Polypharmacy in Heart Failure Patients: In the Era of Guidelines-Based Therapy Optimization

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KEYWORDS

chronic kidney disease; diabetes mellitus; excessive polypharmacy; heart failure; polypharmacy; pulmonary disease

ABSTRACT

Objectives: Comorbidities in heart failure (HF) patients require patients to take large amounts of medication (polypharmacy). This study aimed to assess the proportion of HF patients with polypharmacy and comorbidities that increase the risk of polypharmacy.

Methods: This cross-sectional study was conducted at Cardiovascular Hospital in Cirebon, Indonesia. Samples were taken at outpatient clinics from January to December 2023 using total sampling method. Data was taken from electronic medical records. Patients with incomplete medical record data were excluded from this study.

Key findings: A total of 494 HF patients were included. Most patients were male (53.4%) and aged 45-59 years (46%). Polypharmacy was found in 42.5% of HF patients and 36.7% of them had excessive polypharmacy (≥10 medications). Bivariate analysis showed that age group, ≥3 comorbidities, type 2 diabetes mellitus (T2DM), coronary artery disease (CAD), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), asthma and history of percutaneous coronary intervention (PCI) significantly increased the risk of polypharmacy ($p<0.05$). While from multivariate analysis, T2DM (AOR 12.35; 95%CI 6.78-22.49), CKD (AOR 7.18; 95%CI 2.73-18.91), COPD (AOR 7.15; 95%CI 3.35-15.26), asthma (AOR 11.18; 95%CI 2.22-56.29) and history of PCI (AOR 2.13; 95%CI 1.27-3.57) increased the risk of polypharmacy.

Conclusion: Heart failure patients with T2DM, CKD, history of PCI and pulmonary disease should receive special concern to reduce the risk of polypharmacy. Clinicians must make priority regarding medications that should be given according to recommended guidelines and address the patient's comorbidities.

Introduction

Heart failure (HF) is a clinical syndrome with characteristic features that are influenced by its pathophysiology and etiology. HF is a disease with health burden that impacts mortality, rehospitalization and health costs.[1] The proportion of people with HF globally reaches 1-2% and almost half of them die within 5 years of diagnosis.[2] Epidemiology data showed that the age-standardized prevalence (ASR) for HF in Asia (722.45/100,000 population) was lower than in America (810.42/100,000 population) but higher than in Europe (606.61/100,000 population). The data also showed that the trend of HF prevalence in 2 Asian regions was increasing: Southeast Asia (22.10%) and South Asia (4.22%).[3]

Indonesia is the country with the highest ASR of HF (900.90/100,000 population) in Southeast Asian region, and this number increased by 7.83% compared to the ASR prevalence for 1990 to 2019 period. Indonesia is also the country with the highest 1-year crude mortality rate (34.1%) compared to other Southeast Asia countries.[3] HF patients in Indonesia are dominated by relatively young age (<60 years) and male (66%). The majority risk factors are hypertension (33%), type 2 diabetes mellitus (T2DM) (37%), smoking (28%), dyslipidemia (31%) and coronary artery disease (CAD) (35%).[2]

Heart failure treatment guidelines are divided based on ejection fraction (EF) classification. The 4 main pillars therapy that have been proven to reduce mortality in heart failure with reduced ejection fraction (HFrEF) patients are Beta-Blockers (BBs), Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Neprilysin Inhibitor/Angiotensin Receptor Blocker (ACEi/ARNI/ARB), Mineralocorticoid Receptor Antagonist (MRA), and Sodium-Glucose Co-Transporter 2 (SGLT2) inhibitor. Meanwhile, in heart failure mildly reduced ejection fraction (HFmrEF) and heart failure preserved ejection fraction (HFpEF) patients, only SGLT2 inhibitors that have been proven to reduce the risk of mortality.[4]

Implementation of HF treatment guidelines is very important, but patients must take large amounts of medications. Polypharmacy is defined when the patient taking at least 5 medications.[5] However, another definition of polypharmacy is taking ≥7 medications, and it's more acceptable because HF patients will consume at least 4 medications recommended by guidelines.[6] Patients with comorbidities sometimes have to take more than 10 medications per day.[5] There is a possibility of side effects due to polypharmacy in HF patients, but real world data are still limited, especially in Indonesia. Thus, this study was conducted to determine polypharmacy in HF patients in terms of comorbidities and other characteristic features.

