Original article

Left ventricular ejection fraction in individuals with heart failure and associated factors

Fração de ejeção do ventrículo esquerdo em indivíduos com insuficiência cardíaca e fatores associados

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ABSTRACT | OBJECTIVE: To verify the relationship of modifiable risk factors, clinical complications and drug therapy with left ventricular ejection fraction (LVEF) in individuals with heart failure (HF). **METHODS:** Cross-sectional study with secondary data from a matrix study "Cerebral infarction in patients with heart failure: associated characteristics and left atrial function". The sample consisted of 75 adult individuals treated at a reference outpatient clinic in Salvador, Bahia. LVEF groups were classified: reduced LVEF (LVEFr) ≤ 40%, intermediate LVEF (LVEFi) 40-49% and preserved LVEF (LVEFp) ≥50%. An analysis was carried out using SPSS software and considered statistical significance p≤0.05. **RESULTS:** The sample had a mean age of 62±10 years, the majority were men n=42 (56%), functional class II/IV n=41 (54.7%) and of idiopathic etiology n=33 (44%). LVEF and LVEFp were similar n=31 (41%), followed by LVEFi n=13 (18%). The LVEF subgroups were related to Diabetes Melitus (DM) as a risk factor (p=0.049), Cerebral Vascular Accident (CVA) as a complication (p=0.001), drug therapy with beta blockers (p=0.004) and Converting Enzyme Inhibitors of Angiotensin (ACEI/ARB) (p=0.007). **CONCLUSION:** DM as a risk factor, stroke as a complication and beta-blocker medications and ACE inhibitors/ARBs are related to LVEF in individuals with HF.

KEYWORDS: Heart Failure. Pharmacological Treatment. Ventricular Ejection Fraction. Risk Factors.

RESUMO | OBJETIVOS: Verificar a relação de fatores de risco modificáveis, complicações clínicas e terapia medicamentosa com a fração de ejeção do ventrículo esquerdo (FEVE) em indivíduos com insuficiência cardíaca (IC). **MÉTODOS:** Estudo de corte transversal, com dados secundários de um estudo matriz Infarto cerebral em pacientes com insuficiência cardíaca: características associadas e função atrial esquerda. A amostra composta por 75 indivíduos adultos atendidos em ambulatório de referência em Salvador, Bahia. Os grupos da FEVE foram classificados: FEVE reduzida (FEVEr) ≤ 40%, FEVE intermediária (FEVEi) 40-49% e FEVE preservada (FEVEp) ≥50%. Foi realizado uma análise através do software SPSS e considerado significância estatística p≤0,05. **RESULTADOS:** A amostra apresentou média de idade 62±10 anos, sendo a maioria homens n=42(56%), de classe funcional II/IV n=41 (54,7%) e etiologia idiopática n=33 (44%). A FEVEr e FEVEp foram semelhantes n=31(41%), seguida de FEVEi n=13 (18%). Os subgrupos de FEVE foram relacionados a Diabetes Melitus (DM) como fator de risco (p=0,049), Acidente Vascular Cerebral (AVC) como complicação (p=0,001) e na terapia medicamentosa betabloqueadores (p=0,004) e Inibidores da Enzima Conversora de Angiotensina (IECA/BRA) (p=0,007). **CONCLUSÃO:** O DM como fator de risco, o AVC como complicação e os medicamentos betabloqueadores e IECA/BRA possuem relação com a FEVE de indivíduos com IC.

PALAVRAS-CHAVE: Insuficiência Cardíaca. Tratamento Farmacológico. Fração de Ejeção Ventricular. Fatores de Risco.

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1. Introduction

Heart failure (HF) is understood as the inability of the heart to pump blood to the body and meet tissue metabolic needs. It is characterized by signs and symptoms that can lead to functional and structural changes in the heart, potentially affecting various organs due to low cardiac output, requiring a good clinical evaluation, early diagnosis and etiological differentiation, essential for prognosis.[1]

HF is a public health problem affecting over 26 million patients worldwide. It is responsible for high mortality and hospitalization rates, with a progressive increase in prevalence due to population aging and associated comorbidities.[2] In Brazil, mortality rates reached a total of 27,775 in 2020[3], and morbidity and hospitalization due to HF reached 201,376 in 2022[3], higher than in other countries, possibly due to direct relations between lifestyle, health services, economy and cultural and social history. However, due to advancements and adherence to treatments, an increase in life expectancy after diagnosis is observed, significantly reducing HF-related deaths.[4]

