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Adiposity measurements in association with metabolic syndrome in older men have different clinical implications

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ABSTRACT

Obesity is a major public health problem, and measuring adiposity accurately and predicting its future comorbidities are important issues. Therefore, we hypothesized that 4 adiposity measurements, body mass index (BMI), waist circumference (WC), waist-to-height ratio, and body fat percentage, have different physiological meanings and distinct associations with adverse health consequences. This study aimed to investigate the relationship of these 4 measurements with metabolic syndrome (MetS) components and identify the most associated factor for MetS occurrence in older, non-medicated men. Cross-sectional data from 3004 men, all 65 years of age and older, were analyzed. The correlation and association between adiposity measurements and MetS components were evaluated by Pearson correlation and multiple linear regression. Based on multivariate logistic regression, BMI and WC were significantly associated with MetS and were selected to build a combined model of receiver operating characteristic curves to increase the diagnosis accuracy for MetS. The results show that BMI is independently associated with systolic and diastolic blood pressure; WC and body fat percentage are associated with fasting plasma glucose and log transformation of triglyceride; BMI and WC are negatively associated with high-density lipoprotein cholesterol (HDL-C); and WC is a better discriminate for MetS than BMI, although the combined model (WC + BMI) is not significantly better than WC alone. Based on these results, we conclude that the 4 adiposity measurements have different clinical implications.

Abbreviations: AUC, area under curve; BF%, body fat percentage; BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Log TG, log transformation of triglyceride; MetS, metabolic syndrome; ROC, receiver operating characteristic; SBP, systolic blood pressure; T2DM, type 2 diabetes mellitus; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WC + BMI, combined model of waist circumference and body mass index; WHO, World Health Organization; WHtR, waist-to-height ratio.

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Thus, in older men, BMI is an important determinant for blood pressure and HDL-C. Waist circumference is associated with the risk of fasting plasma glucose, HDL-C, triglyceride, and MetS occurrence. The combined model did not increase the diagnosis accuracy.

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1. Introduction

Throughout the world, the incidence of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) is rapidly increasing. Both are listed as dominant causes of mortality and disability in the Global Burden of Disease Study 2010 [1]. These 2 diseases are found to be significantly related to the clustering of increased adiposity, hypertension, hyperglycemia, and dyslipidemia; thus, the World Health Organization (WHO) published the first criteria for metabolic syndrome (MetS) in 1999 [2]. The definition of MetS was further updated by the National Cholesterol Education Program and the International Diabetes Federation [3–5], and the criteria for MetS were harmonized in 2009 [6]. It is now generally acknowledged that, among the 5 components of MetS, increased adiposity is the most important because this measure is the core of the other 4 components [7]; however, there are many different methods of measuring adiposity.

The most commonly used adiposity measurement is the body mass index (BMI), and the definitions of overweight and obese recommended by the WHO are based on this measurement [8,9]. Waist circumference (WC) is used as one of the criteria of MetS [4,5], and waist-to-height ratio (WHtR) and body fat percentage (BF%) are also commonly used in different conditions. Many studies have been conducted to shed light on the roles of these 4 different measurements. For example, Schneider et al. [10] found that WC or WHtR may better predict the prevalence of cardiovascular risk, and Dervaux et al. [11] concluded that WC is more strongly associated with MetS than BMI in whites. However, Knowles et al. [12] examined these 4 measurements of adiposity in Peruvian people and found that no single adiposity measurement could be identified as the best predictor for MetS. Based on these studies, the identity of the best adiposity measurement for the prediction of MetS remains controversial. Moreover, it should be noted that most of these studies did not exclude subjects who were on medications for hypertension, diabetes mellitus, or hyperlipidemia, and the effects of these drugs are certainly confounding factors that need to be considered.

In many countries, health insurance systems provide complete and affordable medical services, which helps to increase life expectancy and makes aging populations an important issue for health providers and governments. Given that the elderly exhibit a high prevalence of CVD and T2DM, early detection of MetS is particularly crucial for this age group. We hypothesized that the 4 measurements have different physiological meanings and distinct associations with adverse health consequences, such as obesity-related metabolic disorders. In this study, we investigated the relationship of these 4 measurements with MetS components and identified the most associated factor for the occurrence of MetS in older men.

