

Review

Update on the Value of Lung Ultrasound Examination in Acute Decompensated Heart Failure Patients with Various Left Ventricular Ejection Fraction

Hui Zhang^{1,2,†}, Yunlong Zhu^{1,†}, Na Li^{1,2}, Jianping Zeng^{1,2,*} ¹Department of Cardiology, Xiangtan Central Hospital, 411100 Xiangtan, Hunan, China²Graduate Collaborative Training Base of Xiangtan Central Hospital, Hengyang Medical School, University of South China, 421001 Hengyang, Hunan, China*Correspondence: xhjiang2@hnust.edu.cn (Jianping Zeng)

†These authors contributed equally.

Academic Editors: Julio Núñez Villota, Rafael de la Espriella and Alfonso Valle Muñoz

Submitted: 30 June 2022 Revised: 5 August 2022 Accepted: 12 August 2022 Published: 18 October 2022

Abstract

Acute decompensated heart failure (ADHF) is one of the most common causes of hospital admission for cardiovascular diseases. ADHF often affects the elderly population, is associated with high morbidity, admission rate and mortality. Pulmonary congestion (PC) is the most common cause of hospitalization among ADHF patients. Previous studies have shown that lung ultrasound (LUS) serves as a valuable tool for the evaluation of PC in patients with heart failure in terms of diagnosis, guiding of the treatment, and post-discharge monitoring. The use of LUS for ADHF is well described and already widely used in the daily clinical practice. PC might differ in ADHF patients with different left ventricular ejection fraction value and treatment options should be steadily adjusted according to the LUS-derived PC results to improve the outcome. This review summarized the value of LUS examination in patients with ADHF with preserved, mildly reduced, and reduced left ventricular ejection fraction, aiming to expand the rational use of LUS, promote the LUS-guided management and improve the outcome among patients with ADHF.

Keywords: pulmonary congestion; lung ultrasound; ADHF; HFrEF; HFmrEF; HFpEF

1. Introduction

Heart failure (HF) is a global public health problem affecting 26 million people worldwide [1]. Acute decompensated heart failure (ADHF) refers to the acute attack of symptoms and signs of HF [2]. The common causes of ADHF include drug and dietary disorders, arrhythmia, deterioration of renal function, poor control of hypertension, myocardial infarction, and infection [3]. Risk of readmission within 6 months was as high as 50% for ADHF patients hospitalized due to worsening HF [4], and repeated hospitalization will seriously affect the quality of life of ADHF patients. The prognosis of ADHF patients is also poor. After discharge, the 1-year mortality rate is around 40–45% [5,6], and the 5-year mortality rate is about 70–80% [7,8] among ADHF patients.

In the 2016 European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of acute and chronic heart failure, HF patients were classified according to left ventricular ejection fraction (LVEF) [9]. Patients were defined as heart failure with reduced ejection fraction (HFrEF) (LVEF <40%), heart failure with mid-range ejection fraction (HFmrEF) (LVEF 40%–49%), and heart failure with preserved ejection fraction (HFpEF) (LVEF ≥50%) [9]. In the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure, HFmrEF was renamed as heart failure with mildly reduced ejection

fraction (LVEF 41%–49%) [10]. A study on the prognosis of de novo acute heart failure (AHF) and ADHF showed that HFrEF accounted for 60.8%, HFmrEF for 15.1%, and HFpEF for 24.1% respectively of ADHF patients [11]. Onteddu *et al.* [12] reported that HFrEF accounted for 77%, HFmrEF for 11%, and HFpEF for 12%, respectively of ADHF patients. Jayagopal *et al.* [13] showed that HFrEF accounted for 72.4% and HFmrEF and HFpEF accounted for the rest 27.6% of ADHF patients. HFrEF is thus the largest patient group of ADHF. Since HFpEF patients accounted for the main population in the overall HF patients [14], patients with HFrEF are thus more prone to cardiac decompensation than patients with HFmrEF and HFpEF.

HF is the final stage of various heart diseases. Pulmonary congestion (PC) is a common sign of HF and directly related to the major HF symptom (dyspnea) and signs of HF (pulmonary rales, peripheral edema, and vascular congestion) [10]. In case of ADHF, pulmonary edema and the rapid accumulation of fluid within the interstitial and alveolar spaces could lead to more significant dyspnea and respiratory decompensation. The causes of pulmonary edema are multiple, cardiogenic pulmonary edema is usually a result of acutely elevated cardiac filling pressures [15]. Cardiogenic pulmonary edema refers to hemodynamic PC with increased capillary pressures. This could result in increased fluid transfer out of capillaries into the in-



terstitium and alveolar spaces. High capillary pressures can further cause barrier disruption, which increases the permeability and fluid transfer into the interstitium and alveoli. Fluid in alveoli could alter surfactant function and increases surface tension. This vicious circle can lead to more edema formation and to atelectasis with impaired gas exchange [16]. PC is thus the most common feature in patients with ADHF.

2. The Use of Lung Ultrasound for Acute HF in Emergency Department

The use of LUS for ADHF is well described [17,18] and already widely used in the daily clinical practice, especially in emergency department (ED). The emergency department is very important for the diagnosis and treatment of patients with acute dyspnea, and the important etiology of dyspnea is ADHF [19]. The use of LUS images is helpful for the diagnosis of patients with acute respiratory failure, circulatory shock, or cardiac arrest. LUS scores can be used to quantify lung ventilation and thus regulate the parameters of ventilators in mechanically ventilated patients, LUS can also be used for early detection and management of respiratory complications under mechanical ventilation, such as pneumothorax, ventilator-associated pneumonia, atelectasis, and pleural effusions [20]. In the ED, there are two regimens for the use of LUS. One is the bedside lung ultrasound in emergency (BLUE)-protocol, which is primarily used to rapidly diagnose the cause of acute respiratory failure. The other one is the fluid administration limited by lung sonography (FALLS)-protocol, which is used to guide the management of acute circulatory failure [21]. The BLUE protocol is used in the diagnosis of patients with ADHF, which required scanning 12-point of the chest, and 8-point or 6-point is sufficient to quickly diagnose AHF [22,23]. In critically ill patients, 4-point or 2-point can be used to identify lung conditions. Sforza *A et al.* [24] found that bilateral chest LUS was more sensitive and accurate to the diagnosis of AHF than double anterior chest LUS, and with the exacerbation of hypoxemia, the accuracy of anterior chest LUS in the diagnosis of AHF gradually increased and approached that of lateral chest LUS. In the first 6 hours of ED management, there was no significant difference in the degree of PC response caused by LUS-guided treatment compared with usual care in patients with ADHF, but LUS-guided treatment improved PC more quickly within 48 hours [25]. Therefore, repeating LUS examination at 6 hours after admission is meaningful, which could be helpful for the medication adjustment, and for the improvement of the PC status within 48 hours after admission for ADHF patients.

