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Borg, Morten; Løkke, Anders; Rasmussen, Torben Riis

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# Symptoms and lung function follow-up after lung cancer resection

Morten Borg[1], Anders Løkke[2, 3] & Torben Riis Rasmussen[4]

1) Department of Respiratory Diseases, Aalborg University Hospital, 2) Department of Internal Medicine, Lillebaelt Hospital Vejle, 3) Department of Regional Health Research, University of Southern Denmark, 4) Department of Respiratory Diseases and Allergy, Aarhus University Hospital, Denmark

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## ABSTRACT

**INTRODUCTION** In recent decades, lung cancer is being diagnosed at ever earlier stages, leading to higher resection rates and improved survival. Therefore, more patients live with the sequelae of thoracic surgery. The standardised Danish follow-up programme after lung cancer resection includes CT and clinical evaluation at set times.

**METHODS** An e-mail survey was conducted to evaluate local practices at lung cancer investigation sites with respect to the setup of follow-up programmes after lung cancer resection. In addition, 50 consecutive patients were seen three months after their lung cancer resection. Spirometry was performed and patients reported on their use of inhalation medicine, smoking status and quality of life.

**RESULTS** The study revealed heterogeneous setups regarding routine spirometry (5/12 sites) and assessment by a respiratory physician (6/12). In a single-centre study including 50 patients three months after lung cancer resection, 22% of patients were using a bronchodilator even though 50% of patients were obstructive on spirometry and 48% reported shortness of breath (SOB). 17% of patients were active smokers, whereas the majority reported symptoms of a physical nature such as fatigue, SOB and cough.

**CONCLUSIONS** It is important to establish the optimal follow-up setup with an emphasis on detection of recurrence, symptom improvement and smoking cessation. This study highlighted the importance of symptom assessment by a respiratory physician/nurse. A spirometry should be performed if patients experience SOB and the potential benefit of inhalation medicine should be assessed.

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**TRIAL REGISTRATION** not relevant.

In Denmark, lung cancer is the most common cause of cancer-related death in both men and women [1]. The incidence of lung cancer has increased over the past decades with almost 5,000 patients being diagnosed annually [2]. With increased use of CT, lung cancer is now diagnosed at earlier stages and resection rates have increased accordingly [3]. As a result, more patients live as lung cancer survivors with the sequelae of thoracic surgery and loss of lung tissue and function.

Despite curative treatment, lung cancer has a high recurrence rate [4]. Guidelines recommend active surveillance after curatively intended treatment [5] and following surgery; the primary goal of follow-up regimens is to detect any recurrence at early and potentially curative stages. Simultaneously, follow-up visits should emphasise symptom relief and quality of life (QoL). However, the most effective follow-up model for lung

cancer patients has yet to be established [6].

In respiratory medicine, the majority of QoL questionnaires have been developed for use in clinical trials with chronic obstructive pulmonary disease or asthma patients. Some lung cancer-specific validated QoL questionnaires have appeared, e.g. the Lung Cancer Symptom Scale [7] or the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer Module (EORTC QLQ-LC13) [8]. However, none of these guidelines have been translated into Danish.

The standardised Danish follow-up programme includes clinical control and contrast-enhanced CT of the thorax and upper abdomen every three months for the first two years following treatment and every six months in years 3-5 [9]. Depending on the local setup, patients attend standard outpatient visits either at a department of respiratory diseases or at an oncology department. At present, the practice of individual centres regarding spirometry, prescription of inhalation medicine and symptom scoring remain unknown.

This study evaluated the different practices concerning post-operative spirometry among different lung cancer centres in Denmark through an e-mail survey. Furthermore, in a study of 50 patients at the Department of Respiratory Diseases and Allergy, Aarhus University Hospital, Denmark, spirometry was performed three months after lung cancer resection. Furthermore, inhalation medicine use was recorded and a QoL questionnaire including the modified Medical Research Council (mMRC) dyspnoea scale was completed.

## METHODS

An e-mail survey was conducted among the Danish lung cancer centres to determine local practices in the post-operative setup following lung cancer resection. The survey documented which department was responsible for the follow-up visits and CTs, and whether patients routinely received a spirometry and/or visited a respiratory physician three months after resection.

