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ORIGINAL ARTICLE
Heart failure

Remote dielectric sensing to detect acute heart failure in patients with dyspnoea: a prospective observational study in the emergency department

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Aims Remote dielectric sensing (ReDS) enables quick estimation of lung fluid content. To examine if ReDS is superior to other methods in detecting acute heart failure.

Methods and results We included consecutive patients with dyspnoea from the emergency departments at Bispebjerg Hospital, Copenhagen, and performed ReDS, low-dose chest computed tomography (CT), echocardiogram, lung ultrasound, NT-Pro-brain natriuretic peptide (NT-proBNP), and a Boston score evaluation (chest X-ray and clinical signs). ReDS values >35% were used as a cut-off to diagnose pulmonary congestion. Acute heart failure was adjudicated by experts' review of health records but independently of ReDS values. Sub-analyses investigated ReDS in acute heart failure patients with congestion on CT. We included 97 patients within a median of 4.8 h from admittance: 25 patients (26%) were ReDS-positive and 39 (40%) had adjudicated acute heart failure (21 with and 18 without CT congestion). Heart failure patients had median ReDS 33%, left ventricular ejection fraction 48%, and NT-proBNP 2935 ng/L. A positive ReDS detected heart failure with 46% sensitivity, 88% specificity, and 71% accuracy. The AUC for ReDS was like the Boston score ($P = 0.88$) and the lung ultrasound score ($P = 0.74$). CT-congested heart failure patients had higher ReDS values than patients without heart failure (median 38 vs. 28%, $P < 0.001$). Heart failure patients without CT-congestion had ReDS values like patients without heart failure (mean 30 vs. 28%, $P = 0.07$).

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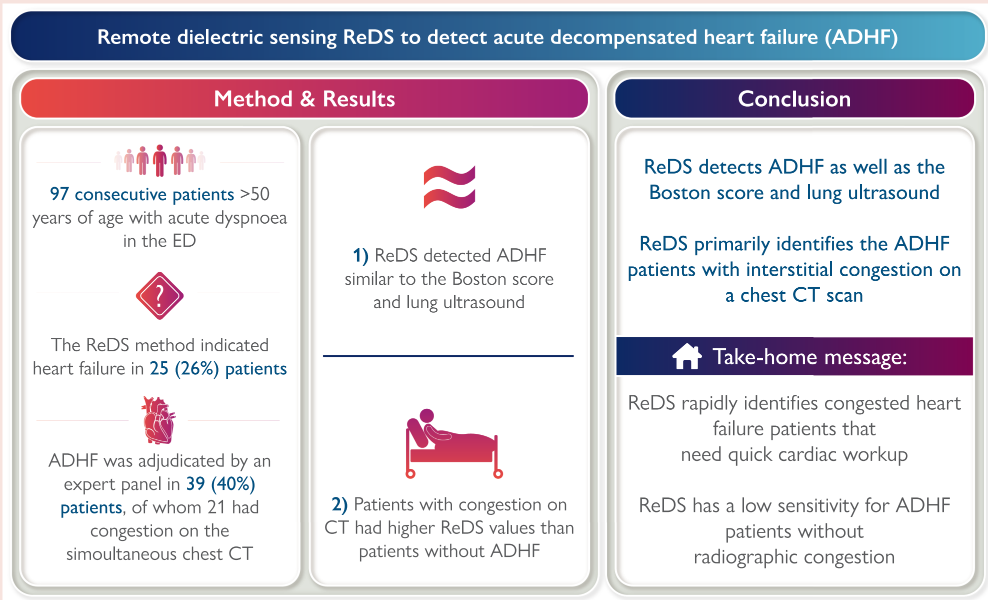
Conclusion ReDS detects acute heart failure similarly to the Boston score and lung ultrasound score, and ReDS primarily identifies the acute heart failure patients who have congestion on a chest CT.

Graphical Abstract



Keywords Remote dielectric sensing technology • Dyspnoea • Acute decompensated heart failure

Introduction

Dyspnoea is a common complaint in the emergency department[1] and half of the patients presenting with dyspnoea have congestive heart failure as the primary or co-primary diagnosis.[1,2] A correct diagnosis is essential for swift therapy and recovery, but diagnosis can be challenging, especially among elderly patients with comorbidities.[3,4] Diagnostic echocardiography in every patient is not possible in a busy emergency department. Approximately 20% of patients presenting with dyspnoea are initially misdiagnosed, and emergency physicians struggle to decide which patients should be referred for instant cardiologic evaluation.[5,6] Thus, simple, immediate, and reliable methods are needed to guide emergency physicians in choosing the right diagnostic strategy.

Remote dielectric sensing (ReDS) is a recent technology that immediately and non-invasively estimates lung fluid content based on electromagnetic energy.[7] The ReDS technology is approved by FDA and CE for lung fluid monitoring. In previous studies, ReDS was correlated to pulmonary wedge pressure[8] and it could accurately discriminate heart failure patients with pulmonary congestion on a chest computed tomography (CT) from normal subjects.[9] A recent study found that ReDS detects pulmonary oedema moderately in emergency patients.[10]

In the real world, patients with acute congestive heart failure present with varying degrees of vascular and interstitial pulmonary congestion. There are at least two phenotypes of pulmonary congestion: one with interstitial tissue congestion displaying radiographic signs of congestion, and one with vascular congestion, without radiographic signs of congestion, that can only be determined after echocardiographic confirmation of elevated left ventricular (LV) filling pressure.[11,12] Because ReDS estimates lung fluid content,[9] we anticipated higher ReDS values in patients with radiographic signs of congestion.

