Anemia and functional capacity in elderly Brazilian hospitalized patients

Anemia e capacidade funcional em idosos brasileiros hospitalizados

La anemia y la capacidad funcional de los ancianos brasileños hospitalizados

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Abstract

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This study evaluated the association between anemia and physical functional capacity in a cross-sectional population-based sample of 709 hospitalized elderly patients aged 60 years and over admitted to the Madre Teresa Hospital, Belo Horizonte, State of Minas Gerais, Brazil. The Mann-Whitney or "t" test, and chi-square or Fisher exact test were used for quantitative and categorical variables, respectively, and hierarchical binary logistic regression was used to identify significant predictors. The presence of anemia was found in 30% of participants and was significantly associated with decreased functionality according to the two measures which were used – ADL (activities of daily living) and IADL (instrumental activities of daily living). Anemia was also independently associated with older age. The results of this study demonstrate a strong association between the presence of anemia and lower levels of functional capacity. Further investigations are needed to assess the impact of anemia treatment on the functionality and independence of older people.

Anemia; Activities of Daily Living; Aged

Resumo

O presente estudo avaliou a associação entre anemia e a capacidade física funcional em idosos hospitalizados. Estudo transversal, com amostra de 709 participantes com idades ≥ 60 anos, internados no Hospital Madre Teresa, em Belo Horizonte, Minas Gerais, Brasil. Foram utilizados os testes de Mann-Whitney ou "t" e qui-quadrado ou teste exato de Fisher para as variáveis quantitativas e categóricas, respectivamente, e um modelo hierárquico de regressão logística foi usado para identificar as variáveis preditoras associadas. A presença de anemia foi encontrada em 30% dos participantes e associada a uma diminuição significativa da funcionalidade em ambos os índices utilizados – AVD (atividades da vida diária) e AIVD (atividades instrumentais da vida diária). A idade avançada também foi independentemente associada com anemia. Os resultados deste estudo demonstraram uma forte associação entre a redução da capacidade funcional e a presença de anemia. Investigações adicionais são necessárias para avaliar o impacto do tratamento da anemia na melhora da funcionalidade e independência em pessoas idosas.

Anemia; Atividades Cotidianas; Idoso

Introduction

Although hemoglobin levels decrease naturally with age, anemia is not considered a natural consequence of the aging process. The main known causes of anemia are nutritional deficiency, chronic diseases and/or renal failure [1,2,3]. Anemia associated with chronic inflammation plays a peculiar role among the elderly and its origin is still not clear. Studies suggest that oxidative stress that accompanies aging may be the real cause of chronic inflammation in the elderly and a major cause of anemia [4].

Anemia is common among the elderly and its presence should always be investigated. It is estimated that one out of every seven to eight elderly people is affected by anemia and among hospitalized individuals and those in nursing homes this proportion rises significantly, often reaching 50% [5,6,7,8,9].

However, studies that have attempted to quantify anemia prevalence in this population have reported discrepant results due to the lack of standard methods and differences in the characteristics of the studied groups [8,9].

Anemia has been highlighted as one of the factors responsible for health decline amongst the elderly population, and has been associated with several symptoms (loss of muscle tone, weakness, fatigue, increase in the number of falls, loss of functional independence, cognitive alterations and depression), and a consequent rise in morbidity and general mortality, even among mild cases [3,8,10,11,12,13,14,15].

It is estimated that by 2020 the elderly population in Brazil will reach 30 million people, representing the sixth largest elderly population in the world, and by 2050 the elderly will make up 30% of the population of the country [16].

However, only a few Brazilian studies have investigated the prevalence of anemia in the elderly population and none of these include hospitalized patients. Furthermore, we found no studies addressing the health consequences associated with anemia [17,18,19].

The aim of the present study was to evaluate the relationship between the presence of anemia upon hospital admission and previous functional capacity, and the influence of socioeconomic and cultural differences, in a sample of Brazilian elderly patients and compare these results to those found in literature outside Brazil.