Furthermore, 50 consecutive patients were seen three months after lung cancer resection in the outpatient clinic of the Department of Respiratory Diseases and Allergy, Aarhus University Hospital, Aarhus, Denmark.
A spirometry was performed by a trained nurse, and patients were asked if they used any inhalation medicine. In addition, the mMRC dyspnoea scale, smoking status and Eastern Cooperative Oncology Group (ECOG) Performance Status were assessed.

For use as a starting point in the consultation, patients completed a small QoL questionnaire focusing on their physical and psychological health. The following physical symptoms could be ticked off; fatigue, shortness of breath (SOB), cough, weight loss, loss of appetite, insomnia, pain, wound discomfort, dizziness, nausea and reduced mobility. The following psychological issues could also be ticked off; emotional distress, nervousness, sadness, anxiety, stress and guilt.

Statistical analyses were conducted using R statistical software (Fox & Leanage, 2016).

### Ethics

As this was a clinically integrated project, the local ethics committee required no formal application.

*Trial registration:* not relevant.

## RESULTS

**Table 1** shows the current practice for follow-up visits for lung cancer resection patients among lung cancer centres in Denmark obtained through an e-mail survey.

**TABLE 1** Lung cancer follow-up visits in Denmark.

| Hospital | Department of 5-yr follow-up | 3-mo. assessment by respiratory physician | Routine spirometry at 3 mos. |
|---|---|---|---|
| *Capital Region* | | | |
| Gentofte | Respiratory medicine | Yes | Yes |
| Bispebjerg | Respiratory medicine | Yes | No |
| *Region Zealand* | | | |
| Næstved | Respiratory medicine | Yes | Yes |
| Roskilde | Respiratory medicine | Yes | Yes |
| *Region of Southern Denmark* | | | |
| Odense | Oncology | No | No |
| Vejle | Oncology | No | No |
| Sønderborg | Oncology | No | No |
| *Central Denmark Region* | | | |
| Aarhus | Oncology | Yes | Yes |
| Randers | Oncology | No | No |
| Viborg | Oncology | No | No |
| Holstebro | Oncology | No | No |
| *North Denmark Region* | | | |
| Aalborg | Respiratory medicine | Yes | Yes |

