

Title: Effects of a respiratory physiotherapy session in patients with LRTI: a pre/post-test study.

Running head: Respiratory physiotherapy in LRTI.

Ana Oliveira^a, Cátia Pinho^{a,b}, Alda Marques^{a,c}

^a Lab 3R – Respiratory Research and Rehabilitation Laboratory, School of Health Sciences, University of Aveiro (ESSUA), Aveiro, Portugal.

^b IT – Aveiro, Instituto de Telecomunicações, University of Aveiro, Aveiro, Portugal

^c Cintesis.UA (Center for Health Technology and Services Research), University of Aveiro, Aveiro, Portugal

Contributor's Statement:

Ana Oliveira carried out data collection and analysis, drafted the manuscript and approved the final manuscript as submitted.

Cátia Pinho carried out data collection and analysis, critically reviewed the manuscript and approved the final manuscript as submitted.

Alda Marques conceptualized and designed the study, obtained the funding, coordinated and supervised data collection, critically reviewed the manuscript and approved the final manuscript as submitted.

Corresponding author: Alda Marques; School of Health Sciences, University of Aveiro (ESSUA), Agrad do Crasto - Campus Universitário de Santiago – Ed. 30, 3810-193 Aveiro, Portugal. Telephone: 00351 234 372 462; Fax: 00351 234 401 597; Email: amarques@ua.pt

Conflict-of-interest statement: The authors report no conflict of interests.

ABSTRACT

Introduction: The role of respiratory physiotherapy (RP) in lower respiratory tract infections (LRTI) has been questioned. However, studies have focused on hospitalised patients, and the presence/absence of an underlying disease has been neglected.

Objectives: To assess the effects of a RP session in community patients with LRTI and to explore the differences between patients with pneumonia (restrictive disease – AR) and those with exacerbations of an obstructive disease (AO).

Methods: A pre/post-test study was conducted. A RP session was applied to patients with LRTI and crackles, wheezes, dyspnoea, perception of sputum and oxygen saturation were collected pre/post session. Comparisons were performed using paired t-tests or Wilcoxon tests.

Results: Thirty patients (14 males, 55.23 ± 17.78 yrs) with pneumonia (AR, $n=12$), exacerbations of chronic obstructive pulmonary disease, acute bronchitis and asthma (AO, $n=18$) were enrolled. After treatment, the total sample presented lower wheeze rates at trachea ($p=0.02$; $r=-0.54$) and less sputum ($p=0.01$; $r=-0.47$). AR patients presented a decrease in the number of crackles ($p<0.05$; $0.30 < d_z < 0.26$) and number and rate of wheezes at chest locations ($p<0.05$; $-0.56 < r < -0.48$). AO patients showed an increase in the number of crackles ($p<0.05$; $0.20 < d_z < 0.31$), wheeze frequency ($p=0.03$; $r=-0.27$) and dyspnoea ($p=0.04$; $r=-0.55$); and a decrease in the number of wheezes at trachea ($p=0.02$; $r=-0.54$).

Conclusions: RP seems effective in reducing wheezes and perception of sputum in patients with LRTI. However, when considering AR and AO diseases separately, further changes in respiratory sounds and dyspnoea emerged. This highlights the importance of considering subgroups of patients with LRTI to develop RP evidence-base practice.

Key words: acute obstructive; acute restrictive, computerised respiratory sounds; physiotherapy

Clinical Trial Registration Number: NCT02053870

Ethical Statement: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 2000 Helsinki declaration. Before data collection, written informed consent was obtained from each participant.

INTRODUCTION

Lower respiratory tract infection (LRTI) defines a wide range of infectious diseases which annually affect 429 million people worldwide(1). Due to its far-reaching spectrum of conditions(2, 3), LRTI may present itself in the form of a restrictive disease (e.g., patients with pneumonia with no other previous respiratory condition) or as an exacerbation of an obstructive disease (e.g., chronic obstructive respiratory diseases).

LRTI is often characterised by the presence of cough, dyspnoea and sputum(3), compromising patients' wellbeing and functionality(4). Respiratory physiotherapy has shown to be effective in relieving such symptoms in patients with stable chronic respiratory diseases(5, 6), however its effectiveness in patients with LRTI has been questioned. A recent Cochrane systematic review assessing the effectiveness of respiratory physiotherapy in pneumonia has reported no effects on patients' health status(7). However, this review only addressed inpatients, therefore the content and structure of the intervention (e.g. techniques, duration and frequency) may not be the most adequate for community patients. Also, an emerging body of evidence is showing promising results when physiotherapy interventions are applied in acute exacerbations of obstructive diseases, at the onset and/or immediately after the exacerbation(8-10). Improvements in sputum expectoration, exercise capacity(9, 10) and health-related quality of life(9); and decrease risk of future hospital admissions(8, 9), have been reported. Although the evidence is still scarce, most patients with LRTI are treated as community patients⁽¹¹⁾ and are living in the community therefore, studies focused on developing, implementing and assessing the outcomes of community-based physiotherapy programs are needed.

According to the authors' best knowledge, there is also no intervention studies in LRTI exploring if the absence or presence of an underlying respiratory disease influences the effects of the physiotherapy treatment. This is of particular relevance, as different underlying

pathophysiologies might affect patients' response to interventions primarily developed to resolve the LRTI condition. This evidence would contribute not only to clarify the role of physiotherapy in patients with LRTI but also to personalise patient's treatment according to their specific background.

Therefore, the primary aim of this study was to assess the effects of a respiratory physiotherapy session in community patients with LRTI. Additionally, a secondary aim was established to explore patients' response to physiotherapy considering their underlying respiratory condition, i.e., restrictive disease with no previous respiratory condition (AR) and exacerbations of an obstructive disease (AO). For this purpose, computerised adventitious respiratory sounds (i.e., crackles and wheezes) were used as primary outcome measures, whilst dyspnoea, perception of sputum and peripheral oxygen saturation were used as secondary outcome measures.

METHODS

Design and Ethics

A parallel study with a pre/post-test design, part of a larger randomised controlled trial (NCT02053870), was conducted with a sample of patients with LRTI living in the community. Patients were classified as restrictive (pneumonia) or obstructive (mucosal infections, acute exacerbation of COPD and asthma) based on their health records (i.e., previous diagnosis of asthma and COPD or no previous diagnosis of a respiratory disease) and medical notes in the emergency department (i.e., diagnosis of a pneumonia, acute exacerbation of COPD or asthma and acute bronchitis). Lung function tests were not taken into consideration as they are not accurate in the assessment of exacerbated patients(12).

Before data collection, full approval from the Institutional Ethics Committee (2010-4-14) was acquired and patients' written informed consents were obtained.

