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**Diagnostic performance of congestion score index evaluated from chest radiography for acute heart failure in the emergency department:
A retrospective analysis from the PARADISE cohort**

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Running title: Diagnostic Value of Radiographic Congestion Scoring for Acute Heart Failure

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Abstract

Background: Congestion score index (CSI), a semi-quantitative evaluation of congestion on chest radiography, is associated with outcome in patients with heart failure (HF). However, its diagnostic value in patients admitted for acute dyspnea has yet to be evaluated.

Methods and Findings: The diagnostic value of CSI for acute HF (adjudicated from patients' discharge files) was studied in the Pathway of dyspneic patients in Emergency (PARADISE) cohort, including patients aged 18 years or older admitted for acute dyspnea in the emergency department of the Nancy University Hospital (France) between January 1, 2015 and December 31, 2015. CSI (ranging from 0 to 3) was evaluated using a semi-quantitative method on chest radiography in consecutive patients admitted for acute dyspnea in the emergency department. Results were validated in independent cohorts (N=224). Of 1,333 patients, mean (SD) age was 72.0 (18.5) years, 686 (51.5%) were men, and mean (SD) CSI was 1.42 (0.79). Patients with higher CSI had more cardiovascular comorbidities, more severe congestion, higher b-type natriuretic peptide (BNP), poorer renal function and more respiratory acidosis. Acute HF was diagnosed in 289 (21.7%) patients. CSI was significantly associated with acute HF diagnosis (adjusted-odds ratio for 0.1-unit CSI increase 1.19, 95%CI 1.16-1.22, $p<0.001$) after adjustment for clinical-based diagnostic score including age, comorbidity burden, dyspnea and clinical congestion. The diagnostic accuracy of CSI for acute HF was >0.80 , whether alone (area under receiver operating characteristic curve [AUROC] 0.84, 95%CI 0.82-0.86) or in addition to the clinical model (AUCROC 0.87, 95%CI 0.85-0.90). CSI improved diagnostic accuracy on top of clinical variables (Net reclassification improvement [NRI]=94.9%) and clinical variables plus BNP (NRI=55.0%). Similar diagnostic accuracy was observed in the validation cohorts (AUROC 0.75, 95%CI 0.68-0.82). The key limitation of our derivation cohort was its single-center and retrospective nature, which was counterbalanced by the validation in the independent cohorts.

Conclusions: In this study, we observed that a systematic semi-quantified assessment of radiographic pulmonary congestion showed high diagnostic value for acute HF in dyspneic patients. Better use of chest radiography may provide an inexpensive, widely, and readily available method for acute heart failure triage in the emergency department.

Author summary

Why was this study done?

- Chest radiography is often performed in patients admitted for acute dyspnea in the emergency department; however, its assessment is generally not standardized.
- Latest guidelines for heart failure emphasize the limitations of chest radiography in its current use.
- A standardized approach to quantify pulmonary congestion from chest radiography could potentially improve its diagnostic performance for acute heart failure.

What did the researchers do and find?

- We studied the diagnostic value of a semi-quantitative approach (the Congestion Score Index) to pulmonary congestion on chest radiography for acute heart failure in a retrospective cohort study of 1,333 patients with acute dyspnea admitted to the emergency department.
- This Congestion Score Index was significantly associated with acute heart failure diagnosis.
- The Congestion Score Index also improved diagnostic accuracy over clinical parameters with or without inclusion of natriuretic peptide.
- This good diagnostic accuracy of the Congestion Score Index was externally validated in independent cohorts (N=224).

What do these findings mean?

- The quantification of radiographic pulmonary congestion using the Congestion Score Index improved diagnostic accuracy for acute heart failure on top of clinical parameters and natriuretic peptide.

Introduction

Acute heart failure (HF) is one of the leading causes of acute dyspnea in the emergency department (ED) (1) and is associated with a higher risk of morbidity and mortality (2, 3). In-hospital mortality is reported to be greater than 10% (4) and has remained stable in the last 30 years. As prognosis is associated with initiation time of specific therapies (5), current guidelines emphasize the importance of early diagnosis and treatment initiation to improve clinical outcomes (5, 6). However, a minority of patients with acute HF (AHF) receive treatment within one hour of admission (5), in contradiction with current recommendations (6). In addition, a third of AHF diagnosis are missed in the ED (7), further delaying access to care. An increasing number of better diagnostic tools for AHF are available in the ED (8-10). However, there is likely room for improving the diagnostic approach to AHF from widely available routine tools including chest radiography (CXR).

Chest radiography is a fast and inexpensive method performed systematically in the ED in patients with acute dyspnea (11-13). It is the first-line diagnostic imaging modality advocated in current guidelines (14). However, its diagnostic accuracy for HF has been reported to be relatively low (15-17). In particular, diagnosing HF in patients with concomitant lung diseases such as chronic obstructive pulmonary disease (COPD) and pneumonia still remains a challenge (18).

A new semi-quantitative approach to pulmonary congestion has recently emerged in the field of HF. Congestion score index (CSI) is a semi-quantitative approach to pulmonary congestion based on a 6-zone evaluation of CXR, scoring each zone from 0 (no congestion) to 3 (intense alveolar pulmonary edema). CSI is a strong risk-stratifier in patients with stable or worsening HF (19-21). However, there are little available data regarding its diagnostic value for AHF.

The aims of the present study are to investigate the diagnostic value of pulmonary congestion assessed with CSI for AHF in patients admitted for acute dyspnea in the ED and, to assess its discriminative value comparatively to and on top of currently used clinical diagnostic models and natriuretic peptide measurements.

Methods

Study population

This study is reported as per the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guideline (**S1 Checklist**). The Pathway of dyspneic patients in Emergency (PARADISE) cohort is a retrospective cohort study including consecutive patients aged 18 years or older who were admitted for acute dyspnea in the ED of the Nancy University Hospital (France) between January 1, 2015 and December 31, 2015 as detailed previously (22, 23). The hospital's electronic charts (Resurgences) were systematically reviewed by investigators to search for the records of all patients admitted for acute dyspnea in the ED. All patients with signs or symptoms of dyspnea, or requiring oxygen therapy for dyspnea during (or prior to) their ED stay were included. Patients with shock or cardiac arrest were excluded from this analysis as dyspnea was not the primary condition triggering ED admission. The PARADISE cohort is consequently a cohort of unselected consecutive patients with acute dyspnea in the ED. In the current study, a total of 1,333 dyspneic patients with available information on CXR at the emergency department were analyzed (**S1 Fig**). Demographic parameters, medical history, physical examination, laboratory findings and treatment received in the ED were retrieved from the patients' electronic records.

External validation was performed on the merged dataset from the HF disease management program entitled "Insuffisance CARDiaque en LORraine (ICALOR)" (24, 25) (included at a different time-period than the data from Nancy University Hospital used in the derivation set) and data from Epinal Hospital (a secondary care hospital located at 70 km from Nancy University Hospital) within the PURPLE multi-centre cohort (NCT03194243). Briefly, we used the data from the previously described(20) 117 patients included in the ICALOR disease management cohort during an hospitalization for acutely decompensated HF in the Cardiology Department, of the Nancy University Hospital (France). We also used the data of 107 consecutive patients admitted for acute dyspnea with available CXR data and discharge diagnosis in the Emergency department of the Epinal hospital. This external validation set allowed us to test CSI in a significantly different setting (mixing cardiology department from a tertiary care hospital and an ED of a secondary care hospital) than our derivation set.

Under French law, no formal institutional Review Board approval is required for data extraction from patient medical records in single center cohorts (the PARADISE and ICALOR cohorts). For the PURPLE cohort, patients were informed through a notice at admission and could refuse their inclusion in the study, although no formal consent was required, in keeping with the framework of the Commission Nationale de l'Informatique et des Libertés (CNIL). The PARADISE cohort was recorded by the local hospital corresponding agent of the CNIL (Number R2016-08) and registered on "clinicaltrials.gov" (NCT02800122). The PURPLE cohort was approved by an ethical board ("Comité de Protection des personnes" – Number 2016-63 – ID RCB 2016-A01877-44) and CNIL (Number DR-2017-098), and registered on "clinicaltrials.gov" (NCT03194243).

Diagnosis of Heart Failure

HF was diagnosed according to ESC guidelines (26). Diagnosis of AHF was coded independently by 2 medical physicians (GG and TH) according to ESC guidelines (26). Each physician had access to all ED medical charts as well as additional hospital admission test results and records (*e.g.*, echocardiography, natriuretic peptide level and patient response to diuretic/bronchodilator therapy) but were blinded to CSI quantification on CXR. Homogenous coding was ensured by a trained senior physician (TC). Importantly, to determine the discharge diagnosis, we focused on the main cause of acute dyspnea rather than background medical history or coexisting conditions.

