Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/5mf48423

SYSTEMIC AND PULMONARY HEMODYNAMIC EFFECTS OF SGLT2 INHIBITORS IN HEART FAILURE WITH COEXISTING LUNG DISEASE

Dr Muhammad Imran Ullah[1], Dr Muhammad Fawad[2]*, Dr Ihsan Ullah[3], Dr Hina Umair[4], Dr Falak Naz[5], Dr Ameer Hamza[6]

[1,2]*Assistant Professor, Department of Medicine, Gomal Medical College - MTI, DI Khan, Pakistan
[3]Assistant Professor, Department of Pharmacology, Saidu Medical College, Swat, Pakistan
[4]Assistant Professor, Department of Physiology, Wah Medical College, NUMS, Wah Cantt, Pakistan
[5]Assistant Professor, Department of Pharmacology, Northwest School of Medicine, Peshawar, Pakistan
[6]Lecturer, Department of Pharmacology, Peshawar Medical College, Peshawar, Pakistan

***Corresponding author:** Dr Muhammad Fawad
Assistant Professor, Department of Medicine, Gomal Medical College - MTI, DI Khan, Pakistan,
Email: drfawadmarwat@gmail.com

ABSTRACT

Background: To evaluate the systemic and pulmonary hemodynamic effects of SGLT2 inhibitors in patients with chronic HF and coexisting lung disease.

Methods: This prospective observational study included 72 patients with HF and chronic lung disease treated at Gomal Medical College and its affiliated hospital between January 2023 and January 2024. Baseline and six-month follow-up assessments included clinical evaluation, echocardiographic measurements of systemic and pulmonary pressures, pulmonary function tests, NT-proBNP levels, and six-minute walk distance (6MWD). Statistical comparisons were made using paired t-tests and McNemar's test.

Results: Mean systolic and diastolic blood pressures decreased significantly after therapy (128.4 ± 12.7 to 122.1 ± 11.9 mmHg, $p = 0.004$; 78.5 ± 8.4 to 74.9 ± 7.8 mmHg, $p = 0.011$), while cardiac output increased (4.21 ± 0.82 to 4.56 ± 0.87 L/min, $p = 0.022$). Pulmonary artery systolic pressure and mean pulmonary artery pressure declined ($p < 0.001$ for both), alongside reductions in 'pulmonary vascular resistance and pulmonary capillary wedge pressure'. NT-proBNP levels fell significantly (1832 ± 651 to 1427 ± 604 pg/mL, $p < 0.001$), and 6MWD improved by a mean of 34 meters ($p < 0.001$). Pulmonary function parameters showed no significant change.

Conclusion: In HF patients with chronic lung disease, SGLT2 inhibitors improved both systemic and pulmonary hemodynamics, enhanced exercise capacity, and reduced cardiac biomarker levels without adversely affecting lung function. These findings support their role as a valuable addition to therapy in this complex patient group.

Keywords: SGLT2 inhibitors, heart failure, pulmonary hypertension, chronic lung disease, hemodynamics, right ventricular function, NT-proBNP

INTRODUCTION

Heart failure (HF) remains a leading cause of morbidity and mortality worldwide, with a substantial proportion of patients affected by coexisting chronic lung disease 'such as chronic obstructive pulmonary disease (COPD) or interstitial lung disease (ILD)'. The coexistence of these conditions poses significant therapeutic challenges, as the overlapping pathophysiological mechanisms amplify circulatory burden and functional limitation. Elevated left-sided filling pressures in HF can lead to post-capillary pulmonary hypertension, which, when combined with pre-capillary changes from lung disease, results in disproportionate strain on the right ventricle[1, 2]. This "dual-hit" mechanism contributes to worsened exercise capacity, increased hospitalizations, and higher mortality rates compared with either condition alone [3].