Sample size

Sample size was calculated to determine the number of participants required to detect a significant difference in crackles' mean number per breathing cycle, detected with computerised respiratory sound analysis. This parameter was chosen since previous studies conducted in patients with LRTI indicated that this variable significantly changes after interventions (effect sizes of 0.74 and 1.65)(13, 14). Data from a pilot study(14) conducted with 6 community patients with LRTI was used to compute the required sample size (pre: 2.15 ± 0.55 vs. post 1.59 ± 1.02 ; effect size of 0.63) for a power of 95% and an alpha of 0.05. Using the sample size calculation of GPower 3 software (University Düsseldorf, Germany), a sample of 28 individuals was required. According to the literature, the choice of a study's power depends on the size of the effect to be detected, which in turn is based on clinical judgement(15). Specifically in the present study, a single session of physiotherapy was being evaluated and thus, small differences in the outcome measures were expected, resulting in small effect sizes. Therefore, in order to detect true differences between pre and post intervention, a larger power was needed in the sample size calculation.

Dropout rates were calculated using evidence from long-term rehabilitation programs (i.e., 30-50%)(16, 17), as no studies reporting on dropout rates in single sessions of respiratory physiotherapy were found. Considering that patients with exacerbations are those with higher probability to dropout(18), the highest percentage was used and a final sample of 41 participants was recruited.

Participants

Patients were recruited from the emergency department of a general hospital and were eligible if they: i) were ≥ 18 years old; ii) presented cough; and iii) had at least one of the following symptoms: sputum, dyspnoea, wheezes or chest pain(3). Exclusion criteria were: i) hospital admission; ii) signs of cognitive impairment; iii) being bedridden or dependent on a

wheelchair; iv) having a score >2 in the CURB criteria(19); and v) presence of comorbidities that could interfere with the tests (e.g., previous history of pulmonary lobectomy and current history of neoplasia, tuberculosis or other infectious diseases).

Intervention

The intervention consisted of conventional medical treatment (i.e., antibiotherapy, bronchodilators and rest)(3) plus respiratory physiotherapy. The respiratory physiotherapy session was conducted 72h after hospital presentation and was composed of approximately: i) 5 minutes of breathing retraining techniques to reduce energy costs of breathing(20); ii) 10 minutes of incentive spirometry to increase pulmonary expansion(21), prevent atelectasis and aid airway clearance(22); iii) 10-15 minutes of active cycle of breathing techniques to mobilise and clear excess bronchial secretions(23); iv) 15 minutes of exercises for thoracic mobility, expansion and flexibility to increase pulmonary volumes(24); and v) 10-15 minutes of education about self-clearing techniques and home-based exercises, to ensure an on-going effective intervention and to encourage patients' self-management of the disease. Sessions lasted on average 60 ± 15 minutes. The same intervention was applied to all participants as prior to the study, it was unknown if patients with or without underlying pathologies would respond differently to these physiotherapy techniques. Thus, the intervention was prepared to tackle mainly the acute condition.

Data collection

Before the session, socio-demographics (gender and age), anthropometric (height and weight), activities limitation resulting from dyspnoea (measured with the modified medical research questionnaire(25)) and lung function tests, assessed with a portable spirometer (MicroLab Micro Medical 36-ML3500-MK8, UK)(26), were collected. Information on computerised respiratory sounds (collected before lung function tests), dyspnoea, perception of sputum and peripheral oxygen saturation were collected before and after the respiratory physiotherapy

session. Data were collected by an independent trained researcher not involved in the respiratory physiotherapy intervention.

Primary outcome measure

Computerised adventitious respiratory sounds (i.e, crackles and wheezes), were recorded according to the Computerised Respiratory Sound Analysis (CORSA) guidelines for short-term acquisitions(27), i.e., participants were in a seated-upright position and respiratory sounds were collected with a digital stethoscope (WelchAllyn Meditron 5079-400) in seven anatomical locations (trachea, left and right: anterior, lateral and posterior locations). The stethoscope was connected to a sound card (Cakewalk UA-25EX), which was plugged to a laptop computer. Data were acquired using the LungSounds@UA interface(28) for 20 seconds in each location. The signal was converted with a 24-bit resolution at a sampling rate of 44.1 KHz and recorded in wav. format(29). Acquired signals were then filtered using a Blackman bandpass filter from 100-2000Hz. Tracheal data were not analysed for crackles parameters, as a recent study has indicated that crackles are not reliable at this anatomical point(30).

All sound files were analysed using automatic algorithms implemented in Matlab 2009 (The MathWorks, Inc, Natick, MA, USA). Breathing cycles were semi-automatically detected using the algorithm developed by Huq and Moussavi (95.5% sensitivity and 95.6% specificity)(31).

Crackles were automatically detected using an algorithm based on fractal dimension and box filtering techniques (89% sensitivity, 95% positive predictive value and 92% overall performance –F-index)(32). Crackles analysis was composed by number, frequency (Hz), initial deflection width (IDW), two-cycle deflection duration (2CD) and largest deflection width (LDW). Wheezes detection was performed based on the algorithm of Taplidou and Hadjileontiadis(33). The parameters extracted were: total number, number of monophonic and polyphonic wheezes, frequency (Hz) and occupation rate. All respiratory sound analysis was performed per breathing phase (inspiration/expiration).

Secondary outcome measures

Dyspnoea was assessed with the modified Borg Scale (34), a vertical scale labelled from 0 to 10 with corresponding verbal expressions of increasing breathlessness intensity. The modified Borg Scale is simple, quick to apply and has shown to be reliable to assess dyspnoea in subjects with respiratory diseases (35, 36).

Perception of sputum was evaluated using a 5 level self-report scale which is a domain of the Breathlessness, cough and sputum scale (37): (1) no sputum production; (2) mild sputum production; (3) moderate sputum production; (4) severe sputum production; and (5) unquantifiable. This scale is validated for patients with stable COPD (38) and has been shown to be sensitive to changes during the course of exacerbations (37).

Peripheral Oxygen saturation (SpO_2) was measured with a pulse oxymeter (Nonin, WristOx₂[™], Model 3150) to ensure patient's safety and monitor the impact of the intervention (i.e., when secretions are removed, regional ventilation may increase and oxygenation should improve). Pulse oximeters have been described as an accurate outcome measure (39).