Methods

Study design and participants

This cross-sectional study was conducted at Hasna Medika Cardiovascular Hospital Cirebon, one of the referral centers for cardiovascular disease in West Java, Indonesia. The research sample was HF patients at outpatient clinics from January to December 2023. The sampling technique used was total sampling. Inclusion criteria were HF patients aged >18 years. Patients with incomplete data were excluded.

Data measurement

Polypharmacy criteria are defined if the patient takes more than 7 medications and excessive polypharmacy if patient takes more than 10 medications. Polypharmacy assessment is based on the type of medication, not medication load. All types of medication taken by patients were included in this study including inhalation medications and supplements. The secondary data were collected from electronic medical records which includes socio-demographic characteristics, type and number of medications, comorbidities, EF classification and history of percutaneous coronary intervention (PCI).

Data analysis

Clinical characteristics of patients were presented in numbers and percentages. Bivariate analysis was assessed with Chi-square or Fisher exact test. Variables with p value <0.25 were included in multivariate analysis model. Multivariate analysis was assessed using logistic regression method. The significance value in bivariate and multivariate analysis was $p<0.05$.

Ethical consideration

All data are confidential and only access by principal investigator. This research has received ethical approval No. 060/LAIKETIK/KEPPKRSGJ/X/2024 from Gunung Jati General Hospital ethics committee.

Results

This study included 494 HF patients as participants. Most patients were male (53.4%) and aged range 45-59 years (46%). Almost half of HF patients in this study received ≥7 drugs and most often received 5 drugs. The results of this study also showed that 34.6% of HF patients had ≥ 3 comorbidities and almost the same distribution of HFrEF, HFmrEF, and HFpEF patients (35%, 31.8% and 33.2%, respectively). Then about 20.9% of HF patients in this study had a history of PCI (Table 1).

Table 1. Clinical Characteristics of HF Patients (n=494)

Characteristics		Frequency	Percentage
Gender	Male	264	53.4
	Female	230	46.6
Age (years)	18-44	44	8.9
	45-59	227	46
	60-74	198	40.1
	≥75	25	5.1
	Mean±SD	58.1±10.48	
Number of medications	≤4	75	15.2
	5	115	23.3
	6	94	19
	≥7	210	42.5
	Min-Max	3-21	
	Mode	5	
Number of comorbidities	< 3	323	65.4
	≥ 3	171	34.6
Ejection fraction	HFrEF (≤ 40%)	173	35
	HFmrEF (41 – 49%)	157	31.8
	HFpEF (≥ 50%)	164	33.2
History of PCI	No	391	79.1
	Yes	103	20.9

Abbreviations: HFrEF: heart failure reduced ejection fraction; HFmrEF: heart failure mildly reduced ejection fraction; HFpEF: heart failure preserved ejection fraction; PCI: percutaneous coronary intervention

Figure 1 shows that 42.5% of HF patients received polypharmacy, and 36.7% among them were excessive polypharmacy (≥10). The three most common comorbidities found in this study were CAD (80.2%), hypertension (23.1%) and T2DM (20%). Whereas only around 2% of patients have asthma, stroke, and dyslipidemia (Figure 2).

