Tarlovskaya E.I., Omarova Yu.V.
Privolzhsky Research Medical University, Nizhny Novgorod, Russia

Analysis of the compliance of the prescribed therapy with the EURO FORTA system in polymorbidic patients of elderly and old age with CHF

Aim	To study the consistency of the prescribed therapy with the EURO FORTA (2018) system in polymorbid patients with chronic heart failure (CHF) according to data of the local registry.
Material and methods	The study included 313 patients with CHF aged 75±8.2 years. The Charlson Comorbidity Index (CCI) and the number of diseases (1–2, 3–5, >5) were calculated for all patients. Inpatient and outpatient treatment was assessed according to the EURO FORTA (2018) system based on polymorbidity degree, age, gender, and CHF type and severity.
Results	For the retrospective analysis of outpatient treatment, 5 groups of patients were isolated based on the drug class in the EURO FORTA system: group 1, patients treated only with class A drugs (3.51%); group 2, class A and B drugs (22.36%); group 3, class A, B, and C drugs (17.25%); group 4, class A, B, C, and D drugs 10.86% (A, B, C, D) and 16.31% (A, B, D); and group 5, patients without an outpatient drug therapy (29.71%). For the analysis of inpatient treatment, 4 groups of patients were isolated based on the drug class in the EURO FORTA system: group 1, patients treated only with class A drugs (0.32%); group 2, class A and B drugs (15.97%); group 3, class A, B, and C drugs (57.19%); and group 4, separately analyzed patients treated with class C and D drugs or only D in combination with class A and B drugs. Thus, 28.11% of patients at the outpatient stage and 82.75% of patients at the inpatient stage received drugs with questionable efficacy/safety profiles (class C); 27.17% of patients at the outpatient stage and 26.52% at the inpatient stage received potentially inappropriate drugs (class D). At the outpatient stage in groups 2-4, most of patients (51.43–70.59%) had >5 diseases (p_{mg}=0.020). At the inpatient stage, there were no significant differences between groups in the number of diseases (p_{mg}=0.349). The groups were comparable in the left ventricular ejection fraction depending on the CHF type (p_{mg}=0.027 and p_{mg}=0.778) at both stages of treatment. For instance, the same patient with preserved left ventricular ejection fraction could be included into EURO FORTA group 2 for the analysis of outpatient treatment while after prescription of the inpatient treatment, he/she could be included into group 3; p_{mg} (intergroup, detecting differences for comparison of 3 groups) exceeded 0.017; therefore, the groups were comparable in the number of CHF patients with reduced, mid-range, and preserved left ventricular ejection fraction.
Conclusion	Every second patient of the study had more than 5 diseases. Every third patient did not take any drugs at the outpatient stage. 28.11% of patients received EURO FORTA class C drugs and 27.17% of patients received class D drugs at the outpatient stage. The drugs to be avoided in CHF, included primarily nonsteroid anti-inflammatory drugs (NSAIDs) and class I and III anti-arrhythmic medications (except for amiodarone). At the inpatient stage, 82.75% of patients received EURO FORTA class C drugs and 26.52% of patients received class D drugs. NSAIDs and ciprofloxacin prevailed among the drugs to be avoided in CHF.

Keywords	Chronic heart failure; EURO FORTA (2018) system; polymorbidity
For citation	Tarlovskaya E.I., Omarova Yu.V. Analysis of the compliance of the prescribed therapy with the EURO FORTA system in polymorbidic patients of elderly and old age with CHF. Kardiologiia. 2021;61(11):57–64. [Russian: Тарловская Е.И., Омарова Ю.В. Анализ соответствия назначенной терапии системе EURO FORTA у полиморбидных пациентов пожилого и старческого возраста с хронической сердечной недостаточностью. Кардиология. 2021;61(11):57–64].

Corresponding author Omarova Yu.V. E-mail: sailor94mihailova@yandex.ru

Chronic heart failure (CHF) is a major cause of hospitalization among patients over 65, which is a significant clinical and economic burden [1]. The problem of simultaneously administering a multitude of drugs in patients with CHF is relevant due to their numerous chronic comorbidities. Each comorbidity requires drug treatment which results in polypragmasy. Polypragmasy is forced upon patients with CHF

due to polymorbidity, but can remain a factor that compromises treatment compliance [2].

