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ORIGINAL RESEARCH

Coexistence of Pre-sarcopenia and Metabolic Syndrome in Arab Men

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Abstract

Objective The present single-center observational study determined the prevalence and coexistence of sarcopenia, pre-sarcopenia, and metabolic syndrome (MetS) among apparently healthy Arab men and whether having both conditions present a unique cardiometabolic profile that is distinct than having the conditions separately.

Methods A total of 471 out of 530 Arab men aged 20–77 years old were included after screening for the presence of pre-sarcopenia (ALM/ht^2 < 7.26 kg/m^2), sarcopenia (presence of both low muscle mass and low function), and MetS. MetS screening was done using the definition by the NCEP-ATP III. Based on the screening results, the participants were classified as control (normal) group (N = 328), MetS only (N = 73), pre-sarcopenia only (N = 64), and MetS + pre-sarcopenia (N = 6).

Results Pre-sarcopenia without MetS was observed in 64 participants (13.6%), while MetS without pre-sarcopenia was observed in 73 participants (15.5%). MetS + pre-sarcopenia was observed only in 6 participants (1.3%). None of the participants had sarcopenia. Age- and BMI-adjusted comparisons showed that those with MetS + pre-sarcopenia had the highest diastolic blood pressure and triglyceride levels as compared to all groups (p values < 0.001). MetS + pre-sarcopenia group also had the highest levels of glucose and the lowest lean arms–legs/BMI ratio than control and pre-sarcopenia groups (p values < 0.001 and 0.005, respectively).

Conclusion The prevalence of pre-sarcopenia + MetS is low among young adult Arab men, but shows a unique cardiometabolic profile that is worse than those having only one of the conditions. Further investigations should be done among Arab women and the elderly.

Keywords Body composition · Bone mineral density · Metabolic syndrome · Sarcopenia

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Introduction

Sarcopenia, a recently known geriatric syndrome, is characterized as a progressive and general loss of skeletal muscle mass and strength with risk of adverse outcomes [1]. While the mentioned working definition for sarcopenia is internationally accepted, its assessment remains slightly debatable since the reference standard for measuring muscle mass is still not considered the gold standard [2, 3]. Nevertheless, a recent meta-analysis by Shafiee and colleagues estimated that the global prevalence of sarcopenia was 10% in both men and women [4]. Age-related loss of muscle mass, coupled with other inflammatory and hormonal imbalances leading to sarcopenia, causes a decrease in muscle mobility, strength, low fatigue resistance, and increased risk for fractures [5]. Accumulating evidence also suggests that sarcopenia leads to a decline in quality of life [6], abdominal aortic calcification [7], falls [8], osteoporosis [9], and increased risk for various chronic disorders such as atherosclerosis, hypercholesterolemia, hyperglycemia, hypertension, insulin resistance [10], and worse outcomes in combination with obesity [11].

Metabolic syndrome (MetS), on the other hand, is a cluster of cardiometabolic factors (i.e., obesity, dyslipidemia, hypertension and elevated blood glucose) that has recently been associated with sarcopenia, most notably among the middle-aged and non-obese elderly with MetS [10]. According to recent evidence, sarcopenia is strongly linked to glycemic impairment and insulin resistance due to low muscle mass [12].

In the Middle-Eastern region in general and the kingdom of Saudi Arabia (KSA) in particular, sarcopenia is a relatively understudied disorder. From the limited evidence available, it was found that sarcopenic obesity was associated with low fitness scores in Saudi men and more so in Saudi women [13]. Furthermore, a recent observational study done among young Saudi men indicated that pre-sarcopenia, or the skeletal muscle mass index (SMI) cut-off, an indicator of muscle mass and a criterion for sarcopenia diagnosis, was much lower (6.51 kg/m^2) [14] than the internationally accepted cut-off (7.26 kg/m^2) as proposed by the European Working Group on Sarcopenia in Older People (EWGSOP) [1]. MetS, on the other hand, is well documented in the Middle East and KSA, with an overall prevalence of 35% as of 2010 and almost 40% in 2018 [15, 16]. To the best of our knowledge, the coexistence of these pathologic entities (MetS, pre-sarcopenia and sarcopenia) has never been studied in the region and in the Arab ethnicity.

