

ORIGINAL ARTICLE

The Effect of Frailty and Cognitive Impairment on Rational Use of Medicine in Older Adults

Yaşlı Yetişkinlerde Kırılganlık ve Bilişsel Değişikliklerin Akılçılı Ilac Kullanımı Üzerindeki Etkisi

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ABSTRACT

Aim: To determine whether frailty and cognitive impairment affect rational use of medicines in older individuals.

Methods: The descriptive cross-sectional study was conducted in eastern Turkey. A total of 251 older individuals aged 60 years were included. In addition to demographic and medical characteristics, frailty status, mental status, and rational use of medicines were measured in a 25-35 minute scale administration period.

Results: The frailty scores of the participants were 1.65 ± 1.22 , rational use of medicines scores were 72.16 ± 16.31 , and mental status scores were 20.83 ± 5.46 . Rational use of medicines had a statistically significant negative correlation with frailty ($r = -.314$) and a statistically significant positive correlation with mental status ($r = .595^{**}$). There was a statistically significant difference in rational use of medicines according to polypharmacy, history of hospitalization, educational status, income, age, and cohabitant variables ($p < 0.05$). Regression analysis showed that the final model of rational use of medicines including mental status score, income, educational status, age, and cohabitant variables explained 43% of the total variance.

Conclusions: Rational use of medicines was adequate in the elderly, but cognitive impairment and frailty negatively affected rational use of medicines. Accordingly, it is recommended that mental status and frailty factors should be taken into consideration to ensure that the use of medicines in older individuals is in accordance with the principles of rational use of medicines.

Keywords: Cognitive impairment, frailty, mental status, older adults, rational use of medicines.

Öz

Amaç: Çalışma yaşlı bireylerde kırılganlık ve kognitif azalmanın akılçılı ilaç kullanımına etkisi olup olmadığını belirlemek amacıyla yapıldı.

Gereç ve Yöntemler: Tanımlayıcı kesitsel tipte yapılan çalışmanın verileri, Mart 2021 – Haziran 2021 tarihleri arasında toplandı. Bilişsel gerileme olmaksızın 60 yaş ve üzerindeki 251 yaşlı birey dahil edildi. Yaşlı bireylerin demografik ve tıbbi özelliklerinin yanında kırılganlık durumu, mental durumu ve akılçılı ilaç kullanımı 25-35 dakikalık bir ölçek uygulama süresinde ölçüldü.

Bulgular: Yaşlıların kırılganlık puanları $1,65 \pm 1,22$, akılçılı ilaç kullanım puanları $72,16 \pm 16,31$ ve mental durum puanları $20,83 \pm 5,46$ olarak bulundu. Akılçılı ilaç kullanımı ile kırılganlık arasında negatif yönde ($r = -.314$); mental durum arasında ise pozitif yönde ($r = .595^{**}$) istatistiksel olarak önemli ilişki bulundu. Akılçılı ilaç kullanımında çoklu ilaç kullanımı, hastanede yatma öyküsü, eğitim durumu, gelir durumu, yaş ve birlikte yaşanan birey değişkenlerine göre istatistiksel olarak önemli değişiklik saptandı ($p < 0,05$). Regresyon analizi yaşlıarda mental durum puanı, gelir durumu, eğitim durumu yaş ve birlikte yaşanan kişi değişkenlerini içeren akılçılı ilaç kullanımına ait nihai modelin toplam varyansın % 43'ini açıkladığını gösterdi.

Sonuçlar: Akılçılı ilaç kullanımı yaşlıarda yeterli düzeydeydi ancak kognitif azalma ile kırılganlık akılçılı ilaç kullanımını olumsuz etkilemiştir. Bu doğrultuda yaşlı bireylerde ilaç kullanımının akılçılı ilaç ilkelerine uygun olabilmesi için mental durum ve kırılganlık faktörlerinin göz önüne alınması önerilmektedir.

Anahtar Kelimeler: Akılçılı ilaç kullanımı, kırılganlık, kognitif azalma, mental durum, yaşlı, yaşlılık

INTRODUCTION

Weakness due to physiological and psychological problems occurring with old age is defined as frailty (1). It has been reported that frailty is more common in the presence of comorbidities and in individuals with low education and socioeconomic status (2, 3). As the level of frailty increases, individuals have difficulty in performing activities of daily living and need assistance. In addition, morbidity and mortality risks also increase (4, 5). Frailty, polypharmacy, and mental changes in the geriatric population significantly increase these risks (6, 7). Studies reporting a close relationship between cognitive dysfunction and frailty show that as the level of frailty increases, impairments and losses in cognitive functions also increase (8-12). Higher level of cognitive function indicate better physiological and psychological health (13, 14).

