Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Rapid Communication

Two cases of chronic obstructive pulmonary disease evaluated by dynamic-ventilatory digital radiography for pulmonary function and assessment of treatment efficacy

Noriyuki Ohkura a,*, Rie Tanaka b, Johsuke Hara a, Naohiko Ogawa a, Miki Abo a, Satoshi Watanabe a, Yuichi Tambo a, Shingo Nishikawa a, Takashi Sone a, Hideharu Kimura a, Kazuo Kasahara a

a Kanazawa University Hospital, Respiratory Medicine, Ishikawa, Japan
b Kanazawa University, College of Medical, Pharmaceutical & Health Sciences, Ishikawa, Japan

ARTICLE INFO

Article history:
Received 8 June 2021
Received in revised form 1 July 2021
Accepted 13 July 2021
Available online 22 August 2021

Keywords:
COPD
Pulmonary function
Spirometry
Dynamic digital radiography

ABSTRACT

Spirometry is a crucial test used in the diagnosis and monitoring of patients with chronic obstructive pulmonary disease (COPD). Severe acute respiratory syndrome coronavirus 2 pandemic has posed numerous challenges in performing spirometry. Dynamic-ventilatory digital radiography (DR) provides sequential chest radiography images during respiration with lower doses of radiation than conventional X-ray fluoroscopy and computed tomography. Recent studies revealed that parameters obtained from dynamic DR are promising for evaluating pulmonary function of COPD patients. We report two cases of COPD evaluated by dynamic-ventilatory DR for pulmonary function and treatment efficacy and discuss the potential of dynamic DR for evaluating COPD therapy.

© 2021 The Authors Published by Elsevier B.V. on behalf of The Japanese Respiratory Society. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

1. Introduction

Spirometry is a crucial test implemented in the diagnosis and monitoring of chronic obstructive pulmonary disease (COPD). However, the production of aerosols could contribute to the transmission of severe acute respiratory syndrome coronavirus 2 during the coronavirus disease 2019 (COVID-19) pandemic [1]. Recent studies have reported the utility of dynamic digital radiography (DR) performed by a flat panel detector (FDP) device [2]. Dynamic-ventilatory DR provides sequential chest radiography images during respiration with lower doses of radiation than conventional X-ray fluoroscopy and computed tomography (CT). These images from dynamic-ventilatory DR allow efficient examination of...
such respiratory kinetic parameters corresponding to the change in the area of the lung, diaphragmatic motion, and change in tracheal diameter [2–5]. Here, we report two cases of COPD evaluated by dynamic-ventilatory DR for pulmonary function and its treatment efficacy. This study aims to analyze the potential of dynamic DR for evaluating COPD therapy.

2. Dynamic-ventilatory digital radiography

Dynamic-ventilatory DR was performed as previously reported [4]. Sequential chest radiography images of the patient breathing slowly to maximum inspiration and maximum expiration were captured at 15 frames per second using a dynamic flat-panel imaging system (Test Model; Konica Minolta, Inc., Tokyo, Japan). The exposures were achieved using the following parameters: 100 kV; 50 mA; 2.5 ms; 15 frames per second; and 2.0 m from the SID. This in turn resulted in effective patient radiation doses of approximately 0.2 mSv per 14 s of a single slow and deep respiratory cycle. The use of dynamic-ventilatory DR for the assessment of pulmonary function was approved by the Medical Ethics Committee of Kanazawa University Hospital (registration number 1729). Both patients provided informed consent.

The lung areas at the points of maximum inspiration (lung area_in) and maximum expiration (lung area_ex) were measured as previously described [4]. The ratio of change in the area of the lung during a respiratory cycle (ratio of lung area change) was calculated as follows: ratio of lung area change = (lung area_ex − lung area_in)/lung area_in. The change in extent of the movement of bilateral diaphragm during a respiratory cycle (diaphragm motion) was also measured as previously described [3].