Radiographic Congestion Score Index

Radiographic CSI was used to quantify the severity of pulmonary congestion in CXR as previously published (19, 20). After dividing the lung field into six topographical zones, each area was assessed as follows: Score 0, no congestion sign; Score 1, cephalization (superior area), perihilar haze or perivascular/peribronchial cuffing or Kerley's A lines (middle area), Kerley's B or C lines (inferior area); Score 2, interstitial or localized/mild alveolar pulmonary edema; Score 3, intense alveolar pulmonary edema (**Fig 1**). To enhance the reproducibility of the severity of confluent edema, a portion of the divided lung fields which was visually similar to the cardiac silhouette was regarded as an intense zone, whereas the field with weaker density was regarded as a mildly intense zone. Lung areas

were not scored when more than one third of the divided lung fields were occupied by pleural effusion (including vanishing tumor), atelectasis or cardiac silhouette. CSI was calculated as the sum of the scores in each zone divided by the number of available zones. An examiner also assessed the presence of pneumonia, pleural effusion, cardiomegaly by cardiothoracic ratio (>50%) and the difficulty in assessing CSI.

CXR was analyzed by a single emergency physician (AD), blinded to clinical data and discharge diagnosis, with no previous training in congestion quantification on CXR prior to that in the present study. After a short training (~3 hours) using a 20-patient sample with a radiographic CSI expert (MK), intra-observer and inter-observer agreement (with MK) was tested on 30 randomly selected patients, while blinded to clinical status and diagnosis. Intra-class correlation coefficients showed good reproducibility (intra-observer agreement, 0.85, 95%CI 0.71-0.93 and inter-observer agreement 0.81, 95%CI 0.64-0.90).

Brest Score

The Brest score was calculated for every patient based on the patients' medical charts. This diagnostic score for AHF in dyspneic patients is based on age, comorbidities (*i.e.* prior history of heart failure, myocardial infarction and COPD), pattern of dyspnea, ST segment abnormalities and signs/symptoms of congestion (*i.e.* rales and leg edema) (27, 28).

Statistical analysis

Categorical variables are expressed as frequencies (percentages) and continuous variables as means \pm standard deviation or median (25th and 75th percentiles) according to the distribution of the variables. Comparisons of demographic, clinical and biological parameters among quartiles of radiographic CSI were analyzed using χ^2 tests for categorical variables and ANOVA or Kruskal-Wallis test for continuous variables.

Inter-observer and intra-observer agreements of CSI were assessed with the intraclass correlation coefficient.

We analyzed 1,333 dyspneic patients with 289 AHF diagnosis - which provided a sizeable statistical power to assess diagnostic performance in a multivariable setting (29). A logistic regression model was used to assess the association of CSI with diagnosis of AHF. Multivariable analyses included relevant confounders as previously shown (22): model 1: age, sex, body mass index (BMI), presence of hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, prior HF admission, use of angiotensin converting enzyme inhibitor/angiotensin receptor blocker, beta-blocker, diuretics, leg edema, jugular venous distension, hemoglobin, white blood cell count, estimated glomerular filtration rate (eGFR, as calculated by the Chronic Kidney Disease Epidemiology Collaboration formula (30)) at admission; model 2: Brest Score. Receiver operating characteristics (ROC) curve was used to determine the diagnostic value of CSI in AHF. All correlation coefficients of variables included in the models were less than 0.50 with CSI, suggesting the absence of important in-model collinearity.

The increase in discriminative value of the addition of CSI for AHF diagnosis on top of the aforementioned potential covariates were assessed using continuous net reclassification improvement (NRI) (31). In addition, in 498 (37.4%) patients who had available brain natriuretic peptide (BNP) measurements, the added value of CSI on the top of the Brest Score and BNP was assessed.

This analysis on the PARADISE cohort was planned in February 2019, although no formal analysis was written. The general analysis intention was to evaluate the diagnostic value of CSI for AHF. Of note, among all patients with available data, chest radiography was assessed, blinded for clinical data and diagnosis, and standard statistical approaches were used. Based on recommendations made during the peer-review process, we conducted restricted cubic spline regression analysis for the association between CSI and AHF diagnosis.

All analyses were performed using R version 3.4.0 (R Development Core Team, Vienna, Austria). A two-sided p-value <0.05 was considered statistically significant. No imputation was performed.

Results

Baseline Characteristics

Less than 10% of the population had no available data on CXR (**S1 Table**). These patients were markedly younger and had less comorbidities than patients who underwent CXR. The characteristics of the PARADISE cohort population across different discharge diagnoses such as AHF, COPD and pneumonia are depicted in **S2 Table**.

In a total of 1,333 patients included in this study, a half were men, mean age was 72.0 ± 18.5 years, mean BMI was 25.5 ± 5.5 kg/m² and less than 10% had a prior admission for HF (7.1%) (**Table 1**). CXR was considered as difficult to interpret during CXR reviewing in 502 patients (37.7%). Mean CSI was 1.42 ± 0.79 . Patients with a higher CSI had more cardiovascular risk factors, comorbidities, more frequent prior HF admission, more severe congestion, inflammation status, higher BNP, poorer renal function and more respiratory acidosis at admission (**Table 1**).

Association of Congestion Score Index with Adjudicated Discharge Diagnosis of Acute Heart Failure

In this study, 289 (21.7%) patients were diagnosed with AHF at discharge. Higher CSI was significantly associated with AHF diagnosis (OR [95% CI] for a 0.1-unit increase in CSI=1.22 [1.19-1.25], $p < 0.001$) even after adjustment for potential clinical confounders (adjusted OR [95% CI] in CSI=1.18 [1.15-1.22], $p < 0.001$) and the Brest score (adjusted OR [95% CI] in CSI=1.19 [1.16-1.22], $p < 0.001$). The association of CSI with AHF diagnosis using restricted cubic spline regression analysis is shown in **Fig 2**. CSI had a linear association with AHF diagnosis ($p > 0.05$ for non-linearity), and higher CSI showed an increased risk of AHF diagnosis (OR [95% CI] for CSI score 1.0=4.09 [2.50-6.71], $p < 0.001$; OR [95% CI] for CSI score 1.5=13.92 [6.32-30.65], $p < 0.001$; OR [95% CI] for CSI score 2.0 =37.03 [16.09-85.26] , $p < 0.001$ - considering CSI score 0.5 as a reference). Similar results were observed after adjustment for the Brest Score (adjusted-OR [95% CI] for CSI score 1.0=3.26 [1.93-5.48], $p < 0.001$; adjusted-OR [95% CI] for CSI score 1.5=9.07 [4.00-20.59], $p < 0.001$; adjusted-

OR [95%CI] for CSI score 2.0 =20.88 [8.83-49.35], $p<0.001$ - considering CSI score 0.5 as a reference) (**Fig 2**).

Diagnostic Value of the Congestion Score Index

In the whole population, CSI exhibited high discrimination for AHF as reflected by an area under the curve (AUC) of 0.84 (0.82 to 0.86) (**Fig 3 & Fig 4**). Similarly, high AUC were observed across subgroups of age, sex and comorbidities (obesity, COPD) or associated diagnosis (pneumonia and pleural effusion) (**Fig 3**). In contrast, subgroups without cardiomegaly assessed by CXR had higher AUC compared to those with cardiomegaly (AUC [95%CI]=0.85 [0.81-0.89] vs. 0.75 [0.70-0.79] respectively). In addition, the diagnostic value of CSI was influenced by the patient's position (AUC [95%CI]=0.83 [0.80-0.89] in sitting position and 0.79 [0.73-0.84] in supine position) as well as the difficulty in assessing CSI (AUC [95%CI]=0.92 [0.86-0.97] for easy, 0.84 [0.80-0.88] for moderate and 0.80 [0.75-0.84] for difficult assessments).

AUC for the Brest score was 0.78 [0.75-0.81]. The combination of CSI and Brest score yielded a high AUC for AHF (AUC [95%CI]=0.87 [0.85-0.90]).

Improvement in Reclassification Associated with Acute Heart Failure Diagnosis

The addition of CSI on top of the Brest score significantly improved reclassification of AHF diagnosis (NRI [95%CI]=94.9 [83.5-106.2], $p<0.001$) (**Fig 4**).

Furthermore, in patients with available BNP data (N=496), CSI still significantly improved reclassification of AHF diagnosis on top of BNP and the Brest score (NRI [95%CI]=55.0 [38.0-72.0], $p<0.001$, delta AUC [95%CI]=2.9 [0.6-5.2], $p=0.015$) (**Fig 4 & Fig 5**). The diagnostic value of the joint use of the Brest score and CSI was not significantly different that the joint use of the Brest score and BNP (NRI [95%CI]=4.4 [-13.3-22.1], $p=0.63$, delta AUC [95%CI]=-1.4 [-5.0-2.1], $p=0.42$). In this subgroup, the Brest score had a moderate accuracy (AUC [95%CI]=0.72 [0.75-0.81]), but the

combination of CSI, BNP and Brest score resulted in high diagnostic value for AHF (AUC [95% CI]=0.85 [0.82-0.89]) (**Fig 5**).

Validation in external cohorts

In the validation cohorts (N=224), more than a half of the patients (56.7%) were men, mean age was 75.8±13.9 years, mean CSI was 1.85±0.87, and 72.7% had a diagnosis of AHF at discharge. The diagnostic performance of CSI was externally validated (AUC [95% CI]=0.75 [0.68-0.82]).