Patients and methods

Studied population

A total of 1,047 elderly ($\geq$ 60 years) inpatients attending a General Hospital in Belo Horizonte, State of Minas Gerais, Brazil were selected between June 2006 and January 2009. The sample included both Brazilian Unified National Health System (SUS) and private health patients. Patients hospitalized within the last 48 hours were randomly selected from the hospital's daily admissions list. A total of 146 patients were excluded due to hospital discharge, death or clinical instability during selection. After analyzing the remaining 901 medical records, another 105 patients were also excluded due to the following reasons: (1) presence of a chronic and severe incapacitating illness leading to total inability to carry out functional tasks (a score of 3 in three or more domains of activities of daily living – ADL); (2) diagnosis with acute or chronic bleeding; (3) diagnosis with neoplastic or chronic kidney disease; and (4) presence of severe visual and/or auditory impairments. Patients that signed an informed consent form (five refusals) underwent cognitive assessment using the Folstein *Mini-Mental State Examination* (MMSE) test with the following scores: $\leq$ 13 for patients who are illiterate; $\leq$ 18 for patients with one to seven years of schooling; and $\leq$ 26 for patients with eight or more years of schooling) [20].

Patients with acceptable results were interviewed by previously trained personnel using a specially designed questionnaire. A total of 82 individuals were excluded after completion of the MMSE, giving a final study sample of 709 patients (Figure 1). This investigation was approved by the Ethics Boards of the Madre Teresa Hospital and Santa Casa located in Belo Horizonte.
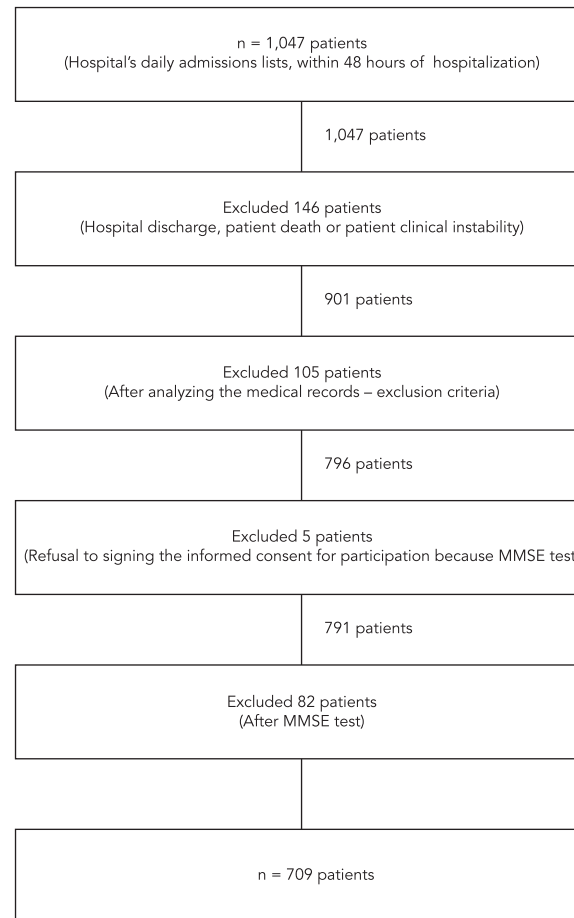
Anemia

Anemia was defined according to World Health Organization (WHO) [21] guidelines (Hb < 120.0g/L for women, and < 130.0g/L for men). Blood samples were collected during the first 48 hours after hospitalization, and Hb was measured using the Beckman Coulter T890 hematology analyzer (Beckman Coulter, Miami, USA).

Physical functional capacity

Physical functional capacity was assessed by self-appraisal, considering the 30 days prior to hospitalization using the Katz index and Lawton scale which are commonly used in research with the elderly [22,23,24,25].

Figure 1

Flowchart describing patient selection criteria.