Statistical analysis

Descriptive statistics were used to characterise the sample. First, differences between pre/post physiotherapy session were explored in all sample with paired sample t-tests for normally distributed data and Wilcoxon signed-rank tests for ordinal/non-normally distributed data. Chi-square tests were used for categorical data. Then, two-way analysis of variance with repeated measurements were used to establish the significant effects of the interaction time X group. For non-parametric and ordinal data, the differences between pre and post-intervention assessments were pooled and then Mann Whitney U-tests were used to compare AR and AO groups. Pre/post differences within groups were performed using paired sample t-tests, for normally distributed data, and Wilcoxon signed-rank tests, for non-normally distributed data. The level of significance was set at 0.05. Statistical analysis was completed with the estimation

of effect sizes for each outcome measure(40). Effect sizes were measured via Partial eta-squared (η^2), for two-way analysis of variance(41), Cohen's d_z for Paired sample t-tests(42) and the rank-biserial correlation (r) for data analysed with Mann Whitney U-tests and Wilcoxon signed-rank tests(43). Effect sizes were interpreted as small ($\eta^2 \geq 0.01$; $d_z \geq 0.2$ (42); $r \geq 0.1$ (43)), medium ($\eta^2 \geq 0.06$; $d_z \geq 0.5$ (42); $r \geq 0.3$ (43)) or large ($\eta^2 \geq 0.14$; $d_z \geq 0.8$ (42); $r \geq 0.5$ (43)) effect, according to the index used. Analyses were performed using SPSS version 20.0 (IBM Corporation, Armonk, NY, USA) and data is presented as mean (standard deviation) or median [interquartile range].

RESULTS

A total of 41 patients were assessed for eligibility and asked about their willingness to participate. Eleven patients refused to participate due to: personal reasons ($n=1$), transport constraints ($n=3$) and disruption of normal routine ($n=7$). Thus, 30 community patients (14 males; 55.23 (17.78) yrs) diagnosed with LRTI were enrolled in the study. Twelve participants presented an AR (i.e., pneumonia with no previous respiratory conditions; $n=12$) and eighteen an AO (i.e., exacerbation of COPD, acute bronchitis and asthma) disease. At baseline, no significant differences were found between the two groups for socio-demographic and clinical characteristics. A detailed description is provided in table 1.

(please insert table 1 about here)

Primary outcome measure

No differences were found in crackles parameters before and after the physiotherapy session considering the average changes among the 30 participants ($p > 0.05$). However, when considering AR and AO diseases as separate groups, a significant decrease in the number of crackles during inspiration (pre 2.01 (1.46) vs. post 1.61 (1.14); $p=0.03$; $d_z=0.30$) and expiration (pre 2.38 (1.67) vs. post 1.98 (1.36); $p=0.04$; $d_z=0.26$) were found after the intervention in

patients with AR diseases. Conversely, patients with AO diseases presented a significant increase in the same parameter (inspiration: pre 1.89 (1.10) vs. post 2.15 (1.44); $p=0.03$; $d_z=0.20$; expiration: pre 2.64 (1.68) vs. post 3.22 (1.99); $p<0.001$; $d_z=0.31$) (Figure 1). Also, significant differences were found between groups for these variables ($p<0.05$; η^2 from 0.05 to 0.09). No differences were found within AR and AO groups for the remaining crackles parameters. A detail description of crackles variables can be found in the online supplementary material.

(please insert figure 1 about here)

Considering the average changes among the 30 participants, a significant decrease in the wheeze occupation rate at trachea was found (pre 2.36 [0 to 5.83] vs. post 0.70 [0 to 2.79]; $p=0.02$; $r=-0.54$). No differences were found for the other wheezes' parameters at trachea or at chest locations ($p>0.05$). However, when considering AR and AO diseases as separate groups, a significant decrease in the inspiratory number of wheezes (pre 0.20 [0.20 to 0.50] vs. post 0 [0 to 0.20]; $p=0.02$; $r=-0.54$), monophonic wheezes (pre 0.20 [0.20 to 0.33] vs. post 0 [0 to 0.20]; $p=0.01$; $r=-0.48$) and wheeze occupation rate (pre 3.86 [2.15 to 11.87] vs. post 0 [0 to 3.07]; $p=0.01$; $r=-0.56$) at chest locations was observed in AR patients. In AO patients, only the frequency (Hz) of inspiratory wheezes increased significantly (pre 233.98 [172.86 to 603.55] vs. post 504.35 [226.08 to 911.43]; $p=0.03$; $r=-0.27$) (Figure 2).

(please insert figure 2 about here)

At trachea, a significant decrease in the expiratory number of wheezes (pre 0.22 [0 to 0.50] vs. post 0 [0 to 0.25]; $p=0.02$; $r=-0.54$), monophonic wheezes (pre 0 [0 to 0.20] vs. post 0 [0]; $p=0.02$; $r=-0.54$) and wheeze occupation rate (pre 3.49 [0 to 5.83] vs. post 0 [0 to 2.08]; $p=0.02$; $r=-0.55$) was observed only in AO patients (Figure 3).

(please insert figure 3 about here)

Significant differences between groups were found only in chest locations for the previously reported variables ($p < 0.05$; η^2 from 0.02 to 0.37). No differences between AR and AO groups for the remaining parameters of wheezes were found. More details on wheezes variables can be found in the online supplementary material.

Secondary outcome measures

Considering the average changes among the 30 participants, a significant improvement in the reported sputum was found (pre 3 [2 to 3] vs. post 2 [2 to 3]; $p = 0.01$; $r = 0.47$). When AR and AO diseases were analysed as separate groups, patients with AO diseases reported significantly less perception of sputum (pre 3 [2 to 3.25] vs. post 2 [1 to 3]; $p = 0.04$; $r = 0.55$) and no differences were found for patients with AR diseases. After intervention, AO patients felt more breathless than before the intervention (pre 0 [0 to 2] vs. post 2 [1 to 3]; $p = 0.02$; $r = 0.47$) and no significant changes were found for SpO₂ in both groups (Table 2). No differences were found between groups for these variables.

(Please insert table 2 about here)

DISCUSSION

According to the authors' best knowledge, this is the first study reporting the effects of one single respiratory physiotherapy session in community patients with LRTI. The expiratory wheeze rate at trachea and the self-reported sputum improved significantly in the overall sample. No other significant differences were found pre/post intervention when analysing all sample. However, when the presence/absence of an underlying disease was taken into consideration, opposite behaviours mainly concerning computerised adventitious respiratory sounds in chest locations and dyspnoea were found in patients with AR and AO diseases. This highlights the importance of exploring the different groups when studying the effects of respiratory physiotherapy in patients with LRTI.

