

## FAT MASS TO FAT-FREE MASS RATIO AND BODY COMPOSITION IN PARTICIPANTS WITH CHRONIC LEG PROBLEMS

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### ABSTRACT

**Background & aim:** Low fat-free mass (FFM) or high fat mass (FM) in older adults are abnormal body composition phenotypes associated with morbidity. The dual burden of excessive FM and low FFM may lead to a higher risk of cardiovascular and other diseases and disability and lower physical performance compared with individuals with normal body composition or low FFM or high FM alone. Both conditions lead to poorer health and can be identified by a high FM/FFM ratio. Because few studies have examined the effects of abnormal body composition using the FM/FFM ratio, the aim of this study is to determine the FM/FFM values by gender in patients with knee and hip pathologies and compare them with body composition parameters. This condition is important when surgery is required because abnormal body composition leads to an increase in infections and other postoperative complications.

**Methods:** A total of 93 participants aged  $64.71 \pm 7.71$  years in women and  $65.9 \pm 9.9$  years in men with a body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> were recruited from the Val-doltra Orthopaedic Hospital (Ankaran, Slovenia). The waist circumference (WC) and anthropometric data (BMI), as well as body composition data (FM, FFM, % of body water, estimated by bioelectrical impedance - BIA) were measured. In addition, the body composition phenotypes (FM/FFM ratio) were calculated.

**Results:** The FM/FFM index was higher in females. The female group with FM/FFM (0.68) and those with a higher FM/FFM (0.92) correlated positively with WC. Male participants were excluded for further analysis because only two males had FM/FFM > 0.80. The FM/FFM of the remaining male participants was  $0.53 \pm 0.09$ .

**Conclusions:** FM/FFM provide information on patient body composition and identify individuals at risk of body composition abnormalities in women only.

**Keywords:** Fat-mass, fat-free mass, waist circumference, older adults, knee, hip.

## RAZMERJE MED MAŠČOBNO MASO IN PUSTO MIŠIČNO MASO TER SESTAVA TELESA PRI BOLNIKI S KRONIČNIMI TEŽAVAMI SPODNJE OKONČINE

### IZVLEČEK

**Izhodišča:** Zmanjšan delež puste mišične mase (FFM) ali povečan delež maščevja (FM) vodi pri starejših odraslih do sprememb v telesni sestavi, ki odstopajo od mejnih vrednosti, kar je povezano z obolevnostjo. Sočasna prisotnost povečane FM in zmanjšane FFM lahko v primerjavi s posamezniki z normalno telesno sestavo ali samo z nizko FFM ali visoko FM poveča tveganje za razvoj srčno-žilnih in drugih bolezni, invalidnost in nižjo telesno zmogljivost. Oba dejavnika poslabšata zdravstveno stanje posameznika, ki ga lahko identificiramo s pomočjo povečanega razmerja FM/FFM. Zato je namen te raziskave določiti vrednosti FM/FFM pri preiskovancih s patologijo kolena in kolka ter jih primerjati s parametri telesne sestave. Poznavanje vrednosti FM/FFM je ključnega pomena v primerih, ko je potreben operativni poseg, saj telesna sestava, ki odstopa od mejnih vrednosti vodi do večjega tveganja za razvoj pooperativnih zapletov.

**Metode:** V raziskavo je bilo vključenih 93 preiskovancev iz Ortopedske bolnišnice Valdoltra (Ankaran, Slovenija), starih  $64,71 \pm 7,71$  let (ženske) in  $65,9 \pm 9,9$  let (moški) z indeksom telesne mase (ITM)  $\geq 25$  kg/m<sup>2</sup>, napotenih na ortopedsko specialistično obravnavo. Izmerjeni so bili antropometrija (ITM), obseg pasu (WC) ter telesna sestava (FM, FFM, % telesne vode, ocenjeni z bioeletrično impedančno analizo-BIA). S pomočjo indeksa FM/FFM so bili določeni fenotipi telesne sestave.

**Rezultati:** Indeks FM/FFM je bil višji pri ženskah. Tako skupina žensk s FM/FFM (0,68), kot skupina z višjim FM/FFM (0,92) sta pozitivno korelirali z obsegom pasu. Ker sta imela samo dva moška FM/FFM  $> 0,80$  smo moške preiskovance iz nadaljnje analize izključili. FM/FFM preostalih moških preiskovancev je znašal  $0,53 \pm 0,09$ .

**Zaključek:** Razmerje FM/FFM nam poda pomembno informacijo o značilnostih pacientove telesne sestave ter pomaga identificirati bolnike, pri katerih obstaja tveganje za spremenjeno telesno sestavo. V naši študiji smo s pomočjo indeksa ugotovili, pomembne značilnosti v spremembi telesne sestave pri preiskovankah ženskega spola.

**Ključne besede:** maščobna masa, pusta mišična masa, obseg pasu, starejši odrasli, koleno, kolka.

## INTRODUCTION

The ageing of the population and the rise in obesity prevalence worldwide are the two major risk factors for non-communicable diseases, including degenerative diseases, sarcopenia, frailty, increased morbidity and mortality, with negative implications for the public health system (Merchant et al., 2021). Elevated body mass index (BMI), waist circumference (WC), and/or waist-to-hip ratio are commonly used to define obesity. BMI needs to be interpreted with caution in older adults as loss of physiological body height may lead to over-interpretation and lack of correlation with the percentage of body fat, the distribution of fat, or body composition (Batsis et al., 2016). Additionally, BMI has a limited ability to distinguish between muscle mass and fat accumulation and does not provide information on body composition (Prado et al., 2012). Therefore, a better understanding of body composition may require more specific measurements, such as fat mass (FM) and fat free mass (FFM), which can be obtained by bioelectrical impedance analysis (BIA) (Prado et al., 2012). The fat mass to fat-free mass ratio (FM/FFM) is an integrated metabolic index for assessing body composition, which evaluates the combined effect of the ratio between FM and FFM (Godziuk, Woodhouse, Prado, & Forhan, 2020; Rugila et al., 2022) In other words, FM/FFM indicates whether the amount of FM is adequate for the amount of FFM in an individual. Theoretically, higher values of the ratio indicate a less favorable balance between FM and FFM, and a high FM/FFM ratio already has negative effects on physical abilities and contributes to morbidity and mortality in many patients (Prado et al., 2012). Despite these clinical associations previously found with FM/FFM in chronic disease, this ratio has not been studied in patients with chronic knee or hip pain. The clinical impact of higher versus lower FM/FFM in these patients requires increased attention due to the accelerated loss of FFM associated with pain, mobility limitations and obesity-related inflammation (Godziuk et al., 2020). In addition, a loss of muscle mass is associated with prolonged hospital stays, infections, and other complications and disability (Prado et al., 2012). Thus, the aim of this study is to determine the FM/FFM values and compare the body composition of patients with higher and lower FM/FFM values by gender. Screening of this ratio may be important in order to identify patients with abnormal body composition, especially if surgery is indicated, to avoid complications after surgery. Our hypothesis is that higher FM/FFM values in these individuals are associated with abnormalities in body composition.

## METHODS

### Study Design

In this cross-sectional study, 93 participants (Caucasian origin), women with a mean age of  $64.71 \pm 7.71$  years and men with a mean age of  $65.90 \pm 9.90$  years with knee and hip problems, referred to an orthopedist for further diagnosis, were recruited at the Valdoltra Orthopaedic Hospital (Ankaran, Slovenia), excluding participants with cancer and acute illness, patients with pacemakers, and patients with a  $BMI \leq 25 \text{ kg/m}^2$ . Participants were examined in 2019 in the departments of the mentioned institution and underwent anthropometric measurement and body composition analysis.

The National Medical Ethics Committee of Slovenia (code 0120-557/2017/4) approved the study. All the participants were fully informed about the procedures before written informed consent was obtained.

### Anthropometric Data

At the study site, body height, body mass and WC were measured according to a standardized protocol. All the measurements were taken between 7 and 8 am after fasting overnight. The body height (cm) of the subjects was measured to the nearest 0.1 cm while standing, without shoes, using a Leicester Height Measure (Invicta Plastics Limited, Oadby, England). The body mass (kg) of the participants wearing light clothing without shoes was measured with an accuracy of 0.1 kg. The WC (cm) was measured in the standing position halfway between the costal arch and the iliac crest with a non-stretchable tape measure. The BMI ( $\text{kg/m}^2$ ) was calculated using the formula body mass (kg) / body height ( $\text{m}^2$ ).

### Body Composition Measurements

FM (kg) and FFM (kg) were estimated by bioelectrical impedance analysis (BIA) using the Tanita BC 418MA (Tanita Corporation, Arlington Heights, IL) and the data was analyzed with the software provided by the manufacturer. The FM to FFM ratio (FM/FFM) was calculated as an index of obesity combined with sarcopenia and the following cut-off values were used (Biolo et al., 2015; Prado et al., 2012): FM/FFM ratio  $< 0.40$  for metabolically healthy obese individuals in whom the increase in FM was minor compared to that in FFM; FM/FFM ratios between 0.40 and 0.80 for obese phenotypes in whom FM predominated FFM, but FFM is still adequately maintained; FM/FFM ratios  $> 0.80$  for obese phenotypes with sarcopenia in whom FM was increased and FFM was reduced.

## Statistics

Statistical analyses were performed using IBM SPSS ver. 26. Univariate data analysis was performed by calculating the frequencies and percentages for qualitative variables, mean and/or median, standard deviation (SD) were calculated for quantitative variables. To assess the normality of the distribution, Kolmogorov-Smirnov and Shaphiro-Wilk tests were performed. Normality was additionally assessed by evaluating the histogram, skewness, and kurtosis.

The independent sample t-test was used to determine the statistically significant differences between the two groups because the variables in both groups followed the normal distribution. The Pearson's correlation coefficient was calculated to determine the association between normally distributed variables.

## RESULTS

The participant characteristics are shown in Table 1. The female and male participants were comparable in age and BMI. Male participants had higher body mass, % body water, FFM and WC whereas FM and the FM/FFM ratio were higher in females. We excluded male participants from further analysis because only two men had FM/FFM > 0.80 ( $1.0 \pm 0.13$ ); the FM/FFM of the remaining male participants was  $0.53 \pm 0.09$ .

Table 1. General characteristics of the participants

Parameters	Men n=37 (45.8%)	Women n = 56 (54.2%)
Age [years]	64.71 ± 7.71	65.90 ± 9.90
<b>Anthropometric measurements</b>		
Body mass [kg]	93.2 ± 16.0	78.9 ± 12.9
Body height [cm]	172 ± 7	160 ± 7
WC [cm]	109 ± 14	101 ± 11
BMI [kg/m <sup>2</sup> ]	31.4 ± 4.8	30.8 ± 5.0
<b>Body composition measurements</b>		
FFM [kg]	59.7 ± 7.1	43.3 ± 4.6
Body water [%]	48.7 ± 3.2	41.1 ± 2.9
FM [kg]	30.4 ± 10.6	43.3 ± 4.6
FM/FFM	0.50 ± 0.16	0.75 ± 0.15

Legend: All the values are mean ±SD, BMI - body mass index, WC - waist circumference, FM - fat mass, FFM - fat free mass, FM/FFM ratio - ratio between fat mass and fat free mass

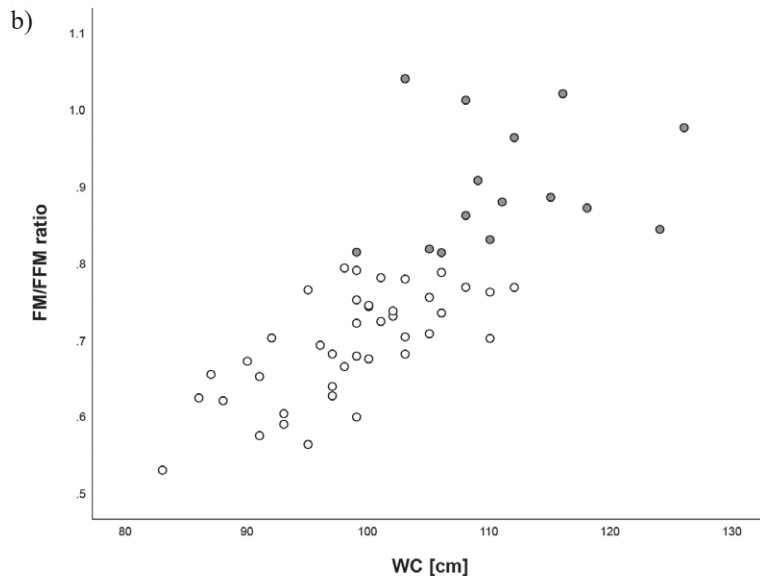
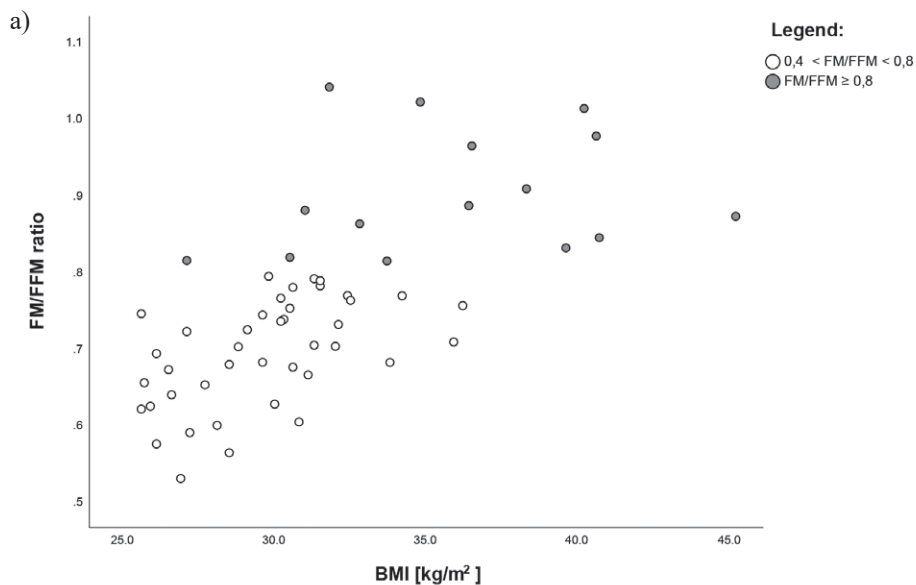
Therefore, we divided the females into two groups based on the cut-off values for the FM/FFM ratio: FM/FFM between 0.40 and 0.80 and FM/FFM  $\geq$  0.80 (Table 2).

Table 2. Body composition data in women with medium and higher FM/FFM ( $0.4 < \text{FM/FFM} < 0.8$  and  $\text{FM/FFM} \geq 0.8$ ).

Parameters	FM/FFM		Independent sample t-test (p)	Cohen d
	0.4 < FM/FFM < 0.8 (n=41)	FM/FFM $\geq$ 0.8 (n=15)		
Age [years]	66.62 $\pm$ 9.82	65.85 $\pm$ 9.55	.704	
Body mass [kg]	72.33 $\pm$ 8.11	91.31 $\pm$ 11.12	< .001	-2.112
Body height [cm]	159.05 $\pm$ 6.94	160.53 $\pm$ 7.58	.318	
WC [cm]	97.07 $\pm$ 7.93	110.18 $\pm$ 9.07	< .001	-1.581
BMI [kg/m <sup>2</sup> ]	28.66 $\pm$ 3.32	35.56 $\pm$ 4.79	< .001	-1.837
Body water [%]	42.38 $\pm$ 2.18	38.13 $\pm$ 1.76	< .001	2.044
FM [%]	38.95 $\pm$ 3.34	46.28 $\pm$ 2.68	< .001	-2.304
FM [kg]	28.3 $\pm$ 4.9	42.4 $\pm$ 7.0	< .001	-2.481
FFM [kg]	41.63 $\pm$ 3.61	46.31 $\pm$ 4.63	< .001	-1.200
FM/FFM ratio	.68 $\pm$ .09	.92 $\pm$ .11	< .001	-2.511