Discussion

Our results show that pulmonary congestion quantified by a simple standardized CXR scoring can efficiently identify patients with AHF in the ED, consistently across the various subgroups (e.g., elderly, overweight, COPD and pneumonia). Furthermore, CSI significantly improved the reclassification of AHF diagnosis on top of the recognized clinical diagnostic markers of AHF and natriuretic peptides. Our findings suggest that a semi-quantified assessment of congestion on CXR could represent a readily available and clinically useful diagnostic tool for AHF in acute dyspneic patients in the emergency department.

Radiographic Congestion Score Index as a Diagnostic Tool for Acute Heart Failure

CXR exhibited a higher diagnostic performance for AHF than usually reported in the literature (15-17). Of note, previous reports assessed the diagnostic value of CXR using a single or combination of typical radiographic signs of congestion using a global evaluation of the lungs (16, 17, 32-34) rather than a systematic approach, with lung segmentation as used in the CSI method. Our group recently showed that more severe pulmonary congestion, quantified by either CSI or lung ultrasound at admission, was associated with higher pulmonary artery systolic pressure (20, 35). This association of CSI with hemodynamic data emphasizes the mechanistic plausibility of our results.

Recent registry data have shown that approximately 20% of patients hospitalized for AHF had concomitant lung diseases such as pneumonia and COPD (36-38), and these patients generally excluded in previous reports assessing the diagnostic value of CXR (17, 18, 39, 40). However, our subgroup analysis provided a remarkably homogenous diagnostic performance of CSI across various subgroups (i.e., elderly, body mass index) and coexisting lung diseases (i.e., COPD and pneumonia). The only factor appearing to decrease the diagnostic value of CSI was cardiomegaly, possibly as a result of the overlapping of relevant information of the lung fields with cardiac silhouette in these patients.

Radiographic Congestion Score Index and Other Diagnostic Measurements: Clinical Parameters and Natriuretic Peptide

In keeping with previous literature data (20, 41), our results showed that patients with more severe pulmonary congestion were predominantly elderly, had higher BMI, more cardiovascular risk factors and comorbidities, severe congestion, poorer renal function and higher inflammatory markers. In the latest guidelines, natriuretic peptide is recommended to rule out non-HF related causes of acute dyspnea, although accumulated data suggested the overall diagnostic accuracy of natriuretic peptide (42-46). However, multiple comorbidity burden (i.e. older age and poor renal function) may lead to diagnostic uncertainty in a sizeable proportion of dyspneic patients (8). BNP, in addition, requires time to measure and is not always available in routine clinical practice. In cases with unequivocal diagnosis of AHF based on clinical parameters, prompt treatment approach is recommended rather than wait for its result (6). In this regard, the Brest score, based on clinical parameters, may be pragmatic tool as well as good diagnostic accuracy for diagnosing HF as previously shown (28). However, in the current study, more than half of dyspneic patients have intermediate scores, suggesting that this clinical score may need to be complemented by more refined strategies in this relatively frequent “grey zone”. The unmet need in clinical practice, even when using the Brest score and natriuretic peptides, thus remains high.

In the current study, CSI was found to improve reclassification of AHF diagnosis on top of the Brest score and BNP. In addition, the combination of CSI and the Brest score improved the diagnostic value (AUC 0.81) to a similar degree of the combination of BNP and the Brest score (AUC 0.82). CSI also significantly improved diagnostic accuracy on top of the Brest Score and BNP, and the combined use of these 3 parameters resulted in an AUC of 0.85. Taken together, these findings further strengthen that CSI may play a complementary role to the clinical model and natriuretic peptides in diagnosing AHF.

Clinical Implications

An early accurate diagnosis and consequently a prompt appropriate management improve outcomes in AHF patients admitted to the ED (47) (5, 48). Our results show that a standardized evaluation of CXR, using CSI, improves diagnosis performance and potentially the ability to swiftly manage AHF in the ED. The assessment of radiographic pulmonary congestion requires training period. However,

this approach may be easily scalable since training for this assessment is fairly simple; the operator (AD) who evaluated all CXRs of this cohort efficiently acquired the technique in the context of this study in a matter of a few hours.

Recent studies showed the clinical utility of lung ultrasound to diagnose AHF in dyspneic patients with high specificity and high sensitivity (10, 27, 49), and its diagnostic accuracy was better than that of CXR(9, 50). Of note, these previous studies did not include quantitative assessment of radiographic pulmonary congestion. In any event, based on the promising results herein, multi-center trials may be warranted to assess the impact of the implementation of CSI on AHF diagnosis in patients with acute dyspnea. Furthermore, further study to compare diagnostic value between CSI on chest radiography and lung ultrasound is worthy undertaking.

Limitations and strengths

The main limitation of our derivation cohort was its single-center and retrospective nature, although the external validation of our results may lead to generalize our findings. The overall proportion of AHF diagnosis was relatively low, which may explain the fact that a low number of patients had congestion signs (i.e., leg edema, rales and jugular venous distention) and cardiovascular diseases. In our center (as in most centers in France), some dyspneic patients known to have HF and all patients with obvious evidence of myocardial ischemia were admitted directly in the intensive cardiac care unit/cardiology ward, not through the ED (51). The proportion of AHF diagnosis possibly due to the health care system may influence our results. However, it should be noted that hospitalization rates for worsening HF in the ED declined over past decades (52), which may result from the development of disease management program to prevent urgent HF hospitalization (53). Indeed, the proportion of AHF diagnosis in the present study was similar to that of dyspneic patients in other contemporary cohorts (45, 54). Ejection fraction was not recorded; thus, we did not evaluate the diagnostic accuracy of CSI across levels of ejection fraction. This parameter, however, is usually not a major determinant of decision-making for acute dyspneic management in the ED (6, 13).

In the derivation cohort, we had no data on CSI in 138 (9.4%) patients who did not undergo CXR or had no available lung field to assess CSI. These patients, however, had better clinical status (i.e., younger age and less severe congestion), and only 8% of these patients (N=11) were diagnosed AHF (**S1 Table**). In addition, all CSI readings were performed blinded for other parameters and diagnoses, suggesting that this limitation is unlikely to have major influence on our findings.

CSI is a semi-quantitative tool with some subjectivity. Although accurate and reproducible scoring was achieved after about 3-hour training period in the current study and one of our previous study (20), more evidence may be needed to ascertain the appropriate learning period.

Lastly, the assessment of CSI was difficult in 502 (37.7%) of patients which may limit its applicability in routine clinical practice. However, the diagnostic value of CSI persisted in these patients (AUC=0.80, 0.75-0.84) and the difficulty in assessing CSI did not influence its diagnostic accuracy ($P_{\text{interaction}}=0.13$).

Conclusions

Our study shows that a semi-quantified assessment of radiographic pulmonary congestion provided diagnostic value for AHF in dyspneic patients of similar magnitude to that of BNP. These results suggest that implementing radiographic CSI in the diagnostic approach to AHF in addition to clinical parameters and BNP measurement could benefit the management of acute heart failure patients. Better use of chest radiography may provide an inexpensive, widely, and readily available method for acute heart failure triage in the emergency department. Multicenter prospective studies are nonetheless needed to confirm the diagnostic value of radiographic CSI.

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S1 Checklist. TRIPOD checklist.

S1 Fig. Flow Chart

S1 Table. Baseline Characteristics of Patients with Available and Unavailable Chest Radiograph

S2 Table. Patient Characteristics across Different Discharge Diagnoses

Fig 1. Radiographic Congestion Score Index

The scoring is performed on six lung fields. The absence of radiographic congestion signs in a lung field is graded as a score of “0”.

Panels A and B provide examples.

A) Example: $CSI = (2+3+3+3+2+1)/6=2.33$. There is diffuse alveolar edema, appearing as intense edema in the left superior field and middle fields.

B) Example: $CSI = (1+1+1+1+1+0)/6=0.83$. Cephalization in superior fields, and peribronchial and perivascular cuffing are visible in middle fields, respectively.”

*Confluent edema was regarded as intense edema, when the density in an area of the divided lung field was visually similar to that of cardiac silhouette.

Fig 2. Association between Congestion Score Index and Discharge Diagnosis of Acute Heart Failure

AHF, acute heart failure

Multivariable model included the Brest score, which was calculated from age, comorbidity burden, dyspnea, ST segment abnormalities and clinical congestion. Dotted lines/shaded regions represent 95% CI.

Fig 3. Diagnostic Value of Radiographic Congestion Score Index for Acute Heart Failure

*Pneumonia was diagnosed at discharge.