Two cross sectional and descriptive studies developed by Murphy et al. (2004)(44) and Vyshedskiy et al. (2011)(45) found that crackles were the most common finding in patients with pneumonia, with a mean number ranging from 6 to 8 crackles per patient. Such is approximately three times higher than the values obtained in our sample. However, it should be noted that in the present study patients were being treated in a community based setting, presented mild severity pneumonia (i.e., CURB<2) and were under the effects of the standard medical treatment for 72 hours, which most likely influenced the respiratory sounds obtained. Contrary to our findings, a study of Piirila (1992)(46) assessing computerised crackles behaviour during the clinical course of pneumonia showed that the number of crackles did not vary during the course of pneumonia. However, direct comparisons are difficult to establish due to methodological constraints. In Piirila's study(46), patients' second evaluation was performed two days after the initial assessment, whilst in our study the second evaluation occurred immediately after the intervention. Also, as the respiratory physiotherapy session involved pulmonary expansion and airway clearance techniques, at the end of the session more airways were probably clear and open, justifying the reduction in crackles number in the AR patients(47). On the other hand, the number of crackles increased in those with AO diseases. Exacerbations of obstructive respiratory diseases are characterised by an excessive production of thicker sputum, (48, 49), which often remains lodged in the lung bases(49), causing small airways to be closed. It is known that respiratory physiotherapy aids to mobilise secretions to the upper airways and ultimately clear them from the respiratory system(10). This movement of secretions to the upper airways may have contributed for allowing more air to pass into smaller and peripheral airways leading them to suddenly open, and therefore increasing crackle production. These results also differ from those found by Marques et al. (2012)⁽⁵⁰⁾, who found no differences in the number of crackles after 20 minutes of active breathing cycle techniques in patients with stable bronchiectasis. Differences may be related

to the different population studied (stable vs. exacerbated) and with the fact that only one intervention with a shorter period of time was applied in Marques' study.

Results on wheeze parameters were more discrete, but generally its behaviour supported crackles findings. The decrease in the inspiratory number and occupation rate of wheezes in patients with AR diseases may support the idea that more airways were open after treatment, causing less bronchiolar constriction(51). The significant increase in the frequency of wheezes in the chest of patients with AO may be explained by the movement of secretions to more central and upper airways, as it is known that high frequency wheezes are produced in more proximal airways(52). A significant decrease in the expiratory number of wheezes was also observed at trachea. Wheezes' production in patients with obstructions diseases is related with either airways oedema or sputum accumulation(53). In pre-intervention, AO patients showed more signs of obstruction, caused by bronchial secretions (54, 55) (i.e., higher rates of self-reported sputum, higher percentage of the breathing cycle occupied by wheezes and lower FEV₁ values). Thus, these findings corroborate the conclusions, that post treatment sputum was being moved and eliminated towards more proximal airway.

Following the respiratory physiotherapy session, all patients reported less sputum and patients with AO diseases reported more dyspnoea. A lower sputum perception at the end of the session was expected and desirable, as it reveals that the respiratory manoeuvres helped patients to expectorate and clean most secretions. These results contrast with a recent Cochrane systematic review which reported that respiratory physiotherapy did not improve sputum weight in inpatients with pneumonia(7). This may be explained not only by the different population studied (i.e., inpatients vs. community patients), but also by the different techniques and evaluation methods used. The studies included in the Cochrane review used mainly conventional techniques and therefore, those, have been discouraged by the current literature in patients with acute respiratory disease (grade B)(23).

The increase of dyspnoea in AO patients may be explained by the respiratory manoeuvres used to mobilise and expel secretions, namely forced expiratory manoeuvres. As previously mentioned, AO patients showed more signs of obstruction, thus a higher number of forced expiratory manoeuvres were needed to remove secretions. These techniques, despite presenting high efficacy(56), also require high levels of physical effort(57), which may explain the higher post intervention dyspnoea. Contrarily, Marques et. al (2012)(50) found a significantly decrease in patients' dyspnoea after the airway clearing session. Differences in the population, techniques and time of the intervention may explain the dissimilarities between studies.

Currently, there has been a large debate on the effects of respiratory physiotherapy in patients with acute and exacerbated conditions. However, based on the best evidence available of the effectiveness of physiotherapy techniques to manage the symptoms of LRTI (23, 24, 58) and from our results, it can now be suggested that community patients with LRTI may benefit from respiratory physiotherapy sessions. Nevertheless, patients with AR diseases may require respiratory physiotherapy interventions focused on exercises for thoracic mobility, expansion and flexibility to increase pulmonary volumes, reduce number of crackles and open airways, whereas patients with AO diseases may need interventions mainly involving techniques for airway clearance to move and expel secretions towards proximal airways.

Limitations and future work

This study has some limitations that need to be acknowledged. Firstly, the absence of a control group. Inclusion of a group of patients receiving only medication would have strengthened the findings regarding the effectiveness of respiratory physiotherapy in patients with LRTI. Secondly, respiratory sounds parameters were evaluated before and after the respiratory physiotherapy session and not between techniques, which impairs to assess the individual effect of each technique. However, in clinical practice, one session of respiratory

physiotherapy often includes more than one technique applied to the patient, which makes the results of this study directly applicable to physiotherapists' clinical practice. Thirdly, it is known that factors such as age and severity of the disease affect respiratory sounds(59, 60). However, the results achieved for the established groups (i.e., AR vs AO groups) were generally homogeneous within groups and a clear difference between them was found, which lead us to believe that the influence of such variables was residual. Nevertheless, future studies with larger samples are needed to increase the statistical power and allow to control for such confounders.

Finally, flows and/or volumes were not controlled during respiratory sounds recordings. These might have affected the results as it is known that crackle frequency depends on volume of inhaled air and the presence of wheezes depends on rate of inhalation. However, patients with LRTI often present severe dyspnoea which causes the use of a mouthpiece or facemask (necessary to assess flows and/or volumes) to be highly uncomfortable or even not tolerated. Furthermore, the primary purpose of this study was to assess the effect of respiratory physiotherapy applied in a community-based clinical setting, where control of airflow is often not practical.

CONCLUSION

One session of respiratory physiotherapy seems effective in reducing wheezes rate at trachea and perception of sputum in patients with LRTI. However, when considering patients with AR and AO diseases separately different responses were observed and further changes in respiratory sounds at chest locations and dyspnoea emerged. These results highlight the importance of analysing patients with LRTI in subgroups to clarify and develop respiratory physiotherapy evidence-base practice in acute respiratory populations. It also emphasises the need of implementing personalised care in future interventions applied to community patients with LRTI.

Acknowledgements

This work was funded by Fundação para a Ciência e Tecnologia, Portugal (project ref. PTDC/SAU-BEB/101943/2008). The authors' grateful acknowledge the contribution of Welch Allyn Company by providing the digital stethoscope used in the respiratory sounds evaluation. The authors are also very grateful to all institutions and patients for their participation in this research study.

