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# Hospital readmission within 30 days of older adults hospitalized in a public hospital

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Older adults have difficulty monitoring their drug therapy in the first thirty days following hospital discharge. This transition care period may trigger hospital readmissions. The study aims to identify the factors associated with the readmission of older adults 30 days after discharge from the perspective of drug therapy. This is a cross-sectional study and hospital admission within 30 days was defined as readmission to any hospital 30 days after discharge. The complexity of the drug therapy was established by the Medication Regimen Complexity Index (MRCI). Readmission risks were predicted by the "Readmission Risk Score – RRS". The multivariate logistic regression was used to identify factors associated with readmission within 30 days after discharge. Two hundred fifty-five older adults were included in the study, of which 32 (12.5%) had non-elective hospital readmission. A higher number of readmissions was observed with increased RRS value, suggesting a linear gradient effect. The variables included in the final logistic regression model were the diagnosis of cancer (OR=2.9, p=0.031), pneumonia (OR=2.3, p=0.055), and High MRCI (> 16.5) following discharge (OR=1.9, p=0.119). The cancer diagnosis is positively associated with hospital readmissions of older adults within 30 days.

Keywords: Patient Readmission. Aged. Drug Therapy.

#### INTRODUCTION

BJPS

As in the demographic and epidemiological transition in Brazil, population aging is a reality in other countries (Mendes *et al.*, 2012). The higher number of older adults in society is associated with an increased burden of chronic noncommunicable diseases, which favors polypharmacy, the use of potentially inappropriate medicines (PIM) for older adults, and a complex drug therapy regimen. These factors contribute to frequent adverse drug events, hospitalizations, hospital readmissions, and other adverse health outcomes among older adults (Hain *et al.*, 2012; Wong *et al.*, 2014).

Unplanned hospital readmissions, especially those occurring 30 days after discharge, are costly to the health system and may directly affect the morbidity and mortality

of the patients. Therefore, it is essential to identify factors related to hospital readmission to enhance the quality of care provided and improve the care transition (Ben-Chetrit *et al.*, 2012; Low *et al.*, 2015; Picker *et al.*, 2015; Zhou *et al.*, 2016).

Unplanned readmissions are influenced by patientrelated factors and care, such as comorbidities, length of hospital stay, number of previous admissions, and laboratory parameters (hemoglobin, creatinine), among others (Zhou *et al.*, 2016). Patients' drug therapy may contribute to hospital readmission due to adverse drug events (ADE) (El Morabet *et al.*, 2018), complex drug therapy (Colavecchia *et al.*, 2017), number of medications prescribed at discharge (Low *et al.*, 2015; Picker *et al.*, 2015), polypharmacy, and PIM (Sehgal *et al.*, 2013).

The older adults may show difficulties understanding the possible drug therapy changes after hospital discharge. Incorrect use of medications during care transition may increase the likelihood of adverse drug events and therapeutic failures, thus contributing to hospital

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readmissions. The first 30 days are known to be the most difficult for older adults to adapt to the new therapeutic routine (Hain *et al.*, 2012).

Therefore, this study aims to identify the factors associated with the readmission of older adults 30 days after discharge from the perspective of drug therapy.

## METHODS

### Design, setting, and study participants

This is a cross-sectional study conducted in a general public hospital with 340 beds responsible for attending civil servants, located in a metropolitan region of southeastern Brazil.

We estimated the minimum inclusion of 246 older adults in the study considering the following assumptions: infinite population, readmission prevalence of 20% (Zhou *et al.*, 2016), 95% confidence interval, 5% error margin, and test statistics on a community. The sample was calculated by OpenEpi software version 2.0.

The study included individuals aged 60 years or over (older adults defined by the World Health Organization for developing countries) hospitalized for more than 24 hours in the Medical and Geriatric Clinic wards from April to November of 2017. The following exclusion criteria were adopted: death during hospitalization, length of hospital stay longer than 60 days, hospital evasion, and contact loss of participants during follow-up. The Research Ethics Committee of the Federal University of Minas Gerais approved the study under N° CAAE 63612216.7.0000.5149, and the patients and responsible signed the Informed Consent Form.

#### **Data collection**

The patients admitted to the hospital were identified by the computerized hospitalization management system and invited to participate in the research. The patient's first admission in the investigation period was considered the hospitalization index. An interview was conducted with the patient to collect sociodemographic information, information on home use of medications, and application of the Vulnerable Elders Survey-13 (VES-13). The VES- 13 is a tool for assessing the vulnerability of older adults, validated in Brazil and with adequate psychometric properties (Luz *et al.*, 2015). Clinical information was collected by consulting the patient's electronic medical record. Two telephone follow-ups were performed after discharge: the first to confirm medications prescribed at hospital discharge, and the second, to verify the outcome. The primary result was readmission within 30 days after hospital discharge, both at the investigated hospital and other health facilities.

The comorbidities assessed were identified using the Charlson Comorbidity Index (CCI) (Charlson *et al.*, 1987). Diagnoses of admission and readmissions were classified according to the 10<sup>th</sup> edition of the International Code of Diseases (ICD-10). High-risk diagnoses were defined as stroke, cancer, diabetes mellitus, chronic obstructive pulmonary disease, heart failure, and pneumonia (Taha *et al.*, 2014).

Polypharmacy was defined as the concomitant use of five or more medications (Runganga, Peel, Hubbard, 2014; Jyrkka *et al.*, 2009), and excessive polypharmacy as the use of 10 or more medications (Taha *et al.*, 2014; Runganga, Peel, Hubbard, 2014; Jyrkka *et al.*, 2009). The following drugs were included in the high-risk category: acetylsalicylic acid + clopidogrel concomitantly, warfarin, enoxaparin, fondaparinux, digoxin, opioid, and insulin (Taha *et al.*, 2014). PIM for the older adults were classified per the 2015 American Geriatric Society(AGS)/Beers criteria (American Geriatrics Society, 2015).

The complexity of the drug treatment regimen prescribed at discharge was determined by calculating the Medication Regimen Complexity Index (MRCI) (George *et al.*, 2004), using the Brazilian version (Melchiors, Correr, Fernandez-Llimos, 2007). The drug therapy complexity was stratified in high complexity: yes (MRCI > 16.5), no (MRCI  $\leq$ 16.5). The cutoff point to define high complexity was that determined in the MRCI normalization for Brazilian older adults (Pantuzza *et al.*, 2018).

The risk of readmission within 30 days was calculated using the "Readmission Risk Score" (RRS). The risk of readmission was estimated using the following equation recommended by the RRS: 8% + (value obtained in RRS x 4%) (Taha *et al.*, 2014).

#### **Statistical analysis**

Descriptive analysis was performed with the frequency for the dichotomous variables, and the numerical variables were described as mean [standard deviation-SD] or median (interquartile range-IQR). Normality analysis was performed per the Shapiro-Wilk Test. The median dichotomized numerical variables. The association between the independent variables and readmission within 30 days was performed per the Chi-square test and Fisher's exact test, observing the assumptions of each test. The study's statistical significance level was considered as p<0.05. Variables with a p-value  $\leq 0.25$  in this univariate analysis were included in the multivariate analysis through the logistic regression model. The Backward stepwise method was used to obtain the final model, with variables remaining at p-value<0.05 or if they contributed to adjusting the model. The adequacy of the final model was evaluated by the Hosmer-Lemeshow test and was considered adequate if the p-value> 0.05. Statistical analysis was performed using SPSS 25.0 Software.

#### RESULTS

A total of 300 older adults people were included in the study, of which 27 (9%) died during hospitalization, one older adult (0.3%) escaped from the hospital, one older adult (0.3%) was transferred to another health service, and three (1%) older adults were excluded due to prolonged hospitalization. Of the 268 discharged patients, five (1.7%) were contact losses, one (0.3%) was a dropout, and seven (2.3%) were exclusions due to elective readmission. Thus, 255 older adults were eligible for the analyses, of which 32 (12.5%) had non-elective readmissions within 30 days after discharge from the hospital [Figure 1].

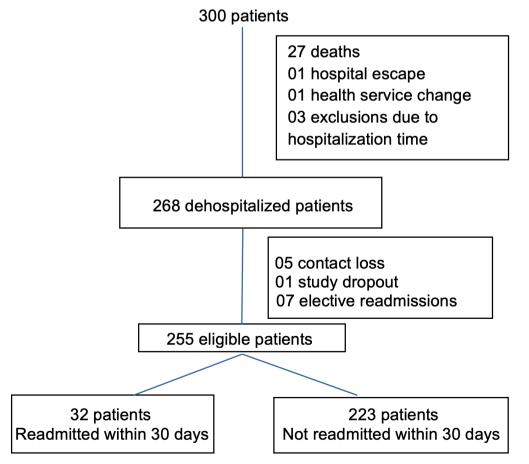


FIGURE 1 - Study flowchart.

Among the 255 older adults followed-up to 30 days after hospital discharge, 146 (57.3%) were female, with a median age of 75 years (IOR 13.0). A predominance of patients from the medical clinic (62%) was observed. The most frequent admission diagnoses among older adults were respiratory diseases (64, 25.1%), diseases of the genitourinary system (43, 16.9%), and diseases of the circulatory system (30, 11.8%). The median of the Charlson Comorbidity Index was 5.0 (IQR 2.0), and the VES13 was 5.0 (IOR 6.0). The most frequent comorbidities among older adults were hypertension (181, 71.0%), diabetes (110, 43.1%), pneumonia (53, 20.8%), chronic kidney disease (45, 17.6%), hypothyroidism (43, 16.9%), heart failure (38, 14.9%), and neoplasms (29, 11.4%). The median length of hospital stay was 12 days (IQR=10). The number of medications used by the patients was higher after discharge (median=6.0; IQR 4.0) than the number of medications used before hospital

admission (median=5.0; IQR 5.0). One hundred sixty-five patients (64.7%) used PIM, with a median of 1 (IQR 1.0) medication per patient.

The frequency of non-elective readmission within 30 days was 32 (12.5%), and the RRS median was 3 (IQR=2). The risk of readmission in 30 days calculated for older adults per the RRS ranged from 8% (RSS=0) to 32% (RSS=6), with a median of 20% (RSS=3). The analysis of the number of hospitalized patients by score value showed growing readmissions with an increasing value of RRS [Figure 2], suggesting a linear gradient effect. We evidenced [Table 1] that the clinical and pharmacotherapeutic characteristics used in calculating RRS had a higher frequency in the readmission group, except for the variable excessive polypharmacy. However, there was no statistically significant difference between the readmitted patients and those who were not in all variables [Table I].

TABLE I - Association between clinical pharmacotherapeutic characteristics used in the calculation of Readmission Risk Score

| Description            | Readmissio   | n within 30 days |                        |                      |  |
|------------------------|--------------|------------------|------------------------|----------------------|--|
| Variable               | Yes<br>n (%) | No<br>n (%)      | Odds Ratio<br>(CI 95%) | <b>p-value</b> 0.306 |  |
| Female                 | 21 (65.6%)   | 125 (56.1%)      | 1.49 (0.69-3.25)       |                      |  |
| Age ≥ 65               | 29 (90.6%)   | 197 (88.3%)      | 1.27(0.36-4.49)        | 1.0001               |  |
| High Risk Diagnosis    | 28 (87.5%)   | 169 (75.8%)      | 2.24 (0.75-6.66)       | 0.139                |  |
| High Risk Drugs        | 12 (37.5%)   | 81 (36.3%)       | 1.05 (0.49-2.26)       | 0.897                |  |
| Excessive polypharmacy | 5 (15.6%)    | 40 (17.9%)       | 0.85 (0.30-2.34)       | 0.748                |  |
| Depression             | 8 (25.0%)    | 38 (17.0%)       | 1.62(0.68-3.89)        | 0.273                |  |
| Palliative care        | 5 (15.6%)    | 17 (7.6%)        | 2.24 (0.77-6.58)       | 0.169 <sup>1</sup>   |  |

<sup>1</sup> Values calculated using Fisher>s Exact Test.

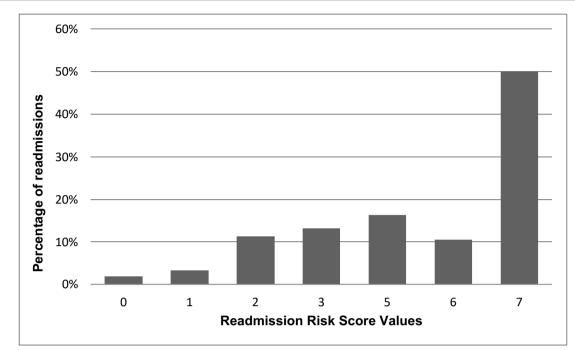


FIGURE 2 - Percentage of patients readmitted according to the Readmission Risk Score value.

In the univariate analysis, hospital readmission in 30 days did not show a statistically significant association (p-value<0.05) with any of the variables. Variables in the group of patients not readmitted differ from those hospitalized because they have a higher frequency of diagnosis of Chronic Obstructive Pulmonary Disease, Diabetes Mellitus, Chronic Kidney Disease, Atrial Fibrillation, use of medicines acetylsalicylic acid combined with clopidogrel, enoxaparin, insulin, and

excessive polypharmacy, but the difference was not statistically significant. The following variables were included in the multivariate model: age, cancer, diabetes mellitus, pneumonia, palliative care, functionality, insulin use, and opioid use. In the final model, cancer with OR=2.9 (CI 1.11-7.70), OR=2.3 (0.98-5.39), and high-complexity drug therapy OR=1.9 (0.85-4.13). However, only cancer showed statistical significance (p-value<0.05) [Table II].

| Description<br>Variable | Readmission occurrence |             | Univariate analysis    |         | Multivariate<br>analysis |         |
|-------------------------|------------------------|-------------|------------------------|---------|--------------------------|---------|
|                         | Yes<br>n (%)           | No<br>n (%) | Odds ratio<br>(CI 95%) | p-value | Odds ratio<br>(CI 95%)   | p-value |
| Sociodemographic        |                        |             |                        |         |                          |         |
| Gender                  |                        |             |                        |         |                          |         |
| Female                  | 21 (65.6%)             | 125 (56.1%) | 1.45 (0.69-3.25)       | 0.306   |                          |         |
| Male                    | 11 (34.4%)             | 98 (43.9%)  |                        |         |                          |         |
| Age                     |                        |             |                        |         |                          |         |

| Description<br>Variable                     | Readmission occurrence |              | Univariate analysis    |         | Multivariate<br>analysis |         |
|---|------------------------|--------------|------------------------|---------|--------------------------|---------|
|   | Yes<br>n (%)           | No<br>n (%)  | Odds ratio<br>(CI 95%) | p-value | Odds ratio<br>(CI 95%)   | p-value |
| ≥75   | 21 (65.6%)             | 119 (53.4%)  | 1.67 (0.77-3.62)       | 0.192   |                          |         |
| <75   | 11 (34.4%)             | 104 (46.6 %) |                        |         |                          |         |
| Clinical                                    |                        |              |                        |         |                          |         |
| Admission of origin                         |                        |              |                        |         |                          |         |
| Geriatrics                                  | 20 (62.5%)             | 138 (61.9%)  | 1.03 (0.48-2.21)       | 0.946   |                          |         |
| Other clinics                               | 12 (37.5%)             | 85 (38.1%)   |                        |         |                          |         |
| Admission time                              |                        |              |                        |         |                          |         |
| ≥12 days                                    | 20 (62.5%)             | 121 (54.3%)  | 1.41 (0.66-3.01)       | 0.381   |                          |         |
| <12 days                                    | 12 (37.5%)             | 102 (45.7%)  |                        |         |                          |         |
| Non-elective admission in the last 6 months |                        |              |                        |         |                          |         |
| Yes   | 10 (31.3%)             | 67 (30.0%)   | 1.06 (0.48-2.36)       | 0.890   |                          |         |
| No  | 22 (68.8%)             | 156 (70.0%)  |                        |         |                          |         |
| VBI   |                        |              |                        |         |                          |         |
| Yes   | 5 (15.6%)              | 32 (14.3%)   | 1.11 (0.40-3.09)       | 0.7921  |                          |         |
| No  | 27 (84.4%)             | 191 (85.7%)  |                        |         |                          |         |
| Heart Failure                               |                        |              |                        |         |                          |         |
| Yes   | 7 (21.9%)              | 31 (13.9%)   | 1.73 (0.69-4.35)       | 0.2851  |                          |         |
| No  | 25 (78.1%)             | 192 (86.1%)  |                        |         |                          |         |
| COPD  |                        |              |                        |         |                          |         |
| Yes   | 4 (12.5%)              | 30 (13.5%)   | 0.92 (0.30-2.81)       | 1.0001  |                          |         |
| No  | 28 (87.5%)             | 193 (86.5%)  |                        |         |                          |         |
| Cancer                                      |                        |              |                        |         |                          |         |
| Yes   | 7 (21.9%)              | 22 (9.9%)    | 2.56 (0.94-6.59)       | 0.0681  | 2.916 (1.105-<br>7.698)  | 0.031   |
| No  | 25 (78.1%)             | 201 (90.1%)  |                        |         | 1                        |         |
| Diabetes Mellitus                           |                        |              |                        |         |                          |         |
| Yes   | 10 (31.3%)             | 100 (44.8%)  | 0.56 (0.25-1.24)       | 0.147   |                          |         |
| No  | 22 (68.8%)             | 123 (55.2%)  |                        |         |                          |         |

| Description<br>Variable       | Readmission occurrence |             | Univariate analysis    |         | Multivariate<br>analysis | n l     |
|-------------------------------|------------------------|-------------|------------------------|---------|--------------------------|---------|
|                               | Yes<br>n (%)           | No<br>n (%) | Odds ratio<br>(CI 95%) | p-value | Odds ratio<br>(CI 95%)   | p-value |
| Pneumonia                     |                        |             |                        |         |                          |         |
| Yes                           | 10 (31.3%)             | 43 (19.3%)  | 1.90 (0.84-4.31)       | 0.159   | 2.302 (0.983-<br>5.390)  | 0.055   |
| No                            | 22 (68.8%)             | 180 (80.7%) |                        |         | 1                        |         |
| Dementia                      |                        |             |                        |         |                          |         |
| Yes                           | 10 (31.3%)             | 69 (30.9%)  | 1.01 (0.45-2.26)       | 0.972   |                          |         |
| No                            | 22 (68.8%)             | 154 (69.1%) |                        |         |                          |         |
| Hypothyroidism                |                        |             |                        |         |                          |         |
| Yes                           | 8 (25.0%)              | 35 (15.7%)  | 1.79 (0.74-4.31)       | 0.189   |                          |         |
| No                            | 24 (75.0%)             | 188 (84.3%) |                        |         |                          |         |
| Chronic Kidney Disease        |                        |             |                        |         |                          |         |
| Yes                           | 5 (15.6%)              | 40 (17.9%)  | 0.85 (0.31-2.34)       | 0.748   |                          |         |
| No                            | 27 (84.4%)             | 183 (82.1%) |                        |         |                          |         |
| Atrial fibrillation           |                        |             |                        |         |                          |         |
| Yes                           | 2 (6.3%)               | 19 (8.5%)   | 0.72 (0.16-3.23)       | 1.0001  |                          |         |
| No                            | 30 (93.8%)             | 204 (91.5%) |                        |         |                          |         |
| SAH                           |                        |             |                        |         |                          |         |
| Yes                           | 25 (78.1%)             | 156 (70.0%) | 1.53 (0.63-3.72)       | 0.341   |                          |         |
| No                            | 7 (21.9%)              | 67 (30.0%)  |                        |         |                          |         |
| Palliative care               |                        |             |                        |         |                          |         |
| Yes                           | 5 (15.6%)              | 17 (7.6%)   | 2.24 (0.77-6.57)       | 0.1691  |                          |         |
| No                            | 27 (84.4%)             | 206 (92.4%) |                        |         |                          |         |
| Depression                    |                        |             |                        |         |                          |         |
| Yes                           | 8 (25.0%)              | 38 (17.0%)  | 1.62 (0.68-3.89)       | 0.324   |                          |         |
| No                            | 24 (75.0%)             | 185 (83.0%) |                        |         |                          |         |
| Charlson Comorbidity<br>Index |                        |             |                        |         |                          |         |
| ≥5                            | 22 (68.8%)             | 121 (54.3%) | 1.86 (0.80-4.10)       | 0.122   |                          |         |
| <5                            | 10 (31.3%)             | 102 (45.7%) |                        |         |                          |         |
| Functionality                 |                        |             |                        |         |                          |         |
| VES 13                        |                        |             |                        |         |                          |         |

| Description<br>Variable | Readmission occurrence |             | Univariate analysis    |         | Multivariate<br>analysis |         |
|-------------------------|------------------------|-------------|------------------------|---------|--------------------------|---------|
|                         | Yes<br>n (%)           | No<br>n (%) | Odds ratio<br>(CI 95%) | p-value | Odds ratio<br>(CI 95%)   | p-value |
| ≥5                      | 22 (68.8%)             | 114 (51.1%) | 2.10 (0.95-4.65)       | 0.062   |                          |         |
| <5                      | 10 (31.3%)             | 109 (48.9%) |                        |         |                          |         |
| Pharmacotherapeutic     |                        |             |                        |         |                          |         |
| AAS + Clopidogrel       |                        |             |                        |         |                          |         |
| Yes                     | 0 (0.00%)              | 8 (3.6%)    | 1.15 (1.10-1.21)       | 0.6011  |                          |         |
| No                      | 32 (100%)              | 215 (96.4%) |                        |         |                          |         |
| Enoxaparin              |                        |             |                        |         |                          |         |
| Yes                     | 0 (0.00%)              | 1 (0.4%)    | 1.14 (1.09-1.20)       | 1.0001  |                          |         |
| No                      | 32 (100%)              | 222 (99.6%) |                        |         |                          |         |
| Insulin                 |                        |             |                        |         |                          |         |
| Yes                     | 3 (9.4%)               | 49 (22.0%)  | 0.92 (0.35-2.43)       | 0.098   |                          |         |
| No                      | 29 (90.6%)             | 174 (78.0%) |                        |         |                          |         |
| Opioid                  |                        |             |                        |         |                          |         |
| Yes                     | 7 (21.9%)              | 25 (11.2%)  | 2.22 (0.87-5.65)       | 0.094   |                          |         |
| No                      | 25 (78.1%)             | 198 (88.8%) |                        |         |                          |         |
| Anticonvulsant          |                        |             |                        |         |                          |         |
| Yes                     | 6 (18.8%)              | 4 (9.8%)    | 2.14 (0.55-8.33)       | 0.3171  |                          |         |
| No                      | 26 (81.3%)             | 37 (90.2%)  |                        |         |                          |         |
| Warfarin                |                        |             |                        |         |                          |         |
| Yes                     | 2 (6.3%)               | 12 (5.4%)   | 1.17 (0.25-5.50)       | 0.6911  |                          |         |
| No                      | 30 (93.8%)             | 211 (94.6%) |                        |         |                          |         |
| ACEI and ARB            |                        |             |                        |         |                          |         |
| Yes                     | 15 (46.9%)             | 97 (43.5%)  | 1.15 (0.55-2.41)       | 0.719   |                          |         |
| No                      | 17 (53.1%)             | 126 (56.5%) |                        |         |                          |         |
| PIM                     |                        |             |                        |         |                          |         |
| Yes                     | 20 (62.5%)             | 145 (65.0%) | 0.90 (0.42-1.93)       | 0.780   |                          |         |
| No                      | 12 (37.5%)             | 78 (35.0%)  |                        |         |                          |         |
| Polypharmacy            |                        |             |                        |         |                          |         |
| Yes                     | 22 (68.8%)             | 152 (68.2%) | 1.03 (0.46-2.28)       | 0.947   |                          |         |
| No                      | 10 (31.3%)             | 71 (31.8%)  |                        |         |                          |         |

**TABLE II** – Univariate and multivariate analysis of the factors associated with the occurrence of readmission of older adults within 30 days

| Description<br>Variable | Readmission occurrence |             | Univariate analysis    |         | Multivariate<br>analysis |          |
|-------------------------|------------------------|-------------|------------------------|---------|--------------------------|----------|
|                         | Yes<br>n (%)           | No<br>n (%) | Odds ratio<br>(CI 95%) | p-value | Odds ratio<br>(CI 95%)   | p-value  |
| Excessive polypharmacy  |                        |             |                        |         |                          |          |
| Yes                     | 5 (15.6%)              | 40 (17.9%)  | 0.85 (0.31-2.34)       | 1.0001  |                          |          |
| No                      | 27 (84.4%)             | 183 (82.1%) |                        |         |                          |          |
| High MRCI               |                        |             |                        |         |                          |          |
| >16.5                   | 20 (62.5%)             | 113 (50.7%) | 1.62 (0.76-3.48)       | 0.210   | 1.874 (0.852-4.126       | 6) 0.119 |
| ≤16.5                   | 12 (37.5%)             | 110 (49.3%) |                        |         |                          |          |

#### DISCUSSION

The occurrence of non-elective readmissions among older adults included in the study 30 days after discharge from the hospitalization index was 12.5% and is independently associated with cancer diagnosis. While in Brazil older adults account for 33.5% of the hospitalizations in the Unified Health System and correspond to 37.7% of the funds paid for hospitalizations (Loyola Filho et al., 2004), no investigations on readmission of older adults within 30 days or more were identified. The frequency of readmissions in a public regional hospital in southeastern Brazil was 18% within one year of hospitalization, however, covering patients of all age groups (Castro, Carvalho, Travassos, 2005). In international studies, older adults' readmission after 30 days ranged from 12% to 19.6% (Robinson, Howie-Esquivel, Vlahov, 2012; Khan et al., 2012; Pugh et al., 2014; Low et al., 2017). The comparison of hospital readmission studies should be carried out with caution and observing the time interval between the hospitalization index and readmission, along with the clinical characteristics of the patients.

The association between cancer diagnosis and hospital readmission within 30 days identified in the study is consistent with a systematic review that examined hospital readmissions in cancer patients and

d., 2017). The comparisondisease affect patientss should be carried outthe increased life expe time interval betweenincidence of cancer ineadmission, along withgrow (Maggiore *et al.*,e patients.it is crucial to implementa cancer diagnosis andof older adults with can30 days identified into the improved provision

found that older adults are a significant predictor, as well as comorbidities and advanced stage of the neoplasm (Khan *et al.*, 2012). Metastatic cancer was a predictor of hospital readmission in 30 days in a study investigating the number of medications' contributions to older adults' readmission. Non-small cell lung cancer, colorectal cancer, and comorbidities are risk factors for readmission of patients with neoplasms (Whitney *et al.*, 2017), and these predictors are frequent in older adults, reinforcing the importance of the association found. It is also worth noting that cancer is one of the risk diagnoses included in the RRS (Taha *et al.*, 2014) and is also included in the "80+ score", a tool developed and validated in Switzerland to estimate the rehospitalization of older adults over 80 years (Alassaad *et al.*, 2015).

Cancer is a disease that mainly affects older adults. It is estimated that more than 50% of cancer diagnoses and about 70% of the mortality associated with the disease affect patients aged 65 or over. Considering the increased life expectancy of the population, the incidence of cancer in the higher age groups tends to grow (Maggiore *et al.*, 2014; Turner *et al.*, 2014). Thus, it is crucial to implement actions to reduce readmission of older adults with cancer within 30 days to contribute to the improved provision of beds for the hospitalization of cancer patients. Measures to curb readmission should be directed toward streamlining care transition, infection

prevention, proactive management of nausea and vomiting (Bell *et al.*, 2017), and appropriate pain management (Mercadante *et al.*, 2017). Older people with multiple diseases and advanced cancer should be part of these actions' priority group (Bell *et al.*, 2017).

Also, medications may be a contributing factor to the readmission of older adults with cancer within 30 days due to adverse reactions to antineoplastic and adjuvant or supportive therapies such as nausea, vomiting, constipation, drowsiness, and even mental confusion during treatment of pain with opioids (Mercadante *et al.*, 2017). Opioid use is one of the components of RRS and the "80+ score" (Taha *et al.*, 2014; Alassaad *et al.*, 2015) and is a contributor to readmission within 30 days (Mercadante *et al.*, 2017). However, there was no significant association with readmission in the hospital investigated, although the use was more frequent among the readmitted older adults.

Borderline association with the diagnosis of pneumonia was detected and explained by pneumonia being a known risk factor for hospital readmission and a predictor of older adults' readmission (Taha *et al.*, 2014). Also, pneumonia is a target disease of readmission reduction programs in the U.S. Medicaid and Medicare health systems (Picker *et al.*, 2015; Zhou *et al.*, 2016).

Another variable included in the logistic model was the MRCI. This index indicates the medication load used by the patient and is negatively associated with clinical health outcomes (Colavecchia et al., 2017; Alves-Conceição et al., 2018). Although the number of drugs affects the complexity of drug treatment, other factors also contribute, such as administration route, dosage form, dose frequency, and special administration instructions. These other factors contributing to drug therapy's complexity are crucial in older adults. A systematic review that examined the association between the complexity of older adults' drug therapy and clinical outcomes found mixed evidence for the association between complex drug therapy and readmission (Alves-Conceição et al., 2018; Wimmer et al., 2016). Other studies showed different methodologies and designs, different cutoff points for complexity, with an evaluation of readmission at different times (90 days and 12 months), hindering comparisons (Yam et al., 2016; Schoonover et

*al.*, 2014). The assessment of the association with the 30day readmission showed that there is no association with readmission for the MRCI cutoff point  $\geq$  15 (Schoonover *et al.*, 2014). This result is close to the finding of this study that adopted the cutoff point of > 16.5 of the MRCI and also found no positive association.

The association between PIM and readmission within 30 days is scarcely investigated. In this study, the use of PIM was higher among older adults readmitted but did not show an association with the outcome. Previous studies have not identified a significant association with readmission within 30 days (Mansur, Weiss, Beloosesky, 2009; Hagstrom *et al*, 2015). However, the lack of association between PIM for older adults and readmission within 30 days found in our study does not limit the importance of reducing PIM use. This measure is known to produce significant benefits by improving the quality of prescription and clinical, economic, and humanistic results (Fabbietti *et al.*, 2018).

Polypharmacy has been described as a risk factor for hospital readmission of older adults, as it is a disease severity and clinical complexity marker. The use of multiple medications may contribute to deteriorating the health status of older adults and is associated with increased risk of adverse drug reactions (Sganga *et al.*, 2017). However, this study did not evidence an association between readmission and polypharmacy / excessive polypharmacy. It is worth mentioning that the research that evaluated readmission within 30 days and investigated the association with polypharmacy was not exclusively in older adults (Picker *et al.*, 2015), and the studies conducted with older adults evaluated readmission at 3 and 12 months (Fabbietti *et al.*, 2018).

The readmission after 30 days may reflect the consequences of the polypharmacy established in the last hospitalization. The lack of association in our study can be attributed to the fact that polypharmacy is quite prevalent in older adults, and its consequences are more pronounced with prolonged use. This evaluation was performed 30 days after discharge from the hospitalization index, so it was impossible to detect the effect in a small sample such as in our study. Another critical aspect of the polypharmacy of older adults, especially those with multimorbidity, is the analysis of polypharmacy's adequacy vis-à-vis the clinical context. From this perspective, the focus of the analysis of polypharmacy shifts from "too many drugs" to "many drugs", considering the multiple diseases of the older adults. The current trend is to avoid inadequate prescription ("too many drugs") and ensure prescriptions that contribute to proper polypharmacy ("many drugs") (Cadogan, Ryan, Hughes 2016), an aspect which should be considered before hospital discharge. The value of cutoff points assumes a limited value in this perspective, which may also explain the lack of association.

RRS proved to be a feasible and practical tool for the investigated hospital. It showed a linear concentration gradient. However, for its inclusion as a hospital risk predictive tool aiming to encourage actions to evaluate readmission in Brazil, it is necessary to develop an adequate validation study to determine the performance of RRS. RRS and the "80+ rating" are examples of a score that includes medications among its predictors (Taha *et al.*, 2014; Alassaad *et al.*, 2015). However, RRS stands out for including data available in the care practice without the need for laboratory parameters, which facilitates the collection process. Another RRS advantage is predicting readmission within 30 days (Taha *et al.*, 2014).

The study shows relevant information to guide actions focused on measures to prevent hospital readmission of the older adults after 30 days of hospitalization index. However, we should consider the limitations of the study. First, caution is required in generalizing the results since this research was carried out in a single public hospital and exclusively serves civil servants. Second, we did not evaluate adverse drug events as a determinant of readmission, which could better elucidate the characteristics of drug therapy as a risk factor for readmission within 30 days. Third, the sample covered a small number of older adults. However, the number of losses was not high. Fourth, visits to the hospital outpatient clinic or other primary care facilities of the public health system were not evaluated, as these establishments are essential elements to help elucidate hospitalization-related adverse events. Fifth, we did not analyze the suitability of prescribed medications for older adults' clinical and functional situation. Finally, the study evaluated only geriatric and medical clinic

older adults. Surgical clinic patients and other specialties were not investigated, compromising the generalization of results. The study's prospective design is a strength, as it provided the most reliable data collection. The outcome was not only evaluated through the electronic medical record of the health institution. Telephone follow-ups were conducted after discharge, allowing the investigation of readmissions in other hospitals and higher accuracy of information regarding the medications prescribed at discharge.

## CONCLUSION

The study showed that the diagnosis of cancer is positively associated with the readmission of the older adults within 30 days after discharge from the hospitalization index. Polypharmacy and the use of potentially inappropriate medication were prevalent among the older adults but did not show a significant association with readmission. Although prevalent among the older adults who were readmitted, the high-complexity drug therapy showed no significant association with readmission within 30 days.

## **DECLARATION OF CONFLICTS OF INTEREST**

The authors declare that there are no conflicts of interest.

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