

# Effects of metabolic syndrome on the correlation between the most common groups of prescribed medications and the risk of fall in Brazilian elderly people

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## Research article

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## **Abstract**

## **Background**

Aging is an irreversible process of all living beings and one of the great challenges we have to face is learning how to live healthier. Several health conditions, such as cardiovascular disease, diabetes, stroke, depression, hypertension, metabolic disorders, and falls, are related to senescence and can directly affect quality of life around the world. In addition to these physiological disorders, the use of medications can directly affect the quality of life of the elderly, and some studies have already reported the correlation between metabolic syndrome, prescription medications, and injury caused by falling.

## **Methods**

This study was conducted with a group of 102 adults over 60 years of age, including volunteers in the city of Viçosa - Minas Gerais, Brazil. The instruments of analysis were performed using three types of tests: The Timed Up and Go (TUG) test, the Functional Reach Test, and the Tandem Test. Two questionnaires were used - the Falls Efficacy Scale-International (FES-I) and quality of life questionnaire (the Short Form [SF]-36) - in order to establish a connection between the intake of prescription of medication and the quality of life of this population. The statistical analysis was performed using R software version 3.2.2.

## **Results**

The analysis of factors indicated that risk of fall was directly related to the amount of medications used by patients. The medicines associated with the risk of falls were grouped into nine categories: 28%, antihypertensive; 17%, anti-cholesterolemic; 8%, cardiovascular agents; 2%, musculoskeletal pain; 2%, hormones; 14%, central nervous system agents; 6%, vitamins, 8%, anti-diabetic; and 15%, other target action medication. When the risk of fall was compared according to each category, the most significant difference in proportion was observed when related to central nervous system.

## **Conclusion**

The data analysis showed that type of medications prescribed should be considered to better understand how some are related to the risk of fall in elderly people. The knowledge of how some prescribed medications can affect the way of life in the elderly community helps to guide some clinicians' orientations to prevent possible injuries.

## **Background**

Aging is an irreversible process of all living beings.<sup>1,2</sup> One of the great challenges we face is to learn how to live in a healthy way with a high quality of life.<sup>3,4</sup> Bad habits acquired in youth such as sedentarism and poor diet increase susceptibility to chronic diseases in adulthood.<sup>5-7</sup> Among the chronic diseases that affect the aging process are Alzheimer's disease, depression, diabetes, systemic arterial hypertension, and heart disease.<sup>8</sup> In the people of this age group, several ill-defined factors predispose them to unintentional falls that subsequently lead to impaired activities of daily living and an increase in mortality.<sup>5,8,9</sup> Recent studies have demonstrated the possibility of the relationship between metabolic syndrome (MetS) and the risk of falling in the elderly population.<sup>8-13</sup> The World Health Organization (WHO) created the first criterion for MetS,<sup>13,14,19,43</sup> and shortly thereafter, the definition of MetS was improved by the European Resistance Insulin Study Group (EGIR), followed by the National Cholesterol Education Program - Adult Treatment Panel III (NCEP - ATPIII)<sup>15-16</sup> and finally by the International Diabetes Federation (IDF). The latter organization has created a more accessible tool for research needs and improved clinical use.<sup>15,20</sup> According to the IDF and other organizations, the central components of MetS are central obesity, increased triglyceride levels, low HDL cholesterol, increased blood pressure, and elevated fasting plasma glucose.<sup>13,16-20</sup> Due to the central components of MetS, it is believed that the individual will become more dependent on certain medications.<sup>21,22</sup> Additionally, the side effects generated by medications and the common alterations in aging increase the risk of the elderly suffering injury due to falls.<sup>10,21-26</sup> The objective of this study was to perform an analysis of the medications used by the Brazilian elderly population. We also sought to investigate the relationship between MetS and the groups of medications prescribed, their interactions and concentrations, and this population's risk of suffering some type of fall.

## Methods

The study was implemented with 102 participants, aged 60 years or older. These participants included a group of volunteers who resided in the municipality of Viçosa-Minas Gerais, Brazil.

**Clinical Data:** Volunteers who participated in the study required a recent laboratory examination or they had completed one within the last six months. The examination included the measurement of cholesterol (HDL), glucose, and triglyceride levels.