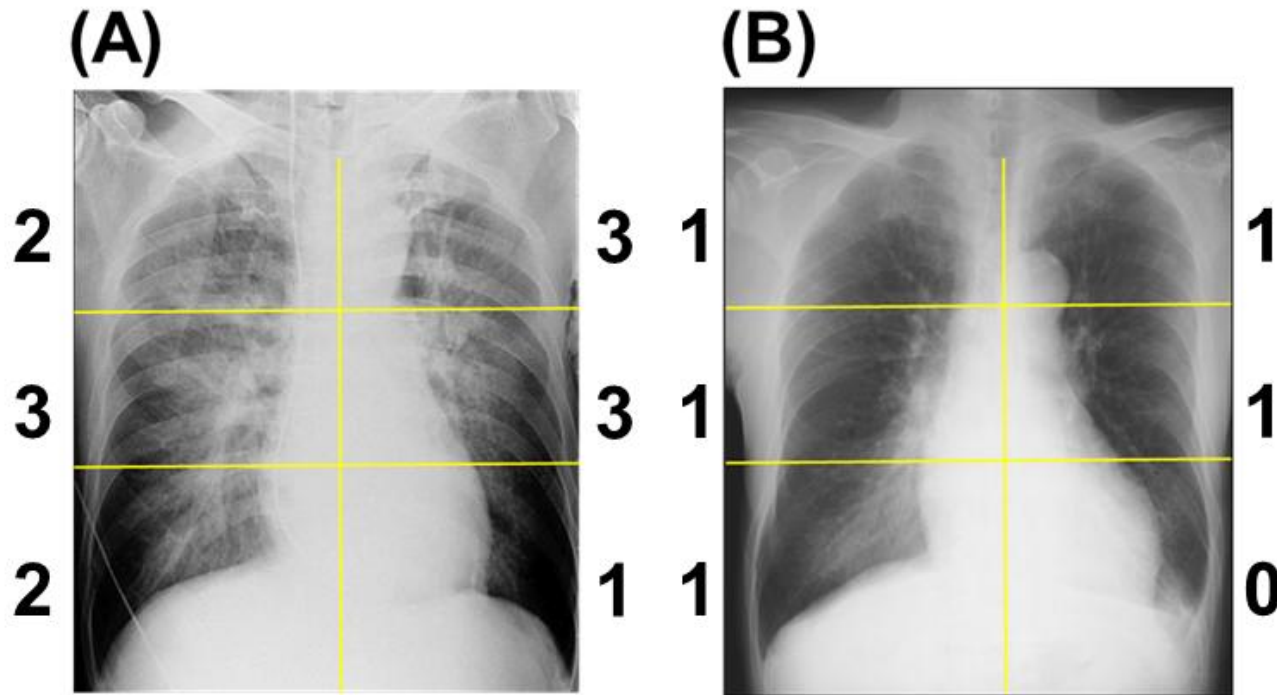
Fig 4, Diagnostic Performance of the Radiographic Congestion Score Index

On the receiving operating characteristic curve for the association between CSI and AHF diagnosis, the red shaded region represents the 90% or greater specificity zone ($CSI \leq 1.3$) whereas the green shaded region represents the 90% or greater sensitivity zone ($CSI > 2.2$). On the top portion of the figure, chest radiography panels illustrate typical examples of radiographies in the 3 zones, with CSI score of “1”, “2” and “3”, respectively from left to right.

Fig 5. Added values of CSI and BNP for the Diagnosis of Acute Heart Failure on Top of the BREST Score in Patients with Available BNP (N=496)

CSI, congestion score index; BNP, b-type natriuretic peptide; AUC, area under the curve; NRI, net classification improvement.

Fig 1. Radiographic Congestion Score Index



	1	2			3
Superior	Cephalization	Interstitial pulmonary edema	Alveolar pulmonary edema		
Middle	Peribronchial cuffing Perivascular cuffing Kerley A line		Localized edema	Confluent mild edema*	Confluent Intense edema*
Inferior	Kerley B line Kerley C line				
No congestive sign; Vanishing tumor / Costophrenic angle					

Fig 2. Association between Congestion Score Index and Discharge Diagnosis of Acute Heart Failure

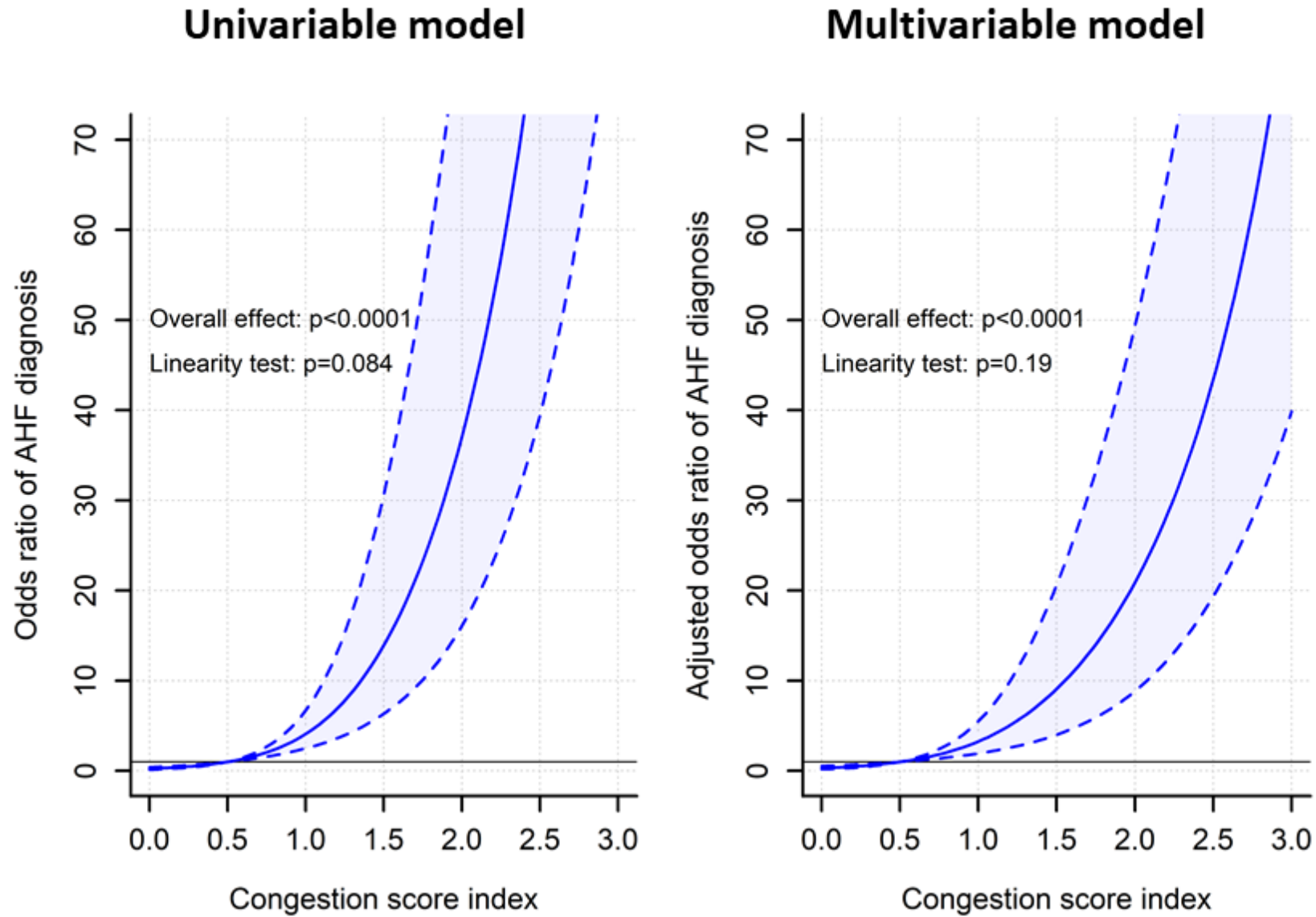


Fig 3. Diagnostic Value of Radiographic Congestion Score Index for Acute Heart Failure

