agreement was fair between BMI and WC (Cohen’s κ = 0.345).

Based on both definitions of BMI and WC, hypertension (54% vs. 33%; p < 0.001 and 44% vs. 31%; p < 0.001) and diabetes mellitus (29% vs. 13%; p < 0.001 and 20% vs. 13%; p = 0.001) were more prevalent among those defined as obese (Table 2). However, WC identified more women (65% vs. 50%; p < 0.001), older participants (65 ± 11 vs. 63 ± 14 years; p = 0.007) and dyslipidemic (46% vs. 34%; p < 0.001) participants as obese. Systolic blood pressure was also significantly higher (140 ± 21 vs. 135 ± 24 mm Hg; p = 0.002) in obese versus nonobese participants defined by WC. Based on BMI, gender, age, dyslipidemia, and systolic blood pressure were not significantly different between obese and nonobese participants (Table 2). Participants defined as obese by WC definition had lower hand grip strength (24.2 vs. 25.9, p = 0.022) compared to nonobese. On the other hand, participants defined as obese by
BMI definition had similar hand grip strength (26.4 vs. 25.2, p = 0.26) compared to nonobese. Participants defined as obese by either WC or BMI definitions, had lower VO$_2$ compared to nonobese participants (Table 2).

**Cardiovascular Structure and Function Based on Obesity Definitions**

In general, participants who were defined by both BMI and WC as obese had larger left ventricular dimensions (online suppl. Table A; for all online suppl. material, see www.karger.com/doi/10.1159/000521729). Participants who were defined by BMI as obese had significantly lower E/A ratio compared to those who were not obese (1.17 ± 0.49 vs. 1.00 ± 0.37; p < 0.001) (Table 3). Left atrial size was also significantly larger in obese individuals in both the BMI group (3.94 ± 0.53 vs. 3.50 ± 0.55; p < 0.001) and WC group (3.73 ± 0.58 vs. 3.46 ± 0.54; p < 0.001). The LAVI was also found to be significantly higher in obese individuals in both the BMI (22.3 ± 7.90 vs. 20.5 ± 7.43; p = 0.020) and WC (22.1 ± 8.3 vs. 20.0 ± 6.9; p < 0.001) groups. Left ventricular ejection fraction percentage was over 70% and not significantly different in both obese and nonobese for both BMI (72.6 ± 8.3 vs. 71.1 ± 9.7; p = 0.074) and WC (72.4 ± 8.4 vs. 72.3 ± 8.7; p = 0.935) (Table 3) (online suppl. Table A).

However, across high or low BMI categories, high WC was associated with more adverse mean E/A and VO$_2$

### Table 3. Key echocardiographic characteristics

| Variables                        | Nonobese                  | Obese                      | p value |
|----------------------------------|---------------------------|----------------------------|---------|
|                                 | mean ± SD 95% conf. interval | mean ± SD 95% conf. interval |         |
| **BMI definition**               |                           |                            |         |
| Left atrial diameter, cm         | 3.50±0.55 3.46–3.53       | 3.94±0.53 3.84–4.04        | <0.001  |
| LAVI (mL/m$^2$)                  | 20.5±7.43 20.0–21.1       | 22.3±7.90 20.8–23.8        | 0.020   |
| LVEF (%)                         | 72.6±8.3 72.0–73.1        | 71.1±9.7 69.3–72.8         | 0.074   |
| Peak velocity flow in MV E peak (m/s) | 0.74±0.17 0.73–0.75      | 0.73±0.18 0.70–0.76        | 0.591   |
| Peak velocity flow in late diastole by MV A peak (m/s) | 0.72±0.21 0.71–0.73       | 0.78±0.19 0.75–0.82        | 0.003   |
| Ratio MV E peak: MV A peak       | 1.13±0.46 1.09–1.16       | 0.98±0.35 0.91–1.04        | <0.001  |
| **WC definition**                |                           |                            |         |
| Left atrial diameter, cm         | 3.46±0.54 3.42–3.50       | 3.73±0.58 3.66–3.79        | <0.001  |
| LAVI (mL/m$^2$)                  | 20.0±6.9 19.5–20.6        | 22.1±8.3 21.1–23.0         | <0.001  |
| LVEF (%)                         | 72.4±8.4 71.7–73.0        | 72.3±8.7 71.4–73.3         | 0.935   |
| Peak velocity flow in MV E peak (m/s) | 0.74±0.17 0.73–0.76      | 0.73±0.17 0.71–0.75        | 0.279   |
| Peak velocity flow in late diastole by MV A peak (m/s) | 0.70±0.21 0.68–0.72       | 0.77±0.19 0.75–0.79        | <0.001  |
| Ratio MV E peak: MV A peak (E/A) | 1.17±0.49 1.13–1.21       | 1.00±0.37 0.96–1.04        | <0.001  |

LVEF, left ventricular ejection fraction; SD, standard deviation.