References

1. World Health Organization. The global burden of disease - 2004 update Switzerland: World Health Organization, 2008.
2. Greene G, Hood K, Little P, Verheij T, Goossens H, Coenen S, et al. Towards clinical definitions of lower respiratory tract infection (LRTI) for research and primary care practice in Europe: an international consensus study. *Prim Care Respir J*. 2011;20(3):299-306, 6 p following
3. Woodhead M, Blasi F, Ewig S, Garau J, Huchon G, Ieven M, et al. Guidelines for the management of adult lower respiratory tract infections--full version. *Clin Microbiol Infect*. 2011;17 Suppl 6:E1-59.
4. Restrepo MI, Anzueto A. Guidelines for the diagnoses and treatment of adult lower respiratory tract infections: a true "European cooperative effort". *Eur Respir J*. 2005;26(6):979-81.
5. Bradley JM, Moran FM, Stuart Elborn J. Evidence for physical therapies (airway clearance and physical training) in cystic fibrosis: An overview of five Cochrane systematic reviews. *Resp Med*. 2006;100(2):191-201.
6. Garrod R, Lasserson T. Role of physiotherapy in the management of chronic lung diseases: An overview of systematic reviews. *Resp Med*. 2007;101(12):2429-36.
7. Yang M, Yan Y, Yin X, Wang BY, Wu T, Liu GJ, et al. Chest physiotherapy for pneumonia in adults. *Cochrane Database Syst Rev*. 2013;2:CD006338.
8. Holland AE. Physiotherapy management of acute exacerbations of chronic obstructive pulmonary disease. *J Physiother*. 2014;60(4):181-8.
9. Puhan MA, Gimeno-Santos E, Scharplatz M, Troosters T, Walters EH, Steurer J. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2011(10):Cd005305.
10. Tang CY, Taylor NF, Blackstock FC. Chest physiotherapy for patients admitted to hospital with an acute exacerbation of chronic obstructive pulmonary disease (COPD): a systematic review. *Physiotherapy*. 2010;96(1):1-13.

11. Singanayagam A, Chalmers JD, Welte T. Epidemiology of CAP in Europe. In: Chalmers J, Pletz M, Aliberti S, editors. *European Respiratory Monograph 63: Community-Acquired Pneumonia*. 63: European Respiratory Society; 2014.
12. The Global Initiative for Chronic Obstructive Lung Disease. *Global Strategy for Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease - 2015 Update*. The Global Initiative for Chronic Obstructive Lung Disease, Inc.; 2015.
13. Beck R, Elias N, Shoval S, Tov N, Talmon G, Godfrey S, et al. Computerized acoustic assessment of treatment efficacy of nebulized epinephrine and albuterol in RSV bronchiolitis. *BMC Pediatr*. 2007;7(22):1-6.
14. Oliveira D. *Dispneia e Sons Pulmonares Adventícios na Infecção Respiratória do Trato Inferior*: University of Coimbra; 2012.
15. Whitley E, Ball J. Statistics review 4: Sample size calculations. *Critical Care*. 2002;6(4):335-41.
16. Garrod R, Marshall J, Barley E, Jones PW. Predictors of success and failure in pulmonary rehabilitation. *Eur Respir J*. 2006;27(4):788-94.
17. Greulich T, Kehr K, Nell C, Koepke J, Haid D, Koehler U, et al. A randomized clinical trial to assess the influence of a three months training program (gym-based individualized vs. calisthenics-based non-individualized) in COPD-patients. *Respir Res*. 2014;15(36):1-8.
18. Fischer MJ, Scharloo M, Abbink JJ, van 't Hul AJ, van Ranst D, Rudolphus A, et al. Drop-out and attendance in pulmonary rehabilitation: the role of clinical and psychosocial variables. *Respir Med*. 2009;103(10):1564-71.
19. Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax*. 2003;58(5):377-82.
20. Main E, Prasad A, Schans CVd. Conventional chest physiotherapy compared to other airway clearance techniques for cystic fibrosis. *Cochrane Database Syst Rev*. 2005.
21. Weiner P, Man A, Weiner M, Rabner M, Waizman J, Magadle R, et al. The effect of incentive spirometry and inspiratory muscle training on pulmonary function after lung resection. *J Thorac Cardiovasc Sur*. 1997;113(3):552-7.
22. Postiaux G. *Fisioterapia respiratória pediátrica, o tratamento guiado por ausculta pulmonar*. 2nd ed: Porto Alegre Artmed; 2004.
23. Bott J, Blumenthal S, Buxton M, Ellum S, Falconer C, Garrod R, et al. Guidelines for the physiotherapy management of the adult, medical, spontaneously breathing patient. *Thorax*. 2009;64 Suppl 1:i1-51.
24. American Association of Cardiovascular and Pulmonary Rehabilitation. *Guidelines for pulmonary rehabilitation programs*. 4rd ed. USA: Human Kinetics; 2011.
25. Doherty DE, Belfer MH, Brunton SA, Fromer L, Morris CM, Snader TC. Chronic Obstructive Pulmonary Disease: Consensus Recommendations for Early Diagnosis and Treatment. *J Fam Practice*. 2006:S1.

26. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. *Eur Respir J*. 2005;26(2):319-38.
27. Rossi M, Sovijarvi ARA, Piirila P, Vannuccini L, Dalmasso FVJ. Environmental and subject conditions and breathing manoeuvres for respiratory sound recordings. *Eur Respir Rev*. 2000;10(77):611-5.
28. Pinho C, Oliveira A, Oliveira D, Dinis J, Marques A. LungSounds@UA interface and multimedia database. *International Journal of E-Health and Medical Communications*. 2014;5(1):81-95.
29. Cheetham B, Charbonneau G, Giordano A, Heliö P, Vanderschoot J. Digitization of data for respiratory sound recordings. *Eur Respir Rev*. 2000;10(77):621-4.
30. Jacome C, Marques A. Computerized Respiratory Sounds Are a Reliable Marker in Subjects With COPD. *Respir Care*. 2015.
31. Huq S, Moussavi Z. Automatic Breath Phase Detection Using Only Tracheal Sounds. 2010 Annual International Conference of the IEEE Engineering in Medicine and Biology Society (Embc). 2010:272-5.
32. Pinho C, Oliveira A, Jácome C, Rodrigues J, Marquesa A. Automatic crackle detection algorithm based on fractal dimension and box filtering. *Procedia Computer Science*. 2015;(in press).
33. Taplidou SA, Hadjileontiadis LJ. Wheeze detection based on time-frequency analysis of breath sounds. *Comput Biol Med*. 2007;37(8):1073-83.
34. Borg G. Borg's Perceived Exertion and Pain Scales. United States of America: Human Kinetics; 1998.
35. Belman MJ, Brooks LR, Ross DJ, Mohsenifar Z. Variability of breathlessness measurement in patients with chronic obstructive pulmonary disease. *Chest*. 1991;99(3):566-71.
36. Simon PM, Schwartzstein RM, Weiss JW, Lahive K, Fencel V, Teghtsoonian M, et al. Distinguishable sensations of breathlessness induced in normal volunteers. *Am Rev Respir Dis*. 1989;140(4):1021-7.
37. Leidy NK, Rennard SI, Schmier J, Jones MK, Goldman M. The breathlessness, cough, and sputum scale: the development of empirically based guidelines for interpretation. *Chest*. 2003;124(6):2182-91.
38. Leidy NK, Schmier JK, Jones MK, Lloyd J, Rocchiccioli K. Evaluating symptoms in chronic obstructive pulmonary disease: validation of the Breathlessness, Cough and Sputum Scale. *Respir Med*. 2003;97 Suppl A:S59-70.
39. Jensen LA, Onyskiw JE, Prasad NG. Meta-analysis of arterial oxygen saturation monitoring by pulse oximetry in adults. *Heart Lung*. 1998;27(6):387-408.
40. Kraemer HC, Kupfer DJ. Size of Treatment Effects and Their Importance to Clinical Research and Practice. *Biological Psychiatry*. 2006;59(11):990-6.
41. Levine TR, Hullett CR. Eta Squared, Partial Eta Squared, and Misreporting of Effect Size in Communication Research. *Hum Commun Res*. 2002;28(4):612-25.
42. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale, New Jersey: Lawrence Erlbaum Associates; 1988.