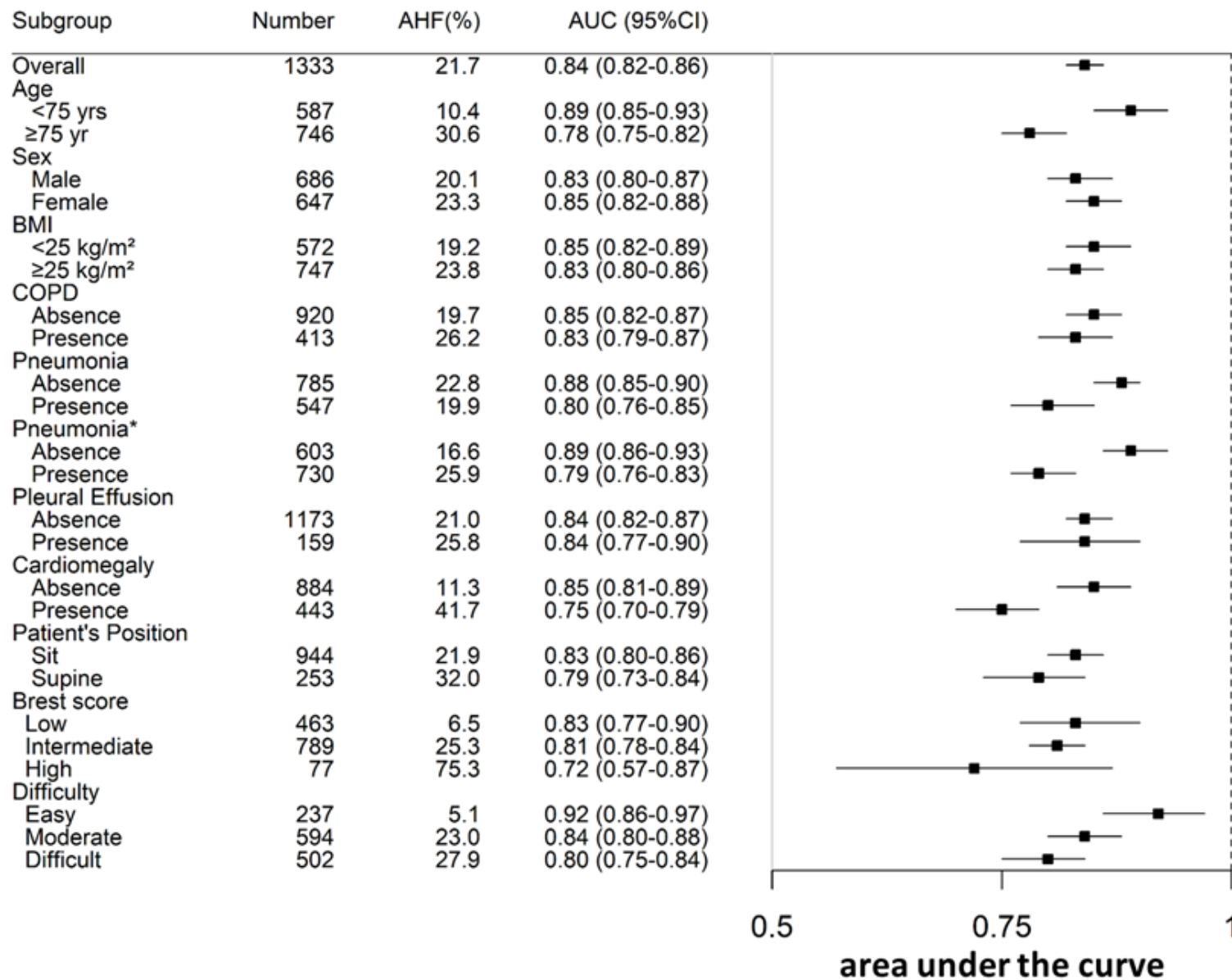


Fig 4, Diagnostic Performance of the Radiographic Congestion Score Index

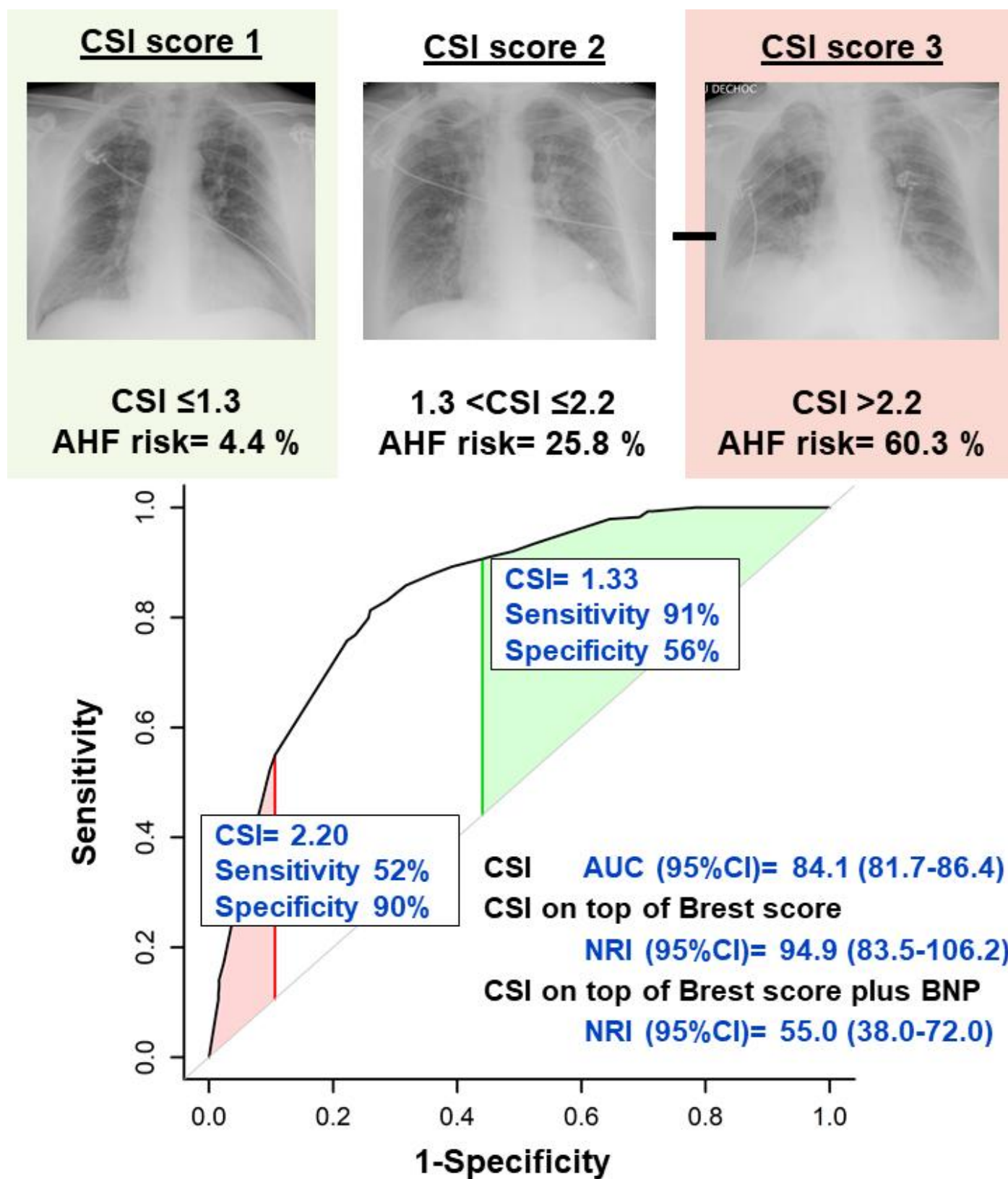
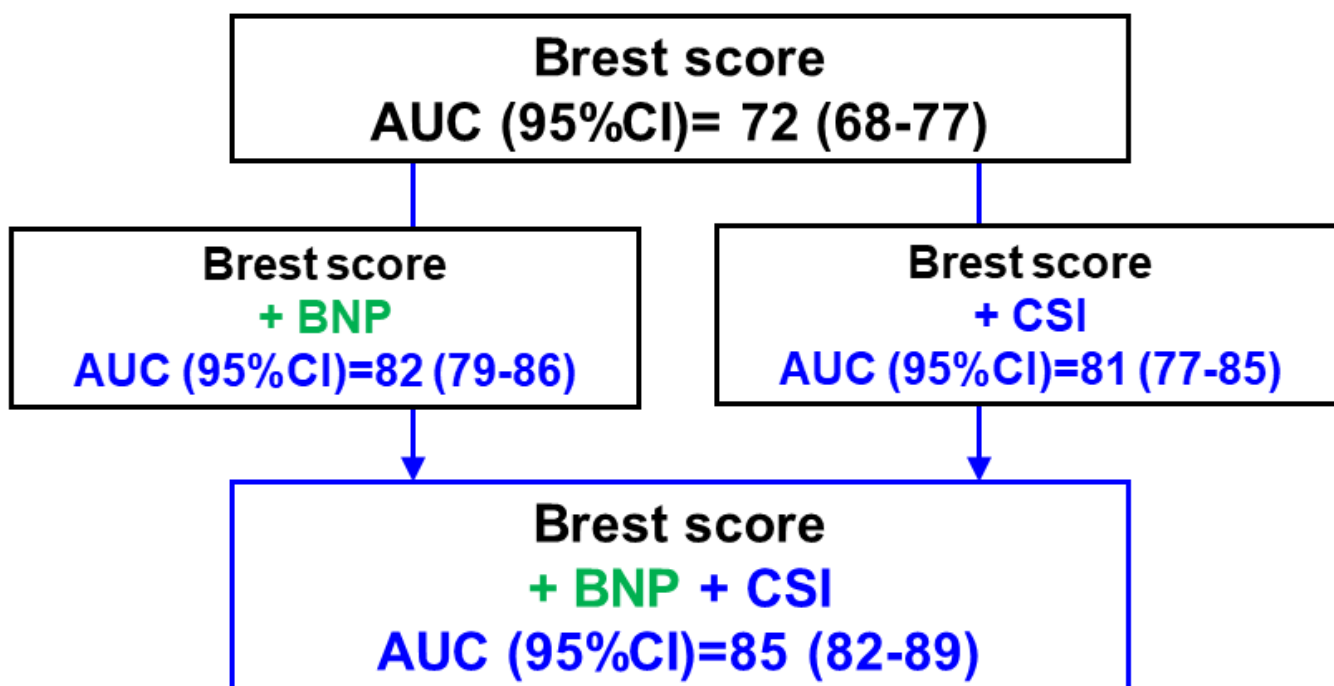


Fig 5. Added values of CSI and BNP for the Diagnosis of Acute Heart Failure on Top of the BREST Score in Patients with Available BNP (N=496)



Baseline model	CSI		BNP	
	delta AUC (95%CI)	NRI (95%CI)	delta AUC (95%CI)	NRI (95%CI)
on top of Brest score	9 (5-12)	75 (59-91)	10 (7-13)	74 (58-90)
on top of Brest score + BNP	3 (1-5)	55 (38-72)	—	—
on top of Brest score + CSI	—	—	4 (2-6)	63 (47-79)

Table 1. Baseline Characteristics according to the Radiographic Congestion Score Index (Quartiles)

Values are mean \pm SD, n (%) or median (25th to 75th percentile)

* p-value adjusted for age and body mass index at admission.

