British Journal of Heart Diseases
2018; 1(1): 112 - 118 . doi: 10.31488/bjhd.105

Research article

Natural history and prognostic value of ultrasound lung artefacts ("comet tail" sign) in patients admitted to hospital for worsening heart failure

Josa-Laorden C*[1], Cleland JG[2], Butcher C[3], Giménez-López I[4], Rubio-Gracia J[1], Sola A[5], Pérez-Calvo JI[1]

1. Aragon Institute of Health Research, IIS-Aragon, Zaragoza, Spain, Internal Medicine Department, Lozano Blesa University Hospital, Spain
2. National Heart and Lung Institute and National Institute of Health Research Cardiovascular Biomedical Research Unit, Royal Brompton and Harefield Hospitals, Imperial College, United Kingdom
3. Heart Rhythm Centre, NIHR Cardiovascular Research Unit Royal Brompton & Harefield Hospitals and National Heart and Lung Institute, Imperial College London, United Kingdom
4. Aragon Institute of Health Research, IIS-Aragon, Zaragoza, Spain. Aragon Institute of Health Sciences (IACS).
5. Department of Experimental Nephrology, IDIBELL, L'Hospitalet del Llobregat, Spain.

*Corresponding autor: Josa-Laorden C, Aragon Institute of Health Research, IIS-Aragon, Zaragoza, Spain. Internal Medicine Department. Lozano Blesa University Hospital, Spain, Tel: +34 679676908; E-mail: claudiajosa@gmail.com

Received: Novemeber 28, 2018; Accepted: December 28, 2018; Published: December 31, 2018

Abstract

Background and Objectives: Identification of pulmonary congestion remains challenging in clinical practice; it's rapid, early, bedside assessment by lung ultrasound might prove useful. The objectives were to assess the presence of comet tail artefacts (CTA) in patients admitted to hospital with worsening heart failure (HF) and to evaluate their relationship to biomarkers, radiographic pulmonary congestion and prognosis. Method: CTA were assessed in eight lung regions; at least two regions of each hemi-thorax had to exhibit at least three CTA for the test to be considered positive (CTA+). Patients were followed during twelve months. Results: 204 patients, median age 81±9 years, 51% were men, 57% had a left ventricular ejection fraction (LVEF) >40% and 51% fulfilled the criteria for CTA+. Patients with CTA+ had higher plasma concentrations of amino-terminal pro-Brain Natriuretic Peptide (NT-proBNP) and were more likely to have lung crackles, jugular venous distension and radiological pulmonary oedema. During follow-up, 22.5% of patients died, mostly for cardiovascular reasons. Being CTA+ on admission was associated with higher mortality (p=0.011, OR=2.19 CI 1.08-4.43). Multi-variable analysis demonstrated that age, length of hospital stay, LVEF and plasma Cystatin-C, NT-proBNP, urea and creatinine were independent predictors of prognosis at one year. CTA status entered the model only when NT-proBNP was removed. Conclusions: In our experience, CTA is often absent in patients admitted to hospital with worsening heart failure but CTA do identify patients with a worse prognosis and might be used as an alternative to NT-proBNP when this test is not available.

Keywords: Heart failure; Comet tail artefact; Kerley-B lines; Prognosis; Pulmonary congestion; NT-proBNP

Introduction

Clinical signs of decompensated heart failure are diagnostically and prognostically important but, unless florid, lack diagnostic sensitivity and specificity, even when elicited by expert clinicians [1-4]. Consequently, European Society of Cardiology (ESC) guidelines recommend investigations including a chest X-ray, plasma natriuretic peptides and echocardiography to confirm the diagnosis [1].

Accumulation of fluid in the pulmonary inter-lobular septa due to increases in left atrial and pulmonary capillary pressure produces a typical pattern of interference known as comet-tail artefacts (CTA) on lung ultrasound (LUS) [5,6]. CTA appear to be the sonographic equivalent of Kerley-B lines (KBL), a well-established radiographic sign of interstitial oedema. Acquisition of images by LUS is quick, painless, safe and inexpensive and easy to teach and learn. Accordingly, CTA might prove a useful bedside test for the diagnosis and monitoring of pulmonary congestion [7,8]. Fluid accumulation often starts long before symptoms of congestion become evident in patients who subsequently require hospital admission for heart failure [9]. Early identification might allow clinicians to increase the intensity of therapy before symptoms become overt, thereby avoiding hospital admission [10]. CTA might also be useful for monitoring therapeutic response.