In ED, LUS can quickly guide the diagnosis and treatment of acute respiratory distress syndrome (ARDS), COVID-19 pneumonia, interstitial lung disease, and other diseases [26–28]. For patients with HF, as long as the patient has signs of PC, whether it is AHF or CHF, HF_rEF,

HF_{mr}EF, or HF_pEF, LUS is an important tool for diagnosis and treatment. Unlike echocardiography, LUS does not require professional operation skills, as long as it avoids the ribs, it can be examined in the whole chest. All ultrasound equipment suitable for the abdomen and superficial organs can meet the requirements of lung ultrasound. Convex array, phased array, and linear array probes can be used for a LUS examination. High frequency linear array probe (7.5~10 MHz) is mainly used for the examination of the chest wall, pleura and sub-pleural lesions. Low frequency convex array probe (2~5 MHz) is suitable for the examination of deep lung tissue lesions and obese people. All these provide convenience for the clinical application of LUS.

3. Clinical Value of Lung Ultrasound Examination in the Diagnosis, Treatment and Monitoring of Acute Decompensated Heart Failure Patients

Lung ultrasound (LUS) examination could sufficiently evaluate PC through detecting the presence and number of B-lines, which indicate pulmonary edema or loss of lung aeration [29]. The advantage of B-line assessment is that it could provide direct information on pulmonary interstitial lesions and can distinguish between hemodynamic congestion and pulmonary interstitial edema. The signs of PC on LUS are often shown as B-line evenly distributed on both sides with smooth pleural line, the regularly spaced B-line shows septal or interstitial edema, while the crowded or combined B-line shows alveolar edema. ADHF patients can sometimes present in the form of many diffused B-lines with strong echo in the whole lung field, at this time, it is called “white lung”. LUS can easily detect pulmonary edema in patients with acute decompensation and in patients at risk for decompensation. LUS could also help characterize patients with cardiogenic pulmonary edema and help identify subgroups who need specific management [30–32]. As a useful tool for evaluating PC, LUS could significantly contribute to the diagnosis of ADHF (Table 1, Ref. [33–35]) and has become standard care in many emergency departments and intensive care settings [36].

LUS is helpful for the early and rapid diagnosis of ADHF and can improve the treatment efficacy for these patients [37]. The most important scheme to reduce PC in clinical practice is the proper use of diuretics. A prospective clinical trial has shown that early intravenous diuretics could reduce in-hospital mortality, while in-hospital mortality increased by 2.1% for each 4-hour delay in the use of intravenous diuretics [38]. BLUSHED-AHF is a multi-center, single-blind prospective clinical study, 130 patients with AHF admitted in the emergency department were enrolled and divided into LUS guided nursing group and routine nursing group at 1:1 ratio within the first 6 hours of treatment [25]. Within 48 hours, the remission of PC was faster in the LUS guided nursing group than that in the routine nursing group [25]. Studies have shown that the risk

Table 1. Study on the diagnostic value of LUS in ADHF patients.

Study	N	Conclusions
Pivetta <i>et al.</i> (2015) [33]	1005	LUS combined with clinical examination can improve the diagnosis of ADHF.
Pivetta <i>et al.</i> (2019) [34]	518	Integration of LUS with clinical assessment for the diagnosis of ADHF in the emergency department seems to be more accurate than the current diagnostic approach based on CXR and NT-proBNP.
Hacıoğulları <i>et al.</i> (2021) [35]	80	In the ED setting, an assessment of B-lines and measurement of IVC diameters are better markers than the B-type natriuretic peptide level, EF, or chest x-ray for diagnosis of ADHF and can be used to make decisions for hospitalization or discharge from the ED.

Abbreviations: LUS, lung ultrasound; ADHF, acute decompensated heart failure; CXR, chest radiography; NT-proBNP, N-terminal pro-B-type natriuretic peptide; ED, emergency department; IVC, inferior vena cava; EF, ejection fraction.

of adverse events and long-term adverse prognosis in patients with HF increases in proportion with the increased number of B-lines [39]. LUS is thus a sensitive tool for risk stratification of ADHF [39]. It can be added to the remote monitoring item of patients with HF and serves as an important tool of telemedicine. Another study clearly showed that timely management of patients at risk of decompensation based on LUS results can reduce the risk of HF deterioration and prevent readmission [40]. Since PC and outcome might differ among ADHF with various LVEF, it is of importance to define PC status in ADHF patients with various LVEF to develop LVEF- and PC-oriented monitoring and therapy strategies for these patients.

4. Pulmonary Congestion in Acute Decompensated Heart Failure Patients with Reduced Ejection Fraction

HFrEF refers to HF patients with LVEF $\leq 40\%$. HFrEF is often initially characterized by decreased cardiac output, which further leads to a series of adverse reactions [41]. Hemodynamic features of left ventricular dysfunction in ADHF with HFrEF include: the temporary effect of deteriorated left ventricle systolic function; subsequent compensation by activating the sympathetic nervous system and renin-angiotensin-aldosterone system (RAAS) [42]. When the heart is severely damaged and decompensated, RAAS activation could not maintain cardiac output to meet the oxygenation needs of vital organs and peripheral circulation. PC, dyspnea and fluid retention form the usual clinical symptoms and signs of HFrEF patients [43]. The reduced cardiac output could lead to progressive retention of blood volume fluid. Progressive increase of systemic filling pressure and right atrial pressure, increased LV end diastolic pressure (LVEDP), which could collectively contribute to the formation of PC. Thus, detecting and monitoring PC plays a central role in the management of ADHF patients with reduced EF.