43. Wendt HW. Dealing with a common problem in Social science: A simplified rank-biserial coefficient of correlation based on the U statistic. *Eur J Soc Psychol.* 1972;2(4):463-5.
44. Murphy RL, Vyshedskiy A, Power VA, Bana D, Marinelli P, Wong-Tse A, et al. Automated lung sound analysis in patients with pneumonia. *Chest.* 2004;124(4):190s-s.
45. Vyshedskiy A, Ishikawa S, Murphy RLH. Crackle Pitch and Rate Do Not Vary Significantly During a Single Automated-Auscultation Session in Patients With Pneumonia, Congestive Heart Failure, or Interstitial Pulmonary Fibrosis. *Respir Care.* 2011;56(6):806-17.
46. Piirila P. Changes in crackle characteristics during the clinical course of pneumonia. *Chest.* 1992;102(1):176-83.
47. Piirila P, Sovijarvi A. Crackles: recording, analysis and clinical significance. *Eur Respir J.* 1995;8:2139-48.
48. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med.* 2007;176(6):532-55.
49. Papi A, Luppi F, Franco F, Fabbri LM. Pathophysiology of Exacerbations of Chronic Obstructive Pulmonary Disease. *Proceedings of the American Thoracic Society.* 2006;3(3):245-51.
50. Marques A, Bruton A, Barney A, Hall A. Are crackles an appropriate outcome measure for airway clearance therapy? *Respir Care.* 2012;57(9):1468-75.
51. Baughman RP, Loudon RG. Quantitation of wheezing in acute asthma. *Chest.* 1984;86(5):718-22.
52. Sovijärvi A, Malmberg L, Charbonneau G, Vanderschoot J, Dalmaso F, Sacco C, et al. Characteristics of breath sounds and adventitious respiratory sounds. *Eur Respir Rev.* 2000;10(77):591-6.
53. Meslier N, Charbonneau G, Racineux JL. Wheezes. *Eur Respir J.* 1995;8(11):1942-8.
54. Cortes S, Jane R, Fiz JA, Morera J. Monitoring of wheeze duration during spontaneous respiration in asthmatic patients. *Conference Proceedings: Annual International Conference Of The IEEE Engineering In Medicine And Biology Society IEEE Engineering In Medicine And Biology Society Conference.* 2005;6:6141-4.
55. The Global Initiative for Chronic Obstructive Lung Disease. *Global Strategy for Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease.* The Global Initiative for Chronic Obstructive Lung Disease, Inc.; 2013.
56. Osadnik CR, McDonald CF, Jones AP, Holland AE. Airway clearance techniques for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev.* 2012;3:Cd008328.
57. Fink JB. Forced expiratory technique, directed cough, and autogenic drainage. *Respir Care.* 2007;52(9):1210-21; discussion 21-3.
58. Pryor J, Prasad S. *Physiotherapy for Respiratory and Cardiac Problems: Adults and Paediatrics.* 4th ed. CL E, editor. UK: Churchill Livingstone; 2008.

59. Gross V, Dittmar A, Penzel T, Schuttler F, Wichert P. The relationship between normal lung sounds age and gender. *Am J Resp Crit Care*. 2000;162:905-9.
60. Pasterkamp H, Kraman SS, Wodicka GR. Respiratory Sounds: Advances Beyond the Stethoscope. *Am J Resp Crit Care*. 1997;156:974-87.

Figures captions

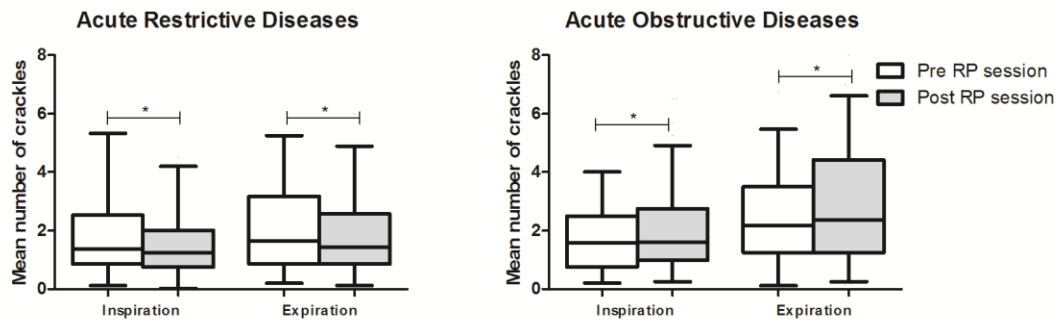


Figure 1 – Mean number of crackles in patients with acute restrictive and acute obstructive diseases. Data are presented as median and 5-95% percentile. Significant differences are identified with * ($p < 0.05$).

