



HAL
open science

Poor in-hospital congestion improvement in acute heart failure patients classified according to LVEF: prognostic implications

Gaetano Ruocco, Nicolas Girerd, Tripti Rastogi, Zohra Lamiral, Alberto Palazzuoli

► To cite this version:

Gaetano Ruocco, Nicolas Girerd, Tripti Rastogi, Zohra Lamiral, Alberto Palazzuoli. Poor in-hospital congestion improvement in acute heart failure patients classified according to LVEF: prognostic implications. *European Heart Journal - Cardiovascular Imaging*, 2024, 10.1093/ehjci/jeae075 . hal-04505174

HAL Id: hal-04505174

<https://hal.univ-lorraine.fr/hal-04505174v1>

Submitted on 14 Mar 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Poor in-hospital congestion improvement in acute heart failure patients classified according to LVEF: prognostic implications.

Gaetano Ruocco MD, FESC^{1*}, Nicolas Girerd MD, PhD, FHFA^{2*}, Tripti Rastogi MD², Zohra Lamiral², Alberto Palazzuoli MD, FESC, FEACVI³

¹ *Cardiology Unit, "Buon Consiglio" Fatebenefratelli Hospital, Naples, Italy*

² *Université de Lorraine, INSERM, Centre d'Investigations Cliniques 1433, CHRU de Nancy, Inserm 1116 and INI-CRCT (Cardiovascular and Renal Clinical Trialists) F-CRIN Network, Nancy, France*

³ *Cardiovascular Diseases Unit, Cardio Thoracic and Vascular Department Le Scotte Hospital, University of Siena, Siena, Italy*

*** Gaetano Ruocco and Nicolas Girerd share the first author position.**

Address for correspondence:

Nicolas Girerd MD, PhD, FHFA

Address: 4, rue du Morvan. 54500 Vandœuvre-Lès-Nancy

E-mail: n.girerd@chru-nancy.fr

Phone: +33383157496 Fax: +33383157324

Short Title: Congestion changes in AHF according to LVEF

Word count: 3226

ABSTRACT

Background: Residual congestion in acute heart failure (AHF) is associated with poor prognosis. However, there is a lack of data on the prognostic value of changes in a combined assessment of in-hospital congestion. The present study sought to assess the association between in-hospital congestion changes and subsequent prognosis according to left ventricular ejection fraction (LVEF) classification.

Methods: Patients (N=244, 80.3±7.6 years, 50.8% male) admitted for acute HF in two European tertiary care centers underwent clinical assessment (congestion score included dyspnea at rest, rales, third heart sound, jugular venous distention, peripheral edema and hepatomegaly; simplified congestion score included rales and peripheral edema), echocardiography, lung ultrasound (LUS) and natriuretic peptides (NP) measurement at admission and discharge. The primary outcome was a composite of all-cause mortality and/or HF re-hospitalization.

Results: In the 244 considered patients (95 HF with reduced EF, 57 HF with mildly reduced EF and 92 HF with preserved EF), patients with limited improvement in clinical congestion score (hazard ratio 2.33, 95%CI 1.51 to 3.61, p=0.0001), NP levels (2.29, 95%CI 1.55 to 3.38, p<0.0001) and the number of B-lines (6.44, 95%CI 4.19 to 9.89, p<0.001) had a significantly higher risk of outcome compared to patients experiencing more sizeable decongestion. The same pattern of association was observed when adjusting for confounding factors. A limited improvement in clinical congestion score and in the number of B-lines was related to poor prognosis for all LVEF categories.

Conclusions: In AHF, the degree of congestion reduction assessed over the in-hospital stay period can stratify the subsequent event risk. Limited reduction in both clinical congestion and B-lines number are related to poor prognosis, irrespective of HF subtype.

INTRODUCTION

Despite the recent advances in heart failure (HF) therapies, approximately 20-30% of HF patients discharged from hospital are re-hospitalized within 30-90 days. [1,2] Acute heart failure (AHF) and acute decompensated heart failure (ADHF) are clinical syndromes characterized by progressive intravascular and interstitial fluid accumulation due to the increase in intracardiac filling pressures. Salt and water retention leads to both pulmonary and systemic congestion which are responsible for traditional symptoms and signs of decompensation such as dyspnea, hepato-renal congestion and peripheral edema. [3] Current scenario may vary according with HF typology, haemodynamic conditions, and disease journey (i.e. new onset vs worsening episode of chronic HF). In this framework, the timely and accurate detection of congestion and its resolution is one of the main objectives in AHF/ADHF management [3-5].

Various congestion assessment tools, such as clinical examination and chest X-ray, are typically employed for congestion detection in acute settings despite limited sensitivity [3-5]. Recently, lung ultrasound (LUS) has been endorsed in emergency departments to accurately diagnose and measure pulmonary congestion through the number of “B-lines” or lung “comets”, which represent ultrasonic reverberations arising from extravascular lung water. [6-8] Indeed, several studies have demonstrated that the number of B-lines is a key prognostic marker in HF [9,10]. Additionally, residual pulmonary congestion at discharge assessed by LUS is reported to be associated with poor prognosis in HF patients. [9,10] Thus, in-hospital assessment of pulmonary congestion and the serial evaluation of its changes could become the “key” for clinicians to better monitor and treat AHF/ADHF patients.

The latest European Society of Cardiology (ESC) 2021 HF guidelines classify HF patients according to left ventricular ejection fraction (LVEF) status, namely heart failure with reduced ejection fraction (HFrEF, LVEF<40%), heart failure with mildly-reduced ejection fraction (HFmrEF, 40%≤ LVEF≤ 49%) and heart failure with preserved ejection fraction (HFpEF, LVEF≥50%). [11] Although several studies have evaluated the clinical characteristics and prognosis of HFrEF, HFmrEF and HFpEF patients, there are very few studies which assessed the congestion burden in these specific patient subgroups.

The present study aimed to assess in-hospital changes/improvement in congestion and its association with prognosis in patients with HF according to LVEF class.

METHODS

Pooled Patient Population

This is a retrospective study combining datasets from two independent cohort studies which enrolled consecutive patients with AHF/ADHF.

The AHF-core study (admission and discharge): This is an ongoing cohort study which includes patients hospitalized for acute HF in the university hospitals of the Grand Est region of France. LUS was conducted within 72 hours of admission and before discharge.

The Siena cohort study (admission and discharge): The Siena cohort study included patients with ADHF and with sinus rhythm as previous shown. All patients underwent echocardiography within 12 hours after admission. Clinical, laboratory and LUS data were assessed both at admission and at discharge. [12]

All patients included in this study underwent clinical assessment, echocardiography, LUS and natriuretic peptides (NP) measurement during hospitalization (B-type natriuretic peptide [BNP] and N-terminal-pro-brain natriuretic peptide [NT-proBNP]).