Over the past decade, sodium–glucose cotransporter 2 (SGLT2) inhibitors have emerged as an important addition to guideline-directed therapy for HF. Originally developed as glucose-lowering agents for type 2 diabetes, these drugs have demonstrated robust cardiovascular benefits in large trials, including reductions in HF hospitalizations and improvements in quality of life in both diabetic and non-diabetic populations. Proposed mechanisms extend beyond glycemic control and include osmotic diuresis, natriuresis, reduction in interstitial fluid volume, improved ventricular loading conditions, and potential modulation of vascular tone[4-6].

While the systemic hemodynamic effects of SGLT2 inhibitors have been well described, their impact on pulmonary vascular parameters, particularly in patients with HF complicated by chronic lung disease, remains less clear. The potential to reduce pulmonary pressures, improve right ventricular performance, and enhance functional capacity could have substantial implications for this high-risk group. However, few studies have focused specifically on this population, and most available data are derived from mixed HF cohorts without detailed pulmonary hemodynamic assessment [7-9].

This study was designed to address this gap by prospectively 'evaluating the effects of SGLT2 inhibitor therapy on systemic and pulmonary hemodynamics, functional capacity, and biomarkers in patients with HF and coexisting chronic lung disease'. By focusing on this subgroup, the aim was to provide clinically relevant insights that could guide therapy in a setting where optimal management remains challenging.

METHODOLOGY

This was a prospective, observational study conducted at Gomal Medical College, Dera Ismail Khan, and its affiliated teaching hospital. The study period extended over 12 months, from January 2023 to January 2024. The hospital serves as a tertiary care center with dedicated cardiology and pulmonology units, allowing for integrated management and follow-up of patients with heart failure and chronic lung disease.

A total of 72 patients were enrolled, all of whom had a confirmed diagnosis of chronic heart failure in accordance with the European Society of Cardiology guidelines and a coexisting chronic lung condition. Lung diseases included 'chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), or other chronic respiratory pathologies diagnosed by a pulmonologist based on clinical evaluation, imaging, and pulmonary function tests'. Participants were recruited consecutively from the cardiology and pulmonology outpatient clinics and inpatient wards.

Inclusion Criteria

- Age 40 years or older
- Established diagnosis of heart failure (HFrEF, HFmrEF, or HFpEF)
- Documented chronic lung disease (e.g., COPD, ILD)
- Stable on guideline-directed medical therapy for heart failure for at least four weeks prior to enrollment
- Planned initiation of SGLT2 inhibitor therapy (dapagliflozin or empagliflozin) as part of standard care

Exclusion Criteria

- 'Acute decompensated heart failure at the time of screening'
- Severe valvular heart disease requiring surgical or interventional management
- Advanced chronic kidney disease (eGFR < 30 mL/min/1.73 m^2)
- Active pulmonary infection or acute exacerbation of lung disease
- Known hypersensitivity to SGLT2 inhibitors
- Pregnancy or breastfeeding

The study protocol was reviewed and approved by the Institutional Ethical Review Committee of Gomal Medical College. All participants provided written informed consent prior to enrollment. Patient confidentiality was maintained throughout the study in compliance with the Declaration of Helsinki.

At enrollment, demographic and clinical data were recorded, including age, sex, body mass index, smoking status, comorbidities, NYHA functional class, and current medications. Physical examination included blood pressure, heart rate, and anthropometric measurements.

Blood pressure and heart rate were measured in a seated position after five minutes of rest using an automated sphygmomanometer. Cardiac output, cardiac index, systemic vascular resistance, and stroke volume were calculated using echocardiography-derived left ventricular outflow tract (LVOT) measurements and Doppler velocity–time integrals.

Pulmonary artery systolic pressure (PASP), mean pulmonary artery pressure (mPAP), pulmonary capillary wedge pressure (PCWP), and right atrial pressure (RAP) were estimated non-invasively using transthoracic echocardiography. 'Pulmonary vascular resistance (PVR) was calculated from Doppler-derived gradients'. Right ventricular function was assessed using tricuspid annular plane systolic excursion (TAPSE) and right ventricular fractional area change (RVFAC).