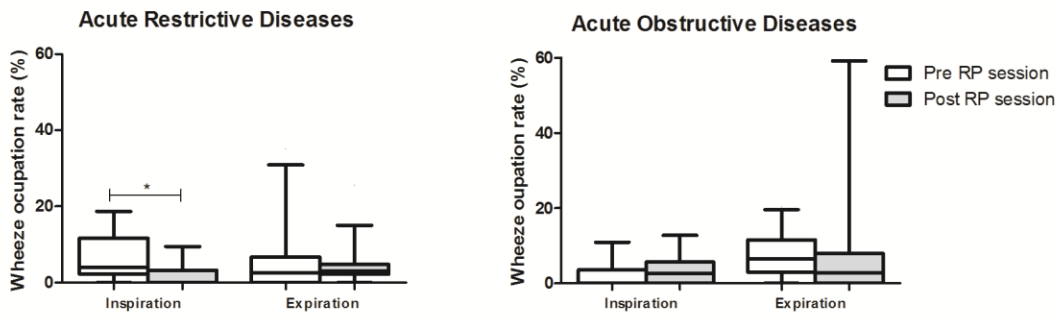


Figure 2 – Wheezes occupation rate in patients with acute restrictive and acute obstructive diseases. Data are presented as median and 5-95% percentile. Significant differences are identified with * ($p < 0.05$).

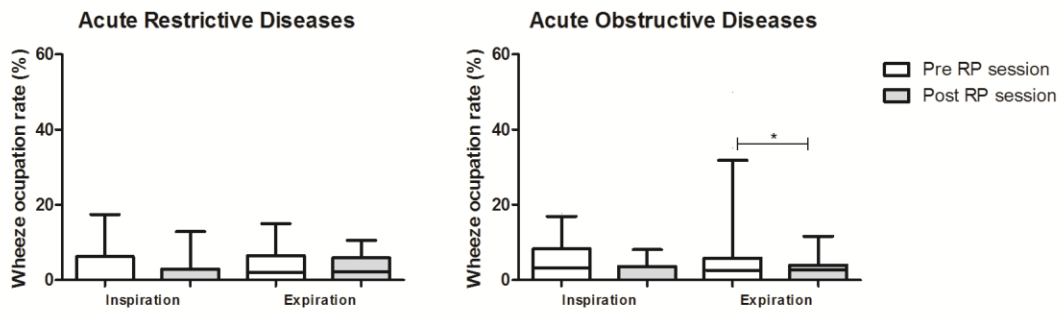


Figure 3 – Wheezes occupation rate in patients with acute restrictive and acute obstructive diseases at trachea. Data are presented as median and 5-95% percentile. Significant differences are identified with * ($p < 0.05$).

Tables with captions

Table 1 - Socio-demographic and clinical characteristics of the participants (n=30).

	Total Sample	Acute Restrictive	Acute Obstructive	p
N. of subjects	30	12	18	-
Gender (M/F)	14/16	6/6	8/10	-
Age (yrs)	55.23 (17.78)	52.83 (17.91)	56.83 (18.02)	0.56
BMI (Kg/m ²)	28.24 (4.85)	26.88 (5.32)	29.15 (4.44)	0.21
mMRC	2 [1-3]	1 [0-2]	2 [1-3]	0.11
FEV ₁ pp (%)	73.87 (21.03)	80.58 (21.90)	69.39 (19.78)	0.16
FVC pp (%)	79.37 (20.86)	82.67 (23.10)	77.17 (19.60)	0.56
FVC/FEV ₁	76.37 (9.61)	80.50 (6.72)	73.61 (10.39)	0.30

Note: values show as n, mean (standard deviation) or median [interquartile range].

Abbreviations: (M/F) – (Male/Female); BMI - body mass index; mMRC - Modified British Medical Research Council questionnaire; FEV₁pp - forced expiratory volume in one second percentage predicted; FVC pp – forced vital capacity percentage predicted.

Table 2 – Descriptive and inferential statistics for the modified Borg scale, sputum and peripheral oxygen saturation.

Clinical variables	Total Sample n=30			Acute Restrictive n=12			Acute Obstructive n=18		
	pre	post	p	pre	post	p	pre	post	p
MBS	0 [0 to 2]	1 [0-2]	0.13	1 [0 to 2]	1 [0 to 2]	0.32	0 [0 to 2]	1.50 [0 to 2.25]	0.02*
Sputum	3 [2 to 3]	2 [2 to 3]	0.01*	2.50 [2 to 3]	2 [2 to 3]	0.68	3 [2 to-3.25]	2 [1 to 3]	0.04*
SPO₂	96.31 (2.16)	96.24 (2.81)	0.85	96.67 (2.31)	96 (3.84)	0.38	96.06 (2.08)	96.39 (1.85)	0.32

Note: values show as mean (standard deviation) or median [interquartile range].

Abbreviations: MBS – modified Borg Scale; SpO₂ - peripheral oxygen saturation.

* statistical differences between pre and post intervention ($p \leq 0.05$).

Online Data Supplement

Effects of a respiratory physiotherapy session in patients with LRTI: a pre/post-test study.

Ana Oliveira, Cátia Pinho, Alda Marques

1 **Table 1**

2 **Table 1** - Summary results of the automatic crackles detection for chest locations at pre and post respiratory physiotherapy session (right and left: anterior,
3 lateral and posterior areas) during inspiration and expiration.

CRACKLES variables	Total Sample n=30			Acute Restrictive n=12			Acute Obstructive n=18			
	pre	post	p	pre	post	p	pre	post	p	
<i>Inspiration</i>	Number	1.94 (1.25)	1.94 (1.35)	1.00	2.01 (1.46)	1.61 (1.14)	0.03*	1.89 (1.10)	2.15 (1.44)	0.03*
	IDW (ms)	2.51 (0.77)	2.48 (0.79)	0.64	2.60 (0.70)	2.45 (0.75)	0.07	2.46 (0.82)	2.48 (0.83)	0.80
	LDW (ms)	2.53 (0.59)	2.53 (0.56)	0.86	2.60 (0.60)	2.64 (0.51)	0.91	2.49 (0.59)	2.46 (0.59)	0.90
	2CD (ms)	10.39 (2.43)	10.26 (2.46)	0.07	10.80 (2.30)	10.57 (2.17)	0.38	10.12 (2.51)	10.05 (2.64)	0.69
	Frequency (Hz)	220.59 (141.85)	218.47 (147.63)	0.65	208.70 (140.06)	213.40 (165.35)	0.40	225.43 (140.44)	221.04 (136.67)	0.92
<i>Expiration</i>	Number	2.54 (1.67)	2.72 (1.86)	0.17	2.38 (1.67)	1.98 (1.36)	0.04*	2.64 (1.68)	3.22 (1.99)	>0.001*
	IDW (ms)	2.72 (0.74)	2.56 (0.74)	0.10	2.77 (0.69)	2.60 (0.73)	0.27	2.69 (0.78)	2.53 (0.76)	0.12
	LDW (ms)	2.61 (0.58)	2.69 (0.53)	0.44	2.68 (0.55)	2.77 (0.54)	0.34	2.57 (0.59)	2.63 (0.52)	0.09
	2CD (ms)	10.79 (2.46)	10.83 (2.25)	0.34	11 (2.37)	11.06 (2.17)	0.51	10.63 (2.52)	10.66 (2.32)	0.92
	Frequency (Hz)	207.85 (132.15)	194.98 (99.10)	0.15	197.06 (87.32)	199.36 (124.24)	0.62	215.73 (155.46)	192.87 (79.35)	0.11

4 Note: values are show as mean (standard deviation).

5 Abbreviations: IDW - initial deflection width; LDW - largest deflection width; 2CD - two-cycle deflection duration.

6 * statistical differences between pre and post intervention (p<0.05)

7

1 **Table 2**

2 **Table 2** - Summary results of the automatic wheeze detection for chest locations at pre and post respiratory physiotherapy session (right and left: anterior,
3 lateral and posterior) during inspiration and expiration.