3. Case report

3.1. Case 1

A 53-year-old man with productive cough was referred to our institution as he was diagnosed with an obstructive disorder on spirometry. The patient was a current smoker, having smoked 40 cigarettes per day for 23 years. He had no history of asthma or rhinitis. His COPD assessment test (CAT) score was 15. Pulmonary function testing revealed an obstructive pattern prior to bronchodilator administration, as follows: VC, 4.15 L (%VC, 111.9%); FVC, 3.57 L (%FVC, 96.2%); FEV1 1.56 L (%FEV1, 49.7%); FEV1/FVC 43.7%; MMF 0.45 L/s, (%MMF, 11.4%); FRC 3.78 L (%FRC, 112.5%); RV 2.42 L (%RV, 136.7%); TLC 6.57 L (%TLC 111.0%); DLco 17.5 ml/min/mm Hg (%DLco, 64.2%). The results of spirometry following bronchodilator administration were as follows: VC, 4.23 L (%VC, 114.0%); FVC, 4.23 L (%FVC, 114.0%); FEV1 1.90 L (%FEV1, 60.5%); FEV1/FVC 44.9%. COPD was diagnosed based on the data, and the patient was started on dual long-acting bronchodilator therapy (indacaterol/glycopyrronium). Three months later, his CAT score and pulmonary function parameters showed significant improvement (Table 1). The ratio of lung area change and bilateral diaphragm motion increased following the treatment. (Figs. 1a and 2, Supplemental file 1a, Supplemental file 1b).

3.2. Case 2

A 76-year-old man, who was scheduled to undergo surgery for lung cancer, was referred to our department after being diagnosed with an obstructive disorder based on spirometry. The patient was a current smoker, having smoked 40 cigarettes per day for 46 years. He also had intermittent asthma

| Table 1 – Response to treatment of patients with COPD as reflected by pulmonary function testing and total CAT scores. |
|---------------------------------------------------------------|
| Case 1                                                      |
| Pretreatment | Post-treatment | Pretreatment | Post-treatment |
| VC (L)       | 4.15           | 4.22         | 2.72           | 3.15           |
| FVC (L)      | 3.57           | 4.22         | 2.72           | 3.15           |
| FEV1 (L)     | 1.56           | 1.94         | 1.54           | 1.82           |
| FEV1/FVC     | 0.44           | 0.46         | 0.57           | 0.58           |
| MMF (L/s)    | 0.45           | 0.59         | 0.51           | 0.49           |
| FRC (L)      | 3.78           | 3.86         | 2.94           | 4.05           |
| RV (L)       | 2.42           | 2.68         | 2.71           | 2.95           |
| TLC (L)      | 6.57           | 6.90         | 5.43           | 6.02           |
| RV/TLC       | 0.37           | 0.38         | 0.50           | 0.49           |
| R5 (cm H2O/L/s) | 5.37       | 3.10         | 3.54           | 2.30           |
| R20 (cm H2O/L/s) | 4.01      | 2.62         | 2.61           | 1.80           |
| X5 (cm H2O/L/s) | 1.36     | 0.48         | 0.93           | 0.50           |
| Fres (Hz)    | 15.30          | 7.50         | 12.18          | 9.90           |
| ALX (cm H2O/L) | 9.56      | 1.50         | 8.22           | 2.37           |
| Total CAT score | 15          | 9            | 4              | 0              |

The table shows treatment course in Case 1 and Case 2 on spirometry, lung volumes using multi-breath helium dilution method, forced oscillation technique and total CAT score.

COPD was diagnosed in Case 1, who was reassessed after 3 months of treatment with indacaterol/glycopyrronium. Asthma/COPD overlap syndrome was diagnosed in Case 2, who was reassessed after 2 weeks of treatment with the combination of fluticasone/formoterol and tiotropium.
and allergic rhinitis since about 40 years of age, although he
did not receive regular treatment for asthma. His CAT score
was 4. Pulmonary function testing revealed an obstructive
pattern prior to bronchodilator administration as follows: VC,
2.72 L (%VC, 85.0%); FVC, 2.72 L (%FVC, 85.0%); FEV₁, 1.54 L (%
FEV₁, 67.2%); FEV₁/FVC 56.6%; MMF 0.51 L/s, (%MMF, 17.9%);
FRC 2.94 L (%FRC, 97.7%); RV 2.71 L (%RV, 140.4%); TLC 5.43 L (%
TLC 100.2%); DLco 13.47 mL/min/mmHg (%DLco, 59.5%). The