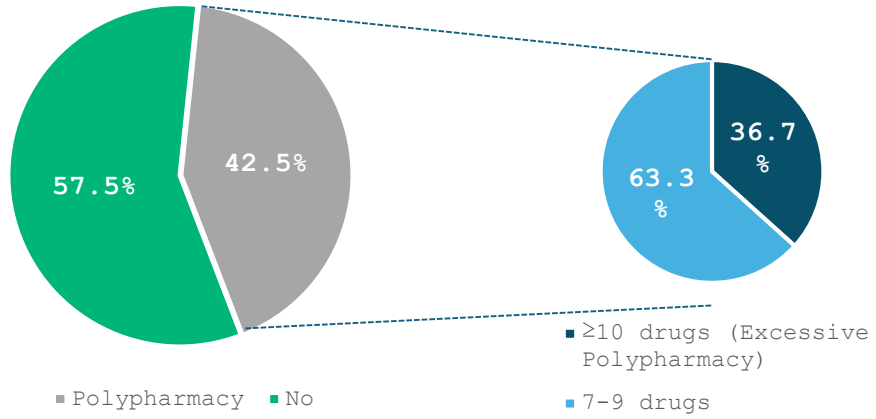

Figure 1. Proportion of polypharmacy and excessive polypharmacy on HF patients

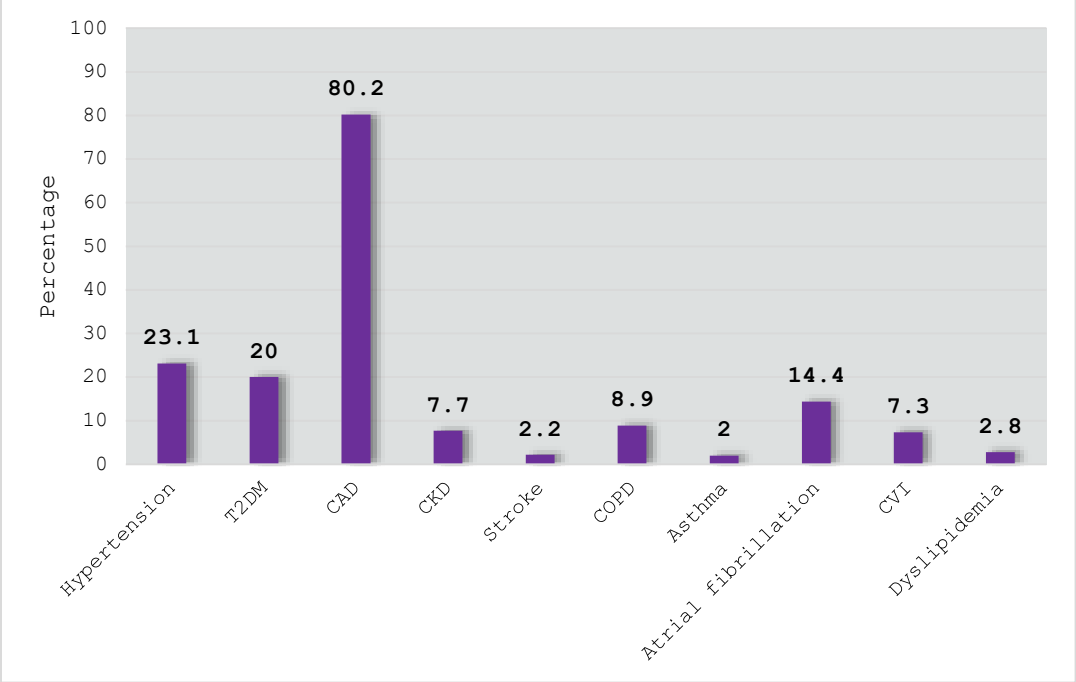

Figure 2. Comorbidities of HF patients

Abbreviations: T2DM: diabetes mellitus type 2; CAD: coronary artery disease; CKD: chronic kidney disease; COPD: chronic pulmonary obstructive disease: CVI: chronic venous insufficiency.

Figure 3 summarize the list of medications consumed by HF patients in this study. Five most common medications consumed by patients were BBs, furosemide, spironolactone, aspirin, and ACEi/ARBs/ARNI with percentages of 98.6%, 90.1%, 72.3%, 71.3%, and 66.0%, respectively. SGLT2i as one of the pillars of HFrEF therapy was only 6.3%. The most common types of T2DM drugs consumed by HF patients were metformin (4.1%) and glimepiride (3.9%). Salbutamol (4.3%) and ipratropium bromide inhalation (2.8%) were the most common medication for HF patients with pulmonary disease in this study.