HF, heart failure; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; BNP, brain natriuretic peptide; PaO₂, partial pressure of oxygen; PaCO₂, partial pressure of carbon dioxide

Table 1. Baseline Characteristics according to the Radiographic Congestion Score Index (Quartiles)

	CSI quartiles					%missing value	p-value	Adjusted p-value*
	Global (N=1333)	Quartile I, <0.84 (N=376)	Quartile II, 0.84-1.40 (N=328)	Quartile III, 1.40-2.00 (N=359)	Quartile IV, ≥2.00 (N=270)			
Age, yrs	72.0 ± 18.5	57.4 ± 20.9	73.4 ± 15.4	79.3 ± 12.6	80.9 ± 11.8	0	<0.001	—
Men, N (%)	686 (51.5 %)	212 (56.4 %)	168 (51.2 %)	166 (46.2 %)	140 (51.9 %)	0	0.06	0.26
Body mass index, kg/m ²	25.5 ± 5.5	24.7 ± 4.8	25.3 ± 5.0	25.5 ± 5.8	26.8 ± 6.4	1.1	<0.001	—
Medical history, N (%)								
Hypertension	729 (54.7 %)	111 (29.5 %)	194 (59.1 %)	236 (65.7 %)	188 (69.6 %)	0	<0.001	0.03
Diabetes mellitus	302 (22.7 %)	50 (13.3 %)	62 (18.9 %)	94 (26.2 %)	96 (35.6 %)	0	<0.001	0.03
Dyslipidemia	280 (21.0 %)	51 (13.6 %)	79 (24.1 %)	82 (22.8 %)	68 (25.2 %)	0	<0.001	0.36
Coronary artery disease	162 (12.2 %)	16 (4.3 %)	36 (11.0 %)	63 (17.5 %)	47 (17.4 %)	0	<0.001	0.001
Atrial fibrillation	313 (23.5 %)	33 (8.8 %)	70 (21.3 %)	107 (29.8 %)	103 (38.1 %)	0	<0.001	0.003
Heart failure	258 (19.4 %)	21 (5.6 %)	47 (14.3 %)	93 (25.9 %)	97 (35.9 %)	0	<0.001	< 0.001
Prior HF admission, N (%)	95 (7.1 %)	6 (1.6 %)	15 (4.6 %)	28 (7.8 %)	46 (17.0 %)	0	<0.001	< 0.001
Medication, N (%)								
ACEi/ARB	444 (34.7 %)	67 (18.3 %)	112 (36.5 %)	142 (40.8 %)	123 (47.7 %)	4.1	<0.001	0.02
Beta-blocker	306 (23.9 %)	45 (12.3 %)	70 (22.8 %)	103 (29.6 %)	88 (34.1 %)	4.1	<0.001	0.047
Spironolactone	64 (5.0 %)	16 (4.4 %)	13 (4.2 %)	19 (5.5 %)	16 (6.2 %)	4.1	0.65	0.88
Diuretics	368 (28.8 %)	40 (10.9 %)	81 (26.4 %)	127 (36.5 %)	120 (46.5 %)	4.1	<0.001	< 0.001
Calcium channel blocker	258 (20.2 %)	24 (6.6 %)	67 (21.8 %)	82 (23.6 %)	85 (32.9 %)	4.1	<0.001	< 0.001
Statin	300 (23.5 %)	58 (15.8 %)	81 (26.4 %)	87 (25.0 %)	74 (28.7 %)	4.1	<0.001	0.58
O ₂ flow, L/min	4.0 (2.0 - 9.0)	3.0 (2.0 - 9.0)	3.0 (2.0 - 9.0)	3.0 (2.0 - 9.0)	5.0 (3.0 - 9.0)	53.0	0.005	0.001
Physical examination, N (%)								
Leg edema	334 (25.1 %)	28 (7.4 %)	65 (19.8 %)	117 (32.6 %)	124 (45.9 %)	0	<0.001	< 0.001
Jugular venous distension	43 (3.3 %)	4 (1.1 %)	8 (2.4 %)	12 (3.4 %)	19 (7.3 %)	1.4	<0.001	0.04
Rales	454 (35.2 %)	63 (17.3 %)	104 (32.3 %)	148 (42.8 %)	139 (54.5 %)	3.4	<0.001	< 0.001
Systolic BP, mmHg	132.1 ± 26.0	129.6 ± 22.7	132.3 ± 26.0	132.9 ± 26.8	134.5 ± 28.9	0.1	0.13	0.98
Diastolic BP, mmHg	73.5 ± 17.6	77.2 ± 16.3	72.4 ± 17.8	71.6 ± 18.1	72.4 ± 18.0	0.1	<0.001	0.40
Heart rate, bpm	95.7 ± 20.7	98.1 ± 19.0	94.7 ± 20.2	94.2 ± 20.1	95.5 ± 23.8	0.4	0.02	0.32
Respiratory rate, /min	26.3 ± 7.9	24.5 ± 7.6	26.5 ± 7.5	26.8 ± 8.0	27.5 ± 8.4	31.3	<0.001	0.19
Congestion score index	1.4 ± 0.8	0.5 ± 0.3	1.2 ± 0.2	1.8 ± 0.2	2.5 ± 0.3	0	<0.001	< 0.001
Laboratory findings								
Hemoglobin, g/dl	12.8 ± 2.0	13.5 ± 1.9	12.8 ± 2.0	12.6 ± 2.0	12.2 ± 2.0	0.3	<0.001	< 0.001
White blood cell count, μl	11300 (8300 - 15400)	10765 (8420 - 14100)	10900 (7700 - 15100)	11575 (7800 - 15600)	12600 (8900 - 16700)	2.0	0.006	0.007
C-reactive protein, mg/dl	6.6 (1.8 - 14.0)	3.9 (0.8 - 10.5)	7.7 (2.3 - 14.8)	7.7 (2.3 - 14.5)	7.1 (2.1 - 15.4)	7.7	<0.001	< 0.001

Sodium, mmol/l	136.9 ± 5.3	137.1 ± 4.9	136.3 ± 5.4	137.0 ± 5.7	137.2 ± 5.0	2.7	0.17	0.003
Potassium, mmol/l	4.1 ± 0.6	4.0 ± 0.5	4.1 ± 0.6	4.2 ± 0.6	4.3 ± 0.7	5.6	<0.001	<0.001
Blood glucose, mmol/l	7.7 ± 3.5	6.8 ± 2.6	7.4 ± 3.0	7.8 ± 3.4	9.3 ± 4.5	3.0	<0.001	<0.001
BUN, mg/dl	25.3 ± 18.0	19.3 ± 15.5	23.5 ± 15.9	27.7 ± 17.5	32.6 ± 20.8	2.9	<0.001	<0.001
eGFR, ml/min/1.73m²	82.6 ± 55.4	96.2 ± 38.4	85.0 ± 42.2	79.8 ± 83.1	65.4 ± 34.4	3.5	<0.001	0.03
BNP, pg/ml	274 (133 - 590)	65 (37 - 183)	155 (83 - 262)	280 (154 - 592)	480 (286 - 837)	62.6	<0.001	<0.001
Blood gas								
PH	7.41 (7.34 - 7.45)	7.43 (7.39 - 7.46)	7.42 (7.37 - 7.46)	7.41 (7.34 - 7.45)	7.36 (7.28 - 7.42)	18.8	<0.001	<0.001
PaO₂, mmHg	65.0 (56.0 - 79.0)	64.0 (58.0 - 78.0)	64.5 (56.0 - 79.5)	64.0 (53.0 - 79.0)	66.0 (57.0 - 79.0)	19.0	0.68	0.57
PaCO₂, mmHg	40.4 (35.0 - 48.0)	39.0 (34.0 - 44.0)	41.0 (35.0 - 47.0)	41.0 (35.2 - 51.0)	42.0 (36.0 - 52.0)	18.8	<0.001	<0.001
Lactate, mmol/L	1.10 (0.80 - 1.60)	1.00 (0.70 - 1.50)	1.00 (0.80 - 1.40)	1.10 (0.80 - 1.70)	1.10 (0.80 - 1.90)	19.5	0.008	<0.001