Given these information, the main objectives of the present cross-sectional study were to determine the prevalence of the coexistence of pre-sarcopenia, sarcopenia, and MetS in Arab men and whether having concomitant conditions present a different cardiometabolic profile as compared to having each disorder alone.

Subjects and Methods

Participant Characteristics

This cross-sectional study was done at the Department of Exercise Physiology, College of Sport Sciences and Physical Activity, in King Saud University (KSU), Riyadh, kingdom of Saudi Arabia (KSA). Participants were recruited via social media and through announcements the bulletin board posted at King Khalid University Hospital (KKUH) of KSU. Details of full recruitment have been mentioned previously [14]. A total of 530 participants initially showed interest based on their responses in the announcement. After screening, 59 were excluded for missing biochemical and body composition values necessary for diagnosis, leaving the final sample size to 471 apparently healthy Arab men aged between 20 and 77 years old. None of the subjects were on medications during the study and none declared any existing chronic diseases (i.e., diabetes mellitus, heart disease, musculoskeletal, neurologic, hepatic, and renal diseases).

Anthropometry and Measures of Whole-body Composition

All anthropometric and body composition indices were measured at the Laboratory of Body Composition at the College of Sports Science and Physical Activity in KSU.

Height (cm) and body weight (kg) were measured. Body mass index (BMI) was calculated by dividing weight (kilograms) by height in squared meters. Waist circumference was measured at the level of the umbilicus using a standard tape measure. Systolic and diastolic blood pressures (mmHg) were measured twice at 15-min interval using a mercurial sphygmomanometer and the average was noted.

Lean soft tissue mass and BMD were determined for the whole body by DXA (Lunar iDXA, GE Healthcare, USA). Total and percent lean mass and TLM/ht^2 were calculated. Appendicular lean mass (ALM) is the sum of arm and leg lean mass, and ALM/ht^2 was also calculated. Pre-sarcopenia was defined as having an ALM/ht^2 < 7.26 kg/m^2 [1]. Handheld dynamometer was used to measure handgrip strength. The mean of two measures was recorded in kg. Weak handgrip strength was defined as < 30 kg [1]. Sarcopenia was defined as having the presence of both low muscle mass and low muscle function according to the criteria set by EWGSOP [1].

Biochemical Analyses

About 10 cc of fasting venous blood samples were collected from each participant and processed for separation of serum samples on the same day the body composition analysis was done. The remaining blood and serum samples were transported to the Biomarkers Research Program (BRP) in King Saud University, Riyadh, KSA in specialized containers for biochemical analyses and storage at − 80 °C. Fasting lipid profile including triglycerides, cholesterol, and level of fasting blood glucose in all recruited individuals were determined by chemical analyzer (Konelab20XTi, Thermo Electron Corporation, Vantaa, Finland).

The definition of MetS used to screen the participants was the one proposed by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) and modified by the American Heart Association (AHA) and the National Heart, Lung and Blood Institute (NHLBI) [17]. Diagnosis of MetS for males was established if the participant has 3 out of 5 features: waist circumference > 102 cm, blood pressure > 130/85 mmHg, fasting triglycerides > 1.7 mmol/l, and/or HDL-cholesterol < 1.03 mmol/l and fasting glucose ≥ 5.6 mmol/l.

Statistical Analysis

Data were analyzed using SPSS (version 21, IBM). Continuous data were presented as mean ± standard deviation (SD) for variables following Gaussian variables and non-Gaussian variables were presented in median (1st and 3rd) percentiles. All categorical variables were presented in percentages (%). All continuous variables were checked for normality using Kolmogorov–Smirnov test, if not normal, then non-Gaussian variable transform to log transform. Analysis of Variance (ANOVA) and Kruskal–Wallis tests were performed to determine differences for Gaussian variables and non-Gaussian variables. Bonferroni corrections were done and p values modified. Univariate Linear Model (GULM) was performed for adjustments. A modified p value < 0.05 was considered statistically significant.