**Fig. 1** – The ratio of the change in lung area over a single respiratory cycle in Case 1 and Case 2. Sequential chest
radiography images of the patient breathing slowly to maximum inspiration and maximum expiration were captured at 15
frames per second using a dynamic flat-panel imaging system (Test Model; Konica Minolta, Inc., Tokyo, Japan). The ratio of
the change in lung area over a single respiratory cycle (maximum inspiration to maximum expiration) was calculated as
follows: ratio of the change in lung area = (lung area at maximum expiration – lung area at maximum inspiration)/lung
area at maximum inspiration. In Case 1, the lung area ratio changed from −0.22 to −0.27 with treatment (Fig. 1a). In Case 2,
the lung area ratio changed from −0.30 to −0.34 with treatment (Fig. 1b).
results of spirometry following bronchodilator administration were as follows: VC, 3.11 L (%VC, 97.8%); FVC, 3.11 L (%FVC, 97.8%); FEV₁ 1.60 L (%FEV₁, 70.8%); FEV₁/FVC 51.4%. The exhaled nitric oxide level was 22 ppb. His peripheral blood eosinophil count was 168/μL, and his total IgE level was 1449 IU/mL. Asthma/COPD overlap syndrome was diagnosed based on the data, and the patient started combination therapy consisting of fluticasone/formoterol and tiotropium. Two weeks following the initiation of combination therapy, the patient’s CAT score and pulmonary function showed significant improvement (Table 1). The ratio of the change in lung area as well as bilateral diaphragm motion increased following the treatment (Figs. 1b and 2, Supplemental file 2a, Supplemental file 2b).

4. Discussion

We evaluated the therapeutic effects of COPD treatments for two patients using dynamic DR in addition with spirometry, measurement of lung volumes, forced oscillation technique, and the determination of CAT scores. The ratio of change in the lung area and the bilateral diaphragm motion during a respiratory cycle increased following the treatment in both cases. These results reflect improvements in pulmonary hyperinflation following treatment with bronchodilators or inhaled corticosteroid. Recent studies have shown that the parameters obtained from dynamic DR are useful measures that reflect the pulmonary function of patients with COPD [3–5]. To the best of our knowledge, this is the first report on the efficacy of dynamic DR in the verification of therapy for COPD.

These findings are consistent with previous findings that the ratio of the change in lung area during a respiratory cycle reflect the severity of airflow limitation [3,4]. On the other hand, the diaphragm motion during tidal breathing have been reported to be larger in COPD patients than in healthy volunteers [6]. Discrepancy of the diaphragmatic movement due to breathing maneuvers is a future issue for elucidation of the pathophysiology of COPD.

The evaluation of pulmonary function by dynamic DR has numerous advantages over other modalities. For instance, dynamic DR can be performed with a patient either in a standing or sitting position, both of which reflect physiologically relevant routine activities. Dynamic DR can be conducted as a supplemental examination to conventional chest radiography. The radiation dose of dynamic DR is lower than that of conventional X-ray fluoroscopy and CT [7]. Dynamic DR, unlike spirometry, does not require forced expiration or techniques that depend on the skill of the operator or on the cooperation of the patient being evaluated. Since dynamic DR is a noninvasive evaluation and is easy to perform, even patients at a critical stage can be repeatedly tested. Additionally, the sequential chest X-ray images provided by dynamic DR [4] during respiration may facilitate the understanding of chest respiratory motions for both the operator and the patient. Therefore, this imaging modality contributes to a patient’s understanding of the disease and thereby increase patient adherence to treatment.

COVID-19 pandemic has led to numerous complications while performing spirometry. The Japanese Respiratory Society recommends using flowchart entitled “Working diagnosis and initial management of COPD during the COVID-19 pandemic”.