Comorbidity, which is closely related to frailty and cognitive impairment in old age, is especially prominent with the problem of polypharmacy. It has been revealed in the literature that inappropriate medicines use is common in the older population (14-17). The most effective way to minimize drug use complications is rational use of medicine. The process of rational drug use requires defining the problem and determining treatment targets. It begins with choosing the most effective, reliable and easy-to-use treatment among these targets. It is a process that includes explaining the applied treatment to the patient in an understandable way and closely monitoring and evaluating the results (17). Studies have shown that older individuals use five or more medicines (18, 19). Another study reported that 44% of frail older patients discharged from hospital

used at least one unnecessary medicine (20). Both over- and underuse of medicines is common in older people and causes serious problems (21).

In addition to the view that cognitive impairment and frailty may increase medicine misuse, side effects of medicine misuse such as functional decline, disability, frailty, cognitive impairment, incontinence, malnutrition, risk of falls, and trauma were reported (22). In this context, it should be kept in mind that incorrect medicine use may lead to frailty and cognitive impairment. In addition, considering that medicine absorption and distribution change with changing fat and water percentages in old age, it is clear that rational use of medicines is vital in this population (23). Despite the extensive literature on medicine use problems in older adults, few studies have addressed the causes of medication misuse or irrational use. Determining the effects of frailty and changes in cognitive function on medication use in older individuals and the strength of these effects is important to ensure rational use of medicines. Therefore, the aim of this study was to determine whether frailty and cognitive impairment have an effect on rational use of medicines in older individuals.

The following research questions are addressed in the study:

1. What is the level of rational use of medicines in older individuals?
2. Does frailty affect the rational use of medicines by older individuals?
3. Do cognitive impairment affect the rational use of medicines of older individuals?

The following research hypotheses are

addressed in the study:

H₁: The level of rational drug use of elderly individuals with high frailty level is significantly lower than non-frail elderly individuals.

H₂: The level of rational drug use of elderly individuals with cognitive impairment is significantly lower than those without cognitive impairment.

H₃: Frailty significantly predicts the level of rational drug use of elderly individuals.

H₄: Cognitive impairment significantly predicts the level of rational medication use of elderly individuals.

MATERIALS and METHODS

The data of this descriptive cross-sectional study were collected between March 2021 and June 2021.

When calculating the sample size, we assumed a frailty prevalence of 30% based on analyses of other studies with older people (33.2% and 27%) (24-26). A sample of 245 older individuals with confidence intervals of 5% and 95% was determined to be necessary. In the study, 350 older people were approached to be surveyed for the study. The scale was completed with 270 participants. Nineteen older individuals incompletely completed the scale and finally 251 patient scales were analyzed. The study included Turkish-speaking individuals aged 60 years and over who agreed to participate. Those who had previously been diagnosed with delirium or psychosis, or who had end-of-life clinical conditions, were excluded.

Data Collection

Data were collected using a survey form

created by the researchers, the FRAIL Scale, the Standardized Mini Mental Test (SMMT), and the Rational Use of Medicines Scale (RUMS) short form. First, the scales were introduced to each participant individually. Then each question was read and the answer given by the participant was marked by the researcher. For the drawing questions in the SMMT scale, the participant made the drawing, then scoring was performed and the results were recorded. The average scale response time for each participant was 25-35 minutes.

FRAIL Scale: The 'FRAIL Scale' developed by Morley et al. in 2012 consists of 5 items (27). The FRAIL Scale has been validated in many countries and has proven to be an effective method for detecting frailty. In this scale, which allows evaluation by questioning the patient's fatigue status, resistance, mobility, weight loss, and other diseases, patients receive 0 or 1 point according to their answer. A total score of 0 is considered non-frail, 1-2 points is considered pre-frail, and >2 points is considered frail (28).

Standardized Mini Mental Test (SMMT): It is a short, useful, and standardized method used to assess cognitive level. It consists of eleven items and is evaluated on a 30-point scale. A score between 24 and 30 points is considered "normal", 18-23 points as "mild dementia", and 17 points and below as "severe dementia" (29, 30).