However, despite reports suggesting that CTA are an accurate and reproducible measure of lung congestion7, image interpretation remains both subjective and prone to inter-operator variability [11]. Also, to the best of our knowledge, the prognostic importance of CTA on LUS in patients admitted with worsening heart failure is unknown. Accordingly, we investigated the prevalence, natural history and prognostic significance of CTA and their relationship to radiological pulmonary oedema and plasma concentrations of amino-terminal pro-brain natriuretic peptide (NT-proBNP) in patients admitted to hospital with worsening heart failure.

Methods

Study population

From February 2013 to July 2014, 204 consecutive patients with worsening heart failure were prospectively enrolled at the University Hospital Lozano Blesa, Zaragoza (Spain). Eligible patients were at least 18 years of age, had been hospitalised with a clinical diagnosis of worsening heart failure and had an NT-proBNP >300 pg/ml. Patients with either new-onset or pre-existing heart failure were included. Those with persistent NYHA class IV symptoms in the month prior to admission, cognitive impairment, a life expectancy less than six months, active neoplasms, pulmonary fibrosis, advanced renal disease (glomerular filtration rate (GFR) less than 30 ml/min/1.73m2 by MDRD (Modification of Diet in Renal Disease), requiring inotropic therapy on admission and unable to provide informed consent were excluded. All patients who agreed to participate in the study provided written informed consent. The study was approved by the Ethics Committee for Clinical Research of Aragon (CEICA), (CI PI13 / 0019).

All patients were offered clinical follow-up at one, three, six and twelve months post discharge. Clinical end-points were overall mortality, unplanned HF re-admissions at one year. Data were collected from computerised records, out-patient clinics visits and follow up phone calls for those unable to attend the hospital.

Investigations

Blood tests

Blood tests were performed within 48 hours of admission and included full blood count, renal function, electrolytes, total protein, albumin, transaminases and biomarkers (NT-proBNP, Cystatin C).

Lung ultrasound (LUS)

Within 24 hours of admission, a bedside thoracic ultrasound was performed with a V-SCAN (General Electrics Healthcare®) and 1.7-3.8 megahertz G3S transducer to identify and quantify CTA. The same experienced physician performed all LUS examinations with the patient reclined at 30 degrees. Both the anterior and lateral hemi-thorax were divided into upper or lower quadrants, resulting in eight quadrants in all. CTA are narrow, vertical, bilateral and diffuse linear echogenic images visualized from the 2nd to 4th intercostal spaces, which reflect differences in acoustic impedance in the lungs. A positive assessment (CTA+) was defined as >3 CTAs per area in at least two areas per hemi-thorax. Patients who were CTA+ had a repeat LUS every 24 hours until the changes had resolved. Those with a negative assessment (CTA-: those who did not meet the threshold defined) had no further LUS during admission.

Chest X-ray

A postero-anterior chest X-ray was performed on admission and assessed by two expert physicians, blinded to the LUS result, clinical background and hemodynamic status of the patient.

Statistical analysis

Baseline categorical data were reported as percentages. Continuous variables were summarised as median [and interquartile range (IQR)]. Statistical comparisons between subject groups at baseline and on follow up were performed using the chi-square or Fisher's exact test for categorical data. For continuous data, the student's t-test or Mann-Whitney U or ANOVA were used for parametric and non-parametric data respectively. A probability value of <0.05 was considered statistically significant. Odds Ratio (OR) was calculated to quantify the association between CTA and mortality.

Cumulative mortality over 12 months according to the presence or absence of CTA was calculated using the Kaplan-Meier (K-M) method. CTA and median plasma NTpro-BNP concentration were used to stratify patients into four groups (Group 1: NT-proBNP <3306 pg/ml and CTA-; group 2: NT-proBNP <3306 pg/ml and CTA+;

group 3: NT-proBNP >3306 pg/ml and CTA-; group 4: NT-proBNP >3306 pg/ml and CTA+). Receiver Operating Characteristics (ROC) curves assessed the utility of NT-proBNP and CTA for predicting mortality.

Relationships of variables with overall mortality at one year were calculated using a Cox proportional hazard model. A multivariable model was generated including the following pre-defined variables; age, sex, length of hospital stay, left ventricular ejection fraction (LVEF), systolic blood pressure, plasma urea and creatinine, NT-proBNP, Cystatin-C and medical history including hypertension, ischaemic heart disease (IHD), diabetes mellitus, chronic kidney disease and chronic obstructive pulmonary disease. The statistical analysis was performed using SPSS version 22.0.

Results

Baseline characteristics (Table 1)

Two hundred and four patients were included in the study. Their median age was 81±9 years, 51% were men and the median hospital stay was 8 days (IQR 2 to 51 days). The most frequent cause for heart failure was hypertension (39%) followed by IHD (29%) and valve disease (mitral and aortic, 9% and 7% respectively). Baseline NYHA functional class, prior to the current admission, was II or III in 172 (84%) patients. One hundred and sixteen patients (57%) had a left ventricular ejection fraction (LVEF) >50%. Prior to admission, 93% of patients were on loop diuretics, 77% on angiotensin-converting enzyme inhibitor (ACEI) or angiotensin-receptor blocker (ARB), 56% on beta-blockers, 34% on mineral receptor antagonists and 64% were receiving anticoagulants.

