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ORIGINAL ARTICLE

Association between frailty and inappropriate prescribing in elderly patients admitted to an Acute Care of the Elderly Unit

Mónica Zuleta[1] | Inés Gozalo[2] | Margarita Sánchez-Arcilla[1] | Jordi Ibáñez[3] | Carmen Pérez-Bocanegra[1] | Antonio San-José[1]

[1]Internal Medicine Department, Geriatric Unit, Vall d'Hebron University Hospital, Barcelona, Spain

[2]Pharmacy Department, Hospital San Rafael, Barcelona, Spain

[3]Internal Medicine Department, Hospital San Rafael, Barcelona, Spain

Correspondence
Mónica Zuleta Barco, Internal Medicine Department, Geriatric Unit, Vall d'Hebron Hospital, Barcelona 08035, Spain.
Email: monica.zuleta@vallhebron.cat

Abstract

Objectives: The aim of this study is to analyze the association between the degree of frailty and inappropriate prescribing patterns at admission to an Acute Care of the Elderly Unit (ACE Unit).

Methods: Prospective observational study conducted in the ACE Unit of an acute hospital in Barcelona city between June and August 2021. Epidemiological and demographic data were collected during hospitalization. Comprehensive geriatric assessment was performed on admitted patients. We recorded frailty (FRAIL scale), extreme polypharmacy (10 or more drugs), central nervous system potentially inappropriate medications-PIMs (STOPP-CNS or group D), cardiovascular potential prescribing omissions-PPOs (START-CV or group A), and anticholinergic burden using the drug burden index (DBI).

Results: Ninety-three patients were included, of whom 48 (51.6%) were male, with a mean age of 82.83 (SD 7.53) years. The main diagnosis upon admission was heart failure in 34 patients (36.6%). Frail patients were older, with more dependence of activities of daily living and more comorbidity than non-frail patients. Additionally, frail patients demonstrated more omissions according to the START-A criteria. No statistically significant differences were observed in term of extreme polypharmacy, PIMs, or anticholinergic burden.

Conclusions: In the current study we found an association between frailty and inappropriate prescribing, specifically with regard to omissions using the START criteria for the cardiovascular system (group A). Notably, frail patients exhibited more omissions compared to their non-frail counterparts, and this difference was statistically significant.

KEYWORDS
frailty, geriatric unit, inappropriate prescribing, polypharmacy

1 | INTRODUCTION

Elderly individuals experience high comorbidity, which often leads to polypharmacy. Although there is no universally accepted definition of polypharmacy, the widely adopted criterion involves the use of five or more medications, and extreme polypharmacy indicates the use of ten or more medications. The prevalence of polypharmacy among community-dwelling elderly ranges from 7% to 45%.[1,2]

In the elderly population, inappropriate prescribing (IP) is a common event and is often linked to polypharmacy, both situations contributing to adverse health outcomes.[2–7] In addition, patients with advanced age and comorbidity face an elevated risk of being prescribed medications with anticholinergic effects. This increased risk is associated with adverse consequences such as cognitive and functional impairment, increased risk of falls, higher rates of hospitalization, and elevated mortality.[8,9]

Several studies have highlighted a significant prevalence of inappropriate prescribing among community-dwelling older adults, nursing homes, and hospitals. Inappropriate prescribing encompasses both overprescribing, characterized by the use of potentially inappropriate medications (PIM), and underprescribing, indicated by possible prescription omissions (PPO).[10–16] A study in our setting showed that, in more than half of the cases, both problems were present simultaneously.[15]

Frailty stands as a common and significant geriatric syndrome, characterized by age-associated decline in physiological reserve and function of multiple organ systems. This condition renders individuals more susceptible to adverse health outcomes.[17] Although there is no universally accepted tool for assessing frailty, a variety of instruments exist. The most commonly used tools include Fried's criteria, the FRAIL scale, and the Rockwood scale, among others.[18,19] Prevalence varies according to the scale used and the setting in which it is assessed. A systematic review by Rónán O'Caoimh et al. estimated the global prevalence of frailty at 12% for physical frailty and 24% for frailty resulting from the accumulation of deficits in 62 countries.[20] The prevalence of frailty tends to increase with age, ranging from 4% to 59% among community-dwelling older people, with higher rates observed in women than in men.[21] The relationship between frailty and inappropriate prescribing lacks strong evidence, with some studies proposing a potentially bidirectional association.[18]

Although there is currently no conclusive evidence that interventions targeting anticholinergic burden lead to improved patient health outcomes, there may be potential benefits in mitigating polypharmacy.[22] Other interventions aiming to enhance appropriate medication use have shown reductions in inappropriate prescribing, but without corresponding improvements in health status.[23]

The aim of this study is to analyze the association between the degree of frailty and inappropriate prescribing patterns at admission to an Acute Care of the Elderly Unit (ACE Unit). Our hypothesis states that there is an association between frailty and different patterns of inappropriate prescribing, including extreme polypharmacy, PIMs, PPOs, and high anticholinergic burden.

2 | MATERIALS AND METHODS

This study is a prospective observational study carried out in the Acute Care of the Elderly Unit (ACE Unit) of a hospital in Barcelona city, Spain. The data were collected from the medical records of patients admitted to the unit between June 2021 and August 2021.

2.1 | Study population

Our ACE unit admitted all patients from Barcelona northern area requiring hospital admission for acute medical illness or exacerbation of chronic pathology. The recommended admission criteria was as follows: individuals aged 75 and above, categorized as frail and pre-frail (FRAIL score>0), with no significant baseline dependence in daily activities of living (Barthel Index >60), and lacking severe baseline cognitive impairment (global deterioration scale (GDS)-Reisberg <6).

2.2 | Methods

Epidemiological and demographic variables were collected, encompassing factors such as age, gender, origin, main diagnosis at the time of admission, length of stay, and discharge destination. The assessment of baseline status included an evaluation of frailty, using the FRAIL scale,[24] cognitive function assessed though GDS-Reisberg scale,[25] prior diagnosis of dementia, basic and instrumental activities of daily living (measured by the Barthel Index and Lawton Index, respectively),[26,27] and comorbidity evaluated by the Charlson Comorbidity Index.[28] Additionally, we documented geriatric syndromes such as dysphagia (assessed through medical records), risk of malnutrition using the Short Nutritional Assessment Questionnaire (SNAQ),[29] risk of falls (assessed through medical records), and risk of pressure ulcers evaluated by the Norton scale.[30] Within the first 48 hours of admission, cognitive status was assessed with the Pfeiffer test and the presence of delirium with the 4AT scale.[31,32]

Inappropriate prescribing was identified based on the following criteria: extreme polypharmacy (defined as 10 or more drugs), potentially inappropriate medication affecting the central nervous system (STOPP-CNS or group D) and potential prescribing omissions related to the cardiovascular system (START-CV or group A) using the STOPP/START criteria version 2,[33] and anticholinergic burden measured by the drug burden index (DBI).[34]

Comprehensive geriatric assessment (CGA) was performed by the hospital geriatric team, and evaluation of inappropriate prescribing was performed by the hospital pharmacy team.

2.3 | Statistical analysis

To analyze the sample, patients were divided into frail (FRAIL 3 or more) and non-frail (FRAIL<3). The sample was analyzed using the average and standard deviation (SD) for continuous variables.

Frequencies and percentages were used for categorical variables. To compare between subgroups in the present study, the Student's *t* test was used for continuous variables. To compare the results of the categorical variables, the χ^2 was applied. When the result was less than 5, Fisher's test was indicated. The statistically significant value was 0.05.

3 | RESULTS

Ninety-three patients were included in the study, of whom 48 (51.6%) were male, with a mean age of 82.83 (SD 7.53) years. The majority, 87 patients (93.5%), were from home or nursing homes, and the main diagnosis upon admission was heart failure in 34 patients (36.6%). The mean FRAIL score was 2.92 (SD 1.23), and 22 (23.7%) patients had dementia. Most patients demonstrated considerable comorbidity, as reflected by a Charlson Index mean of 3.3 (SD 2.27). Participants exhibited mild dependence for basic activities of daily living and moderate dependence for instrumental activities of daily living. On admission, the mean number of medications was 11.75 (SD 4.71), and 64 (68.8%) patients had extreme polypharmacy. A summary of the baseline characteristics of the study population is provided in Table 1.

We observed noteworthy differences in our comparative analysis of patients based on the degree of frailty. Frail patients (FRAIL score of 3 or more) were significantly older than non-frail counterparts (84.52 vs. 78.96, $P<0.001$). In addition, frail patients were more likely to be discharged to places other than their homes compared to non-frail patients, with a statistically significant difference (35.4% vs. 11.1%, $P=0.022$). Frail patients showed a higher functional dependence in basic and instrumental activities of daily living, as indicated by lower scores on the Barthel Index (76.77 vs. 86.30; $P=0.002$) and Lawton Index (3.60 vs. 5.58; $P=0.002$), respectively. Those who were frail also had higher comorbidity, with a higher Charlson Index (3.65 vs. 2.26, $P=0.005$), and a higher risk of malnutrition (SNAQ 2.02 vs. 1.58, $P=0.009$). Regarding geriatric syndromes such as dysphagia, risk of falls, risk of pressure ulcers, or delirium, our analysis revealed no statistically significant differences among frail and non-frail patients. Summary of significant results is presented in Table 2.

Regarding inappropriate prescribing (IP), our findings indicate that frail patients showed a higher prevalence of omissions (OPI) according to START criteria in group A in comparison to non-frail patients. This difference reached statistical significance, as 55.4% of frail patients had one or more START criteria, in contrast to non-frail patients, where 25.9% had one or more START criteria. However, no statistically significant differences were observed for extreme polypharmacy, potentially inappropriate prescribing according to group D STOPP criteria, or anticholinergic burden. The results are summarized in Table 3.

4 | DISCUSSION

In our current study, we identified a significant association between frailty and inappropriate prescribing, specifically in terms of omissions using the START criteria of group A. Frail patients showed a higher incidence of omissions on admission, compared to non-frail patients, and this difference was statistically significant. However, no statistically significant differences were observed when analyzing frailty in relation to other inappropriate prescribing variables, such as extreme polypharmacy, STOPP criteria, or anticholinergic burden.

According to the Comprehensive Geriatric Assessment (CGA), frail patients were characterized by older age, higher probability of discharge to out-of-home settings, higher dependency in activities of daily living, and higher comorbidity. In addition, in relation to geriatric syndromes, frail patients were at higher risk of malnutrition.

These results are consistent with previous research. Martinot et al. in their study concluded that the presence of PIMs increased the risk of developing frailty, with NSAIDs being the most commonly reported PIMs.[3] Another study found the association between frailty and IP restricted to drug classes such as anticholinergics, benzodiazepines, z-substances, and antipsychotics.[35] Meid et al.

TABLE 1 Baseline demographics and clinical characteristics.

Measures	Total: 93 patients
Age, years, mean (SD)	82.83 (7.53)
Gender, male, *n* (%)	48 (51.6)
Length of stay, days, mean (SD)	8.46 (5.37)
Origin at admission, *n* (%)	
Home[a]	87 (93.5)
Others[b]	6 (6.5)
Destiny at discharge, *n* (%)	
Home[a]	66 (71.0)
Others[c]	27 (29.0)
Main diagnosis, *n* (%)	
Heart failure	34 (36.6)
COPD	14 (15.1)
FRAIL score, mean (SD)	2.92 (1.23)
GDS, mean (SD)	2.32 (1.26)
Dementia, *n* (%)	22 (23.7)
Barthel Index, mean (SD)	76.56 (19.23)
Lawton Index, mean (SD)	4.18 (2.80)
Charlson Index, mean (SD)	3.3 (2.27)
Number of medications, mean (SD)	11.75 (4.71)
Polypharmacy, *n* (%)	
5 and more	86 (92.5)
10 and more	64 (68.8)

Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; GDS, global deterioration scale; SD, standard deviation.

[a]Home: own home, nursing home.

[b]Others: other acute hospital, intermediate hospital.

[c]Others: other acute hospital, intermediate hospital, hospital-at-home (HaH), death.

TABLE 2 Characteristics according to the presence of frailty.

	Non-Frail (27)	Frail (65)	*p*
Age, years, mean (SD)	78.96 (8.8)	84.52 (6.3)	<0.001
Gender, male, *n* (%)	15 (55.6)	32 (49.8)	0.581
Length of stay, days, mean (SD)	7.41 (4.6)	8.77 (5.5)	0.266
Origin at admission, *n* (%)			
Home[a]	27 (100.0)	59 (90.8)	0.103
Others[b]	0 (0.0)	6 (9.2)	
Destiny at discharge, *n* (%)			
Home[a]	24 (88.9)	42 (64.6)	0.022
Others[c]	3 (11.1)	23 (35.4)	
Main diagnosis, *n* (%)			
Heart failure	7 (25.9)	27 (41.5)	0.518
COPD	7 (25.9)	7 (10.8)	
Barthel Index, mean (SD)	86.30 (17.9)	72.77 (19.2)	0.002
Lawton Index, mean (SD)	5.58 (2.6)	3.60 (2.6)	0.002
Charlson Index, mean (SD)	2.26 (1.8)	3.65 (2.2)	0.005
SNAQ, mean (SD)	1.58 (0.7)	2.02 (0.6)	0.009
Dementia, *n* (%)	6 (22.2)	16 (25)	0.777
Pfeiffer, mean (SD)	2.50 (2.2)	2.83 (2.2)	0.552
Number of medications, mean (SD)	11.59 (4.8)	11.78 (4.7)	0.860

Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; SNAQ, Short Nutritional Assessment Questionnaire.

[a]Home: own home, nursing home.

[b]Others: other acute hospital, intermediate hospital.

[c]Others: other hospital, intermediate hospital, hospital-at-home (HaH), death.

TABLE 3 Patterns of inappropriate prescribing according to the presence of frailty.

	Non-Frail (27)	Frail (65)	*p*
Extreme polypharmacy, *n* (%)	18 (66.7)	45 (69.2)	0.810
STOPP-D, mean (SD)	0.56 (0.6)	0.46 (0.6)	0.511
STOPP 0, *n* (%)	14 (51.9)	39 (60.0)	
STOPP 1+, *n* (%)	13 (48.1)	26 (40.0)	
START-A, mean (SD)	0.26 (0.4)	0.69 (0.7)	<0.001
START 0, *n* (%)	20 (74.1)	29 (44.6)	
START 1+, *n* (%)	7 (25.9)	36 (55.4)	
Anticholinergic burden, mean (SD)	1.0 (0.7)	0.83 (0.7)	0.283
High, *n* (%)	13 (48.1)	27 (41.5)	
Medium or low, *n* (%)	14 (51.8)	38 (68.5)	

Note: Anticholinergic burden assessed using Drug Burden Index.

Abbreviations: START-A, START criteria of group A; STOPP-D, STOPP criteria of group D.

conducted a study on omissions using the START criteria of the cardiovascular group, revealing a high prevalence of omissions associated with frailty.[36] Gutiérrez-Valencia et al. did not find a direct association between frailty and polypharmacy in their multivariate analysis, but observed a higher prevalence of START criteria in frail patients, suggesting a trend towards a higher rate of omissions in institutionalized frail individuals.[37] In our study, frail patients showed a higher rate of omissions, although they did not have advanced frailty, severe dependence, or advanced dementia. Furthermore, there was no difference in the origin of patients between frail and non-frail individuals, which could explain the observed trend towards a higher rate of omissions.

There is limited evidence from randomized controlled trials assessing the benefits of interventions aimed at improving inappropriate prescribing in older people. In addition, most of these trials do not take into account the presence or degree of frailty in older populations. Interventions in these studies vary widely, ranging from hospital pharmacist recommendations to multidisciplinary approaches addressing inappropriate prescribing.[38–40] In future intervention studies targeting inappropriate prescribing in older people, the inclusion of frailty as a support is highly recommended. This would provide evidence-based personalized management, taking into account the degree of frailty of the elderly population.

Our study has several limitations that should be acknowledged. First, it is a single-center design with a small sample size, which limits the applicability of our findings and reduces the statistical power of our results. Moreover, being an observational study, we cannot establish causal relationships between variables. We used a simplified version of the STOPP/START criteria, which may not reflect the full spectrum of possible medication-related problems in our population. In addition, the STOPP criteria of group D in our study could introduce bias due to a potentially higher anticholinergic burden. The use of START criteria of group A was due to the high prevalence of heart failure diagnoses among our patients, which may not be applicable to different settings.

Despite these limitations, our study has some strengths. First, we performed a comprehensive geriatric assessment, which allowed for a more holistic assessment of the health status of our participants. In addition, we considered degrees of frailty of the patients, which provided additional information on their health status. In addition, we adopted a personalized approach to address the different profiles of inappropriate prescribing, which increases the clinical relevance of our findings.

5 | CONCLUSIONS

Our study found a notable association between frailty and inappropriate prescribing, specifically in terms of omissions among the cardiovascular medication spectrum according to the STOPP/START criteria. Evidence suggests that frail patients manifest a higher prevalence of omissions on admission compared to their non-frail counterparts, a distinction that reaches statistical significance in our sample.

These findings underscore the importance of further research to better understand the nature of the relationship between

inappropriate prescribing and frailty. Future studies should explore whether this association is unidirectional or bidirectional and further examine the underlying mechanisms driving this connection. The ultimate goal is to develop early interventions aimed at preventing adverse outcomes in the most vulnerable demographics in the future.

AUTHOR CONTRIBUTIONS

M. Z. wrote the entire manuscript and all the authors reviewed the manuscript.

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CONFLICT OF INTEREST STATEMENT

All authors declare that they have no financial conflicts of interest.

ETHICS STATEMENT

This is a prospective observational study without control group, with usual care intervention and anonymous participant data. No follow-up or medical records were taken after discharge. It has the approval of the Ethics Committee of Vall d'Hebron Hospital and adheres to the Declaration of Helsinki (1964) and its later amendments (current version dating from 2013).

ORCID

Mónica Zuleta https://orcid.org/0009-0009-4669-4531

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