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┌─────────────────────────────────────────────────────────────────────┐
│                         n = 1,047 patients                            │
│  (Hospital's daily admissions lists, within 48 hours of hospitalization)│
└─────────────────────────────────────────────────────────────────────┘
                              │
                         1,047 patients
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┌─────────────────────────────────────────────────────────────────────┐
│                       Excluded 146 patients                           │
│    (Hospital discharge, patient death or patient clinical instability)│
└─────────────────────────────────────────────────────────────────────┘
                              │
                         901 patients
                              │
┌─────────────────────────────────────────────────────────────────────┐
│                       Excluded 105 patients                           │
│        (After analyzing the medical records – exclusion criteria)     │
└─────────────────────────────────────────────────────────────────────┘
                              │
                         796 patients
                              │
┌─────────────────────────────────────────────────────────────────────┐
│                        Excluded 5 patients                            │
│ (Refusal to signing the informed consent for participation because MMSE test)│
└─────────────────────────────────────────────────────────────────────┘
                              │
                         791 patients
                              │
┌─────────────────────────────────────────────────────────────────────┐
│                       Excluded 82 patients                            │
│                         (After MMSE test)                             │
└─────────────────────────────────────────────────────────────────────┘
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│                         n = 709 patients                             │
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The Katz index (ADL) was applied to assess the amount of care and assistance the subjects needed to perform basic daily life activities (personal hygiene and grooming, dressing and undressing, functional transfers – getting from bed to wheelchair, getting onto or off of toilet, etc., bowel and bladder management, self-feeding) [26]; The Lawton Instrumental Activities of Daily Living (IADL) Scale was used to evaluate more complex activities (ability to use the telephone, shopping, food preparation, housekeeping, laundry, means of transportation, responsibility for taking medications, ability to handle finances) [27].

Patients were considered to have suffered a loss of functional capacity when they required help to perform any of the activities detailed by the Katz index and Lawton scale. Functional limitations were classified into the following categories according to the respective ADL and IADL scores: none – ADL score of 0 and IADL score of 27; moderate – ADL score of 3 in one to two tasks and/or an IADL score of 1 in one to four domains; and severe – ADL score of 3 in $\geq$ three tasks and/or an IADL score of 1 in $\geq$ five domains. The number of activities with functional loss, as well as the total score for each measure, was registered for all participants.

Covariates

The following sociodemographic variables were included in this study: age, gender, education, family background, former and/or current professional activity, and income. The following

medical variables were also assessed: hospitalization type (scheduled, emergency, clinical or surgical); diagnosis; comorbidities; smoking history; number of daily prescribed medications (during the 30 days prior to hospitalization); hospitalizations in the previous year; medical complications during hospital stay; length of stay in hospital (including ICU); and mortality.

Statistical analysis

Univariate analysis was carried out to compare anemic and non-anemic groups. The "t-test" or Mann-Whitney test (Anderson-Darling to test for normality) and chi-square or Fisher's exact tests were used for quantitative and categorical variables, respectively. Hierarchical binary logistic regression models including the social demographic and medical variables were constructed to identify significant predictor variables for both the ADL and IADL. Characteristics presenting a p-value ≤ 0.2 from the univariate analysis were included in the initial (full) models. Those variables with a p-value ≤ 0.05 after fitting the initial model were carried forward to the final model (backward selection). Model adjustment was evaluated using the Hosmer & Lemeshow test. All procedures were carried out using the Epi Info version 3.5 (Centers for Disease Control and Prevention, Atlanta, USA) and SPSS version 12 (SPSS Inc., Chicago, USA) statistical packages.

Results

The mean age of the sample was 73.2 ± 8.2 years, 51.6% were women and 213 participants (30%, n = 709) had anemia. No significant gender differences were found. Mean Hb levels in anemic and non-anemic participants were 113.0 ± 10.6 and 138.5 ± 10.5g/L, respectively (Table 1).

Anemic patients were older, had a lower level of education level and income, were taking more medications and had a higher number of comorbidities (congestive cardiac insufficiency, arrhythmia, diabetes, peripheral vascular disease and chronic renal insufficiency). It was also found that the this group had lower cognitive performance based on the MMSE, had been hospitalized for urgent or clinical treatment more times in the previous year, and length of hospital stay, including intensive care (Table 1) was greater.