This syndrome can be classified by symptom severity, disease progression and left ventricular ejection fraction (LVEF), a parameter verified by echocardiography. LVEF can be considered preserved (≥50%), intermediate (40-49%) or reduced (<40%) and is directly related to disease etiology, comorbidities and symptoms affecting individual comfort.[1] LVEF is an indicator observed for treatment choice; when reduced (<40%), there is a greater tendency to use specific drugs, better hospitalization control, and reduced deaths.[5]

HF treatment significantly reduces morbidity and mortality, improving the quality of life of those with the disease. Treatment can be achieved through lifestyle changes and drugs that control the syndrome. HF is considered a severe disease and is the leading cause of cardiovascular death, directly influenced by comorbidities, increasing the risk of complications in individuals. However, when drug treatment follows national and international guidelines, there is a significant reduction in complications and mortality, improving the quality of life of these individuals.[6]

Risk factors directly influence HF prognosis, being comorbidities that alter cardiac function and worsen clinical outcomes, increasing hospitalization and morbidity and mortality risks. They can be classified as modifiable or non-modifiable. Modifiable factors include diabetes mellitus, hypertension and smoking; non-modifiable factors include sex and age, contributing to the development of various cardiovascular diseases.[7] These comorbidities can exacerbate HF complications, worsening prognosis and quality of life[8], increasing mortality risk, necessitating specific management to identify individuals at high risk due to associated comorbidities for HF complication prevention.[9]

Nurses play a crucial role in caring for heart failure patients by assessing potential complications and monitoring drug therapy. They are also essential in early risk factor identification, promoting health education, managing HF clinically, and providing psychological support for self-care and medication adherence, all of which reduce morbidity and mortality risks and improve the quality of life of those with HF.[10]

Conducting studies that relate LVEF classification with modifiable risk factors, clinical complications and drug treatment is scarce in national literature. New studies can favor the application of specific strategies that reduce secondary morbidity, hospitalizations and mortality in individuals with HF. Such actions can improve the care provided and the quality of life of HF patients.

Given this context, this study aims to verify the relationship between modifiable risk factors, clinical complications and drug therapy with left ventricular ejection fraction (LVEF) in individuals with heart failure (HF).

2. Method

This cross-sectional study uses secondary data from a matrix study titled "Cerebral infarction in patients with heart failure: associated characteristics and left atrial function." Conducted at one of the largest cardiology reference outpatient clinics for HF patients in Salvador, Bahia. HF diagnosis followed the European Society of Cardiology (ESC) recommendations for individuals with HF signs and symptoms.[11] LVEF subgroups were: reduced LVEF (LVEFr) ≤ 40%, intermediate LVEF (LVEFi) 40-49%, and preserved LVEF (LVEFp) ≥50%. According to NYHA (New York Heart Association), HF functional class has been the most used to classify symptom severity since 1920. This classification is recommended by HF guidelines and is based on activity tolerance and symptom presence or absence, consisting of four categories: I- Asymptomatic; II- Mild symptoms; III- Moderate symptoms; IV- Severe symptoms at rest.[1]

An amendment was submitted to the Research Ethics Committee (CEP) for authorization to analyze other variables from the pre-existing database. The methods of choosing these variables were those available in the database and authorized for use. The amendment was submitted in June 2023, and after ethical approval, the following variables compared with LVEF subgroups were: sociodemographic and clinical characterization (age, sex, race/color, HF functional class, and HF etiology), modifiable risk factors (ex-smoking, alcoholism, atrial fibrillation - AF, systemic arterial hypertension - SAH, diabetes mellitus - DM, dyslipidemia, coronary artery disease - CAD, dilated cardiomyopathy), clinical complications (cerebral vascular accident - CVA on cranial CT), and medications in use: oral anticoagulant (Vitamin K antagonist and New anticoagulants - NOACS; acetylsalicylic acid - ASA; diuretics; beta-blockers; calcium channel blockers; angiotensin-converting enzyme inhibitors - ACEI; angiotensin receptor blockers - ARB; amiodarone; digoxin; and statins).

Inclusion criteria were adult individuals (over 18 years) diagnosed with HF. The exclusion criterion was the existence of incomplete data in the medical record.