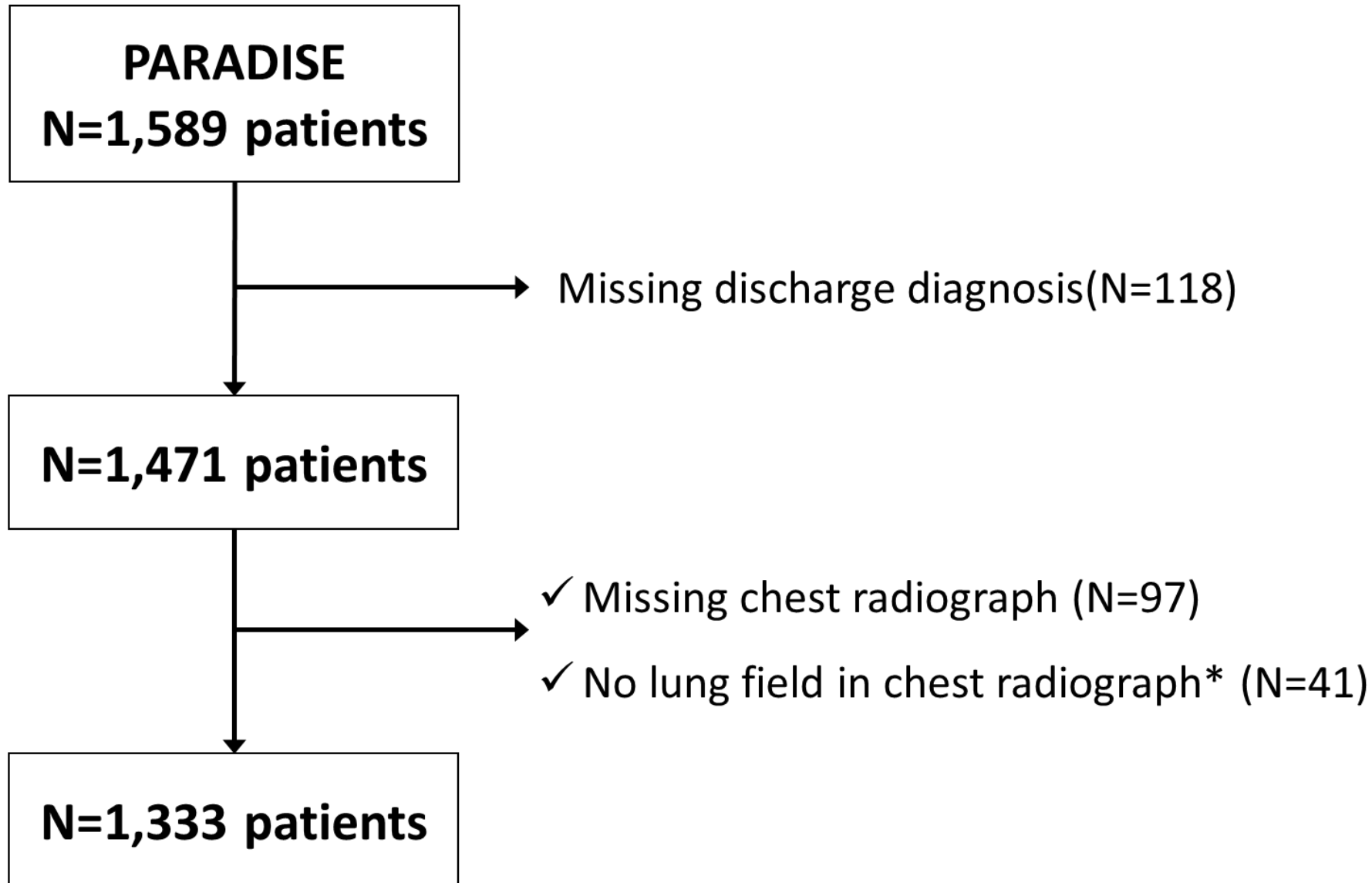
S1 Checklist. TRIPOD checklist

Section/Topic Item Checklist Item Page			
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	Title page
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	Abstract section
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	Introduction section Paragraph 1-3
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	Introduction section Paragraph 4
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	Study population (Methods) Paragraph 1
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	Study population (Methods) Paragraph 1
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centers.	Study population (Methods) Paragraph 1
	5b	Describe eligibility criteria for participants.	Study population (Methods) Paragraph 1
	5c	Give details of treatments received, if relevant.	—
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	Diagnosis of Heart Failure (Methods) Paragraph 1
	6b	Report any actions to blind assessment of the outcome to be predicted.	Diagnosis of Heart Failure (Methods) Paragraph 1
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	Radiographic Congestion Score Index (Methods) Paragraph 1
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	Radiographic Congestion Score Index (Methods) Paragraph 2
Sample size	8	Explain how the study size was arrived at.	Statistical analysis (Methods) Paragraph 3
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	Statistical analysis (Methods) Paragraph 5
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	Statistical analysis (Methods) Paragraph 3
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	Statistical analysis (Methods) Paragraph 3
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	Statistical analysis (Methods) Paragraph 3
Risk groups	11	Provide details on how risk groups were created, if done.	—
Results			

Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	S1 Fig
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	Baseline Characteristics (Results) Paragraph 1 and 2 & S1 Fig
Model development	14a	Specify the number of participants and outcome events in each analysis.	Association of Congestion Score Index with Adjudicated Discharge Diagnosis of Acute Heart Failure (Results) Paragraph 1
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	Association of Congestion Score Index with Adjudicated Discharge Diagnosis of Acute Heart Failure (Results) Paragraph 1
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	Diagnostic Value of the Congestion Score Index (Results) Paragraph 1 and 2
	15b	Explain how to use the prediction model.	Diagnostic Value of the Congestion Score Index (Results) Paragraph 1 and 2
Model performance	16	Report performance measures (with CIs) for the prediction model.	Diagnostic Value of the Congestion Score Index (Results) Paragraph 1 and 2
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	Limitations and strengths (Discussion) Paragraph 1- 4
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	Discussion Paragraph 1- 5
Implications	20	Discuss the potential clinical use of the model and implications for future research.	Discussion Paragraph 1 (Clinical implications -Paragraph 1)
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	—
Funding	22	Give the source of funding and the role of the funders for the present study.	Funding

S1 Fig. Flow Chart

*Patients had no available lung field in their chest radiograph due to pleural effusion, atelectasis or cardiac silhouette.



S1 Table. Baseline Characteristics of Patients with Available and Unavailable Chest Radiograph

	Global (N=1,471)	Chest radiograph Unavailable (N=138)	Chest radiograph Available (N=1,333)	p-value
Age, yrs	70.1 ± 20.1	51.4 ± 24.7	72.0 ± 18.5	<0.0001
Men, N (%)	750 (51.0 %)	66 (47.8 %)	684 (51.3 %)	0.44
Body mass index, kg/m ²	25.5 ± 5.5	25.2 ± 4.8	25.5 ± 5.5	0.80
Medical history, N (%)				
Hypertension	773 (52.5 %)	44 (31.9 %)	729 (54.7 %)	<0.0001
Diabetes mellitus	318 (21.6 %)	16 (11.6 %)	302 (22.7 %)	0.003
Dyslipidemia	298 (20.3 %)	18 (13.0 %)	280 (21.0 %)	0.027
Coronary artery disease	176 (12.0 %)	14 (10.1 %)	162 (12.2 %)	0.49
Atrial fibrillation	327 (22.2 %)	14 (10.1 %)	313 (23.5 %)	0.0003
Heart failure	275 (18.7 %)	17 (12.3 %)	258 (19.4 %)	0.044
Prior HF admission	95 (7.1 %)	NA	95 (7.1 %)	NA
Medication, N (%)				
ACEi/ARB	468 (33.1 %)	24 (18.0 %)	444 (34.7 %)	0.0001
Beta-blocker	323 (22.9 %)	17 (12.8 %)	306 (23.9 %)	0.004
Spironolactone	70 (5.0 %)	6 (4.5 %)	64 (5.0 %)	0.80
Diuretics	387 (27.4 %)	19 (14.3 %)	368 (28.8 %)	0.0004
Calcium channel blocker	276 (19.5 %)	18 (13.5 %)	258 (20.2 %)	0.066
Statin	323 (22.9 %)	23 (17.3 %)	300 (23.5 %)	0.11
O ₂ flow, L/min	4.0 (2.0 - 9.0)	6.0 (3.0 - 9.0)	4.0 (2.0 - 9.0)	0.024
Physical examination, N (%)				
Leg edema	345 (23.5 %)	11 (8.0 %)	334 (25.1 %)	<0.0001
Jugular venous distension	45 (3.1 %)	2 (1.5 %)	43 (3.3 %)	0.38
Rales	454 (35.2 %)	NA	454 (35.2 %)	NA
Systolic BP, mmHg	131.8 ± 25.7	128.8 ± 22.0	132.1 ± 26.0	0.17
Diastolic BP, mmHg	73.7 ± 17.4	75.9 ± 14.9	73.5 ± 17.6	0.032
Heart rate, bpm	95.6 ± 20.7	95.0 ± 20.8	95.7 ± 20.7	0.71
Respiratory rate, /min	26.2 ± 8.0	24.3 ± 8.9	26.3 ± 7.9	0.004
Laboratory findings				
Hemoglobin, g/dl	12.8 ± 2.0	12.6 ± 2.1	12.8 ± 2.0	0.73
White blood count	11200 (8200 - 15400)	10100 (8100 - 14000)	11300 (8300 - 15400)	0.20
C-reactive protein, mg/dl	65.8 (17.8 - 140.0)	42.0 (10.5 - 102.4)	66.4 (18.0 - 140.0)	0.18
Sodium, mmol/l	137.0 ± 5.4	138.6 ± 8.0	136.9 ± 5.3	0.32
Potassium, mmol/l	4.1 ± 0.6	4.1 ± 0.6	4.1 ± 0.6	0.92
Blood glucose, mmol/l	7.7 ± 3.5	7.5 ± 3.2	7.7 ± 3.5	0.78
BUN, mg/dl	25.5 ± 19.2	28.9 ± 38.0	25.3 ± 18.0	0.43
eGFR, ml/min/1.73m²	82.5 ± 54.9	79.9 ± 37.0	82.6 ± 55.4	0.75
BNP, pg/ml	269 (125 - 586)	115 (59 - 280)	274 (133 - 590)	0.011
Blood gas				
PH	7.41 (7.34 - 7.45)	7.40 (7.31 - 7.46)	7.41 (7.34 - 7.45)	0.94
PaO₂, mmHg	65.0 (56.0 - 79.0)	65.0 (52.0 - 80.5)	65.0 (56.0 - 79.0)	0.81
PaCO₂, mmHg	40.0 (35.0 - 48.0)	39.5 (32.5 - 47.5)	40.4 (35.0 - 48.0)	0.46
Lactate, mmol/L	1.10 (0.80 - 1.60)	1.05 (0.75 - 1.55)	1.10 (0.80 - 1.60)	0.64
Diagnosis of AHF at discharge	300 (20.4 %)	11 (8.0 %)	289 (21.7 %)	0.0001