Rational Use of Medicines Scale (RUMS): The scale consists of 21 items in a single dimension. The items are scored on a 5-point Likert-type scale according to the occurrence of the statements (1-Never, 2-Rarely, 3-Sometimes, 4-Most of the time and 5-Always). Only item 17 is scored in reverse. The sum of all scale items, including

the reverse item included in reverse gives the "total scale score". The total score of the RUMS varies between 21 and 105. As the total score obtained from the RUMS increases, rational use of medicines increases. When evaluating the total score obtained from the RUMS, if the total score obtained is between 21 and 52, it is considered as "low level", between 53 and 67 as "medium level", and between 68 and 105 as "high level"³¹. Cronbach's alpha internal consistency coefficient of the RUMS was determined as 0.84.

Statistical Analysis

Data analyses were performed in 2022 using SPSS 22 software. First, descriptive statistics, t tests, and ANOVA were used to compare rational use of medicines by demographic characteristics, followed by Pearson correlation and forward stepwise multiple regression to investigate the association between rational use of medicines and cognitive and frailty. Correlation strength was interpreted as $0.7 \leq r =$ strong correlation, $0.5 \leq r < 0.7 =$ moderately strong correlation, $0.3 \leq r < 0.5 =$ weak correlation, and $r \leq 0.3 =$ very weak correlation (32).

Ethics Statement

Approval was obtained from Inonu University Health Sciences Non-Interventional Clinical Research Ethics Committee (2021/1750). The study was conducted in accordance with the Declaration of Helsinki. All participants provided voluntary consent online and their participation was confidential. Permission to use the scale was obtained from the authors.

RESULTS

The mean age of the 251 participants included in the study was 72.59 (SD: 6.59) and the age range was between 60 and 85.

There was a negative correlation between age and RUMS ($r = -.379$) and SMMT ($r = -.411$) scores, and a weak positive correlation with the frailty score ($r = .333$). Most of the participants were female (54.2%), had primary education (50.2%), had an income below 2825 TL (42.6%), and lived with their spouse (42.2%). It was determined that 43.8% used multiple medicines, 19.9% had had an accident in the last year, and 30.7% had been hospitalized at least once in the last year. Rational use of medicines of the participants was significantly higher in those with a bachelor's degree or higher. Rational use of medicines scores of the participants whose income was 2825 TL or less, who lived with their children, used multiple medicines, and had a history of hospitalization were significantly lower ($p < 0.05$). The frailty level of the participants was higher in those who were illiterate, lived with their children, used multiple medicines, and had a history of hospitalization and accidents in the last year ($p < 0.05$). The mental scores of the participants were lower in women, illiterates, those with an income of 2825 TL or less, those living with their children, those using multiple medicines, and those with a history of hospitalization ($p < 0.05$) (Table 1).

The rational use of medicines score of the participants was 72.16 (SD: 16.31), the frailty score was 1.65 (SD: 1.22), and the SMMT score was 20.83 (SD: 5.46). There was a negative correlation between rational use of medicines and frailty ($r = -.314$) and a positive and moderately significant correlation with the SMMT score ($r = .595$) (p values $\leq .005$). It was determined that 48.6% of the participants were pre-frail and 26.7% were frail. Rational use of medicines and mental change scores decreased in pre-frail and frail participants compared

Table 1: Comparison of RUMS, FRAIL and SMMT scale scores by demographic characteristics (n=251)