Legend: All values are mean  $\pm$  SD, BMI - body mass index, WC - waist circumference, FM - fat mass, FFM - fat free mass, FM/FFM ratio - ratio between fat mass and fat free mass

Forty-one of the women were classified in the obesity phenotype group: FM/FFM ratio ( $0.68 \pm 0.09$ ), while fifteen women had an obesity phenotype combined with a low FFM: FM/FFM ratio ( $0.92 \pm 0.11$ ). In addition, women with a higher FM/FFM ratio ( $\geq 0.8$ ) exhibited significantly greater body mass, BMI, WC, FFM and FM and a significantly lower % of body water when compared to the group with a lower FM/FFM. Pearson's correlation analysis revealed a significant, positive correlation in both groups between FM/FFM and BMI (overall:  $r = 0.742$ ,  $p < 0.01$ ; for  $0.4 < \text{FM/FFM} < 0.8$ :  $r = 0.659$ ,  $p < 0.01$ ; for  $\text{FM/FFM} \geq 0.8$ :  $r = 0.676$ ,  $p < 0.01$ , Figure 1a) and WC (overall:  $r = 0.768$ ,  $p < 0.01$ ; for  $0.4 < \text{FM/FFM} < 0.8$ :  $r = 0.741$ ,  $p < 0.01$ ;  $\text{FM/FFM} \geq 0.8$ :  $r = 0.542$ ,  $p < 0.01$ , Figure 1b). In addition, a significant, negative correlation was identified between FM/FFM and % of body water (overall:  $r = -0.907$ ,  $p < 0.01$ ; for  $0.4 < \text{FM/FFM} < 0.8$ :  $r = -0.869$ ,  $p < 0.01$ ; for  $\text{FM/FFM} \geq 0.8$ :  $r = -0.874$ ,  $p < 0.01$ , Figure 1c).



Figures 1a, 1b: Scatter diagrams of the FM/FFM ratio and BMI (a) and WC (b).

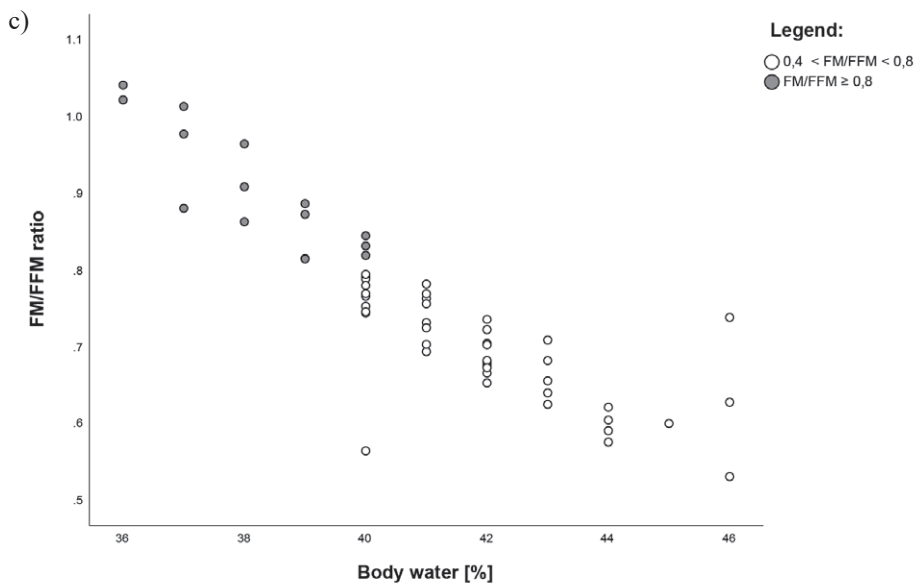


Figure 1c: Scatter diagrams of the % of body water.

## DISCUSSION

In this cross-sectional study, the majority of the participants with hip or knee joint problems and associated leg pain were obese with normal FFM, while obesity associated with lower FFM was only found in women. A higher FM/FFM ( $> 0.8$ ) is significantly associated with worse body composition parameters (body mass, BMI, WC, FM, FFM) in female patients.

The ageing process in the increasing population of older adults is associated with an increase in chronic health conditions and a high prevalence of functional limitations and disabilities associated with a decrease in muscle mass and strength (Delmonico & Beck, 2017). In addition, obese adults have greater skeletal muscle mass than normal body mass adults of the same age and sex, as we confirmed in this study. These differences are the result of muscle anabolism induced by the loading effect of the higher body mass in obesity (Biolo et al., 2015; Morse & Soeldner, 1964).

In our study, the FM/FFM ratio in both female groups correlated strongly and positively with WC. The WC is a surrogate marker for assessing the risk of visceral/abdominal fat accumulation (Ma et al., 2021). The association between abdominal fat and muscle mass loss is explained by several mechanisms. Abdominal obesity is characterized by systemic inflammation, oxidative stress and insulin resistance, which affect muscle proteolysis and inhibit protein synthesis (Biolo et al., 2015). Adipose tissue is actively involved in metabolic regulation and secretes pro-inflammatory cytokines such



as interleukin-6 (IL -6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), as well as the hormone leptin. The pro-inflammatory cytokines have effects on the brain, liver, and pancreas, which control appetite, carbohydrate and fat metabolism, and energy balance (Dhawan & Sharma, 2020; Roubenoff, 2000). The increase in FM and the accompanying release of pro-inflammatory cytokines lead to insulin resistance, which reduces the normal anabolic effect of insulin on amino acid transport in muscle (Kim et al., 2000). In addition, there is evidence that leptin reduces growth hormone secretion, suppressing another important anabolic stimulus (Obradovic et al., 2021).

In addition, there are a number of explanations for the association between body fat, muscle mass and musculoskeletal pain, including the upregulation of pro-inflammatory cytokines released by adipose tissue (Younger, Kapphahn, Brennan, Sullivan & Stefanick, 2016). Inflammation triggered by pro-inflammatory cytokines is known to be associated with physical pain, particularly in women (Walsh et al., 2018). In addition, a higher FM/FFM is a determinant factor of physical inactivity (Rugila et al., 2022). According to the FM/FFM ratio, obese women in this study had predominantly more fat mass and less muscle mass. This could be a result of the different distribution of body fat between the sexes (Prado et al., 2012). Physical activity became more difficult in this condition and their habitual level decreased further. The FM/FFM ratio may help reinforce the notion that body composition is a more informative measure of risk for musculoskeletal pain and immobility (Walsh et al., 2018). Taken together, these findings support the hypothesis that a higher FM/FFM ratio ( $> 0.8$ ) may associate obesity with an additional decrease of FFM due to immobility and inflammation. This could be important information for sarcopenia screening in participants scheduled for surgery to avoid complications.

This study should be considered in light of certain limitations. First, the study included a relatively small sample size. Second, there is a lack of additional measurements of inflammatory markers and muscle function, which would certainly be of interest. Finally, this study is cross-sectional.

## CONCLUSIONS

A higher value of the FM/FFM ratio, studied for the first time in participants with chronic knee or hip pain, was significantly associated with abdominal obesity and is useful for identifying individuals at risk of body composition abnormalities. The clinical implications of an FM/FFM  $> 0.8$  in these participants require increased attention, as accelerated loss of FFM and complications may occur if surgery is indicated.

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