Currently, a variety of analytical algorithms are used to prevent polypragmasy: Beers criterion proposed by the Gerontological Society of America; STOPP/START criteria; McLeod criterion [3, 4].

The EURO FORTA (Fit fOR The Aged) system allows drug therapy to be evaluated on the basis of age and associated pathologies. The EURO FORTA system is based on the principles of evidence-based medicine and the analysis of medical practice data. The system is designed to help increase treatment efficacy in elderly patients based on their clinical characteristics and protect them from the sequelae of misuse, irregular use, and incorrect combinations of the most commonly used drugs. All drugs are divided into several classes (EURO FORTA) depending on how beneficial they are for elderly patients [5, 6].

Class A (A-bsolutley): drugs with proven clear benefits in terms of the efficacy/safety ratio in elderly patients with a specific disease.

Class B (B-beneficial): drugs with proven benefits in elderly patients with relatively limited efficacy or safety.

Class C (C-areful): drugs with an ambiguous efficacy/safety profile. If a patient requires many drugs, they should be administered with caution due to possible side effects or find other treatment options.

Class D (D-on't): drugs that should not be administered to elderly patients in the first place. It is recommended that other treatment options be found.

Objective

To study the compliance of the allocated treatment to the EURO FORTA system in the polymorbid patients with CHF in the local register.

Material and Methods

The study included 313 patients admitted to the City CHF Treatment Center from 1 February 2019 to 1 October 2020.

Inclusion criteria: patients with CHF hospitalized in the City CHF Treatment Center of the Nizhny Novgorod City Clinical Hospital No. 38.

Exclusion criteria: age<18 years; pregnancy and lactation; comatose states, delirious states, chronic alcohol intoxication and/or substance addiction; severe cognitive impairments; mental disorders; refusal to sign the informed consent to participate in the observational study.

The mean age was 75±8.216 years. The mean age of male (n=142, 45.37%) and female patients (n=171, 54.63%) was 73.79±7.968 years and 76.01±8.306 years, respectively. Female patients were older than male patients (p=0.022).

CHF was diagnosed based on the common criteria following the clinical guideline [7]. Echocardiography was performed, in order to determine left ventricular ejection fraction (LVEF; Simpson's method). CHF with preserved LVEF (HFpEF) was diagnosed with LVEF≥50%, with midrange ejection fraction (HFmrEF) with LVEF 40–49%, and reduced ejection fraction (HFrEF) with LVEF<40%. [22] HFpEF was established if N-terminal pro-brain natriuretic propeptide (NT-proBNP) was elevated and/or in the presence of diastolic dysfunction and/or structural changes of the heart (LV hypertrophy or left atrial enlargement).

66.77% of patients had HFpEF, 19.81% had HFmrEF, and 13.42% of patients had HFrEF.

All patients with CHF were treated following the clinical guideline with consideration for the associated pathologies.

The Charlson comorbidity index and the number of comorbidities were analyzed: 1–2 comorbidities; 3–5 comorbidities; and more than 5 comorbidities.

Outpatient and inpatient management was evaluated by EURO FORTA (2018) in 313 patients with CHF (274 patients over the age of 65 years, 39 patients over 60 years; ≥6 drugs administered) depending on the degree of polymorbidity, age, sex, type and severity of CHF (CHF stages I to III).

The causes of hospitalization, the incidence and severity of acute kidney damage (AKD) and anemia, and the incidence of death in hospital (9 (2.87%) of patients died in the hospital) were assessed.

AKD was diagnosed based on the clinical guideline [8]. Since there was no information in the baseline kidney function (creatinine levels and glomerular filtration rate (GFR)) in most patients with suspected AKD, Table 1 was used (adapted from [9]) This allowed proper baseline serum levels of creatinine to be established depending on race, sex and age with a determined level of GFR (75 mL/min/m^2) [8, 9].

Anemia was diagnosed if hemoglobin was <130 g/L in male patients and <120 g/L in female patients. Hemoglobin levels <129/119–90 g/L, 89–70 g/L, and <70 g/L corresponded to mild, moderate, and severe anemia.

The study was carried out following the Ethical Principles for Medical Research Involving Human Subjects of the World Medical Association Declaration of Helsinki (developed initially in 1964 and amended in 2000). All patients included (local register) signed

ISSN 0022-9040. Kardiologiia. 2021;61(11). DOI: 10.18087/cardio.2021.11.n1619

Table 1. Baseline serum creatinine levels in the Caucasian patients corresponding to GFR 75 mL/min/m²

Age, years	Serum creatinine, μmol/L	
	Male	Female
20–24	115	88
25–29	106	88
30–39	106	80
40–54	97	80
55–65	97	71
> 65 years	88	71

GFR, glomerular filtration rate.

the informed consent approved by the local Ethics Committee.

The electronic database was created using Microsoft Office Excel 2019, taking into account the current requirements for relational databases. Statistical analysis of the data obtained was performed using Statistica 10.0. The Kolmogorov-Smirnov test and the Shapiro-Wilk test were used to test the distribution normality of traits. The quantitative variables were expressed using the median (Me) and the interquartile range [25th percentile; 75th percentile] if the distribution was non-normal; and the mean and standard deviation (M±SD), if the distribution was normal. The Kruskal-Wallis test was used to compare the variables between three groups with non-normal distribution. Qualitative variables were compared using the Yates' χ^2 test. If the number of cases in one of the comparison groups was less than 5, the two-tailed Fischer test was used. The data is expressed as absolute and relative values (n (%)). The multigroup value pmg<0.017 was adopted as the significance level for the null hypothesis to compare independent groups. Logistic regression analysis was performed, in order to identify the factors associated with adverse events (determine the probability of an event (outcome) depending on the independent variables).

Results

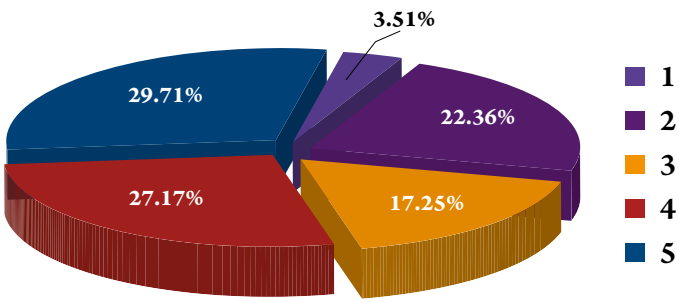
Arterial hypertension (AH) and coronary artery disease (CAD) were diagnosed in 99.04% and 67.09% of patients, respectively. 65.49% of patients had cardiac arrhythmias, such as atrial fibrillation (AF) or atrial flutter. 20.45% of patients had chronic pulmonary disease. 21.72% had cancer, 38.98% had diabetes mellitus, and 14.69% of patients had various arthropathies. Almost all (99.04%) patients with CHF had chronic kidney disease (CKD), 45.05% of patients had anemia of various severity.

Depending on the drug class (EURO FORTA), patients were divided in five groups (Figure 1): Group 1 (only group A drugs) – 3.51% of patients; Group 2 (group A and B drugs) – 22.36%; Group 3 (group A, B and C drugs) – 17.25%; Group 4 (group A, B, C, and D) – 10.86% (A, B, C, D) and 16.31% (A, B, D); Group 5 – did not receive drug therapy at the outpatient stage (29.71%).

In hospital: Group 1 (only group A drugs) – 0.32% of patients; Group 2 (group A and B) – 15.97%; Group 3 (group A, B and C) – 57.19%; Group 4 (A, B, C and D) – 25.56% (A, B, C, D) and 0.96% (A, B, D) (Figure 2).

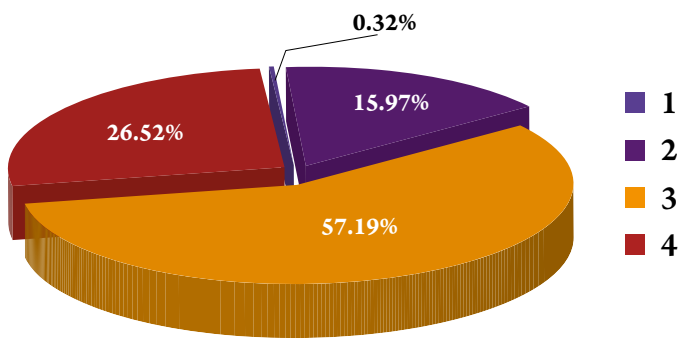
Patients were comparable in terms of age (rmg=0.994 and rmg=0.893, respectively) and Charlson comorbidity index (rmg=0.425 and rmg=0.335) at the outpatient and inpatient stages. Comorbidity increased in a linear progression with age. There was

Figure 1. Patient groups with respect to the EURO FORTA drug groups at the outpatient stage



Groups: Group 1 (only group A drugs); Group 2 (group A and B drugs); Group 3 (group A, B, and C drugs); Group 4 (group A, B, C, and D); Group 5 (no drug therapy at the outpatient stage).

Figure 2. Patient groups with respect to the EURO FORT drug groups at the inpatient stage



Groups: Group 1 (only group A drugs); Group 2 (group A and B drugs); Group 3 (group A, B, and C drugs); Group 4 (group A, B, C, and D).

Table 2. Characteristics of patient groups depending on the drug classes administered (EURO FORTA), at the outpatient and inpatient stages, taking into account the number of comorbidities in patients with CHF

Stages	Number of comorbidities	0 (n=93)	A (n=11)	B (n=70)	C (n=54)	D (n=85)	p_{mg}
Outpatient, n / %	1–2	16/17.20	–	8/11.43	5/9.26	4/4.71	0.020
	3–5	30/32.26	6/54.54	26/37.14	12/22.22	21/24.71	
	> 5	47/50.54	5/45.46	36/51.43	37/68.52	60/70.59	
	Number of comorbidities	**0 (n=0)**	**A (n=1)**	**B (n=50)**	**C (n=179)**	**D (n=83)**	**p_{mg}**
Inpatient, n / %	1–2	–	–	6/12	23/12.85	4/4.82	0.349
	3–5	–	1/100	14/28	55/30.73	25/30.12	
	> 5	–	–	30/60	101/56.42	54/65.06	

a direct correlation between age and the Charlson index (r=0.360; p<0.0001). 59.11% of patients with CHF had more than 5 comorbidities, 1–2 and 3–5 comorbidities were diagnosed in 33 (10.54%) and 95 (30.35%) patients, respectively.

At the outpatient stage, patients with > 5 comorbidities prevailed (51.43–70.59%) in Groups 2–4 (pmg=0.020) (Table 2).

There were no intergroup differences in the analysis of patient groups based on CHF type (HFpEF, HFrEF and HRmrEF). This takes into consideration the EURO FORTA classes (O, A, B, C, D) at the outpatient (pmg=0.027) and inpatient (pmg=0.778) stages (since pmg was >0.017). At the outpatient stage, patients with CHF stage IIB predominated in Groups 1, 3 and 4 (63.64%, 51.86% and 47.06%, respectively; pmg=0.041). Patients with IIA prevailed in Groups 2 and 5 (58.57% and 48.39%, respectively). At the inpatient stage, the patient groups did not differ depending on the CHF stage (pmg=0.096; Table 3).

Patients were hospitalized due to the following: acute decompensated CHF (63.26%); heart arrhythmias (AF – 17.57%); hypertensive crisis with hypertensive encephalopathy; acute left ventricular insufficiency; acute coronary syndrome; AKD (7.98%); pneumonia (1.59%); unstable angina (7.67%) or other reasons (AKD, sick sinus syndrome, atrioventricular block grade II; 1.93%) (pmg=0, 829).

Analysis of the administration of different EURO FORTA drug classes established that drugs with ambiguous efficacy / safety profile (class C) were administered at the outpatient stage in 28.11% of patients. 27.17% of patients received potentially unsuitable drugs (Class D). At the inpatient stage, 82.75% of patients received EURO FORTA class C drugs, and 26.52% of patients received class D drugs.

Class C drugs used at the outpatient stage were: cardiac glycosides (4 patients with AF); amiodarone (3 patients with AF); moxonidine (1 patient with AH); beta-blockers three years after MI (n=2); and spironolactone (n=23). Four patients took two drugs of this class simultaneously, while twenty patients also took class C and class D drugs.

Table 3. Characteristics of patient groups depending on the drug classes administered (EURO FORTA), at the outpatient and inpatient stages, with consideration for CHF stages

Parameter	CHF stage	0 (n=93)	A (n=11)	B (n=70)	C (n=54)	D (n=85)	p_{mg}
Outpatient, n / %	I	13/13.98	–	5/7.14	3/5.55	13/15.29	0.041
	IIA	45/48.39	4/36.36	41/58.57	20/37.04	31/36.47	
	IIB	33/35.48	7/63.64	24/34.29	28/51.86	40/47.06	
	III	2/2.15	–	–	3/5.55	1/1.18	
Parameter	**CHF stage**	**0 (n=0)**	**A (n=1)**	**B (n=50)**	**C (n=179)**	**D (n=83)**	**p_{mg}**
Inpatient, n / %	I	–	–	7/14	16/8.93	11/13.25	0.096
	IIA	–	1/100	31/62	74/41.34	35/42.17	
	IIB	–	–	11/22	84/46.93	37/44.58	
	III	–	–	1/2	5/2.8	–	

CHF, chronic heart failure.

ISSN 0022-9040. Kardiologiia. 2021;61(11). DOI: 10.18087/cardio.2021.11.n1619

Outpatient administration of spironolactone was associated with a high risk of AKD (odds ratio (OR) 2.683; 95% confidence interval (CI) 1.261–5.706; p=0.01), including with baseline creatinine (OR 2.814; 95% CI 1.322–5.989; p=0.007); AKD associated with CKD (OR 2.168; 95% CI 1.027–4.575; p=0.042), and AF (OR 2.992; 95% CI 1.115–8.031; p=0.03).

At the inpatient stage, the following class C drugs were administered: cardiac glycosides (47 patients with AF); amiodarone (40 patients with AF); moxonidine (21 patients with AH); spironolactone (n=214); levofloxacin (9 patients with pneumonia, chronic obstructive pulmonary disease (COPD)). 48 (29.09%) and 3 (1.81%) patients took simultaneously 2 and 3 drugs of this class, respectively, and 64 (77.1%) patients also took 2 class C and class D drugs.

The following class D drugs were administered at the outpatient stage: nonsteroidal anti-inflammatory drugs (NSAIDs; n=68); acetylsalicylic acid (2 patients with AF); antiarrhythmic drugs of class I and class III, except for amiodarone (n=8); glibenclamide (n=1); calcium channel blockers (CCBs) – non-dihydropyridine CCBs (2 patients with AHA); and dihydropyridine CCBs (1 patient with CAD 3 years after MI).

Outpatient administration of NSAIDs was associated with a high risk of AKD with baseline assessment of creatinine (OR 1.806; 95% CI 1.049–3.112; p=0.033) and anemia (OR 1.784; 95% CI 1.040–3.062; p=0.036), including severe anemia (OR 3.734; 95% CI 1.049–13.296; p=0.042).

Inpatient administration of class D: NSAIDs (n=47); antiarrhythmic drugs class I and III except for amiodarone (n=6); glibenclamide (n=2); ciprofloxacin (15 patients to treat urinary tract infection, pneumonia, COPD). 12 (12.12%) patients took two drugs of this class simultaneously.

Inpatient administration of NSAIDs was associated with a high risk of severe anemia (OR 6.769; 95% CI 1.874–24.453; p=0.004).

Discussion

At the outpatient stage, 30.03% of patients did not receive drug treatment. This data is confirmed by Stegman et al. [10], who by using the Morisky–Green questionnaire established that 51.3% of patients with CHF are non-compliant in 12 months.

We found that 27.17% of patients received drugs with the ambiguous efficacy/safety profile (class C), while 28.11% of patients received potentially unsuitable drugs (class D) at the outpatient stage. At

ISSN 0022-9040. Kardiologiia. 2021;61(11). DOI: 10.18087/cardio.2021.11.n1619

the inpatient stage, 82.75% of patients received EURO FORTA class C drugs, while 26.52% of patients received class D drugs.

Similar data was obtained from a Brazilian trial which included 418 patients. The annual frequency of administering potentially unsuitable drugs was 44.1 episodes (95% CI 35.2–54.7) per 1000 people. Nifedipine, glibenclamide, and diclofenac sodium were the most commonly used drugs. The risk factors for using potentially unsuitable drugs were polypragmasy (relative risk RR 3.00; 95% CI 1.31–6.88) and diabetes mellitus (RR 1.57; 95% CI 1.03–2.39) [11]. The prevalence of polypragmasy and drug misuse is a real problem for patients not only with CHF over 65 years of age. Terol-Fernández et al [12] showed that 35.5% of all patients over 65 years of age with a variety of pathologies received unsuitable drugs according to the STOPP criteria. According to the PRISCUS trial, the rate of inappropriate drug therapy in elderly patients is relatively stable (about 23%) in Germany. Patients taking unsuitable drugs are at a greater risk of developing side effects and being hospitalized [13]. According to the STARTREC trial, 58% of patients of 70 years of age and older receive at least one potentially unsuitable drug according to the STOPP/START criteria. The misuse of benzodiazepines, NSAIDs, and proton pump inhibitors is the most common [14].

The general prevalence of administering unsuitable drugs varies from 20% to 79%, depending on the population of interest or country. However, inappropriate administration is associated in almost all trials with a sharp increase in the incidence of side effects, hospitalizations, and deaths [15].

According to our register, the drugs to be avoided in elderly patients according to the EURO FORTA system (Class D) at the outpatient stage were: NSAIDs (80%); antiarrhythmic drugs class I and class III except for amiodarone (9.41%); at the inpatient stage; NSAIDs (56.63%) and ciprofloxacin (18.07%). According to our findings, patients took NSAIDs to treat mainly arthralgia (osteoarthritis – 78.26%, gout – 19.56%, ankylosing spondylitis – 2.18%). Another trial in elderly patients found that arthritis (5.35%), back pain (4.95%), knee pain (3%), and leg pain (2.3%) were the most common causes of the use of NSAIDs. The most commonly administered NSAIDs were diclofenac (36.5%), indomethacin (22.5%) and ibuprofen (22.5%) [16].

Vardeny et al. [17] established that the risk of hyperkalemia and kidney failure was higher in patients with HFrEF and initial kidney dysfunction, as well as in the group with GFR decreasing within one year, especially during the spironolactone therapy. The authors concluded that the benefits of spironolactone were observed primarily in patients with reduced GFR. Impaired kidney function was associated with poor prognosis, but spironolactone reduced the risk of death.

There is evidence that NSAIDs can cause AKD by inhibiting prostaglandin synthesis, thus reducing blood flow to the kidneys and/or inducing interstitial nephritis [18].

The advantages of the EURO FORTA system were confirmed in several controlled clinical trials [19, 20], which demonstrated significant improvements in the quality of treatment and the reduced incidence of side effects. Michalek et al. [21] showed that the administration of drugs following EURO FORTA principles, when compared to the standard treatment approach, in 114 elderly patients resulted in an 84% decrease in the incidence of uncontrolled falls in hospitals.

The two-center clinical trial by Wehling et al. [19] included 409 patients admitted to geriatric clinics (over the age of 65 years + ≥3 drugs and over the age of 60 years old + ≥6 drugs). They were evaluated using the EURO FORTA criteria. After training physicians, the percentage of Class A drugs increased ($p<0.0001$), and the percentage of Class D drugs ($p<0.0005$) decreased before discharge from hospital. The revision of drug treatment with consideration of the EURO FORTA system allowed a reduction in the incidence of adverse drug reactions, improvement in the quality of life of patients, as well as improved kidney function [19].

There is no current national data on the frequency of administering potentially unrecommended drugs in patients with CHF and the frequency of administering potentially dangerous drug combinations in cardiac patients.

Conclusion

One in two patients with chronic heart failure included in the study had more than five comorbidities. One in three patients did not take drugs at the outpatient stage. The EURO FORTA class C and class D drugs were administered at the outpatient stage to 28.11% and 27.17% of patients, respectively. Nonsteroidal anti-inflammatory drugs (80%) and antiarrhythmic drugs class I and class III, except for amiodarone (9.41%), are the major drugs to be avoided in chronic heart failure. The EURO FORTA class C and class D drugs were administered at the inpatient stage by 82.75% and 26.52% of patients, respectively. Nonsteroidal anti-inflammatory drugs (56.63%) and

ISSN 0022-9040. Kardiologiia. 2021;61(11). DOI: 10.18087/cardio.2021.11.n1619

ciprofloxacin (18.07%) are the major drugs to be avoided in chronic heart failure.

Outpatient administration of spironolactone was associated with a greater risk of acute kidney damage and atrial fibrillation. Nonsteroidal anti-inflammatory drugs administered at the outpatient stage were associated with a greater risk of acute kidney damage, when assessed by the baseline creatinine levels and anemia. Nonsteroidal anti-inflammatory drugs administered in the hospital are associated with a greater risk of developing severe anemia.

No conflict of interest is reported.

The article was received on 20/03/2021

REFERENCE

1. Azad N, Lemay G. Management of chronic heart failure in the older population. Journal of Geriatric Cardiology. 2014;11(4):329–37. DOI: 10.11909/j.issn.1671-5411.2014.04.008
2. Sushinsky V.E., Pristrom M.S. Ways of improving adherence to treatment in patients with coronary heart disease. Medical news. 2016;5:77–80. [Russian: Сушинский В.Э., Пристром М.С. Пути повышения приверженности к лечению у пациентов с ишемической болезнью сердца. Медицинские новости. 2016;5:77-80]
3. Ministry of Health of Russian Federation. Pharmacotherapy in elderly and senile people. Methodical guidelines. Av. at: https://rgnkc.ru/images/metod_materials/Farmakoterapiya_2018.pdf. 2018. [Russian: Министерство здравоохранения Российской Федерации. Фармакотерапия у лиц пожилого и старческого возраста. Методические руководства. 2018. Доступно на: https://rgnkc.ru/images/metod_materials/Farmakoterapiya_2018.pdf]
4. Sychev D.A., Bordovsky S.P., Danilina K.S., Ilyina E.S. Inappropriate prescribing in older people: STOPP/START criteria. Clinical pharmacology and therapy. 2016;25(2):76–81. [Russian: Сычев Д.А., Бордовский С.П., Данилина К.С., Ильина Е.С. Потенциально нерекомендованные лекарственные средства для пациентов пожилого и старческого возраста: STOP/START критерии. Клиническая фармакология и терапия. 2016;25(2):76-81]
5. Pazan F, Weiss C, Wehling M. The EURO-FORTA (Fit fOR The Aged) List: International Consensus Validation of a Clinical Tool for Improved Drug Treatment in Older People. Drugs & Aging. 2018;35(1):61–71. DOI: 10.1007/s40266-017-0514-2
6. Pazan F, Gercke Y, Weiss C, Wehling M, Marcum ZA, Gokula M et al. The U.S.-FORTA (Fit fOR The Aged) List: Consensus Validation of a Clinical Tool to Improve Drug Therapy in Older Adults. Journal of the American Medical Directors Association. 2020;21(3):439.e9-439.e13. DOI: 10.1016/j.jamda.2019.07.023
7. Tereshchenko S.N., Galyavich A.S., Uskach T.M., Ageev F.T., Arutyunov G.P., Begrambekova Yu.L. et al. 2020 Clinical practice guidelines for Chronic heart failure. Russian Journal of Cardiology. 2020;25(11):311–74. [Russian: Терещенко С.Н., Галявич А.С., Ускач Т.М., Агеев Ф.Т., Арутюнов Г.П., Беграмбекова Ю.Л. и др. Хроническая сердечная недостаточность. Клинические рекомендации 2020. Российский кардиологический журнал. 2020;25(11):311-74]. DOI: 10.15829/1560-4071-2020-4083
8. Smirnov A.V., Rumyantsev A.Sh. Acute kidney disease. Part I. Nephrology. 2020;24(1):67–95. [Russian: Смирнов А.В., Румянцев А.Ш. Острое повреждение почек. Часть I. Нефрология. 2020;24(1):67-95]. DOI: 10.36485/1561-6274-2020-24-1-67-95
9. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. American Journal of Kidney Diseases. 2002;39(2 Suppl 1):S1-266. PMID: 11904577
