BMJ Open Respiratory Research

Inspiratory crackles—early and late—revisited: identifying COPD by crackle characteristics

Hasse Melbye ,[1] Juan Carlos Aviles Solis,[1] Cristina Jácome,[2] Hans Pasterkamp[3]

To cite: Melbye H, Aviles Solis JC, Jácome C, *et al*. Inspiratory crackles—early and late—revisited: identifying COPD by crackle characteristics. *BMJ Open Resp Res* 2021;**8**:e000852. doi:10.1136/bmjresp-2020-000852

Received 2 December 2020
Revised 2 February 2021
Accepted 5 February 2021

[1]General Practice Research Unit, Department of Community Medicine, Faculty of Health Sciences, UIT The Arctic University of Tromsø, Tromso, Norway
[2]Center for Health Technology and Services Research (CINTESIS), University of Porto Faculty of Medicine, Porto, Portugal
[3]Department of Pediatrics and Child Health, University of Manitoba Faculty of Medicine, Winnipeg, Manitoba, Canada

Correspondence to
Professor Hasse Melbye; hasse.melbye@uit.no

ABSTRACT

Background The significance of pulmonary crackles, by their timing during inspiration, was described by Nath and Capel in 1974, with early crackles associated with bronchial obstruction and late crackles with restrictive defects. Crackles are also described as 'fine' or 'coarse'. We aimed to evaluate the usefulness of crackle characteristics in the diagnosis of chronic obstructive pulmonary disease (COPD).

Methods In a population-based study, lung sounds were recorded at six auscultation sites and classified in participants aged 40 years or older. Inspiratory crackles were classified as 'early' or 'late and into the types' 'coarse' and 'fine' by two observers. A diagnosis of COPD was based on respiratory symptoms and forced expiratory volume in 1 s/forced inspiratory vital capacity below lower limit of normal, based on Global Lung Function Initiative 2012 reference. Associations between crackle characteristics and COPD were analysed by logistic regression. Kappa statistics was applied for evaluating interobserver agreement.

Results Of 3684 subjects included in the analysis, 52.9% were female, 50.1% were ≥65 years and 204 (5.5%) had COPD. Basal inspiratory crackles were heard in 306 participants by observer 1 and in 323 by observer 2. When heard bilaterally COPD could be predicted with ORs of 2.59 (95% CI 1.36 to 4.91) and 3.20 (95% CI 1.71 to 5.98), annotated by observer 1 and 2, respectively, adjusted for sex and age. If bilateral crackles were coarse the corresponding ORs were 2.65 (95% CI 1.28 to 5.49) and 3.67 (95% CI 1.58 to 8.52) and when heard early during inspiration the ORs were 6.88 (95% CI 2.59 to 18.29) and 7.63 (95%CI 3.73 to 15.62). The positive predictive value for COPD was 23% when early crackles were heard over one or both lungs. We observed higher kappa values when classifying timing than type.

Conclusions 'Early' inspiratory crackles predicted COPD more strongly than 'coarse' inspiratory crackles. Identification of early crackles at the lung bases should imply a strong attention to the possibility of COPD.

Key messages

What is the key question?

- In the diagnosis of chronic obstructive pulmonary disease (COPD), is it more useful to focus on the timing of crackles than on the crackle type?

What is the bottom line?

- Pulmonary crackles are divided into two types, 'fine' and 'coarse' and coarse inspiratory crackles are regarded to be typical of COPD. In bronchial obstruction crackles tend to appear early in inspiration, and this characteristic of the crackle might be easier for a listener to recognise than the crackle type.

Why read on?

- The study shows that crackles identified as 'early' are more strongly associated with COPD than crackles identified as 'coarse'. The timing of crackles is easier to identify than the crackle type.

INTRODUCTION

Crackles are respiratory sounds often heard in chronic obstructive pulmonary disease (COPD) as well as in restrictive conditions, such as heart failure, lung fibrosis and pneumonia.[1] Forgacs proposed that crackles heard during inspiration were related to sudden opening of airways.[2] Since the inflation of the lungs happens sequentially, and the basal parts inflate later during inspiration than the central parts,[3] crackles may be described by time of appearance. Few years after Forgacs published his findings, Nath and Capel observed clear differences in the timing of crackles between patients with bronchial obstruction, in whom early crackles usually were heard, and patients with restrictive lung defects, who had late crackles.[4] This difference could be explained by the site of airway closure, that is, central airways in obstructive and peripheral airways in restrictive defects.