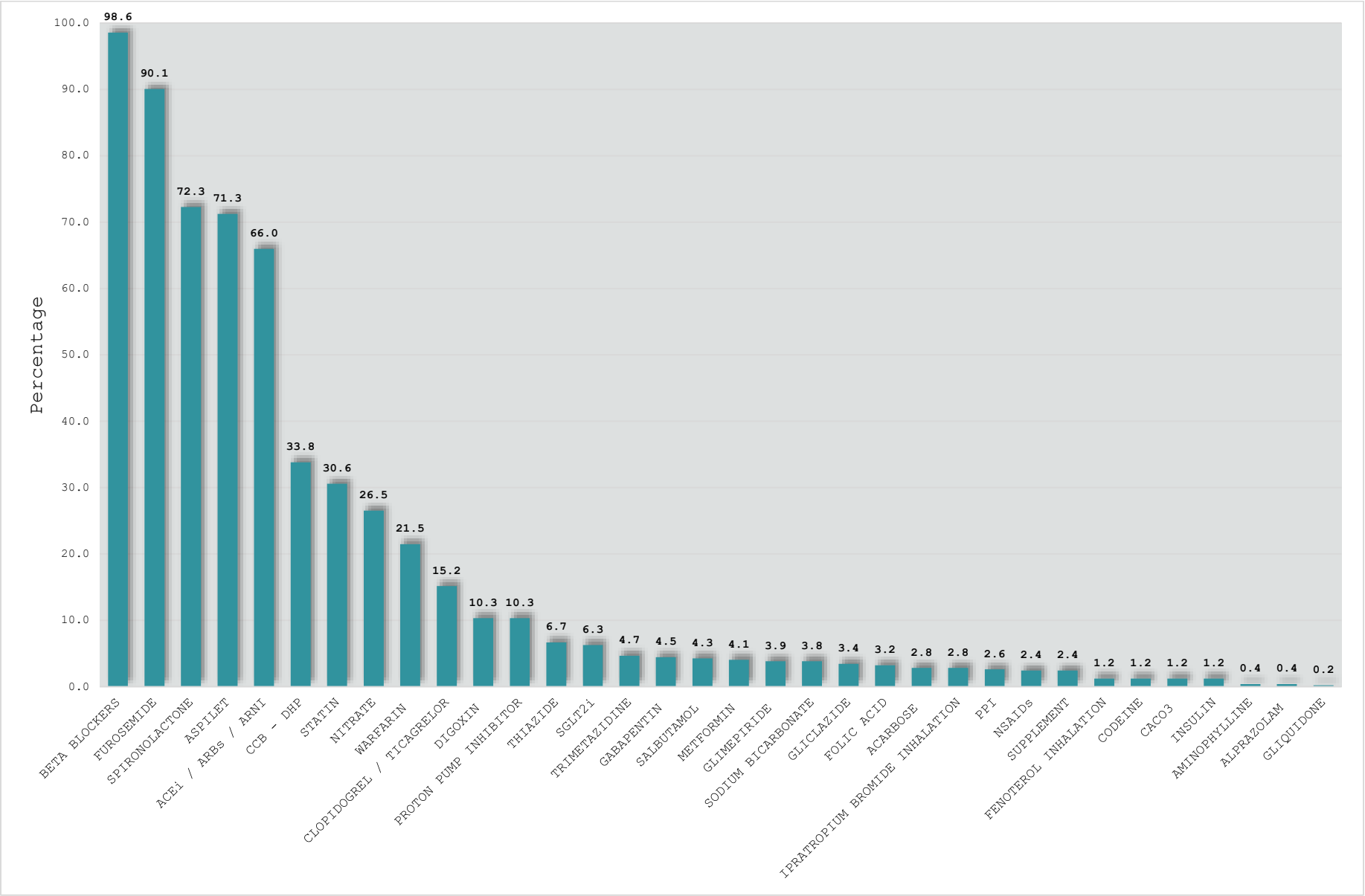

Figure 3. Proportion of medication taken by HF patientsAbbreviations: ACEi: angiotensin-converting enzyme inhibitors; ARBs: angiotensin receptor blockers; ARNI: angiotensin receptor neprilysin inhibitor; CCB-DHP: calcium channel blockers-dihydropyridine; SGL T2i: sodium-glucose cotransporter-2 inhibitors; PPI: proton pump inhibitors; NSAIDs: non-steroidal anti-inflammatory drugs; CaCO3: calcium carbonat