Clinical congestion definition

Patients were evaluated by two physicians at admission and discharge to assess the degree of clinical congestion, with 1 point attributed for each of the following signs: dyspnea at rest, pulmonary rales, third heart sound, jugular venous distention, peripheral edema and hepatomegaly, all mentioned in the European Society of Cardiology scientific statement on “Assessing and grading congestion in acute heart failure” [5] and previously used by our team [12]. Simplified congestion score was based solely on pulmonary rales and peripheral edema.

Echocardiography

Echocardiography was performed at hospital admission. Left ventricular (LV) systolic and diastolic volumes and LVEF were determined using apical two- and four chamber views by the modified Simpson’s biplane method. Left ventricular diastolic function was evaluated by pulsed Doppler transmitral flow velocity, including: early diastolic velocity (E wave), late diastolic velocity (A wave) and their ratio (E/A), deceleration time (DT) of E wave. Early diastolic myocardial velocity (e') was obtained by tissue Doppler imaging (TDI) on the basal septal and basal lateral walls at the level of the

mitral annular site measuring five consecutive beats. The E/e' ratio was calculated from the mean of the two TDI measurements divided by the pulsed doppler E wave measured by placing the sample volume in the LV chamber between the two mitral leaflets during the diastolic phase. TAPSE was obtained by placing the M-mode cursor laterally to the tricuspid annulus. PASP was estimated by continuous Doppler at the tricuspid valve level as the sum of 4 * squared peak velocity of tricuspid regurgitation and the estimate of right atrial pressure based on inferior vena cava (IVC) diameter and collapsibility.

Lung Ultrasound (LUS)

Measurements were collected for each LUS zone. Eight LUS zones were analyzed for each patient. In the Siena cohort, the maximum number of vertical reverberation artifacts (B-lines) was counted in a single intercostal space for each zone and the sum of all 8 zones was considered as the total number of B-lines. In the AHF-core cohort study, the number of B-lines counts were calculated from those obtained with the twenty-eight-point method and converted to 8 zone counts as previously reported. [9]

Study Outcomes

The primary outcome was the composite of all-cause mortality and/or HF re-hospitalization. All patients were followed after discharge in each institution. Median follow-up duration in the AHF-core study was 90 (57 - 90) days and 156 (65 - 180) days in the Siena cohort study.

Statistical Analysis

Patients with heart failure were divided into three subgroups according to LVEF: HF_rEF (LVEF \leq 40%), HF_{mr}EF (40% <LVEF <50%) and HF_pEF (LVEF \geq 50%).

Categorical data are presented as number and percentages, and normally and non-normally distributed continuous variables as mean and standard deviation (SD). Continuous variables were compared using ANOVA or Kruskal-Wallis tests as required, while chi-squared test or Fisher's exact test was used for categorical variables.

To assess the association between congestion changes and subsequent outcome, limited improvement in congestion was defined as an improvement in congestion below the median for each clinical, NP and LUS congestion variables. The thresholds used for limited improvement of each congestion variable were as follows: delta complete clinical congestion score \geq -2, delta simplified clinical congestion score \geq -1, delta NP Z score > 0, delta BNP > -411, delta B-lines >-10. Crude and adjusted Cox proportional hazard regression models were used to assess the relationship between congestion changes and clinical outcome during follow-up. In these models, interactions between LVEF category and the association of congestion variables with outcome were tested using interaction terms in survival models. Hazard ratios and their 95% confidence intervals are reported.

Results yielding a p value <0.05 were considered statistically significant. All analyses were performed using SAS version 9.4.6 (SAS Institute Inc., Cary, N.C., USA) and R version 3.6.1 (2019-07-05).

RESULTS

Baseline characteristics in the overall study population and according to LVEF class

A total of 244 patients were included (50.8% men, mean age 80.3 ± 7.6 years). The proportion of ischemic heart disease (IHD), atrial fibrillation (AF) and chronic kidney disease (CKD) were 43.2%, 24.2% and 71.7 %, respectively. Mean admission clinical congestion score was 2.5 ± 1.2 and mean admission BNP and mean NT-proBNP levels were 1354.1 ± 964.9 pg/mL and 16324.2 ± 20737.6 pg/mL, respectively. Mean LVEF was 41.6 ± 12.5 and mean B-lines at admission was 30.6 ± 9.2 .

When sub-dividing the study population according to LVEF, there were 95 HFrEF patients, 57 HFmrEF patients and 92 HFpEF patients. Patients with HFrEF were more likely to be male (63.2% vs. 47.4% vs. 40.2% ; $p=0.006$) and had a higher prevalence of IHD (82.1% vs. 33.3% vs. 8.8% ; $p<0.001$) compared to HFmrEF and HFpEF patients. Moreover, patients with HFrEF demonstrated a significantly higher admission congestion score (3.0 ± 1.0 vs. 2.5 ± 1.2 vs. 2.0 ± 1.1 ; $p<0.001$) and admission BNP levels (1597.2 ± 1069.9 vs. 1324.3 ± 914.9 vs. 1121.1 ± 819.5 pg/mL ; $p=0.001$) relative to HFmrEF and HFpEF patients. Similarly, congestion score at discharge (complete) ($p=0.0008$) and BNP levels ($p=0.0009$) were significantly higher in HFrEF patients compared to HFmrEF and HFpEF patients. The number of B-lines at admission ($p=0.14$) and at discharge ($p=0.11$) did not differ significantly among the groups [Table 1].

In our cohort of 244 patients, 175 were identified with chronic kidney disease (CKD), defined by an estimated glomerular filtration rate (eGFR) of less than 60 ml/min/m^2 . When examining the association between eGFR levels (categorized as $eGFR<30 \text{ ml/min/m}^2$, 30 to less than 60 ml/min/m^2 , and $eGFR \geq 60 \text{ ml/min/m}^2$) and the number of B-lines at the time of admission, we found no statistically significant difference across the eGFR groups ($p=0.26$). This lack of significant difference persisted in the number of B-lines at the time of discharge across the same eGFR categories ($p=0.31$), as illustrated in Supplementary Figure 1.

Association between limited improvement in congestion and outcome

Univariate Cox regression analysis showed that patients who experienced limited improvement in clinical congestion score ($p=0.0001$), NP levels ($p<0.0001$) and the number of B-lines ($p<0.001$) had a poor outcome. Multivariable Cox regression analysis confirmed a similar trend after adjustment for age, sex, coronary artery disease, CKD, AF and initial value of the considered congestion variable [Table 2].

When assessing the changes in clinical congestion, NP values and B-lines according to HF_rEF, HF_{mr}EF and HF_pEF class, the limited improvement in clinical congestion score and in the number of B-lines were related to poor prognosis independently of LVEF classification. Among all variables, limited improvement in NP values during hospitalization was the only variable not significantly related to prognosis in HF_pEF [Figure 1].

Interplay between limited improvement in clinical, imaging and biological congestion

In view of the above findings, the study population was divided into 7 subgroups according to the limited/no improvement in congestion variables using a Venn diagram. As showed in Figure 2, there were 35 patients with only limited/no improvement in simplified clinical congestion score, 30 patients with only limited/no improvement in the number of B-lines, 14 patients with only limited/no improvement in NP level, 20 patients with limited/no improvement in both simplified congestion score and NP level, 22 patients with limited/no improvement in both simplified congestion score and B-lines count, 33 patients with limited/no improvement in both B-lines count and NP level and 48 patients with limited/no improvement in simplified congestion score, B-lines count and NP level. [Figure 2A] When analyzing the outcome occurrence rate among the 7 subgroups, limited improvement in clinical and/or NP level was associated with a poorer outcome whereas the limited improvement in B-lines count was associated with a high risk of adverse events occurrence irrespective of the presence of the two other components (17% vs. 62% vs. 36% vs. 10% vs. 59% vs. 88% vs. 73%; $p < 0.001$) [Figure 2B].

Prognostic value of limited improvement in congestion according to LVEF class

The pattern of association between limited congestion improvement and outcome was similar in all LVEF subtypes [Figure 3].

DISCUSSION

Congestion plays a central role in HF progression and re-hospitalization and its assessment is a critical goal in HF management. [13,14] Several scores for clinical congestion evaluation and severity have been proposed although none have been extensively assessed to date and their related prognostic accuracy remains to be clarified. [15,16] Our study focused on the in-hospital evaluation of clinical and pulmonary congestion both at admission and at discharge. We demonstrate that the limited improvement in clinical congestion score, number of B-lines and natriuretic peptide levels from admission to discharge was related to poor outcome. In addition, the limited improvement in either clinical congestion score or B-lines count was associated with a higher risk of event regardless of LVEF class. A limited improvement in B-lines during hospital stay was associated with a numerically greater increase

in event risk than limited improvement in clinical congestion score or natriuretic peptide levels. Hence, the limited improvement in B-lines count constituted the key congestion variable predicting worse prognosis in AHF.

To the best of our knowledge, this is the first study highlighting the prognostic role of in-hospital LUS changes in AHF/ADHF according to LVEF classification. AHF is a clinical syndrome characterized by fluid overload which manifests as clinical congestion. According to the traditional clinical classification, congestion status and perfusion state represent the main factors driving outcome in AHF patients. [3] In line with these observations, a recent analysis of the ESC-EORP-HFA Heart Failure Long-Term Registry demonstrated that, among 7865 AHF patients, “wet” patients had a worse prognosis; in addition, among the discharged patients, 30.9% had residual congestion, and had a higher 1-year mortality compared to patients discharged without congestion (28.0 vs. 18.5%). [17] Additionally, a recent study including 1000 patients showed that pulmonary congestion assessed through chest X-ray was related to poor prognosis, with a worsening of prognosis with increasing pulmonary congestion. [18] Given that LUS assessment appears to be superior to chest X-ray in detecting pulmonary congestion as shown in a head-to-head meta-analysis, accurate assessment of pulmonary congestion trajectories throughout the course of hospitalization is an invaluable tool for risk stratification. [19]

Moreover, our study showed that the analysis of the number of B-lines at admission and at discharge did not significantly change across eGFR strata (categorized as $eGFR < 30$ ml/min/m², 30 to less than 60 ml/min/m², and $eGFR \geq 60$ ml/min/m²). These findings are different with respect to the available studies. Indeed, an analysis of 97 AHF patients performed by Pugliese et al. demonstrated that patients with CKD presented higher percentage of patients with B-lines number >15 than patients without CKD. In this analysis the contemporary presence of congestion and CKD was related to poor prognosis and also to inflammatory status. [20]

LUS is a rapid and reliable tool for assessing pulmonary congestion since it reflects real-time pulmonary congestion and pulmonary circulation status. Imanishi et al. confirmed the direct correlation between B-lines count and pulmonary capillary wedge pressure and thus the prognostic weight of residual pulmonary congestion in AHF. [21] Several studies assessing residual pulmonary congestion at discharge revealed the worse prognosis in patients with higher B-lines count. [9,10,21,22] Our study confirms that a limited reduction in B-lines count (lesser than 9) was related to poor prognosis as well as the lack of improvement in clinical congestion.

Although all congestion signs are related to poor outcome in AHF, there is absence of concordance among the various congestion markers. [16] This lack of concordance likely results from the fact that every patient shows a different congestion phenotype which could be related to a different HF picture, etiology and LVEF classification. Despite the fact that peripheral congestion, intravascular congestion

and pulmonary congestion are all aspects of the same pathophysiological process, they can all occur differently. Our findings are in agreement with a previous study including both HFrEF and HFpEF patients demonstrating the significant prognostic value of discharge B-lines count in all patients; a significant association between discharge B-lines and outcome was also separately confirmed in HFrEF and HFpEF. [12] Furthermore, a multicenter study including 125 patients with HFrEF and 83 patients with HFpEF, showed demonstrated the residual pulmonary congestion, defined as the number of B-lines at discharge greater than 15, was related to poor prognosis independently from LVEF and from biohumoral and echocardiographic data. [23] Another report including approximately 1000 patients showed that pulmonary congestion detected through LUS (B-lines count>30) had a significant relationship with worse prognosis in HFpEF. [24] Conversely, Cogliati et al. did not find an association between outcome and B-lines, and only inferior vena cava (IVC) diameter at discharge was related to poor outcome. [25] Their findings suggested the prognostic weight of intravascular congestion in HFrEF patients who exhibited increased central venous pressure, a condition typically associated with systemic fluid accumulation and underlying right HF. Indeed, in HFpEF, prevalent pulmonary congestion assessed by LUS and its relationship with prognosis may result from fluid redistribution due to increased vascular resistance/stiffness, subsequently leading to reduced capacitance in the large veins as well as increased arterial resistance. [26]

Although various studies have analyzed congestion burden in both HFrEF and HFpEF, few studies have assessed such burden in HFmrEF. To this end, our study confirmed that the limited/no improvement in clinical congestion and B-lines during hospitalization was related to poor prognosis independently from LVEF phenotype. Accordingly, HFmrEF patients with limited improvement in congestion demonstrated poor outcome, mainly related to poor B-lines improvement.

Thus, in-hospital assessment of congestion through clinical, laboratory examination and LUS at admission and after treatment could represent a valuable tool in recognizing high-risk profile patients. Patients with residual congestion were more prone to occurrence of adverse events, regardless of LVEF class. Our study further demonstrates the prognostic role of residual congestion as well as residual pulmonary congestion assessed by LUS. Congruent with these findings, Kang et al. showed that the combination of conventional congestion assessment and B-lines before discharge aided physicians in risk stratification of hospitalized HF patients. [27] Hence, limited congestion improvement during hospitalization may be related to unsuccessful or insufficient in-hospital treatment, diuretic resistance, or delay in prescribing newer HF therapies prior to discharge. A recent analysis of BLUSHED-AHF trial confirmed the better prognosis in patients with LUS reduction from emergency department to discharge; however, this benefit was significant and evident in patients without tachycardia, tachypnea, hypotension, hyponatremia, uremia, advanced age, or history of myocardial infarction at admission. [28] Indeed, in keeping with the latter, the ongoing IMP-OUTCOME trial will explore B-lines-guided

intensive HF management in the post-discharge period in patients discharged with residual pulmonary congestion. [29] Therefore, the in-hospital monitoring of pulmonary congestion through LUS could be done together with echocardiography assessment evaluating PASP, inferior cave vein (ICV) and left ventricular filling pressures in order to better stratify patients with high risk of adverse events. This approach was applied by Ohman J et al. who demonstrated that in 60 AHF patients, E/e decrease within hospitalization was a significant congestion parameter able to evaluate pulmonary congestion resolution in relation to better prognosis; however, pulmonary congestion resolution assessed by LUS, remained the only congestion variables related to good outcome at 6 months. [30] In this line, further studies are necessary to investigate the value of congestion monitoring and resolution to guide therapies in AHF patients.

LIMITATIONS

This study is a retrospective analysis of consecutive AHF patients, evaluated with a post-hoc research objective in mind. The methodology for recording B-lines differed between the two centers, utilizing either a 28-point or an 8-zone approach, which was later standardized. A notable limitation was the absence of echocardiographic assessments prior to discharge, which would have been valuable for a more detailed understanding of the changes in PASP, IVC size, and E/e' ratio throughout the hospital stay. Additionally, information on heart failure treatments during hospitalization was not comprehensively available for all patients, hindering the examination of the relationship between decongestive therapies and congestion patterns. Furthermore, data on heart failure triggers and comprehensive biomarker profiles during the acute phases were not accessible, thus precluding their analysis in relation to in-hospital congestion trends.

CONCLUSIONS

Limited improvement in clinical congestion, NP values and B-lines count is a strong predictor of poor prognosis irrespective of LVEF class. The prognostic value of limited improvement in B-lines appeared more stringent than that of other congestion parameters, making it a cardinal variable to monitor during hospital stay. Further studies should determine whether strategies intended to minimize discharge congestion (especially focusing on B-lines) can improve clinical outcome following discharge.

Conflict of interests: none to declare.

Funding resources: none.

Data availability: The study data are available for sharing after specific request to the corresponding author (Prof. Nicolas Girerd).

REFERENCES

1. Palazzuoli A, Evangelista I, Ruocco G, Lombardi C, Giovannini V, Nuti R et al. Early readmission for heart failure: An avoidable or ineluctable debacle? *Int J Cardiol.* 2019 Feb 15;277:186-195. doi: 10.1016/j.ijcard.2018.09.039. Epub 2018 Sep 13.
2. Vaduganathan M, Bonow RO, Gheorghiade M. Thirty-day readmissions: the clock is ticking, *JAMA* 309 (2013) 345–346.
3. Gheorghiade M, Pang PS. Acute heart failure syndromes. *J Am Coll Cardiol.* 2009 Feb 17;53(7):557-573. doi: 10.1016/j.jacc.2008.10.041.
4. Weintraub NL, Collins SP, Pang PS, Levy PD, Anderson AS, Arslanian-Engoren C et al; American Heart Association Council on Clinical Cardiology and Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Acute heart failure syndromes: emergency department presentation, treatment, and disposition: current approaches and future aims: a scientific statement from the American Heart Association. *Circulation.* 2010 Nov 9;122(19):1975-96. doi: 10.1161/CIR.0b013e3181f9a223.
5. Gheorghiade M, Follath F, Ponikowski P, Barsuk JH, Blair JE, Cleland JG et al; European Society of Cardiology; European Society of Intensive Care Medicine. Assessing and grading congestion in acute heart failure: a scientific statement from the acute heart failure committee of the heart failure association of the European Society of Cardiology and endorsed by the European Society of Intensive Care Medicine. *Eur J Heart Fail.* 2010 May;12(5):423-33. doi: 10.1093/eurjhf/hfq045.
6. Pellicori P, Platz E, Dauw J, Ter Maaten JM, Martens P, Pivetta E et al. Ultrasound imaging of congestion in heart failure: examinations beyond the heart. *Eur J Heart Fail.* 2021 May;23(5):703-712. doi: 10.1002/ejhf.2032.
7. Platz E, Jhund PS, Girerd N, Pivetta E, McMurray JJV, Peacock WF et al; Study Group on Acute Heart Failure of the Acute Cardiovascular Care Association and the Heart Failure Association of the European Society of Cardiology. Expert consensus document: Reporting checklist for quantification of pulmonary congestion by lung ultrasound in heart failure. *Eur J Heart Fail.* 2019 Jul;21(7):844-851. doi: 10.1002/ejhf.1499.
8. Gargani L, Girerd N, Platz E, Pellicori P, Stankovic I, Palazzuoli A et al. Lung ultrasound in acute and chronic heart failure. A Clinical Consensus Statement of the European Association of Cardiovascular Imaging (EACVI). *Eur Heart J Cardiovasc Imaging.* 2023 Jul 14;jead169. doi: 10.1093/ehjci/jead169.
9. Coiro S, Rossignol P, Ambrosio G, Carluccio E, Alunni G, Murrone A et al. Prognostic value of residual pulmonary congestion at discharge assessed by lung ultrasound imaging in heart failure. *Eur J Heart Fail.* 2015 Nov;17(11):1172-81. doi: 10.1002/ejhf.344.

10. 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 Fail.* 2019 Oct;7(10):849-858. doi: 10.1016/j.jchf.2019.07.008.
11. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M et al; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021 Sep 21;42(36):3599-3726. doi: 10.1093/eurheartj/ehab368.
12. 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. *Clin Res Cardiol.* 2018 Jul;107(7):586-596. doi: 10.1007/s00392-018-1221-7.
13. Girerd N, Seronde MF, Coiro S, Chouihed T, Bilbault P, Braun F et al; INI-CRCT, Great Network, and the EF-HF Group. Integrative Assessment of Congestion in Heart Failure Throughout the Patient Journey. *JACC Heart Fail.* 2018 Apr;6(4):273-285. doi: 10.1016/j.jchf.2017.09.023.
14. Palazzuoli A, Evangelista I, Nuti R. Congestion occurrence and evaluation in acute heart failure scenario: time to reconsider different pathways of volume overload. *Heart Fail Rev.* 2020 Jan;25(1):119-131. doi: 10.1007/s10741-019-09868-0.
15. Lee MMY, Campbell RT, Claggett BL, Lewis EF, Docherty KF, Lindner M et al. Health-related quality of life in acute heart failure: association between patient-reported symptoms and markers of congestion. *Eur J Heart Fail.* 2022 Sep 25. doi: 10.1002/ejhf.2699.
16. Haag S, Jobs A, Stiermaier T, Fichera CF, Paitazoglou C, Eitel I et al. Lack of correlation between different congestion markers in acute decompensated heart failure. *Clin Res Cardiol.* 2022 Jun 1. doi: 10.1007/s00392-022-02036-9.
17. Chioncel O, Mebazaa A, Maggioni AP, Harjola VP, Rosano G, Laroche C et al; ESC-EORP-HFA Heart Failure Long-Term Registry Investigators. Acute heart failure congestion and perfusion status - impact of the clinical classification on in-hospital and long-term outcomes; insights from the ESC-EORP-HFA Heart Failure Long-Term Registry. *Eur J Heart Fail.* 2019 Nov;21(11):1338-1352. doi: 10.1002/ejhf.1492.
18. Pan D, Pellicori P, Dobbs K, Bulemfu J, Sokoreli I, Urbinati A et al. Prognostic value of the chest X-ray in patients hospitalised for heart failure. *Clin Res Cardiol.* 2021 Nov;110(11):1743-1756. doi: 10.1007/s00392-021-01836-9.
19. Maw AM, Hassanin A, Ho PM, McInnes MDF, Moss A, Juarez-Colunga E et al. Diagnostic Accuracy of Point-of-Care Lung Ultrasonography and Chest Radiography in Adults With Symptoms Suggestive of Acute Decompensated Heart Failure: A Systematic Review and Meta-

- analysis. *JAMA Netw Open*. 2019 Mar 1;2(3):e190703. doi: 10.1001/jamanetworkopen.2019.0703
20. Pugliese NR, Fabiani I, Conte L, Nesti L, Masi S, Natali A et al. Persistent congestion, renal dysfunction and inflammatory cytokines in acute heart failure: a prognosis study. *J Cardiovasc Med (Hagerstown)*. 2020 Jul;21(7):494-502. doi: 10.2459/JCM.0000000000000974.
 21. Imanishi J, Maeda T, Ujiro S, Masuda M, Kusakabe Y, Takemoto M et al. Association between B-lines on Lung Ultrasound, Invasive Hemodynamics and Prognosis in Acute Heart Failure Patients. *Eur Heart J Acute Cardiovasc Care*. 2022 Dec 22:zuac158. doi: 10.1093/ehjacc/zuac158.
 22. Zhu Y, Li N, Wu M, Peng Z, Huang H, Zhao W et al. Impact of B-lines-guided intensive heart failure management on outcome of discharged heart failure patients with residual B-lines. *ESC Heart Fail*. 2022 Aug;9(4):2713-2718. doi: 10.1002/ehf2.13988.
 23. Pugliese NR, Mazzola M, Bandini G, Barbieri G, Spinelli S, De Biase N et al. Prognostic Role of Sonographic Decongestion in Patients with Acute Heart Failure with Reduced and Preserved Ejection Fraction: A Multicentre Study. *J Clin Med*. 2023 Jan 18;12(3):773. doi: 10.3390/jcm12030773.
 24. 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 Fail*. 2021 Aug;8(4):2660-2669. doi: 10.1002/ehf2.13206.
 25. 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. *Eur J Intern Med*. 2022 Mar;97:69-77. doi: 10.1016/j.ejim.2021.11.010.
 26. Cotter G, Metra M, Milo-Cotter O, Dittrich HC, Gheorghide M. Fluid overload in acute heart failure--re-distribution and other mechanisms beyond fluid accumulation. *Eur J Heart Fail*. 2008 Feb;10(2):165-9. doi: 10.1016/j.ejheart.2008.01.007.
 27. Kang Y, Zhong XK, Chen QW, Yang ZX, Chen XJ, Yu PM et al. Prognostic values of B-lines combined with clinical congestion assessment at discharge in heart failure patients. *ESC Heart Fail*. 2022 Oct;9(5):3044-3051. doi: 10.1002/ehf2.14041.
 28. Harrison NE, Ehrman R, Collins S, Desai AA, Duggan NM, Ferre R et al. The prognostic value of improving congestion on lung ultrasound during treatment for acute heart failure differs based on patient characteristics at admission. *J Cardiol*. 2024 Feb;83(2):121-129. doi: 10.1016/j.jjcc.2023.08.003.

29. Zhu Y, Li N, Wu M, Peng Z, Huang H, Zhao W et al. Impact of B-lines-guided intensive heart failure management on outcome of discharged heart failure patients with residual B-lines. *ESC Heart Fail.* 2022 Aug;9(4):2713-2718. doi: 10.1002/ehf2.13988.
30. Öhman J, Harjola VP, Karjalainen P, Lassus J. Assessment of early treatment response by rapid cardiothoracic ultrasound in acute heart failure: Cardiac filling pressures, pulmonary congestion and mortality. *Eur Heart J Acute Cardiovasc Care.* 2018 Jun;7(4):311-320. doi: 10.1177/2048872617708974.

Table 1: Characteristics of patients with heart failure overall and according to LVEF classification (HFpEF, HFmrEF and HFrEF) in the AHF-CORE and Siena cohorts

Characteristic	N	Overall	HFrEF (LVEF <40%)	HFmrEF (40<=LVEF <50%)	HFpEF (LVEF >=50%)	P-value
		(n=244)	(n=95)	(n=57)	(n=92)	
		Mean ± SD / n(%)	Mean ± SD / n(%)	Mean ± SD / n(%)	Mean ± SD / n(%)	
Age (years)	244	80.3 ± 7.6	80.9 ± 7.0	80.8 ± 7.5	79.5 ± 8.3	0.40
Men	244	124 (50.8 %)	60 (63.2 %)	27 (47.4 %)	37 (40.2 %)	0.006
Risk factors – n. (%)						
Previous HF	28	16 (57.1 %)	7 (58.3 %)	4 (57.1 %)	5 (55.6 %)	1.00
Ischemic heart disease (IHD)	243	105 (43.2 %)	78 (82.1 %)	19 (33.3 %)	8 (8.8 %)	<0.0001
AF	244	59 (24.2 %)	24 (25.3 %)	15 (26.3 %)	20 (21.7 %)	0.77
CKD	244	175 (71.7 %)	66 (69.5 %)	43 (75.4 %)	66 (71.7 %)	0.73
Clinical examination and BNP						
Heart rate (bpm)	244	89.1 ± 9.6	88.9 ± 10.7	88.2 ± 10.8	89.8 ± 7.3	0.67
Systolic blood pressure (mmHg)	244	128.7 ± 18.1	116.6 ± 16.1	128.7 ± 12.8	141.3 ± 13.9	<0.0001
Edema at admission	243	176 (72.4 %)	90 (94.7 %)	41 (71.9 %)	45 (49.5 %)	<0.0001
Rales at admission	244	220 (90.5)	83 (87.4)	51 (89.5)	86 (94.5)	0.24
Admission congestion score (complete)	241	2.5 ± 1.2	3.0 ± 1.0	2.5 ± 1.2	2.0 ± 1.1	<0.0001
0	241	1 (0.4 %)	0 (0.0 %)	1 (1.8 %)	0 (0.0 %)	
1	241	63 (26.1 %)	9 (9.7 %)	15 (26.3 %)	39 (42.9 %)	
2	241	57 (23.7 %)	22 (23.7 %)	15 (26.3 %)	20 (22.0 %)	<0.0001
3	241	53 (22.0 %)	23 (24.7 %)	9 (15.8 %)	21 (23.1 %)	
4	241	67 (27.8 %)	39 (41.9 %)	17 (29.8 %)	11 (12.1 %)	
Admission congestion score (simplified)	243	1.6 ± 0.5	1.8 ± 0.4	1.6 ± 0.5	1.4 ± 0.5	<0.0001
0	243	2 (0.8 %)	0 (0.0 %)	1 (1.8 %)	1 (1.1 %)	
1	243	86 (35.4 %)	17 (17.9 %)	20 (35.1 %)	49 (53.8 %)	<0.0001
2	243	155 (63.8 %)	78 (82.1 %)	36 (63.2 %)	41 (45.1 %)	
Discharge congestion score (complete)	239	0.9 ± 1.2	1.2 ± 1.3	0.9 ± 1.2	0.7 ± 1.2	0.0008
0	239	125 (52.3 %)	34 (36.2 %)	31 (55.4 %)	60 (67.4 %)	
1	239	56 (23.4 %)	30 (31.9 %)	13 (23.2 %)	13 (14.6 %)	0.0008
2	239	21 (8.8 %)	14 (14.9 %)	5 (8.9 %)	2 (2.2 %)	

3	239	22 (9.2 %)	8 (8.5 %)	3 (5.4 %)	11 (12.4 %)	
4	239	15 (6.3 %)	8 (8.5 %)	4 (7.1 %)	3 (3.4 %)	
Discharge congestion score (simplified)	240	0.7 ± 0.8	0.8 ± 0.8	0.6 ± 0.8	0.5 ± 0.8	0.002
0	240	130 (54.2 %)	37 (38.9 %)	32 (57.1 %)	61 (68.5 %)	
1	240	64 (26.7 %)	36 (37.9 %)	15 (26.8 %)	13 (14.6 %)	0.0011
2	240	46 (19.2 %)	22 (23.2 %)	9 (16.1 %)	15 (16.9 %)	
BNP at admission	233	1354.1 ± 964.9	1597.2 ± 1069.9	1324.3 ± 914.9	1121.1 ± 819.5	0.001
BNP at discharge	230	887.3 ± 838.0	1117.1 ± 948.1	792.4 ± 715.0	701.6 ± 728.6	0.0009
NT-proBNP at admission	11	16324.2 ± 20737.6	33053.3 ± 26763.4	10632.3 ± 12298.6	3864.0 ± 1954.0	0.15
NT-proBNP at discharge	11	12315.6 ± 20317.0	25400.3 ± 31241.8	5618.3 ± 5803.8	4254.0 ± 4201.2	0.15
<i>Echocardiography and LUS</i>						
LVEF (%)	244	41.6 ± 12.5	28.4 ± 6.4	42.8 ± 2.7	54.5 ± 4.5	< 0.0001
B-lines count (highest scoring within a zone) at admission	244	30.6 ± 9.2	31.6 ± 9.4	30.1 ± 10.2	29.8 ± 8.4	0.14
B-lines count (highest scoring within a zone) at discharge	240	20.9 ± 9.2	22.4 ± 9.4	20.5 ± 9.7	19.6 ± 8.6	0.11

Abbreviations: LVEF: Left Ventricular Ejection Fraction, HFrEF: Heart Failure with reduced Ejection Fraction, HFmrEF: Heart Failure with mildly reduced Ejection Fraction, HFpEF: Heart Failure with preserved Ejection Fraction, BNP: B-type natriuretic peptide, NT-proBNP: N-terminal-pro-brain natriuretic peptide, LUS: Lung Ultrasound

Complete congestion score was based on 1 point being attributed for each of the following signs: dyspnea at rest, pulmonary rales, third heart sound, jugular venous distention, peripheral edema and hepatomegaly. Simplified congestion score was based solely on pulmonary rales and peripheral edema.

Table 2: Association between limited improvement in congestion and the composite of death or re-hospitalization for heart failure - Overall.

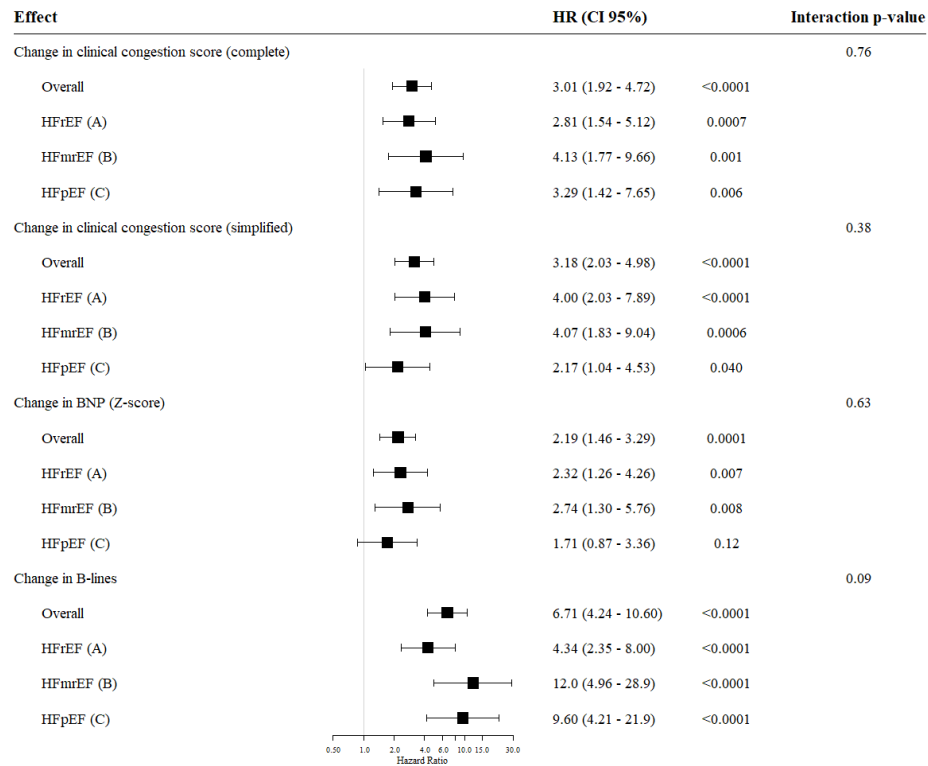
	n/N	Univariable		Adjusted ¹	
		HR (95%CI)	P-value	HR (95%CI)	P-value
Limited clinical congestion improvement					
Based on complete clinical congestion score	185/237	2.33 (1.51 - 3.61)	0.0001	3.01 (1.92 - 4.72)	<0.0001
Based on simplified clinical congestion score	186/240	2.04 (1.36 - 3.07)	0.0006	3.18 (2.03 - 4.98)	<0.0001
Limited NP improvement					
Based on median NP Z score change	125/241	2.17 (1.49 - 3.17)	<0.0001	2.19 (1.46 - 3.29)	0.0001
Relative reduction from admission >30%	62/241	0.93 (0.62 - 1.41)	0.74	1.14 (0.75 - 1.73)	0.55
Based on median BNP change	115/230	2.29 (1.55 - 3.38)	<0.0001	2.59 (1.69 - 3.99)	<0.0001
Limited LUS improvement					
Based on median B-lines change	116/240	6.44 (4.19 - 9.89)	<0.0001	6.71 (4.24 - 10.60)	<0.0001

¹ adjusted for age, sex, coronary artery disease, chronic kidney disease, atrial fibrillation and initial value of the considered congestion variable

Complete congestion score was based on dyspnea at rest, pulmonary rales, third heart sound, jugular venous distention, peripheral edema and hepatomegaly. Simplified congestion score was based solely on pulmonary rales and peripheral edema.

The thresholds used for each congestion variable are as follows: delta complete clinical congestion score ≥ -2 , delta simplified clinical congestion score ≥ -1 , delta NP Z score > 0 , delta BNP > -411 , delta B-lines > -10 .

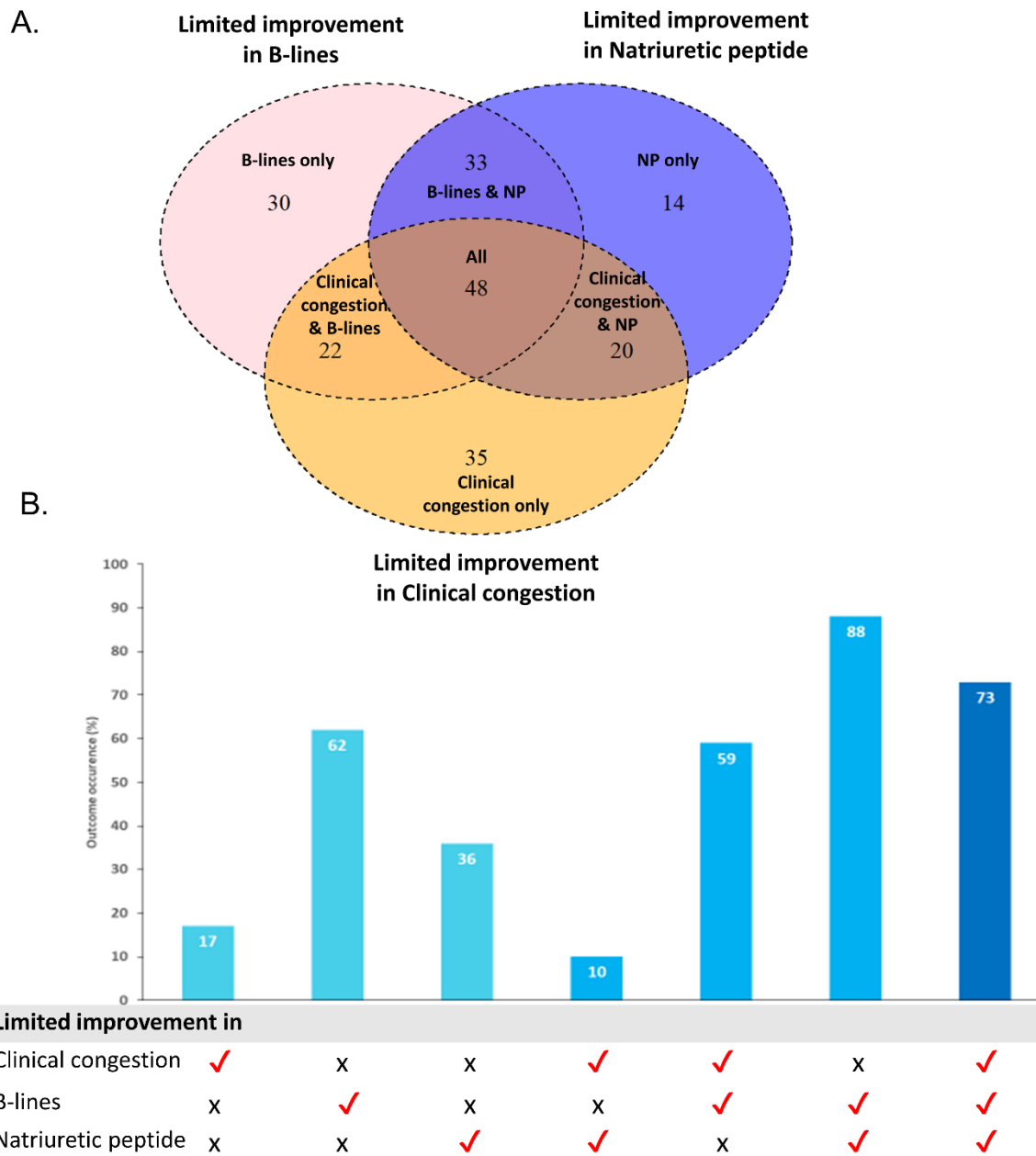
Figure 1: Association between limited improvement in congestion and the composite of death or rehospitalization for heart failure according to HF subtype.



Legend: Models are adjusted for age, sex, coronary artery disease, chronic kidney disease, atrial fibrillation and initial value of the considered parameter.

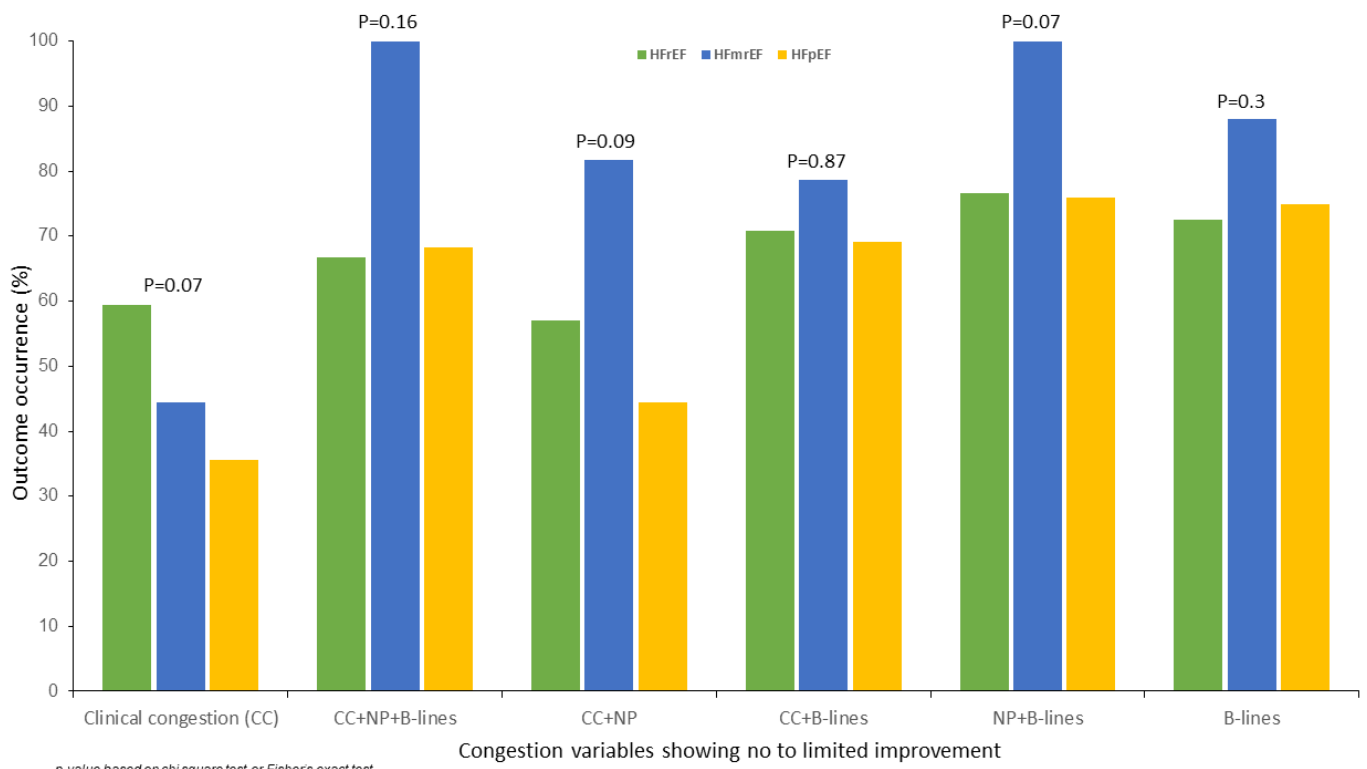
The thresholds used for each congestion variable are as follows: delta complete clinical congestion score ≥ -2 , delta simplified clinical congestion score ≥ -1 , delta NP Z score > 0 , delta BNP > -411 , delta B-lines > -10 .

Figure 2: Venn diagram according to limited/no congestion improvement in congestion parameters (A); Outcome occurrence rate according to limited/no improvement congestion groups (Chi-square test, $p < 0.001$) (B).



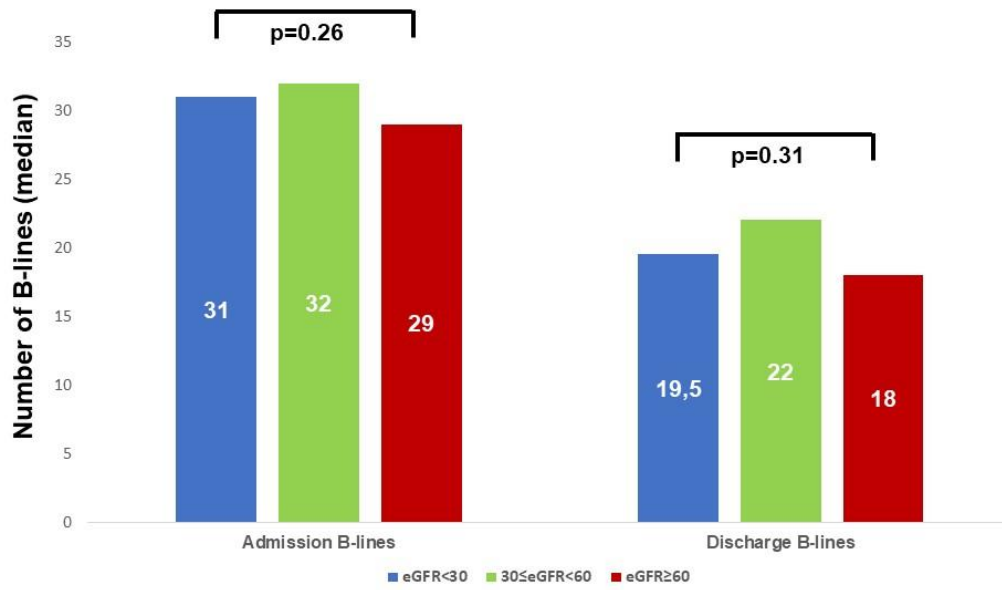
Legend: (✓) indicates the limited to no/ congestion improvement in the congestion parameter.
 (x) indicates improvement in the congestion variable.

Figure 3: Percentage of patients with outcome occurrence according to limited/no improvement congestion



variables and HF subtype

Supplementary Figure 1. Median differences of admission and discharge number of B-lines according to eGFR strata



Supplementary Figure 1