The nonanemic patients had a more active lifestyle, and were more likely to perform a professional activity and/or live alone (30.3 vs. 15.5, Table 1).

Medical complications associated to hospitalization were reported in 17.6% of participants.

Acute respiratory insufficiency (13.6 vs. 7.7) and acute renal insufficiency (4.2 vs. 1.6) were significantly higher among anemic patients. Smoking history was not a differentiating factor (Table 1).

The overall rate of mortality was 9.5% and, despite being higher in anemic patients, there was no significant difference between the two groups (6.1 vs. 3.4, Table 1).

A considerable reduction in physical functional capacity was observed in the anemic patients, both in terms of higher total scores and the number of activities with functional loss (Table 2). It is important to note, however, that the majority of participants did not present any functional decline according to the results of the Katz and Lawton measures (646/91% and 499/71%, respectively). In light of these results, multivariate analysis was carried out using logistic models (ADL – Katz score of 0 = reference, score of ≥1 = risk; IADL – Lawton score of 27 = reference, score of ≤ 26 = risk). All sociodemographic and medical variables, except hypertension and coronary heart disease, were included in the initial analysis (full models).

The results of the final logistical regression models fitted to the ADL and IADL scores are presented in Table 3. Anemic patients presented a high level of functional loss in both models: ADL (OR = 12.7; 95%CI: 6.3-25.9); IADL (OR = 15.9; 95%CI: 10.7-23.7). Anemia was independently associated with older age in the ADL model (OR = 1.04; 95%CI: 1.02-1.06).

Discussion

Prevalence of anemia in the study population was 30%. Other studies of the elderly in Brazil have reported anemia prevalence rates ranging from 4.3% to 31.8% [17,18,19].

A systematic review conducted by Gaskell et al. [9] found that average anemia prevalence in the elderly population was 17% (varying between 3% and 50%), while in four studies conducted with more than 13,000 hospitalized patients, anemia prevalence varied between 40% and 72%.

The lower prevalence rate found by this study is probably due to the stringent inclusion criteria adopted, which excluded a number of potential anemic patients. It should be emphasized that our intention was not to estimate the prevalence of anemia in the study population, but rather to investigate the possible association between anemia and previous functional decline. It is also possible that the wide diversity of cultural and sociodemographic characteristics among the study population contributed to the lower prevalence rate.

Table 1

Sociodemographic, economic and clinical characteristics of the sample.

Characteristics	Anemic (n = 213)	Nonanemic (n = 496)	p-value
Age (years) * [mean ± SD]	75.9 ± 8.5	72.1 ± 7.8	< 0.001
Female [n (%)]	121 (56.8)	245 (49.4)	0.07
Education (years) [n (%)]			
None/Up to 1	32 (15.0)	46 (9.2)	
1-7	124 (58.2)	261 (52.6)	0.041
8-14	38 (17.8)	111 (22.4)	
15 or over	19 (8.9)	78 (15.7)	
Living alone [n (%)]	19 (8.9)	75 (15.1)	0.01
Current professional activity [n (%)]	33 (15.5)	150 (30.3)	< 0.001
Average monthly income (R$) ** [median, 25-75%]	700.00 (350-1,600)	900.00 (350-2,300)	0.053
Comorbidities [n (%)]			
Hypertension	161 (75.6)	376 (75.8)	0.95
Congestive heart failure	63 (29.6)	53 (10.7)	< 0.001
Coronary heart disease	91 (42.7)	211 (42.5)	0.96
Peripheral artery disease	26 (12.2)	35 (7.0)	0.025
Arritmia	47 (22.0)	69 (13.9)	0.007
Diabetes mellitus	76 (35.7)	121 (24.4)	0.002
Chronic renal insufficiency	26 (12.2)	7 (1.4)	< 0.001
Number of comorbidities [mean ± SD]	3.4 ± 1.2	2.6 ± 1.1	< 0.001
Smoker [n (%)]	26 (12.2)	53 (10.79)	0.142
Number of medications used [n (%)]			
0-3	74 (34.7)	229 (46.1)	
4-6	94 (44.1)	200 (40.3)	0.038
≥ 7	45 (21.1)	67 (13.5)	
Previous hospitalization [n (%)]	100 (46.9)	154 (31.09)	< 0.001
Previous hospitalization ICU [n (%)]	46 (21.69)	60 (12.1)	< 0.001
Types of hospitalization 1 [n (%)]			
Scheduled	39 (18.3)	140 (28.2)	0.005
Emergency	174 (81.4)	356 (71.8)	
Types of hospitalization 2 [n (%)]			
Clinical	124 (58.7)	214 (43.3)	< 0.001
Surgery	89 (41.3)	282 (56.6)	
Creatinine g/dL ** [median, 25-75%]	1.2 (0.9-1.6)	1.0 (0.8-1.2)	< 0.001
MMSE score * [mean ± SD]	23.5 ± 3.8	25.1 ± 3.6	< 0.001
Number of days in ICU [mean ± SD]	4.6 ± 6.8	3.3 ± 5.4	0.0046
Number of days of hospitalization ** [median, 25-75%]	8 (4-14)	6 (3-10)	< 0.001
Complications [n (%)]			
Acute respiratory insufficiency	29 (13.6)	38 (7.79)	0.013
Acute renal insufficiency	9 (4.2)	8 (1.69)	0.037
Mortality [n (%)]	13 (6.1)	17 (3.4)	0.105

ADL: activities of daily living; IADL: instrumental activities of daily living; MMSE: *Mini Mental State Examination*; SD: standard deviation.

Note: all percentages were calculated relative to the total population.

* p-value based on t-test;

** p-value based on the Mann-Whitney non-parametric test for continuous variables and on the chi-square or Fisher's exact test for categorical variables.

Table 2

Functional capacity: Katz and Lawton's measures.

Functional capacity (in the 30 days prior to hospitalization)	Anemic (n = 213)	Non anemic (n = 496)	p-value *
Katz (ADL)			
Total score [mean ± SD]	0.7 ± 1.5	0.04 ± 0.4	< 0.001
Number of disabilities, [mean ± SD]	0.5 ± 1.0	0.03 ± 0.3	< 0.001
Bathing [%]	22.5	1.2	< 0.001
Dressing [%]	18.3	0.4	< 0.001
Going to the toilet [%]	3.3	0.2	0.001
Transfer [%]	5.2	0.4	< 0.001
Continence [%]	5.2	0.8	< 0.001
Feeding [%]	0.0	0.0	< 0.001
Lawton (IADL)			
Total score [mean ± SD]	23.1 ± 3.5	26.4 ± 1.9	< 0.001
Number of disabilities [mean ± SD]	3.3 ± 2.7	0.4 ± 1.4	< 0.001
Ability to use the telephone [%]	8.9	0.8	< 0.001
Transportation [%]	47.0	8.9	< 0.001
Shopping [%]	55.4	8.7	< 0.001
Food preparation [%]	32.9	3.8	< 0.001
Housekeeping [%]	56.8	7.9	< 0.001
Hand works [%]	11.7	1.2	< 0.001
Laundry [%]	54.5	6.8	< 0.001
Responsibility for own medications [%]	31.0	3.2	< 0.001
Ability to handle finances [%]	29.6	3.2	< 0.001

ADL: activities of daily living; IADL: instrumental activities of daily living; SD: standard deviation.

Note: all percentages were calculated relative to the total population.

* p-values are based on the Mann-Whitney non-parametric test for continuous variables and on the chi-square or Fischer's exact test for categorical variables.

Table 3

Variables associated with anemia after multivariate analysis – final models.

Variables	Katz (ADL) model OR (95%CI)	Lawton (IADL) model OR (95%CI)
ADL/IADL	12.7 (6.3-25.9)	15.9 (10.9-23.7)
Age (years)	1.04 (1.02-1.06)	-
Model adjustment *	0.771	0.767

ADL: activities of daily living; IADL: instrumental activities of daily living; OR: odds ratio; 95%CI: 95% confidence interval.

* Hosmer & Lemershow test.

The results show that older individuals are more likely to develop anemia. This finding corroborates the findings of the majority of studies which demonstrate that prevalence of anemia increases proportionately with age [8,9,14,28,29,30].

This study also shows that there is a direct association between aging and a decrease in functional capacity. On average, the likelihood of a decline in functional performance is 1.06 times (ADL) and 1.11 times (IADL) greater for each ad-

ditional year of life; thus, with a five-year increase in age the likelihood is 5.30 and 5.55 times greater, respectively. The association between aging and functional decline is a common finding in the literature [31,32,33,34,35,36].

Although some studies observed gender differences in anemia prevalence [3,37,38], no significant gender differences were observed by this study. However, it interesting to note that women were twice as vulnerable to a decline in functional performance than men, corroborating the results of other studies. Although females have a greater life expectancy, the proportion of years lived without disability is smaller than in males [39,40,41].

The results also show a strong association between anemia and physical functional loss in the models tested: patients with anemia on admission to hospital were 12.7 (ADL) or 15.9 (IADL) times more likely to have low physical functional capacity during the 30 days prior to admission. This decline in functionality of the elderly was observed both in terms of the total score and the number of compromised activities. This is the first study to address the association between anemia and decreased physical functional capacity among a sample of the Brazilian population. The results of this study are similar to the findings of studies undertaken outside Brazil which evaluated anemia and functional capacity among the elderly [8,9,14,42,43,44].

Studies have reported hemoglobin values similar the findings of our study (> 10g/dL) suggesting that anemia in the elderly generally tends to be mild [29,45,46].

There is currently a debate about a possible change in the hemoglobin threshold level recommended by WHO for the diagnosis of anemia, with some authors claiming that small reductions in hemoglobin are a normal consequence of aging [38,47,48]. However, several studies have shown that even mild anemia in the elderly is associated with several deleterious effects on the health, including increased morbidity and mortality. Therefore, even mild anemia should be considered a warning sign of possible health problems, including serious underlying disease [3,10,22,49,50]. In line with this, our study shows that, despite mean hemoglobin levels slightly below those recommended by WHO [21], a number of negative health consequences were observed in anemic elderly patients, even those with mild anemia [3, 22].

Regarding family arrangements, our results showed that a higher proportion of anemic elderly patients lived with a family member than non anemic patients. On the other hand, a significantly higher proportion of nonanemic patients reported living alone. Furthermore, elderly people living alone showed a lower level of functional capacity loss than those living with family members [32,33,34,51]. This is probably because it is necessary to be functionally active to perform essential daily tasks and activities.

It has been shown that a large proportion of Brazilian elderly live in multigenerational residential arrangements, especially those with low income and low socioeconomic status. In contrast, those living in better socioeconomic conditions are more likely to live alone or with a partner, following the pattern observed in more developed countries [31].

It is possible that elderly people living with their families are more vulnerable to health conditions that compromise their independence, whereas those living alone experience better health and are more independent with respect to self-care and social relations. However, due to the cross-sectional design of this study, a causal pathway cannot be established.

With regard to occupation, our results show that roughly a quarter of the sample was engaged in a regular professional activity and that this proportion was higher among nonanemic patients. Although no association between professional activity and anemia or functional capacity was identified, it is plausible that regular professional activity requires good health.

No significant association was found between income, education level and anemia, corroborating other studies [3,22,52].

The rate of hospitalization in the year preceding the study was higher among anemic patients and the results of the multivariate analysis showed that the likelihood of disability in individuals that reported previous hospitalization was twice as great. These results are consistent with the findings of other studies [13,14,53]. The presence of chronic diseases and comorbidities, usually long term illnesses, is frequent in this population, increasing the probability of clinical instability and the need of frequent hospitalization and repeated hospitalization may be used as an estimate of frailty in this group [54].