Information obtained was stored in a database and statistically analyzed using SPSS version 24.0 software. Nominal variables were described in number and percentage, and the continuous variable (age) was expressed in mean and standard deviation according to normality verified by the Kolmogorov-Smirnov test. In bivariate analysis, Pearson's Chi-square (X^2) test was used to verify the relationship of LVEF with other variables (risk factors, complications, and drug therapy). The statistical significance level was 95% ($p<0.05$).

The Research Ethics Committee approved the study under opinion number 6.107.383 and CAAE 21847713.0.0000.0045.

3. Results

The sociodemographic and clinical characteristics of individuals with heart failure are described in Table 1. The left ventricular ejection fraction showed the same percentage of reduced and preserved (41%). Of the total participants (n=75), the mean age was 62±10 years, majority male (56%), of black race/color (49.3%). Clinically, a significant percentage of NYHA functional class II/IV (54.7%) and idiopathic etiology (44%) followed by Chagas etiology (36%) was observed.

Table 1. Sociodemographic and clinical characteristics of individuals with Heart Failure, Salvador, Bahia, 2024

Sociodemographic and clinical characteristics	Total	Reduced LVEF (≤40%)	Intermediate LVEF (40-49%)	Preserved LVEF (≥50%)
	N (%) n= 75(100)	N (%) n= 31(41)	N (%) n= 13(18)	N (%) n= 31(41)
Age, years **(μ±)****	62±10	62±10	56±8	64±11
Sex				
Male	42 (56)	19(45.2)	9(21.4)	14(33.3)
Female	33 (44)	12(36.4)	4(12.1)	17(51.5)
Race/color				
Mixed	32 (42.7)	13(40.6)	6(18.7)	13(40.6)
Black	37 (49.3)	16(43.2)	5(13.6)	16(43.2)
White	6 (8)	2(33.3)	2(33.3)	2(33.3)
Functional class HF (NYHA)				
I	20(26.7)	6(30.0)	4(20.0)	10(50.0)
II	41(54.7)	18(43.9)	6(14.6)	17(41.5)
III	14(18.7)	7(50.0)	3(21.4)	4(28.6)
HF etiology				
Idiopathic	33(44.0)	12(36.4)	8(24.2)	13(39.4)
Chagas	27(36.0)	13(48.1)	2(7.5)	12(44.4)
Ischemic	10(13.3)	4(40.0)	2(20.0)	4(40.0)
Hypertensive	3(4.0)	2(66.6)	1(33.4)	-
Rheumatic	1(1.3)	-	-	1(100.0)

HF - Heart failure; NYHA - New York Heart Association.
Source: the authors (2024).

Table 2 describes the relationship between modifiable risk factors and clinical complications of HF according to LVEF. It was observed that 50% of individuals with DM had LVEFr and showed statistical significance (p=0.049); CVA was the HF complication that showed a relationship with LVEF (p=0.001), and 72.8% of individuals (n=16/22) with CVA had reduced LVEF.

Table 2. Risk factors and clinical complications related to left ventricular ejection fraction, Salvador, Bahia, 2024

Risk factors and clinical complications	Total	Reduced LVEF (≤40%)	Intermediate LVEF (40-49%)	Preserved LVEF (≥50%)	
	N (%) n=75(100)	N (%) n=31(41)	N (%) n=13(18)	N (%) n=31(41)	p-value*
Ex-Smoker	39(52.0)	19(48.7)	5(12.9)	15(38.4)	0.335
Alcoholism	18(24.0)	9(50.0)	4(22.3)	5(27.7)	0.405
AF	13(17.3)	6(46.1)	2(15.4)	5(38.5)	0.926
SAH	60(80.0)	26(43.3)	9(15.0)	25(41.7)	0.538
DM	20(26.7)	10(50.0)	6(30)	4(20)	0.049
Dyslipidemia	42(56.0)	15(35.7)	6(14.2)	21(50.1)	0.226
CAD	47(62.7)	22(46.8)	7(14.9)	18(38.3)	0.444
Dilated cardiomyopathy	32(42.7)	12(37.5)	8(25.0)	12(37.5)	0.318
HF complications					
CVA on CT	22(29.3)	16(72.8)	3(13.6)	3(13.6)	0.001

AF - Atrial fibrillation; SAH - Systemic arterial hypertension; DM - Diabetes mellitus; CAD - Acute coronary disease; CVA - Cerebral vascular accident; CT - Computed tomography. *Pearson's Chi-square (X^2) test.
Source: the authors (2024).