The primary aim was to examine the value of ReDS to detect or rule out acute heart failure among consecutive patients with dyspnoea in an emergency department. Furthermore, we aimed to compare ReDS with a lung ultrasound[13,14] and Boston score.[15] Finally, we examined how ReDS values are affected by radiographic congestion on a chest CT scan.

Method

Design

A prospective single-centre observational study was performed in the emergency department at Bispebjerg University Hospital, Copenhagen, Denmark. The National Ethics Committee approved the study protocol on Health Research Ethics in Copenhagen, Denmark (Project-id: H-17000869).

Population

On 110 randomly selected workdays from October 2018 to August 2019, we screened all consecutive patients with a same-day hospital contact between 2 a.m. and 1.30 p.m. The main inclusion criteria were acute dyspnoea and age of 50 years or above. Acute dyspnoea was defined as self-reported sudden onset of dyspnoea or worsening of chronic dyspnoea within 14 days, combined with at least one abnormal objective parameter supporting respiratory imbalance

(*Figure 1*). We excluded patients requiring intensive care or ventilation, acute coronary syndrome requiring telemetry, and patients who refused or could not consent. The protocol demanded that all study examinations had to be done as fast as possible and no later than 12 h after admittance, otherwise, the patient was excluded (*Figure 1*).[13,16]

Patients underwent a clinical examination, arterial blood gas, and phlebotomy as part of the clinical routine. All patients provided initial informed written consent for the package of the protocolled study procedures that were performed on every patient: ReDS, lung ultrasound, chest X-ray, low-dose chest CT, and echocardiography.

Remote dielectric sensing technology

ReDS (FDA: K150095 and CE: 3900874CE01) provides an estimate of the percentage of lung fluid content within the range of 15–60%.[7] Values within the range of 20–35% are normal by standard, and values above 35% were defined as positive for pulmonary congestion (positive ReDS).[7,9] Patients were measured once on the right hemithorax in a sitting position. After applying the ReDS vest, ReDS each measurement lasted 30 s.

Radiology

CT scans were used as the reference standard for determining the presence or absence of pulmonary congestion. A multi-slice CT scan (Somatom Definitions Flash, Siemens Medical Solutions, Forschheim, Germany) was acquired during a single breath-hold without spirometry for detecting inspiration status. The mean CT-radiation dose was 1.3 mSv (95% CI: 1.2–1.4). The CT scans were reviewed by two specialized thoracic radiologists, independently of each other, and blinded to clinical information including chest X-rays and ReDS measurements. The radiologists assessed signs of pulmonary congestion on CT, and we defined CT with interstitial congestion based on the agreement between the two observers. In case of no agreement, the CT was classified as 'without congestion'.[17] In concert with the CT, a chest X-ray was also taken.

Symptoms, clinical signs of heart failure, and Nt-proBNP levels

We used modified Boston criteria as a clinical and radiographic measure of the signs and symptoms of heart failure.[15] The New York Heart Association functional classification (NYHA) was used to grade the severity of dyspnoea in the Boston score and replaced the categories of 'rest dyspnoea', 'dyspnoea while walking on level area' and 'dyspnoea while climbing' with NYHA IV, NYHA III, and NYHA II, respectively. Orthopnoea and paroxysmal nocturnal dyspnoea were used accordingly to the Boston score. The score gave a total from 0 to 12, where 0–4 marks 'unlikely heart failure', 5–7 'possible heart failure', and 8–12 marks 'definite heart failure' (*Table 1*).

NT-Pro-brain natriuretic peptide (NT-proBNP) was measured in blood samples at admission and analysed with the Roche Elecsys technique. NT-proBNP results were available for the diagnosing adjudication panel.

Lung ultrasound

Certified investigators performed lung ultrasounds according to international recommendations using a 14-zone protocol, including 8 anterior zones and 6 posterior zones.[14] We used a Sonosite X-Porte Ultrasound System device with a 2.5–3.5 MHz cardiac probe. One video sequence of 4 s was saved for all lung ultrasound zones, and two blinded certified reviewers assessed B-lines and pleural effusion according to guidelines.[13,14] One zone with at least 3 B-lines on each hemithorax was considered positive for congestion. For this study, we created a continuous lung ultrasound score on a scale from 0 to 5 points based on the presence of bilateral B-lines and pleural effusion. A score of 3 corresponds to the traditional criterion of pulmonary congestion based on at least 3 B-lines in at least one zone on both sides (see supplementary material online, *Table S1*).[13,14]

Echocardiography

Dedicated specialists in cardiology performed the comprehensive transthoracic echocardiography, and readings were approved by at least two cardiologists, who were heart failure specialists and accredited in echocardiography by the European Society of Cardiology (ESC). Echocardiograms were performed according to the 2016 ESC guidelines,[18] including a systematic evaluation of LV filling pressure and diastolic dysfunction.[11,12] Cardiac dysfunction was classified as reduced left ventricular ejection fraction (LVEF) < 40% (HFrEF), mildly reduced LVEF from 40 to 49% (HFmrEF), and preserved LVEF 50% or greater (HFpEF).[11] However, severe valve disease (HFvhd), was noted separately to distinguish it from HFpEF.