Table 2 presents bivariate analysis on several variables. The results of the study showed that there was no significant difference between gender in the risk of polypharmacy. HF patients with ≥3 comorbidities had crude OR 3.43 (95% CI, 2.33-5.06) to had polypharmacy compared to those with <3 comorbidities. HF patients with T2DM, CAD, CKD, COPD and asthma were associated with polypharmacy (p<0.05). The highest crude OR was T2DM (10.95; 95% CI 6.16-19.46). The risk of polypharmacy based on EF category was not significantly different in this study. History of PCI increased the risk of polypharmacy (crude OR 2.03; 95% CI, 1.31-3.14).

Table 2. Bivariate Analysis of Polypharmacy in HF Patients (n=494)

Variables	Polypharmacy		P-value	Crude OR (95%CI)
	Yes (≥7 medications)	No (<7 medications)		
Gender				
Male	119 (45.1)	145 (54.9)	0.217	Reff.
Female	91 (39.6)	139 (60.4)		0.8 (0.56–1.14)
Age group				
18-44	14 (31.8)	30 (68.2)		
45-59	109 (48)	118 (52)	0.047*	
60-74	74 (37.4)	124 (62.6)		
≥75	13 (52)	12 (48)		
Number of comorbidities	104 (32.2)	219 (67.8)	<0.001*	Reff.
< 3	106 (62)	65 (38)		3.43 (2.33–5.06)
≥ 3				
Comorbidities				
Hypertension	51 (44.7)	63 (55.3)	0.583	1.13 (0.74–1.72)
T2DM	83 (83.8)	16 (16.2)	<0.001*	10.95 (6.16–19.46)
CAD	180 (45.5)	216 (54.5)	0.008*	1.89 (1.18–3.03)
CKD	32 (84.2)	6 (15.8)	<0.001*	8.33 (3.41–20.33)
Stroke	5 (45.5)	6 (54.5)	1.00	1.13 (.34–3.75)
COPD	33 (75)	11 (25)	<0.001*	4.63 (2.28–9.4)
Asthma	8 (80)	2 (20)	0.015*	5.58 (1.17–26.57)
Atrial fibrillation	23 (32.4)	48 (67.6)	0.062	0.61 (0.36–1.03)
CVI	12 (33.3)	24 (66.7)	0.247	0.657 (0.32–1.35)
Dyslipidemia	8 (57.1)	6 (42.9)	0.261	1.84 (0.63–5.37)
Ejection fraction				
HFrEF	74 (42.8)	99 (57.2)	0.989	
HFmrEF	66 (42)	91 (58)		
HFpEF	70 (42.7)	94 (57.3)		
History of PCI	58 (56.3)	45 (43.7)	0.001*	2.03 (1.31–3.14)

T2DM: diabetes mellitus type 2; CAD: coronary artery disease; CKD: chronic kidney disease; COPD: chronic pulmonary obstructive disease: CVI: chronic venous insufficiency; HFrEF: heart failure reduced ejection fraction; HFmrEF: heart failure mildly reduced ejection fraction; HFpEF: heart failure preserved ejection fraction; PCI: percutaneous coronary intervention; OR: odds ratio.
*P-value < 0.05

Multivariate analysis at Table 3 showed that HF patients with T2DM, CKD, COPD, asthma and history of PCI increased the risk of polypharmacy. HF patients with T2DM had the highest adjusted OR (AOR) 12.35; 95% CI, 6.78-22.49. HF patients with COPD (AOR 7.15; 95%CI 3.35-15.26) and asthma (AOR 11.18; 95%CI 2.22-56.29) in this study also had higher risk of polypharmacy.