Demographic Characteristics		RUMS	FRAIL	SMMT
		r/p	r/p	r/p
Age (years)		-.379**	.333*	-.411**
	72.59 (6.59)	60-85	.001	*.001
				.001
		n (%)	M(SD)	M(SD)
Sex	Female	136 (54.2)	71.81 (16.82)	1.74 (1.17)
	Male	115 (45.8)	72.58 (15.75)	1.54 (1.28)
	Test		t= -.370	t= 1.254
	p Value		p=.712	p=.211
				p=.032
Education	Illiterate	21 (8.4)	71.04(24.23)	2.52(.98)
	Primary School	126 (50.2)	67.96(14.72)	1.62(1.20)
	Middle School	52 (20.7)	77.07(13.58)	1.55(1.33)
	University and above	52 (20.7)	77.88(16.00)	1.46(1.14)
	Test		KW= 22.734	KW=12.538
	p Value		p=.000	p=.006
				p=.000
Income Level ¶	Less than 2825 TL	107 (42.6)	64.58(14.92)	1.78(1.13)
	Between 2826 and 3999 TL	92 (36.7)	77.30(15.26)	1.55(1.37)
	4000 TL and over	52 (20.7)	78.67(14.67)	1.55(1.12)
	Test		F= 23.955	F= 1.073
	p Value		p=.000	p=.344
				p=.000
Cohabitants	With child/children	57 (22.7)	62.22 (18.24)	2.35 (1.24)
	With spouse	106 (42.2)	75.69 (13.14)	1.33 (1.11)
	With spouse and child/children	55 (21.9)	73.69 (15.28)	1.47 (1.18)
	Alone	33 (13.1)	75.45 (17.41)	1.75 (1.17)
	Test		F= 10.35	F= 9.86
	p Value		p=.000	p=.000
				p=.000
Polypharmacy	Yes	110 (43.8)	67.36 (17.61)	2.17 (1.17)
	No	141 (56.2)	75.91 (14.19)	1.24(1.10)
	Test		t= -4.259	t= 6.371
	p Value		p=.000	p=.000
				p=.000
Hospitalization (within the last year)	Yes	77(30.7)	68.10(18.50)	2.28(1.12)
	No	174 (69.3)	73.96(14.95)	1.37(1.16)
	Test		t= -2.657	t= 5.768
	p Value		p=.008	p=.000
				p=.001
History of accidents (within the last year)	Yes	50 (19.9)	69.70(17.77)	2.18(1.08)
	No	201 (80.1)	72.78(15.91)	1.52(1.22)
	Test		t= -1.196	t= 3.463
	p Value		p=.233	p=.001
				p=.085

*p<0.05; M = mean; FRAIL: Frailty scale, SD=Standard deviation; t= Student's t test; U= Mann Whitney U Test, RUMS: Rational Use of Medicine Scale, SMMT: Standardized Mini Mental Test, ¶= Variances are homogeneous according to Levene's test result. According to the Post Hoc test Tukey HSD, the group with an income of 2825 TL made the difference. #= According to Levene's test result, variances are homogeneous. According to the Post Hoc test Tukey HSD, the group showing the difference was those living with their children.

to non-frail participants. The decrease in rational use of medicines in frail participants was statistically significant. Among the participants, 39.8% had dementia and 24.3% had severe dementia. The decrease in rational use of medicines in individuals with dementia according to the severity of dementia was statistically significant (Table 2, Figure 1).

Potential influencing factors that showed statistically significant associations by t-test,

ANOVA, KW, or correlation were selected for forward stepwise regression analysis. Since no predictor variable was highly associated with rational use of medicines, all variables were included in the analysis. Components of rational use of medicines included SMMT, frailty score, polypharmacy, cohabitant(s), caregiver, age, education, and income.

Five variables, namely SMMT, income, education, age, and cohabitant(s), explained the final model ($F = 136.134$, $p <$

Table 2: Impact of frailty and mental status on rational use of medicines (n=251)

		RUMS		
		Mean (SD)	r	p
RUMS		72.16 (16.31)		
FRAIL Scale		1.65 (1.22)	-.314**	.001
SMMT Scale		20.83 (5.46)	.595**	.001
Frailty Status	n(%)	Mean (SD)	F	P
Non-frail	62 (24.7)	78.61(11.93)		
Pre-frail	122 (48.6)	71.73 (15.53)	8.774	.001¶
Frail	67 (26.7)	66.98 (19.16)		
Mental Status				
Normal	90 (35.9)	82.13 (12.01)		
Dementia	100 (39.8)	70.93 (14.19)	49.163	.001#
Serious Dementia	61 (24.3)	59.49 (15.72)		

**p<.001, FRAIL: Frailty scale, RUMS: Rational Use of Medicine Scale, SMMT: Standardized Mini Mental Test,

¶=Variances are homogeneous according to Levene's test result. Post Hoc test Tukey HSD test showed that there was a difference between normal and frail and pre-frail.

#=The variances were homogeneous according to Levene's test result. Post Hoc test Tukey HSD test showed that there was a difference between normal, dementia, and severe dementia.