Miglioranza *et al.* [44] evaluated the association between PC and decompensation HF patients with LVEF $< 45\%$, they found that in the outpatient department of HF, the degree of PC, assessed by LUS, was significantly corre-

lated with decompensation. B-lines ≥ 15 can be considered as a quick and reliable biomarker of decompensation in outpatients with heart failure and reduced LVEF. A study evaluated the association between PC incidence and short-term and long-term prognosis in patients with AHF and reduced LVEF, results showed that there was no significant difference in PC among AHF patients with chronic obstructive pulmonary disease (COPD) and other comorbidities and different EF, while there was a stronger association between the degree of PC and early events after discharge ($p = 0.022$) [44]. Scali *et al.* [45] evaluated the effect of exercise-induced PC on prognosis in patients with HFrEF and found that twelve-month event-free survival was 95% in the 36 patients with stress B-lines < 30 (best cut-off identified by receiver operating characteristic curve analysis) versus 7% in patients with ≥ 30 B-lines ($p < 0.0001$). Bajraktari *et al.* [46] verified that LUS and B-type natriuretic peptide (BNP) guided follow-up care can improve the survival rate of patients with HFrEF.

5. Pulmonary Congestion in Acute Decompensated Heart Failure Patients with Mildly Reduced Ejection Fraction

HFmrEF is defined as a clinical syndrome with an EF of 41%–49%, typical HF symptoms and signs in patients with structural heart disease. In all patients with heart failure, the prevalence rate of HFmrEF is around 10%–20% [47]. Compared with the population of HFrEF and HFpEF, patients with HFmrEF showed general clinical characteristics between HFpEF and HFrEF [47]. Patients with HFmrEF can be further divided into three subgroups: HFmrEF improved (previous LVEF $< 40\%$), HFmrEF deteriorated (previous LVEF $> 50\%$), HFmrEF remained unchanged (previous LVEF was 41%–49%).

Although the concept of HFmrEF has been proposed for several years, and the research on HFmrEF is far less than HFrEF and HFpEF. At present, there are relatively few studies focusing on PC in patients with HFmrEF. The results of previous clinical studies on PC status in HFmrEF patients are sometimes difficult to interpret, since the enrolled “HFmrEF” patients in previous studies are in fact

“HFpEF” or “HFrEF” patients per current definition. Skrodumova *et al.* [48] explored PC status in ADHF patients with HFmrEF through LUS. They found that after the remission of ADHF, pulmonary interstitial congestion was still dominant (the distance between B-lines was 7 mm), there was a small amount of pulmonary edema (the distance between B-lines was 3 mm), and the number of B-lines was related to the simultaneous detection of N-terminal pro-B-type natriuretic peptide (NT-proBNP) level and readmission. Obviously, more clinical studies are needed to explore the PC situation and change post various HF treatments in ADHF patients with HFmrEF.

6. Pulmonary Congestion in Acute Decompensated Heart Failure Patients with Preserved Ejection Fraction

HFpEF is defined as: (1) patients with symptoms and signs of heart failure; (2) LVEF $\geq 50\%$; and (3) objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides [10]. The pathophysiology of HFpEF is heterogeneous, including diastolic dysfunction, inflammation and oxidative stress/endothelial dysfunction, chronotropic dysfunction and cardiac reserve dysfunction, pulmonary hypertension and abnormal ventricular arterial coupling [49]. In HFpEF patients, parameters describing left ventricular filling may be normal or only slightly impaired. Exercise is helpful to reveal diastolic abnormalities that cannot be seen under resting conditions [50].

The main feature of HFpEF patients is the increased cardiac filling pressure at rest and further increased during exercise, the symptoms of ADHF patients with HFpEF are thus mainly related to PC. Reddy *et al.* [51] found that interstitial lung water was increased in ADHF patients with HFpEF, even during low-intensity exercise. The acute development of PC in HFpEF patients was associated with increased pulmonary capillary hydrostatic pressure and systemic venous hypertension associated with impaired RV-PA coupling. Simonovic *et al.* [52] evaluated the risk factors of PC in patients with HFpEF during exercise. They found that the formation of B-lines in patients with HFpEF during exercise was related to the deterioration of diastolic function, that is, PC was related to further aggravated diastolic dysfunction in patients with HFpEF. Rueda-Camino *et al.* [53] used bedside lung ultrasound to evaluate the PC status of HFpEF patients before discharge, the study found that patients with B-lines >15 at discharge faced 2.5 times higher risk of rehospitalization for acute heart failure than patients with B-lines <15 .

7. Effects of Pulmonary Congestion-Guided Treatment in Acute Decompensated Heart Failure Patients with Different Ejection Fraction

As a whole, there are relatively few studies on PC status among ADHF patients with HFpEF, HFmrEF, and HFrEF. Most clinical trials are either in non-ADHF patients or ADHF patients without ejection fraction stratification. It is still controversial whether there are differences in PC status in ADHF patients with different LVEF (Table 2, Ref. [54–61]). Yang *et al.* [55] showed that B-lines measured by lung ultrasound were positively correlated with early transmitral velocity to tissue Doppler mitral annular early diastolic velocity ratio (E/e') and NT-proBNP, but negatively correlated with LVEF in both the HFpEF and HFrEF patients. The correlation of B-lines with E/e' and NT-proBNP was superior to LVEF, especially in the HFpEF group. It has also been shown that E/e' is useful for estimating pulmonary capillary wedge pressure in ADHF patients with HFpEF, but not with HFrEF [62]. Van Aelst *et al.* [63] evaluated the congestion markers [brain natriuretic peptide (BNP), mid-regional pro-atrial natriuretic peptide (MR-proANP), soluble CD146 (sCD146), and inferior vena cava (IVC)] in ADHF patients with HFpEF and HFrEF and demonstrated similar hemodynamic congestion in these patients. In contrast, other studies evidenced worse pulmonary congestion in ADHF patients with HFrEF as compared to ADHF patients with HFpEF. A multicenter prospective study included 314 patients with ADHF. The results showed that HFrEF patients had more severe PC and intravascular congestion than HFpEF patients at admission. In terms of response to diuretic treatment, the two HF phenotypes also showed some differences [61]. ADHF patients with HFrEF experienced greater remission of intravascular congestion after diuretics, while ADHF patients with HFpEF showed greater remission of PC [61]. Similarly, other studies demonstrated that the degree of PC was higher in HFrEF patients than that in HFpEF patients [56,57], which may be the reason why HFrEF patients are more prone to decompensation.