*Abdominal circumference:* For all participants, abdominal circumference was measured (this measurement was performed by positioning a tape measurer along a horizontal plane between the lower rib margin and the upper border of the iliac crest).

*MetS:* Based on the criteria of the NCEP-ATP III group, MetS was defined by the presence of hypertension and two or more of the following criteria:<sup>10,13-18</sup>

1. Abdominal obesity: From NCEP-ATP III the waist circumference is  $\geq 102$  cm in men and  $\geq 88$  cm in women. But according to the IDF, the waist measurement parameters for South and Central America

are established according to data from South Asia, where waist circumference associated with MetS has values of  $\geq 90$  cm in men and  $\geq 80$  cm in women. The criteria from IDF were used in this study.<sup>20</sup>

2. Hypertriglyceridemia: triglycerides  $\geq 150$  mg/dL
3. High density lipoprotein cholesterol (HDL):  $\leq 40$  mg/dL for men and  $\leq 50$  mg/dL for women.
4. Alteration of glucose metabolism: high fasting glycemia  $\geq 100$  mg/dL.
5. Blood pressure parameters were defined according to the criteria established by the NCEP-ATP III group, where the value considered as consistent with MetS was  $\geq 130/85$  mmHg.

*Medication analysis:* The volunteers had to present their list of medications in current use, the time of consumption, the dosages, and the reason for their use.

*Tests for fall risk analysis:* Three tests were performed: 1. *Timed Up & Go (TUG)* test: The (TUG) test was used as a test for functional mobility and fall risk analysis.<sup>27</sup> The TUG test is a simple test that measures the likelihood that an elderly person will fall.<sup>28</sup> A standard chair is used, and the participant is invited to stand up, walk a line 3 meters away, and return to the seat. The timer was triggered from the point at which the patient's buttocks moved from the seat and made contact with the back of chair. The volunteers for whom it took  $\geq 13$  seconds to perform the test were identified as having a higher risk of falling.<sup>27,28</sup> The chronometer used was a mobile device model X1069 G(Motorola).

**2. Gait analysis:** Participants performed the Tandem test, which consists of walking in a straight line drawn on the floor and placing the non-dominant foot heel in front of the toes of the dominant foot at each step.<sup>29</sup> The scoring for the test was determined according to the following characteristics: The participant who completed 10 steps in the straight line was deemed as having good performance and normal balance. If the participant completed 7-9 steps, he/she was considered to have an average balance deficit, but no risk of falling was assessed. If the participant completed 4-7 steps, they demonstrated a moderate deficit in balance, which lead to some concern about the risk of falling. Finally, the participants who achieved completion of less than 4 steps were considered as having a high level of balance deficit and thus were considered to be at high risk of falling.<sup>29,30</sup>

**3. Functional Reach Test:** In the Functional Reach Test, participants standing in the orthostatic position next to a wall marked with a straight tape measure were instructed to perform a trunk flexion movement. During this movement, the extended arm demarcated the limit of its antero-posterior movement, without involving the movement of the legs, which must maintain their alignment from the beginning to the end of the movement. Values  $\geq 15$  test score indicated that there was a deficit in balance that can lead to a greater risk of falling.<sup>30,31</sup>

**Mean arterial pressure (MAP):** The MAP is a term to describe an average blood pressure in an individual. It is defined as the average arterial pressure during a single cardiac cycle. The equation for the MAP is as follows:  $MAP = \frac{1}{3}$  systolic blood pressure (SBP) +  $\frac{2}{3}$  diastolic blood pressure (DBP).<sup>32</sup>

**Falls history:** The volunteers participating in the study were questioned about the occurrence of falls within a one-year period.