Although Nath and Capel proposed that the timing of crackles could be clinically helpful, which was also supported by Piirilä *et al*,[1] recent guidelines for diagnosing COPD[5] and heart failure[6] do not mention the distinction between early and late crackles. Instead, another subdivision based on crackle characteristics is frequently referred to, namely 'coarse' versus 'fine'. These crackle types are defined by the duration of each single crackle.[1] Coarse crackles may be caused by sudden opening of obstructed central

bronchii, while fine crackles are related to opening of distal airways.[1 7–9] Coarse and early crackles are related to each other, since coarse crackles tend to appear early during inspiration[9] and both coarse and early crackles are commonly heard in obstructive lung diseases.[1 7] The clinical usefulness of differentiating coarse from fine crackles has however been questioned due to low agreement between clinicians in identifying these crackle characteristics.[10] Yet these conclusions have been mainly based on small datasets, and we hypothesise that the distinction between 'early' and 'late' will generate higher agreement and possibly also be more useful in clinical practice.

In the seventh Tromsø study (2015–2016), lung sound recordings from six chest locations were classified in more than 4000 participants,[11] and the presence of COPD could be evaluated in most of these. The possible role of crackle characteristics (early/late and coarse/fine) when identifying obstructive lung conditions could now be re-evaluated in a non-selected general population.

The aim of this study was therefore to assess the diagnostic value of early vs late, and coarse vs fine inspiratory crackles heard at the lung bases, for the identification of COPD. Further, we wanted to evaluate the agreement between clinicians in identifying these crackle characteristics.

METHODS

Study population

The Tromsø study was established in 1974, and seven iterations of the study have been carried out, with the last health survey performed between May 2015 and October 2016. Main features of the methodology and study design have been previously described.[12] All Tromsø residents 40 years and older (n=32 591) received an invitation by mail to participate in the first visit of Tromsø 7. A random sample was selected for a second visit including 20% of those aged 40–59 years and 60% of those aged 60–84 years, and those who attended the first visit were invited. Thus, in this cross-sectional study, our sample consists of randomly selected participants attending the second visit of the seventh survey of the Tromsø study (Tromsø 7).

Patient and public involvement

The Tromsø Study has been strongly supported by the Tromsø municipality and the inhabitants of Tromsø, and the response rate has never been lower than 65%. Based on pathological test results, participants have been invited for further examinations or been advised to visit their general practitioner (GP). In terms of spirometry in the seventh survey, a GP visit was recommended to Tromsø 7 participants with forced expiratory volume in 1 s (FEV1) <70% predicted and not followed by a doctor due to a lung disease. A GP visit was also recommended if lung consolidation was suspected by the examining physician during lung sound recording. The Tromsø Study share results with the municipality of Tromsø for health surveillance.

Data collection

Information on participants' diseases and smoking habits was retrieved from self-administered questionnaires, and daily smoking was categorised as never, former or current. The participants answered the question 'Do you cough about daily for some periods of the year'. At the second visit, the participants answered the modified Medical Research Council questionnaire (mMRC) on dyspnoea.[13]

Spirometry was performed using SensorMedics Vmax 20c Encore (VIASYS Healthcare Respiratory Technologies, Yorba Linda, California, USA). Calibration was done daily. We followed the standards of the American Thoracic Society/European Respiratory Society (ERS).[14] Tests with FEV1 <0.3 L or with expiration lasting less than 3 s were regarded invalid. Postbronchodilator measurement was not carried out, the procedure was deemed too cumbersome to be included in this comprehensive survey. We used the Global Lung Function Initiative (2012) as a reference with the fifth percentile among healthy never smokers as lower limit of normal (LLN).[15] Participants were advised to take their medications for asthma and COPD as usual.

Lung sounds were recorded at six locations of the chest,[11] 15 s at each site, with a Sennheiser microphone MKE2-EW inserted in the tube of a Littmann Classic II stethoscope and using a Sennheiser wireless system EW112-PG3-G (Sennheiser electronic, Wedemark, Germany). The presence of crackles during inspiration and expiration was determined by two observers (physicians) who, using high-quality head-sets, independently classified the recordings, blinded for other information.[11] When the observers disagreed, they discussed the respective recordings with a third more experienced observer (HM). The recordings judged to contain crackles (certainly or likely), were evaluated in a second round, again independently by two observers, one of the observers of the first round (JCAS, physician with no specialty, observer (1) and one experienced lung sound researcher (HP, paediatric pulmonologist, observer (2). In the second round the crackles were categorised as 'certain', 'uncertain' and 'not present'. The certain crackles were subclassified as 'coarse' or 'fine' and as 'early', 'late' or 'both early and late'. In order to evaluate the importance of all early crackles, those classified as 'both early and late' were grouped together with 'early' crackles. The category 'crackles elsewhere' include inspiratory crackles heard at other locations and also expiratory crackles. When classifying the lung sounds, the observers watched spectrograms of the recordings.[16]