Results

A total of 471 Arab men 418 Saudis (88.7%) and 53 (11.3%) non-Saudi Arabs [Yemeni, Syrian, Moroccan, Egyptian, Lebanese and Sudanese] participated in this cross-sectional study. Pre-sarcopenia was observed in 64 participants (13.6%), while MetS alone was observed in 73 participants (15.5%). MetS + pre-sarcopenia was observed only in 6 participants (1.3%). Overall, a total of 90 participants had elevated triglycerides, 14 (15.6%) of whom had pre-sarcopenia; 173 had low HDL-cholesterol, 27 (15.6%) of whom had pre-sarcopenia; 137 (29.1%) had elevated glucose, 20 (14.6%) of whom had pre-sarcopenia; and 112 (23.8%) had elevated blood pressure, 15 (13.4%) of whom had pre-sarcopenia.

Table 1 shows the clinical characteristics and comparisons of subjects according to the presence/absence of pre-sarcopenia and presence/absence of MetS. Overall, 70 participants had pre-sarcopenia (14.9%) and 79 participants had MetS (16.8%). Age- and BMI-adjusted comparisons revealed that participants with pre-sarcopenia had significantly higher triglyceride levels than those without pre-sarcopenia ($p < 0.01$). Furthermore and as expected, majority of the body composition indices were significantly lower among participants with pre-sarcopenia than those without. On the other hand and also as expected, age and BMI comparisons revealed that majority of the cardiovascular indices were significantly higher in the MetS group than those without MetS (p values < 0.01), except HDL-cholesterol which was significantly lower in the MetS group ($p < 0.01$). Among the body composition indices, the MetS group had significantly higher percentages of body fat in different areas (legs, trunk, android, fat trunk/total, fat legs/total, and fat arms–leg/trunk) as well as visceral volume and visceral mass (p values < 0.01). The rest of the comparisons are seen in Table 1.

In Table 2, we compared the characteristics of control (normal) participants ($N = 328$) among those with MetS only ($N = 73$), pre-sarcopenia only ($N = 64$), and with both MetS and pre-sarcopenia ($N = 6$), adjusted for age and BMI. Those with MetS and pre-sarcopenia had the highest diastolic blood pressure and triglyceride levels as compared to all groups (p values < 0.001). They also had the highest levels of glucose and the lowest lean arms–legs/BMI ratio but were significant only between normal and pre-sarcopenia groups (p values < 0.001 and 0.005, respectively). The pre-sarcopenia group had the lowest percentages of lean composition in all groups except for lean arms–legs/BMI where the pre-sarcopenia group was significantly the highest (p values < 0.001). They also had the lowest mean waist circumference in all groups. The MetS group were the oldest, had the highest mean BMI, waist circumference and lean arms–legs/height^2 ratio. The rest of the comparisons are found in Table 2.

Table 3 shows the age- and BMI-adjusted comparisons between body composition indices including handgrip strength according to the presence and co-presence of MetS and pre-sarcopenia. Those with MetS and pre-sarcopenia had the weakest handgrip strength as compared to other groups ($p < 0.001$). As expected, the pre-sarcopenia group had the lowest BMD and indices of fat % (arms, legs, trunk, android, and FMI) as compared to other groups (p values < 0.001). The rest of the comparisons are shown in Table 3.