Table 3 describes the relationship between drug therapy and LVEF. It is observed that the relationship of beta-blocker use (p=0.004) and ACEI/ARB (p=0.007) with LVEF types, with the total individuals using beta-blockers (66.6%) having preserved LVEF. All individuals with reduced and preserved LVEF used ACEI/ARB.

Table 3. Relationship of drug therapy according to left ventricular ejection fraction, Salvador, Bahia, 2024

Drug therapy	Total	Reduced LVEF (≤40%)	Intermediate LVEF (40-49%)	Preserved LVEF (≥50%)	
	N (%) n=75(100)	N (%) n=31(41%)	N (%) n=13(18%)	N (%) n=31(41%)	P- value*
ACO	**19(25.3)**	**10(52.6)**	**2(10.5)**	**7(36.8)**	0.452
Vitamin K antagonist	13(68.42)	8(61.5)	-	5(38.5)	
NOACS	6(31.58)	2(33.3)	2(33.3)	2(33.3)	
ASA	41(54.7)	20(48.8)	5(12.2)	16(39.0)	0.258
Diuretics	69(92.0)	31(44.9)	11(15.9)	27(39.1)	0.097
Beta-blocker	27(36.0)	6(22.2)	3(11.1)	18(66.6)	0.004
Calcium channel blocker	49(65.3)	19(38.8)	9(18.3)	21(42.8)	0.823
ACEI/ARB	73(97.3)	31(42.5)	11(15.0)	31(42.5)	0.007
Amiodarone	49(65.3)	18(36.7)	11(22.4)	20(40.8)	0.239
Digoxin	49(65.3)	17(34.7)	11(22.4)	21(42.8)	0.156
Statins	42(56.0)	20(47.6)	6(14.3)	16(38.0)	0.435

ACO - Oral anticoagulant; NOACS - New anticoagulants; ASA - Acetylsalicylic acid; ACEI - Angiotensin-converting enzyme inhibitors; ARB - Angiotensin receptor blockers. NOACS - New anticoagulants. *Pearson's Chi-square (X^2) test.
Source: the authors (2024).

4. Discussion

In this study, it was possible to verify a relationship between left ventricular ejection fraction with DM, CVA, and the use of beta-blockers and ACEI/ARB in individuals with heart failure. Individuals with reduced LVEF showed higher percentages of DM and CVA, and all used ACEI/ARB. Regarding beta-blockers, they were used mainly by individuals with preserved LVEF.

Regarding clinical and sociodemographic characterization, this study corroborates with other research revealing that HF mainly affects the elderly and male individuals with reduced LVEF.[12] Clinically, individuals with functional class II prevailed, those who have difficulty performing activities, some work impairment, and are symptomatic. NYHA classification allows evaluating individuals according to their clinical condition and symptom severity, assisting in determining specific therapy and reducing the risk of death.[13]

The idiopathic origin of HF was higher among individuals, but the significant number of patients with Chagas disease-induced HF, a precursor to clinical deterioration and poor disease prognosis, usually caused by dilated cardiomyopathy affecting left ventricular function, explained why most Chagas patients have reduced LVEF.[14] It is worth noting that although the World Health Organization certified the eradication of vector transmission in Brazil, small endemic foci are still found, mainly in Bahia[15], which may explain the number of patients with this etiology in this study.

Analyzing the risk factors related to left ventricular ejection fraction, it was observed that individuals with reduced LVEF present more modifiable risk factors such as DM, which can be explained by diastolic dysfunction caused by hyperglycemia and insulin resistance altering myocardial structure, causing fibrosis. These patients have worse prognoses as the pathology increases HF complications, and those with reduced ejection fraction have a higher mortality risk compared to those with preserved ejection fraction.[16] On the other hand, systemic arterial hypertension is the most prevalent chronic disease and significantly interferes with disease prognosis, contributing to HF development and clinical deterioration.[17]

CVA considered a clinical complication after HF diagnosis regardless of LVEF, showed statistical significance with LVEF[18] subgroups, being more frequent in individuals with reduced LVEF, increasing their mortality risk. Research shows a relationship between CVA risk and reduced LVEF, with these individuals developing complications more often, even those undergoing antithrombotic treatment, and those with LVEF <15% having double the risk of developing CVA, corroborating this study where most patients with complications had reduced LVEF.[19]

Studies confirm that most HF patients have a 2-5 times higher risk of developing CVA compared to non-HF patients[20], possibly explained by the disease's pathophysiology, which reduces cerebral blood flow, increases cardioembolic events, and inflammation risks[18], all predisposing to ischemic CVA. Additionally, this predisposition may relate to other HF-related risk factors like hypertension, AF and diabetes mellitus, which are risk predictors for CVA development. In this study, all CVA[21] cases were ischemic after HF diagnosis.