Definition of COPD

Global initiative for chronic Lung Disease (GOLD) recommends that a COPD diagnosis should be restricted to patients with typical symptoms.[5] We considered a diagnosis of COPD when FEV1/(forced vital capacity) was lower than LLN (5% percentile) and the participant had answered yes to the question 'do you get short of breath

when hurrying on a level surface or walking up a slight hill' (mMRC=1 or higher) or to the question 'do you cough about daily for some periods of the year'. COPD severity was categorised by the GOLD grades: (1) ≥80% predicted, (2) 50–79% predicted, (3–4) <50% predicted.[5]

Statistical analysis

Participants' characteristics were described as frequencies and determined by COPD status (presence or absence), and differences between groups were analysed with χ^2 tests. Predictive values of crackle characteristics were evaluated by univariable logistic regression for the two observers separately. Main findings were adjusted for age and sex. Positive predictive values of the strongest COPD predictors were calculated, also in a subgroup of former or current smokers, statistical significance was analysed with χ^2 test. The presence of crackle characteristics among the participants with COPD was analysed by severity groups, using χ^2 test for trend. To study to which degree participants were classified with both early and coarse crackles and both late and fine crackles, such concordance in identification was evaluated by kappa statistics. Such analysis was also applied to assess the agreement between the two observers. SPSS statistical software V.26 (IBM) was used.

Written consent was provided by all study participants.

RESULTS

Lung sounds were recorded and COPD status was evaluated in 3684 participants. Of these, 53.1% were women with a mean age of 63.2 (SD 10.6) years and 46.9% were men with a mean age of 63.5 (SD 10.5) years. Other characteristics of the study sample are shown in table 1. In the first round of classification, 588 were deemed to have certain or likely crackles and these were included in the second round of classification. Here, observer 1 identified certain crackles in 388 subjects, and basal inspiratory crackles in 306 of these. Observer 2 identified certain crackles in 461 subjects, and 323 with basal inspiratory crackles. Basal inspiratory crackles were heard in 16.2% and 15.2% of those with COPD, by observer 1 and 2, respectively, approximately twice as often as in those without COPD (table 1).

Table 1 Characteristics of the 3684 participants by COPD status

	All (n=3684)	No COPD (n=3480)	COPD (n=204)	
	n (%)	n (%)	n (%)	P value
Gender				
Male	1734 (47.1)	1631 (46.9)	103 (50.5)	0.3
Female	1950 (52.9)	1849 (53.1)	101 (49.5)	
Age				
40–64 years	1838 (49.9)	1760 (50.6)	78 (38.2)	0.001
65–84 years	1846 (50.1)	1720 (49.4)	126 (61.8)	
Smoking (27 missing)				
Current	442 (12.1)	377 (10.9)	65 (31.9)	<0.001*
Previous	1729 (47.3)	1609 (46.6)	120 (58.8)	
Never	1486 (40.6)	1467 (42.5)	19 (9.3)	
Self-reported diseases				
Hypertension (102 missing)	1287 (35.9)	1222 (36.1)	65 (32.8)	0.3
Myocardial infarction (155 missing)	171 (4.8)	155 (4.7)	16 (8.2)	0.03
Heart failure (158 missing)	101 (2.9)	96 (2.9)	5 (2.6)	0.8
Atrial fibrillation (156 missing)	277 (7.9)	255 (7.6)	22 (11.3)	0.06
Diabetes (124 missing)	219 (6.2)	211 (6.3)	8 (4.1)	0.2
COPD (143 missing)	140 (4.0)	79 (2.4)	61 (31.9)	<0.001
Asthma (129 missing)	393 (11.1)	331 (9.8)	62 (32.0)	<0.001
Crackles				
Observer 1	388 (10.5)	351 (10.1)	37 (18.1)	<0.001
Observer 2	461 (12.5)	422 (12.1)	39 (19.1)	0.003
Basal inspiratory crackles				
Observer 1 unilateral	221 (6.0)	200 (5.7)	21 (10.3)	<0.001*
Bilateral	85 (2.3)	73 (2.1)	12 (5.9)	
Observer 2 unilateral	246 (6.7)	228 (6.6)	18 (8.8)	0.001*
Bilateral	77 (2.1)	64 (1.8)	13 (6.4)	

*Analysed by χ^2 for trend.
COPD, chronic obstructive pulmonary disease.