Table 3. Multivariate Analysis of Polypharmacy in HF Patients

Predictors	Full Model		Final Model	
	P-value	Adjusted OR (95%CI)	P-value	Adjusted OR (95%CI)
Age ≥65 vs 18-64	0.059	0.62 (0.37–1.02)	-	-
Comorbidities ≥ 3	0.475	1.21 (0.72–2.04)	-	-
T2DM	<0.001	11.14 (5.96–20.83)	<0.001	12.35 (6.78–22.49)
CAD	0.22	1.42 (0.81–2.49)	-	-
CKD	<0.001	7.12 (2.56–19.79)	<0.001	7.18 (2.73–18.91)
COPD	<0.001	7.05 (3.11–16.01)	<0.001	7.15 (3.35–15.26)
Asthma	0.004	10.91 (2.12–56.17)	0.003	11.18 (2.22–56.29)
History of PCI	0.015	1.94 (1.14–3.31)	0.004	2.13 (1.27–3.57)

Abbreviations: T2DM: diabetes mellitus type 2; CAD: coronary artery disease; CKD: chronic kidney disease; COPD: chronic pulmonary obstructive disease; PCI: percutaneous coronary intervention; OR: odds ratio.

Discussion

Heart failure patients, especially those with HFrEF, will receive at least 4 types of drugs which are the 4 main pillars of therapy: BBs, ACEi/ARB/ARNI, MRA, and SGLT2i.[4] It cannot be denied that comorbidities in HF patients will increase the number of medications. A previous study showed that every additional 1 comorbidity in HF patients would increase the risk of polypharmacy (OR 1.58; 95%CI 1.46-1.70).[7] Interestingly, our finding showed that 77 of 210 patients (36.7%) in the polypharmacy category was excessive polypharmacy. The medications taken by HF patients are related to comorbidities and symptoms, make clinician difficult to avoid polypharmacy. On the other side, there was a risk of rehospitalization in HF patients because of side effects and drug interactions from excessive polypharmacy, although these side effects do not affect the risk of death.[7]

Bivariate analysis in this study showed that T2DM, CKD, COPD, asthma and history of PCI had significantly increased polypharmacy. Clinically, T2DM and CKD are closely related to heart function, known as cardio-renal-metabolic (CVRM) syndrome. Treatment of CVRM requires combination of medications. Thus, when a patient falls into HF state, polypharmacy is often unavoidable. Frequently, HF patients with CKD will face obstacles in optimizing GDMT due to hyperkalemia and decreased kidney function.[8]

Polypharmacy on HF Patients with T2DM and CKD

Heart failure and T2DM usually coexist and occur in 20% of chronic and 40% of acute cases.[9] The prevalence and incidence of HF is increased in T2DM, as well as the risk of mortality which increases up to 10-fold. Current antihyperglycemic therapy has been shown to reduce the risk of mortality and HF hospitalization, such as SGLT2i. The combination of metformin and SGLT2i is also known to be beneficial reduce the incidence of HF and decrease of mortality.[10] With the existence of new T2DM medications and are followed by at least 4 pillars of GDMT therapy, polypharmacy in T2DM – HF patients is often unavoidable. Our study revealed that 20% of HF patients had T2DM (Figure 2), with 83% of them had polypharmacy.

The concomitant of CKD will complicate the treatment of T2DM in HF patients. Approximately more than 50% of HF patients have CKD as comorbidities, and the severity of renal dysfunction is

associated with high mortality rates. Even though, an increased risk of mortality already occur in the early phase of renal dysfunction.[11] Our study revealed that 7.7 % of HF patients had CKD and 32 % of them accounted for polypharmacy. The multivariate analysis (Table 3) showed that HF patients with T2DM had 12.35 higher risk of polypharmacy, while CKD 7.18 higher risk. A good strategy is needed to reduce unnecessary medications in HF patients, so that polypharmacy can be minimized.