Almost half (49%) of patients hospitalised for HF were CTA-. Of those who were CTA+ on admission, 70% had >3 CTA in all eight lung segments. Patients who were CTA+ had higher median plasma NT-proBNP (p=0.006) and lower haemoglobin (p=0.08) and triglycerides (p=0.04) concentrations. The greater the number of segments affected by CTA, the higher the NT-proBNP (p=0.011). Clinical signs of congestion such as lung crackles (p=0.022) and raised jugular venous pressure (JVP) (p=0.033) were more common in CTA+ patients. Of patients with radiological alveolar (13%) or interstitial (72%) pulmonary oedema, 78% (p=0.003) and 46% (p=0.044) respectively were CTA+. Pleural effusion, which might have been expected to be associated with CTA, were not (p=0.99) (Table 1).

Natural History of CTA

CTA+ persisted for a mean of 3 (± 2.5 days). CTA+ resolved within the first 24 hours after intravenous diuretics in 36% of patients but persisted for at least 72 hours in 34% and for longer than four days in 29%. Some patients (n=14) remained CTA+ throughout the period of observation, even amongst patients considered well enough for discharge. The right upper lobe was the segment with the most persistent CTA.

Outcomes

Ten patients (5%) died during the index hospital admission (7 due to HF, one due to stroke and two due to septicaemia). During follow-up, 16 patients (8%) died during the first month after discharge, 31 (16%) by six months and 46 (22.5%) by twelve months. Of these, 15 (88,2%), 19 (55,9%) and 20 (42,6%) occurred without a re-admission for heart failure. Of those who died, 33 (81%) were cardiovascular. Patients who died were older (p=0.001), had had a longer hospital stay (p=0.027) and higher plasma concentrations of urea (p<0.0001), creatinine (p=0.034), NT-proBNP (p<0.0001) and Cystatin C (p=0.014) at admission but had similar LVEF as compared to those that survived (Table 2).

The presence of CTA on admission was associated with higher mortality at twelve months (29.8% if CTA+ vs. 15.0% if CTA-, p=0.011, OR=2.19 CI 1.08-4.43). Thir-

Table 1. Baseline characteristics of the patients included, defined by CTA results.

	Global (n=204)	CTA- (n=100, 49%)	CTA+ (n=104, 51%)	p-value
Age	81 (9)	80 (10)	81 (5)	81 (5)
Men	103 (50.5)	46 (46.5)	56 (47)	56 (47)
Length stay (days)	8 (6.5)	8 (6)	9 (7)	9 (7)
NYHA II prior to admission	119 (61)	59 (62.1)	58 (58.6)	58 (58.6)
NYHA III prior to admission	45 (23)	20 (21.1)	25 (25.3)	25 (25.3)
Chronic decompensated HF	163 (80)	160 (78.4)	156 (76.5)	156 (76.5)
LVEF	54 (24)	54 (24)	53 (25)	53 (25)
Hypertension	172 (85)	83 (85.6)	87 (84.5)	87 (84.5)
Ischaemic heart disease	74 (37)	35 (36.1)	39 (37.9)	39 (37.9)
Chronic Kidney Disease	54 (27)	24 (24.7)	30 (29.1)	30 (29.1)
Diabetes mellitus	80 (40)	41 (42.3)	38 (36.9)	38 (36.9)
Heart rate (bpm)	81 (28)	80 (21)	85 (28)	85 (28)
Atrial Fibrillation (%)	118 (58)	46 (44)	58 (56)	58 (56)
SBP (mmHg)	140 (43)	140 (26)	140 (35)	140 (35)
Lung Crackles	138 (68)	59 (62)	79 (77)	79 (77)
Peripheral oedema	155 (76)	71 (74)	84 (82)	84 (82)
Elevated JVP	115 (56)	47 (49)	66 (64)	66 (64)
Cystatin C (mg/L)	1.45 (0.7)	1.41 (0.8)	1,48 (0,6)	1,48 (0,6)
NTproBNP (pg/mL)	3306 (5388)	2722 (3375)	4403 (6431)	4403 (6431)
Haemoglobin (g/dL)	12.2 (2.3)	12.5 (2.6)	11.8 (2.8)	11.8 (2.8)
Urea (mg/dL)	0.6 (0.3)	0.5 (0.8)	0.6 (0.4)	0.6 (0.4)
Creatinine (mg/dL)	1,1 (0,6)	1,1 (0,6)	1,2 (0,6)	1,2 (0,6)
Albumin (g/dLdl)	3.2 (0.5)	3.2 (0.5)	3.1 (0.5)	3.1 (0.5)
Total cholesterol (mg/dL)	145 (40)	144 (45)	139 (41)	139 (41)
Triglycerides(mg/dL)	88 (42)	93 (43)	85 (41)	85 (41)
Pleural effusion	61 (30)	30 (30)	31 (30)	31 (30)
Radiological alveolar pulmonary oedema	27 (13.3)	6 (6.1)	21 (20.4)	21 (20.4)
Radiological interstitial pulmonary oedema	147 (72)	77 (77)	67 (65)	67 (65)

Table 1. Patient characteristics for patients with and without CTA at baseline using students t-test for continuous and normally distributed variables, Chi square test for categorical variables and Mann-Whitney test for non-parametric data. Results are expressed as number (percentage) and median (interquartilic range), as appropriate. COPD: chronic obstructive pulmonary disease; DBP: diastolic blood pressure; JVP: jugular vein pressure; LVEF: left ventricle ejection fraction; NYHA: New York Heart Association; NT-proBNP: N-terminal pro-brain natriuretic peptide; SBP: Systolic blood pressure

Table 2. Patients' characteristics according to 12-month mortality.

	Dead (n=46, 22.5%)	Alive (n=158, 77.5%)	p-value
Age (years)	83 (6)	80 (11)	0.001
Length of hospital stay (days)	12 (9)	8 (5)	0.027
LVEF < 50%	22 (54)	57 (39)	0.094
Urea (mg/dL)	0.7 (0.3)	0.51 (0.3)	0.000
Creatinine (mg/dL)	1.2 (0.6)	1.1 (0.6)	0.034
Haemoglobin (g/dL)	11.8 (7.9)	12.4 (3)	0.011
Red cell distribution width (%)	16.8 (3)	15.5 (2.3)	0.003
Albumin (g/dL)	3.1 (0.6)	3.2 (0.5)	0.025
Cystatin C (mg/L)	1.58 (0.7)	1.41 (0.7)	0.014
NTproBNP (pg/ml)	7318 (12962)	2969 (4390)	0.000
Positive CTA	31 (67.4)	73 (46.2)	0.011
Days positive CTA	2 (3)	2 (3)	0.181

Table 2. Patients' characteristics according to 12-month mortality, using students t-test for continuous and normally distributed variables, Chi square test for categorical variables and Mann-Whitney test for non-parametric data. Results are expressed as number (percentage) and median (interquartilic range), as appropriate.
CTA: comet tail artifact; LVEF: left ventricular ejection fraction; NT-proBNP: N-terminal pro-brain natriuretic peptide.

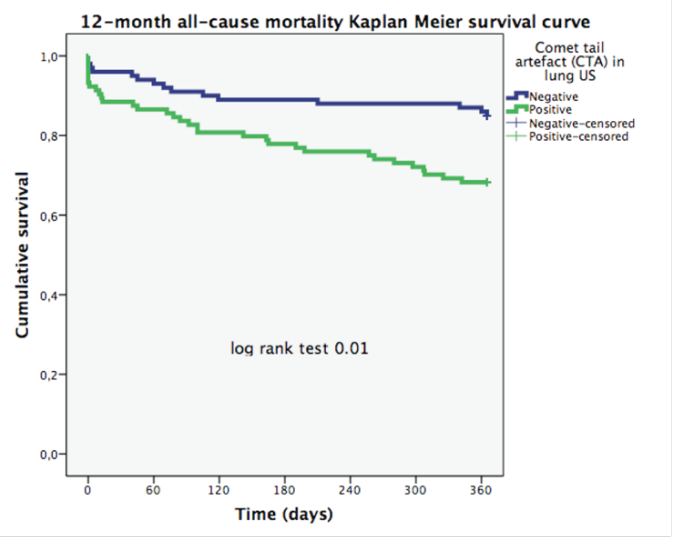

Figure 1. Kaplan-Meier 12-month all-cause survival curves defined by LUS result (negative vs positive).

ty-one (67.4%) of the patients who died were CTA+ on admission. Survival curves showed poorer outcomes in those who were CTA+ (Log Rank 0.01) (Figure 1).
No relationship was found between persistence of CTA+ and hospital readmission rate. Kaplan Meier 12-month survival curve showed no differences in survival according to duration of CTA+ (Log-rank 0.543) (Figure 2).

Univariate regression analysis showed that the strongest predictors of 12-month all-cause mortality were Cystatin C [Exp(B)=3.3, p=0.009], NT-proBNP [Exp(B)=2.1, p<0.0001] and being CTA+ [Exp(B)=2.2, p=0.013] on admission (Table 3). Adjusted multivariable analysis demonstrated that age, length of hospital stay, LVEF, Cystatin C, NT-proBNP and plasma urea and creatinine were independent predictors of prognosis at one year (Table 3). CTA entered the model when NT-proBNP was excluded.

Twenty-four patients (12%) were readmitted within the first month; 60 (29%) within 6 months and 81 (40%) within 12-months. Rates of the composite outcome (cardiovascular mortality or re-admission for heart failure) were similar in patients who were CTA+ (52%) or CTA- (41%) p=0.118. If CTA disappeared (from CTA+ to CTA-) within the first three days, CTA+ patients were less likely to experience re-admissions by 12 months (38% vs 60.0%; p=0.037), but not the composite outcome (50.0% vs 64.5%; p=0.175). However, caution in the interpretation of re-admission rates is required because out of hospital deaths preclude re-admission.

Outcomes according combined NT-proBNP values and CTA status at admission.

Patients were classified according to median NT-proBNP (3,306ng/L) and CTA+/- at admission (Table 4). Patients who had above median NT-proBNP and were CTA+ had the highest mortality at 12 months (41.0%) and those with values below median and CTA- the lowest (10.2%) (Figure 2). Receiver Operating Characteristics (ROC) curves also showed that combining CTA status and NT-proBNP (CTA+/- and NT-proBNP: AUC=0.674 CI 0.581-0.767) was superior than either alone (CTA+/-: AUC=0.619 CI 0.521-0.718; NT-proBNP: AUC=0.633 CI 0.535-0.731).

For the composite, patients with above median NT-proBNP had higher event rates at 12 months

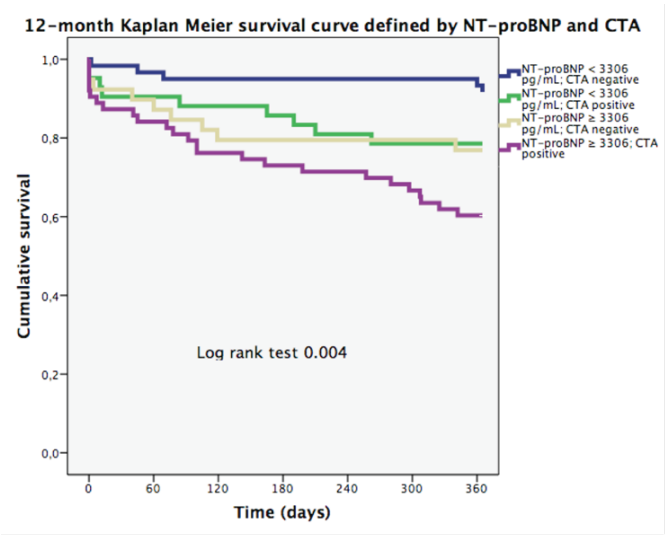

Figure 2. Kaplan-Meier 12-month survival estimate according to NT-proBNP (pg/mL) and CTA at admission. Group 1: NT-proBNP < 3306 pg/ml and CTA negative (mortality 10.2%). Group 2: NT-proBNP < 3306 pg/ml and CTA positive (mortality 23.1%). Group 3: NT-proBNP > 3306 pg/ml and CTA negative (mortality 19.0%) and group 4: NT-proBNP > 3306 pg/ml and CTA positive (mortality 41.0%).

Table 3. Univariate and multivariable regression analysis for 12-month overall mortality.

	Univariate Cox regression analysis			**Multivariable Cox regression analysis**			**Multivariable COX without NT-proBNP**		
	Exp (B)	95% CI	p-value	Exp (B)	95% CI	p-value	Exp (B)	95% CI	p-value
Sex	1.146	0.643-2.044	0.644						
Age	1.087	1.034-1.141	0.001	1.114	1.046-1.187	0.001	1.116	1.046-1.191	0.001
Hospital stay	1.867	1.175-2.967	0.008	1.735	1.025-2.939	0.004	1.760	1.018-3.045	0.043
Ischaemic heart disease	1.200	0.661-2.179	0.549						
Arterial hypertension	1.957	0.701-5.465	0.200						
Diabetes mellitus	1.267	0.704-2.282	0.430						
Chronic kidney disease	1.898	1.045-3.447	0.035						
LVEF	0.456	0.185-1.123	0.088	0.263	0.083-0.829	0.023	0.170	0.059-0.492	0.001
Cystatin C	3.312	1.344-8.162	0.009	5.926	1.144-30.707	0.034	5.408	0.989-29.577	0.052
NT-proBNP	2.114	1.549-2.886	0.000	1.695	1.140-2.522	0.009			
Plasma urea	1.844	1.119-2.884	0.007	3.110	1.399-6.911	0.005	2.604	1.226-5.531	0.013
Plasma creatinine	1.470	0.891-2.424	0.131	0.121	0.021-0.705	0.019	0.187	1.226-5.531	0.013
Presence of CTA	2.181	1.177-4.041	0.013	1.564	0.865-3.283	0.213	2.061	1.274-3.823	0.042

Table 3. Univariate and multivariate Cox regression analysis for 12-month overall mortality, with and without NT-proBNP included in the analysis. CI: confidence interval; CTA: comet tail artifact; Exp(B): exponentiation of the B coefficient; LVEF: left ventricular ejection fraction; NT-proBNP: N-terminal pro-brain natriuretic peptide.

Table 4. Clinical outcomes (all-cause mortality and composite all-cause mortality + HF readmissions) defined by the combination of NT-proBNP and LUS (CTA) on admission.

	NT-proBNP < 3306 pg/mL			NT-proBNP > 3306 pg/mL			Global p-value
	CTA- (n=60; 59%)	CTA+ (n=39; 39%)	p-value	CTA- (n=60; 59%)	CTA+ (n=39; 39%)	p-value	
NT-proBNP, median (IQR)	1726 (1382)	1727 (1649)	0.852	5285 (4355)	7696 (7823)	0.005	0.000
All-Cause Mortality							
6-months	3 (5)	6 (14)	0.104	7 (18)	17 (28)	0.038	0.009
12-months	6 (10)	8 (19)	0.191	9 (23)	23 (38)	0.04	0.004
Composite all-cause mortality + HF re-admissions							
6-months	14 (24)	13 (31)	0.391	17 (44)	31 (50)	0.530	0.021
12-months	19 (32)	16 (38)	0.501	22 (56)	38 (61)	0.627	0.006

Table 4. Clinical outcomes classified by the combination of NT-proBNP and LUS (CTA) on admission. Results are expressed as number (percentage) and median (interquartilic range), as appropriate.
CTA: comet tail artifact; NT-proBNP: N-terminal pro-brain natriuretic peptide

(p=0.006), whether patients were CTA- (56.4%) or CTA+ (63.9%) compared to those with NT-proBNP below median (32.2% and 38.1% respectively).

Discussion

Published studies suggest that LUS is a simple and accurate tool to assist clinicians in differentiating between respiratory and cardiac causes of dyspnoea [12-15]. This may be true, but the main determinant of admission for many patients with worsening heart failure is peripheral oedema rather than breathlessness [16]. Although patients admitted with worsening peripheral oedema may often have interstitial pulmonary oedema and breathlessness on slight exertion this may not always be the case and such cases may not have CTA. Indeed, in our cohort, only 50% of patients fulfilled the criteria for CTA+ at admission for worsening heart failure. Whilst there may have been some diagnostic uncertainty in our patients, there was a substantial amount of clinical data and information from other investigations to corroborate the presence of HF, which casts doubt on the diagnostic utility of LUS for worsening heart failure in this setting using existing criteria.

Previous publications [6] have suggested that CTA

were strongly associated with the radiological appearance of pulmonary interstitial fluid with a high sensitivity and specificity (93% and 93% respectively). In a cohort of patients admitted with breathlessness [17], all those with cardiogenic radiologically-confirmed pulmonary oedema on chest radiograph had positive Kerley-B lines, compared to 8% of patients admitted with chronic obstructive pulmonary disease (COPD). Studies that show a high sensitivity and specificity for CTA [6,18] were performed in medical intensive care units that tend to admit patients in acute respiratory distress. Our patients were admitted to general medical units and included patients admitted predominantly for the management of severe peripheral oedema albeit usually accompanied by breathlessness on slight exertion; many patients had neither pulmonary interstitial (28%) nor alveolar oedema (87%). The prevalence of CTA in our study appears more in line with that reported for outpatients with severe chronic HF[19,20]. A lower burden of pulmonary interstitial fluid accumulation might explain the lower prevalence of CTA in our study. However, the absence of CTA should not be equated with the absence of severe heart failure; many patients who did not fulfil the criteria for a positive CTA test had grossly elevated NT-proBNP and subsequent mortality was high.

An alternative explanation for the low prevalence of CTA in our cohort is that, by mistake, we included patients with dyspnoea from non-cardiac aetiologies, However, patients were included only if they demonstrated clinical and radiological signs and symptoms of HF and had an elevated NT-proBNP (median concentration 3306 pg/mL) [1]. Most of our patients had also had previous admissions for heart failure. Moreover, mortality rates (around 5% during admission and 23% at 1-year follow-up) are in keeping with that reported in most registries and studies for HF suggesting that a correct diagnosis had been established in our cohort. Our results concur with previous studies, reporting that CTA on LUS are more common in older patients, those with more severe cardiac dysfunction with a lower LVEF [21] and higher plasma NT-proBNP [4,14,19,22,23] and a higher prevalence of hypoalbuminemia [24] and anaemia.

As far as we are aware, this is the first study to explore the relationship between CTA and prognosis. Patients who had a positive CTA test had a worse prognosis and those who had both CTA and a plasma NT-proBNP concentration above the median had the worst prognosis over the following year. The availability of both, pocket-LUS [25,26] and NT-proBNP, makes it feasible to combine these tests for risk stratification in daily clinical practice. However, after adjusting for other patient characteristics, the association between a positive CTA test and prognosis was no longer significant. As patients may improve with therapy, it is not surprising that many clinical measures of the severity of heart failure at the time of admission, including CTA and natriuretic peptides are not strong predictors of long term prognosis. However, our results also suggest that resolution of CTA during hospitalization does not predict subsequent outcome. LUS has been used to monitor and guide therapy in patients admitted to hospital with acute HF exacerbations [27,28]. Previous studies have reported that resolution of CTA was related to clinical recovery, with a drop in plasma concentrations of natriuretic peptides and radiographic clearance of pulmonary oedema [27,28]. We could not confirm this. In our cohort, many patients were considered ready for discharge even though CTA had not resolved.

Quantification of CTA will be, to some extent, operator dependent. We did not assess inter- and intra-observer reproducibility. Our findings require confirmation by other operators and in other, larger populations. We used published criteria [29,30] to define a positive CTA test. However, there will be a range of severity for pulmonary interstitial oedema. Perhaps grading the severity of CTA both in terms of number of lung regions affected and the number of CTA per region. Ranking CTA as absent, mild, moderate or severe may be more useful than simply considering a test positive or negative. Such an analysis requires careful consideration and analysis and is beyond the scope of the present report.

Conclusions

In our experience, many patients admitted for worsening heart failure do not have a positive CTA test. This may be because the threshold criteria for a positive CTA has been set too high or because many patients admitted with worsening heart failure do not have pulmonary oedema. A positive CTA test is associated with a worse prognosis and improves risk stratification when added to plasma NT-proBNP but not in multi-variable models. Failure of CTA to resolve during admission does not preclude being considered fit for discharge and does not indicate a worse prognosis, therefore repeating LUS regularly during or after admission may not have clinical value. Re-evaluating the grading system for CTA might improve their clinical utility.

References

1. McMurray JJ, Adamopoulos S, Anker SD, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2012; 14:803-69.
2. Kociol RD, McNulty SE, Hernandez AF, et al. NHLBI Heart Failure Network Steering Committee and Investigators. Markers of decongestion, dyspnea relief, and clinical outcomes among patients hospitalized with acute heart failure. Circ Heart Fail. 2013;6:240-5.
3. Lala A, McNulty SE, Mentz RJ, et al. Relief and Recurrence of Congestion During and After Hospitalization for Acute Heart Failure: Insights from DOSE-AHF and CARRESS-HF. Circ Heart Fail. 2015;8:741-8.