Table 2 Unadjusted OR and 95% CIs of crackles for COPD by location

	Observer 1			Observer 2		
	n	OR (95% CI)	P value	n	OR (95% CI)	P value
No certain or doubtful crackles	3096	1 (reference)		3096	1 (reference)	
Crackles by location						
Certain inspiratory crackles at one lung base	221	1.91 (1.19 to 3.08)	0.008	246	1.44 (0.87 to 2.39)	0.2
Certain inspiratory crackles at both lung bases	85	3.00 (1.60 to 5.63)	0.001	77	3.70 (2.00 to 6.86)	<0.001
Certain crackles elsewhere*	82	0.94 (0.34 to 2.59)	0.9	138	1.12 (0.54 to 2.33)	0.8
Questionable crackles†	200	0.56 (0.25 to 1.29)	0.2	127	0.59 (0.22 to 1.63)	0.3

*Expiratory crackles are included.
†Classified as possible crackles in first round of classification, but as uncertain or no crackles in second round.
COPD, chronic obstructive pulmonary disease.

The unadjusted ORs of crackle characteristics for identifying COPD are shown in (tables 2 and 3). The age-adjusted and sex-adjusted OR for COPD of inspiratory crackles at one lung base was 1.73 (95% CI 1.07 to 2.81) for observer 1 and 1.29 (95% CI 0.77 to 2.16) for observer 2, while the ORs of inspiratory crackles at both lung bases were 2.59 (95% CI 1.36 to 4.91) and 3.20 (95% CI 1.71 to 5.98), respectively. Crackles elsewhere, including certain inspiratory or expiratory crackles, were not significantly associated with COPD, neither were crackles deemed as likely in the first round, but rejected as absent or uncertain in the second round.

When the bilateral crackles could be classified as coarse, the age and sex adjusted ORs were 2.65 (95% CI 1.28 to 5.49) and 3.67 (95% CI 1.58 to 8.52), whereas fine crackles were not related with COPD. The timing

Table 3 Unadjusted OR and 95% CI of crackles for COPD by crackle characteristics

	Observer 1			Observer 2		
	n	OR (95% CI)	P value	n	OR (95% CI)	P value
No certain crackles	3296	1 (reference)		3223	1 (reference)	
Coarse versus fine						
Fine inspiratory crackles one lung base, no inspiratory crackles on the other	36	1.10 (0.26 to 4.63)	0.9	116	0.84 (0.34 to 2.07)	0.7
Fine inspiratory crackles both lung bases	9	2.34 (0.29 to 18.84)	0.4	17	2.47 (0.56 to 10.90)	0.2
Coarse crackles one lung base[2]	196	2.25 (1.39 to 3.63)	0.001	149	2.39 (1.41 to 4.05)	0.001
Coarse inspiratory crackles both bases	65	3.01 (1.46 to 6.19)	0.003	38	4.19 (1.82 to 9.65)	0.001
Early* versus late						
Late inspiratory crackles at one lung base, no inspiratory crackles on the other	155	1.16 (0.58 to 2.31)	0.7	130	0.44 (0.14 to 1.39)	0.2
Late inspiratory crackles at both lung bases	37	1.07 (0.26 to 4.49)	0.9	17	0	1.0
Early inspiratory crackles at one lung base	94	3.84 (2.20 to 6.73)	<0.001	139	2.41 (1.40 to 4.15)	0.002
Early inspiratory crackles at both lung bases	20	8.03 (3.05 to 21.16)	<0.001	37	8.90 (4.39 to 18.02)	<0.001
Both early and coarse						
Early and coarse inspiratory crackles at one lung base	84	4.75 (2.73 to 8.28)	<0.001	102	3.45 (1.98 to 6.01)	<0.001
Early and coarse inspiratory crackles at both lung bases	13	5.62 (1.53 to 20.62)	0.009	18	9.27 (3.44 to 25.00)	<0.001
Other certain crackles	291	1.16 (0.70 to 1.94)	0.6	341	0.97 (0.58 to 1.62)	0.97

*'Early crackles' and 'both early and late crackles' are included in the category 'early'.
COPD, chronic obstructive pulmonary disease.