Polypharmacy on HF Patients with Pulmonary Disease

Asthma and chronic inflammatory lung disease are risk factors for HF and CAD. The risk is higher for those with COPD.[12] The concomitant of asthma and COPD in HF patients undoubtedly raises the number of medications taken by patients, which raises the risk of polypharmacy or excessive polypharmacy.[7] In our study, about 8.9% HF patients had COPD and 2% had asthma. Both diseases significantly increased the risk of polypharmacy. The number of respiratory drugs needed for asthma and COPD varies depending on how severe the symptoms are. The greater the intensity of the disease's symptoms, the more treatment is required.

Treatment of HF patients with asthma and COPD requires specific attention to ensure that the symptoms of the diseases are properly controlled while not causing harmful side effects to the cardiovascular (CV) system.[13,14] There are some evidences indicates that certain asthma or COPD medications may negatively impact CV system, while some HF medications may exacerbate asthma or COPD symptoms. [15,16] The medication related to pulmonary disease that is often given to HF patients is long-acting beta-agonist plus inhaled corticosteroids and oral bronchodilators.[5,17] In our study as shown in Figure 3, the therapy given for COPD and asthma was salbutamol (6.68%), combination of fenoterol and ipratoprium bromide (3.85%), fenoterol (2.23%), and aminophylline (1.21%).

The multivariate analysis in this study found that both asthma and COPD had higher risk of polypharmacy. Based on this study, asthma and COPD were major contributors to polypharmacy in HF patients. Careful consideration in therapy to reduce the impact of polypharmacy is as important as providing appropriate therapy for HF, asthma, and COPD. This is a dilemma for clinicians. Therefore, in the treatment of HF patients with asthma or COPD, inhalation therapy is recommended rather than oral therapy, as well as prescribing one inhaler is preferred.

Polypharmacy on HF patients with Atrial Fibrillation

Atrial fibrillation (AF) is most common arrhythmia in HF patients. The occurrence of AF is related to the severity of HF, rises from <10% in New York Heart Association (NYHA) class I to >50% in NYHA class IV.[18] In this study, 14.4% of HF patients experienced AF, and consequently the patient must receive oral anticoagulant (OAC). As seen in Figure 3, warfarin is the drug of choice for OAC in this study. Heart rate control strategies for AF patients is essential.[19] In HFrEF patients, BBs are one of the pillars treatment that must be given in addition to its role as heart rate control in AF. When BBs alone are not adequate, digoxin can be used as a combination therapy. Even though study showed that digoxin did not improve survival, but symptoms related to heart rate will be better.[20]

Another consideration is to perform catheter ablation for AF. Study showed that catheter ablation for AF in HF patients was associated with a significantly lower rate of mortality and rehospitalization compared to medication alone.[21] However, this procedure is not easy and carries risks, especially in HF patients who are still relatively unstable.[22] A successful catheter ablation procedure will reduce the risk of HF patients taking AF-related medications (polypharmacy).

Limitations of Study

This research was conducted in a cardiovascular hospital therefore polypharmacy patterns will differ in hospitals with other characteristics. This study presented single-time data and did not assess patterns of therapy changes in HF patients.

Conclusion

Many HF patients receive polypharmacy, some even receive excessive polypharmacy. HF patients with T2DM, CKD, history of PCI, and pulmonary disease should be of particular concern due to increased risk of polypharmacy. Clinicians must make priority considerations regarding medications that should be given according to recommended guidelines and address the comorbidities suffered by patient.

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Conflict of interest

No conflict of interest.

References

1. Khan MS, Shahid I, Bennis A, Rakisheva A, Metra M, Butler J. Global epidemiology of heart failure. Nat Rev Cardiol 2024;21(10):717–34.

2. Reyes EB, Ha JW, Firdaus I, Ghazi AM, Phrommintikul A, Sim D, et al. Heart failure across Asia: Same healthcare burden but differences in organization of care. International Journal of Cardiology 2016;223:163–7.

3. Feng J, Zhang Y, Zhang J. Epidemiology and burden of heart failure in asia. JACC: Asia 2024;4(4):249–64.

4. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Bohm M, et al. 2023 focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal 2023;1–13.

5. Unlu O, Levitan EB, Reshetnyak E, Kneifati-Hayek J, Diaz I, Archambault A, et al. Polypharmacy in older adults hospitalized for heart failure. Circ: Heart Failure 2020;13(11):e006977.

6. Schuler J, Dückelmann C, Beindl W, Prinz E, Michalski T, Pichler M. Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria. Wien Klin Wochenschr 2008;120(23–24):733–41.

7. Minamisawa M, Claggett B, Suzuki K, Hegde SM, Shah AM, Desai AS, et al. Association of hyper-polypharmacy with clinical outcomes in heart failure with preserved ejection fraction. Circ: Heart Failure [Internet] 2021 [cited 2024 Oct 20];14(11). Available from: https://www.ahajournals.org/doi/10.1161/CIRCHEARTFAILURE.120.008293

8. Green D, James B, Hussain N. Pharmacological management of cardio-renal-metabolic disease including new potassium binders. Medicine 2023;51(3):176–9.

9. Dei Cas A, Khan SS, Butler J, Mentz RJ, Bonow RO, Avogaro A, et al. Impact of diabetes on epidemiology, treatment, and outcomes of patients with heart failure. JACC: Heart Failure 2015;3(2):136–45.

10. Standl E, Schnell O, McGuire DK. Heart failure considerations of antihyperglycemic medications for type 2 diabetes. Circulation Research 2016;118(11):1830–43.

11. Kadowaki T, Komuro I, Morita N, Akiyama H, Kidani Y, Yajima T. Manifestation of heart failure and chronic kidney disease are associated with increased mortality risk in early stages of type 2 diabetes mellitus: analysis of a japanese real-world hospital claims database. Diabetes Ther 2022;13(2):275–86.

12. Ingebrigtsen TS, Marott JL, Vestbo J, Nordestgaard BG, Lange P. Coronary heart disease and heart failure in asthma, COPD and asthma-COPD overlap. BMJ Open Resp Res 2020;7(1):e000470.

13. Cazzola M, Page CP, Hanania NA, Calzetta L, Matera MG, Rogliani P. Asthma and cardiovascular diseases: navigating mutual pharmacological interferences. Drugs 2024;84(10):1251–73.

14. Prosser TR, Bollmeier SG. Assessment of medication regimen complexity of COPD regimens in individuals visiting community pharmacies. COPD 2023;Volume 18:1499–510.

15. Ruiz-Laiglesia FJ, Garcés-Horna V, Formiga F. Comprehensive therapeutic approach for patients with heart failure and comorbidity. Revista Clínica Española (English Edition) 2016;216(6):323–30.

16. Matera MG, Hanania NA, Maniscalco M, Cazzola M. Pharmacotherapies in older adults with COPD: challenges and opportunities. Drugs Aging 2023;40(7):605–19.

17. Wu P, Jiang Y qun, Si F li, Wang H ying, Song X bo, Sheng C feng, et al. Pharmaceutical treatment status of patients with COPD in the community based on medical internet of things: a real-world study. npj Prim Care Respir Med 2024;34(1):10.

18. Bergau L, Bengel P, Sciacca V, Fink T, Sohns C, Sommer P. Atrial fibrillation and heart failure. JCM 2022;11(9):2510.

19. Alobaida M, Alrumayh A. Rate control strategies for atrial fibrillation. Annals of Medicine 2021;53(1):682–92.

20. Fauchier L, Laborie G, Clementy N, Babuty D. Beta-blockers or digoxin for atrial fibrillation and heart failure? Cardiac Failure Review 2016;2(1):35.

21. Marrouche NF, Boersma L, Sanders P, Vogt J. Catheter ablation for atrial fibrillation with heart failure. NEJM 2018;

22. Huang HD, Waks JW, Contreras-Valdes FM, Haffajee C, Buxton AE, Josephson ME. Incidence and risk factors for symptomatic heart failure after catheter ablation of atrial fibrillation and atrial flutter. Europace 2016;18:521–30.