Table 1 Clinical characteristics of subjects

Parameters	Pre-sarcopenia		MetS	
	Normal ($N=401$)	Pre-Sarc ($N=70$)	Normal ($N=392$)	MetS ($N=79$)
Age (year)[#]	32.2 ± 10.5	33.1 ± 12.8	31.0 ± 10.1	39.1 ± 13.2
BMI (kg/m^2)[#]	29.1 ± 5.1	22.6 ± 2.9	27.2 ± 4.9	32.7 ± 4.4
Waist (cm)	94.7 ± 13.5	80.5 ± 11.2	89.4 ± 12.4	108.2 ± 11.9**
Systolic BP (mmHg)	117.5 ± 12.9	114.6 ± 12.8	115.8 ± 12.1	125.3 ± 14.2**
Diastolic BP (mmHg)	75.3 ± 10.0	75.3 ± 10.5	73.6 ± 9.4	84.1 ± 10.6**
Glucose (mmol/l)	5.1 (4.7–5.7)	5.2 (4.8–5.7)	5.1 (4.6–5.5)	5.8 (5.1–6.7)**
Triglycerides (mmol/l)	1.1 (0.8–1.5)	1.2 (0.8–1.5)**	1.0 (0.8–1.4)	1.8 (1.3–2.3) **
HDL-cholesterol (mmol/l)	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	0.95 ± 0.2**
Lean/height^2	18.6 ± 1.9	15.4 ± 0.9**	17.9 ± 2.1	19.2 ± 1.8
Lean arms–legs	27.1 ± 3.9	20.4 ± 2.7**	25.8 ± 4.4	27.9 ± 4.4
Lean Arms–Legs/BMI	0.95 ± 0.1	0.91 ± 0.1*	0.96 ± 0.1	0.86 ± 0.1
Lean arms–legs/height^2	9.2 ± 1.0	6.9 ± 0.9**	8.7 ± 1.3	9.4 ± 1.1
Handgrip strength (kg)	43.5 ± 7.5	37.7 ± 7.1**	42.7 ± 7.7	42.2 ± 7.3
Thigh strength (kg)	76.6 ± 23.5	63.5 ± 24.3**	75.4 ± 23.9	70.9 ± 24.6
BMD (g/cm^2)	1.3 ± 0.2	1.1 ± 0.1**	1.2 ± 0.1	1.3 ± 0.1
% fat region	32.0 ± 7.9	28.1 ± 7.4**	30.1 ± 7.9	38.0 ± 4.7
Lean (g)	55.1 ± 7.5	44.6 ± 4.2**	52.8 ± 8.0	56.9 ± 7.2
Fat arms	2.9 ± 1.1	1.9 ± 0.6*	2.6 ± 1.0	3.6 ± 1.0
Fat legs	9.7 ± 3.8	6.4 ± 2.0**	8.7 ± 3.7	11.2 ± 3.5**
Fat trunk	14.9 ± 6.9	9.7 ± 4.9**	12.7 ± 6.2	21.6 ± 5.7**
Fat android	2.6 ± 1.4	1.6 ± 1.1**	2.2 ± 1.3	3.9 ± 1.2**
Fat gynoid	4.5 ± 1.9	3.0 ± 1.1*	4.1 ± 1.8	5.6 ± 1.6
Lean arms	6.7 ± 1.1	5.2 ± 0.7**	6.5 ± 1.2	6.8 ± 1.0
Lean legs	20.4 ± 3.1	15.1 ± 2.7**	19.3 ± 3.6	21.1 ± 3.6
Fat/height (FMI)	10.9 ± 2.9	9.8 ± 2.7**	10.3 ± 2.8	12.9 ± 1.8
Fat trunk/total	0.51 ± 0.1	0.49 ± 0.1**	0.5 ± 0.1	0.6 ± 0.1**
Fat legs/total	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.3 ± 0.1**
Fat arms–leg/trunk	0.9 ± 0.2	1.0 ± 0.3	0.95 ± 0.2	0.70 ± 0.1**
Visceral volume (cm^3)	989 (486–1563)	518 (246–990)**	726 (377–1257)	1859 (1393–2454)**
Visceral mass (g)	934 (466–1471)	469 (229–892)**	685 (349–1175)	1759 (1346–2315)**

Data presented as Mean ± SD and Median (1st–3rd) percentiles for Gaussian and non-Gaussian variables

*,**Represented p value significant at 0.05 and 0.01 level

Lastly, Fig. 1 shows the significant positive correlation between ALM/height^2 and BMD ($R=0.54$, $p<0.001$).