Spirometry was performed according to American Thoracic Society/European Respiratory Society standards. Forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC ratio were expressed as percentages of predicted values based on reference equations. Diffusing capacity for carbon monoxide (DLCO) was measured when feasible.

Blood samples were collected after an overnight fast to measure NT-proBNP, serum creatinine, estimated glomerular filtration rate (eGFR), electrolytes, hemoglobin, glycated hemoglobin (HbA1c), uric acid, and high-sensitivity C-reactive protein (hs-CRP). Arterial blood gases were obtained from the radial artery in a resting state to assess PaO_2, $PaCO_2$, and oxygen saturation.

'Exercise capacity was evaluated using the six-minute walk distance (6MWD) test performed along a standardized hospital corridor under supervision'. The test was conducted according to American Thoracic Society guidelines, with encouragement provided at fixed time intervals.

Participants were reassessed at six months after initiating SGLT2 inhibitor therapy. Follow-up evaluations repeated all baseline measurements, including systemic and pulmonary hemodynamics, laboratory investigations, pulmonary function tests, and functional assessments. The primary outcomes were changes in pulmonary artery pressures, pulmonary vascular resistance, and NT-proBNP. Secondary outcomes included 'changes in systemic blood pressure, cardiac output, right ventricular function, 6MWD, and renal function'. Adverse events related to SGLT2 inhibitors, such as volume depletion, hypotension, urinary tract infections, and diabetic ketoacidosis, were documented.

Data were analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation (SD) and compared between baseline and follow-up using paired t-tests for normally distributed data. Non-parametric variables were analyzed with the Wilcoxon signed-rank test. Categorical variables were presented as frequencies and percentages, with changes over time assessed using McNemar's test. A p-value < 0.05 was considered statistically significant.

RESULTS

The study enrolled 72 patients with heart failure and coexisting chronic lung disease. The mean age was 64.2 ± 9.1 years, with a predominance of male participants (59.7%). The average BMI was 27.5

± 3.9 kg/m². Hypertension (75.0%) and type 2 diabetes mellitus (68.1%) were the most common comorbidities, followed by coronary artery disease (45.8%) and chronic kidney disease (29.2%). Among respiratory conditions, chronic obstructive pulmonary disease was present in 36.1% and interstitial lung disease in 13.9% of participants. Over a quarter (26.4%) had a prior diagnosis of pulmonary hypertension. Most participants were in NYHA Class III (62.5%), with the remainder in Class II (37.5%). Slightly more than half (56.9%) had heart failure with reduced ejection fraction (HFrEF), while 43.1% had preserved ejection fraction (HFpEF). The majority were receiving optimal guideline-directed medical therapy, including beta-blockers (84.7%), loop diuretics (80.6%), ACEi/ARB/ARNI (73.6%), and mineralocorticoid receptor antagonists (65.3%). Pulmonary medications, such as inhalers, were used by 40.3% of the cohort.

Table 1. Baseline Demographic and Clinical Characteristics of Participants (n = 72)

Variable	Mean ± SD / n (%)
Age (years)	64.2 ± 9.1
Male sex	43 (59.7%)
BMI (kg/m²)	27.5 ± 3.9
Current smoker	18 (25.0%)
Hypertension	54 (75.0%)
Diabetes mellitus type 2	49 (68.1%)
Chronic kidney disease	21 (29.2%)
COPD	26 (36.1%)
Interstitial lung disease	10 (13.9%)
Coronary artery disease	33 (45.8%)
Pulmonary hypertension (diagnosed)	19 (26.4%)
NYHA Class II	27 (37.5%)
NYHA Class III	45 (62.5%)
Heart failure type – HFrEF	41 (56.9%)
Heart failure type – HFpEF	31 (43.1%)
Loop diuretics	58 (80.6%)
Beta-blockers	61 (84.7%)
ACEi/ARB/ARNI	53 (73.6%)
Mineralocorticoid receptor antagonists	47 (65.3%)
Pulmonary medications (inhalers)	29 (40.3%)