Regarding cognitive capacity, the performance of anemic patients in the MMSE test was worse, and patients with lower levels of physical functional capacity also obtained generally low scores confirming associations between cognitive impairment, anemia and functional capacity already reported in the literature [35,55,56,57,58].

The overall rate of mortality was 9.5%; the rate was higher among anemic patients but this difference was not significant. This result contrasts with the findings of other studies [3,14,30,46,59]; however, it should be noted that participants were not followed up after the hospital stay.

The autonomy of elderly people, in terms of self-care and living environment, is directly related to functional capacity. Disability cannot be considered a static situation, but rather a dynamic and complex process that involves a number of individual and environmental factors.

The association between anemia and decreased physical functional capacity is well documented in the literature [8,9,10,13,22,58]. The signs and symptoms associated with anemia in the elderly vary according to several factors, including anemia duration. In chronic anemia, spontaneous complaints of older patients are generally less common. Often without realizing it, the elderly progressively decrease levels of physical activity until it becomes asymptomatic.

A decrease in hemoglobin levels, with a consequent decrease in the number of red blood cells, causes a reduction in the flow of oxygen in all organs, which has clinical manifestations. These symptoms increase with physical activity, which requires a greater oxygen supply [60]. As a consequence, the elderly progressively reduce their routine activities leading to a progressive level of functional dependency.

Although it is still not clear whether active interventions for the treatment of anemia are beneficial to all older people, many studies have shown the clear benefits of early diagnosis and treatment of anemia for various diseases, such as congestive heart failure [61,62] and chronic kidney disease [63], with significant improvements in functional capacity, cognitive functions and quality of life.

The cross-sectional nature of our study can be considered a limitation, since it was not possible to determine the temporal relations between the variables. Furthermore, the fact that information concerning functionality was self-reported may have resulted in errors when qualifying disability.

Conclusion

Anemia is recognized as a significantly independent predictor for morbidity, frailty and functional loss in the elderly, and is potentially modifiable. The results of this study of a sample of Brazilian hospitalized elderly showed that there was an association between the presence of anemia and reduced functional capacity. Since the measurement of hemoglobin levels is routine with hospitalized elderly and in outpatient services, the presence of anemia may be used as an important marker of the risk of functional decline. Further research is still needed to evaluate improvements in functionality and independence in the elderly as a result of anemia treatment.

Resumen

Este estudio evaluó la asociación entre la anemia y la capacidad física funcional en ancianos hospitalizados. Se trató de un estudio transversal con una muestra de 709 participantes con edad ≥ 60 años, ingresados en el hospital Madre Teresa, Belo Horizonte, Minas Gerais, Brasil. Se aplicó el Mann-Whitney o "t" y chi-cuadrado o la prueba exacta de Fisher para las variables cuantitativas y categóricas, respectivamente, así como un modelo jerárquico binario de regresión logística para identificar predictores significativos. La presencia de anemia se encontró en un 30% de los participantes y se asoció con una disminución significativa de la funcio-nalidad en ambos índices utilizados – AVD (actividades de la vida diaria) y de AIVD (actividades instrumentales de la vida diaria). La edad avanzada también se asocia de forma independiente con la anemia. Los resultados de este estudio demostraron una fuerte asociación entre una menor capacidad funcional y la presencia de anemia. Se necesitan más investigaciones para evaluar los efectos del tratamiento de la anemia en la mejora de la funcionalidad y la independencia de los ancianos.

Anemia; Actividades Cotidianas; Anciano

Contributors

R. M. Bosco, L. S. M. Pereira and C. M. F. Antunes participated in project conception, data interpretation, drafting and approval of the final version of this article. E. P. S. Assis participated in data collection and drafting and approval of the final version of this article. R. R. Pinheiro and L. C. V. Queiroz contributed to data analysis and interpretation and drafting of this article.

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