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

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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 in 323 by observer 2. When central inspiratory 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.

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. Nath and Capel proposed that crackles heard during inspiration were related to sudden opening of airways. Since the inflation of the lungs happens sequentially, and the basal parts inflate later during inspiration than the central parts, crackles may be described by time of appearance. Few years after Foggacs 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. 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., recent guidelines for diagnosing COPD and heart failure 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. 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 inspiration9 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 charac-
teristics.1 0 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,1 1 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 diag-
nostic 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 agree-
ment between clinicians in identifying these crackle
characteristics.

METHODS
Study population
The Tromsø study was established in 1974, and seven iter-
ations 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.1 2 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 physi-
cian 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.1 3

Spirometry was performed using SensorMedics Vmax
20c Encore (VIASYS Healthcare Respiratory Technolo-
gies, Yorba Linda, California, USA). Calibration was
done daily. We followed the standards of the American
Thoracic Society/European Respiratory Society (ERS).1 4
Tests with FEV1 <0.3 L or with expiration lasting less than
3 s were regarded invalid. Postbronzchodilator measure-
ment 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).1 5 Participants
were advised to take their medications for asthma and
COPD as usual.

Lung sounds were recorded at six locations of the
chest,1 1 15 s at each site, with a Sennheiser microphone
MKE2-EW inserted in the tube of a Litmann 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 (physi-
cians) who, using high-quality head-sets, independently
classified the recordings, blinded for other informa-
tion.1 1 When the observers disagreed, they discussed
the respective recordings with a third more experi-
enced 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 inspira-
ory crackles heard at other locations and also expi-
ratory crackles. When classifying the lung sounds, the
observers watched spectrograms of the recordings.1 6

Definition of COPD
Global initiative for chronic Lung Disease (GOLD)
recommends that a COPD diagnosis should be restricted
to patients with typical symptoms.1 6 We considered a diag-
nosis 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.3

### Statistical analysis

Participants’ characteristics were described as frequencies and determined by COPD status (presence or absence), and differences between groups were analysed with χ² 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 χ² test. The presence of crackle characteristics among the participants with COPD was analysed by severity groups, using χ² 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.

### 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).

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<thead>
<tr>
<th>Table 1 Characteristics of the 3684 participants by COPD status</th>
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<td>Gender</td>
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*Analysed by χ² for trend.

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 2 | Unadjusted OR and 95% CIs of crackles for COPD by location |
|----------------------------------|-----------------|-----------------|
| **Observer 1**                   | **Observer 2**  |
| **n**                            | **OR (95% CI)** | **P value**     |
| **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.

| Table 3 | Unadjusted OR and 95% CIs of crackles for COPD by crackle characteristics |
|----------------------------------|-----------------|-----------------|
| **Observer 1**                   | **Observer 2**  |
| **n**                            | **OR (95% CI)** | **P value**     |
| **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. |
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 predictive 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
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.

**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, 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.

The diagnosis of COPD was based on spirometry and symptoms. Postbronchodilator spirometry was not obtained, and some participants might therefore have been overdiagnosed. 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 15s 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. 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 airflow. Other factors that could explain the lower predictive value of crackle type compared with their timing include effects of their amplitudes, their frequency content, 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, and it has also been successfully used by the ERS’s Task Force for Lung Sounds.

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 and asthma. The PPVs found in our study are similar to those found for high COPD questionnaire scores. 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. 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.

When basal inspiratory crackles are identified in a patient with dyspnoea, the clinicians has to consider heart failure and other restrictive conditions in addition to the obstructive diseases. In a recent study from Japan, early and fine inspiratory crackles were found in severe interstitial lung disease. 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. 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.

REFERENCES

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;18:981–975.