After six months of SGLT2 inhibitor therapy, notable improvements were observed in both systemic and pulmonary hemodynamics. Systolic and diastolic blood pressures decreased significantly ($p = 0.004$ and $p = 0.011$, respectively), accompanied by a modest but significant reduction in resting heart rate ($p = 0.018$). Cardiac output and cardiac index improved ($p = 0.022$ and $p = 0.027$), while systemic vascular resistance declined ($p = 0.013$). Pulmonary artery pressures showed marked reductions, with PASP decreasing from 42.3 ± 8.5 mmHg to 37.4 ± 7.9 mmHg ($p < 0.001$) and mPAP from 28.1 ± 6.2 mmHg to 24.7 ± 5.8 mmHg ($p < 0.001$). Left-sided filling pressure, as reflected by PCWP, also improved significantly ($p < 0.001$), along with a reduction in pulmonary vascular resistance ($p = 0.002$). Right ventricular function, assessed by TAPSE, improved modestly ($p = 0.029$). Functional capacity, measured by the '6-minute walk distance, increased by an average of 34 meters ($p < 0.001$)'.

Table 2. Systemic and Pulmonary Hemodynamic Parameters at Baseline and 6-Month Follow-up After SGLT2 Inhibitor Therapy (n = 72)

Parameter	Baseline (Mean ± SD)	Follow-up (Mean ± SD)	p-value
SBP (mmHg)	128.4 ± 12.7	122.1 ± 11.9	0.004
DBP (mmHg)	78.5 ± 8.4	74.9 ± 7.8	0.011
Heart rate (bpm)	79.2 ± 10.3	75.1 ± 9.7	0.018
'Cardiac output (L/min)'	4.21 ± 0.82	4.56 ± 0.87	0.022
'Cardiac index (L/min/m²)'	2.39 ± 0.43	2.58 ± 0.45	0.027
SVR (dyn·s/cm⁵)	1421 ± 182	1342 ± 176	0.013
PASP (mmHg)	42.3 ± 8.5	37.4 ± 7.9	<0.001
mPAP (mmHg)	28.1 ± 6.2	24.7 ± 5.8	<0.001
PCWP (mmHg)	18.7 ± 4.3	15.9 ± 3.9	<0.001
PVR (Wood units)	3.52 ± 0.84	3.02 ± 0.79	0.002
TAPSE (mm)	17.6 ± 2.9	18.9 ± 3.1	0.029
6MWD (m)	322 ± 55	356 ± 58	<0.001

Biochemical analysis revealed a significant reduction in NT-proBNP levels from 1832 ± 651 pg/mL at baseline to 1427 ± 604 pg/mL at six months ($p < 0.001$), indicating improved cardiac strain. Renal function showed a small but statistically significant increase in eGFR ($p = 0.042$). Hemoglobin levels remained stable throughout the study period ($p = 0.117$). Arterial oxygenation improved modestly, with mean PaO_2 increasing by 3.5 mmHg ($p = 0.009$). Pulmonary function tests demonstrated slight increases in FEV_1 and FVC; however, these changes were not statistically significant ($p = 0.084$ and $p = 0.157$, respectively), consistent with the chronic, fixed nature of lung impairment in the study cohort.

