Low health related quality of life associated with fractures in obese postmenopausal women in Santa Maria, Brazil

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1. Introduction

Obesity is a prevalent health disorder associated with high public health costs, mainly with the rapidly rising tendency of weight gain in the global population (Guo et al., 2009). As the population ages, bone fractures also remain a significant health condition that impacts a high burden of the quality of life in obese subjects (Nielsen et al., 2012; Compston et al., 2014; Palacios et al., 2014). The proportion of fractures occurring in obese people is significant, considering that clinical risk factors for fracture are similar in obese and non-obese subjects, although patterns of fracture and falling may diverge (Premaor et al., 2014). The association between obesity and fracture is no longer controversial; while there is no difference in the incidence of fractures in obese and non-obese women, fractures proved to be site-dependent in obese postmenopausal women (Prieto-Alhambra et al., 2012; Compston et al., 2011).

Regardless of their association, both obesity and fractures are individually associated with low health-related quality of life (HRQL), especially its physical function measures, in the postmenopausal population (Sanfelix-Genoves et al., 2011; Jia & Lubetkin, 2005; Katz et al., 2000). Nevertheless, few studies assessed the combined effect of both obesity and fractures over HRQL in postmenopausal women (Compston et al., 2014). We assume that these conditions add a greater impact on quality of life when occurring together than when lonely prevalent. Therefore, our study aims to explore the effect of both obesity and fractures over HRQL in postmenopausal women.

2. Methods

2.1. Study setting

The study design has been described elsewhere (Copes et al., 2015), but in brief, women aged 55 years or older who attended at least once a primary care facility of Santa Maria, Brazil in the 24 months before the study were invited to participate. The recruitment was from March 1, 2013, to August 31, 2013. Women with cognitive impairment and communicative deficit were excluded from the survey. This cross-sectional study was approved by the Center for Continuing Education in Health of the Health Department of the Municipality of Santa Maria (Ofício 492/2012/SMS/NEPeS) and by the Ethics Committee of the Federal University of Santa Maria (CAAE 11166012.6.0000.5346). All participants provided informed consent, and all study procedures were in...
agreement with the Declaration of Helsinki and the Brazilian Resolution 466/12.

2.2. Measurements

A validated translation into Portuguese of the GLOW study questionnaire (Compston et al., 2014) - authorized by the respective study authors and The Center for Outcomes Research, University of Massachusetts Medical School - was administered to the studied women. This questionnaire includes information about demographic characteristics, lifestyle, previous fractures, family history of fractures, menopause, medications, and comorbidities. Falls were evaluated with the following question: “In the last 12 months, how many times have you fallen?” and for this study it was considered a dummy variable (fall or no-fall). The SF-36 questionnaire (Ware & Gandek, 1998) (license number QM016471) was administered to assess HRQL. Weight was measured in kilograms by weighing-machines validated by the Brazilian National Institute of Metrology, Quality, and Technology with the study participant wearing light clothing without shoes. Height was measured according to the recommendations of the World Health Organization (WHO). BMI was calculated dividing the weight in kilograms by the square of height in meters. Obesity was defined as BMI ≥ 30 kg/m². Fractures were set as any clinical self-reported fracture (excluding hand, feet, head, and high-impact fractures) that occurred after the age of 45 years. The risk of fractures was assessed through the Fracture Risk Assessment Tool (FRAX®, OMS) without BMD measurement.

2.3. Statistical analysis

Statistical analysis was performed using SPSS for Windows, version 19 (IBM Brazil, São Paulo – Brazil). Data were reported as mean (standard deviation), prevalence rate (percent), and proportion, and distribution. The studied women were categorized into four groups, according to their BMI score (obese if BMI ≥ 30/20-30 if BMI < 30) and to the presence/absence of previous fractures. The ANOVA was performed to identify significant differences between continuous variables. Univariate general linear models were used for FRAX® calculated fracture risks. The Bonferroni correction was applied to the Post Hoc tests. The Chi-square test was used to assess differences between nominal variables. Associations were considered significant when the p-value was < 0.05. Linear generalized models were used to evaluate the association between the SF-36 component scores and all variables with P < 0.05. The best model was chosen based on the lower model Chi-square.