2. Methods and materials

2.1. Study participants

From January 2010 to December 2012, males (65 years of age and older) were enrolled during routine health examinations at the MJ Health Screening Centers in Taiwan, with the cross-sectional study conducted in 2013. The MJ Health Screening Centers are private membership clinics around Taiwan that provide regular health screening services for more than 1 million persons since its inception in 1988 [13]. Written informed consent was collected from each participant, and the study protocol was approved by the institutional review board of the MJ Health Screening Centers. Data were recorded anonymously, with any information related to the identification of individuals removed.

Initially, a total of 7142 records were obtained. Those with significant major medical diseases; those with a history of hypertension, diabetes mellitus, or hyperlipidemia; and those receiving medications for these diseases or other medications known to affect blood glucose, lipid, or blood pressure (BP) were excluded. The categories of medications considered to potentially alter serum glucose concentrations included corticosteroids, diuretics, β -blockers, and others. In addition, subjects with acute illnesses, such as fever or abnormal hydration status, were also excluded. After all exclusions, 3004 men were eligible for data analysis.

2.2. Anthropometric measurements and laboratory data

Following a minimal 10-hour fast, participants visited the clinic at 8 AM. An interview conducted by a member of the senior nursing staff obtained information about medical history, lifestyle, alcohol intake, smoking, and physical exercise. All participants were measured wearing light clothing and no shoes.

Four different measurements of adiposity were conducted:

1. BMI was calculated as the weight (kilograms) divided by the square of the height (meters) (kilograms per square meter) [14].
2. WC (centimeters) was taken at the midway point between the inferior margin of the last rib and the crest of the ilium in a horizontal plane [15].
3. WHtR was calculated as the WC (centimeters) divided by height (meters) (centimeters per meter) [14].
4. BF% was measured using the Tanita TBF Body Composition Analyzer (Tanita Corp, Tokyo, Japan), which provided a print-out of measured bioelectrical impedance and calculated body fat. It is shown that the Tanita bioimpedance analysis measurements are highly correlated with both dual-energy X-ray absorptiometry and underwater weighing methods [16].

Quality control procedures and employee training programs were conducted by the senior staff to ensure that the measurements, such as height and body weight, were performed with standardized techniques at each site. The apparatuses used for adiposity measurements at each site were regularly examined for accuracy and reproducibility.

The nursing staff measured systolic BP (SBP) and diastolic BP (DBP) using mercury sphygmomanometers with appropriately sized cuffs on the right arms of the participants, following a minimal 5-minute rest in a sitting position. Two measurements were taken more than 1 minute apart, and the average was recorded. We only measured BP in the sitting position from 1 arm, as recommended by the American Heart Association [17].

Venous blood samples were drawn from the antecubital vein for biochemical analyses. Plasma was separated from blood within 1 hour and stored at -70°C . Fasting plasma glucose (FPG) was determined using the glucose oxidase method (YSI 203 glucose analyzer; Scientific Division, Yellow Spring Instrument Company, Inc, Yellow Spring, OH). Both total cholesterol (TC) and triglyceride (TG) levels were measured using the dry, multilayer analytical slide method (Fuji Dri-Chem 3000 analyzer; Fuji Photo Film Corporation, Minato-Ku, Tokyo, Japan). Serum high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) concentrations were determined using an enzymatic assay following dextran sulfate precipitation (Model 7150; Hitachi Corporation, Tokyo, Japan).

2.3. Definition of the MetS

We measured the components of MetS using the latest criteria that were harmonized in 2009 [6]. According to these criteria, MetS is clinically defined by the presence of 3 or more of the following: central obesity (elevated WC ≥ 90 cm in men for Asians), elevated TG (≥ 150 mg/dL), reduced HDL-C (< 40 mg/dL for men), elevated BP (SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg), and/or elevated FPG concentration (≥ 100 mg/dL).

2.4. Statistical analyses

Analyses were performed using SPSS version 20.0 (IBM, Somers, NY). Data were tested for normal distribution with the Kolmogorov-Smirnov test and for homogeneity of variances with Levene's test. Continuous variables were expressed as means \pm standard deviation. The TG value was logarithmically transformed before statistical analysis to reduce the influence of extreme right skewedness because it was not normally distributed. An independent-sample t test was used to evaluate the anthropometric data and metabolic components between participants with and without MetS.

Correlations between adiposity measurements (dependent variable) and each metabolic component (independent variable) were evaluated by Pearson correlation. To further evaluate which of the 4 adiposity measurements were independently associated with MetS components, multiple linear regression analysis was performed. With this method, whether the 4 adiposity measurements had the same impact on the MetS components could be evaluated simultaneously by using standardized coefficients (β). Furthermore, multivar-

iate logistic regression analysis was applied to calculate the adjusted coefficients (B) of adiposity measurements for the association with abnormal MetS components and MetS itself. We focused on the measurements for accessing adiposity. Because the anthropometric measure of body weight is not sufficient for the clinical assessment of body fat and the calculations of BMI and WHtR considered height, we did not include body weight and height in the regression model.

Finally, receiver operating characteristic (ROC) curves of the adiposity measurements for discriminating MetS were constructed. The area under curve (AUC) and 95% confidence interval (CI) were also estimated and compared. To further increase the diagnosis accuracy, combined models with more than 1 measurement were built. Only measurements significantly related to MetS in the multivariate logistic regression were selected for further model establishment. Among them, each related measurement was separately included in the model and then combined model. The diagnosis accuracy of different models was then compared via AUC using MedCalc version 12.2.1 (MedCalc Software, Ostend, Belgium). All statistical tests were 2 sided, and $P < .05$ was considered statistically significant.

3. Results

Among the 3004 participants, 698 participants (23.2%) were diagnosed with MetS. The anthropometric variables, BP, and serum biochemistries are shown in Table 1. There is no significant difference in age between subjects with and without MetS (MetS+, MetS-, respectively). The MetS+ group

Table 1 – Anthropometric and clinical characteristics of the study subjects with (+) or without (–) MetS

Variables	Total (N = 3004)	MetS (–) (n = 2306)	MetS (+) (n = 698)	P ^a
Age, y	70.0 \pm 4.5	70.0 \pm 4.4	70.1 \pm 4.5	.845
Height, cm	164.2 \pm 5.8	163.9 \pm 5.8	165.2 \pm 5.8	<.001
Weight, kg	63.1 \pm 9.3	61.1 \pm 8.5	70.0 \pm 8.5	<.001
BMI, kg/m ²	23.4 \pm 3.0	22.7 \pm 2.7	25.6 \pm 2.7	<.001
WC, cm	83.7 \pm 8.7	81.5 \pm 7.8	91.0 \pm 7.3	<.001
WHtR, cm/m	51.0 \pm 5.2	49.8 \pm 4.8	55.1 \pm 4.5	<.001
BF%, %	20.6 \pm 5.3	19.6 \pm 5.0	24.0 \pm 4.9	<.001
SBP, mm Hg	132.4 \pm 19.3	129.9 \pm 19.3	140.9 \pm 16.7	<.001
DBP, mm Hg	75.6 \pm 11.2	74.2 \pm 10.9	80.2 \pm 10.7	<.001
FPG, mg/dL	103.5 \pm 19.2	100.7 \pm 15.5	112.6 \pm 26.1	<.001
TC, mg/dL	200.0 \pm 33.9	198.6 \pm 33.0	204.5 \pm 36.2	<.001
HDL-C, mg/dL	51.6 \pm 13.9	54.3 \pm 13.6	42.8 \pm 10.7	<.001
LDL-C, mg/dL	125.1 \pm 30.6	124.3 \pm 30.0	127.8 \pm 32.4	.007
TG, mg/dL	116.4 \pm 58.5	100.3 \pm 46.1	169.3 \pm 63.9	<.001
Log TG	2.02 \pm 0.20	1.96 \pm 0.18	2.20 \pm 0.18	<.001
MetS component ^b , n	1.70 \pm 1.17	1.19 \pm 0.75	3.37 \pm 0.59	<.001

Data are shown as means \pm SD.

^a The Student's t test for unpaired data was used for the comparison of mean values between MetS(–) and MetS(+).

^b Number of abnormal MetS components: WC ≥ 90 cm, SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg, FPG ≥ 100 mg/dL, HDL-C < 40 mg/dL, TG ≥ 150 mg/dL.

Table 2 – Pearson correlation coefficients (*r*) between MetS components and measurements of adiposity

	SBP	DBP	FPG	HDL-C	Log TG ^a
BMI	0.161	0.192	0.153	−0.334	0.330
WC	0.146	0.173	0.176	−0.352	0.353
WHtR	0.158	0.163	0.164	−0.336	0.344
BF%	0.121	0.168	0.173	−0.280	0.356

All $P < .001$.

^a The TG value was logarithmically transformed before statistical analysis because it was not normally distributed.

had significantly higher BMI, WC, WHtR, BF%, SBP, DBP, FPG, TC, LDL-C, and log transformation of TG (Log TG), but lower HDL-C.

The results of Pearson correlation between adiposity measurements and each metabolic component are shown in Table 2. All of the correlations reached statistical significance; however, the coefficients (*rs*) are small. The coefficients between measurements of adiposity with SBP, DBP, and FPG were less than 0.20, whereas those with HDL-C and Log TG were around or above 0.30. In Table 3, the results of multiple linear regression analysis are listed. Body mass index was the only one found to be associated with SBP after the adjustment of all other methods. A similar finding was noted for the DBP. Both WC and BF% were associated with FPG and Log TG. Body mass index and WC were negatively associated with HDL-C.

These relationships were evaluated again from a different aspect with multivariate logistic regression (Table 4). In this analysis, the occurrence of abnormal MetS was regarded as an outcome variable. The results are similar to those presented in Table 3. In addition, it is worthwhile to note that BMI and WC were independently associated with the risk of MetS occurrence.

Because both BMI and WC were independently associated with the occurrence of MetS, they were selected for the model of the ROC curve, separately (Fig.). The AUCs were 0.783 (CI, 0.765–0.802) for BMI and 0.820 (CI, 0.801–0.838) for WC. The AUC of the combined model (WC + BMI) was increased to 0.822 (CI, 0.804–0.840). The *P* value of the comparison of AUCs between BMI and WC was .014, and that between BMI and combined model was .009. No difference of AUCs between the WC and combined model was found ($P = .890$).

Table 3 – Adjusted standardized coefficients (β) in multiple linear regression analysis between MetS components and measurements of adiposity

	SBP	DBP	FPG	HDL-C	Log TG ^a
BMI	0.172	0.142	NS	−0.112	NS
WC	NS	NS	0.160	−0.253	0.191
WHtR	NS	NS	NS	NS	NS
BF%	NS	NS	0.117	NS	0.208

The coefficients listed were at $P < .05$ level unless NS was specified. All are adjusted for age, alcohol intake, smoking, and exercise. Abbreviation: NS, non-significance.

^a The TG value was logarithmically transformed before statistical analysis because it was not normally distributed.

Table 4 – Adjusted coefficients (β) in multivariate logistic regression analysis of 4 different adiposity measurements for the association with abnormal MetS components and MetS

	SBP	DBP	FPG	HDL-C	TG	MetS
BMI	0.103	0.102	NS	0.080	NS	0.079
WC	NS	NS	0.036	0.055	0.053	0.152
WHtR	NS	NS	NS	NS	NS	NS
BF%	NS	NS	0.048	NS	0.057	NS

The coefficients listed were at $P < .05$ level unless NS was specified. All are adjusted for age, alcohol intake, smoking, and exercise. Having abnormal MetS components is defined as subjects with SBP ≥ 130 mm Hg, DBP ≥ 85 mm Hg, FPG ≥ 100 mg/dL, HDL-C < 40 mg/dL, and TG ≥ 150 mg/dL.

Abbreviation: NS, non-significance.

4. Discussion

Obesity in both developed and developing countries is a major public health problem. The morbidity and mortality caused by obesity not only lead to many medical complications, such as CVD and T2DM, but also account for extensive social and financial burdens [18]. Therefore, the accurate estimation of obesity and prediction of its related morbidities are important issues to address.