Table 4 Frequency of COPD in subgroups with basal inspiratory crackles identified by both observers among all participants and in those who reported current or former smoking

	All participants			Former or current smokers		
	n	COPD, n (%)	P value	n	COPD n (%)	P value
All	3684	204 (5.5)		2171	185 (8.5)	
Basal inspiratory crackles, one or both lungs						
Yes	263	29 (11.0)	<0.001	194	29 (14.9)	0.001
No	3421	175 (5.1)		1977	156 (7.9)	
Basal inspiratory crackles, both lungs						
Yes	71	11 (15.5)	<0.001	53	11 (20.8)	0.001
No	3613	193 (5.3)		2118	174 (8.2)	
Basal coarse inspiratory crackles, one or both lungs						
Yes	162	22 (13.6)	<0.001	124	22 (17.7)	<0.001
No	3522	182/5.2)		2047	163 (8.0)	
Basal coarse inspiratory crackles, both lungs						
Yes	34	7 (20.6)	<0.001	28	7 (25%)	0.002
No	3650	197 (5.4)		2143	178 (8.3)	
Basal early inspiratory crackles, one or both lungs						
Yes	87	20 (23.0)	<0.001	74	20 (27.0)	<0.001
No	3597	184 (5.1)		2097	165 (7.9)	
Basal early inspiratory crackles, both lungs						
Yes	13	5 (38.5)	<0.001	11	5 (45.5)	<0.001
No	3671	199 (5.4)		2160	180 (8.3)	
Basal inspiratory crackles, early and coarse, one or both lungs						
Yes	64	14 (21.9)	<0.001	54	14 (25.9)	<0.001
No	3620	190 (5.2)		2117	171 (8.1)	
Basal inspiratory crackles, early and coarse, both lungs						
Yes	6	3 (50.0)	<0.001	6	3 (50.0)	<0.001
No	3678	201 (5.5)		2165	182 (8.4)	

COPD, chronic obstructive pulmonary disease.

of crackles had even greater impact on the predictive value. When early inspiratory crackles were heard at both lung bases the OR for COPD was 6.88 (95% CI 2.59 to 18.29) for observer 1 and 7.63 (95% CI 3.73 to 15.62) for observer 2. Late crackles were not related with COPD. When the crackles were classified as both early and coarse the respective ORs were 4.77 (95% CI 1.29 to 17.62) and 7.90 (95% CI 2.90 to 21.49).

When basal inspiratory crackles were agreed on by both observers, the frequency or positive predicte value (PPV) for COPD was 11% (table 4). In the subsample who reported current or former daily smoking, the frequency was 14.9%. The PPVs found when the basal inspiratory crackles were 'early' were considerably higher than when coarse crackles were reported. The highest PPV, 50%, was found when both observers reported 'early' and 'coarse' crackles bilaterally (table 4).

The prevalence of both coarse and early basal inspiratory crackles increased by increasing severity of COPD (p<0.001), while no change in prevalence was found for fine and late crackles (figure 1).

The concordance of classifying basal inspiratory crackles as early and coarse had a kappa of 0.50 (95% CI 0.43 to 0.56) and 0.64 (95% CI 0.59 to 0.69) for observers 1 and 2, respectively. The corresponding concordances between fine and late crackles had kappas of 0.22 (95% CI 0.15 to 0.29) and 0.53 (95% CI 0.46 to 0.61).

The two observers agreed well on identifying basal inspiratory crackles (table 5). The agreement was somewhat poorer when it came to identifying the timing (early from late) and even more so when it came to type (fine from coarse).

DISCUSSION

Main findings

The present study confirmed that crackles heard during inspiration over the basal parts of the lungs are related to COPD. However, this applied only to early inspiratory and coarse crackles. We found no such association for other

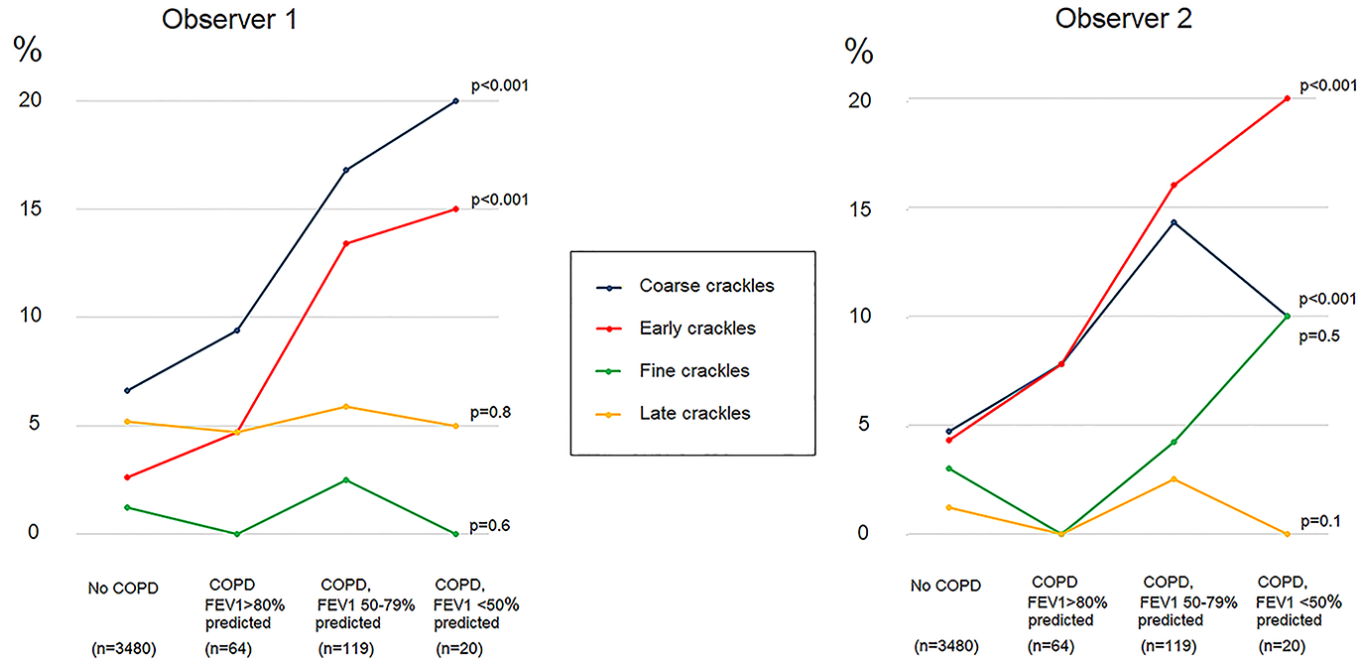

Figure 1 Prevalence (%) of characteristics (timing and type) of basal inspiratory crackles (unilateral or bilateral) by COPD severity. The p values refer to χ^2 tests for trend. COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 s.

types of crackles. The positive predictive value for COPD reached 50% when both observers heard basal inspiratory crackles over both lungs, which were both early and coarse. The prevalence of early and coarse crackles increased with increasing severity of COPD, while the prevalence of late and fine crackles remained unchanged across the different stages of COPD, suggesting another origin than bronchial obstruction. We found early crackles during inspiration to be more strongly associated with COPD than the acoustic perception of a coarse character. The interobserver agreement on timing was also superior to the agreement on type, as we were expecting.

Table 5 Agreement between the two observers on classification of crackles

	Kappa	95% CI
Among all participants in the second round of classification (n=588)		
Basal inspiratory crackles either lung	0.65	0.59 to 70.9
Among 263 participants classified by both observers to have unilateral/ bilateral basal inspiratory crackles		
Fine or coarse crackles either lung	0.24	0.13 to 0.36
Early* or late crackles either lung	0.40	0.30 to 0.51

*'Early crackles' and 'both early and late crackles' are included in the category 'early'.

Strengths and limitations

Among the strengths of this study are the large sample of participants and the rigorous process to classify lung sounds. We examined a sample of the general population who were mainly in a stable clinical state, and only a few of those with COPD were examined during an exacerbation. In patients with COPD, the prevalence of crackles tend to increase during exacerbations,[17] and a stronger association between crackles and COPD would probably be found if patients with COPD with exacerbations had been a particular focus of this study. Visualising spectrograms during the classification might have been of additional help in assessing the timing and type of crackles.[16]

The diagnosis of COPD was based on spirometry and on symptoms. Postbronchodilator spirometry was not obtained, and some participants might therefore have been overdiagnosed.[18] However, it was an advantage to have lung function measurements from the same day as the lung sounds were recorded.

The subclassification of crackles was done by only two observers, and their capabilities in classifying lung sounds are probably not representative of the average physician, Even these two observers differed considerably in their classification, for example, with observer 2 annotating fine crackles more than twice as frequently and also finding the characteristics 'coarse' and 'early' more strongly related to each other. However, this did not result in significant differences in the ability of such crackles to predict COPD.