### Table 4. Multivariate regression model for E/A ratio

| Variables        | Obesity based on BMI | Obesity based on WC | p value |
|------------------|----------------------|---------------------|---------|
|                  | adjusted $R^2$       | standard coefficient ($\beta$) | std. Error | p value |
|                  |                      | std. coefficient ($\beta$) | std. Error | p value |
| Hypertension     | 0.139                | -0.288              | -0.288±0.031 | <0.001 |
| Diabetes mellitus| -0.156               | -0.156±0.042        | <0.001   |
| BMI, kg/m$^2$    | -0.059               | -0.059±0.043        | 0.168    |
| WC, cm           | -0.114               | -0.114±0.024        | <0.001   |
| Dyslipidemia     | -0.032               | -0.032±0.034        | 0.035    |
| Age, years       | -0.021               | -0.021±0.0001       | <0.001   |
| Female           | 0.037                | 0.037±0.023         | 0.107    |
measurements (Fig. 1a, b). Among those low BMI, high WC was associated with more adverse mean LAVI (Fig. 1c).

Multiple linear regression analysis was performed in BMI and WC groups to assess association of the E/A ratio with obesity status after adjustment for significant covariates (Table 4). Adjusted $R^2$ value was 13.9% and 45.5% for BMI and WC groups, respectively. When adjusted for hypertension and diabetes mellitus, BMI was not associated with cardiovascular function. In contrast, WC was associated with E/A ($\beta = -0.114$, $SE = -0.114 \pm 0.024$, $p < 0.001$), independent of age and diabetes mellitus. With each 1 cm increase in WC, E/A ratio declined by 0.114.

**Discussion**

Based on a cohort of older adults, the prevalence of obesity varied depending on the definition used. The prevalence of obesity was higher at 35.7% based on WC, and only 12.8% based on BMI. Although both definitions identified more adverse alterations in cardiovascular structure and function, only WC was independently associated with impaired E/A. Importantly, even within nonobese BMI category, high WC was associated with impairments in E/A, aerobic capacity, and LA structure.

Comparing between definitions of BMI versus WC, WC identified the presence of obesity in adults who were older in age, whereas BMI did not differentiate between
adults with older age. Although both definitions are intrinsically different and are not interchangeable, these prevalence rates highlight the importance of using appropriate definitions of obesity, particularly among older adults with aged biology.

The limited ability of BMI to identify obesity among older adults has been previously appreciated [16]. At extremes of age and weight, BMI has limited utility [17, 18]. Apart from age, older adults have fluctuating body weights, related to ageing or accumulation of systemic illnesses [19, 20]. We observed that those defined as obese by WC had lower hand grip strength, a possible reflection of concomitant muscle sarcopenia. Our findings concur with studies that have found associations between abdominal adiposity and poorer physical outcomes in sarcopenic adults [21]. This adds to the body of evidence that shows inverse associations between muscle strength and adiposity-related obesity markers, particularly among older adults [22–24].

Our findings are novel because they depict distinct associations between WC and cardiovascular structure and function among older adults. WC was linearly associated with impairments in myocardial function, namely E/A, a common early manifestation of myocardial ageing. Left atrial size was larger among the obese as defined by both BMI and WC definitions, a well-recognized risk factor for atrial fibrillation development [25, 26]. While cardiometabolic complications of central adiposity are well established in current literature [2, 30], while our cross-sectional study cannot prove generalizability. The observational study design does not imply causality between markers of obesity and cardiovascular disease. Adaptive versus pathogenic responses arising from medication treatment are unknown. Furthermore, for purposes of cardiovascular risk assessment, WC is an accepted marker of central adiposity [36]. Our findings are based on Asian older adults, utilizing obesity cut-offs and functional features as targets useful for monitoring response to therapies, to reduce burdens of central obesity-related cardiovascular disease [33–35].

We acknowledge limitations in our study. In the absence of body fat measurements, the use of WC may only represent an incomplete measure of body fat composition. However, WC is not interchangeable with body fat [5]. Furthermore, for purposes of cardiovascular risk assessment, WC is an accepted marker of central adiposity [36]. Our findings are based on Asian older adults, utilizing obesity cut-offs based on prior Asian data. Hence our findings may not be extrapolated to cohorts of non-Asian descent. Importantly, we recognize that BMI may not be an accurate measure of obesity for Asians. The Asian phenotype of obesity comprises of higher proportions of visceral fat in the central abdominal regions (“central obesity”) compared to Western populations [37–40]. Similar studies from other cohorts would be necessary to confirm our observations and improve generalizability. The observational study design does not imply causality between markers of obesity and cardiovascular function. Adaptive versus pathogenic responses cannot be differentiated based on this clinical study design. We did not correct for details such as medication data hence effects arising from medication treatment are unknown. This is a low-risk community cohort, hence marginal values in some of the observed measurements may reflect underestimation rather than overestimation of clinical significance. Even so, the large study sample provided reasonable sample power.

**Conclusion**

The prevalence of obesity varied depending on the definition used. WC identified higher prevalence of obesity, possibly related to central adiposity. Across BMI catego-
ries, WC identified more adverse measurements in E/A, aerobic capacity, and LA structure. WC may better characterize the impact of obesity on cardiovascular ageing.

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**Statement of Ethics**

Written informed consent was obtained from the participants upon enrolment. The SingHealth Centralised Institutional Review Board (CIRC/2014/628/C) had approved the study protocol.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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