**Falls Efficacy Scale-International (FES-I):** This is a questionnaire that assesses the individual's concern about suffering falls when performing their daily activities. The FES-I is a questionnaire modified by Chris Todd and Lucy Yardley through the Falls Efficacy Scale (FES), which was developed by Tinetti. It consists of 16 questions focused on activities of daily living and social life, with answers to each item having a score from 1 to 4 (1 = not worried, 2 = worried, 3 = very worried, and 4 = extremely worried). The scoring system ranges from 16 to 64 points. A score of 16-19 points indicates the participant has little concern about falling. Values of 20-27 characterize a moderate preoccupation with concern about falling, while values ranging from 28-64 points indicate the participant maintains great concern about suffering a fall.<sup>33,34</sup>

**Quality of Life Questionnaire (the Short Form [SF]-36):** This is a questionnaire that measures health status. It calculates the cost-benefit ratio of a health treatment. It consists of eight scales, which are the weighted sums of questions in each section. The lower the score, the greater the degree of disability, and the higher the score, the lesser the degree of disability. A score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability, which is associated with a perceived excellent quality of life.<sup>26,35</sup>

## Results

MetS-correlated variables such as MAP ( $P = 0.004185$ ), HDL ( $P = 0.000726$ ), and Triglycerides ( $P = 0.002466$ ) are shown to be the most significant factors associated with an increased risk of falls in elderly people, according to the logistic regression results (Table S1). Another significant factor which also can be emphasized among MetS factors is the number of medications prescribed to correct MetS ( $P = 0.005742$ ). When the principal components approach was performed to retrieve the correlation among all the studied factors, the number of medications prescribed, and the risk of falls behaved as strong components, especially in patients with a history of fall (Fig. 1). When the classes of medications were considered, the proportions among the falls risk (Fig. 2A) and the non-falls risk group (Fig. 2B) have shown considerable differences by chi-square test analysis ( $P = 0.01586$ ). A deeper analysis showed that the medications of fall risk patients could be grouped into the following categories: 28%, antihypertensive; 17%, anti-cholesterolemic; 8% non-antihypertensive cardiovascular medications; 2%, musculoskeletal pain; 14%, central nervous system agents; 6%, vitamins; 8% anti-diabetics; and 15%, medications with other target action. When the risk of fall was compared among each category, the most significant difference in proportion was observed when related to central nervous system, and other target action medications, which is the opposite of what is reported in the literature. Also, a significant correlation was observed for central nervous system agents. As some categories of medications could influence the way of life, we performed a survey to evaluate quality of life using the SF-36 questionnaire. The SF-36 consists of eight scaled scores, which are the weighted sums of the questions in their section where we use the following scores (vitality, mental health and physical functioning). The performance of

the logistic regression in the two groups, one with MetS and the other with risk of fall, showed distinct profiles. The MetS group had vitality ( $P = 0.000535$ ) and mental health ( $P = 0.028382$ ) as the most significant scores. The number of medications ( $P = 0.000102$ ) was the only significant factor in the fall risk group.

## Discussion

Our study showed that the medications used for the correction of hypertriglyceridemia and insulin resistance is another important factor to explain the occurrence of falls in the population aged greater than 60 years. In previous studies<sup>10,16,36–38</sup> participants diagnosed with the MetS presented with a higher prevalence of hypertension relative to the group without MetS (18.4% versus 10.6%,  $P < 0.001$ ). Another study demonstrated a higher fall rate in those MetS in comparison to those without MetS (45.7% versus 23.3%,  $P < 0.001$ ), and abdominal obesity, hypertriglyceridemia, elevated blood pressure, and serum glucose levels were identified as the main factors that may lead to falls. However, in these studies there was no direct analysis examining the relationship between falls with visual abnormalities and the use of medications.

Seeking to better understand how MetS generates a higher occurrence of falls in the elderly<sup>39</sup>, we further analyzed the drug interaction and the risk of falls (assessing the individual in an orthostatic position while touching the ground with his or her hand or knee). Analysis of the medications was performed by observing the class, the side effects, the proportion ingested, and the time of consumption (Table S2). One study demonstrated that the use of psychotropic medications increases wounds and fractures of the femur.<sup>22</sup> Other studies reported that the use of phenothiazine, tricyclic antidepressants, barbiturates, and benzodiazepines has a high association with a risk of falls, and may lead to fractures.<sup>21–23</sup> However, in this study, there was no clear association between diuretics and antihypertensive agents and an increased risk of falls. The result of logistic regression analysis in another study showed that a fall could be a consequence of patients who have a fever, due to associated hypotension and malaise that may be present.<sup>10</sup> In a different study,<sup>37</sup> the researchers found that there is no increased risk of falls in users of antihypertensive medications compared to non-users of the medications (adjusted odds ratio = A = 1.13; confidence interval [CI] 95% = 0.88–1.46). Our data demonstrated that the highest fall rate is related to the use of central nervous system medicines and another target action, resulting in 14% and 15% respectively. The relationship was also<sup>40</sup> who found between the use of statins and the side effect of myalgia, in addition to causing other serious pathologies in skeletal muscle. Various physiological mechanisms appear to contribute to the loss of muscular strength of the lower extremities in the elderly.<sup>41</sup> Results also demonstrate that balance training can be a useful strategy in balance rehabilitation and fall prevention, especially in the population studied. This can lead to an improvement in their quality of life and less public health costs.<sup>42</sup> A deeper study is still required to understand how some classes of medications affect the way of living in elderly people.

## Conclusion

Our study showed that the types of medications can actually impact the rate of falls in elderly people. Certainly, a deeper analysis is required to understand the physiological mechanism behind this relation. Then clinicians would be able to guide those old people and their carriers to prevent falls, and thus causing less public spending on the public health care system. Consequently, a better quality of life in this population may be achieved.

## Abbreviations

**1. MetS**

Metabolic Syndrome

**2.TGU**

Timed Up and Go

**3.FES-I**

Falls Efficacy Scale – International

**4.SF-36**

Short-form health survey

**5.WHO**

World Health Organization

**6.EGIR**

European Resistance Insulin Study Group

**7.NCEP-ATP III**

National Cholesterol Education Program – Adult Treatment Panel III

**8.IDF**

International Diabetes Federation

**9.HDL**

High Density Lipoproteins

**10. MAP**

Mean arterial pressure

## Declarations

**Ethics approval and consent to participate:** Ethical approval was received from the Universidade Federal de Viçosa committee with the CONEP Resolution 466/2012 with the number 3.259.354. Any contact can be made by the email: cep@ufv.br.

**Consent for publication:** Not Applicable.

**Availability of data and material:** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that they have no competing interests.

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**Authors' contributions:** ESS, WCS and ATRV made substantial contributions to the design of this work. ESS designed the experimental setting, performed the experiment, analysed and interpreted the data, and was the major contributor in writing the manuscript. ATR performed the statistics analysis and helped the interpretation of the results. WCS contributed to the data acquisition and the ethical revision.

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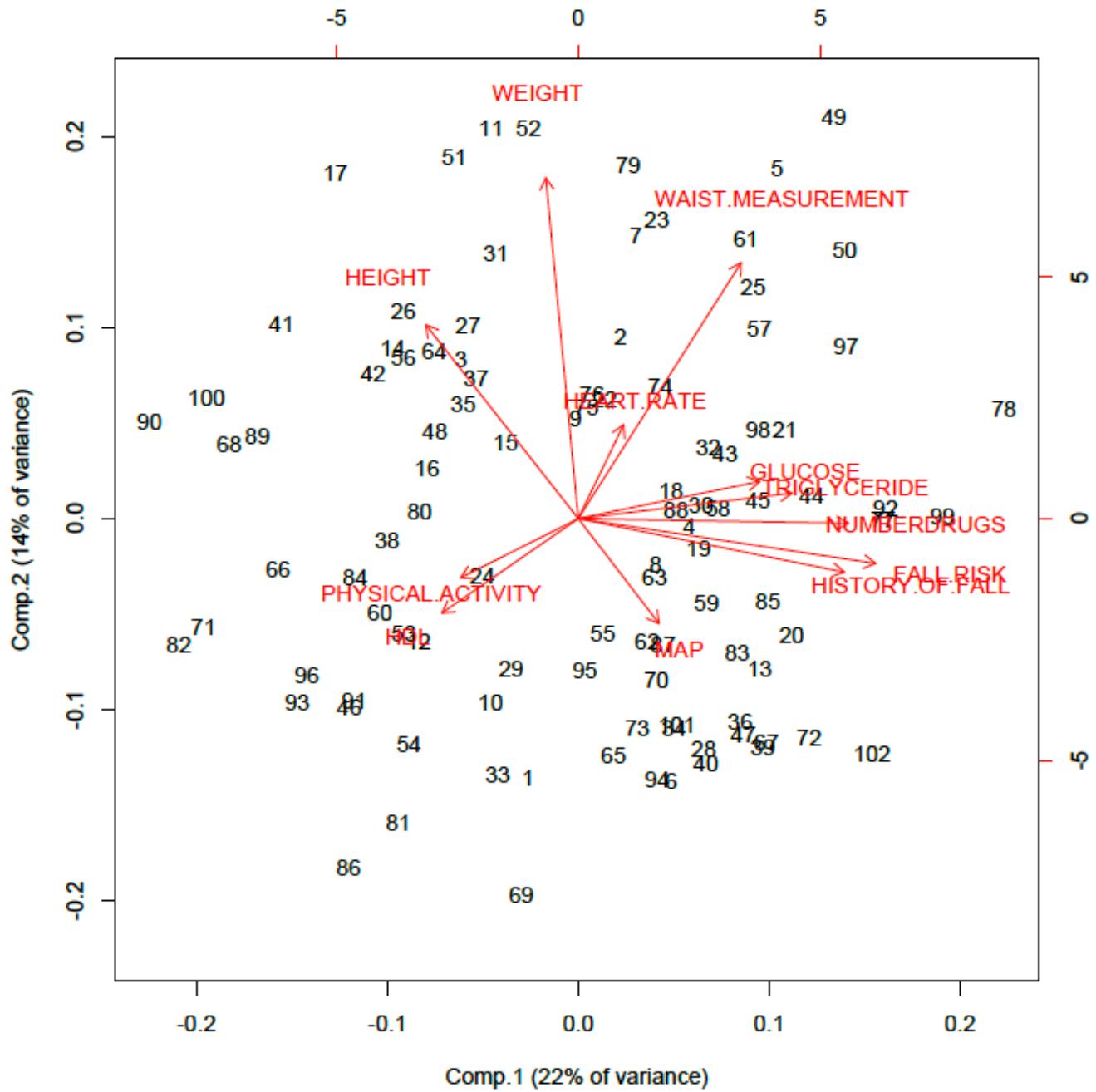
## Tables

Due to technical limitations, Tables 1 and 2 are only available as a download in the supplemental files section

## Supplemental Legends

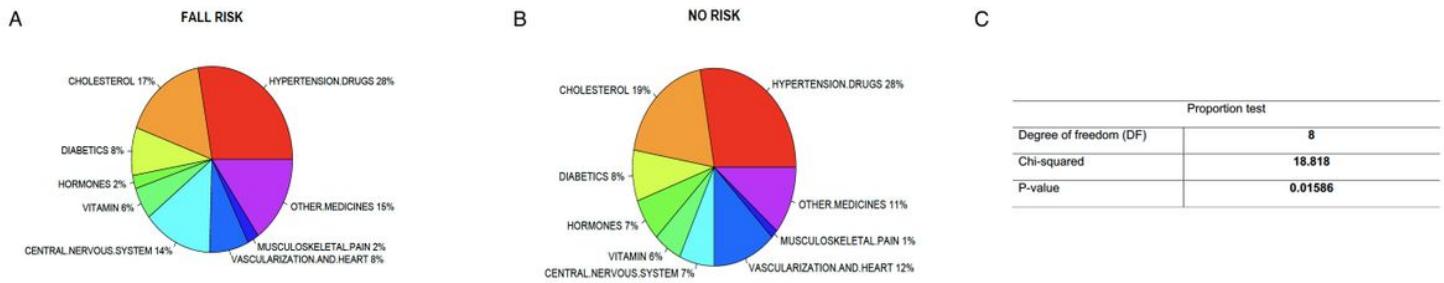
**Figure S1:** 3D graphics of the groups of MetS and risk of fall according to number of medications, vitality and mental health scores (SF-36).

## Figures



**Figure 1**

The biplot shows the correlations among the metabolic syndrome (MetS) factors, the number of medications, and risk of falls (red arrows). The plot numbers represent individuals and the red arrows show tendency according to the variance components.



**Figure 2**

Proportion of classes of medications comparing fall risk (A) and non-fall risk groups (B). The proportion test (C) indicates a statistical significance between the two groups.

## Supplementary Files

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