The tedious classification process might have made the result less generalisable, since it is probably easier

to make judgements on timing and quality of crackles when watching a recording of 15 s than during conventional chest auscultation in real-world clinical practice. The diagnostic values might have been overestimated. In cardiac auscultation, the description of acoustic events such as murmurs is well established and relatively easy in comparison to pulmonary auscultation, given the frequency of the cardiac cycle. We are not aware of data regarding the average number of respiratory cycles that are typically auscultated in routine clinical examination. In fact, some recommendations are focused more clearly on the number of auscultation sites to be assessed and would accept as little as one complete breath per location.[19] The recordings in our study captured usually three or more respiratory cycles per site. Both observers had the advantage to listen repeatedly, but even in clinical practice three breaths or more should be sufficient to decide on the type and timing of crackles during the inspiratory phase.

The recordings in the present study were obtained while subjects were taking slightly deeper breaths than at rest and airflow was not captured. Auscultatory detection of crackles, particularly of those with coarse sound characteristics, becomes more difficult with increasing lung sound intensity, that is, at higher airflows.[20] Other factors that could explain the lower predictive value of crackle type compared with their timing include effects of their amplitudes,[1] their frequency content,[21] and related transmission through stethoscopes, as well as the auditory performance of listeners.

It is a limitation that we did not use a commercially available stethoscope. However, the stethoscope is described in detail,[11] and it has also been successfully used by the ERS's Task Force for Lung Sounds[22]

Implications for clinical practice and the future of the stethoscope

In terms of screening a general adult population for COPD, basal inspiratory crackles can only indicate that a patient might have this disease. However, when they occur early during inspiration, the clinician has reason to suspect COPD, and even more so when heard bilaterally, although such crackles may also indicate bronchiectasis[23] and asthma.[17] The PPVs found in our study are similar to those found for high COPD questionnaire scores[24 25] But, identification of crackles cannot match the questionnaires in terms of sensitivity.

The limited sensitivity we observed, particularly in mild to moderate COPD, reminds us that in most patients with COPD no crackles are heard. However, when listening to the chest wheezes or diminished breath sounds are also useful signs for identifying COPD.[26 27] The sensitivity of chest auscultation for COPD is, accordingly, considerably higher than for early inspiratory crackles alone. Anyway, a suspicion of COPD will in most cases rely on smoking history and symptoms.[27]

When basal inspiratory crackles are identified in a patient with dyspnoea, the clinicians has to consider heart failure[28] and other restrictive conditions[1] in addition to the obstructive diseases. In a recent study from Japan, early and fine inspiratory crackles were found in severe interstitial lung disease.[29] When the inspiratory crackles are both early and coarse, a strong attention to the possibility of COPD is timely. In the near future, electronic stethoscopes with automatic machine learning based classification and interpretation of lung sounds might be helpful in this respect.[30] Differentiation between coarse and fine and between early and late crackles can probably be taken into account in future devices and mHealth solutions, being thus more easily integrated in routine clinical practice.

CONCLUSION

Early inspiratory crackles at the lung bases predicted COPD more strongly than did coarse inspiratory crackles. However, both the timing and type of crackles should be considered when crackles are heard and COPD can be suspected.

Acknowledgements We thank the study participants and the staff of the Tromsø Study.

Contributors HM designed the study, took part in data collection and lung sound classification, and led the analysis and writing. JCAS collected data, classified sounds and contributed to analysis and writing. CJ and HP classified sounds and contributed to analysis and writing.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The Tromsø study protocol was performed in accordance with the Declaration of Helsinki and was approved by the Regional Committee for Medical and Health Research Ethics, North Norway (2014/940/REK Nord).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

ORCID iD

Hasse Melbye http://orcid.org/0000-0002-9773-3141

REFERENCES

1 Piirilä P, Sovijärvi AR. Crackles: recording, analysis and clinical significance. *Eur Respir J* 1995;8:2139–48.
2 Forgacs P. Crackles and wheezes. *Lancet* 1967;2:203–5.
3 Dollfuss RE, Milic-Emili J, Bates DV. Regional ventilation of the lung, studied with boluses of 133xenon. *Respir Physiol* 1967;2:234–46.
4 Nath AR, Capel LH. Inspiratory crackles--early and late. *Thorax* 1974;29:223–7.
5 GOLD. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2, 234-246, 2020. Available: https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMV.pdf