The 4 different adiposity measurements are generally considered to be interchangeable. However, there is evidence that these measurements have substantially different physiological meanings [19,20]. For example, on one hand, BMI is the most commonly used anthropometric measure for the assessment of total body adiposity, but the numerator in the BMI calculation does not distinguish between lean and fat mass. On the other hand, WC is the estimation of visceral fat or central obesity. Nevertheless, it does not account for height, which may affect WC because taller individuals tend to have larger WCs. Taking these into consideration, WHtR might be a better index of central obesity. Finally, although BF% measures the percentage of fat in the body, this measure does not distinguish between subcutaneous and visceral fat. In the present study, we sought to re-evaluate the complicated relationships between these measurements and MetS, and see if our results may clarify which measure is more relevant for MetS.

These 4 measurements have previously been assessed and compared in many clinical studies [19,20]; however, most of these studies did not exclude subjects who were on medications for hypertension, hyperglycemia, or dyslipidemia. Thus, the relationships reported by these studies were potentially influenced by medications. In the current study, subjects on medications for any of the MetS components were excluded. Furthermore, although the general population is gradually aging, few studies have focused on the elderly. We identified the measures that were most strongly correlated with each MetS component and MetS itself in older men, and the best diagnostic model for discriminating MetS was determined using ROC curves. We believe that the results of this study can be used extensively in practice and are not only novel but also important. Notably, the BMIs of

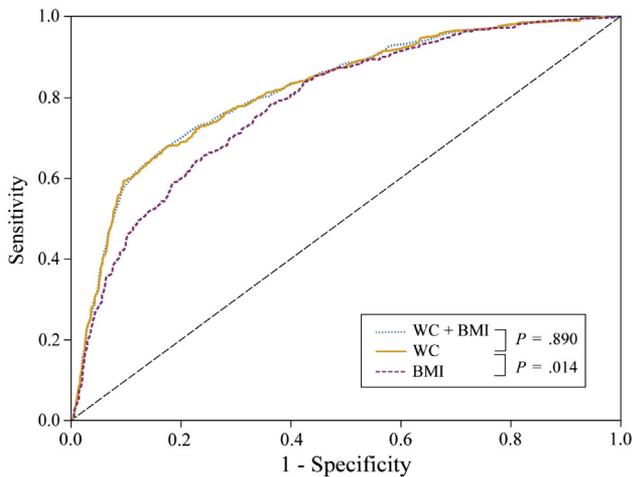


Fig. – Estimation and comparison of ROC curves of the adiposity measurements for discriminating the occurrence of MetS. The AUC and 95% CI were 0.783 (0.765–0.802) for BMI, 0.820 (0.801–0.838) for WC, and 0.822 (0.804–0.840) for WC + BMI. The P value of comparison between BMI and WC was .014; BMI and WC + BMI, .009; and WC and WC + BMI, .890.

the participants enrolled in the present study were in a reference range because we excluded subjects with severe diseases, thus eliminating extreme data. Because the extreme values were removed, the ranges of data were narrow and may account for the weak relationships between pairs of the 8 variables in the Pearson correlation.

Our study shows that elevated BP is independently correlated with BMI in older men, thus in accordance with the widely reported association between BP and BMI. For example, Tuan et al. [21] examined 7336 Chinese adults (18–65 years old) who participated in the 2004 China Health and Nutrition Survey and revealed that the waist indices, including WC and WHtR, do not perform better than BMI in predicting hypertension risk. However, Yalcin et al. [22] conducted a cross-sectional descriptive study of 1727 Turks (18–65 years old) and found that WC was an independent risk factor for elevated BP in men and that BMI had a greater association with elevated BP than WC in women. The possible underlying link between adiposity and BP might be attributable to overweight-associated sympathetic activation, which contributes to the increased incidences of cardiovascular complications [23].