Adjudication of pulmonary and cardiac diagnoses

The final diagnoses of pulmonary and cardiac diagnoses were adjudicated by two cardiologists and two pulmonologists after patient discharge. They reviewed clinical data, medication, specifically intensification of intravenous or oral diuretics, routine clinical radiology reports, blood tests and echocardiography. CT and lung ultrasound images were not assessed by the adjudication panel.

A diagnosis of acute decompensated heart failure (ADHF) was ascertained by at least two cardiologists, and in the case of disagreement, the diagnosis was discussed with a third cardiologist. Criteria adhered to the ESC guidelines based on clinical signs, elevated NT-proBNP, a chest X-ray reading, echocardiographic cardiac dysfunction,[11] and evidence of elevated LV filling pressure (Grade II or Grade III) as a sign of pulmonary vascular congestion.[12] However, the adjudicators did not require Grade II or III elevated LV filling pressure in a few patients who fulfilled all criteria and already had received acute relevant therapy for triggers like a high blood pressure or fast a supraventricular tachyarrhythmia.

We defined *interstitial* congestion as radiographic congestion on a CT assessed by both independent radiologists. Correspondingly, we defined *vascular* congestion as an adjudicated ADHF diagnosis without radiographic congestion on chest CT.

Statistical analyses

The primary outcome of the study was the adjudicated ADHF diagnosis, including both patients with and without radiographic CT congestion. In sub-analyses, we examined ReDS in relation to ADHF patients with and without radiographic congestion on the chest CT. The main discriminatory exposure variable was ReDS dichotomized using 35% as the cut-point. However, we also examined ReDS as a continuous variable compared with the continuous Boston score and lung ultrasound score. Because we used NT-proBNP for adjudication, it was only examined as an exploratory exposure variable.

The diagnostic value of ReDS was evaluated against the primary outcome measure ADHF and was assessed by 2×2-tables and receiver operating characteristic (ROC)-curves with area under the curve (AUC). We compared the AUC of each modality against ADHF, and thresholds for indicating heart failure were ReDS >35%, lung ultrasound score of 3 or more (see supplementary material online, *Table S1*),[13,14] and Boston score of 8 or more.[15]

As appropriate, we report data as means and standard deviations (SD), medians and interquartile ranges (IQR), or counts and percentages. Histograms and Shapiro-Wilks test of normality assessed distributions of variables. The independent samples *t*-test, the χ^2 test/Fisher's exact test, the Wilcoxon rank-sum, and the Kruskal Wallis test were used for statistical comparisons. Two-sided tests were used, and *P*-values of