6 Ponikowski P, Voors AA, Anker SD. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of cardiology (ESC). developed with the special contribution of the heart failure association (HFA) of the ESC. *Eur J Heart Fail* 2016;2016:891–975.
7 Bohadana A, Izbicki G, Kraman SS. Fundamentals of lung auscultation. *N Engl J Med* 2014;370:744–51.
8 Jácome C, Marques A. Computerized respiratory sounds in patients with COPD: a systematic review. *COPD* 2015;12:104–12.
9 Vyshedskiy A, Murphy R. Crackle pitch rises progressively during inspiration in pneumonia, CHF, and IPF patients. *Pulm Med* 2012;2012:1–4.
10 Melbye H, Garcia-Marcos L, Brand P, *et al*. Wheezes, crackles and rhonchi: simplifying description of lung sounds increases the agreement on their classification: a study of 12 physicians' classification of lung sounds from video recordings. *BMJ Open Respir Res* 2016;3:e000136.
11 Aviles-Solis JC, Jácome C, Davidsen A, *et al*. Prevalence and clinical associations of wheezes and crackles in the general population: the Tromsø study. *BMC Pulm Med* 2019;19:173.
12 Jacobsen BK, Eggen AE, Mathiesen EB, *et al*. Cohort profile: the Tromso study. *Int J Epidemiol* 2012;41:961–7.
13 Mahler DA, Ward J, Waterman LA, *et al*. Patient-Reported dyspnea in COPD reliability and association with stage of disease. *Chest* 2009;136:1473–9.
14 Miller MR, Hankinson J, Brusasco V, *et al*. Standardisation of spirometry. *Eur Respir J* 2005;26:319–38.
15 Quanjer PH, Stanojevic S, Cole TJ, *et al*. Multi-Ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J* 2012;40:1324–43.
16 Aviles-Solis JC, Storvoll I, Vanbelle S, *et al*. The use of spectrograms improves the classification of wheezes and crackles in an educational setting. *Sci Rep* 2020;10:8461.
17 Melbye H, Al-Ani S, Spigt M. Drop in lung function during asthma and COPD exacerbations - can it be assessed without spirometry? *Int J Chron Obstruct Pulmon Dis* 2016;11:3145–52.
18 Johannessen A, Omenaas ER, Bakke PS, *et al*. Implications of reversibility testing on prevalence and risk factors for chronic obstructive pulmonary disease: a community study. *Thorax* 2005;60:842–7.
19 Prakash S, Mullick P, Pawar M. Pulmonary auscultation: a need to revisit this skill. *Br J Anaesth* 2015:115.
20 Kiyokawa H, Greenberg M, Shirota K, *et al*. Auditory detection of simulated crackles in breath sounds. *Chest* 2001;119:1886–92.
21 Kiyokawa H, Yonemaru M, Horie S, *et al*. [Frequency analysis of crackles recorded with a stethoscope-equipped recorder]. *Nihon Kyobu Shikkan Gakkai Zasshi* 1995;33:1341–7.
22 Pasterkamp H, Brand PLP, Everard M, *et al*. Towards the standardisation of lung sound nomenclature. *Eur Respir J* 2016;47:724–32.
23 Habesoglu MA, Ugurlu AO, Eyuboglu FO. Clinical, radiologic, and functional evaluation of 304 patients with bronchiectasis. *Ann Thorac Med* 2011;6:131–6.
24 Samukawa T, Matsumoto K, Tsukuya G, *et al*. Development of a self-scored persistent airflow obstruction screening questionnaire in a general Japanese population. The Hisayama study. *In J Chron Obstruct Pulmon Dis* 2017;12:1469–81.
25 Weiss G, Steinacher I, Lamprecht B, *et al*. Development and validation of the Salzburg COPD-screening questionnaire (SCSQ): a questionnaire development and validation study. *NPJ Prim Care Respir Med* 2017;27:4.
26 Oshaug K, Halvorsen PA, Melbye H. Should chest examination be reinstated in the early diagnosis of chronic obstructive pulmonary disease? *Int J Chron Obstruct Pulmon Dis* 2013;8:369–77.
27 Melbye H, Stylidis M, Aviles-Solis JC. Prediction of chronic heart failure and chronic obstructive pulmonary disease in a general population: the Tromsø study. *ESC Heart Fail* 2020;4150. [Epub ahead of print: 07 Oct 2020]. doi:10.1002/ehf2.13035
28 Fonseca C, Morais H, Mota T, *et al*. The diagnosis of heart failure in primary care: value of symptoms and signs. *Eur J Heart Fail* 2004;6:795–800.
29 Fukumitsu T, Obase Y, Ishimatsu Y, *et al*. The acoustic characteristics of fine crackles predict honeycombing on high-resolution computed tomography. *BMC Pulm Med* 2019;19:153.
30 García-Ordás MT, Benítez-Andrades JA, García-Rodríguez I, *et al*. Detecting respiratory pathologies using Convolutional neural networks and variational Autoencoders for unbalancing data. *Sensors* 2020;20:1214.