DOI: 10.37990/medr.1183707 Med Records 2023;5(2):255-61

MEDICAL RECORDS-International Medical Journal

Research Article

Polypharmacy in the Elderly: A Double-Edged Sword

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Abstract

Aim: Polypharmacy is a very important geriatric syndrome related to critical health conditions. The purpose of this study is to research the association of polypharmacy with comprehensive geriatric assessment's (CGA) various parameters which are indicators of health and life quality in older individuals.

Material and Methods: 515 older adults admitted to a university hospital were included in this cross-sectional study. Along with CGA, European Quality of Life (EQ-5D) was performed on the participants. Geriatric Depression Scale (GDS) was used to evaluate depressive symptoms. Daily living activities were assessed by using Lawton & Brody index of Instrumental Activities of Daily Living (IADL) and Katz Index of Activities of Daily Living (ADL). The Full Mini-Nutritional Assessment (MNA) questionnaire was performed to evaluate nutritional status.

Results: The participants' mean age was 72.2±6.3 years and 58.6% of them were female. 242 participants using 5 or more drugs were included in the polypharmacy group. The polypharmacy group had lower IADL, MNA, EQ-5D, Hand Grip Strength (HGS), and gait speed scores and higher GDS scores compared to those without polypharmacy. According to the correlation analysis results, the number of the medications had a moderate positive correlation with GDS scores and a moderate negative correlation with EQ-5D and MNA.

Conclusion: As the number of medications increases; patients tend to have depression, malnutrition, and a decline in functional status. Polypharmacy also impairs the quality of life. We should address polypharmacy as a crucial health problem, optimize the number of medications and thereby make the health condition better.

Keywords: Polypharmacy, depression, daily living activities, malnutrition, quality of life

INTRODUCTION

The aging population has been constantly rising around the world and multimorbidity and geriatric syndromes are increasing consequently. Polypharmacy due to morbidity, which is a component of geriatric syndromes, is also increasing and turning into a serious health problem (1). Some physiological changes arising with aging make elderly susceptible to the drugs. Therefore, polypharmacy leads to more often unintended consequences among older individuals through drug-drug interactions and adverse reactions (2). Falls, frailty, impairment in cognition and physical function, increased hospitalization and recurrent readmission, prolonged hospital stay, decreased drug adherence, reduced medication efficacy and increased mortality have been linked to polypharmacy which is also a great economic burden (3).

The definition of the polypharmacy is using potentially inappropriate drugs and/or concurrently multiple medications including prescribed and over-the-counter drugs (4). Even though the exact number of drugs in polypharmacy is still not clear and has been defined variously, using five or more drugs per day is generally considered polypharmacy, given the number of drugs alone (5). "Excessive polypharmacy" is defined as using ≥10 medications concurrently (6). Older adults are more susceptible to side effects and interactions of the drugs because of the high rates of the comorbidities in comparison with the younger adults (7). Prescribing numerous drugs may cause inappropriate drug use, an increase in adverse reactions, decreased medication adherence, repetition of therapy, and interactions between drugs. Thus, polypharmacy is associated with impairment in nutrition and physical function, decline in cognitive functions and

CITATION
Ozturk E, Ganidagli S, Ozturk ZA. Polypharmacy in the Elderly: A Double-Edged Sword. Med Records. 2023;5(2):255-61. DOI:1037990/medr.1183707

Received: 04.10.2022 **Accepted:** 14.11.2022 **Published:** 23.03.2023
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increase of geriatric syndromes (2,8). Status of the nutrition, cognitive and functional capacity are markers of health quality in older ages (9,10). Sarcopenia is known as one of the major risk factors for frailty, and polypharmacy is also known to be associated with sarcopenia (11,12). Frailty in the elderly is a multi-dimensional geriatric syndrome that may cause a decline in functional ability, falls, delirium, hospitalization, and death (13). There is a close relationship between polypharmacy and multimorbidity, and both these conditions independently increase the frailty and hospitalization risk. A decline in physical performance is also a consequence of polypharmacy (14). A poorer cognitive capability and disability in instrumental activities are also shown to be negative outcomes of polypharmacy (15,16).

Various health-related conditions influencing life quality such as polypharmacy, comorbidities, and malnutrition, and disability trigger depression (17). Late-life depression is a common health problem and affected by gender, socioeconomic status, physical activity, and nutrition, is associated with serious consequences ending up morbidity and mortality (18). There is a relationship between polypharmacy and depression, and depression may be a better independent predictive factor for polypharmacy than the other comorbid diseases (19). Lower depression scores have been shown to increase adherence to medication in the general population (20).

The aim of this study is to research the association of polypharmacy with CGA's various parameters that are indicators of health status and quality of life in the elderly.

MATERIAL AND METHOD

This cross-sectional study was conducted with 515 older individuals aged 65 and over who applied to geriatric outpatient clinic of a university hospital between the dates May 2022 and August 2022. Patients who have cognitive disorders impairing cooperation, cancer, aphasia, inflammatory and neuromuscular diseases, and comorbidities severely restricting to assess muscle functions like severe osteoarthritis, neuropathy and peripheral artery disease were excluded. The medical histories of the participants including comorbid diseases and polypharmacy were questioned. Concurrently use of five and more different drugs in a day was described as "Polypharmacy" (5). Epi Info software was used to calculate the sample size. The minimum sample size was 298 participants at the level of $\alpha = 0.05$ with 95% power. We conducted the study with the approval of the local ethics committee.

The components of the comprehensive geriatric assessment consist of evaluating the nutritional status, fall risk, instrumental activities of daily living, activities of daily living, sarcopenia, mental status, and depressive symptoms.

All of the questionnaires were performed using the validated forms and in the Turkish language. In order to evaluate depressive symptoms, the GDS was used which is coded according to responses to questions. Negative responses were coded as 0 point whereas positive responses were coded as 1 point. Some questions were reversely coded. The scores 14 points and over were considered as "depression", those between 0 and 10 as "no depression" and those between 11 and 13 as "possible depression".

The criteria of the Working Group on Sarcopenia in Older People (EWGSOP2) were used in order to diagnose sarcopenia. The bioelectric impedance analyzer branded Tanita SA165 A-0950U3 was used to measure muscle mass and handgrip strength (muscle strength) was measured by Jamar hydraulic hand dynamometer. The values lower than 32 kilograms for males and 22 kilograms for females were considered as low hand grip strength (HGS). The values lower than 0.823 for females and 1.049 for males were considered as low muscle mass after calculating skeletal muscle mass index (SMMI) adjusted for body mass index (BMI). The speed of the gait lower than ≤ 0.8 m/s was considered as low gait speed.

The dependence of the participant in physical activities including feeding, transferring, dressing, continence, toileting, and bathing was evaluated by the questionnaire of Katz Index of Activities of Daily Living (ADL). Scores were given 0 to 6 and higher scores were considered as greater independence. The dependence of the participant in physical activities including using the telephone and public transportation, housekeeping, food preparation, managing money, shopping, doing laundry, and taking routine medicines was evaluated by the questionnaire of Lawton & Brody index of Instrumental Activities of Daily Living (IADL) Scores were given 0 to 8 and higher scores were considered as greater independence.

The Mini Nutritional Assessment questionnaire (MNA) was used to evaluate the status of nutrition. Scores above 24 were considered as "normal nutritional status", those below 17 were considered as "malnutrition" (MN), and those between 17 and 23.5 as "risk of malnutrition" (MNR).

The cognitive status of the participants was evaluated by using the mini-mental state examination questionnaire (MMSE). In the test maximum score for orientation is 10 points, attention and calculation is 5 points, registration is 3 points, language/visuospatial construction is 9 points, and recall is 3 points. The scores 24 and below were considered as "suggesting dementia". In the "orientation" item, the participants were asked questions like “Which city do you live in?”, “Which year?” or "What building are you currently in?" etc. In the item "attention and calculation" the participant were asked to count backwards; in the "registration" and "recall" they were asked to listen, repeat and then recall certain words, and in the "language/visuospatial construction" they were asked to implement some orders and try to draw the same what they see on the page.

In order to evaluate life quality, the European Quality of Life-5 Dimensions questionnaire (EQ-5D) was used. 5 aspects of health status including anxiety/depression,

usual activities, mobility, pain/discomfort, and self-care were questioned and the index score was calculated. Negative values scores mean that person is unconscious, bedridden, and dependent while the score "0" means death and the score "1" shows flawless health.

The independent samples t-test and Mann–Whitney U test were used to compare two independent groups of variables. The relationship between categorical variables was assessed with the $\chi 2$ test and numerical variables with Spearman's rank correlation coefficient. SPSS for Windows version 22.0 was used and a p-value of <0.05 was accepted as statistically significant.

RESULTS

The mean age of the participants was 72.2±6.3 years and 58.6% were female. Of the participants, 242 were considered as having polypharmacy based on the number of the drugs they used. The rate of chronic diseases was higher in the polypharmacy group, except cerebrovascular disease. Polypharmacy group had lower IADL, MNA, EQ-5D, HGS, and gait speed scores and higher GDS scores and antidepressant user rates compared to those without polypharmacy (Table 1). The frequency of sarcopenia was higher in the polypharmacy group, although there was no statistically significant difference.

Table 1. Socio-demographic characteristics and CGA results of the participants (n=515)

Variables	Polypharmacy (-) (n=273)	Polypharmacy (+) (n=242)	p	Total (n=515)
Gender				
Female	158 (57.9%)	144 (59.5%)	0.708	302 (58.6%)
Male	115 (42.1%)	98 (40.5%)		213 (41.4%)
Age†	72.2±6.3	72.2±6.4	0.942	72.2±6.3
Number of comorbidities#	2 (0-6)	3 (1-8)	<0.001*	2 (0-8)
Number of medications#	2 (0-4)	6 (5-20)	<0.001*	4 (0-20)
Comorbidities				
Hypertension	132 (48.4%)	165 (68.2%)	<0.001*	297 (57.7%)
Diabetes mellitus	96 (35.2%)	147 (60.7%)	<0.001*	243 (47.2%)
Coronary artery disease	52 (19.0%)	93 (38.4%)	<0.001*	145 (28.2%)
Asthma/COPD	21 (7.7%)	42 (17.4%)	<0.001*	63 (12.2%)
Neurodegenerative diseases	25 (9.2%)	49 (20.2%)	<0.001*	74 (14.4%)
Cerebrovascular disease	9 (3.3%)	13 (5.4%)	0.245	22 (4.3%)
Antidepressant use	6 (2.2%)	20 (8.3%)	0.002*	26 (5.0%)
ADL†	4.0±1.7	4.0±1.7	0.913	4.0±1.7
IADL†	5.9±2.0	5.4±2.3	0.004*	5.7±2.2
GDS#	6 (0-30)	9 (2-30)	<0.001*	7.5 (0-30)
MMSE†	24.2±5.1	23.4±5.7	0.093	23.8±5.4
MNA†	23.1±5.2	21.6±5.3	0.002*	22.4±5.3
EQ-5D#	0.70 (-0.27-1.00)	0.41 (-0.53-1.00)	<0.001*	0.52 (-0.53-1.00)
BMI†	29.2±5.2	29.9±5.4	0.167	29.5±5.3
Sarcopenia	85 (32.4%)	89 (38.7%)	0.148	174 (35.4%)
HGS (kg)†				
Female	20.7±6.5	18.2±6.4	0.001*	19.5±6.6
Male	27.8±7.0	27.2±6.8	0.380	27.5±6.9
SMMI (BMI)†				
Female	0.80±0.16	0.80±0.16	0.896	0.80±0.16
Male	1.18±0.19	1.18±0.17	0.880	1.18±0.18
Gait speed †	0.84±0.28	0.76±0.28	0.001*	0.80±0.28

*p<0.05; †Data are presented as Mean±SD. #Data are presented as median (min-max)
CGA, comprehensive geriatric assessment; COPD, Chronic obstructive pulmonary disease; ADL, Katz Index of Activities of daily living; IADL, Lawton & Brody index of Instrumental Activities of Daily Living; GDS, The Geriatric Depression Scale; MMSE, Mini Mental State Examination; MNA, The Mini Nutritional Assessment Tool; EQ-5D; European Quality of Life-5 Dimensions; HGS handgrip strength; SMMI skeletal muscle mass index

Number of the medications had a negative moderate correlation with EQ-5D and MNA scores, a negative weak correlation with IADL, HGS and gait speed scores, and a positive moderate correlation with GDS scores according to the correlation analysis results (Table 2, Table 3).

Table 2. Correlation analysis results between the variables

		Number of medications	Age	Number of diseases	ADL	IADL	EQ-5D
Number of medications	r		0.047	0.513**	-0.070	-0.224**	-0.423**
	p		0.290	0.000	0.114	0.000	0.000
Age	r	0.047		-0.008	-0.079	-0.256**	-0.306**
	p	0.290		0.853	0.073	0.000	0.000
Number of diseases	r	0.513**	-0.008		0.114**	-0.123**	-0.343**
	p	0.000	0.853		0.010	0.005	0.000
ADL	r	-0.070	-0.079	0.114**		0.537**	0.545**
	p	0.114	0.073	0.010		0.000	0.000
IADL	r	-0.224**	-0.256**	-0.123**	0.537**		0.655**
	p	0.000	0.000	0.005	0.000		0.000
EQ-5D	r	-0.423**	-0.306**	-0.343**	0.545**	0.655**	
		0.000	0.000	0.000	0.000	0.000	

r: Spearman rank correlation coefficient; ** Significant at 0.01 level. ADL, Katz Index of Activities of daily living; IADL, Lawton & Brody index of Instrumental Activities of Daily Living; EQ-5D; European Quality of Life-5 Dimensions

Table 3. Correlation analysis results between the variables

		Number of medications	GDS	MMSE	MNA	HGS	Gait speed
Number of medications	r		0.313**	-0.086	-0.305**	-0.153**	-0.145**
	p		0.000	0.051	0.000	0.001	0.001
GDS	r	0.313**		-0.286**	-0.315**	-0.335**	-0.215**
	p	0.000		0.000	0.000	0.000	0.000
MMSE	r	-0.086	-0.286**		0.104*	0.297**	0.222**
	p	0.051	0.000		0.018	0.000	0.000
MNA	r	-0.305**	-0.315**	0.104*		0.233**	0.240**
	p	0.000	0.000	0.018		0.000	0.000
HGS	r	-0.153**	-0.335**	0.297**	0.233**		0.502**
	p	0.001	0.000	0.000	0.000		0.000
Gait speed	r	-0.145**	-0.215**	0.222**	0.240**	0.502**	
		0.001	0.000	0.000	0.000	0.000	

r: Spearman rank correlation coefficient; ** Significant at 0.01 level. ADL, Katz Index of Activities of daily living; IADL, Lawton & Brody index of Instrumental Activities of Daily Living; EQ-5D; European Quality of Life-5 Dimensions

DISCUSSION

In our study we found that polypharmacy is significantly related to depression, decline in instrumental daily activities, impaired nutritional status, and worsening in life quality. The number of the comorbidities was higher in the polypharmacy group. Having multiple comorbid diseases is the most important reason for polypharmacy. On top of that, polypharmacy increases the risk of geriatric syndromes and the rates of morbidity and mortality in older people (3). Increasing rates of multimorbidity is closely related to a decrease in life quality and decline in functional capacity (21).

Previous studies have shown that polypharmacy is associated with impaired physical functioning in older adults (14,16), and this close relationship is thought to be a bidirectional cause-effect relationship (22). In the

current study, gait speed and IADL scores were lower in the polypharmacy group whereas ADL scores found to be similar. “Polypharmacy” itself and “excessive polypharmacy” were shown to be related to disabilities in IADL (15,23). However, in another study in which polypharmacy was defined as using six and more drugs, there was not any association between polypharmacy and ADL scores (24). There may be a reasonable explanation of this situation: IADL includes activities such as using the telephone, preparing food or doing laundry those are more complicated than ADL because of the dependence of instruments. Due to the same reason, it also requires superior cognitive functions than ADL that includes basic living activities like feeding, bathing or toileting. "Excessive polypharmacy" has shown to be closely associated with a decrease in cognitive capacity (15). More drugs mean more dependence in basic living activities (25). Therefore using fewer drugs may only affect the IADL while excessive numbers of drugs can impair both of IADL and ADL.

Functional independence is rather strong predictor of life quality and a worsening in functional status is closely related to depressive symptoms (26). Depression in the elderly is still highly under-recognized syndrome and has a rate as 40%–60% of cases (27), and depressive symptoms among community-dwelling older adults have a substantial ratio ranging from ~8 to 16% (28). The relationship between polypharmacy and depression has been shown previously (17), and moreover, depression may be a better independent predictor of polypharmacy than the other comorbid diseases (19). Depression has also shown to be associated with drug nonadherence in general population (20). Thus, in depressive patients with additional comorbidities, having polypharmacy and medication nonadherence can make the treatment process more complicated and lead to worsening the condition of the patient’s diseases.

In our study we found that MNA scores were significantly lower in polypharmacy group, and there was also a moderate negative correlation between MNA scores and the number of medications (Table 3). Although an explicit relationship has been found between polypharmacy and malnutrition in the previous studies (15,29,30), the mechanism of it is not obvious. Nutritional status of elderly is a very important subject that should be definitely addressed because of its influence on the pharmacology of a lot of drugs (31). In addition, a wide variety of drugs may cause malnourishment through a lot of side effects including nausea, anorexia, early satiety, reduced feeding ability, dysphagia, constipation and diarrhea (32,33). Regulating pharmacotherapy and decreasing the number of drugs may be a reasonable way in order to improve patient's nutritional status (34).

With the modern pharmacotherapy, increasing variety of drugs caused increased adverse reactions and drug interactions, and polypharmacy itself has started to show detrimental effects on the various aspects of health. In the current study, our results have shown that polypharmacy has negatively affected the quality of life in line with previous studies (35).

We depicted that there was no difference regarding sarcopenia and MMSE scores in both groups. Although there was no difference, HGS was lower in polypharmacy group. Although there was not significantly difference, the frequency of sarcopenia was higher in the polypharmacy group. The precise association between polypharmacy and sarcopenia remains unknown. Although some studies in the literature are supporting the relationship of polypharmacy with sarcopenia (36), a recent study has shown that the strength and mass of muscle in sarcopenic patients with stroke was not positively affected after "deprescribing" (34). Sarcopenia is a consequence of a various of predisposing factors, such as physiological changes by getting older, deficiency in nutrition, chronic comorbid diseases, and insufficient physical activity (37). These predisposing factors may be the reason of these conflicting results.

One of the limitations of the study is that the participants' number is relatively limited. Second, since the study is cross-sectional, we cannot mention a cause-effect relationship. Despite these limitations, the study has also some strengths. First, a comprehensive geriatric evaluation was performed, thereby investigating other conditions that could affect the results. Second, along with the CGA, quality of life was also evaluated. Thus, a multidimensional assessment of the health status of older adults included the study was provided.

CONCLUSION

In conclusion, depending on the outcomes of our study we can conclude that as the number of the medications used by patients increase; the detrimental effects of the drugs on the health emerges a tendency to depression, malnutrition, and a decline in functional status. Polypharmacy also impairs the quality of life which is an overall health term and indicator of optimal aging. It will be wise to address the polypharmacy as a crucial health problem, optimize the number of the medications and thereby make the health condition better of an older patient having multiple comorbidities.

Financial disclosures: *The authors declare that this study received no financial support.*

Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Approval for the study was granted by the Gaziantep University Medical Faculty ethical committee (no. 2022/155).*

Authors' contributions: *Author EÖ designed the study,*

performed manuscript writing; Authors SG performed data collection and analysis; Author ZAO reviewed the manuscript and provided critical revisions. All authors have approved the final article.

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