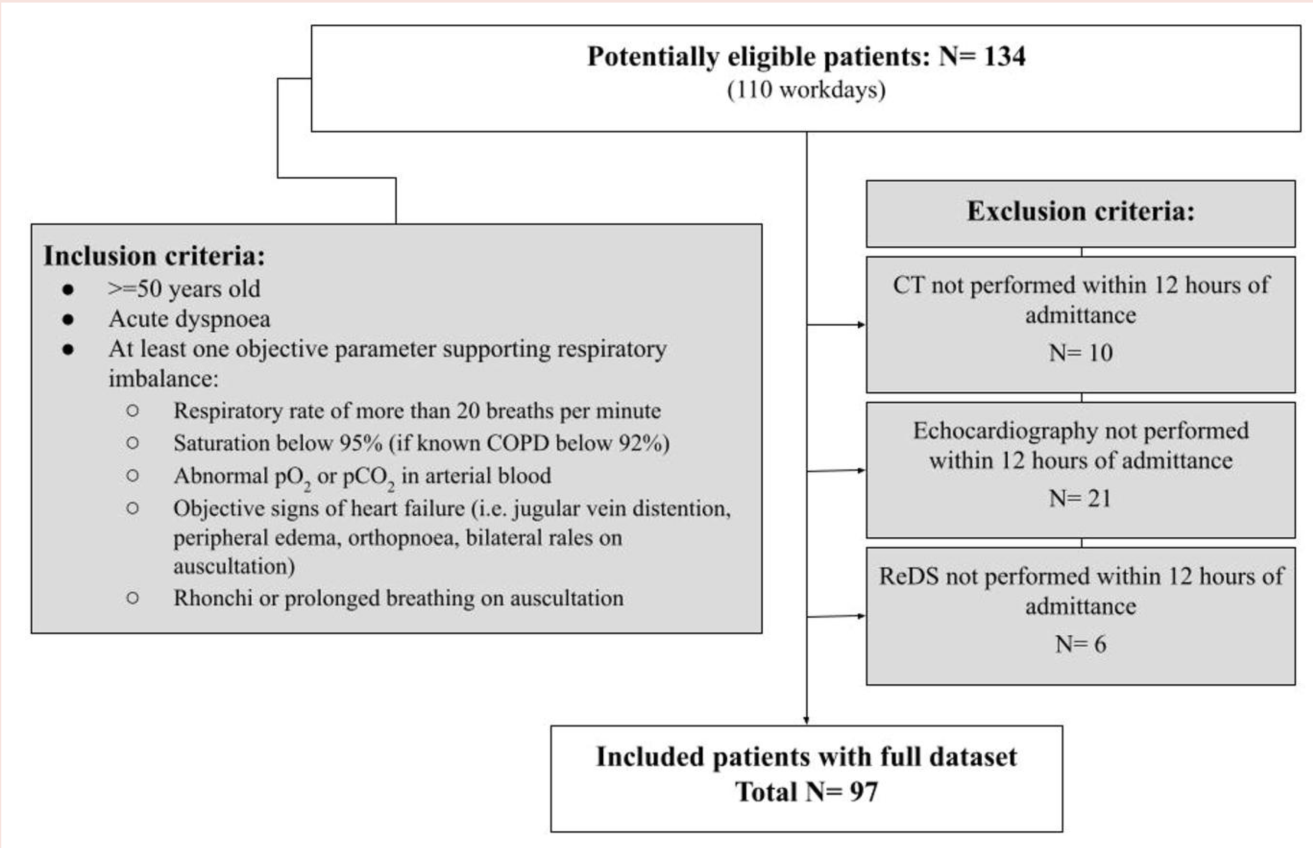


Figure 1 CONSORT diagram of inclusion.

<0.05 were considered statistically significant. Interrater agreements were measured with kappa statistics. We used the ANOVA test to compare ReDS values in ADHF patients with and without CT congestion and non-ADHF patients and illustrated differences with boxplots. In the ANOVA test, the displayed *P*-values were adjusted for comparison of multiple groups. The Bonferroni correction was used for adjustment for multiple group comparisons.

The required sample size was based on an assumed prevalence of ADHF in 30% of dyspnoeic patients in the emergency department.[1,2] The power was 0.80 with alpha 0.05 to detect a kappa-value of 0.85 against a null hypothesis corresponding to a kappa-value of 0.65. Thus, the minimum sample required was 90 patients.[19] We performed the statistical analyses with SAS Studio version 3.7 (SAS Institute, Cary NC) and Rstudio version 3.6.0.[20]

Results

We included 97 patients among 134 eligible patients (*Figure 1*). Ineligibility reasons were the inability to provide informed consent, acute referral to intensive care unit due to critical respiratory and hemodynamic instability, or acute coronary syndrome. We excluded 37 patients because examinations were not performed simultaneously (*Figure 1*). A positive ReDS examination occurred in 25 (25.7%) patients and was associated with higher NT-proBNP levels, Boston score, chest X-ray signs of heart failure, lung ultrasound score (0–2, 3, and 4–5 points), and more abnormal echocardiographic parameters (*Tables 1 and 2*).

We adjudicated ADHF in 39 (40.2%) patients (*Table 3*). ADHF was more frequent in ReDS-positive than ReDS-normal patients (72.0 vs. 29.2%, $P < 0.001$. Although most ReDS normal patients did not have ADHF (70.8%), still, 8.3% had ADHF with CT-congestion (*Table 3*). ADHF was also significantly correlated to the lung ultrasound score and the Boston score (respectively, $P < 0.001$) (see supplementary material online, *Table S2*).

At hospital admittance, ADHF patients had a higher frequency of atrial fibrillation, systolic blood pressure >140 mmHg, and elevated levels of NT-proBNP and troponin T (see supplementary material online, *Table S3*). Moreover, patients with chronic obstructive pulmonary disease (COPD) exacerbations and CT-verified emphysema had less ADHF (see supplementary material online, *Table S3*).

A positive ReDS detected ADHF with a sensitivity of 46% and specificity of 88% and with a kappa value of 0.36 (95% CI: 0.18–0.54, $P < 0.001$) (*Table 4*). Notably, ReDS diagnosed the subgroup with CT-congested ADHF better with a sensitivity of 67%, specificity of 84% and accuracy of 80% ($P < 0.001$) (*Table 4*).

The CT-congested ADHF patients had higher ReDS values than patients without ADHF (median 38 vs. 28%, $P < 0.001$) (*Figure 2*). ADHF patients without CT-congestion had ReDS values that were not significantly different from non-ADHF patients (median 30 vs. 28%, adjusted $P = 0.07$) or CT-congested ADHF patients (mean 30 vs. 38%, adjusted $P = 0.23$).

In ROC analyses, ReDS detected ADHF with an AUC of 0.74 (*Figure 3*), not different from the Boston score or the lung ultrasound score (AUC = 0.77 and AUC = 0.71, $P = 0.69$ and $P = 0.73$ for direct comparison with ReDS) (*Figure 3*). NT-proBNP had a higher AUC than ReDS to detect ADHF (AUC = 0.89, $P = 0.02$). Sub analyses indicated that ReDS could improve the Boston score and the lung ultrasound score to detect ADHF (AUC 0.83 vs. 0.77, $P = 0.03$, and AUC 0.80 vs. 0.71, $P = 0.06$) (see supplementary material online, *Figure S1*).