Regarding drug therapy according to left ventricular ejection fraction, ACEI/ARB use was in totality for both reduced and preserved LVEF groups. The Brazilian HF guideline states these patients need specific pharmacological treatments for clinical improvement and reduced HF morbidity and complications. ACEI/ARB use has been recommended since 1997 as the first medication class to reduce morbidity, mortality, and hospitalization rates in individuals with reduced LVEF.[22]

Despite no statistical significance, over 90% of individuals investigated in this study used diuretics, and 100% of those with reduced LVEF had this medication prescribed. Diuretics are widely used in HF patients to minimize congestion and volume overload despite no randomized clinical trials identifying increased survival in outpatients.[1]

Beta-blocker use prevailed in individuals with preserved LVEF. This pharmacological class acts differently, blocking adrenergic receptors according to the drug and its selectivity, such as carvedilol blocking β1, β2, and α1, and metoprolol having affinity only with β1.[23] Both show efficacy in HF treatment, reducing mortality rates and clinical deterioration.

The main treatment goal for preserved LVEF is treating comorbidities influencing HF and mainly decreasing blood pressure levels[24], explaining why most in this subgroup use beta-blockers. However, studies show that beta-blocker use in preserved LVEF patients relates to no prognosis improvement[25] and no evidence of reduced mortality risk, and the effects are not well elucidated.[26]

Vitamin K antagonists were the most used anticoagulants in the studied groups, predominantly in reduced LVEF patients. Despite increasing hemorrhage risks, they reduce fatal CVA risk.[27] NOACS were less used, suggesting that during this period, studies were consolidating NOACS risks with ischemic events[28], possibly considering the cost of acquiring these drugs[29], given that the studied patients are from a public health institutions.

HF patients generally have a therapeutic plan with multiple drugs, requiring systematic follow-up to ensure good adherence. LVEF directly affects drug choice, with the plan being individually tailored according to each patient's classification, contributing to treatment, reducing morbidity and mortality, and improving quality of life.[1] One factor improving therapeutic adherence in HF is telemonitoring by specialized professionals like nurses[30], who conduct health education guidance and reduce secondary morbidity, hospitalizations and mortality. Such actions can reflect improved care and the quality of life of HF patients.

This study's limitation is being conducted in a single center with a small convenience sample. However, it was performed at one of Bahia's largest cardiology reference outpatient clinics. New studies with larger sample sizes are needed.

5. Conclusion

Individuals with reduced LVEF (LVEFr) showed more modifiable risk factors and clinical complications. They used more specific drugs to control the syndrome compared to intermediate (LVEFi) and preserved LVEF (LVEFp) groups.

DM as a modifiable risk factor influenced HF diagnosis, mainly in the LVEFr subgroup. CVA showed a relationship as an HF clinical complication, with individuals evolving to ischemic CVA after HF diagnosis, mainly in the LVEFr subgroup. Drug therapy with ACEI/ARB relates to both reduced and preserved LVEF and beta-blocker use to the preserved LVEF subgroup.

Finally, this study's results can assist in developing nursing professionals' knowledge, aiming to improve the care provided and promoting clinical excellence in caring for individuals diagnosed with HF.

Author contributions

Santos CO, Gama GGG, and Carvalho MMCO participated in project conception, data analysis, interpretation, article writing, or critical review of relevant intellectual content. All authors reviewed and approved the final version and are responsible for all aspects of the work, ensuring the accuracy and integrity of any part of the work.

Conflicts of interest

No financial, legal, or political conflicts involving third parties (government, companies, private foundations, etc.) were declared for any aspect of the submitted work (including but not limited to grants and funding, advisory board participation, study design, manuscript preparation, statistical analysis, etc.).