3. Results

In total, 1301 women were assessed for eligibility. Of those, 239 refused to participate, and 5 were excluded. From the 1057 women who completed the study questionnaire, 981 had their weight and height measured and composed the study group. The mean (standard deviation) age was 67.1 (7.6) years, with mean BMI of 29.3 (5.5) kg/m². The main characteristics of these women are shown in Table 1. The prevalence of obesity and fractures were 40.9% and 16.5%, respectively. The non-protective effect of obesity on fractures are described in detail elsewhere (Copes et al., 2015), in short, the frequency of fractures was 17.3% (67/387) in obese women and 16.0% (57/354) in non-obese women, P = 0.60. The most frequent fracture sites were [\(n/\text{total n}, P\), in obese vs. non-obese, respectively]: wrist (27/387 vs. 39/594, 0.8); humerus (13/387 vs. 17/594, 0.71); Rib (7/387 vs. 21/594, 0.12); clinical vertebral (4/387 vs. 8/594, 0.77); hip (3/387 vs. 7/594, 0.75) and clavicle (3/387 vs. 4/594, 1.00).

In the univariate analysis (Table 1), obese women with fractures had a significantly higher prevalence of comorbidities and tobacco use and had lost at least 5 kg in the last year in a significantly lower proportion. Besides, non-obese women with fractures were older, had a higher hospitalization rate, were more likely to be taking calcium and suffered significantly more falls. The four groups presented low education level (<8 years), low prevalence of alcohol abuse, a high proportion of medical consultation in the previous year (around 70%) and had health insurance coverage around 50%. The FRAX® scores were higher in non-obese women when compared with all other categories (Table 1). Obese women have higher Major Fracture FRAX® scores when compared with obese women without fractures (P < 0.0001). Non-obese women with fractures have higher scores when compared with all other categories (all P values < 0.0001).

Regarding quality of life, obese women with fractures had significantly lower SF-36 component scores, except for vitality, social functioning and mental health, which did not present significant differences among the groups. The SF-36 mental and physical components summaries are displayed in Fig. 1.

Table 1

| Characteristics of the studied women. | Non-obese without fracture | Obese without fracture | Non-obese with fracture | Obese with fracture | P** |
|--------------------------------------|-----------------------------|------------------------|------------------------|-------------------|-----|
| Age (yrs)                            | 67 (7.8)                    | 65.4 (6.8)             | 72.4 (8.1)             | 67.3 (6.8)        | <0.0001 |
| BMI (kg/m²)                          | 25.8 (3.0)                  | 34.4 (4.2)             | 25.7 (3.1)             | 35.2 (3.8)        | <0.0001 |
| Comorbidity                          | 63.0%                       | 76.6%                  | 79.8%                  | 80.6%             | <0.0001 |
| Tobacco use                          | 16.4%                       | 6.6%                   | 7.4%                   | 6.1%              | <0.0001 |
| Alcohol abuse                        | 0.2%                        | 0%                     | 1.5%                   | 0.092             |     |
| Medical consultation                 | 65.4%                       | 69.1%                  | 66.0%                  | 78.5%             | 0.173 |
| Hospitalization                      | 17.2%                       | 19.4%                  | 32.6%                  | 19.7%             | 0.007 |
| Health insurance                     | 57.8%                       | 52.1%                  | 62.4%                  | 44.4%             | 0.206 |
| Weight loss                          | 17.5%                       | 8.9%                   | 25.0%                  | 6.5%              | <0.0001 |
| Calcium                              | 18.0%                       | 15.6%                  | 28.7%                  | 23.4%             | 0.024 |
| Alendronate                          | 7.3%                        | 5.1%                   | 10.6%                  | 7.9%              | 0.294 |
| Vitamin D                            | 12.4%                       | 7.7%                   | 12.8%                  | 9.5%              | 0.171 |
| Hormone therapy                      | 5.1%                        | 2.2%                   | 1.1%                   | 3.1%              | 0.087 |
| Falls                                | 29.9%                       | 33.9%                  | 50.5%                  | 39.4%             | 0.001 |
| Education                            | <8 yr                       | 75.0%                  | 75.4%                  | 84.9%             | 0.561 |
| ≥8 < 12 yr                           | 17.9%                       | 18.3%                  | 12.8%                  | 17.5%             |     |
| ≥12 years                            | 7.1%                        | 6.2%                   | 2.3%                   | 7.0%              |     |
| FRAX® - risk of major fracture**     | 5.7 (4.0)                   | 4.4 (3.6)              | 13.1 (7.4)             | 7.0 (3.3)         |     |
| FRAX® - risk of hip fracture**       | 2.2 (3.1)                   | 1.4 (2.7)              | 6.2 (5.9)              | 2.2 (2.02)        |     |
| SF-36 components                     |                             |                        |                        |                   |     |
| Physical functioning                 | 74.1 (22.8)                 | 64.0 (26.0)            | 60.2 (26.9)            | 53.8              | <0.0001 |
| Role-physical                        | 76.5 (28.7)                 | 71.9 (31.1)            | 70.9 (32.8)            | 64.5              | 0.011 |
| Bodily pain                          | 60.9 (26.7)                 | 53.3 (28.0)            | 50.8 (27.6)            | 44.0              | <0.0001 |
| General health                       | 69.0 (22.8)                 | 67.7 (22.7)            | 67.9 (23.2)            | 58.7              | 0.011 |
| Vitality                             | 64.1 (24.1)                 | 62.7 (24.3)            | 62.6 (22.6)            | 57.9              | 0.291 |
| Social functioning                   | 83.0 (26.8)                 | 82.9 (26.0)            | 76.0 (32.0)            | 77.6              | 0.088 |
| Role-emotional                       | 84.1 (23.1)                 | 80.1 (28.0)            | 83.3 (26.6)            | 75.8              | 0.046 |
| Mental health                        | 66.4 (23.4)                 | 65.8 (23.9)            | 67.0 (25.0)            | 62.1              | 0.585 |

** At ANOVA test for age, BMI, and SF-36 categories. Univariate general linear model for FRAX® calculated fracture risks. For the remaining characteristics, P value from Chi-square test.

* Reported at least one of the following: Asthma, COPD, Osteoarthritis, Rheumatoid Arthritis, Heart Failure, High Blood Pressure, Ischaemic Heart Disease, Parkinson Disease, Multiple Sclerosis, Cancer, Diabetes, Inflammatory Intestinal Disease.

* The Bonferroni correction was used for Post Hoc analysis. Obese women have higher Major Fracture FRAX® scores when compared with obese women without fractures (P < 0.0001). Non-obese women with fractures have higher scores when compared with all other categories (all P values < 0.0001).
In the linear generalized model, obesity, fractures and the presence of comorbidities were independently associated with a lower SF-36 physical component score (Table 2).

4. Discussion

We found a lower HRQL in obese postmenopausal women with fractures when compared with obese women without fractures and non-obese women with fractures. Many studies show that obesity and fractures are two main health conditions responsible for a great negative impact over HRQL, mainly its physical component (Sanfelix-Genoves et al., 2011; Jia & Lubetkin, 2005; Katz et al., 2000; Fontaine & Barofsky, 2001). What our findings suggest is that, although obese subjects have a worse HRQL per se – i.e. they achieve lower scores in HRQL questionnaires compared to non-obese subjects –, fractures might exert a further negative impact over this low HRQL even greater than that exerted over non-obese individuals with a fracture. In other words, we hypothesized that fractures and obesity might have a synergic effect on the decrease in HRQL, particularly over its physical component.

The impact of fractures on HRQL is well known. The GINERISK study by Palacios et al. with 4157 Spanish osteoporotic postmenopausal women showed a lower score in both the specific Cervantes Scale and the generic SF-12v2 Health Survey in those with osteoporosis. Interestingly, the HRQL loss was greater in women with prior osteoporosis fractures (Palacios et al., 2014). The Australian study AusICUROS applied the EQ-5D-3L questionnaire to both sexes adults over 50 years and described a low to moderate reduction in HRQL in subjects who suffered a low-impact fracture. Moreover, this loss of HRQL was sustained for at least 12 and 18 months, for hip and spine fractures, respectively (Abimanyi-Ochom et al., 2015). The latter could explain in part the low HRQL found in cross-sectional studies (Sanfelix-Genoves et al., 2011; Adachi et al., 2003) such as ours.

The impact of a fracture on HRQL appears to vary according to the fracture site. The GLOW study is a large multinational cohort that recruited 60,397 post-menopausal women. Women with hip, spine, or upper leg fractures had the lower HRQL assessed by EuroQol EQ-5D tool and the SF-36 (Adachi et al., 2010). On the other hand, the cross-section analysis of the Canadian Multicenter Osteoporosis Study that included 5516 men and women over 50 years found the lowest HRQL in pelvic, lower limbs, and rib fractures (Adachi et al., 2003). Moreover, the detrimental in HRQL was worst after a hip, ankle or vertebral fracture in the AusICUROS study (Abimanyi-Ochom et al., 2015). Intriguingly, the association between obesity and fractures is also site dependent. While obese women had fewer fractures of the wrist, hip, and pelvis they have more fractures at the ankle, lower and upper leg, humerus, and spine (Compston et al., 2011). Our study did not have the power to explore the association between fracture site and obesity (Copes et al., 2015).