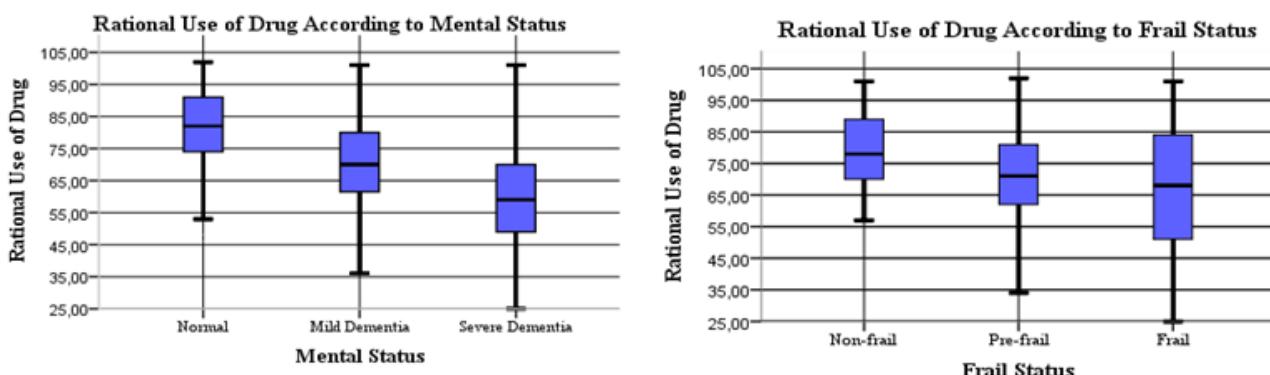


Figure 1. Impact of frailty and mental status on rational use of medicines

Table 3. Factors predicting rational use of medicines in the older adults

Variables	B	SE	β	t	p	Adj. R2	F	p
(Constant)	54.875	10.611		5.172	.000			
SMMT	1.562	.175	.523	8.928	.000			
Income Status	6.629	1.289	.312	5.144	.000			
Educational Level	-3.833	1.155	-.214	-3.318	.001	.435	136.134	<.001
Age	-.290	.118	-.129	-2.455	.015			
Cohabitants	1.679	.831	.098	2.021	.044			

Stepwise multiple regression was performed to identify predictors of rational use of medicines. SE: Standard error, SMMT: Standardized Mini Mental Test,

.001). These variables explained 43% of the total variance in rational use of medicines. The standardized regression coefficient on rational use of medicines was highest for SMMT ($\beta = .52$), followed by income ($\beta = .31$), education ($\beta = -.214$), age ($\beta = -.129$), and cohabitant(s) ($\beta = .098$) (Table 3).

DISCUSSION

To the best of our knowledge, this is the first study to report the relationship between frailty, mental status, and rational use of medicines in the older adults living in a Turkish population. This study had three important findings. First, the rational use of medicines was adequate and the participants were pre-frail and mildly demented. Second, rational use of medicines was negatively affected in those with increased frailty and severity of dementia. Finally, factors such as mental status, income, education, age, and cohabitant(s) were found to predict rational use of medicines. The participants were pre-frail and mildly demented, our results reflect the general condition of individuals of similar age in Türkiye (33). Although many national and international studies have pointed to inappropriate drug use in older adults, the rational drug use scores of the

elderly were found to be adequate in our study. These studies particularly emphasise polypharmacy, negative effects of factors such as comorbidity, number of medication use and anxiety on medication use have been reported (34-37). Although rational use of medicine scores were high in our study, it was observed that the variables reported in the literature affected the level of rational use of medicine.

Akin et al. found the prevalence of frailty, pre-frailty, and non-frailty as 10%, 45.6%, and 44.4%, respectively (38). Participants of the present study were more frail (pre frail %48.6, frail %26.7). The 7.1% prevalence of frail adults in rural Türkiye reported by Çakmur and the prevalence of frailty in Sweden, Denmark, the Netherlands, Germany, Austria, Switzerland, and France, respectively 8.6%, 12.4%, 11.3%, 12.1%, 10.8%, 5.8%, and 15.0% are quite lower compared to our results (33). In the Mediterranean region, the prevalence of frailty is 14.7% in Greece and 23.0% in Italy, so even in similar regions, the prevalence of frailty can vary (39). These results show that there is a significant level of frailty in older adults, but there are differences in prevalence. It is clear that this frailty in older adults may have many negative consequences.