Fig. 2 – Bilateral diaphragmatic motions in Case 1 and Case 2. Case 1: The extent of movement of the right diaphragm from maximum inspiration to maximum expiration changed from 37.1 mm to 36.4 mm with treatment. The extent of movement of the left diaphragm from maximum inspiration to maximum expiration changed from 45.0 mm to 48.0 mm with treatment. Case 2: The extent of movement of the right diaphragm from maximum inspiration to maximum expiration changed from 39.6 mm to 45.9 mm with treatment. The extent of movement of the left diaphragm from maximum inspiration to maximum expiration changed from 45.0 mm to 48.0 mm with treatment.
pandemic” for the diagnosis of COPD in cases where spirometry cannot be performed [8]. In the flowchart, the evaluation of treatment efficacy relies exclusively on the changes of CAT score. However, dynamic-ventilatory DR system could be used by physicians to confirm treatment efficacy.

However, the limitations of the study should be considered. First, we cannot show the minimal clinical important difference values obtained from the dynamic-ventilatory DR yet. Second, asynchrony of chest wall motion as well as vertebral deformity may affect parameters such as diaphragmatic motion, and lung area change rate. These 2 cases did not exhibit asynchrony of chest wall motion and vertebral deformity (Supplemental file 1a, 2a). Therefore, we need to consider if abnormal findings on chest X-ray may affect the parameters achieved using dynamic-ventilatory DR. Therefore, further investigations are required to address these issues.

In conclusion, dynamic-ventilatory DR is a promising tool for monitoring the pulmonary function of patients with COPD.

**Conflict of interest**

This study was supported by Konica Minolta, Inc. (Tokyo, Japan). NOhkura received honoraria for writing promotional material for a device by Konica Minolta, Inc. RT received honoraria for writing promotional material for a device by Konica Minolta, Inc. NOhkura has been reimbursed by Konica Minolta Inc. for attending several conferences. RT has been reimbursed by Konica Minolta Inc. for attending several conferences. KK has been reimbursed by Konica Minolta Inc. for attending several conferences. KK received a research grant from Konica Minolta, Inc.

**Acknowledgements**

The authors would like to thank Noritsugu Matsutani for his assistance with this study.

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resinv.2021.07.005.

**REFERENCES**

[1] Anderson EL, Turnham P, Griffin JR, Clarke CC. Consideration of the aerosol transmission for COVID-19 and public health. Risk Anal 2020;40(5):902–7.

[2] Tanaka R. Dynamic chest radiography: flat-panel detector (FPD) based functional X-ray imaging. Radiol Phys Technol 2016;9(2):139–53.

[3] Hida T, Yamada Y, Ueyama M, Araki T, Nishino M, Kurosaki A, et al. Decreased and slower diaphragmatic motion during forced breathing in severe COPD patients: time-resolved quantitative analysis using dynamic chest radiography with a flat panel detector system. Eur J Radiol 2019;112:28–36.

[4] Ohkura N, Kasahara K, Watanabe S, Haraj A, Abe M, Sone T, et al. Dynamic-ventilatory digital radiography in air flow limitation: a change in lung area reflects air trapping. Respiration 2020;99(5):382–8.

[5] Watase S, Sonoda A, Matsutani N, Muraoka S, Hanaoka J, Nitta N, et al. Evaluation of intrathoracic tracheal narrowing in patients with obstructive ventilatory impairment using dynamic chest radiography: a preliminary study. Eur J Radiol 2020;129:109141.

[6] Yamada Y, Ueyama M, Abe T, Araki T, Abe T, Nishino M, et al. Difference in diaphragmatic motion during tidal breathing in a standing position between COPD patients and normal subjects: time-resolved quantitative evaluation using dynamic chest radiography with flat panel detector system (“dynamic X-ray phrenicography”). Eur J Radiol 2017;87:76–82.

[7] Tanaka R, Sanada S, Kobayashi T, Suzuki M, Matsui T, Matsui O. Computerized methods for determining respiratory phase on dynamic chest radiographs obtained by a dynamic flat-panel detector (FPD) system. J Digit Imag 2006;19(1):41–51.

[8] Shibata Y, Muro S, Yokoyama A, Hashimoto S. Statement from the Japanese Respiratory Society: working diagnosis and initial management of COPD during the COVID-19 pandemic. Respir Investig 2021;59(4):385–8.