WHEEZE variables	Total Sample n=30			Acute Restrictive n=12			Acute Obstructive n=18			
	pre	post	p	pre	post	p	pre	post	p	
<i>Inspiration</i>	Number	0.11 [0 to 0.25]	0.10 [0 to 0.25]	0.31	0.20 [0.20 to 0.50]	0 [0 to 0.20]	0.01*	0 [0 to 0.20]	0.13 [0 to 0.25]	0.20
	mWh	0.10 [0 to 0.25]	0 [0 to 0.25]	0.38	0.20 [0.20 to 0.33]	0 [0 to 0.20]	0.01*	0 [0 to 0.20]	0.11 [0 to 0.25]	0.26
	pWh	0 [0]	0 [0]	0.58	0 [0]	0 [0]	0.07	0 [0]	0 [0]	0.27
	%Wh	2.15 [0 to 5.79]	2.22 [0 to 4.58]	0.19	3.86 [2.15 to 11.87]	0 [0 to 3.07]	0.01*	0 [0 to 3.69]	2.58 [0 to 5.74]	0.30
	Frequency (Hz)	282.70 [172.87 to 501.97]	480.21 [226.08 to 911.43]	0.07	257.26 [173.26 to 501.97]	468.58 [213.29 to 845.02]	0.78	233.98 [172.86 to 603.55]	504.35 [226.08 to 911.43]	0.03*
<i>Expiration</i>	Number	0.20 [0 to 0.50]	0.20 [0.11 to 0.35]	0.79	0.13 [0.13 to 0.50]	0.16 [0.13 to 0.33]	0.59	0.20 [0.12 to 0.43]	0.25 [0 to 0.40]	0.20
	mWh	0.20 [0 to 0.33]	0.18 [0 to 0.33]	0.37	0.13 [0 to 0.50]	0.16 [0 to 0.33]	0.62	0.20 [0 to 0.33]	0.20 [0 to 0.33]	0.11
	pWh	0 [0 to 0.12]	0 [0]	0.66	0 [0]	0 [0]	0.50	0 [0 to 0.13]	0 [0 to 0.11]	0.97
	%Wh	2.74 [0 to 6.24]	2.94 [1.55 to 6.70]	0.85	2.51 [0 to 5.51]	3.07 [2.16 to 4.87]	0.88	3.07 [2.09 to 6.91]	2.84 [0 to 7.97]	0.16
	Frequency (Hz)	409.73 [249.96 to 535.32]	397.01 [203.39 to 596.02]	0.28	407.22 [288.03 to 551.20]	430.63 [222.49 to 597.09]	0.79	412.23 [224.21 to 536.26]	369.45 [196.45 to 557.38]	0.83

4 Note: values are show as median [inter-quartile range].

5 Abbreviations: mWh – number of monophonic wheezes; pWh – number of polyphonic wheezes; %Wh – wheeze occupation rate.

6 * statistical differences between pre and post intervention ($p < 0.05$).

7

8

1 **Table 3**

2 **Table 3** - Summary results of the automatic wheeze detection at trachea in pre and post respiratory physiotherapy session during inspiration and expiration.

	WHEEZE variables	Total Sample n=30			Acute Restrictive n=12			Acute Obstructive n=18		
		pre	post	p	pre	post	p	pre	post	p
<i>Inspiration</i>	Number	0 [0 to 0.20]	0 [0 to 0.13]	0.50	0 [0 to 0.38]	0 [0 to 0.08]	0.14	0 [0 to 0.20]	0 [0 to 0.21]	0.57
	mWh	0 [0 to 0.20]	0 [0 to 0.13]	0.51	0 [0.20 to 0.33]	0 [0 to 0.08]	0.14	0 [0 to 0.05]	0 [0 to 0.14]	0.48
	pWh	0 [0]	0 [0]	1	0 [0]	0 [0]	0.32	0 [0]	0 [0]	0.66
	%Wh	0 [0 to 5.38]	0 [0 to 3.35]	0.36	0 [0 to 0.38]	0 [0 to 1.93]	0.14	0 [0 to 4.62]	0 [0 to 3.92]	0.96
	Frequency (Hz)	319.20 [240.48 to 557.63]	410.74 [181.87 to 573.38]	0.72	450.61 [197.95 to 898.77]	474.29 [195.13 to 599.71]	0.66	319.20 [248.19 to 485.70]	347.19 [142.11 to 564.59]	0.18
<i>Expiration</i>	Number	0.16 [0 to 0.43]	0.06 [0 to 0.25]	0.06	0.05 [0 to 0.31]	0.13 [0 to 0.28]	0.67	0.22 [0 to 0.50]	0 [0 to 0.25]	0.02*
	mWh	0.11 [0 to 0.33]	0 [0 to 0.25]	0.14	0.05 [0 to 0.23]	0.13 [0 to 0.24]	0.40	0.20 [0 to 0.43]	0 [0 to 0.25]	0.20
	pWh	0 [0]	0 [0]	0.11	0 [0]	0 [0]	0.66	0 [0 to 0.20]	0 [0]	0.02*
	%Wh	2.36 [0 to 5.83]	0.70 [0 to 2.79]	0.02*	1.01 [0 to 6.27]	2.19 [0 to 5.13]	0.56	3.49 [0 to 5.83]	0 [0 to 2.08]	0.02*
	Frequency (Hz)	356.34 [285.87 to 551.59]	384.57 [285.29 to 819.05]	0.25	530.19 [306.73 to 866.70]	384.57 [210.48 to 507.33]	0.89	325.02 [285.21 to 504.33]	422.89 [289.33 to 876.44]	0.25

3 Note: values are show as median [inter-quartile range].

4 Abbreviations: mWh – number of monophonic wheezes; pWh – number of polyphonic wheezes; %Wh – wheeze occupation rate.

5 * statistical differences between pre and post intervention (p<0.05).

6

7