Echocardiography, radiology, and ReDS examinations were performed almost simultaneously within a median time of 1.2–1.6 h

Table 1 Modified Boston criteria for heart failure in relation to ReDS

	Positive ReDS *N*: 25	Normal ReDS *N*: 72	Total *N*: 97	*P*-value
History[a]				
NYHA II, *N* (%)	8 (32.0)	22 (30.6)	30 (30.9)	|
NYHA III, *N* (%)	12 (48.0)	31 (43.1)	43 (44.3)	0.784
NYHA VI, *N* (%)	5 (20.0)	18 (25.0)	23 (23.7)	|
Orthopnoea, *N* (%)	17 (68.0)	31 (43.1)	48 (49.5)	**0.032**
Paroxysmal nocturnal dyspnoea, *N* (%)	14 (56.0)	45 (62.5)	59 (60.8)	0.566
Clinical examination				
Heart rate (per minute), mean (SD)	87.2 (78.4–95.9)	93.1 (87.8–98.4)	90.0 (78.0–101.0)	0.254
Jugular venous elevation, *N* (%)	1 (4.0)	0 (0)	1 (1.0)	0.258
Lung crackles basilar, *N* (%)	5 (20.0)	6 (8.3)	11 (11.3)	0.113
Lung crackles more than basilar, *N* (%)	3 (12.0)	16 (22.2)	19 (19.6)	0.384
Wheezing, *N* (%)	2 (8.0)	10 (13.9)	12 (12.4)	0.723
Chest X-ray				
Alveolar pulmonary oedema, *N* (%)	8 (32.0)	8 (11.3)	16 (16.7)	**0.017**
Interstitial pulmonary oedema, *N* (%)	12 (48.0)	12 (16.9)	24 (25.0)	**0.002**
Accentuated flow shift, *N* (%)	11 (44.0)	13 (18.1)	24 (24.7)	**0.011**
Bilateral pleural effusion, *N* (%)	11 (44.0)	8 (11.1)	19 (20.0)	**<0.001**
Enlarged heart (ratio >0.50), *N* (%)	15 (60.0)	22 (35.5)	37 (38.1)	**0.034**
Boston score				
Total Boston score, median (IQR)	8.0 (6.0–9.0)	6.0 (4.0–8.0)	7.0 (5.0–8.0)	**0.017**
Heart failure unlikely (score 0–4), *N* (%)	2 (8.0)	21 (29.2)	23 (23.7)	|
Heart failure possible (score 5–7), *N* (%)	10 (40.0)	29 (40.3)	39 (40.2)	**0.027**
Heart failure definite (score 8–12), *N* (%)	13 (52.0)	22 (30.6)	35 (36.1)	|

[a]No patient had NYHA group I.

between comparative methods (see supplementary material online, *Table S4*). The median duration for one ReDS-measurement, including application, was 1.5 min (IQR: 1.0–1.8 min). During hospital admission, intravenous diuretics were given to 28 of the 39 ADHF patients and to 4 patients without ADHF (see supplementary material online, *Table S4*). Only five (5.2%) patients had diuretics administrated between study examinations. The median time from admittance to the intravenous diuretic administration was 4.9 h. Of the 18 ADHF patients with CT congestion, 17 (94.4%) had intravenous diuretics administrated within a median time of 3.9 h (see supplementary material online, *Table S4*).

Regarding reproducibility, for the overall estimation of lung ultrasound congestion based on either 3 or more B-lines or pleural effusion, the kappa value was 0.89.[13] Similarly, the two radiologists agreed on adjudicated pulmonary congestion on CT with a kappa value of 0.83 (95% CI 0.72–0.94, <0.0001).

Discussion

We examined whether ReDS could identify acute heart failure in consecutive emergency patients with dyspnoea and a high frequency of pulmonary comorbidity. We conclude that a positive ReDS examination has a high specificity for detecting ADHF. The objective ReDS method has an overall accuracy that parallels full clinical examination, chest X-ray, and lung ultrasound. Notably, in a sub analysis, ReDS primarily identifies those ADHF patients who have congestion on a chest CT scan rather than ADHF patients with sole vascular congestion and no radiographic congestion.

Previous proof-of-concept studies reported high accuracies of ReDS to detect CT measured lung fluid content in selected heart failure populations.[7,9] ReDS also correlated well with pulmonary capillary wedge pressure and were found to have a high negative predictive value (94.9%) to exclude patients with PCWP >17 mm Hg.[8] But these results were obtained in a mixed cohort of patients with heart failure and heart transplantation and cannot be directly adopted into an unselected emergency population.[8] Our study is the first study to examine the value of ReDS to detect acute heart failure among emergency patients and to directly compare ReDS with other clinical methods to detect heart failure in the emergency department.