10. Shtegman O.A., Polikarpov L.S., Novikov O.M. Adherence to treatment in outpatients with chronic heart failure. Siberian Medical Journal (Tomsk). 2013;28(2):78–82. [Russian: Штегман О.А., Поликарпов Л.С., Новиков О.М. Приверженность к лечению амбулаторных больных хронической сердечной недостаточностью. Сибирский медицинский журнал (г. Томск). 2013;28(2):78-82]
11. de Araújo NC, Silveira EA, Mota BG, Neves Mota JP, de Camargo Silva AEB, Alves Guimarães R et al. Potentially inappropriate medications for the elderly: Incidence and impact on mortality in a cohort ten-year follow-up. PLOS ONE. 2020;15(10):e0240104. DOI: 10.1371/journal.pone.0240104
12. Terol-Fernández J, Faus-Felipe V, Díez-Rodríguez M, del Rio-Urenda S, Labajos-Manzanares MT, González-Correa JA. Prevalence of inappropriate prescription to polymedicated patients over 65 years old in a rural health area. Revista de Calidad Asistencial. 2016;31(2):84–98. DOI: 10.1016/j.cali.2015.08.006
13. Jäger C, Freund T, Steinhäuser J, Stock C, Krisam J, Kaufmann-Kolle P et al. Impact of a tailored program on the implementation of evidence-based recommendations for multimorbid patients with polypharmacy in primary care practices–results of a cluster-randomized controlled trial. Implementation Science. 2017;12(1):8. DOI: 10.1186/s13012-016-0535-y
14. Cruz-Esteve I, Marsal-Mora JR, Galindo-Ortego G, Galván-Santiago L, Serrano-Godoy M, Ribes-Murillo E et al. Potentially inappropriate prescribing in older Spanish population according to STOPP/START criteria (STARTREC study). Atención Primaria. 2017;49(3):166–76. DOI: 10.1016/j.aprim.2016.02.013
15. Renom-Guiteras A, Meyer G, Thürmann PA. The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries. European Journal of Clinical Pharmacology. 2015;71(7):861–75. DOI: 10.1007/s00228-015-1860-9
16. Abdu N, Mosazghi A, Teweldemedhin S, Asfaha L, Teshale M, Kibreab M et al. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): Usage and co-prescription with other potentially interacting drugs in elderly: A cross-sectional study. PLOS ONE. 2020;15(10):e0238868. DOI: 10.1371/journal.pone.0238868
17. Vardeny O, Wu DH, Desai A, Rossignol P, Zannad F, Pitt B et al. Influence of Baseline and Worsening Renal Function on Efficacy of Spironolactone in Patients With Severe Heart Failure. Journal of the American College of Cardiology. 2012;60(20):2082–9. DOI: 10.1016/j.jacc.2012.07.048
18. Fairweather J, Jawad ASM. Cardiovascular risk with nonsteroidal anti-inflammatory drugs (NSAIDs): the urological perspective. BJU International. 2012;110(11):E437. DOI: 10.1111/j.1464-410X.2012.11679_4.x

19. Wehling M, Burkhardt H, Kuhn-Thiel A, Pazan F, Throm C, Weiss C et al. VALFORTA: a randomised trial to validate the FORTA (Fit fOR The Aged) classification. Age and Ageing. 2016;45(2):262–7. DOI: 10.1093/ageing/afv200
20. Pazan F, Burkhardt H, Frohnhofen H, Weiss C, Throm C, Kuhn-Thiel A et al. Changes in prescription patterns in older hospitalized patients: the impact of FORTA on disease-related over- and under-treatments. European Journal of Clinical Pharmacology. 2018;74(3):339–47. DOI: 10.1007/s00228-017-2383-3
21. Michalek C, Wehling M, Schlitzer J, Frohnhofen H. Effects of "Fit fOR The Aged" (FORTA) on pharmacotherapy and clinical endpoints – a pilot randomized controlled study. European Journal of Clinical Pharmacology. 2014;70(10):1261–7. DOI: 10.1007/s00228-014-1731-9

ISSN 0022-9040. Kardiologiia. 2021;61(11). DOI: 10.18087/cardio.2021.11.n1619