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References

1. Rohde LEP, Montera MW, Bocchi EA, Clausell NO, Albuquerque DC, Rassi S, et al. Diretriz Brasileira de Insuficiência Cardíaca Crônica e Aguda. Arq Bras Cardiol. 2018;111(3):436–539. https://doi.org/10.5935/abc.20180190

2. Fernandes ADF, Fernandes GC, Mazza MR, Knijnik LM, Fernandes GS, Vilela AT, et al. A 10-year trend analysis of heart failure in the less developed Brazil. Arq Bras Cardiol. 2020;114(2):222–31. https://doi.org/10.36660/abc.20180321

3. Ministério da saúde. DATASUS [Internet]. Brasília, DF: Ministério da Saúde; 2020. Available from: http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sim/cnv/obt10uf.def

4. Cestari VRF, Garces TS, Sousa GJB, Maranhão TA, Neto JDS, Pereira MLD, et al. Spatial Distribution of Mortality for Heart Failure in Brazil, 1996 – 2017. Arq Bras Cardiol. 2022;118(1):41–51. https://doi.org/10.36660/abc.20201325

5. Silva-Cardoso J, Brás D, Canário-Almeida F, Andrade A, Oliveira L, Pádua F, et al. Neurohormonal modulation: The new paradigm of pharmacological treatment of heart failure. Revista Portuguesa de Cardiologia. 2019;38(3):175–85. https://doi.org/10.1016/j.repc.2018.10.011

6. Cardoso J, Espíndola MD, Cunha M, Netto E, Cardoso C, Novaes M, et al. Is current drug therapy for heart failure sufficient to control the heart rate of patients? Arq Bras Cardiol. 2020;115(6):1063-9. https://doi.org/10.36660/abc.20190090

7. Francisco PMSB, Assumpção D, Borim FSA, Senicato C, Malta DC. Prevalence and co-occurrence of modifiable risk factors in adults and older people. Rev Saude Publica. 2019;53:1–13. https://doi.org/10.11606/S1518-8787.2019053001142

8. Van Deursen VM, Damman K, Van Der Meer P, Wijkstra PJ, Luijckx GJ, Van Beek A, et al. Comorbidities in Heart Failure. Heart Fail Rev. 2014;19(2):163–72. https://doi.org/10.1007/s10741-012-9370-7

9. Conde-Martel A, Hernández-Meneses M. Prevalence and prognostic meaning of comorbidity in heart failure. Rev Clin Esp. 2016;216(4):222–8. https://doi.org/10.1016/j.rce.2015.08.005

10. Barbosa CC, Perinote LCSC, Gomes RC, Oliveira FT, Costa JS. Cuidados de enfermagem no paciente com insuficiência cardíaca congestiva descompensada. Brazilian Journal of Health Review. 2024;7(2):e69175. https://doi.org/10.34119/bjhrv7n2-442

11. McDonagh TA, Metra M, Adamo M, Baumbach A, Böhm M, Burri H, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2021;42(36):3599–726. https://doi.org/10.1093/eurheartj/ehab368

12. Khan SS, Beach LB, Yancy CW. Sex-Based Differences in Heart Failure: JACC Focus Seminar 7/7. Journal of the American College of Cardiology. Elsevier Inc. 2022;79(15):1530–41. https://doi.org/10.1016/j.jacc.2022.02.013

13. Huo X, Pu B, Wang W, Peng Y, Li J, Lei L, et al. New York Heart Association Class and Kansas City Cardiomyopathy Questionnaire in Acute Heart Failure. JAMA Netw Open. 2023;6(10):e2339458. https://doi.org/10.1001/jamanetworkopen.2023.39458

14. Nunes MCP, Beaton A, Acquatella H, Bern C, Bolger AF, Echeverría LE, et al. Chagas Cardiomyopathy: An Update of Current Clinical Knowledge and Management: A Scientific Statement From the American Heart Association. Circulation. 2018;138(12):e169–209. https://doi.org/10.1161/CIR.0000000000000599

15. Braga JCV, Reis F, Aras R, Dantas Costa N, Bastos C, Silva R, et al. Clinical and therapeutics aspects of heart failure due to Chagas disease. Arq Bras Cardiol. 2006;86(4):296-301. https://doi.org/10.1590/S0066-782X2006000400010

16. Mentz RJ, Kelly JP, von Lueder TG, Voors AA, Lam CSP, Cowie MR, et al. Noncardiac Comorbidities in Heart Failure With Reduced Versus Preserved Ejection Fraction. J Am Coll Cardiol. 2014;64(21):2281–93. https://doi.org/10.1016/j.jacc.2014.08.036

