Original Article

Bronchoscopic Intervention Reduces Dyspnea in Severely Symptomatic Patients With Central Malignant Airway Obstruction

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Abstract

Context. Malignant central airway obstruction (MCAO) is a serious and often life-threatening condition.

Objectives. We aimed to investigate the effects of endoscopic interventions on dyspnea, Quality of life (qoL), and physiological measurements in patients with MCAO.

Methods. This was a single-center prospective cohort study. All patients referred to Uppsala University Hospital, Sweden, for bronchoscopic interventions due to MCAO between January 1, 2015, and December 31, 2019, were eligible for inclusion. Patients were evaluated pre- and postoperatively by heart rate (HR), respiratory rate (RR), forced expiratory volume in 1 second (FEV1), oxygen saturation. The NRS dyspnea scale, the Cancer Dyspnea Scale (CDS), the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC QLQ-C30) and QLQ-lung cancer-13 (EORTC-QLQ LC13), and ECOG-WHO Performance Status (ECOG-PS).

Results. The study group comprised 44 patients (56% women, 69.3 ± 6.8 years). No procedure-related deaths occurred. The first postoperative day the following measurements had decreased: RR (19.9 ± 4.9 vs. 17.1 ± 3.9, $P = 0.0027$), CDS score (13.6 ± 1.43 vs. 5.8 ± 4.9, $P = 0.0003$), NRS dyspnea score (5.6 ± 2.2 vs. 2.3 ± 2.4, $P < 0.001$). The FEV1 increased from 1.23 ± 0.45 to 1.51 ± 0.57, ($P = 0.0014$). At 1 month follow up the CDS score had decreased further to 5.2 ± 4.1, ($P = 0.0001$), the QLQ-C30 dyspnea score from 76.5 ± 25.7 to 41.2 ± 27.7, ($P = 0.001$) and the QLQ-LC13 dyspnea score from 62.5 ± 6.4 to 32.3 ± 5.5, ($P = 0.003$). The QLQ-C30 Global Health Scale (GHS) score increased from 33.9 ± 4.9 to 47.0 ± 18.7, ($P = 0.0124$). Significant changes were only seen in patients with preoperative ECOG PS ≥2.

Conclusion. Most patients with MCAO benefit from bronchoscopic intervention and those with worse ECOG PS may benefit even more in terms of symptom relief. J Pain Symptom Manage 2025;70:38–45.

Key Words
Lung cancer, interventional bronchoscopy, dyspnea, malignant central airway obstruction

Abbreviations: ASA, American Society of Anesthesiologists; CDS, Cancer Dyspnea Scale; ECOG-WHO PS, Eastern Cooperative Oncology Group-world Health Organisation Performance Status; EORTC, European Organisation for Research and Treatment of Cancer; FEV1, Forced Expiratory Volume in 1 seconds; GHS, Global Health Scale; MCAO, Malignant Central Airway Obstruction; NRS, Numerical Rating Scale; QoL, Quality of Life; QLQ-C30, Quality of Life Questionnaire-Core 30; QLQ-LC13, Quality of Life Questionnaire-Lung Cancer 13; RR, Respiratory Rate; VAS, Visual Analogue Scale

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Key Message

Bronchoscopic intervention improves lung function and QoL and decreases dyspnea in patients with MCAO.

Introduction

Lung cancer is one of the most common forms of cancer worldwide.[1] About 20%−30% of patients with lung cancer will develop a partial or total obstruction of the airway,[2] resulting in atelectasis, and in patients with marginal lung function, respiratory failure. Dyspnea and stridulous breathing are common symptoms.[3] The obstruction is caused either by the intraluminal growth of the tumor or compression from an extrinsic tumor mass. In addition to lung cancer, esophageal cancer, lymphoma and, rarely, metastases from other cancer forms can cause malignant central airway obstruction (MCAO). Oncological treatment may ameliorate symptoms but seldom cure the patient from advanced disease. Different modalities of intraluminal treatment can reduce obstruction in the trachea and bronchia: mechanical debulking with microdebrider, cryoablation or laser, photodynamic therapy, brachytherapy and/or airway stenting.[4-7] The overall survival in patients with malignant central airway obstruction is one to two months, but this can be prolonged with endoluminal intervention.[5,8,9] The patient's Quality of Life (QoL) can also be augmented by interventional bronchoscopy.[10]

Dyspnea is a subjective symptom of respiratory distress that may indicate a threat to the airways, and that is often reported in patients with MCAO. This may cause anxiety, decreased stamina and functional impairment.[11] However, the degree of airway obstruction does not always correspond to the patient's experience of dyspnea.[12] Therefore, it is essential to assess the patient's experience of dyspnea and not only the change in airway patency to be able to predict the benefit of a palliative intervention.