Table 3. Laboratory and Functional Outcomes at Baseline and 6 Months (n = 72)

Variable	Baseline (Mean ± SD)	Follow-up (Mean ± SD)	p-value
NT-proBNP (pg/mL)	1832 ± 651	1427 ± 604	<0.001
eGFR (mL/min/1.73 m²)	62.8 ± 12.9	65.4 ± 13.2	0.042
Hemoglobin (g/dL)	13.1 ± 1.4	13.4 ± 1.3	0.117
PaO_2 (mmHg)	75.4 ± 7.8	78.9 ± 8.1	0.009
FEV_1 (% predicted)	69.8 ± 8.9	71.6 ± 9.1	0.084
FVC (% predicted)	74.1 ± 9.2	75.4 ± 9.4	0.157
FEV_1/FVC ratio	0.71 ± 0.06	0.72 ± 0.05	0.211

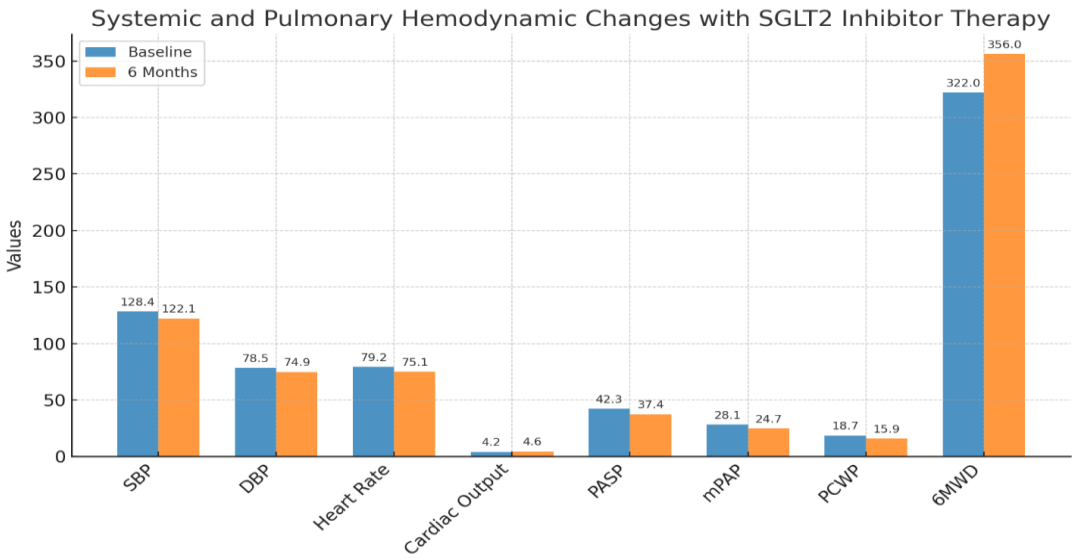

Figure 1

Bar chart showing baseline versus 6-month follow-up changes in key systemic and pulmonary hemodynamic parameters.

DISCUSSION

In this prospective observational study, initiation of 'SGLT2 inhibitor therapy in patients with chronic heart failure and coexisting lung disease was associated with significant improvements in both systemic and pulmonary hemodynamics over a six-month follow-up period'. Reductions in systolic and diastolic blood pressure, systemic vascular resistance, and heart rate were paralleled by increases in cardiac output and cardiac index, suggesting an overall enhancement in forward flow and afterload reduction. These systemic changes were accompanied by favorable pulmonary effects, with notable reductions in pulmonary artery systolic pressure, mean pulmonary artery pressure, pulmonary capillary wedge pressure, and pulmonary vascular resistance. Functional capacity, as measured by the 6-minute walk distance, also improved substantially, indicating that these hemodynamic benefits translated into tangible gains in exercise tolerance.

Our findings align with large randomized controlled trials and mechanistic studies that have demonstrated cardiovascular benefits of SGLT2 inhibitors beyond glucose lowering. The DAPA-HF and EMPEROR-Reduced trials reported significant reductions in heart failure hospitalizations 'and improvements in quality of life with dapagliflozin and empagliflozin, respectively, in patients with reduced ejection fraction, irrespective of diabetes status' [10-12]. Although those trials did not focus specifically on pulmonary hemodynamics, post-hoc analyses have suggested that SGLT2 inhibitors may attenuate pulmonary congestion through diuretic and natriuretic effects, reduction of left atrial pressures, and modulation of interstitial fluid distribution.

