Age- and Sex-Specific Changes in visceral fat mass Throughout the Lifespan

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Article

Keywords:

Posted Date: August 29th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1985973/v1

Abstract

Background

High visceral fat mass (VFM) is a risk factor for cardiovascular diseases, type 2 diabetes mellitus and malignancy, however, normative data are limited. The aim of this study was to provide reference data for VFM from a large apparently healthy Caucasian adult population.

Materials and methods

Volunteers aged 20-93 years from the Copenhagen City Heart Study had a standardized whole-body Dual-energy X-ray Absorptiometry (DXA) scan performed using the iDXA (GE Lunar). Total and regional fat mass was assessed, and VFM was quantified using the CoreScan^{TM} application.

Results

We included 1277 participants [708 women (mean±SD age: 56 ± 19 years, height: 1.66 ± 0.07 m, body mass index: 24.64 ± 4.31 kg/m^2 and 569 men, age: 57 ± 18 years, height: 1.80 ± 0.07 m, body mass index: 25.99 ± 3.86 kg/m^2]. Visceral fat mass was associated with age in both sexess, but men had significantly higher VFM both in mass (g) and after normalization to body size (height, m^2) and total fat mass ($p<0.001$). With the same BMI, body fat % (BF %) and fat mass index (total fat mass/height^2 (FMI)), men had significantly higher VFM. In contrast, VFM increased more in women with high values of android-gynoid ratio, while this relationship was linear in men.

Conclusion

Normative data of visceral fat mass (VFM) from a large healthy Danish cohort aged 20-93 years are presented. Notably, VFM increased with age in both sexes, but men had significantly higher VFM compared to women with the same BMI, BF % and FMI.

Introduction

The worldwide prevalence of obesity, defined by the World Health Organization as a body mass index (BMI) ≥ 30 kg/m^2 in adults, is continually increasing and has tripled since 1975 (1). In addition, more than 39% of adults were overweight (BMI ≥ 25 kg/m^2) and 13% obese in 2016 (1, 2).

BMI is a widely acknowledged index used to define and classify overweight adults (1). Even though BMI is an easy, fast, and low-cost way of describing populations, there are limitations in individual assessments. Hence, an athlete with large muscle mass and low fat mass can be classified as overweight or even obese; and conversely, a person with a low muscle mass but high fat mass may fall within the normal range (18.5–24.9 kg/m^2) (1–3).

More recently, increased visceral fat mass (VFM), has been proven to be a strong independent risk factor for diseases such as cardiovascular disorders, type 2 diabetes mellitus and malignancy (3–5). Notably, individuals with high VFM have more insulin resistance compared to obese individuals with primarily high subcutaneous fat (6). Furthermore, non-obese patients with known coronary artery disease have a high frequency of increased VFM, increased plasma glucose concentration and hypertension without correlation to BMI or age (7, 8). On the other hand, a reduction of VFM, but not subcutaneous fat mass, has been shown to significantly reduce blood pressure in patients with hypertension (9) and improve other cardiovascular risk factors (7, 8). Thus, quantification of VFM as a modifiable risk factor is interesting for the individual patient - and in a population healthcare setting highlighting the need for an easy, safe, efficient, and accessible method to correctly measure VFM.

Different methods can be used to quantify adipose tissue mass with Magnetic Resonance Imaging (MRI) and x-ray computed tomography (CT) considered as gold standards for assessment of VFM (4, 5, 8, 10–12). Even though these modalities are accurate, both have limitations preventing their use in large populations and follow-up examinations. MRI is time consuming and expensive, whereas CT exposes the individual to ionizing radiation (~ 2mSv (12)). These factors are further exacerbated if whole body examinations are required to assess total and regional fat tissue (5, 8, 10).

In contrast, dual-energy x-ray absorptiometry (DXA) holds several advantages compared to CT and MRI as it is fast, inexpensive and can be done with minimal exposure to ionizing radiation (4–5μSv (12, 13)). DXA scanners measure attenuation of calibrated X-ray beams in body tissues at two different energy levels enabling measurement of relative tissue composition (whole-body or regional), enabling the calculation of bone -, fat - and lean tissue masses (2, 10, 12, 14, 15). Thus, whole body DXA scans enable measurements of body fat percentage (BF%) as well as regional adipose tissue such as the android/gynoid ratio (A/G ratio) reflecting adipose tissue from the abdomen and hips, respectively. The A/G ratio often serves as a proxy for visceral fat, and fat mass index (FMI). FMI is calculated as total fat mass (kg) divided by height squared (m^2) and is a normalisation of fat mass to body size that, unlike BMI, is independent of lean mass. Large population-based studies have previously been published on healthy individuals with regards to reference values for these measures (16) and, importantly, several studies have shown excellent correlation between DXA, MRI and CT scanning for assessment of fat mass (4, 5, 8, 10). Recent developments such as the CoreScan™ application (GE Lunar, Madison, Wisconsin, USA) have enabled estimation of VFM, making assessment of VFM by DXA scanning an attractive method both in absolute mass (g), normalised to percentage of total fat mass (VF/TF%) or height squared (visceral fat index, VFI, g/m^2). A severe limitation of current reference values for VFM using DXA scanning is that they are limited to young individuals (10). Therefore, the aim of this study is to provide normative data for VFM, and derived indices measured by DXA scanning in a large apparently healthy adult population with a wide age distribution, and to describe the effect of age and sex. A secondary aim is to describe the relationship between VFM and classic measures of adipose tissue composition including BMI, BF%, FMI and A/G ratio.