Discussion

The present study is the first in the Middle East to determine the prevalence of sarcopenia, pre-sarcopenia, and MetS in a cohort of apparently healthy Arab men in Riyadh, KSA. None of the participants had sarcopenia, 15% had pre-sarcopenia, and less than 2.0% had both pre-sarcopenia and MetS. The present findings also showed that elevated glucose and dyslipidemia were the more common MetS risk factors among Arab men with pre-sarcopenia. The low rate of pre-sarcopenia and MetS in the cohort does not supersede previous findings on the link between sarcopenia, a disease related to aging, with metabolic disturbances, as the population studied was relatively young.

The most recent prevalence of the Saudi elderly (defined as a Saudi citizen ≥ 60 years old) population was estimated at 5.2% as of 2015 [18]. Given the small prevalence of senior citizens in KSA, it makes sense that sarcopenia, a disease arguably considered as limited to the elderly, cannot be considered as an immediate public health threat to the general community at the present times. Nevertheless, as the elderly population continues to grow globally, and with an alarming prevalence of other age-related metabolic diseases in the Arab population, it is worthy to investigate whether certain cardiometabolic abnormalities are potential risk factors for sarcopenia in this particular ethnic group.

The prevalence of sarcopenia in the present study is not in agreement with other epidemiologic observations,

Table 2 Comparisons between participants according to the presence of MetS and/or pre-sarcopenia

Parameters	Normal	MetS	Pre-Sarc	MetS & Pre-Sarc
N (%)	328	73	64	6
Age (year)[#]	30.9 ± 9.5	37.9 ± 1.4	31.4 ± 1.5	56.6 ± 5.3
BMI (kg/m^2)[#]	28.1 ± 4.8	33.1 ± 0.4	22.1 ± 0.5	27.7 ± 1.5
Waist (cm)	91.6 ± 11.9	108.5 ± 1.2[a]	78.2 ± 1.3[a,b]	104.8 ± 4.3[a,c]
Systolic Blood Pressure (mmHg)	115.9 ± 11.7	124.6 ± 1.5[a]	113.3 ± 1.5[b]	134.5 ± 6.2
Diastolic blood pressure (mmHg)	73.6 ± 9.0	83.3 ± 1.1[a]	73.6 ± 1.2[b]	93.3 ± 3.9[a,b,c]
Glucose (mmol/l)	5.1 ± 0.8	6.0 ± 0.1[a]	5.2 ± 0.1[b]	7.3 ± 0.4[a,c]
HDL-cholesterol (mmol/l)	1.2 ± 0.3	0.95 ± 0.03[a]	1.2 ± 0.04[b]	0.94 ± 0.11
Triglycerides (mmol/l)	1.02 (0.7–1.4)	1.3 (1.0–2.3)[a]	1.2 (0.8–1.5)[a,b]	2.2 (1.9–2.5)[a,b,c]
Lean/height^2 (FFMI)	18.4 ± 1.9	19.5 ± 0.2	15.3 ± 0.2[a,b]	16.2 ± 0.7[a,b]
Lean arms–legs	26.9 ± 3.8	28.5 ± 0.4	20.2 ± 0.5[a,b]	22.2 ± 1.5[a]
Lean arms–legs/BMI	0.97 ± 0.14	0.87 ± 0.01	0.92 ± 0.02[a,b]	0.80 ± 0.05[a,c]
Lean arms–legs/height^2	9.1 ± 0.9	9.6 ± 0.1	6.9 ± 0.1[a,b]	7.4 ± 0.4[a,b]

Data presented as Mean ± SE for Gaussian variables, while Median (1st Quartile–3rd Quartile) are presented for non-Gaussian variable. Superscripts used for post hoc Bonferroni test "a," "b," and "c" indicate significant difference from Normal, MetS, and pre-sarcopenia, respectively