In particular, the increase in older adults increases the incidence of comorbidities and the rate of polypharmacy (40). The increase in polypharmacy rates also brings the concept of frailty to the agenda and there are many studies supporting this phenomenon (33, 41-43). Arslan et al. (2020) found that the number of chronic diseases and frailty score were statistically significantly higher in older adults with polypharmacy (41). Similarly, Çakmur (2015) found that comorbidity and polypharmacy are associated with frailty (33). Clinically, frailty and polypharmacy often coexist and one condition can lead to the emergence of the other, synergistically compromising the health outcomes of older people. This highlights the importance of interventions to prevent or reverse frailty. The results of this study may highlight the need to manage both frailty and polypharmacy simultaneously, and prevention of frailty may be of greater importance, especially to prevent the progression of moderate frailty to severe frailty.

Considering the significant association of frailty with polypharmacy in the literature and the findings in our study that frailty negatively affects rational use of medicines, we emphasize that both polypharmacy can be prevented and frailty can be regressed with rational use of medicines. However, the conclusion that frailty negatively affects rational use of medicines cannot be explained only by polypharmacy. Considering that rational use of medicines is "the set of rules that patients should follow for the society and themselves to use medicines in accordance with their clinical needs, in a dose that meets individual needs and in an adequate time interval", it is inevitable that a frail older

adult cannot provide all these parameters (44). Therefore, our findings suggest that supporting frail older people in the rational use of medicines to be able to make the best use of it.

In previous studies as well as in our study, it has been observed that the rational use of medicines and frailty status of older adults are significantly affected by sociodemographic characteristics. It is thought that an increase in the level of education has important contributions on cognitive functions and is an important factor in preventing vulnerability (45). This again draws attention to the importance of the educational status of older adults in rational use of medicines, which is closely related to education. In the study conducted by Hatipoğlu and Özyurt (2016), it is seen that nuclear family structure, income status, and higher education level increase the rates of rational use of medicines (46). In another study, it was observed that attitudes towards rational use of medicines were lower in individuals with low income living in rural areas (47).

When we analyzed the effect of changes in mental status on rational use of medicines, we found significant negative effects even in mild dementia. The difference between mild dementia and severe dementia in terms of rational use of medicines may indicate the importance of rational use of medicines in older adults. Studies have shown that inappropriate medicine use is common in older people with cognitive impairment. In these studies, co-morbidities, recent hospitalization, functional impairment, communication problems have been associated with the risk of inappropriate medicine use (48, 49-53). In our study, we concluded that

factors such as gender, educational status, income, cohabitants, polypharmacy, and hospitalization status should be evaluated together, which may cause changes in mental status scores that may interfere with rational use of medicines. It has been reported that the negative effects of memory loss, decreased intellectual functions, reasoning, and language disorders on decision-making capacity in patients with advanced dementia affect adherence to treatment and cause communication difficulties (48, 54). In this context, many studies have emphasized the need to avoid medicines that may affect cognition or trigger delirium when treating patients with cognitive impairment (48-50, 55). These concerns should be carefully considered by physicians and nurses to overcome barriers to pharmacological treatment of complex patients with severe cognitive impairment (50, 56). This can be based on a set of criteria developed by Holmes and colleagues to identify inappropriate medicine treatment that may or should not be stopped or started in patients with advanced dementia (52). The Holmes criteria were established to reduce polypharmacy and high-risk or minimally beneficial medicine use in older adults.

Finally, when we explained rational use of medicines in older adults with a model, we found that several factors, namely, cognitive status, income status, educational status, age, and cohabitant(s), explained rational use of medicines in older adults. These results indicate that all outcomes should be considered together and the factors that pose the highest risk should be taken into consideration in the care of older adults.

Limitations

There are some limitations that require careful interpretation of our results. First, although we identified age-related comorbidities, we did not consider disease severity. Second, we measured polypharmacy in terms of medicine use but did not consider the duration of the use of each medication. Finally, although the rational use of medicines score was found to be statistically significantly lower in frail older adults, total frailty was not found to be effective on rational use of medicines according to the results of the regression analysis. This suggests that frailty is influenced by many complex factors and further studies should be conducted to examine the relationship between frailty and rational use of medicines. In future studies, it is recommended to examine the effect of disease severity and duration of medication use on rational use of medicines in older adults due to the effect of frailty and mental status.

CONCLUSIONS and RECOMMENDATIONS

Rational use of medicines has a serious importance in older adults. In the present study, it was observed that the rational use of medicines was adequate and the participants were pre-frail and mildly demented. Rational use of medicines was negatively affected in those with increased frailty and dementia severity, and factors such as mental status, income, educational status, age, and cohabitant(s) predicted rational use of medicines. Special interventions are needed to improve rational use of medicines in frail and demented older adults.

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