The present study adds to this evidence by focusing on a subgroup often underrepresented in major heart failure trials those with chronic lung disease. This population faces dual circulatory burdens: elevated left-sided filling pressures from heart failure and increased pulmonary vascular load from chronic respiratory pathology. Both mechanisms contribute to worsening right ventricular function, reduced exercise capacity, and higher mortality [13-15]. In our cohort, the observed improvement in right ventricular performance, reflected by higher TAPSE values, supports the hypothesis that unloading both the systemic and pulmonary circulations may alleviate right ventricular strain.

A possible explanation for the pulmonary vascular effects observed here involves the interplay between left-sided unloading and direct vascular modulation. By lowering PCWP, SGLT2 inhibitors may reduce post-capillary pulmonary hypertension. Furthermore, emerging experimental data suggest these agents may improve endothelial function, reduce oxidative stress, and attenuate vascular remodeling all potentially relevant in chronic lung disease–associated pulmonary hypertension [16-18]. While our study was not designed to confirm these mechanisms, the magnitude of change in mPAP and PVR suggests that benefits are unlikely to be solely attributable to diuresis.

Renal function, an important consideration in heart failure pharmacotherapy, showed modest improvement in eGFR, consistent with prior reports of renal protection in SGLT2 inhibitor trials [19] This is particularly relevant for patients with combined cardiac and pulmonary disease, where polypharmacy and frequent diuretic use may predispose to renal decline. The significant reduction in NT-proBNP further supports a sustained reduction in myocardial wall stress.

Despite these strengths, some findings warrant careful interpretation. Pulmonary function parameters (FEV_1, FVC) did not improve significantly, likely reflecting irreversible airway or parenchymal changes in chronic lung disease. This underscores that while SGLT2 inhibitors can improve hemodynamics and functional capacity, they are unlikely to reverse structural pulmonary impairment. Additionally, while no severe adverse effects were recorded, the possibility of genitourinary infections or rare ketoacidosis episodes remains, as described in earlier pharmacovigilance studies[20]

A major strength of this study is the comprehensive assessment of both systemic and pulmonary circulations using echocardiography, functional testing, and laboratory biomarkers. The prospective design and consistent follow-up reduce recall bias. However, limitations include the single-center setting, modest sample size, and lack of invasive right heart catheterization, which remains the gold standard for pulmonary hemodynamic measurement. Additionally, the absence of a control group

limits the ability to attribute changes solely to SGLT2 inhibitor therapy, as concurrent optimization of heart failure medications may have contributed.

These results suggest that SGLT2 inhibitors may hold particular value in heart failure patients with concomitant lung disease, where reducing both systemic and pulmonary vascular burdens is crucial. Incorporating these agents early in therapy may improve not only cardiac function but also right ventricular adaptation to pulmonary load, potentially reducing morbidity in this high-risk group.

CONCLUSION

In patients with chronic heart failure and coexisting lung disease, six months of SGLT2 inhibitor 'therapy was associated with significant improvements in systemic and pulmonary hemodynamics, enhanced functional capacity, and reductions in NT-proBNP levels'. These benefits occurred without major safety concerns and in the context of stable pulmonary function. While the mechanisms require further elucidation, our findings support the inclusion of SGLT2 inhibitors as part of a comprehensive, multidisciplinary approach to managing this complex patient population. Larger, controlled trials with invasive hemodynamic monitoring are warranted to confirm these effects and explore long-term outcomes.