Interestingly, in older men, FPG was independently correlated with both WC and BF%. Similar results were reported in a study performed by Wildman et al. [24], which was a national cross-sectional study of 15540 Chinese adults aged 35 to 74 years. These authors demonstrated that the likelihood of T2DM increased with successive WC tertiles. In contrast, BMI tertiles were not associated with the likelihood of T2DM. Although these interesting findings are not identical to ours, they further support our hypothesis that these measurements have different clinical implications. Compared with this study, the results of the research carried out by Li et al. [25] are more convincing. A total of 3916 Chinese adults (30–70 years old) without MetS or T2DM were enrolled at baseline and

followed up for a maximum of 5.5 years. The results showed that subjects with high BF% had a greater risk of the incidence of MetS or T2DM than those with low BF%. Given the abundant number of studies examining this topic, there is no proper explanation for this discrepancy between FPG and different adiposity measurements. However, we can postulate that glucose metabolism is more strongly related to visceral fat, which can be more precisely estimated by the WC and/or adiposity. Moreover, this “central obesity” is proven to be the core of insulin resistance and related to many endocrine, inflammatory, neural, and cell-intrinsic pathways [26]. These effects of obesity eventually lead to CVD and/or T2DM.

Our study showed that HDL-C was independently correlated with BMI and WC and TG was independently correlated with WC and BF%. Other studies report similar findings. For example, in 2007, Menke et al. [27] examined a nationally representative sample of 12608 American adult participants in the third National Health and Nutrition Examination Survey. Waist circumference, total body fat, BF%, BMI, and skinfold thickness were compared. The results revealed that WC maintains a stronger association with CVD risk factors, including low HDL-C and high TG, than other measures of adiposity [27]. In 2008, a meta-analysis performed by Lee et al. [20] concluded that, for the detection of dyslipidemia in both men and women, statistical evidence supports the superiority of measures of centralized obesity, especially WHtR, over BMI. This association between dyslipidemia and abdominal obesity may be mediated through an etiopathological mechanism [28]. Intra-abdominal fat has a particularly active metabolism and is instrumental in increasing the flux of free fatty acids carried to the liver from enlarged deposits of mesenteric and omental fat [29]. High levels of free fatty acids interact with the secretion of the lipoproteins [30], modify TG and HDL-C blood levels [31], and influence plasma insulin-glucose metabolism, BP, and fibrinolysis [28,32].

One of the purposes of our study was to build a model that could further improve the diagnosis accuracy of adiposity measurements. Both BMI and WC were independently related to MetS in multivariate logistic regression, and thus, were selected and placed into the model. To our knowledge, there are only a few studies using similar methods, but most of these studies show inconsistent results [33,34]. These findings indicate that, although these measurements are not identical, they share some overlapping physiological meanings. Although both BMI and WC were independently correlated with the occurrence of MetS and, when combined, these 2 measurements increased the AUC of ROC, this difference did not reach statistical significance. This lack of a significant difference may be because BMI is highly correlated with WC, and thus, the combination of these measurements did not increase the discriminative power of the model. Our data suggest that WC is a better measurement for discerning MetS than other measurements in older men.

There are several limitations that should be addressed concerning our study. First, this was a cross-sectional study and provides less consolidated evidence than studies with longitudinal or randomized epidemiologic designs. However, we did not attempt to investigate the incidence of these measurements; rather, we sought to investigate the relationships between these measurements. Thus, this limitation

should be considered minor. Second, because this study was conducted in a single ethnic group, generalizing or extrapolating these results to other ethnic groups should be performed with caution. Further well-designed longitudinal studies of different ethnic groups are needed to support our findings. Despite these 2 limitations, our study cohort was large, and we believe that the results are informative. Initially, we included both sexes in this study; thus, we also have data on women. However, because some of the results from females differed greatly from those of males, we chose to not include both sexes for the sake of simplicity.

In conclusion, we accept our hypothesis that 4 adiposity measurements, BMI, WC, WHtR, and BF%, have different physiological meanings and distinct associations with adverse health consequences. Our study shows that, in older men, BMI is an important determinant for BP and HDL-C, but WC is the associated factor with FPG, HDL-C, TG, and the occurrence of MetS. The model that combined WC and BMI did not further increase the diagnosis accuracy. Although the 4 measurements that we examined are seemingly interchangeable, they have diverse physiological meanings and different relationships with each of the MetS components.

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