There is scanty literature on PC status among ADHF patients with different LVEF, there are even fewer studies reporting the impact of various interventions on PC outcomes in ADHF patients with HFpEF, HFmrEF and HFrEF. EPICC Study is a randomized, multicenter, single-blind clinical trial [64]. The protocol aims to prove that LUS-guided therapy improves the 6-month prognosis of HF patients. It will reveal whether HFrEF and HFpEF would have the same response to LUS-guided therapy [64]. More researchers are needed to demonstrate the distribution of lung water and mechanism of PC in ADHF patients with HFpEF, HFmrEF, and HFrEF in order to test the effects of targeted therapy on PC remission in these patients.

Table 2. Pulmonary B-line correlation studies with different ejection fraction.

Study	Cohort	Zone	Position	N	Follow-up	Conclusions
Coiro <i>et al.</i> (2017) [54]	Hospitalized patients with AHF	28	Supine position	HFrEF (N = 59) (EF ≤40%) HFpEF (N = 51) (EF >40%)	-	LUS can identify patients with high BNP, but cannot identify patients with elevated E/e', and also shows a prognostic role independent of atrial fibrillation status, EF or quantification time; The optimal B-line threshold seems to vary according to the quantitative time during hospitalization.
Yang <i>et al.</i> (2017) [55]	Hospitalized patients with ADHF	8	Supine position	HFrEF (N = 32) (EF <50%) HFpEF (N = 50) (EF ≥50%)	6 months	There was no difference in B-lines between HFrEF and HFpEF; It has a good correlation between B-lines and E/e', especially in the HFpEF group.
Palazzuoli <i>et al.</i> (2018) [56]	Hospitalized patients with AHF	8	Semirecumbent position	HFrEF (N = 95) (EF <50%) HFpEF (N = 67) (EF ≥50%)	6 months	Compared with HFpEF patients, HFrEF patients had more B-lines and congestion at admission and discharge.
Mozzini <i>et al.</i> (2018) [57]	Hospitalized patients with AHF	-	Supine position	HFrEF (N = 35) (EF <40%) HFmrEF (N = 35) (EF 40–49%) HFpEF (N = 50) (EF ≥50%)	-	LUS can accelerate the discharge time of HF patients, and the B-lines clearance time of HFrEF patients is longer than that of HFpEF and HFmrEF patients.
Dwyer <i>et al.</i> (2018) [58]	Outpatients with HF	8	Supine position	HFrEF (N = 73) (EF <50%) HFpEF (N = 46) (EF ≥50%)	12 months	Patients with HFpEF and HFrEF had similar congestion spectrum.
Ceriani <i>et al.</i> (2020) [59]	Hospitalized patients with ADHF	28	Semirecumbent position	HFrEF (N = 74) (EF <50%) HFpEF (N = 75) (EF ≥50%)	4 years	The ultrasound score before discharge in HFpEF group was significantly lower than that in HFrEF group. The assessment of PC by LUS at discharge is related to the long-term mortality of hospitalized patients with heart failure.
Gargani <i>et al.</i> (2021) [60]	Hospitalized cardiac conditions patients with AHF and non-AHF	28	Supine position	HFrEF (N = 199) (EF <50%) HFpEF (N = 97) (EF ≥50%)	14.4 months	B-lines >30 indicates that the prognosis of patients with HFrEF and HFpEF is poor. And B-line has more significant prognostic value for patients with HFpEF.
Cogliati <i>et al.</i> (2021) [61]	Hospitalized patients with ADHF	11	Semirecumbent position	HFrEF (N = 142) (EF ≤45%) HFpEF (N = 172) (EF >45%)	90 days	At admission, the degree of PC in HFrEF was stronger than that in HFpEF. And the rate of congestion relief in HFrEF patients was faster than that in HFpEF.

Abbreviations: N, patients enrolled; ADHF, acute decompensated heart failure; HF, heart failure; AHF, acute heart failure; LUS, lung ultrasound; PC, pulmonary congestion; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; E/e', the ratio of early transmitral velocity to tissue Doppler mitral annular early diastolic velocity; BNP, pro-B-type natriuretic peptide.

The treatment of ADHF mainly focuses on the remission of congestion. Persistent PC is a sign of poor prognosis in patients with ADHF [59]. The reduction in pulmonary venous congestion following the use of diuretics leads to a rapid improvement in dyspnea [65]. Although diuretics are important to alleviate congestion and symptoms in decompensated patients, randomized controlled trials have not demonstrated a prognostic benefit of these drugs up to now [66]. Angiotensin converting enzyme inhibitors (ACEI) can reduce cardiac filling pressure, mean arterial pressure, systemic vascular resistance and increase cardiac output in patients with congestive HF [66]. A clinical trial suggested that the benefits of high-dose mineralocorticoid receptor antagonists (MRA) therapy in acutely decompensated chronic heart failure (ADCHF) included lower natriuretic peptide levels, less congestion, better renal function, and less need for an intravenous diuretic [67]. Therefore, ACEI and MRA should also be considered as drugs to relieve PC regardless of EF (Fig. 1).

In patients with ADHF, the outcome of HF_rEF was the worst in comparison with HF_pEF and HF_mrEF [11]. Kawase Y *et al.* [68] demonstrated that carperitide was associated with effective decongestion in the short term and satisfactory prognosis in the long term in AHF patients with moderate–severe PC, but carperitide was not associated with better clinical outcome in patients with no–mild pulmonary congestion. Selvaraj S *et al.* [69] proved that sacubitril/valsartan improved congestion more than enalapril. Reducing congestion in the outpatient setting is independently associated with improved quality of life and reduced cardiovascular events, including mortality. Sodium-glucose cotransporter-2 inhibitors (SGLT-2i) can help HF_rEF patients by normalizing salt-water homeostasis to prevent clinical edema/congestion, so as to reduce hospitalization due to HF, improve functional status, quality, and duration of life in patients with HF_rEF [70].

The characteristics of HF_mrEF patients are between HF_rEF and HF_pEF. At present, there is no medication intervention study on the remission of PC among HF_mrEF patients. In clinical practice, the treatment of HF_mrEF patients is similar to that of HF_rEF patients [71]. Drugs that alleviate PC in patients with HF_rEF might also be effective for HF_mrEF. However, this hypothesis should be validated with future clinical studies focusing on the effects of relevant therapy on PC status for HF_mrEF patients in the setting of ADHF.