Only one other study has evaluated ReDS in an emergency department. Rafique Z, *et al.*[10] found that ReDS values above 35% detected pulmonary congestion in dyspnoeic emergency patients with a moderate sensitivity of 79% and specificity of 62% and an accuracy of 68%. Similarly, we found a 71% accuracy for ReDS to detect ADHF. However, our study included more comorbid patients reflected in a 37% prevalence of pneumonia, and 50% had known COPD (*Table 2*; see supplementary material online, *Table S3*). In contrast to Rafique *et al*, we found a high specificity of 88% but a low sensitivity of 46% for ReDS to detect ADHF. The reason may be that our broad adjudicated ADHF diagnosis included those with definitely elevated LV filling pressure on a comprehensive echocardiogram. We found a better accuracy when restricting the outcome to ADHF patients with radiographic congestion (*Table 4*).

Thus, apart from testing ReDS in an emergency cohort with a high frequency of pulmonary comorbidity, our significant new finding is that a positive ReDS primarily detects the ADHF patients presenting with interstitial congestion, here demonstrated on a CT. In a comorbid emergency population, ADHF patients may present with merely pulmonary vascular congestion, but those patients had ReDS values similar to non-ADHF patients.

Table 2 Baseline characteristics for positive and normal ReDS-examinations

	Positive ReDS *N*: 25	Normal ReDS *N*: 72	Total *N*: 97	*P*-value
Patient characteristics				
Age (years), mean (SD)	73.3 (68.8–77.7)	72.5 (70.1–75.0)	72.7 (70.6–74.8)	0.772
Sex (male), *N* (%)	18 (72.0)	41 (56.9)	59 (60.8)	0.184
BMI (kg/m^2), median (IQR)	27.2 (24.2–32.4)	25.9 (22.3–28.7)	26.0 (22.7–30.1)	0.100
BMI >39 kg/m^2, *N* (%)	1 (4.0)	2 (2.8)	3 (3.1)	1.000
BMI <22 kg/m^2, *N* (%)	3 (12.0)	15 (20.8)	18 (18.6)	0.389
History of heart failure, *N* (%)	7 (28.0)	18 (25.0)	25 (25.8)	0.768
History of COPD, *N* (%)	7 (28.0)	44 (61.1)	51 (52.6)	**0.004**
History of asthma, *N* (%)	4 (16.0)	15 (20.8)	19 (19.6)	0.773
Known renal insufficiency, *N* (%)	4 (16.0)	7 (9.7)	11 (11.3)	0.467
Diabetes Mellitus I/II, *N* (%)	12 (48.0)	13 (18.1)	25 (25.8)	**0.003**
Peripheral pedal oedema, *N* (%)	9 (36.0)	18 (25.0)	27 (27.8)	0.290
Fever, *N* (%)	4 (16.0)	11 (15.3)	15 (15.5)	1.000
C-reactive protein (mg/L), median (IQR)	11.0 (7.0–42.0)	20.5 (6.5–56.5)	16.0 (7.0–55.0)	0.338
NT-ProBNP (ng/l), median (IQR)	2021.2 (800.0–4465.3)	683.3 (225.8–2355.3)	997.9 (257.1–2934.6)	**0.037**
Lung ultrasound				
No interstitial syndrome (score 0–2), *N* (%)	16 (64.0)	52 (72.2)	68 (70.1)	|
Interstitial syndrome (score 3), *N* (%)	1 (4.0)	15 (20.8)	16 (16.5)	**0.003**
Interstitial syndrome AND pleural effusion (score 4–5), *N* (%)	8 (32.0)	5 (5.0)	13 (13.4)	|
Echocardiographic parameters				
Ejection fraction (%), median (IQR)	50.0 (37.5–56.0)	60.0 (45.0–60.0)	55.0 (40.0–60.0)	**0.021**
Lateral e' (cm/s), mean (SD)	8.0 (6.9–9.1)	9.3 (8.6–10.0)	9.0 (6.9–10.2)	0.067
E/e', median (IQR)	13.6 (9.6–17.2)	10.2 (7.5–13.0)	10.6 (8.0–14.2)	**0.004**
Tricuspid regurgitation gradient max velocity (cm/s), median (IQR)	2.9 (2.6–3.3)	2.8 (2.3–3.1)	282.0 (232.0–315.0)	0.112
Index LA-volume (mL/m2), median (IQR)	43.0 (34.6–49.9)	29.9 (22.0–38.6)	32.3 (24.7–44.0)	**0.002**
LV filling pressure and diastolic dysfunction, *N* (%)				
Grade 1 or indeterminate/normal	7 (28.0)	44 (61.1)	51 (52.6)	|
Grade 2 (elevated LV filling pressure)	11 (44.0)	17 (23.6)	28 (28.9)	**0.001**
Grade 3 (elevated LV filling pressure)	4 (16.0)	1 (1.4)	5 (5.2)	|

Table 3 Final diagnoses in relation to ReDS

	Positive ReDS *N*: 25	Normal ReDS *N*: 72	Total *N*: 97	*P*-value
Adjudicated final diagnoses[a]				
All ADHF, *N* (%)	18 (72.0)	21 (29.2)	39 (40.2)	<0.001
CT-congested ADHF, *N* (%)	12 (48.0)	6 (8.3)	18 (18.6)	<0.001
CT-non-congested ADHF, *N* (%)	6 (24.0)	15 (20.8)	21 (21.6)	0.781
No ADHF, *N* (%)	7 (28.0)	51 (70.8)	58 (59.8)	<0.001

[a]Assessed by an expert panel

Pulmonary disease may increase lung density in pulmonary fibrosis and decrease lung density in emphysema, which theoretically confounds the diagnostic value of ReDS.[21] In this real-world scenario of consecutive patients with a high rate of comorbidity, a positive ReDS was associated significantly with ADHF patients who had pulmonary interstitial congestion on a simultaneous chest CT. It is a novel observation that the predefined threshold of ReDS 35%, was too high to detect ADHF patients with mainly vascular congestion but without interstitial or radiographic congestion on CT.

The study limitations were the single-centre design, the limited sample size, and that examinations were not performed in the evenings and nights. Still, it was a strength that all tests were finished within a median of 4.8 h because it warranted patients had a similar cardiorespiratory state for every examination. The 97-patient sample size was arbitrary set as there were no previous studies to guide a formal sample size calculation. For these reasons, it may be regarded as an important pilot study to guide further use and research of this modality. Still, we do not anticipate an excellent diagnostic value of ReDS if a larger study with the same type of patients had been performed. The inclusion rate was reduced because a high rate of acute patients were unable to provide informed consent. We speculate the ReDS method could be useful in these, and future studies should try to include such patients, perhaps in a cluster design. A limitation is that we did not exclude patients according to their BMI. Thus, we included 18 patients with BMI <22 and 3 patients BMI >39, and ReDS has not been validated in these patient groups.

Patients with severe acute pulmonary oedema or needing mechanical ventilation were excluded, and these rarely represent a diagnostic problem, so our results apply to the large contingency of patients with grey zone symptoms and a less obvious clinical presentation.

One strength of the study was the adjudicated reference ADHF diagnosis based on comprehensive echocardiographic evidence for cardiac

Table 4 Diagnostic value of ReDS

N = 97	All ADHF		CT-congested ADHF	
	Yes	No	Yes	No
Positive ReDS	18	7	12	13
Normal ReDS	21	51	6	66
P-value		**<0.0001**		**<0.0001**
	Diagnostic measurement	**(95% CI)**	**Diagnostic measurement**	**(95% CI)**
Sensitivity (%)	46	(31–62)	67	(45–88)
Specificity (%)	88	(80–96)	84	(75–92)
Accuracy (%)	71	(62–80)	80	(73–88)
Negative predictive value (%)	72	(54–90)	92	(85–98)
Positive predictive value (%)	71	(60–81)	48	(28–68)
Odds ratio	6.2	(2.3–17.1)	10.2	(3.2–32.0)
Negative likelihood ratio	0.6		0.4	
Positive likelihood ratio	3.8		4.2	

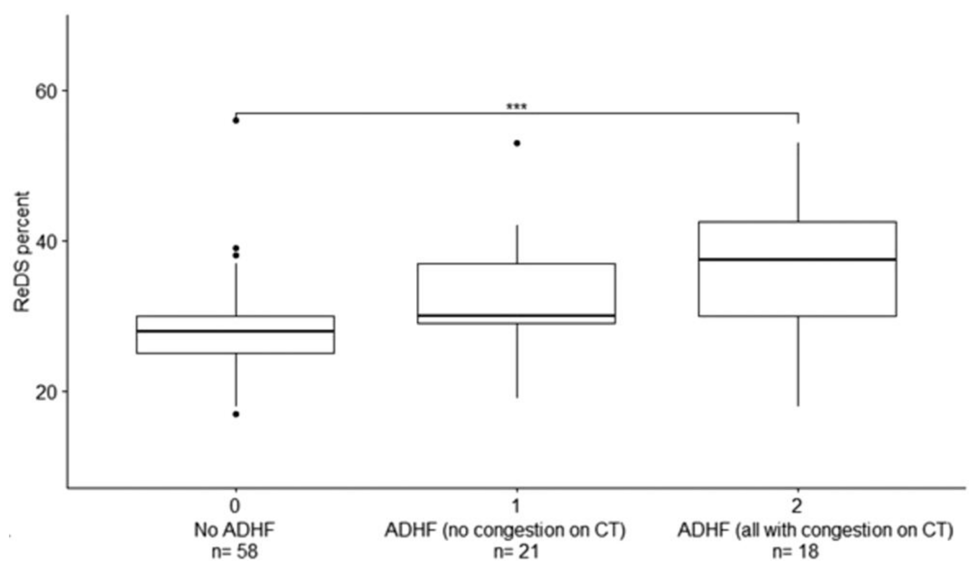


Figure 2 Boxplots of ReDS values in selected ADHF subgroups. Reported *P*-values are adjusted for pairwise comparisons between multiple groups. Median ReDS values (IQR) (%): No ADHF (– congestion) (*N* = 58): 28.0 (25.0–30.0)ADHF (– congestion) (*N* = 21): 30.0 (29.0–37.0) ADHF (+ congestion) (*N* = 18): 37.5 (29.0–43.0). *** Significant difference between the groups ($P < 0.001$).

dysfunction and elevated LV filling pressure[11,12] and the expert panel that judged whether acute symptoms and signs were due to ADHF. We used the ESC/AHA recommended classification for LV filling pressure.[12] It is a limitation that this echocardiographic classification of cardiac filling pressures has not been validated in acute patients. Still, it is currently the best renowned non-invasive method to estimate cardiac filling pressures. Another strength is that this study was investigator-initiated and -designed, and therefore not influenced by industry.