4. Gustafsson M, Alehagen U, Johansson P. Imaging congestion with a pocket ultrasound device - prognostic implications in patients with chronic heart failure. J Card Fail. 2015; 21:548-54.
5. Ziskin MC, Thickman DI, Goldenberg NJ, et al. The comet tail artifact. J Ultrasound Med. 1982;1:1-7.
6. Lichtenstein D, Mezière G, Biderman P. The comet tail artifact. An ultrasound sign of alveolar-interstitial syndrome. Am J Respir Critic Care Med. 1997;156:1640-6.
7. Bedetti G, Gargani L, Corbisiero A, Frassi F, Poggianti E, Mottola G. Evaluation of ultrasound lung comets by hand-held echocardiography. Cardiovasc Ultrasound. 2006;4:34.
8. Cardim N, Fernandez C, Ferrerira D, et al. Usefulness of a new miniaturized echocardiographic system in outpatient cardiology consultations as an extension of physical examination. J Am Soc Echocardiogr. 2011;24:117-24.
9. Schiff GD, Fung S, Speroff T, et al. Decompensated heart failure: symptoms, patterns of onset, and contributing factors. Am J Med. 2003;114:625-30.
10. Yu CM, Wang L, Chau E. Intrathoracic impedance monitoring in patients with heart failure: correlation with fluid status and feasibility of early warning preceding hospitalization. Circulation. 2005;112:841-8.
11. Damy T, Kallvikbacka-Bennett A, Zhang J, et al. Does the physical examination still have a role in patients with suspected heart failure?. Eur J Heart Fail. 2011;13:1340-8.
12. Liteplo AS, Marill KA, Villen T, et al. Emergency thoracic ultrasound in the differentiation of the etiology of shortness of breath (ETUDES): sonographic B-lines and N-terminal pro-brain-type natriuretic peptide in diagnosing congestive heart failure. Acad Emerg Med. 2009;16:201-10.
13. Cardinale L, Volpicelli G, Binello F, et al. Clinical application of lung ultrasound in patients with acute dyspnea: differential diagnosis between cardiogenic and pulmonary causes. Radiol Med. 2009;114:1053-64.
14. Gargani L, Frassi F, Soldati G, Tesorio P, Gheorghiade M, Picano E. Ultrasound lung comets for the differential diagnosis of acute cardiogenic dyspnoea: a comparison with natriuretic peptides. Eur J Fail. 2008;10:70-7.
15. Manutani D, Nagdev A. Three-view bedside ultrasound to differentiate acute decompensated heart failure from chronic obstructive pulmonary disease. Am J Emerg Med. 2013;31:759e3-5.
16. Shoaib A, Waleed M, Khan S, et al. Breathlessness at rest is not the dominant presentation of patients admitted with heart failure. Eur J Heart Fail. 2014;16:1283-91.
17. Lichtenstein D, Mezière G. A lung ultrasound sign allowing bedside distinction between pulmonary edema and COPD: the comet-tail artifact. Intensive Care Med. 1998;24:1331-4.
18. Baldi G, Gargani L, Abramo A, et al. Lung water assessment by lung ultrasonography in intensive care: a pilot study. Intensive Care Med. 2013;39(1):74-84.
19. Miglioranza MH, Gargani L, Sant´Anna RT, et al. Lung ultrasound for the evaluation of pulmonary congestion in outpatients: a comparison with clinical assessment, natriuretic peptides, and echocardiography. JACC Cardiovasc Imaging. 2013;6:1141-51.
20. Kataoka, H. Ultrasound pleural effusion sign as a useful marker for identifying heart failure worsening in established heart failure patients during follow-up. Congest Heart Fail. 2012;18:272-7.
21. Frassi F, Gargani L, Gligorova S, Ciampi Q, Mottola G, Picano E. Clinical and echocardiographic determinants of ultrasound lung comets. Eur J Echocardiogr 2007;8:474-9.
22. Januzzi JL, Troughton R. Are serial BNP measurements useful in heart failure management? Serial natriuretic peptide measurements are useful in heart failure management. Circulation 2013;127:500-7.
23. Moe GW, Ezekowitz JA, O´Meara E, et al. The 2014 Canadian Cardiovascular Society Heart Failure Management Guidelines Focus Update: anemia, biomarkers, and recent therapeutic trial implications. Can J Cardiol. 2015;31:3-16.
24. Polat N, Aydin M, Yildiz A, et al. The prognostic significance of serum albumin in patients with acute decompensated systolic heart failure. Acta Cardiol. 2014;69:648-54.
25. Dalen H, Gundersen GH, Skjetne K, et al. Feasibility and reliability of pocket-size ultrasound examinations of the pleural cavities and vena cava inferior performed by nurses in an outpatient heart failure clinic. Eur J Cardiovasc Nurs. 2015;14:286-93.
26. Mancuso FJ, Siqueira VN, Moises VA, et al. Focused cardiac ultrasound using a pocket-size device in the emergency room. Arq Bras Cardiol. 2014;103:30-7.
27. Volpicelli G, Caramello V, Cardinale L, Mussa A, Bar F, Francisco MF. Bedside ultrasound of the lung for the monitoring of acute decompensated heart failure. AM J Emerg Med. 2008;26:585-91.
28. Noble VE, Murray AF, Capp R, Syvia-Reardon MH, Steele DJ, Liteplo A. Ultrasound assessment for extravascular lung water in patients undergoing hemodialysis. Time course for resolution. Chest. 2009;135:1433-9.
29. Volpicelli G MA, Garofalo G, Cardinale L, et al. Bedside Lung Ultrasound in the Assessment of Alveolar-Interstitial Syndrome. Am J Emerg Med. 2006; 24: 689-96.
30. Lichtenstein D MG, Biderman P, Gepner A, et al. The Comet-tail Artifact. An Ultrasound Sign of Alveolar-Interstitial Syndrome. Am J Respir Crit Care Med. 1997;156:1640-6.

To cite this article: Josa-Laorden C, Cleland JG, Butcher C, et al. Natural history and prognostic value of ultrasound lung artefacts ("comet tail" sign) in patients admitted to hospital for worsening heart failure. British Journal of Heart Diseases. 2018: 1:1.