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Sarcopenic Obesity-A Minireview-Does it Lead to a Greater Incident of Type 2 Diabetes, Metabolic Syndrome or Mortality than When Sarcopenia or Obesity Exist Separately

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Abstract

Sarcopenia is an age related process that is characterized by a progressive loss of skeletal muscLe and strength. This condition is of major health concern in older adults since it has been associated with metabolic impairments, cardiovascular disease(CVD) risk factor along with physical and functional disability and increases the risk of early mortality. Sarcopenia often coexists with obesity leading to a specific condition called ''sarcopenic obesity''(SO). Current evidences implicate that SO maybe associated with a large number of metabolic disorders and an increased risk of mortality than obesity or sarcopenia alone. However few studies have been conducted in this field and with contradictory results. Cross sectional studies in SO subjects have documented greater prevalence of cardiovascular risk factors and metabolic syndrome in these subjects. A strong association of inflammatory markers compared with sarcopenia only subjects have been found. While some longitudinal studies have shown that SO Does not apparently confer any greater mortality risk than sarcopenia alone. Thus we conducted a systematic review to analyze the coexistence of the 2 and relative increased incidence of Type2 diabetes mellitus (T2DM) in SO and its long term outcomes in studies that had used biomedical impedance, dual XRay absorptiometry with BMI, WC etc along with free fat mass, free fat muscle mass etc.

Keywords: *SO,T2DM,; Sarcopenia; Mortality, BIA, BMI, DXA*

Introduction

A situation where there is obesity coexisting with sarcopenia has been called sarcopenic obesity SO)([1-7] There still are problems regarding accepting this phenomenon as far as the definition is concerned and its negative effects on health potentially, mainly those diseases related to obesity, i.e. the cardio-metabolic disease [8,9], like type 2 diabetes mellitus (T2DM), Cardiovascular diseases (CVS), Dyslipidemia, and metabolic syndrome [5,6,1011]. It has been speculated that the 2 components of SO might synergistically increase the negative effects on health, but this is still debatable[14-16].

Various studies have been conducted with a specific focus on finding the association between SO and T2DM, yet data regarding a particular focus that subjects with SO have greater chances of developing hyperglycemia, high Hb A1c, Insulin resistance(IR) etc remain still contradictory and need to be clarified further [11,12-23]. Thus we tried to give a systematic review to interpret the published data with the idea of finding the prevalence of sarcopenia in adults who were overweight and obesity and to find if SO had an association with greater risk of T2DM, according to the PICO process [24-26] as explained herein P-population: Subjects with overweight and obesity

groups, they were defined as body mass index(BMI), body fat percentage, waist circumference (WC), etc][27]. I-who tried to get treatment (weight loss or any other treatment if recruited from a clinical setting] otherwise untreated if individuals were recruited from the general population;C-Comparison: Comparison of subjects with sarcopenia and those without SO and with the healthy control group (if available);O-outcome i) Prevalence of SO, although it was defined in the studies-low muscle mass, low muscle strength, low physical performance, increased visceral adiposity, enhanced waist circumference etc and assessed by bioelectrical impedance (BIA), Dual energy X-ray absorptiometry ((DXA), handgrip, etc among the whole obesity groups ii)the prevalence of T2DM however it was defined in the studies (fasting plasma glucose and glycated haemoglobin A1c, oral glucose tolerance test etc in the SO and non –SO groups.

Methods

We carried out a pubmed review using the Mesh terms sarcopenia, obesity, sarcopenic obesity, type 2 diabetes mellituson the pattern of PRISMA reporting [28,29].

Results

We found a total of 1105 articles of which we selected 57 articles for this review, after ruling out animal studies and duplicate studies. No meta-analysis was carried out .

Synechalet al [30] in 2012 carried out a cross sectional examination where they assessed dynapenic obesity, which was defined as low leg muscle strength that was associated with abdominal obesity in a total of 1963 subjects with abdominal obesity. 566 of these had dynapenic obesity (no data as per gender available). The mean age and mean BMI in the dynapenic obesity and non dynapenic obesity groups were 65.4+_ 9.9 years and 29.9+_4.6kg/m^2 and 65.5+_9.6years and 30.8+_4.5kg/m^2 respectively. Moreover 130 of the 566 subjects with dynapenic obesity had T2DM as compared to 196 of the 1397 subjects without dynapenic obesity group[30].

Lu et al in 2013[18] finished a cross-sectional study, where they examined SO which was defined as the presence of obesity (BMI>25kg/m^2) and sarcopenia that was based on the skeletal muscle index that was estimated by BIA.180 subjects got recruited (n=60 males, n=120 females). 35/60 males had SO as compared to 80/120 females. Irrespective of the gender the Mean age and BMI in the SO group were 61.1+_9.9 years and 27.8+_2.6kg/m^2 and 69.9+_7.3years and 26.8+_1·6kg/m^2 in the non-SO groups. In a cross-sectional study, Poggoiogalle et al.[31] utilized DXA with SO defined as the presence of obesity (BMI>3kg/m^2) and sarcopenia (ASMM:height<6.54 and <4.82kg/m^2 for males and females respectively) or ASMM:weight<0.2827 and 0.2347 for males and females respectively) In this study 727 subjects with ob esity(141 males and 586 females)had SO. The mean ages of 45.6+_13.53 and 45.76+_13.58 years and BMI of 37.56+_5.99 and 37.80+_5.77kg/m^2 respectively for each gender.68/141 male patients had SO as compared to 350/586 female patients. Additionally 155/418 patients had prediabetes or T2DM in the SO group, in contrast to 70/309 patients in the non-SO group. Ma etal. [32] conducted in 2016 itself a cross-setional study regarding SO, which was taken as by BMI and sex specific 24-h urine creatinine secretion in 310 patients (166 females and 144 males) with obesity (BMI>30kg/m^2) 54/144 males and 52/166 females had SO. The mean BMI and age of the SO group were 34.1+_4.0kg/m^2 and 71.8+_7.6years, while they were 34.9+_4.4 kg/m^2 and 67.8+_6.8yrs in the non-SO group, respectively. Moreover 40/106 patients had T2DM in the SO group, as compared to 51/204 patients in non-SO –group[32].

Xiao J et al.[33]conducted a retrospective study on the prevalence of SO and how it correlated with patients presenting for weight loss regarding health outcomes if weightloss was done in a bariatric surgery setting. After determining the body composition using BIA, SO definition was done by a fat mass-fat free index (FMI:FFMI) ratio>than the 95% percentile of sex, BMI and ethnicity specific-population representative references. A sample of a total of 144 adults presenting with obesity (n=99 females, n=45 males) got enrolled. Mean age and BMI was 55.6+_11.5years and 46.6+_8.1kg/m^2. Of the enrolled 144 patients 73 had SO (though data/gender is not available). Mean age and BMI of subjects with obesity only were 56.6+_12.7yrs and 44+_7.6kg/m^2, as compared to54.6+_10.1 yrs and 49.1 +_8.3kg/m^2 in those with SO. Moreover 34/73 patients had T2DM in the SO group in contrast to 36/71 patients in the non-SO group[33].

Further Kang etal. [34]carried out a large cross sec-

tional study for assessing the relationship between SO and metabolic syndrome in postmenopausal women. Definition of SO was the co-presence of sarcopenia (ASM/weight<1 standard deviation before the mean of the reference group) and a BMI cutoff point for obesity that referred to the score 25kg/m^2on the grounds of Asia –Pacific obesity criteria. In this study n=1555 females had obesity, out of which 855 had SO, having a mean age of 62.91+_0.44yrs along with a BMI of 27.93+_0.11kg/m^2. While 700 had no SO, with a mean age of 61.05+_9.44 years along with a mean BMI of 26.80+_0, 07kg/m^2. Further 165/855 subjects had T2D in the SO group and 105/700 patients in the SO group had T2D[34].

Aubertin-Leheudre etal. in 2017[35] tried to study the relationship between dynapenic obesity along with metabolic risk factors in older adults (over 70years). dynapenic obesity was considered when low hand –grip strength was present. It was present in 19.9 females, and <=31.9in males)associated with a mean BMI of 34.9+_4.8kg/m^2. Total number of subjects were 670 with obesity(n=213males, n=457females), of these 256 had dynapenic obesity, with a mean age of 78.0+_4.6 yrs along with a mean BMI of 34.8+_4.8kg/m^2, as compared to 414 who did not have dynapenic obesity having a mean age of 76.3+_4.7yrs and a BMI of 35.6+_4.8kg/m^2. Moreover, 81/256 subjects in the dynapenic obesity group had T2DM, in contrast to 133/414 subjects in the non dynapenic obesity group had T2DM[35].

A large cross-sectional study was carried out by Park et al.[36] in two sites in 2018, that had 53, 818 adults who were overweight and had obesity in both sexes(n=38820 males and n=14998 females) of which 6513 had SO whose definition was two standard deviations of the mean of the skeletal muscle mass index for young adults which was tested by BIA and WC of >=90cm for men and >=85cm for women. The mean age and BMI of these subjects were 40.5+_9.2years and 26.9+_2.2kg/m^2 respectively as compared to the ones with SO, having a mean age of 40.0+_11.3 years and a mean BMI of30.7+_3.4kg/m^2. Further 391/6513 subjects had T2DM in the SO group in comparison to 2176/47505 subjects in the non SO group[36].

Kriedieh et al[37] carried out a cross-sectional study that was controlled in 2018, where body composition, measurements were done using BMI with the definition that besides appendicular lean mass (ALM) also involving BMI, and subjects were considered to be having SO if ALM:BMI was <0.512. A total of n=154females with overweight and obesity having a mean age of 33.26+_14.65 years and a mean BMI of 31.42+_4.94kg/m^2.31/154 female subjects had SO. Furthermore, 4/31 subjects had T2D, in comparison to 3/123 subjects in non-SO group[37].

Khazem etal.[38] conducted a cross-sectional study that was controlled in 2018 that involved 72 male adults having overweight and obesity, having a mean age of 32.79+_13.65years and a mean BMI of 33,.69+_5.84kg/m^2. They utilized 3 separate definitions as proposed by Batsis et al.[39], Levine and Cummins[22], and Oh etal.[40] on the basis of ALM:BMI(and ALM:weight) x100% for defining SO.They assessed body composition by BIA. On the basis of each formula, prevalence of SO differed based on the clinical perspective, 50/72 subjects had a decreased lean body mass with prevalence rate of 69.4%. Further more 3/50 patients had T2DM in the SO group in contrast to 1/22 patients in non-SO group[38] .

Scott et al.in 2018[41] performed a large sampled study with the aim of investigating the cross-sectional correlation between SO and components of the metabolic syndrome in community dwelling older men with SO, where definition used was the co-presence of sarcopenia as ALM/height<7.26 kg/m^2 in addition to hand grip strength <0 30%. 525 males having obesity were part of this study, of which 80 had SO, having a mean age of 80.3+_6.5years and mean BMI of 27.2+_2.3 kg/m2 and 445 did not have SO, having a mean age of 75.9+_4.7years and mean BMI of 30.7+_3.4kg/m^2. Moreover, 29/80 subjects in the SO group had T2DM in contrast to 177/445 subjects in the non–SO group[41].

Further Abete etal.[42] conducted a cross-sectional study based on the baseline data from the PREDIMED Plus Study. A total of 1535 subjects (48 %women) with overweight /obesity(body mass index:32.5+_3.3kg/m^2;age 65.2+_4.2 years old)and metaboli syndrome categorized as per sex specific tertiles(T)of the sarcopenic index(SI) as assessed by DAX scanning. Anthropometrical measurements, biochemical markers, dietary intake, and PA information were collected. Linear regression analysis were carried out to evaluate the association between variables. Subjects in the

1st SI tertiles were older, less physically active, showed higher frequency of abdominal obesity and diabetes and consumed higher saturated fat and less vitamin C than subjects from the other two tertiles (allp<0.05). Multiple adjusted linear regression models evidenced significant positive associations across tertiles of SI with adherence to the Mediterranean dietary score (ptrend<0.05), PA)Ptrend<0.0001) and this 30 s chair stand test (ptrend <0.0001) while significant negative associations were found with aninadequate Vitamin C consumption(ptrend <0.05), visceral fat and leukocyte count(all p trend<0.0001), and some white cell subtypes(neutrophils and monocytes), neutrophil to lymphocyte ratio and platelet count (all ptrend <0.05). When models were additionally adjusted by potential mediators (inflammatory markers, diabetes and WC), no relevant changes were observed, only dietary variables lost. Thus concluding Diet and PA are important regulatory mediators of systemic inflammation, that is directly involved in the sarcopenic process. A healthy dietary pattern with exerciseis a promising strategy to limit age related sarcopenia[42].

Kemmler W tried to find out if changes in muscle mass and function were comparable across body since it is well known that muscle mass and function declines with aging process. They hypothesized that both i) fat free mass(FFM) and ii)function decline at a significantly higher rate in the lower versus the upper extremities. An observational study wasconducted for 24 months, including the community dwelling men living in the area of Northern Braveria got included in the Fraconian Sarcopenic Obesity(FranSO), astudy conducted by the Institute of Medical Physics University of Erlangen-Numberg, Germany. 177 men participated with a mean age(77.5+_4, 5years within the lowest skeletal muscle mass index (SMI) quartile of the Fran SO study were included for the present 24mth analysis. Measurements used were FFM (Direct segmental, multifrequency BIA(DSM-BIA), handgrip strength (hand dynamometer), and 10m habitual gait velocity (photo sensors were assessed a baseline and 24 –month follow up. Lower extremity fat free mass (LEFFM):-2.0+_2.4%), handgrip strength(-12 .8+_11.0%) and gait velocity (-3.5+_9.0%) declined significantly (p<0.001) during the follow up period, while upper extremity FFM remained unchanged (UEFFM) but contrary to our expectation the decline of hand strength representing upper extremity muscle function was 3.7 fold higher(P<0.01), as compared with decline in gait velocity. Thus concluding medical experts involved in diagnosis, monitoring and management of sarcopenia should consider that parameters that constitute morphologic and functional sarcopenia criteria feature different rates of declining age in aging process[43].

Further Anastacio etal.[44], prospectively assessed changes in BC, prevalence and associated factors with respect to sarcopenia, sarcopenic obesity following transplantation. They evaluated patients at 2 different times for BC, 4.0+_3.2yand 7.6+_3.1y after transplantation. BC data were obtained using BIA. The FFM Index and fat mass index were calculated, and subsequently patients were classified into following categories: sarcopenic; obesity; sarcopenic obesity. Atotal of 100 subjects were evaluated(52.6+_13.3years;57% males). The FFM Index reduced(17.92+_2.5 to 17.5+_3.5kg/m^2), fat mass index increased (8.5+_3.5 to9.0+_4.0;p<0.05), prevalence of sarcopenia(19.0-22.0%), obesity(32-37%) and SO(0-2.0%) also increased, although not significantly. The female gender was associated with sarcopenia. Thus concluding that the fat increased over the years after surgery and the lean mass reduced, although not significantly. Sarcopenia and obesity were present following transplantation; however SO was not a reality observed in these patients[44].

Discussion

The basic idea of this review was to assess the association regarding prevalence of sarcopenia in subjects presenting with overweight and obesity along with seeing if any potential correlation exists between SO and T2DM in this particular population. Main observations were that sarcopenia involves 40-45% of subjects presenting with overweight and obesity in both sexes and the presence of sarcopenia along with overweight and obesity together raise the risk of T2DM by nearly 38% in contrast to those having overweight and obesity alone. The basic mechanism for this association is unclear ,yet it appears that two directional interaction within obesity, chronic inflammation,IR and sarcopenia[ ]. Important is chronic inflammation plays a critical role in the pathogenesis of TDM. Thus it is hypothesized that co-presence of overweight/obesity and SO might have as additive effect with chronic inflammation being the common denominator pres-

ent in both problems, which accelerates the glucose impairment more i.e. prediabetes, IR and T2DM[19].

Clinical effects of findings in this review is spreading the awareness of sarcopenia prevalence can be present in overweight/obesity can be highlighted to both clinicians and patients. Hence it is important to do screening for SO in subjects with overweight/obesity, as this problem also appears to be correlated with T2DM.

Strengths of this review is that not many reviews have attempted to study prevalence of SO in males and females having 0verweight /obesity. Studies done on this topic ,showed very variable results that varied from 0-100% based on the definition applied for SO [45,46]. Greater prevalence gets reported in studies that accounted for body mass (BMI), while a lower prevalence rate where this was not the defining factor[37,47]. Low prevalence might also get explained by utilizing definitions which have been developed to start with from studies done in older cohorts and these might be applicable to younger adults as well[42].

Limitations are, that results are required to be interpreted in caution with regard to the association between SO and the prevalence of T2DM, as the cross-sectional design of the studies (i.e .non cohort) included in this review indicates only simple associations between SO and T2DM at best and does not give solid information as far as the causal relationships between the 2 conditions [48, 49]. Thus these studies lack proof to determine whether SO causes onset of deterioration of T2DM and very few studies have investigated this longitudinally, the actual effect of SO on health [50.To overcome these shortcomings, longitudinal studies are required for studying the actual effect of SO on the onset and progression of T2DM.

Conclusions

Sarcopenia prevalence has been found among adults with overweight and obesity at a high prevalence irrespective of the gender,and this condition appears to be associated with a greater risk of T2DM.Therefore clinicians need to be aware of this in their clinical settings to manage their patients better ,both obesity and T2DM.

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