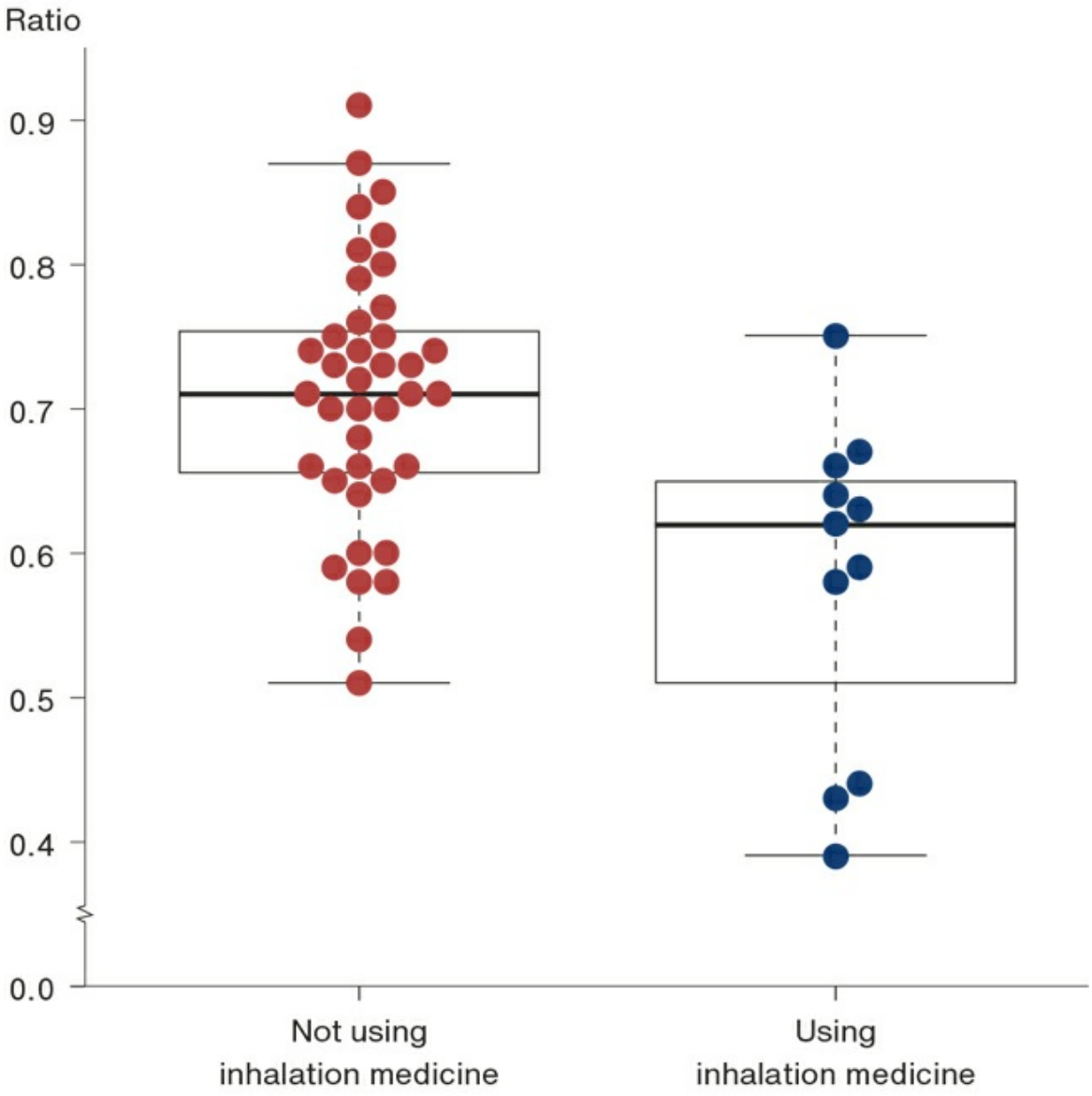
Characteristics of the study patients are presented in **Table 2**. Additionally, characteristics of users and non-users of bronchodilator inhalation medicine are shown. At the three-month follow-up visit, eleven patients (22%) were using bronchodilator inhalation medicine, whereas 25 (50%) were obstructive on post-operative spirometry and 24 (48%) reported SOB. The forced expiratory volume, first second (FEV1)/forced vital capacity (FVC) ratios among users and non-users of inhalation medicine are depicted in **Figure 1**. Users of inhalation medicine had significantly lower FEV1% and FEV1/FVC ratio ($p < 0.05$), whereas their mMRC score was significantly higher ($p < 0.05$) than that of patients not using inhalation medicine. Further characteristics, such as age, BMI, ECOG Performance Status, smoking status, tobacco pack years and lung cancer stage did not significantly differ between the groups.

**TABLE 2** Patient characteristics.

| | | Inhalation medicine | |
|---|---|---|---|
| | **All patients** | **users** | **non-users** |
| n | 50 | 11 | 39 |
| Age, mean (± SD), yrs | 67 (± 11) | 71 | 66 |
| Female sex, % | 52 | 64 | 49 |
| Tobacco pack yrs, mean (± SD) | 32 (± 16) | 39 | 30 |
| BMI, mean (± SD), kg/m² | 26 (± 4) | 24.7 | 26.2 |
| ECOG PS, mean | 1.0 | 1.0 | 0.9 |
| FEV1, mean, % | 73 | 61* | 77 |
| FEV1/FVC ratio, mean | 0.68 | 0.58* | 0.71 |
| mMRC dyspnoea scale score, mean | 0.9 | 1.6* | 0.7 |
| Active smokers, % | 14 | 9 | 15 |
| Lung cancer stage I-IV, mean | 1.8 | 1.5 | 1.9 |

ECOG PS = Eastern Cooperative Oncology Group Performance Status; FEV1 = forced expiratory volume 1st sec; mMRC = modified Medical Research Council; SD = standard deviation.
*) $p < 0.05$ (Wilcoxon signed-rank test).