Materials And Methods

Study population

Data was gathered from the Copenhagen Sarcopenia Study, which is a population-based cross-sectional study conducted at Copenhagen University Hospital Rigshospitalet - Glostrup, from December 2013 to June 2016. Details on study population recruitment have previously been published (17).

In short, a subpopulation of 3 000 men and women aged 20–93 years were invited through the Copenhagen City Heart Study to participate in the Copenhagen Sarcopenia Study(17). All subjects were home-dwelling and characterized by being apparently healthy. Exclusion criteria were pregnancy, acute or chronic medical illness, cancer, surgery within the last 3 months, use of corticosteroids, and any history of compromised ambulation or prolonged immobilization. Written, informed consent was obtained from all participants, and all investigations were conducted in accordance with the Declaration of Helsinki II and approved by the Ethical Committee of Copenhagen (H-3-2013-124).

Anthropometric measurements

All measurements were carried out by three designated and trained technicians. Height (m) was measured without shoes to the nearest 0.1 cm. Weight (kg) was measured wearing light clothing (hospital shirt) to the nearest 0.1 kg and subsequently BMI was calculated (kg/m^2). (17)

Dual-energy X-ray absorptiometry

Whole body DXA scans were performed using the iDXA fan beam densitometer (GE Lunar, Madison, Wisconsin, USA). The same scanner was used for all body scans and was carried out by one of three designated and trained technicians. Subjects had been asked to remove jewellery, empty their pockets and take off their shoes before being positioned within the scanning field. A standard protocol for imaging and positioning was followed meticulously. Analyses of all exams were performed using Encore software version 16.0. No hardware or software changes were made during the study period.

Total fat mass (TFM (kg)) was measured on the whole-body scan enabling calculations of body fat percentage (total fat mass/weight x 100) and FMI (total fat mass (kg)/height (m) squared. A/G ratio was measured as the ratio of the measured fat mass in standardized android and gynoid regions of interest. Visceral fat mass ((VFM) g) was calculated using the CoreScan™ application in a standard region of interest with subsequent calculation of visceral fat index (VFI (g/m^2)) and VF/TF%. (17)

Statistical analysis

All analyses were performed using IBM SPSS Statistics 25. Data distribution was assessed by visual inspection of histograms with superimposed normality curve. Normally distributed data including anthropometric measures are summarised using means and standard deviations. Skewed data (VFM, VFI and VFM%TFM) are summarised using centiles. Prior to statistical analysis skewed data were successfully normalised using square root transformations.

One-way ANOVA was used to compare outcome variables between the different age groups in the same sex. Effects of sex and age on outcome variables were assessed using general linear model. The level of significance was set at 5% (α = 0,05) using two-tailed testing corrected for multiple comparisons using the Bonferroni method.

Results

A total of 1 277 volunteers (women 708, men 569) aged 21 to 93 years participated in the present study. Sex specific anthropometric data (height, weight and BMI) are presented as an overview in table 1, and by age decades in Table 2 (women) and Table 3 (men). Whole body measures of adipose tissue (BF% and FMI) are also presented in Table 2 (women) and table 3 (men) and visualized according to age in Fig. 1. Direct and derived measures of VFM (VF/TF%, VFI and A/G-ratio) are summarized by age decades in Table 4 (women) and Table 5 (men) and distributions in relation to age are shown in Fig. 2.

In general, men had a significantly higher BMI compared to women ($p < 0.001$), and BMI increased in both men and women with increasing age (Tables 2 & 3) reaching a maximum at age 70–79 and then declining in age groups 80–89.

VFM, VF/TF% (visceral fat mass /total fat mass %), VFI and A/G-ratio increased with age in both men and women peaking in the 70–79-year-olds after which, no significant change was found. However, at all ages VFM, VF/TF%, VFI and A/G-ratio were significantly higher ($p < 0.001$) and increased more (steeper slope) in men compared to women (Fig. 2a-d) with peak values in men that were more than double their female equivalent (Fig. 2a-d).

BF% and FMI showed a parallel distribution in men and women, with women having a significantly higher BF% and FMI than men across all age groups ($p < 0.001$). In both sexes, BF% and FMI increased progressively with higher age group peaking in the 70–79-year-olds after which, no significant change was found.

Plots of VFM by BMI, BF%, FMI and A/G-ratio (Fig. 3a-d), respectively, showed significant differences between the sexes. Men had higher VFM per unit BMI, BF% and FMI, and the difference between sexes increased with increasing values of BMI, BF% and FMI. For A/G-ratio a nearly linear relationship was found in men, while VFM seemed to increase more in women at high A/G ratios.

Plots of VFM as a percentage of BF% compared to BMI, BF%, FMI and A/G-ratio illustrate sex differences, with continuous higher values among men, despite eliminating any effect caused by body composition (Fig. 4a-d).

Discussion

The main novel contributions of this study are reference values for VFM and derived normalized values (VFI and VF/TF%) in both sexes in a large apparently healthy Caucasian population with a wide age

range obtained using the GE Lunar iDXA. These normative data can be used as a reference standard in a clinical setting and for population research purposes, especially in studies on risk assessment and effect of interventions such as lifestyle modification, medical treatment and illnesses such as cachexia and anorexia. (18, 19)

We found, that VFM increased in both sexes with increasing age until a certain age then plateaued (Fig. 2), correlating with a concomitant increase in body fat percentage and FMI (Fig. 2). Importantly, however, men in all age groups had significantly higher values compared to women. This was also true after normalization to height squared (VFI), a commonly used measure of body size, and to total fat mass (VF/TF %) (Fig. 3). Notably, men had a higher VFM compared to women with the same body fat percentage and FMI (Fig. 3). A subdivision of age groups showed a significantly higher VFM after normalization of BF% and BMI, in men and women in the ages + 60 years compared to 20–39 years (table 4). In Fig. 4, we eliminated body composition and found a continuous higher percentage of VFM in men increasing with BMI and FMI.

Hence, higher VFM in men is a sex and age specific trait independent of body size and obesity *per se*. Furthermore, as BMI increases, VFM increases more in males compared to females, regardless of body composition. Thus, BMI underestimates VFM in men compared with women with the same BMI, and this difference increases with higher BMI values.

In a study by Miazgowski *et al.* total and regional adipose tissue including VFM was measured in a young population (20–29 years) providing a normal reference in young adults using the same manufacturer (GE-healthcare Lunar Prodigy)(10). In agreement with their results, we found a higher body fat percentage in our young population of women aged 20–29 years compared to men, and that young men had more than double VF/BF% compared to women. In the present study, we extend this normal reference to an entire adult population including both young, middle aged and old subjects of both sexess.

As these data originate from an apparently healthy population, it is unknown whether this is a normal or even healthy phenomenon, or if this translates into disease risk prediction.

This leads to the main limitation of this study, as we trusted the apparent reported health of the subjects. We did not control hospital records or public registries for prior recorded admissions or diagnoses. Neither did we control for prescribed medicine in general. Hence, it is possible that a small number of examined subjects were diseased in one way or another, although our previous data support the cohort is fairly healthy (20–22). Obtaining and controlling for this information would be paramount for later studies of the disease prediction abilities of VFM quantification by DXA. Despite this caveat, follow-up studies correlating measures of VFM burden to disease endpoints such as cardiovascular morbidity and mortality and risk of development of type 2 diabetes mellitus and/or cancer are highly warranted. Due to the relative low cost, availability, fast acquisition, fast analysis easy applicability in large populations, and minimal exposure to ionizing radiation, DXA scanning is currently an optimal choice for such studies.

Other possible implementations to future analyses are measurement of intervention effects on VFM such as lifestyle changes or medication; however, for such purposes the interscan variability of the DXA scanner needs to be determined.

Conclusion

In conclusion the present data provide normative data from a healthy Caucasian population aged 18–93 years. Notably, we found, that visceral fat mass increased with age in both sexess regardless of body composition, however, at all ages the increase was significantly higher in men compared to women, indicating that visceral fat mass is a sex specific trait. The possibilities of DEXA scans are almost endless, and even though more research is necessary, it is our hope that these data can be used as future reference standards.

Declarations

Competing Interests

The authors declare no competing financial interests

Acknowledgements

We would like to thank Tim E. Nørst for his great assistance in data collection for this article.

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Tables

Tables 1 to 5 are available in the Supplementary Files section

Supplementary Files

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- Table1.jpg
- Table2.jpg
- Table3.jpg
- Table4.jpg
- Table5.jpg