Alongside with fractures, obesity alone also has been associated with a poor HRQL in several studies (Jia & Lubetkin, 2005; Katz et al., 2000; Fontaine & Barofsky, 2001). The Nurses Health Study has shown a dose-dependent effect of BMI on HRQL (Fine et al., 1999). Furthermore, both physical and mental components of SF36 are affected in some studies (Fontaine & Barofsky, 2001). The obese women in our study had a decrement in the physical component, especially the physical functioning and bodily pain. Mannucci et al. have described that the impairment in physical functioning is greater in women (Mannucci et al., 1999) which could help to explain our findings.

Although some studies had evaluated the effect of comorbidities in the HRQL of obese people, only few studies assessed fractures as such. The cross-sectional FRAVO study by Sanfelix-Genoves et al. assessed 804 Spanish postmenopausal women age 50 years or older with the SF-12 Questionnaire. They did not find a greater decrement in HRQL in obese women (BMI > 35 kg/m²) with vertebral fracture (Sanfelix-Genoves et al., 2011). Conversely, the GLOW study described that obese women with fracture underwent a longer period of hospitalization for treatment and had poorer functional status and HRQL than non-obese women (Compston et al., 2014).

Our investigation has some limitations. First, data were obtained from a cross-sectional survey and, therefore, are unable to predict cause-consequence associations between fractures in obese patients and lower HRQL. Second, fractures were self-reported and not radiographically verified, although other studies had already shown that such information proved to be reliable (Chen et al., 2004). Finally, there is a possibility of inaccuracies in self-reports, but such imprecision would be equally distributed among the groups. Notwithstanding, our study also has some strengths: 1) we believe our sample to be representative of our primary care postmenopausal population due to thorough sampling; 2) we assessed height according to WHO recommendations and used calibrated scales; and 3) all data collection as standardized and the interviewers trained to increase the reproducibility.

### Table 2

|                | B     | 95% CI  | P       |
|----------------|-------|---------|---------|
| Obesity        | -2.6  | -3.8, -1.4 | <0.0001 |
| Fracture       | -3.2  | -4.9, -1.6 | <0.0001 |
| Tobacco use    | -1.0  | -2.8, 0.8  | 0.29    |
| Age            | -0.6  | -0.1, 0.03 | 0.17    |
| Comorbidity    | -5.4  | -6.7, -4.1  | <0.0001 |

a All variables with \( P < 0.05 \) entered in the models. The best model was chosen based on the AIC criteria.

![Fig. 1. SF-36 Physical component summary and mental component summary. * P values refer to ANOVA test among the groups. The P value for the Post Hoc LSD test was: < 0.0001, D vs. A; 0.003 D vs. B; and 0.076 D vs. C.](image)
Above all, our findings also have many clinical consequences. With the population rapid weight gain and aging, it becomes a public health issue to approach this health conditions altogether, aiming at minimizing their effect on HRQL. The acknowledgment of the impact of fractures in obese patients may help healthcare providers more fully understand the importance of their prevention and treatment in this specific population.

Tools developed to assess fracture likelihood, as the FRAX algorithm, would be expected to be modified, since they do not perfectly fit for obese people, underestimating fracture probability and often leaving obese women at undertreatment (Premao et al., 2013). Therefore, obese-specific fracture probability tools may be created. Moreover, the obese population may have special needs regarding osteoporosis treatment, so that studies designed to assess the antifracture efficacy of different drugs in obese patients may be necessary.

In conclusion, our results strongly suggest that fractures make a significant contribution to the overall reduction in HRQL in the obese population, leaving a field to further studies with higher levels of evidence to explain this association better. The rapid increase in obesity worldwide and the high morbidity caused by fractures in obese subjects urges the necessity of effective obesity-focused prevention and treatment strategies aimed at enhancing global quality of life.

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Ethics approval

Approval for this study was obtained from the Federal University of Santa Maria Ethic Committee [Comitê de Ética em Pesquisa da UFSM (CEP – UFSM); CAAE 04320312.2.0000.5346] and from the Municipality of Santa Maria City [Núcleo de Educação Permanente em Saúde (Ofício 492/2012/SMS/NEPeS) da Secretaria de Saúde da prefeitura de Santa Maria].

Competing interests

All authors state that they have no conflict of interest regarding this manuscript.

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