**FIGURE 1** FEV1/FVC ratio of users and non-users of bronchodilator inhalation medicine.

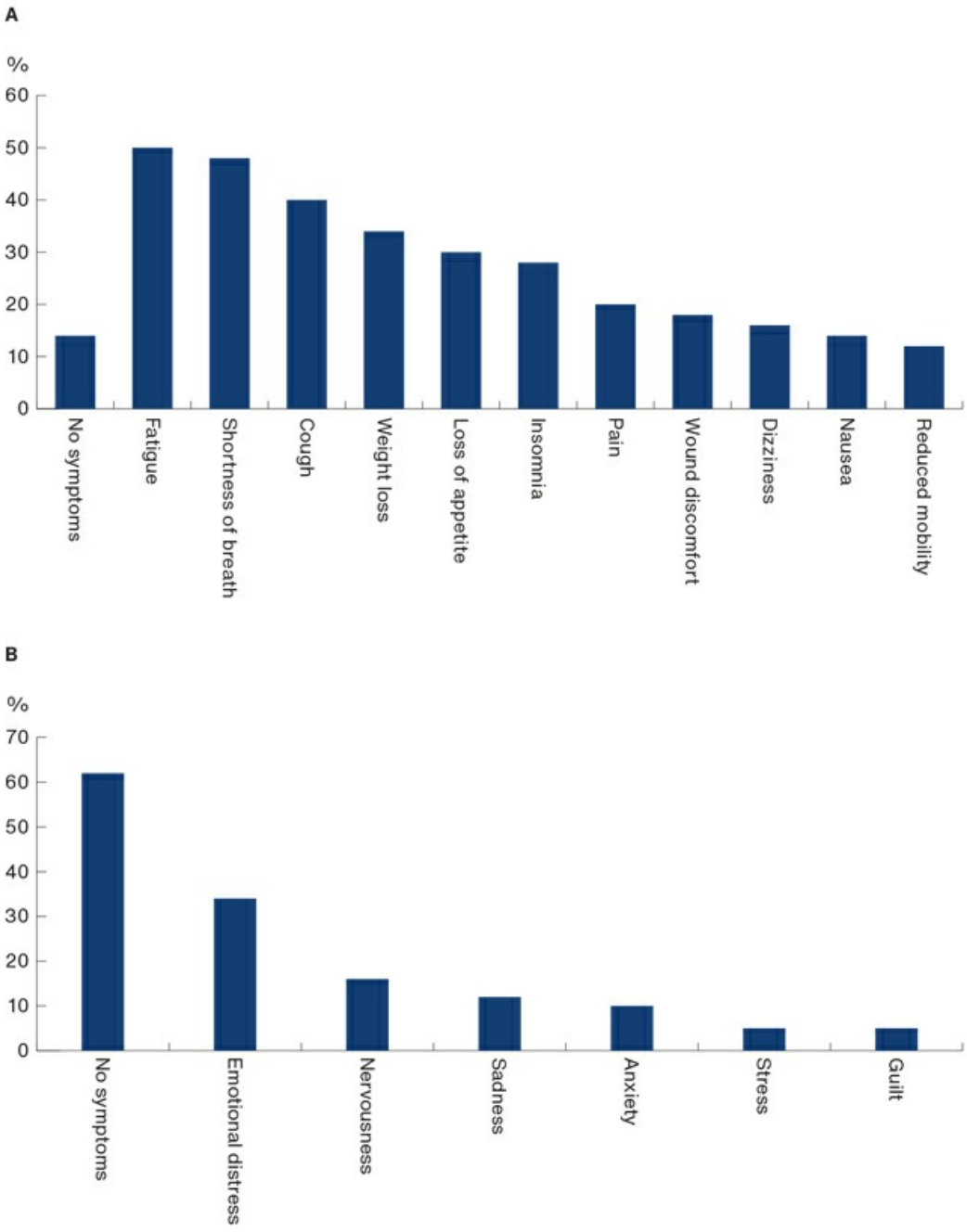



FEV1 = forced expiratory volume 1st sec; FVC = forced vital capacity.

At the post-operative visit, seven patients (14%) were still active smokers, whereas 16 (32%) had abandoned smoking during the lung cancer investigation or in the three-month post-operative period. Hence, the majority of patients who smoked at the time of investigation had now quit smoking (16 out of 23; 70%).

The results of the QoL questionnaire in which physical and psychological symptoms could be ticked off are depicted in **Figure 2**. The primary symptoms were fatigue, SOB and cough.

**FIGURE 2** Physical (**A**) and psychological (**B**) symptoms.




## DISCUSSION

The present paper revealed a heterogeneous setup in Denmark regarding follow-up after lung cancer resection with five out of 12 centres performing routine post-operative spirometry. Additionally, the study of 50 consecutive patients found a relatively infrequent use of inhalation medicine among those with an obstructive spirometry. Smoking tobacco was still used by a minority of patients. According to a QoL questionnaire, the majority of patients had symptoms of a physical nature three months after their lung cancer resection and 48% of patients reported SOB.

Follow-up visits are conducted at 12 different sites in Denmark by either the oncology or respiratory medicine department (Table 1). Six of the 12 sites provide patients with a three-month follow-up visit performed by a respiratory physician, whereas five of 12 sites perform routine spirometry at the three-month follow-up visit. The study found that a large proportion of patients with obstruction do not use inhalation medicine even though they experience SOB (Figure 1, Table 2). Increased SOB is a well-known consequence of lung cancer resection [10], and the majority of lung cancer patients are previous or active smokers and will often have some degree of pre-operative lung function impairment. Although the optimal follow-up scheme after lung cancer resection has yet to be established [6], we believe that this study highlighted the importance of patients being routinely assessed by either a respiratory physician or a specialised respiratory nurse following lung cancer resection. If patients experience SOB, a spirometry should be performed, and the potential benefit of bronchodilator inhalation medicine should be assessed by a respiratory physician. Furthermore, adherence to any prescribed inhalation medicine should be checked.

Only a minority of patients (22%) were using bronchodilator inhalation medicine at the three-month follow-up visit. Table 2 compares the two groups that either used or did not use bronchodilator inhalation medicine. Even though patients who used inhalation medicine generally had a lower FEV1 and FEV1/FVC ratio, a large proportion of non-users who experienced SOB were obstructive on spirometry (Figure 1). The two groups of users and non-users of bronchodilator inhalation medicine did not differ in terms of characteristics such as ECOG Performance Status, lung cancer stage, tobacco pack years or BMI. Therefore, we conclude that a symptom-centred anamnesis, preferably with the use of a lung cancer-specific validated QoL questionnaire, in combination with a spirometry is necessary to detect patients who may benefit from inhalation medicine. Furthermore, patients who may be candidates for pulmonary rehabilitation programmes and/or cardiovascular work-up should be identified. At present, such a QoL questionnaire has not been translated into Danish and validated, and further research in this area is warranted.

Continued tobacco use after the diagnosis of lung cancer is related to poor treatment outcomes, increased risk of surgical complications [11], lower QoL [12] and affected survival chances [13]. Hence, smoking cessation is pivotal when dealing with lung cancer [14]. We find that the majority of patients who smoke at the initiation of their lung cancer investigation will quit during the next three months (70%). This is a relatively high percentage of patients compared with the 51% patients who quit smoking following acute myocardial infarction [15]. However, according to this study, 14% of patients are still active smokers three months after their lung cancer resection. Potentially, some patients might also take up smoking again. This highlights the importance of smoking cessation support during lung cancer investigation, which should be integrated into the follow-up visits after lung cancer resection.

A QoL questionnaire was used as a starting point for the three-month follow-up visit. The results were in line with those reported by previous studies [10]. Most patients experienced issues of a physical nature; primarily fatigue, SOB and cough (Figure 2), whereas psychological issues were less common. Hence, according to this study, the focus of symptom relief should be on physical symptoms. As previously proposed [16], a QoL screening questionnaire may establish that the minority of patients have psychological problems; these patients may be referred for adequate support at either their family doctor or a psychologist.

## CONCLUSIONS

This study highlighted the importance of routine assessment by a respiratory physician or specialised respiratory nurse following lung cancer resection. If patients who experience SOB, a spirometry should be performed and the potential benefit of inhalation medicine should be assessed. Furthermore, apart from CT surveillance of any recurrence, follow-up outpatient visits should emphasize smoking cessation and symptom relief. Results from this study will expect symptoms to be primarily of a physical nature, whereas patients with

substantial psychological symptoms may be identified using a short QoL screening questionnaire and then referred for adequate support.

### Limitations

Due to the sample size of the study, a risk of type 2 error exists. Furthermore, results describing the setup of follow-up at different sites were based on an e-mail survey only.

**Correspondence** *Morten Borg*. E-mail: moklb@rn.dk

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