Table 3 Comparisons between participants' body composition according to the presence of MetS and/or pre-sarcopenia

Parameters	Normal	MetS	Pre-Sarc	MetS & Pre-Sarc
N	328	73	64	6
Handgrip strength (kg)	43.6 ± 7.5	42.7 ± 0.8	38.8 ± 0.9[a,b]	35.7 ± 3.0[a,b]
Thigh strength (kg)	77.6 ± 23.5	71.1 ± 2.8	63.2 ± 3.0[a,b]	68.7 ± 9.7
BMD (g/cm^2)	1.24 ± 0.11	1.3 ± 0.01	1.1 ± 0.01[a,b]	1.1 ± 0.05[b]
Fat arms	2.7 ± 1.1	3.7 ± 0.1	1.8 ± 0.1[a,b]	2.9 ± 0.4[c]
Fat legs	9.3 ± 3.8	11.4 ± 0.4[a]	6.2 ± 0.4[a,b]	8.5 ± 1.4[c]
Fat trunk	13.5 ± 6.3	21.7 ± 0.6[a]	8.8 ± 0.7[a,b]	20.0 ± 2.4[a,c]
Fat android	2.3 ± 1.3	3.9 ± 0.2[a]	1.5 ± 0.1[a,b]	3.5 ± 0.5[a,c]
Fat gynoid	4.3 ± 1.9	5.7 ± 0.2	2.9 ± 0.2[a,b]	4.3 ± 0.7[c]
Lean arms	6.7 ± 1.1	6.9 ± 0.1	5.2 ± 0.1[a,b]	5.7 ± 0.4[a,b]
Lean legs	20.2 ± 2.9	21.5 ± 0.4	14.9 ± 0.4[a,b]	16.5 ± 1.2[b]
Fat/height^2 (FMI)	10.4 ± 2.8	12.9 ± 0.3	9.5 ± 0.3[a,b]	12.9 ± 1.1[c]
Fat trunk/total	0.50 ± 0.06	0.57 ± 0.01[a]	0.48 ± 0.01	0.62 ± 0.02[a]
Fat legs/total	0.36 ± 0.05	0.30 ± 0.01[a]	0.36 ± 0.01[b]	0.26 ± 0.02[a,c]
Fat arms–leg/trunk	0.94 ± 0.2	0.71 ± 0.03[a]	1.01 ± 0.03	0.6 ± 0.1[a,c]
Visceral volume (cm^3)	776 (411–1333)	1845 (1369–2423)	448 (210–877)	2076 (1636–2735)

Data presented as Mean ± SE for Gaussian variables, while Median (1st Quartile – 3rd Quartile) are presented for non-Gaussian variable. Superscripts used for post hoc Bonferroni test "a," "b," and "c" indicate significant difference from Normal, MetS, and pre-sarcopenia, respectively

primarily because of the younger population studied and perhaps the sarcopenia definition applied may be incompatible in the Arab population [19]. Interestingly however, the pre-sarcopenia prevalence noted (13.6%) modestly matches the prevalence observed among similarly aged adult Brazilians submitted for hematopoietic stem cell transplantation (14.4%) [20]. As previously pointed out, the current definition for sarcopenia as established by reputed international organizations may not be applicable in the Arab population [14], but the cut-off obtained from local studies may also be too premature for use in the general public until larger studies have been conducted. Furthermore, with the exception of circulating triglycerides, the cardiometabolic indices among pre-sarcopenic participants were not different compared to non-sarcopenic participants. This was in accordance to a similar study done in Japan [21]. Obesity was also not a risk factor to pre-sarcopenia in this population, in contrast to adult Koreans who found that sarcopenic obesity predisposed to MetS by as much as three times as compared to non-sarcopenic subjects [22].

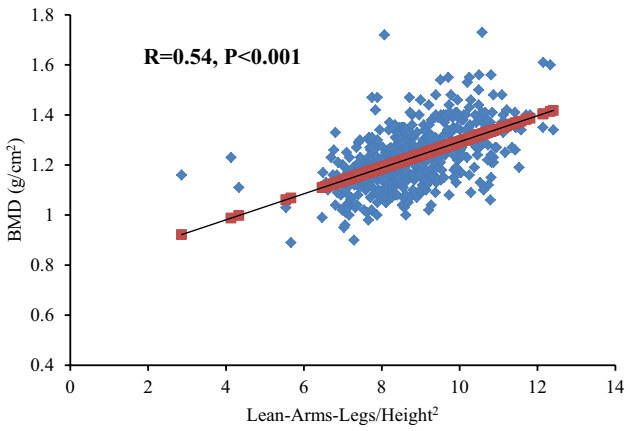

Fig. 1 Association between BMD (g/cm^2) and (Lean arms–legs)/Height^2 in all subjects

Earlier studies with the respect to the association between MetS and fitness proposed that having a lower physical fitness level is an effective determinant in MetS [23–27]. It is still not understood how the interaction between MetS and low muscle mass promotes reductions in age-linked muscle power loss. The present results nevertheless showed that the significant differences in select body composition parameters between MetS and non-MetS participants may mean that MetS in Arab men also has an influence, albeit modest, in overall fitness.

Lastly, the significant association between BMD and select lean muscle mass index elicited in the present cohort confirms that lean mass exerts a greater effect than fat mass in terms of bone loss, at least in Arab men [28].

The authors acknowledge several limitations. The number of participants with both MetS and pre-sarcopenia is extremely small and does not allow to draw significant conclusions. Furthermore, the significantly higher diastolic blood pressure and levels of triglycerides among participants with both MetS and pre-sarcopenia compared to those with only MetS and pre-sarcopenia need to be interpreted with caution since the big discrepancy in group sizes is subject to type 2 error. Gait speed, a parameter included in the algorithm proposed by the European Union of Geriatric Medicine Society (EUGMS), was also not assessed and could have influenced the present results. Lastly, the cross-sectional design limits the findings to, at best, suggestive. The present findings nevertheless have some merits, given the high number of participants that were assessed and the novelty of findings with respect to the Arab ethnicity, particularly in men.

In conclusion, the prevalence of pre-sarcopenia is relatively low among young adult Arab males, with only a few cases having both Mets + pre-sarcopenia. Among those with pre-sarcopenia, the most common cardiometabolic (MetS) features include dyslipidemia, elevated blood glucose, and blood pressure. Those with MetS + pre-sarcopenia showed a clinically worse cardiometabolic profile as compared to those having only of the conditions. A similar study should be extended among Arab women. Further studies involving the strictly elderly population might provide more insights.

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Authors' Contributions SMY, SAA, DA, KSA, MNKK, MSA, JYR, NMA. SMY, SAA, and NMA conceptualized the study. SAA secured the funding and ethical approval. SMY and SS drafted the manuscript. DA, KSA, MSA, and NMA contributed in the data collection, interpretation, and writing of the manuscript. SS and JYR performed the critical review and revision of the manuscript. MNKK performed data analysis and contributed in the drafting of the manuscript. All authors have read and approved the final version of the manuscript.

Availability of Data and Materials Data are available from the corresponding author on reasonable request.

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Compliance with Ethical Standards

Conflict of interest Sobhy M. Yakout, Shaea A. Alkahtani, Dara Al-Disi, Khalid S. Aljaloud, Malak Nawaz Khan Khattak, Majed S. Alokail, Jean-Yves Reginster, Shaun Sabico, Nasser M. Al-Daghri declare that they have no conflict of interest.

Ethics Approval Ethical approval was obtained from the ethics committee of KSU, Riyadh, KSA (IRB No. E-16-1785). All participants who expressed their interest in the study signed a consent prior to inclusion.

Human and Animal Rights and Informed Consent The study was approved by the KSU Institutional Review Board (IRB No. E-16-1785). Written consent was obtained from all patients who were included in the study.

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