As for ADHF patients with HF_pEF, literature on therapy and PC status is also limited. Park *et al.* [72] found that among patients with HF_pEF (LVEF $\geq 50\%$), the mortality of patients with relatively lower LVEF was almost twice that of patients with stable LVEF. In HF_pEF patients, the presence of orthopnea and PC predicted a higher risk of adverse cardiovascular events [73]. SGLT-2i have emerged as osmotic diuretics that may have utility in the treatment of HF_pEF, by reducing renal glucose reabsorption and in-

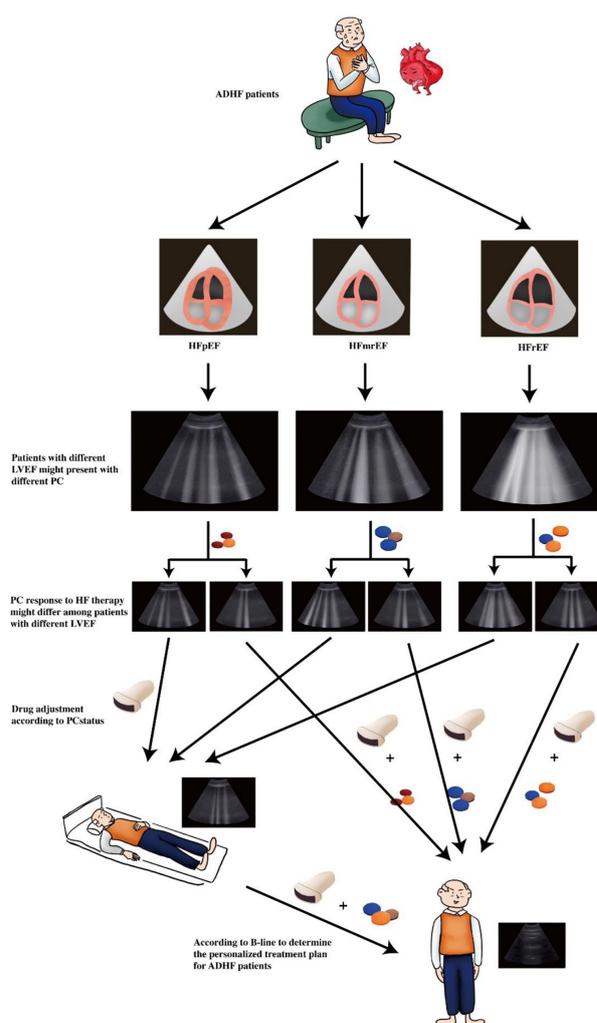


Fig. 1. Clinical value of lung ultrasound examination in ADHF patients with different left ventricular ejection fraction (LVEF). ADHF patients with different LVEF might have different pulmonary congestion (PC) status and response to therapy might also be different, repeated pulmonary congestion evaluation by lung ultrasound might be helpful for guiding drug adjustment aiming to attenuate pulmonary congestion in ADHF patients with different LVEF.

creasing urinary glucose excretion, SGLT-2i can thus relieve PC through natriuresis and diuresis [74,75]. Málek F *et al.* [76] demonstrated that selective blockade of sympathetic signaling to the splanchnic circulation by surgical ablation of the right greater splanchnic nerve (GSN) can reduce pulmonary capillary wedge pressure (PCWP) in HF_pEF patients to improve quality of life and exercise capacity. Again, there is still no study describing the effects of relevant therapy on PC for HF_pEF patients in the setting of ADHF.

8. Conclusions

LUS is a valuable tool to detect PC in ADHF patients and should be readily used in ADHF patients during hospitalization, before discharge and post discharge in the form of follow up or telemedicine. PC might increase in proportion to decreasing LVEF in ADHF patients. Timely detection and management of PC and regular PC monitoring by LUS post discharge might improve the outcome of ADHF patients. Importantly, response to diuretic and other heart failure medications might differ among ADHF patients with different LVEF. Obviously, more efforts are needed to monitor the responses and efficacy of applied treatment in ADHF patients with HFpEF, HFmrEF and HFrEF to find the best therapy options in terms of preventing the hospital readmission and improving the quality of life and outcome among ADHF patients with various LVEF.

Author Contributions

JPZ guides the writing idea and structural framework of this manuscript. HZ and YLZ are responsible for writing this manuscript and collecting relevant references. HZ, YLZ and NL were responsible for the production of image and tables in this paper. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

Funding

This manuscript supported by Natural Science Foundation of Hunan Province (2022JJ70042), Hunan Province, China, Scientific Bureau of Xiangtan City (SF-YB20201023), Xiangtan City, Hunan Province, China, and Committee of Development Reform of Hunan Province (2019-875), Changsha, Hunan Province, China.

Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M, *et al.* The Global Health and Economic Burden of Hospitalizations for Heart Failure: lessons learned from hospitalized heart failure registries. *Journal of the American College of Cardiology.* 2014; 63: 1123–1133.
- [2] Sinnenberg L, Givertz MM. Acute heart failure. *Trends in Cardiovascular Medicine.* 2020; 30: 104–112.
- [3] Hammond DA, Smith MN, Lee KC, Honein D, Quidley AM. Acute Decompensated Heart Failure. *Journal of Intensive Care Medicine.* 2018; 33: 456–466.
- [4] Desai AS, Stevenson LW. Rehospitalization for Heart Failure: predict or prevent? *Circulation.* 2012; 126: 501–506.
- [5] Crespo-Leiro MG, Anker SD, Maggioni AP, Coats AJ, Filipatos G, Ruschitzka F, *et al.* European Society of Cardiology Heart Failure Long-Term Registry (ESC-HF-LT): 1-year follow-up outcomes and differences across regions. *European Journal of Heart Failure.* 2016; 18: 613–625.
- [6] Blecker S, Paul M, Taksler G, Ogedegbe G, Katz S. Heart Failure-Associated Hospitalizations in the United States. *Journal of the American College of Cardiology.* 2013; 61: 1259–1267.
- [7] Lassus JPE, Siirilä-Waris K, Nieminen MS, Tolonen J, Tarvasmäki T, Peuhkurinen K, *et al.* Long-term survival after hospitalization for acute heart failure—Differences in prognosis of acutely decompensated chronic and new-onset acute heart failure. *International Journal of Cardiology.* 2013; 168: 458–462.
- [8] Goldberg RJ, Ciampa J, Lessard D, Meyer TE, Spencer FA. Long-term Survival after Heart Failure: a contemporary population-based perspective. *Archives of Internal Medicine.* 2007; 167: 490–496.
- [9] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, *et al.* 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *European Heart Journal.* 2016; 18: 891–975.
- [10] McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, *et al.* 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *European Heart Journal.* 2021; 42: 3599–3726.
- [11] Choi KH, Lee GY, Choi J, Jeon E, Lee H, Cho H, *et al.* Outcomes of de novo and acute decompensated heart failure patients according to ejection fraction. *Heart.* 2018; 104: 525–532.
- [12] Onteddu SH, Wangchuk G, Sharma AJ, Mohan JC. Acute decompensated heart failure in a North Indian community hospital: Demographics, clinical characteristics, comorbidities and adherence to therapy. *Indian Heart Journal.* 2020; 72: 27–31.
- [13] Jayagopal PB, Abdullakutty J, Sridhar L, Nanjappa V, Joseph J, Vaidyanathan PR, *et al.* Acute decompensated heart failure (ADHF) during COVID-19 pandemic—insights from South India. *Indian Heart Journal.* 2021; 73: 464–469.
- [14] Kitzman DW, Gardin JM, Gottdiener JS, Arnold A, Boineau R, Aurigemma G, *et al.* Importance of heart failure with preserved systolic function in patients > or = 65 years of age. CHS Research Group. *Cardiovascular Health Study. The American Journal of Cardiology.* 2001; 87: 413–419.
- [15] King KC, Goldstein S. Congestive Heart Failure and Pulmonary Edema. In *StatPearls.* StatPearls Publishing: Treasure Island (FL). 2022.
- [16] Dobbe L, Rahman R, Elmassry M, Paz P, Nugent K. Cardiogenic Pulmonary Edema. *The American Journal of the Medical Sciences.* 2019; 358: 389–397.
- [17] Marini C, Fragasso G, Italia L, Sisakian H, Tufaro V, Ingalina G, *et al.* Lung ultrasound-guided therapy reduces acute decompensation events in chronic heart failure. *Heart.* 2020; 106: 1934–1939.
- [18] Leidi F, Casella F, Cogliati C. Bedside lung ultrasound in the evaluation of acute decompensated heart failure. *Internal and Emergency Medicine.* 2016; 11: 597–601.
- [19] Gheorghide M, Pang PS. Acute Heart Failure Syndromes. *Journal of the American College of Cardiology.* 2009; 53: 557–573.
- [20] Mojoli F, Bouhemad B, Mongodi S, Lichtenstein D. Lung Ultrasound for Critically Ill Patients. *American Journal of Respiratory and Critical Care Medicine.* 2019; 199: 701–714.
- [21] Lichtenstein DA. BLUE-Protocol and FALLS-Protocol: two applications of lung ultrasound in the critically ill. *Chest.* 2015; 147: 1659–1670.

- [22] Leidi A, Soret G, Mann T, Koegler F, Coen M, Leszek A, *et al.* Eight versus 28-point lung ultrasonography in moderate acute heart failure: a prospective comparative study. *Internal and Emergency Medicine.* 2022; 17: 1375–1383.
- [23] Buessler A, Chouihed T, Duarte K, Bassand A, Huot-Marchand M, Gottwalles Y, *et al.* Accuracy of several Lung Ultrasound Methods for the Diagnosis of Acute Heart Failure in the ED: A Multicenter Prospective Study. *Chest.* 2020; 157: 99–110.
- [24] Sforza A, Carlino MV, Guarino M, Romano G, Paladino F, de Simone G, *et al.* Anterior vs lateral symmetric interstitial syndrome in the diagnosis of acute heart failure. *International Journal of Cardiology.* 2019; 280: 130–132.
- [25] Pang PS, Russell FM, Ehrman R, Ferre R, Gargani L, Levy PD, *et al.* Lung Ultrasound–Guided Emergency Department Management of Acute Heart Failure (BLUSHED-AHF): A Randomized Controlled Pilot Trial. *JACC: Heart Failure.* 2021; 9: 638–648.
- [26] Hussain A, Via G, Melniker L, Goffi A, Tavazzi G, Neri L, *et al.* Multi-organ point-of-care ultrasound for COVID-19 (PoCUS4COVID): international expert consensus. *Critical Care.* 2020; 24: 702.
- [27] Huang D, Ma H, Xiao Z, Blaivas M, Chen Y, Wen J, *et al.* Diagnostic value of cardiopulmonary ultrasound in elderly patients with acute respiratory distress syndrome. *BMC Pulmonary Medicine.* 2018; 18: 136.
- [28] Staub LJ, Mazzali Biscaro RR, Kaszubowski E, Maurici R. Lung Ultrasound for the Emergency Diagnosis of Pneumonia, Acute Heart Failure, and Exacerbations of Chronic Obstructive Pulmonary Disease/Asthma in Adults: a Systematic Review and Meta-analysis. *The Journal of Emergency Medicine.* 2019; 56: 53–69.
- [29] Russell FM, Ferre R, Ehrman RR, Noble V, Gargani L, Collins SP, *et al.* What are the minimum requirements to establish proficiency in lung ultrasound training for quantifying B-lines? *ESC Heart Failure.* 2020; 7: 2941–2947.
- [30] Pirrotta F, Mazza B, Gennari L, Palazzuoli A. Pulmonary Congestion Assessment in Heart Failure: Traditional and New Tools. *Diagnostics.* 2021; 11: 1306.
- [31] Platz E, Jhund PS, Girerd N, Pivetta E, McMurray JJV, Peacock WF, *et al.* Expert consensus document: Reporting checklist for quantification of pulmonary congestion by lung ultrasound in heart failure. *European Journal of Heart Failure.* 2019; 21: 844–851.
- [32] Li N, Zhu Y, Zeng J. Clinical value of pulmonary congestion detection by lung ultrasound in patients with chronic heart failure. *Clinical Cardiology.* 2021; 44: 1488–1496.
- [33] Pivetta E, Goffi A, Lupia E, Tizzani M, Porrino G, Ferreri E, *et al.* Lung Ultrasound-Implemented Diagnosis of Acute Decompensated Heart Failure in the ED: A SIMEU Multicenter Study. *Chest.* 2015; 148: 202–210.
- [34] Pivetta E, Goffi A, Nazerian P, Castagno D, Tozzetti C, Tizzani P, *et al.* Lung ultrasound integrated with clinical assessment for the diagnosis of acute decompensated heart failure in the emergency department: a randomized controlled trial. *European Journal of Heart Failure.* 2019; 21: 754–766.
- [35] Hacıoğluoğulları F, Yılmaz F, Yılmaz A, Sönmez BM, Demir TA, Karadaş MA, *et al.* Role of Point-of-Care Lung and Inferior Vena Cava Ultrasound in Clinical Decisions for Patients Presenting to the Emergency Department with Symptoms of Acute Decompensated Heart Failure. *Journal of Ultrasound in Medicine.* 2021; 40: 751–761.
- [36] Lee FCY. Lung ultrasound—a primary survey of the acutely dyspneic patient. *Journal of Intensive Care.* 2016; 4: 57.
- [37] Price S, Platz E, Cullen L, Tavazzi G, Christ M, Cowie MR, *et al.* Expert consensus document: Echocardiography and lung ultrasonography for the assessment and management of acute heart failure. *Nature Reviews Cardiology.* 2017; 14: 427–440.
- [38] Matsue Y, Damman K, Voors AA, Kagiya N, Yamaguchi T, Kuroda S, *et al.* Time-to-Furosemide Treatment and Mortality in Patients Hospitalized with Acute Heart Failure. *Journal of the American College of Cardiology.* 2017; 69: 3042–3051.
- [39] Platz E, Campbell RT, Claggett B, Lewis EF, Groarke JD, Docherty KF, *et al.* Lung Ultrasound in Acute Heart Failure: Prevalence of Pulmonary Congestion and Short- and Long-Term Outcomes. *JACC: Heart Failure.* 2019; 7: 849–858.
- [40] Mohebbi D, Kittleson MM. Remote monitoring in heart failure: current and emerging technologies in the context of the pandemic. *Heart.* 2021; 107: 366–372.
- [41] MacIver DH, Dayer MJ. An alternative approach to understanding the pathophysiological mechanisms of chronic heart failure. *International Journal of Cardiology.* 2012; 154: 102–110.
- [42] Fukata M. Acute Decompensated Heart Failure in Patients with Heart Failure with Reduced Ejection Fraction. *Heart Failure Clinics.* 2020; 16: 187–200.
- [43] Hartupée J, Mann DL. Neurohormonal activation in heart failure with reduced ejection fraction. *Nature Reviews Cardiology.* 2017; 14: 30–38.
- [44] Miglioranza MH, Gargani L, Sant’Anna RT, Rover MM, Martins VM, Mantovani A, *et al.* Lung Ultrasound for the Evaluation of Pulmonary Congestion in Outpatients: a comparison with clinical assessment, natriuretic peptides, and echocardiography. *JACC: Cardiovascular Imaging.* 2013; 6: 1141–1151.
- [45] Scali MC, Cortigiani L, Simionuc A, Gregori D, Marzilli M, Picano E. Exercise-induced B-lines identify worse functional and prognostic stage in heart failure patients with depressed left ventricular ejection fraction. *European Journal of Heart Failure.* 2017; 19: 1468–1478.
- [46] Bajraktari G, Pugliese NR, D’Agostino A, Rosa GM, Ibrahim P, Perçuku L, *et al.* Echo- and B-Type Natriuretic Peptide-Guided Follow-up versus Symptom-Guided Follow-up: Comparison of the Outcome in Ambulatory Heart Failure Patients. *Cardiology Research and Practice.* 2018; 2018: 3139861.
- [47] Rickenbacher P. Heart failure with “mid-range” ejection fraction: a new clinical entity? *Therapeutische Umschau.* 2018; 75: 170–173. (In German)
- [48] Skorodumova EG, Kostenko VA, Skorodumova EA, Siverina AV, Rysev AV, Gayvoronskiy IV, *et al.* Prognostic value of the ultrasonic determination of the degree of interstitial edema in patients with intermediate ejection fraction of the left ventricle after treating acute decompensation of heart failure. *Kardiologiya.* 2020; 60: 80–85. (In Russian)
- [49] Zhou Y, Zhu Y, Zeng J. Research Update on the Pathophysiological Mechanisms of Heart Failure with Preserved Ejection Fraction. *Current Molecular Medicine.* 2021. (in press)
- [50] Tadic M, Cuspidi C, Calicchio F, Grassi G, Mancia G. Diagnostic algorithm for HFpEF: how much is the recent consensus applicable in clinical practice? *Heart Failure Reviews.* 2021; 26: 1485–1493.
- [51] Reddy YNV, Obokata M, Wiley B, Koeppe KE, Jorgenson CC, Egbe A, *et al.* The haemodynamic basis of lung congestion during exercise in heart failure with preserved ejection fraction. *European Heart Journal.* 2019; 40: 3721–3730.
- [52] Simonovic D, Coiro S, Deljanin-Ilic M, Kobayashi M, Carluccio E, Girerd N, *et al.* Exercise-induced B-lines in heart failure with preserved ejection fraction occur along with diastolic function worsening. *ESC Heart Failure.* 2021; 8: 5068–5080.
- [53] Rueda-Camino JA, Saiz-Lou EM, del Peral-Rodríguez LJ, Satué-Bartolomé JÁ, Zapatero-Gaviria A, Canora-Lebrato J. Prognostic utility of bedside lung ultrasound before discharge in patients with acute heart failure with preserved ejection fraction. *Medicina Clínica.* 2021; 156: 214–220.
- [54] Coiro S, Porot G, Rossignol P, Ambrosio G, Carluccio E, Tritto

- I, *et al.* Corrigendum: Prognostic value of pulmonary congestion assessed by lung ultrasound imaging during heart failure hospitalisation: A two-centre cohort study. *Scientific Reports*. 2017; 7: 43972.
- [55] Yang F, Wang Q, Zhi G, Zhang L, Huang D, Shen D, *et al.* The application of lung ultrasound in acute decompensated heart failure in heart failure with preserved and reduced ejection fraction. *Echocardiography*. 2017; 34: 1462–1469.
- [56] Palazzuoli A, Ruocco G, Beltrami M, Nuti R, Cleland JG. Combined use of lung ultrasound, B-type natriuretic peptide, and echocardiography for outcome prediction in patients with acute HFrEF and HFpEF. *Clinical Research in Cardiology*. 2018; 107: 586–596.
- [57] Mozzini C, Di Dio Perna M, Pesce G, Garbin U, Fratta Pasini AM, Ticinesi A, *et al.* Lung ultrasound in internal medicine efficiently drives the management of patients with heart failure and speeds up the discharge time. *Internal and Emergency Medicine*. 2018; 13: 27–33.
- [58] Dwyer KH, Merz AA, Lewis EF, Claggett BL, Crousillat DR, Lau ES, *et al.* Pulmonary Congestion by Lung Ultrasound in Ambulatory Patients with Heart Failure with Reduced or Preserved Ejection Fraction and Hypertension. *Journal of Cardiac Failure*. 2018; 24: 219–226.
- [59] Ceriani E, Casazza G, Peta J, Torzillo D, Furlotti S, Cogliati C. Residual congestion and long-term prognosis in acutely decompensated heart failure patients. *Internal and Emergency Medicine*. 2020; 15: 719–724.
- [60] Gargani L, Pugliese NR, Frassi F, Frumento P, Poggianti E, Mazzola M, *et al.* Prognostic value of lung ultrasound in patients hospitalized for heart disease irrespective of symptoms and ejection fraction. *ESC Heart Failure*. 2021; 8: 2660–2669.
- [61] Cogliati C, Ceriani E, Gambassi G, De Matteis G, Perlini S, Perrone T, *et al.* Phenotyping congestion in patients with acutely decompensated heart failure with preserved and reduced ejection fraction: the Decongestion during therapY for acute decOmpensated heart failure in HFpEF vs HFrEF- DRY-off study. *European Journal of Internal Medicine*. 2022; 97: 69–77.
- [62] Matsushita K, Minamishima T, Goda A, Ishiguro H, Kosho H, Sakata K, *et al.* Comparison of the reliability of E/E' to estimate pulmonary capillary wedge pressure in heart failure patients with preserved ejection fraction versus those with reduced ejection fraction. *The International Journal of Cardiovascular Imaging*. 2015; 31: 1497–1502.
- [63] Van Aelst LNL, Arrigo M, Placido R, Akiyama E, Girerd N, Zannad F, *et al.* Acutely decompensated heart failure with preserved and reduced ejection fraction present with comparable haemodynamic congestion. *European Journal of Heart Failure*. 2018; 20: 738–747.
- [64] Bailón MM, Rodrigo JMC, Lorenzo-Villalba N, Cerqueiro JM, García JC, Manuel EC, *et al.* Effect of a Therapeutic Strategy Guided by Lung Ultrasound on 6-Month Outcomes in Patients with Heart Failure: Randomized, Multicenter Trial (EPICC Study). *Cardiovascular Drugs and Therapy*. 2019; 33: 453–459.
- [65] Futterman LG, Lemberg L. Diuretics, the most Critical Therapy in Heart Failure, yet often Neglected in the Literature. *American Journal of Critical Care*. 2003; 12: 376–380.
- [66] Jobs A, Abdin A, de Waha-Thiele S, Eitel I, Thiele H, de Wit C, *et al.* Angiotensin-converting-enzyme inhibitors in hemodynamic congestion: a meta-analysis of early studies. *Clinical Research in Cardiology*. 2019; 108: 1240–1248.
- [67] Ferreira JP, Santos M, Almeida S, Marques I, Bettencourt P, Carvalho H. Mineralocorticoid receptor antagonism in acutely decompensated chronic heart failure. *European Journal of Internal Medicine*. 2014; 25: 67–72.
- [68] Kawase Y, Hata R, Tada T, Katoh H, Kadota K. Effects of Carperitide on Degree of Pulmonary Congestion in Treatment of Acute Heart Failure. *Circulation Journal*. 2018; 82: 2079–2088.
- [69] Selvaraj S, Claggett B, Pozzi A, McMurray JJV, Jhund PS, Packer M, *et al.* Prognostic Implications of Congestion on Physical Examination among Contemporary Patients with Heart Failure and Reduced Ejection Fraction: PARADIGM-HF. *Circulation*. 2019; 140: 1369–1379.
- [70] Hernandez M, Sullivan RD, McCune ME, Reed GL, Gladysheva IP. Sodium-Glucose Cotransporter-2 Inhibitors Improve Heart Failure with Reduced Ejection Fraction Outcomes by Reducing Edema and Congestion. *Diagnostics*. 2022; 12: 989.
- [71] Koufou EE, Arfaras-Melainis A, Rawal S, Kalogeropoulos AP. Treatment of Heart Failure with Mid-Range Ejection Fraction: What Is the Evidence. *Journal of Clinical Medicine*. 2021; 10: 203.
- [72] Park JJ, Park CS, Mebazaa A, Oh I, Park H, Cho H, *et al.* Characteristics and outcomes of HFpEF with declining ejection fraction. *Clinical Research in Cardiology*. 2020; 109: 225–234.
- [73] Jering K, Claggett B, Redfield MM, Shah SJ, Anand IS, Martinez F, *et al.* Burden of Heart Failure Signs and Symptoms, Prognosis, and Response to Therapy: The PARAGON-HF Trial. *JACC: Heart Failure*. 2021; 9: 386–397.
- [74] Lam CSP, Voors AA, de Boer RA, Solomon SD, van Veldhuisen DJ. Heart failure with preserved ejection fraction: from mechanisms to therapies. *European Heart Journal*. 2018; 39: 2780–2792.
- [75] Heise T, Jordan J, Wanner C, Heer M, Macha S, Mattheus M, *et al.* Pharmacodynamic Effects of Single and Multiple Doses of Empagliflozin in Patients with Type 2 Diabetes. *Clinical Therapeutics*. 2016; 38: 2265–2276.
- [76] Málek F, Gajewski P, Zymliński R, Janczak D, Chabowski M, Fudim M, *et al.* Surgical ablation of the right greater splanchnic nerve for the treatment of heart failure with preserved ejection fraction: first-in-human clinical trial. *European Journal of Heart Failure*. 2021; 23: 1134–1143.