

Identification of risk factors for falls in people with multiple sclerosis: a systematic review of prospective studies

Identificação de fatores de risco para quedas em indivíduos com esclerose múltipla: uma revisão sistemática de estudos prospectivos

Identificación de los factores de riesgo de caídas en individuos con esclerosis múltiple: una revisión sistemática de estudios prospectivos

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ABSTRACT | The objective of this study was to identify demographic, clinical, and instrumental variables associated with falls in people with multiple sclerosis (MS), via systematic review, based on prospective data. The search was conducted in these databases: Medline, Web of Science, Bireme e CINAHL via a search strategy that combined the descriptors “multiple sclerosis”, “falls”, “accidental falls”, “fall risk”, “postural control” and “balance”, followed by manual search. Eligibility criteria were prospective cohort studies with a minimum 3-month follow-up of falls that assessed the association of a demographic, clinical or instrumental variable in relation to a higher fall risk in people with MS. The modified Newcastle-Ottawa Quality Assessment Scale was used for study quality assessment. A total of 357 studies were identified, of which 12 were included in the systematic review and 1,270 patients were included. In this study, 740 (58.26%) patients were classified as fallers, 396 (31.18%) patients had recurrent falls (≥ 2 falls within the stipulated period) and 530 patients (41.74%) were classified as non-fallers. Except for spasticity and dual task cost in gait speed, all investigated variables showed conflicting results regarding their association with a higher fall risk. More studies with clinical homogeneity phenotypes of MS individuals and using validated assessment instruments are necessary to establish a robust association of other

clinical, instrumental, and demographic variables with a higher fall risk.

Keywords | Multiple Sclerosis; Accidental Falls; Fall Risk; Systematic Review.

RESUMO | O objetivo deste estudo foi identificar, a partir de uma revisão sistemática, variáveis clínicas, instrumentais e demográficas associadas com maior risco de queda em indivíduos com esclerose múltipla (EM), com base em dados prospectivos. A pesquisa foi conduzida nas bases de dados Medline, Web of Science, Bireme e CINAHL, utilizando os descritores “esclerose múltipla”, “quedas”, “quedas acidentais”, “risco de quedas”, “controle postural” e “equilíbrio”, seguido de buscas manuais. Foram considerados elegíveis estudos de coorte prospectivos, com período mínimo de acompanhamento das quedas de três meses, que avaliassem a associação de determinada variável demográfica, clínica ou instrumental em relação a maior risco de queda em indivíduos com EM. A escala de Newcastle-Ottawa modificada foi utilizada para avaliação da qualidade metodológica dos estudos incluídos. Foram identificados 357 estudos, 12 dos quais foram incluídos na revisão sistemática, com total de 1.270 pacientes incluídos. Destes, 740 (58,26%) pacientes apresentaram um ou mais episódios de queda, 396 (31,18%) apresentaram episódios

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de queda recorrentes (2≥ quedas no período estipulado), e 530 (41,74%) não apresentaram nenhum episódio. Com exceção da espasticidade e do impacto da dupla tarefa na velocidade da marcha, todas as variáveis investigadas apresentaram resultados conflitantes quanto às suas associações a maior risco de quedas. São necessários mais estudos que apresentem homogeneidade dos fenótipos clínicos de indivíduos com EM, além da utilização de instrumentos de avaliação validados, a fim de estabelecer uma associação robusta de outras variáveis clínicas, instrumentais e demográficas com maior risco de queda.

Descritores | Esclerose Múltipla; Quedas Acidentais; Risco de Quedas; Revisão Sistemática.