Values are mean ±SD, n (%) or median (25th to 75th percentile)

HF, heart failure; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; BNP, brain natriuretic peptide; PH, potential of hydrogen; PaO₂, partial pressure of oxygen; PaCO₂, partial pressure of carbon dioxide; AHF, acute heart failure.

S2 Table. Patient Characteristics across Different Discharge Diagnoses

	Acute heart failure (N=289)				non acute heart failure (N=1044)			p-value
	ACS (N=12)	Lung disease (N=189)	AF (N=8)	Others (N=80)	COPD/ Asthma (N=286)	Bronchitis/ Pneumonia (N=541)	Others (N=217)	
Age, yrs	82.0 ± 9.7	82.7 ± 9.3	77.6 ± 11.3	80.6 ± 11.9	67.5 ± 17.4	73.2 ± 18.0	61.9 ± 22.3	<0.001
Men, N (%)	6 (50.0 %)	90 (47.6 %)	6 (75.0 %)	36 (45.0 %)	150 (52.4 %)	271 (50.1 %)	127 (58.5 %)	0.17
Body mass index, kg/m ²	25.3 ± 5.1	27.1 ± 6.8	29.1 ± 4.0	26.3 ± 5.6	25.6 ± 5.9	25.2 ± 5.0	24.4 ± 4.7	<0.001
Medical history, N (%)								
Hypertension	10 (83.3 %)	141 (74.6 %)	4 (50.0 %)	56 (70.0 %)	136 (47.6 %)	295 (54.5 %)	87 (40.1 %)	<0.001
Diabetes mellitus	5 (41.7 %)	71 (37.6 %)	4 (50.0 %)	29 (36.2 %)	57 (19.9 %)	106 (19.6 %)	30 (13.8 %)	<0.001
Coronary artery disease	5 (41.7 %)	36 (19.0 %)	3 (37.5 %)	19 (23.8 %)	41 (14.3 %)	46 (8.5 %)	12 (5.5 %)	<0.001
Atrial fibrillation	5 (41.7 %)	83 (43.9 %)	4 (50.0 %)	30 (37.5 %)	48 (16.8 %)	114 (21.1 %)	29 (13.4 %)	<0.001
Heart failure	5 (41.7 %)	86 (45.5 %)	5 (62.5 %)	42 (52.5 %)	39 (13.6 %)	61 (11.3 %)	20 (9.2 %)	<0.001
Prior HF admission, N (%)	2 (16.7 %)	37 (19.6 %)	4 (50.0 %)	22 (27.5 %)	11 (3.8 %)	13 (2.4 %)	6 (2.8 %)	<0.001
Medication, N (%)								
ACEi/ARB	7 (63.6 %)	80 (43.7 %)	3 (37.5 %)	40 (51.3 %)	85 (30.8 %)	179 (34.8 %)	50 (24.0 %)	<0.001
Beta-blocker	4 (36.4 %)	63 (34.4 %)	6 (75.0 %)	34 (43.6 %)	39 (14.1 %)	123 (23.9 %)	37 (17.8 %)	<0.001
Diuretics	3 (27.3 %)	84 (45.9 %)	4 (50.0 %)	35 (44.9 %)	80 (29.0 %)	135 (26.2 %)	27 (13.0 %)	<0.001
Statin	8 (72.7 %)	55 (30.1 %)	4 (50.0 %)	24 (30.8 %)	67 (24.3 %)	108 (21.0 %)	34 (16.3 %)	<0.001
O ₂ flow, L/min (N=627)	9.0 (3.0 - 12.0)	4.0 (3.0 - 9.0)	6.0 (3.0 - 9.0)	6.0 (2.0 - 9.0)	3.0 (2.0 - 6.0)	4.0 (2.0 - 9.0)	6.0 (2.5 - 9.0)	0.063
Physical examination, N (%)								
Leg edema	6 (50.0 %)	108 (57.1 %)	4 (50.0 %)	45 (56.2 %)	58 (20.3 %)	86 (15.9 %)	27 (12.4 %)	<0.001
Jugular venous distension	3 (27.3 %)	13 (7.0 %)	0 (0.0 %)	7 (9.0 %)	4 (1.4 %)	11 (2.1 %)	5 (2.3 %)	<0.001
Rales	6 (50.0 %)	124 (67.8 %)	5 (83.3 %)	45 (59.2 %)	75 (27.0 %)	158 (30.4 %)	41 (19.2 %)	<0.001
Systolic BP, mmHg	130.0 ± 26.8	139.1 ± 27.7	131.0 ± 26.3	138.3 ± 31.9	132.5 ± 23.6	128.3 ± 25.9	132.9 ± 24.0	<0.001
Heart rate, bpm	104.8 ± 21.7	92.1 ± 20.6	101.1 ± 21.0	92.1 ± 23.2	96.8 ± 19.4	97.7 ± 20.6	92.9 ± 21.0	0.001
Respiratory rate, /min	26.3 ± 9.8	28.3 ± 8.2	23.2 ± 4.4	26.0 ± 7.2	25.8 ± 6.8	26.6 ± 8.3	24.7 ± 8.4	0.006
Congestion score index	2.2 ± 0.5	2.1 ± 0.6	2.5 ± 0.4	2.2 ± 0.6	1.1 ± 0.7	1.4 ± 0.7	0.9 ± 0.7	<0.001
Laboratory findings								
Hemoglobin, g/dl	13.2 ± 1.8	12.4 ± 1.8	12.7 ± 3.5	12.1 ± 2.0	13.5 ± 1.8	12.6 ± 2.0	13.0 ± 2.1	<0.001
White blood count, μl	14118 (11300 - 18005)	13212 (9100 - 16470)	15540 (10140 - 19540)	12203 (7800 - 15180)	11905 (8420 - 14300)	13005 (8000 - 16200)	11348 (8100 - 13600)	0.005
C-reactive protein, mg/dl	3.5 (1.0 - 7.1)	7.8 (2.6 - 13.8)	2.0 (1.1 - 5.2)	2.2 (1.0 - 6.5)	3.0 (1.0 - 9.1)	10.2 (4.3 - 17.6)	2.4 (0.8 - 11.2)	<0.001
Sodium, mmol/l	136.9 ± 3.4	137.5 ± 4.3	138.1 ± 4.6	136.3 ± 5.8	136.6 ± 4.6	136.8 ± 6.1	137.2 ± 4.5	0.026
Potassium, mmol/l	4.2 ± 0.6	4.2 ± 0.7	4.3 ± 0.4	4.4 ± 0.6	4.2 ± 0.5	4.1 ± 0.6	4.1 ± 0.5	<0.001
Blood glucose, mmol/l	12.6 ± 4.5	8.9 ± 3.9	12.4 ± 10.3	9.3 ± 4.5	7.0 ± 2.5	7.6 ± 3.3	7.0 ± 2.8	<0.001
BUN, mg/dl	27.1 ± 12.1	30.3 ± 17.8	30.5 ± 15.7	33.9 ± 26.4	19.9 ± 14.3	26.7 ± 19.0	20.8 ± 12.1	<0.001
eGFR, ml/min/1.73m ²	71.0 ± 26.9	65.6 ± 28.5	57.8 ± 24.0	63.2 ± 36.8	91.9 ± 36.9	84.7 ± 74.6	89.0 ± 35.3	<0.001

Values are mean \pm SD, n (%), median (25th to 75th percentile) or mean (25th to 75th percentile) in white blood cell count

ACS, acute coronary syndrome; AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; HF, heart failure; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate.