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Original article

Comparison of Malnutrition Assessment Tools in Terms of Revealing the Relationship Between Polypharmacy and Inappropriate Drug Use and Malnutrition

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Abstract. Malnutrition is prevalent among older adults and is associated with morbidity and mortality. This study aims to investigate the relationship between malnutrition and polypharmacy in older adults. We also tested which malnutrition test had a stronger relationship with polypharmacy. We conducted a cross-sectional study for four months. We assessed malnutrition by mini nutritional assessment short-form (MNA-SF), long-form (MNA-LF), and Global Leadership Initiative on Malnutrition criteria (GLIM). We evaluated potentially inappropriate medication (PIM) use was by TIME criteria (Turkish Inappropriate Medication Use in the Elderly) criteria. Data analysis was done by SPSS version 22. The study population was composed of 93 women and 57 men, of mean age 73 +/- 9 years. Polypharmacy was present in 73% (n=110) of them. MNA-SF, MNA-LF and GLIM scores were correlated with presence of polypharmacy (p=0.036, p=0.002, p=0.045). MNA-LF was associated with polypharmacy in linear regression analysis (r^2=0.06, p=0.046). PIM use was also found to be negatively related to MNA-LF scores (p=0.049, r=-0.166). We demonstrated a cut-off value of 6.5 of drug numbers for being malnourished (sensitivity 80%; specificity 88%; CI:95%; AUC:0.844; p<0.01). In this study, we concluded that malnutrition and polypharmacy, two common geriatric syndromes, are associated with each other. According to the results of our study, we can say that MNA-LF is a powerful malnutrition assessment tool to demonstrate the malnutrition polypharmacy relationship. Prospective studies to evaluate effect of correction of malnutrition on polypharmacy could be useful.

Key words: malnutrition, mini-nutritional assessment, polypharmacy, potentially inappropriate medication

Introduction

Nutrition is an essential determinant of health status, especially in older adults. Undernutrition, sarcopenia, frailty, obesity, and micronutrient deficiencies are nutritional disorders (1). Malnutrition is "a state resulting from lack of intake or uptake of nutrition that leads to decreased fat-free mass and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease" (2). Malnutrition and unintentional weight loss cause progressive decrement in general health status, impairment in physical and cognitive functional status, the increase in the utilization of health care services, and mortality (3). Geriatric patients also suffer from the consideration that poor nutritional status is a normal consequence of aging. To overcome the underdiagnoses, nutritional evaluation should be a routine part of the geriatric work-up. Several diagnostic tools were developed to evaluate patients for malnutrition. According to the European Society for Clinical Nutrition and Metabolism (ESPEN) guideline, before the malnutrition diagnosis, the criteria for being "at nutritional risk" under any validated nutritional risk screen-

ing tool must be fulfilled. If there is a nutritional risk, two alternative sets of diagnostic criteria will confirm the diagnosis; i.e. either diminished body mass index (BMI) <18.5 kg/m2 or combined weight loss and reduced BMI (age-dependent cut-offs) or reduced gender-dependent fat-free mass index (FFMI)(1). American Society of Parenteral and Enteral Nutrition (ASPEN) and the Academy of Nutrition and Dietetics (Academy) determined six criteria for the diagnosis of malnutrition; low energy intake, loss of weight, muscle mass loss, loss of subcutaneous fat tissue, fluid accumulation, and loss of handgrip strength, at least two of the criteria should be fulfilled for the diagnosis of malnutrition (3). Nutritional assessment tools that developed depending on these criteria are useful in the diagnosis of malnutrition in geriatric patients. Mini Nutritional Assessment (MNA®) is an easy-applied, valid nutritional screening tool for free-living and clinically appropriate older adults. MNA is also an assessment tool (4). It contains questions specific to the geriatric population related to nutritional and general health status (3). MNA is recommended for routine geriatric assessments by the European Society for Clinical Nutrition and Metabolism (ESPEN)(1). Rubenstein and colleagues developed the MNA short-form (MNA-SF), which had high sensitivity, specificity, and correlation to the full MNA to use in time-restricted conditions(5). A new criterion was published by the Global Leadership Initiative on Malnutrition (GLIM), for diagnosing malnutrition in adults (6).

Only 1 % of older adults who do not have comorbidities are malnourished. Malnutrition has been usually together with other geriatric syndromes like sarcopenia, frailty, dementia, depression, multimorbidity, and polypharmacy (7). Polypharmacy is the use of multiple medicines for multimorbid conditions in older adults (8). Polypharmacy is related to adverse outcomes as mortality, falls, adverse drug reactions, increased hospitalizations, and early readmission to the hospital (9). This study aimed to investigate the relationship between malnutrition and polypharmacy in older adults. Also, we aimed to reveal which malnutrition test has a stronger relationship with polypharmacy.

Methods

Participants

This cross-sectional study was conducted for a period of 4 months from September 2019 to January 2020. Patients applied to the outpatient clinic of geriatrics were taken in the study. The study was approved by the Gaziantep University Local Research Ethics Committee. All participants gave informed consent.

Exclusion criteria

Patients, who were under 65 years of age, had already diagnosis of malnutrition and using nutritional support products were excluded from the study.

Comprehensive geriatric assessment

The standardized form of mini-mental state examination (MMSE) was used for cognitive evaluation, the Katz index for evaluation of daily living abilities (ADL), Lawton Brody index for assessment of instrumental activities of daily living (IADL), Tinetti Balance-Gait Evaluation Scale to evaluate the risk of fall and Yesavage Geriatric Depression scale (GDS) for evaluation of psychological status.

In MMSE patients were tested about six different areas; orientation, registration, attention, calculation, language, and recall (10). Scores of ≤24 were valid for the presence of dementia. Katz index of ADL assessed patients for personal hygiene, continence, dressing, feeding, and ambulating. Scores range between 0 and 6, higher scores mean higher independence (11). The Lawton Brody index was used for evaluating IADL like cleaning and tidying home, marketing, managing medications, preparing meals, communicating with others, using transportation, and doing financial management, higher scores mean higher independence (12). Tinetti Balance-Gait Evaluation Scale was used for determining the risk of falls. In this scale, a score of >24 means low risk of fall, 19-23 moderate risk of fall, and <19 high risks of fall (13). GDS scores of 5 and higher are valid for depression (14).

Nutritional assessment

Malnutrition was assessed by a mini nutritional assessment, short-formed (MNA-SF)(4), long-form (MNA-LF)(3), and the Global Leadership Initiative on Malnutrition criteria (GLIM)(6). MNA-SF is the first part of the MNA test and takes only a few minutes to complete. The maximum score for MNA-SF is 14; a score of 12 points or greater indicates that the patient has an acceptable nutritional status and the full MNA is not needed to be done. However, a score of 11 points or below is an indication to proceed with the MNA-LF. Completing the MNA-LF takes 10 to 15 minutes. The maximum score for the second part is 16 and the maximum score for MNA-LF is 30. Scores <17 are evaluated as malnutrition, 17-23.5 is evaluated as the risk for malnutrition, and 24-30 is accepted as normal. GLIM criteria are new criteria for diagnosing malnutrition. These criteria are based on the verification of phenotypic criteria, such as low body mass index, non-volitional loss of weight, or reduced muscle mass, associated with etiological variables, such as reduced food intake, the presence of inflammation, or disease burden. Also, the severity of malnutrition can be classified as moderate and severe according to body mass index, loss of weight, and muscle mass.

Evaluation of polypharmacy

Polypharmacy was assessed from the database of the Social Security System. The number and name of the drugs that patients used were recorded. The use of 5 to 9 drugs was accepted as polypharmacy, ≥10 drugs were accepted as excessive polypharmacy (15). Patients were evaluated for potentially inappropriate medication (PIM) use in the light of TIME (Turkish Inappropriate Medication Use in the Elderly) criteria (16).

Statistics

The variables were evaluated for the normality of their distribution using the Kolmogorov–Smirnov test. All data had showed a normal distribution. Numerical variables were presented as mean ± standard deviation. Categorical variables were shown as frequencies. For the comparison of two groups, we used an independent sample t-test. Chi-square test, Pearson correlation analysis, and linear regression model were used to evaluate the relationship between variables. The IBM SPSS for Windows, version 22.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis.

Results

The study population was composed of 93 women and 57 men, of mean age 73 +/- 9 years. Nineteen percent of the patients were malnourished according to MNA-SF, and 11% of the patients were malnourished according to MNA-LF. Twenty-one percent of the patients were diagnosed as severely malnourished and 29% of them moderately by GLIM criteria. The nutritional status of patients was summarized in table 1. Polypharmacy and excessive polypharmacy were reported in 73 and 12% of the study population, respectively. The presence of polypharmacy and the number of used drugs were revealed to be negatively related to MNA-SF, MNA-LF, and positively related to GLIM scores. The results were summarized in table 2. We found that MNA-LF was independently associated with polypharmacy in linear regression analysis (r^2=0.06, p=0.046). Scores of MNA-SF, MNA-LF, and GLIM were independent variables, polypharmacy was the dependent variable. Thirty-eight percent of patients were using PIM according to TIME crite-

Table 1. Nutritional status of patients

	MNA-SF*	MNA-LF*	GLIM*
Normal	54 (36%)	68 (45%)	74 (50%)
Risk of malnutrition	67 (45%)	64 (43%)	44 (29%) (moderate malnutrition)
Malnutrition	29 (19%)	17 (11%)	32 (21%) (severe malnutrition)

MNA-SF*= Mini nutritional assessment short form; MNA-LF*= Mini nutritional assessment long form; GLIM*= Global leadership initiative on malnutrition

Table 2. Relationship between malnutrition and polypharmacy

	Presence of polypharmacy	Number of drugs used
MNA-SF*	r= -0.195*, p=0.018	r= -0.475**, p<0.001
MNA-LF*	r= -0.264**, p=0.002	r= -0.628**, p<0.001
GLIM*	r= 0.176*, p=0.024	r= 0.462* , p<0.001

MNA-SF*= Mini nutritional assessment short form
MNA-LF*= Mini nutritional assessment long form
GLIM= Global leadership initiative on malnutrition

ria. Malnutrition was also revealed to be related to PIM use when evaluated with MNA-LF (r=0.166, p=0.049). We found a cut-off value of 6.5 of drug number for being malnourished, according to MNA-LF in ROC (Receiver operating characteristic) curve (sensitivity 80%; specificity 88%; CI=95%, p<0.001; AUC:0.844) (Figure 1).

Total Tinetti test score was found to be related to polypharmacy (r=-0.175, p=0.048, respectively). Additionally, geriatric depression scale scores were positively correlated with polypharmacy (r=0.223, p=0.023). Furthermore, no relationship was found with MMSE, ADL, and IADL. Results of comprehensive geriatric assessment tests and relationships with polypharmacy were summarized in table 3. Table 4 shows the height, body weight, fat mass, muscle mass, fat-free mass, and body mass index (BMI) of groups.

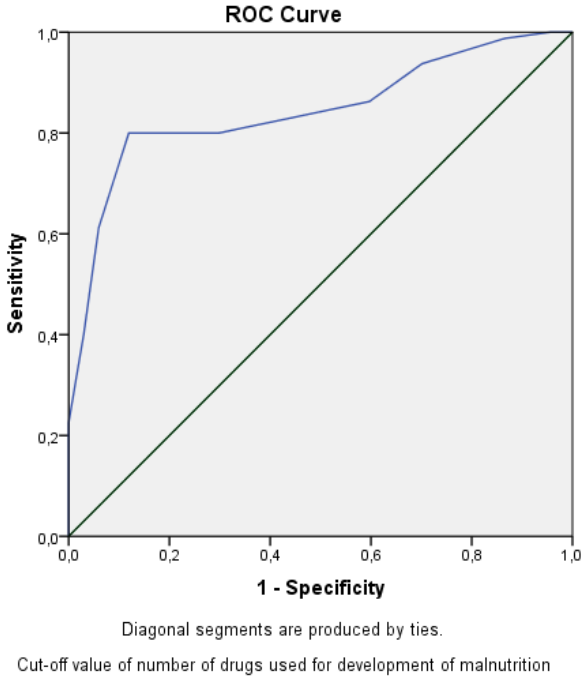

Figure 1. MNA-LF in ROC (Receiver operating characteristic) curve

Discussion

In our study, we found that the presence of polypharmacy was related to malnutrition. It was negatively correlated with MNA-SF, MNA-LF, and positively related to GLIM scores. There were a few studies that were done to evaluate the relationship between polypharmacy and malnutrition. Tamang and his colleagues revealed that polypharmacy increases the risk of malnutrition 3-folds in Nepal (17). This evidence is compatible with our findings. They evaluated malnutrition

Table 3. Relationship between comprehensive geriatric assessment and polypharmacy

	Presence of polypharmacy (n=110) mean±SD	Absence of polypharmacy (n=40) mean±SD	p=
MMSE*	21.91±6.71	21.92±7	0.081
ADL*	5.16±1.1	5.32±1.13	0.418
IADL*	4.95±2.77	5±2.87	0.305
GDS*	11.61±6.69	8.97±5.45	0.023*
Tinetti total	26.83±8.04	29.5±6.25	0.048*
Tinetti balance	19.8±6.12	21.83±4.78	0.083
Tinetti gait	6.97±2.5	7.63±2.16	0.092

MMSE* = Mini-mental state examination
ADL* = Activities of daily living
IADL* = Instrumental activities of daily living
GDS* = Geriatric depression scale

Table 4. Body composition of groups

	polypharmacy present (n=110) mean±SD	polypharmacy absent (n=40) mean±SD	p=
body weight (kg)	80.6±16.38	75.6±12.9	0.535
height (cm)	160.5±9.85	157.56±8.8	0.289
body mass index (kg/m2)	31.2±5.5	30.56±5.23	0.716
fat mass (kg)	23.1±9.24	23.16±9.06	0.470
fat-free mass (kg)	50.9±10.35	47.92±9.07	0.293
muscle mass (kg)	29±6.06	27.57±6.15	0.218

kg:kilogram; kg/m2:kilogram/square meter; cm:centimeter

with MNA, and they did not give any information about PIM use. Our study is the first study that evaluated the relationship between the presence of polypharmacy, the number of drugs used, and malnutrition by using more than one malnutrition assessment tool.

Additionally, we evaluated the PIM use. GLIM was used firstly in our study for the evaluation of the relationship between malnutrition and polypharmacy. We had an opportunity to compare the nutrition assessment tools about which one is more potent to show the relationship with polypharmacy. Our study revealed that the relationship between MNA-LF and polypharmacy is stronger than others. That finding can advise other researchers to use MNA-LF principally in polypharmacy studies.

We found a cut-off value as 6.5, and because this number has a fraction, we can say the use of 7 or more drugs increases the risk of malnutrition. Polypharmacy has more than 24 distinct definitions in the literature and the exact cut-off of the number of drugs required to be considered polypharmacy varies, ranging from more than 4 to more than 10(16). Our study revealed a cut-off number bigger than 4, which is used commonly to define polypharmacy. There was no relationship between inappropriate drug use and malnutrition in our study. After all, Kucukdaglı and her colleagues found PIM use according to Beers 2012 criteria caused a 2.69-fold increase in the risk of malnutrition(18). In that study, more than a third of the study population was denoted to be using at least one PIM. In our study, the result was similar; 38 % of them were using at least one PIM.

In a study from Spain, PIM use was detected in 35.4% of primary care patients by 2012 Beers criteria(19). The prevalence of PIM was recorded as 38.6% in patients admitted to tertiary care centers in Hong-Kong and 87.3% in India, respectively, according to the Beers 2012 criteria (20,21). The prevalence of PIM use in our study was compatible with the studies that were done in Istanbul, Spain, and Hong-Kong. They also showed a relationship between PIM use and malnutrition like our study. Different from those studies we evaluated PIM by TIME criteria which is the newest. They evaluated PIM use with Beers in 2012. Our study is the first study that evaluated PIM use with TIME criteria. We also found low Tinetti total scores in patients who were in the polypharmacy group. Similar to our study, the relationship between disturbance in balance and polypharmacy was shown by many researchers, such as Zia and colleagues (22). Geriatric depression scale scores were also positively related to polypharmacy. Leszek et al. showed the relation between polypharmacy and depression in a previous study, too (23).

Most of the studies evaluate the relationship between the use of a specific group of medicine and malnutrition. Over 250 medications have been implicated as having a potentially harmful effect on nutritional status through disturbance in taste sensation, intestinal absorption, and metabolism of essential elements(24). Long-term, high-dose aspirin use was found to be related to decreased vitamin C levels, which can lead to thinning of gastric mucosa with subsequent gastritis, peptic ulcer disease, nausea, anorexia, and malnutrition (25). Soysal and her colleagues studied the effect of acetylcholinesterase inhibitors (AchEIs) on malnutrition. They found that there was no significant difference in nutritional parameters and body mass index in AchEIs users and non-users (26).

Varma et al. mentioned more than 20 drugs which can cause reduced food intake. Antiarrhythmic, antihypertensive, antibiotic, analgesic, antiepileptic and antipsychotic drugs were present in the list (27). Some antacid, diuretic, antiparkinsonian, and anticoagulant drugs were denoted as drugs that cause mineral and vitamin deficiencies in the same paper.

All those studies make us thought that malnutrition is related to polypharmacy. Present studies were not able to explain the whole mechanism. The relationship between them was tried to be explained by several mechanisms. One of them is, inappropriate and multiple drug use can cause damages in the gastrointestinal (GI) tract. Disturbances in the GI tract can cause impairments in tasting, swallowing, digestion, and absorption. All these distortions in the gastrointestinal tract can cause malnutrition. The other one is that malabsorption causes decrement in the efficiency of drug treatments, and the need for additional drug use increases. Malnutrition also disturbs the bioavailability of drugs and increases the demand for new drugs. These interactions can give rise to a vicious circle (28). Multimorbidity usually co-occurs with polypharmacy and is one of the causes of malnutrition

The major limitation of our study is the number of patients that are evaluated. It could also be better to explain which drugs caused malnutrition and which effect of the drug caused malnutrition.

Conclusion

Malnutrition and polypharmacy are two of the common geriatric syndromes, and their incidences increase with age. Both of them impair quality of life, increases morbidity and mortality, and financial cost burden (29). Acute or chronic illnesses, inflammation, decreased appetite can cause malnutrition and they can be a natural consequence of aging. Malnutrition and polypharmacy seem to be related to each other. More studies could clarify this relationship better.

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Ethical approval:
Procedures were completed under the institutional ethical standards of the responsible committee on human experimentation and the Declaration of Helsinki(30). Gaziantep University Local Research Ethics Committee approved the study protocol. All the patients gave informed consent.

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The authors have no conflict-of-interest report.

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