REFERENCES

1. Kirschbaum, K., et al., *SGLT2 inhibitor therapy and pulmonary artery pressure in patients with chronic heart failure—further evidence for improved hemodynamics by continuous pressure monitoring.* 2022. **111**(4): p. 469-472.
2. King, N.E. and E.J.P.C. Brittain, *Emerging therapies: The potential roles SGLT2 inhibitors, GLP1 agonists, and ARNI therapy for ARNI pulmonary hypertension.* 2022. **12**(1): p. e12028.
3. Patoulias, D., et al., *Meta-Analysis Assessing the Cardiovascular Efficacy of Sodium-Glucose Co-Transporter-2 Inhibitors in Patients With Chronic Obstructive Pulmonary Disease.* 2022. **174**: p. 188-189.
4. Cuthbert, J.J., P. Pellicori, and A.L.J.I.J.o.G.M. Clark, *Optimal management of heart failure and chronic obstructive pulmonary disease: Clinical challenges.* 2022. **15**: p. 7961.
5. Cazzola, M., et al., *Cardiovascular diseases or type 2 diabetes mellitus and chronic airway diseases: mutual pharmacological interferences.* 2023. **14**: p. 20406223231171556.
6. Monda, V.M., et al., *Heart failure with preserved ejection fraction and obstructive sleep apnea: a novel paradigm for additional cardiovascular benefit of SGLT2 inhibitors in subjects with or without type 2 diabetes.* 2022. **39**(11): p. 4837-4846.
7. Butt, J.H., et al., *Heart failure, chronic obstructive pulmonary disease and efficacy and safety of dapagliflozin in heart failure with mildly reduced or preserved ejection fraction: Insights from DELIVER.* 2023. **25**(11): p. 2078-2090.
8. Packer, M., C.S. Wilcox, and J.M.J.C. Testani, *Critical analysis of the effects of SGLT2 inhibitors on renal tubular sodium, water and chloride homeostasis and their role in influencing heart failure outcomes.* 2023. **148**(4): p. 354-372.
9. Polecka, A., et al., *Association between obstructive sleep apnea and heart failure in adults—a systematic review.* 2023. **12**(19): p. 6139.
10. Stöllberger, C., J. Finsterer, and B.J.E.R.o.C.T. Schneider, *Adverse events and drug–drug interactions of sodium glucose co-transporter 2 inhibitors in patients treated for heart failure.* 2023. **21**(11): p. 803-816.
11. Anker, S.D., et al., *Empagliflozin in patients with type 2 diabetes mellitus and chronic obstructive pulmonary disease.* 2022. **186**: p. 109837.
12. Cazzola, M., et al., *Hyperglycaemia and chronic obstructive pulmonary disease.* 2023. **13**(21): p. 3362.
13. Omar, M., et al., *Effect of empagliflozin on hemodynamics in patients with heart failure and reduced ejection fraction.* 2020. **76**(23): p. 2740-2751.
14. Perrotta, G.J.J.C.M., *Heart Failure (HF): recent innovations in clinical therapy and critical profiles of acute and chronic forms.* 2022. **9**: p. 49-76.

15. Anker, S.D., et al., *Patient phenotype profiling in heart failure with preserved ejection fraction to guide therapeutic decision making. A scientific statement of the Heart Failure Association, the European Heart Rhythm Association of the European Society of Cardiology, and the European Society of Hypertension.* 2023. **25**(7): p. 936-955.
16. Li, Z., H. Zhao, and J.J.F.i.C.M. Wang, *Metabolism and chronic inflammation: the links between chronic heart failure and comorbidities.* 2021. **8**: p. 650278.
17. Jasinska-Piadlo, A. and P.J.H. Campbell, *Management of patients with heart failure and preserved ejection fraction.* 2023. **109**(11): p. 874-883.
18. Palazzuoli, A., G. Ruocco, and E.J.H.F.R. Gronda, *Noncardiac comorbidity clustering in heart failure: an overlooked aspect with potential therapeutic door.* 2022. **27**(3): p. 767-778.
19. Wang, X., et al., *SGLT2 inhibitors break the vicious circle between heart failure and insulin resistance: targeting energy metabolism.* 2022. **27**(3): p. 961-980.
20. Gulea, C., et al., *Impact of COPD and asthma on in-hospital mortality and management of patients with heart failure in England and Wales: an observational analysis.* 2022. **12**(6): p. e059122.