17. Pereira AWS, Miranda BCB, Pereira BWS, Coutinho RET. Arterial hypertension and heart failure: critical analysis of new drugs. Revista Brasileira de Hipertensão. 2021;28(1):27–34. https://doi.org/10.47870/1519-7522/2021280127-34

18. Barkhudaryan A, Doehner W, Scherbakov N. Ischemic stroke and heart failure: Facts and numbers. An update. Journal of Clinical Medicine. 2021;10(5);1–14. https://doi.org/10.3390/jcm10051146

19. Di Tullio MR, Qian M, Thompson JLP, Labovitz AJ, Mann DL, Sacco RL, et al. Left Ventricular Ejection Fraction and Risk of Stroke and Cardiac Events in Heart Failure: Data from the Warfarin Versus Aspirin in Reduced Ejection Fraction Trial. Stroke. 2016;47(8):2031–7. https://doi.org/10.1161/STROKEAHA.116.013679

20. Adelborg K, Szépligeti S, Sundbøll J, Horváth-Puhó E, Henderson VW, Ording A, et al. Risk of Stroke in Patients with Heart Failure: A Population-Based 30-Year Cohort Study. Stroke. 2017;48(5):1161–8. https://doi.org/10.1161/STROKEAHA.116.016022

21. Kim W, Kim EJ. Heart failure as a risk factor for stroke. Journal of Stroke. 2018;20(1):33–45. https://doi.org/10.5853/jos.2017.02810

22. Malgie J, Clephas PRD, Brunner-La Rocca HP, de Boer RA, Brugts JJ. Guideline-directed medical therapy for HFrEF: sequencing strategies and barriers for life-saving drug therapy. Heart Failure Reviews. Springer. 2023;28:1221–34. https://doi.org/10.1007/s10741-023-10325-2

23. Liu B, Zhang R, Zhang A, Wang G, Xu J, Zhang Y, et al. Effectiveness and safety of four different beta-blockers in patients with chronic heart failure. MedComm. 2023;4(1):e199. https://doi.org/10.1002/mco2.199

24. Patel AH, Natarajan B, Pai RG. Current Management of Heart Failure with Preserved Ejection Fraction. International Journal of Angiology. 2022;31(3):166–78. https://doi.org/10.1055/s-0042-1756173

25. Hikoso S, Kida H, Sunaga A, Nakatani D, Okada K, Dohi T, et al. β-blockers may be detrimental in frail patients with heart failure with preserved ejection fraction. Clinical Research in Cardiology. 2023;113:842–855. https://doi.org/10.1007/s00392-023-02301-5

26. Meyer M, Du Fay Lavallaz J, Benson L, Savarese G, Dahlström U, Lund LH. Association Between β-Blockers and Outcomes in Heart Failure With Preserved Ejection Fraction: Current Insights From the SwedeHF Registry. J Card Fail. 2021;27(11):1165–74. https://doi.org/10.1016/j.cardfail.2021.04.015

27. Beggs SAS, Rørth R, Gardner RS, Mcmurray JJV. Anticoagulation therapy in heart failure and sinus rhythm: a systematic review and meta-analysis. Heart. 2019;105:1325–34. https://doi.org/10.1136/heartjnl-2018-314381

28. Shpak M, Ramakrishnan A, Nadasdy Z, Cowperthwaite M, Fanale C. Higher incidence of ischemic stroke in patients taking novel oral anticoagulants. Stroke. 2018;49(12):2851–6. https://doi.org/10.1161/STROKEAHA.118.022636

29. Kumana CR, Cheung BMY, Siu DCW, Tse HF, Lauder IJ. Non-vitamin K Oral Anticoagulants Versus Warfarin for Patients with Atrial Fibrillation: Absolute Benefit and Harm Assessments Yield Novel Insights. Cardiovascular Therapeutics. 2016;34:100–6. https://doi.org/10.1111/1755-5922.12173

30. Boyne JJJ, Van Asselt ADI, Gorgels APM, Steuten LMG, De Weerd G, Kragten J, et al. Cost-effectiveness analysis of telemonitoring versus usual care in patients with heart failure: The TEHAF-study. J Telemed Telecare. 2013;19(5):242–8. https://doi.org/10.1177/1357633X13495478