Clinical methods like lung ultrasound, and clinical examinations including chest X-ray detect ADHF as well as ReDS. This is a novel observation, but plausible because all methods indirectly estimate the lung fluid content. Each method has its advantages, but ReDS can be measured by less experienced medical staff in less than five minutes. Thus, ReDS can easily be combined with other diagnostic methods, and sub analyses also indicated that ReDS improves the Boston criteria and lung ultrasound to detect ADHF. Lung ultrasound detected ADHF with a lower diagnostic value than reported in other studies. However, our study differed as we examined patients above 50 years of age with a high rate of comorbidities, and we did not excluded patients with known pulmonary fibrosis or emphysema.[13]

NT-proBNP had a higher AUC than ReDS to diagnose ADHF. It is plausible that NT-proBNP detects ADHF with both vascular and interstitial congestion compared with ReDS which primarily identifies patients with interstitial congestion. Furthermore, the AUC for

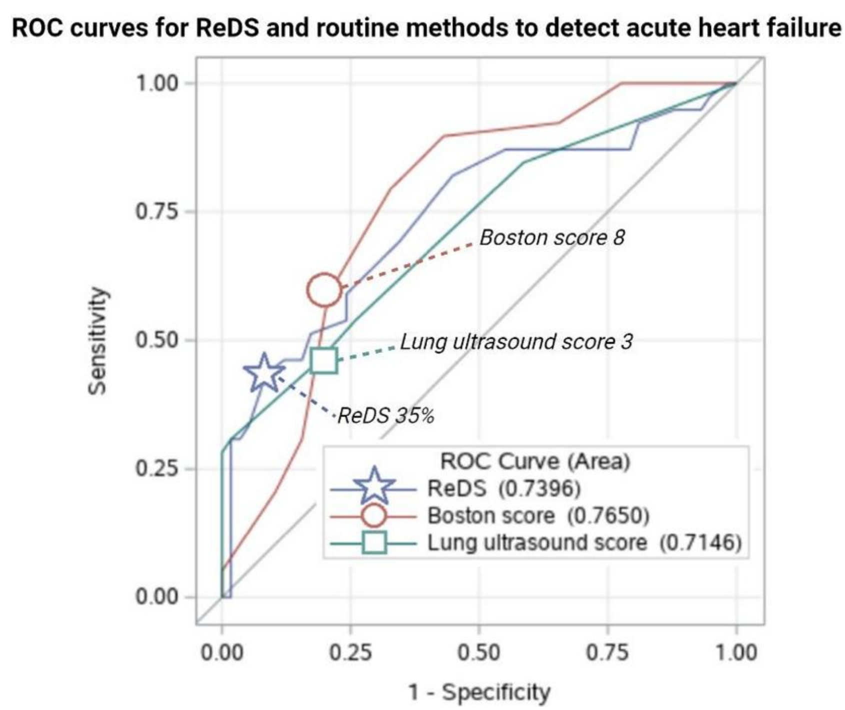


Figure 3 ROC curves of ReDS, Boston criteria and lung ultrasound against ADHF.

NT-proBNP was inflated because the adjudicating expert panel was aware of the NT-proBNP levels. Thus, we do not find that ReDS adds diagnostic value to current clinical practice, including NT-proBNP. However, ReDS can provide a rapid assessment before the complete clinical examination, chest X-ray, and NT-proBNP, thereby ensuring fast triage in the emergency department, where a positive ReDS examination should prompt cardiac workup. Acute heart failure with radiographic interstitial congestion will be picked up by ReDS, which is relevant because only 12% of the dyspnoeic patients had diuretics administrated within 3 h from admittance (see supplementary material online, *Table S2*). Hence, a positive ReDS examination could prompt diuretic treatment in more relevant patients.

Lead author biography

Anne Sophie Olesen graduated from Copenhagen University of Medicine in 2020. During the medical study, Anne Sophie completed a research year at the Department of Cardiology, Bispebjerg University Hospital, where she included the study population, of which this article is applied on. Anne Sophie has clinical experience from working as a physician at the internal medical department at Gentofte Hospital, and in the emergency department at Bispebjerg University Hospital.

Anne Sophie is especially interested in examining and improving diagnostic and prognostic issues among acute dyspnoeic patients and will proceed this research under guidance from prof. Olav W. Nielsen.

Data availability

The authors have full control of all data, and some of the data underlying this article will be shared on reasonable request to the senior (last) author Prof. Olav W. Nielsen.

Supplementary material

Supplementary material is available at *European Heart Journal Open* online.

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