RESUMEN | El objetivo de este estudio fue identificar, a partir de una revisión sistemática, variables clínicas, instrumentales y demográficas asociadas con un mayor riesgo de caída en individuos con esclerosis múltiple (EM), con base en datos prospectivos. La búsqueda se realizó en las bases de datos: Medline, Web of Science, Bireme y CINAHL, utilizando los descriptores “esclerosis múltiple”, “caídas”, “caídas accidentales”, “riesgo de caídas”, “control postural” y “equilibrio”, seguido de búsquedas manuales. Se consideraron elegibles los

estudios de cohorte prospectivos con un período de seguimiento mínimo de caídas de tres meses, que evaluaron la asociación de una variable demográfica, clínica o instrumental en relación con el mayor riesgo de caídas en individuos con EM. La escala modificada de Newcastle-Ottawa se utilizó para evaluar la calidad metodológica de los estudios incluidos. Se identificaron 357 estudios, 12 de los cuales se incluyeron en la revisión sistemática, con un total de 1.270 pacientes incluidos. De estos, 740 (58,26%) pacientes tuvieron uno o más episodios de caída, 396 (31,18%) presentaron episodios de caída recurrentes (2≥ caídas en el período estipulado), y 530 (41,74%) no presentaron ningún episodio. Con excepción de la espasticidad y del impacto de la doble tarea en la velocidad de la marcha, todas las variables investigadas presentaron resultados conflictivos en cuanto a sus asociaciones a mayor riesgo de caídas. Se requieren más estudios que presenten homogeneidad de los fenótipos clínicos de pacientes con EM, además del uso de instrumentos de evaluación validados, para establecer una asociación robusta de otras variables clínicas, instrumentales y demográficas con mayor riesgo de caída.

Palabras clave | Esclerosis Múltiple; Caídas Accidentales; Riesgo de Caídas; Revisión Sistemática.

INTRODUCTION

Multiple sclerosis (MS) is a chronic, demyelinating and neurodegenerative disease that affects the central nervous system, constituting one of the main causes of disability in Western adults^{1,2}. MS indexes have been alarmingly growing in most countries, reaching more than 2.5 million individuals worldwide³. This disease requires special attention from the Brazilian health system, since it is estimated the prevalence of approximately 8.69 MS cases every 100,000 inhabitants⁴, which can represent a huge burden for long-term health and socioeconomic resources.

The disease etiology is not yet completely elucidated, however, it is believed to be an autoimmune disease resulted from the interaction between environmental and genetic factors^{5,6}. The large distribution of lesions is recognized as one of the main consequences of the disease and results in a variety of signs and symptoms, such as muscle weakness, paresthesia, pain, fatigue, heat hypersensitivity and visual, sensory, motor, gastrointestinal, sphincter and cognitive alterations^{5,7}.

The consequences of these problems associated with MS represent great concern and may potentialize the incidence of falls⁸. Previous studies have shown that more

than 50% of individuals with MS have a falling episode during a period of three to six months of follow-up, causing fractures, limitations in the activities of daily living (ADL) performance, restrictions on participation and reduction in the perception of quality of life⁹⁻¹¹. In addition, between 62% and 78% of the falling episodes occur at home in the daytime, mostly during the performance of basic ADL such as moving, gait between rooms and personal hygiene^{12,13}.

Systematic reviews with meta-analysis have identified that using an auxiliary device in gait, cognitive and balance dysfunctions, a higher level of disability, besides a (primary or secondary) progressive subtype of the disease are associated with a higher fall risk in this population. However, these studies included, mostly, investigations that assessed falls retrospectively, which may cause an underestimation of the falls frequency and minimization of the findings validity^{14,15}. Additionally, Gunn et al. (2015)¹⁶ identified that, although ADL, gait and balance training programs promote benefits in the capability of individuals with MS, the magnitude of this effect does not significantly impact on outcome measures related with falls.

To date, no systematic review has elucidated the factors associated with the occurrence of accidental falls

in individuals with MS by selecting only data prospectively collected through fall journals during the minimum period of three months, as advocated by the European guidelines for the study of falls¹⁷. Since the development of this systematic review substantively contributes to decision-making in health, the identification of factors associated with higher fall risk may be valuable for the development, assessment and implementation of efficient intervention programs aimed at preventing falls.

Therefore, this study aimed to identify clinical, instrumental, and demographic variables associated with a higher fall risk in individuals with MS, via systematic review, based on prospective data.

METHODOLOGY

This study consists of a systematic review of prospective cohort studies. The review was performed according to the PRISM (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendations, seeking standardization of the study conduction and the report of systematic reviews.

Search strategy

To expand or restrict the search, we used Boolean operators (AND, OR). The study was conducted in the electronic databases Medline, Web of Science, Bireme and CINAHL using the descriptors “multiple sclerosis”, “falls”, “accidental falls”, “fall risk”, “postural control”, “balance” and their respective terms in Portuguese. The references of the articles were also consulted, seeking for the detection of further studies. All the literature published until the last search performed, according to the established criteria, was considered; the articles were included if they were available in English, Portuguese, Spanish and French. The last search was conducted in April by two individuals with training and experience in the use of databases.

Eligibility criteria

Original articles were considered eligible according to the following inclusion criteria: (1) prospective cohorts published from January 2008 to April 2018; (2) identification of clinical, instrumental and demographic variables associated with the fall risk; (3) prospective follow-up of falls during the minimum period of three months¹⁷. In turn, the following exclusion criteria

were adopted: (1) evaluation of the incidence of falls retrospectively; (2) follow-up of the fall incidence during periods that were shorter than three months; (3) abstracts, unpublished data and review articles.

Due to the limited level of evidence found, it was not possible to stratify individuals with MS according to their level of disability, thus, all the studies were included independently of the MS clinical phenotype. Outcome measures were variables related to higher fall risk, including parameters such as gait, patient perceptions, balance, use of auxiliary devices or medications, and performance-based tests and scales (such as The Berg Balance Scale and the Timed Up and Go test).

Moreover, due to the wide variety of definitions of falls and classifications for individuals who have falling episodes, these variables were not considered in our inclusion criteria.

Selection of studies and data extraction

After the search for the articles in the predetermined databases and removal of duplicate articles, three authors (LGO Silva, TKM Melo and EC Barboza) evaluated titles and abstracts seeking to identify studies that explored the topic of interest. Subsequently, the three authors individually applied the inclusion and exclusion criteria after reading the full text. In case of discrepancies, they discussed the article in question and deliberated until consensus.

The name of the first author, journal, year of publication, study design, frequency of falls, size and sociodemographic characteristics of the sample, follow-up time (in months) and results of outcome measures associated with higher fall risk were extracted from the eligible studies for the elaboration of tables.

The results are presented using the odds ratio (OR), and their respective confidence interval (CI) values at 95%. OR is used to identify whether a given exposure variable is a risk factor for an outcome measure in particular¹⁸. An OR=1 indicates no difference between groups; an OR>1 indicates a greater chance of the outcome measure occurring in the exposed group; an OR<1 indicates a lower chance of the outcome measure occurring in the exposed group.

Analysis of methodological quality

The quality of the articles was evaluated using the Newcastle–Ottawa scale. Which is a valid scale for evaluating the methodological quality of non-randomized studies¹⁹. Due to the absence of a validated minimum score

in the literature, the articles were evaluated according to the bias risk classification used by the systematic review of a similar topic¹⁵. Therefore, the studies were classified as low risk of bias (6-9 points), medium risk of bias (4-5 points) and high risk of bias (1-3 points).

RESULTS

We identified 357 studies after the search in the databases and one study via the references consultation in the articles found, 318 studies remained after the removal of the duplicates.

The evaluation of the titles and abstracts resulted in 43 studies tracked to apply the eligibility criteria. Thus, 12 articles were selected to perform the systematic review, as illustrated in the flow diagram (Figure 1). Nilsagård et al.⁹ showed results of outcome measures in the same population in two distinct studies, therefore, only the findings of the first study were included to avoid duplication.

We included 1,270 individuals with MS from the 12 selected articles. A total of 740 (58.26%) patients were classified as fallers, 396 (31.18%) patients had recurrent falls (2≥falls in the stipulated period) and 530 individuals (41.74%) were classified as non-fallers (Table 1).

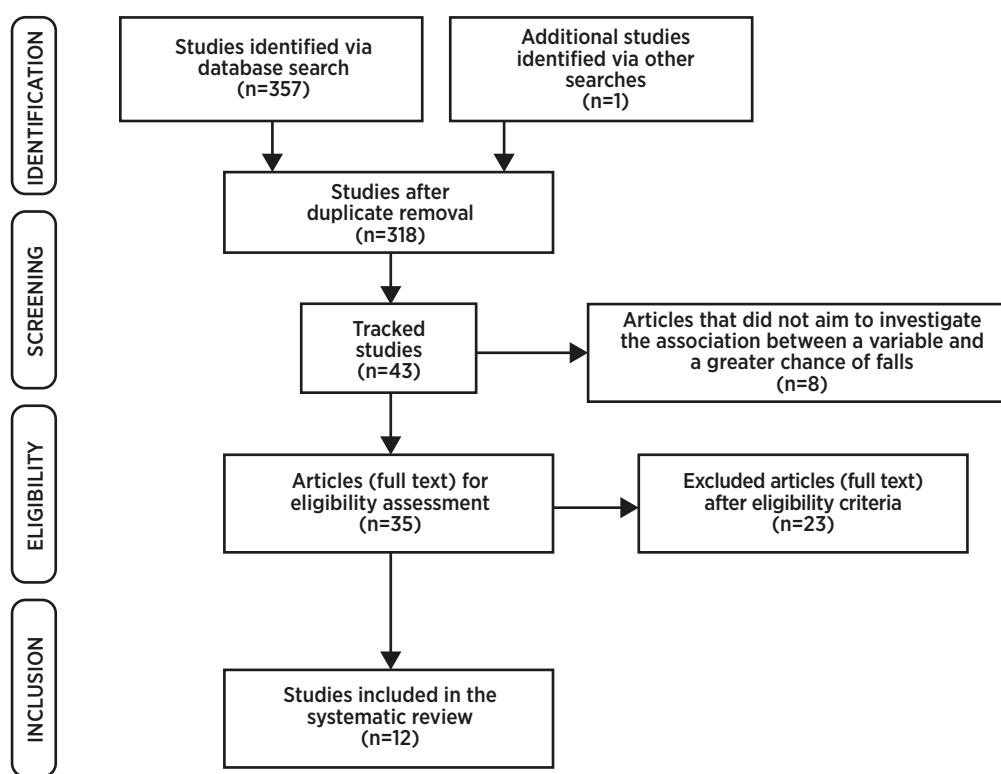


Figure 1 - Flowchart of selected studies

Table 1 - Characteristics of the selected studies

| First author/year | Sample size | % Non-fallers (≥1) | % Recurrent falls (≥2) | % Fallers | Follow-up Time | Variables related to falls |
|---------------------------------|-------------|--------------------|------------------------|-----------|----------------|---|
| Nilsagård (2009) ¹⁰ | 76 | 63.15% (48) | 57.89% (44) | NA | 3 months | Age, EDSS, gender, use of medications, spasticity, MS subtype, use of an auxiliary gait device, sensitivity, fear of falling, Berg balance scale, timed up and go test, four square step test, 12-item multiple sclerosis walking, urinary tract dysfunctions, dual task, cognition |
| Kasser (2011) ²⁰ | 92 | 52% (48) | 35% (32) | NA | 12 months | Gait, muscular strength, balance, sensory orientation |
| Prosperini (2013) ²¹ | 100 | 41% (41) | 19% (19) | 2% (2) | 3 months | Berg balance scale and static posturography |

(continues)

Table 1. Continuation

| First author/year | Sample size | % Non-fallers (≥1) | % Recurrent falls (≥2) | % Fallers | Follow-up Time | Variables related to falls |
|--------------------------------|-------------|--------------------|------------------------|--------------|---------------------|--|
| Gunn (2013) ²² | 148 | 70.3% (104) | 52.7% (78) | NA | 3 months | Spasticity, age, gender, MS subtype, urinary tract dysfunctions, EDSS, use of an auxiliary gait device, use of medications and cognition |
| Hoang (2014) ²³ | 210 | 60% (126) | 32.85% (69) | 57.9% (121) | 6 months | Balance, manual dexterity, gait speed, cognition |
| Cameron (2015) ²⁴ | 248 | 57.66% (143) | NA | 44.35% (110) | 6 months | Urinary tract dysfunctions |
| Nilsagård (2016) ²⁵ | 47 | 47% (22) | 29% (14) | NA | 3 months | 6-minute walk test and maximum distance walked |
| Mazumder (2015) ²⁶ | 54 | 75.9% (41) | 63% (34) | 44.4% (24) | 12 months | Fear of Falling |
| Etemadi (2017) ²⁷ | 60 | 63.33% (38) | 43.3% (26) | NA | 6 months | Dual task |
| Zelaya (2017) ²⁸ | 51 | 62.74% (32) | 29% (15) | NA | 3 months | Urinary tract dysfunctions |
| Comber (2018) ²⁹ | 100 | 56% (56) | 34% (34) | NA | 3 months | Use of medicines |
| Tajali (2017) ³⁰ | 84 | 49% (41) | 37% (31) | NA | 6 months | Timed up and go test, fear of falling, 12-item multiple sclerosis walking scale, dual task |
| TOTAL | 1.270 | 58.26% (740) | 31.18% (396) | 42% (257) | Average: 5.5 Months | |

EDSS: Expanded Disability Status Scale of Kurtzke; MS: Multiple sclerosis.

Analysis of methodological quality

Most of the studies showed low and medium risk of bias (Table 2). The follow-up periods ranged from three

months to one year, with an average of 5.5 months of follow-up. The methodological quality of the studies included ranged between 6 and 8 points (Table 2), according to the adapted scale of Newcastle-Ottawa^{15,19}.

Table 2 – Newcastle-Ottawa Scale adapted for evaluation of the methodological quality of the non-randomized studies included in this systematic review

| Study | Selection | | Comparability | | | Outcomes | | Score |
|-------------------|-----------|---|---------------|----|---|----------|---|-------|
| | A | B | C | D | E | F | G | |
| Nilsagård (2009) | * | * | * | ** | * | * | | 7 |
| Kasser (2011) | * | * | * | ** | * | * | * | 8 |
| Prosperini (2013) | * | * | * | ** | * | * | * | 8 |
| Gunn (2013) | * | * | * | ** | * | * | * | 8 |
| Hoang (2014) | * | * | * | ** | * | * | * | 8 |
| Cameron (2015) | | * | | ** | * | * | * | 6 |
| Nilsagård (2016) | * | * | * | ** | * | * | * | 8 |
| Mazumder (2015) | * | * | * | ** | * | * | * | 8 |
| Etemadi (2017) | * | * | * | ** | * | * | * | 8 |
| Zelaya (2017) | * | | | ** | * | * | * | 6 |
| Comber (2018) | * | * | * | ** | * | * | * | 8 |
| Tajali (2017) | * | * | * | ** | * | * | * | 8 |

Point; A: representativeness – truly representative () (includes all types of MS and disability levels); some representativeness (**) (limited to the specific classification of MS or level of disability); convenience group (O) (limited to a specific group or level of disability); no description (O); B: selection of unexposed subjects – same community (*) ; from another community (O); no description (O); C: method of assessing risk factors – validated objective measures (*) ; non-validated objective measures (**) ; self-report (O); no description (O); D: comparability of subjects – control group with EDSS and age (**); control group with age (*) ; without control group (O); E: assessment of outcomes: external observation or validated measures (*) ; prospective diary (*) ; retrospective self-report (O); not performed or not described (O); F: observation period – more than three months (*) ; less than three months (O); G: appropriate follow-up: complete (*) (all subjects included); subjects who did not do follow-up do not cause bias or is a description of predicted loss (*) ; lower than 80% follow-up and there was no description of the loss (O).

Summarization of the main findings

The heterogeneity observed regarding the methods of assessment and reports of outcome measures, besides the variability of follow-up periods, hinders the performance of a systematic review with meta-analysis, preventing a critical analysis of the subject.

Use of medicines

Three studies (424 participants) assessed the association between the use of medications and a higher fall risk^{10,29,24}. Genitourinary system and sex hormones medications cause a greater chance of the individual having one or more falling episodes (OR=4.16; 95%CI=1.294–13.369) or two or more falling episodes (OR=5.154; 95%CI=1.427–18.609)²⁹. Additionally, for each the nervous system medication used, the chances of falling increase 43% (OR=1.43; 95%CI=1.09–1.93), while the use of antineoplastic and immunosuppressants medicines resulted in a 48% reduction in the chance of falls (OR=0.52; 95%CI=0.28–0.95)²⁴. In contrast, the association between the consumption of medications and falls was not observed by Nilsagård et al.¹⁰ (OR=1.22; 95%CI=0.45–3,27).

Fear of falling

Three studies (278 participants) sought to evaluate the association between fear of falling and a higher fall risk. Two studies assessed the fear of falling via the Falls Efficacy Scale-International (FES-I), a validated scale for assessing fear of falling in individuals with MS, while a study used patients' self-reports. The fear of falling was found to be strongly associated with the risk of recurrent falls in the next three months (OR=1.22; 95%CI=1.04–1.43)²⁶, while this association was not observed in the studies by Nilsagård et al.¹⁰ and Gunn et al.²², showing respectively OR=1.01 (95%CI=0.96–1.06) and OR=0.95 (95%CI=0.57–1,58).

Urinary tract dysfunctions

The relation between urinary tract dysfunctions and falls was investigated by three studies (275 participants)^{10,22,28}. Different methods based on self-reported patients were used to obtain outcome measures related to urinary tract dysfunctions. Individuals who showed falling episodes

had a higher prevalence of urinary tract dysfunctions when compared to individuals who did not have falling episodes²⁸. Recurrent falls were associated with urinary urge-incontinence (OR=57.57; 95%CI=3.43–966.05)²⁸ and with frequent urinary dysfunctions (OR=1.08; 95%CI=0.41–2.80)¹⁰. In contrast, the presence of urinary urgency self-report was not found to be associated with a higher probability of an individual experiencing a falling episode (OR=1.08; 95%CI=0.41–2.80)²².

Use of auxiliary devices

Two studies (224 participants) evaluated the association between the use of an auxiliary gait device and higher fall risk^{10,22}. Interestingly, the use of an auxiliary device was found to be associated with a greater chance of the individual falling (OR=2.27; 95%CI=1.23–4.37), which is potentially increased by five times if the individual used the auxiliary device in his/her home and in external environment¹⁰. In contrast, Gunn et al.²² did not observe any association between the use of an auxiliary gait device and higher fall risk (OR=1.16; 95%CI=0.55–2,42).

Kurtzke Expanded Disability Status Scale

The level of disability assessed via the Kurtzke Expanded Disability Status Scale (EDSS) was associated with a higher fall risk in two studies (224 participants)^{10,22}. The odds of an individual having a falling episode were doubled at each point added in the EDSS (OR=1.99; 95%CI=1.22–3.40)¹⁰, although no relation has been observed in other studies (OR=0.81; 95%CI=0.49–1.35)²².

Dual task

The impact of performing dual task in relation to higher fall risk was explored by three studies (220 participants)^{10,27,30}. Different assessment instruments were used among the studies, including the cognitive timed up and go (TUG), GAITRite and changes in gait speed during the 2-minute walk test (2MW) and the timed 25-foot walk test (T25FW). The cost of the dual task in gait speed caused a greater chance for an individual to have recurrent falls (OR=1.23; 95%CI=1.02–4,45)²⁷, while performing cognitive tasks during TUG, 2MW and T25FW was not associated with future falls^{10,30}.

Spasticity

Two studies (224 participants) listed the evaluation of spasticity via the Modified Ashworth scale (MAS)^{10,22} as one of the variables associated with a higher fall risk. The authors observed that the score of 1 in the scale is associated with a higher fall risk when compared to higher scores (OR=7.88; CI95%=2.16–28.80), indicating a nonlinear relation between the variables²². Additionally, Nilsagård et al.¹⁰ found a 14% increase in the chance of an individual falling to each point added in the MAS.

Berg Balance Scale

Individuals who had falling episodes had poorer performance in the Berg balance scale when compared to individuals who did not fall ($p < 0.001$)²¹. The mean scores between the individuals in the scale ranged between 28 and 56 points for individuals without falls, and between 9 and 58 for individuals who had falling episodes¹⁰. Worst performance in the test was not associated with a higher fall risk during the observation period (OR=0.94; 95%CI=0.85–1.01)^{10,21}.

Cognition

Three studies investigated the association between cognitive functions and falls using different assessment instruments and different aspects of cognitive processing^{10,22,23}. Hoang et al.²³ showed that frequent falls were associated with poorer performance in the trails A and B test, indicating the influence of the reduction of executive functions in relation to the falling episodes.

Cognitive dysfunctions were not associated with a higher fall risk in the studies by Gunn et al.²² and Nilsagård et al.¹⁰, however, the evaluation instruments cover specific aspects of cognition that may not reflect a higher fall risk, demanding the evaluation of other aspects of cognitive processing.

Multiple sclerosis subtype

The relapsing-remitting (RR) subtype was the most prevalent in most of the studies, followed by the secondary-progressive (SP) and primary-progressive (PP) sub-types. Although individuals who had the progressive subtype (PP or PS) were more likely to have falling episodes

when compared to RR subtype, no statistical association between RR, SP or PP subtypes and a higher fall risk was observed in the studies^{10,22}.

DISCUSSION

The findings regarding the influence of drug use, dual task, MS subtype, use of auxiliary device, urinary tract dysfunctions, cognition, fear of falling and level of disability in the increased fall risk showed differences. However, spasticity was directly associated with a higher risk of an individual with MS to have falling episodes.

The necessity to identify factors that negatively contribute to the fall risk is crucial in individuals with MS, as these different elements interact as decisive and predisposing agents for less mobility and impaired physical performance. In this aspect, we understand that the fall risk is an incident that requires attention, since it can be an aggravating factor associated with the level of disability and a potential cause in the decline in quality of life, which can significantly compromise the daily activities of these individuals^{9,31}.

Although our results show a lower sample size and include only investigations that analyzed the falls prospectively, our findings regarding the frequency of falls are similar when compared to systematic reviews that investigated variables associated with the fall risk, including mostly retrospective cohort studies^{14,15}. Previous data demonstrated that older adults with MS have a twice greater probability of having harmful falls when compared to older adults without MS³². Additionally, although severe falls have a considerable financial and personal impact, only four studies have reported the amount of falls that resulted in injuries^{26,21,23}. Therefore, we recommend that the next studies describe the incidence of harmful falls and seek to understand the negative outcomes associated with this aggravation. Finally, it is possible that the conflicting results observed between the studies are resulted from the different methods of evaluating the variables, variability of the sample composition and divergent follow-up periods.

An important finding of this review was that spasticity is associated with a higher risk of an individual falling. Previous studies have shown that spasticity is associated with a higher fall risk in individuals with cerebrovascular accident^{33,34}. Therefore, understanding the impact of spasticity of lower limbs is crucial to identify complications and develop rehabilitation programs, since it plays an

important role in the development of contractures, limitations of motor function and reduced quality of life³⁵⁻³⁷. However, we emphasize that the instruments used for the spasticity assessment have limitations regarding their validity and reliability for individuals with MS, demanding the development of new instruments for the assessment³⁸.

During the association assessment between the presence of urinary tract dysfunctions and a higher fall risk, three studies used different questionnaires that are not validated to identify urinary symptoms. Moreover, different criteria for classification of individuals that have falls can minimize the validity of the findings and hinder the comparison between the studies. Several complex mechanisms can contribute to the association between urinary tract dysfunctions and falling, including the presence of urge-incontinence, which may cause an increase in gait speed in individuals with MS in an unsafe way when going to the bathroom, or resulting from the adverse effects of medications used for the neurogenic bladder control^{28,39}.

Therefore, the alteration in balance is one of the most common MS symptoms, which can cause falls and insecurity in the gait^{21,40}. Balance is one of the bases for all voluntary motor skills, therefore, it needs an intense integration between visual, vestibular and somatosensory systems for its maintenance⁴¹. The identification of balance alterations as a factor associated with the fall risk in individuals with MS is essential because it allows the development of specific treatment and prevention strategies, in addition to promoting the optimization of rehabilitation programs⁴⁰. In this context, the Berg balance scale is an often used instrument to assess balance alterations in individuals with MS⁴². A recent systematic review with meta-analysis did not show a strong enough level of evidence to justify the use of the Berg balance scale to identify the fall risk in individuals with MS, therefore, even if individuals who have falling episodes have worse performance on the scale when compared to those who do not have falling episodes, this instrument should be used with caution due to the multifactorial nature of falls⁴³.

The association between the use of medications and higher fall risk is already established in older adults^{44,45}. On the other hand, the use of multiple medications, mainly anticholinergic medications, is common in individuals with MS, potentially causing side effects such as blurred vision and dizziness²⁴. Therefore, the change in the prescription is a potential modifiable target for the

prevention of falls. Notably, the studies included in this review showed samples with distinct MS subtypes, causing divergent results between the association of medication use and falling.

The fear of falling is a clinical characteristic of multifactorial etiology present in approximately 60% of individuals with MS^{11,46}, which potentially results in functional decline and limitation of ADL performance^{46,47}. In this study, the fear of falling showed conflicting results regarding its association with the fall risk, however, this variable should be considered during the elaboration of rehabilitation programs, due to functional impairments associated with this condition. Thus, it is recommended to develop multifaceted interventions that include motor and cognitive aspects during their therapeutic approach^{10,26,22}.

Although the sample heterogeneity and the assessment methods have prevented the conduction of meta-analysis, causing the summarization of the main findings, this study is the first systematic review to identify factors associated with higher fall risk only via studies that assessed falls using prospective data for a minimum period of three months, as recommended by the European guidelines for the study of falls¹⁷. Moreover, the divergent definitions between the conceptualization of falling and the classification of the individuals who have falling episodes in the studies stand out as limitations of this review.

Due to the wide variety of clinical manifestations corresponding to the foci of disseminated lesions, it should not be expected that individuals diagnosed with MS have the same clinical evolution⁴⁸. However, even with the heterogeneity of the profiles, we could identify factors inherent to the disease that are associated with a higher fall risk using the theoretical framework advocated by the International Classification of Functioning, in order to initiate interventions aimed at its prevention. Thus, knowing the risk factors enables to implement strategies aimed at reducing the incidence and damage of falls, as well as promoting a qualification of health care.

As such, rehabilitation programs aimed at the promotion and prevention of falls in individuals with MS should focus on intrinsic (physical, cognitive and behavioral) and extrinsic (environmental factors and use of assistive technology) variables, to understand the interaction of these components in each specific fall situation. Furthermore, interventions that incorporate gait, balance and functional task training have a greater effect

on reducing falls compared to other types of intervention that aim only at mobility training (gait or mobility training programs, in general)⁴⁹. In all the dimensions of the fall prevention programs, the potential of multidisciplinary work is emphasized for a full approach of the phenomena that interfere in risk factors. Thus, multi-professional action demands the conduction of strategies shared by many health professionals.

CONCLUSION

According to the results of this systematic review, spasticity, and impact of the dual task on gait speed were associated with a higher fall risk in individuals with MS. Our findings reinforce the necessity to develop more studies that include similar clinical profiles of MS, besides the use of validated assessment instruments to identify other potential variables associated with higher fall risk.

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