Only a few studies have evaluated how the experience of dyspnea and QoL in patients with MCAO is altered after tracheobronchial intervention.[9,10] This study aimed to identify which patients with airway compromise will benefit the most from endoluminal procedures and describe the effects of such interventions on dyspnea and QoL. We hypothesized that even patients with poor general condition benefit from the treatment.

Methods

Study Design and Study Population

This was a prospective cohort study. The Ear-Nose-Throat, Head and Neck department in Uppsala, Sweden, is a tertiary referral entre for advanced airway diseases. All patients referred to our center for endoscopic therapeutical procedures due to malignant airway compromise between January 1, 2015, and December 31, 2019, were eligible to participate in the study. Exclusion criteria were severe distress, cognitive impairment, difficulty understanding Swedish and age below 18 years. A written consent was obtained from all patients at admission to the department. The data cutoff occurred on October 31, 2020.

Assessments

The Visual Analogue Scale (VAS)/Numeric Rating Scale (NRS) is a one-dimensional self-rating scale that can be used to evaluate dyspnea.[13-16] The Cancer Dyspnea Scale (CDS) has been developed to better describe the experience of dyspnea in patients with cancer[17]. The CDS is multidimensional and measures the physical and emotional function as well as the level of discomfort in cancer patients. It has been validated in lung cancer patients[15] and is translated and validated in Swedish by Henoch et al.[18] The European Organisation for Research and Treatment of Cancer (EORTC) has developed a 13 item quality of life questionnaire validated in cancer patients (EORTC QLQ-C30)[19] and in lung cancer patients specifically (EORTC Quality of life questionnaire for Lung Cancer [QLQ-LC13]).[20]

The Eastern Cooperative Oncology Group World Health Performance Status (ECOG-WHO PS) is an established measure of functional status[21] and is frequently used as a prognostic factor in oncology.

Breathing parameters were evaluated by measurement of respiratory rate (RR), forced expiratory flow in 1 seconds (FEV1) in absolute values and in per cent of predicted (best value of three measurements), using a portable device (COPD6™, Vitalograph, Ireland), and heart rate and oxygen saturation (%) by a standard pulse oximeter without or with oxygen supplement as needed. The surgeon or the research nurse performed the measurements at the ward.

The day before surgery, the following scales and questionnaires were evaluated: ECOG-WHO PS, CDS, NRS for dyspnea, QLQ-C30, and, when appropriate, QLQ-LC-13.

The following measurements were repeated on postoperative day 1: Heart and respiratory rates, oxygen saturation, FEV1, and the NRS and CDS questionnaires. The first 19 consecutive patients had the physical measurements repeated, and the CDS, EORTC—C30/LC-13 completed, at 1 month postoperatively at a scheduled follow-up at their local hospital. Due to a lack of consistency in the follow-up procedure (response in 7/19 patients) the protocol was changed to mailing the questionnaires directly to the home address of surviving patients at 1 month postoperatively instead.

The Swedish Ethical Review Authority (EPN 2013/304) approved the study.

Surgical Procedure

Surgery was performed under total intravenous anesthesia and under jet ventilation through a rigid bronchoscope. Treatment options included debulking the intraluminal tumor with an Nd YAG (neodymium-doped yttrium aluminum garnet) laser or microdebrider, stent placement in the trachea/bronchus, or both. Depending on the localization of obstruction, self-expanding metallic stents, Ultraflex ™ (Boston Medical) or Carina Y-stent™ (Micro-Tech), were used. Only covered stents were used.

The choice of treatment was based solely on clinical features on previous examinations and findings during surgery by the surgeon following standard clinical routine. Normally, in a patient with intraluminal tumor naïve to oncologic treatment only debulking was performed whereas in patients with advanced disease refractory to nonsurgical treatment stents were used.

Statistical Analyses

Continuous data were presented as mean ± SD (median ±IQR for time to follow-up), and categorical data were presented as frequencies and percentages. Baseline data was stratified by ECOG-WHO PS (PS 0-1 and ≥2). The t-test was used for continuous variable comparisons, and the chi-square test was used for categorical data comparisons. Paired t-test was used to analyze differences in measurement values between baseline and follow-up. Treatment effects were visualized using waterfall charts. The relationships between change in FEV1 and change in CDS and NRS dyspnea scores were analyzed using univariable linear regression and visualized using scatter plots with regression lines. Survival was visualized using Kaplan-Meyer survival function graphs, and differences between groups were analyzed using the log-rank test.

Results

The study population consisted of 44 patients with MCAO (Fig. 1). Baseline data are presented in Table 1. In one patient, information about ECOG PS was

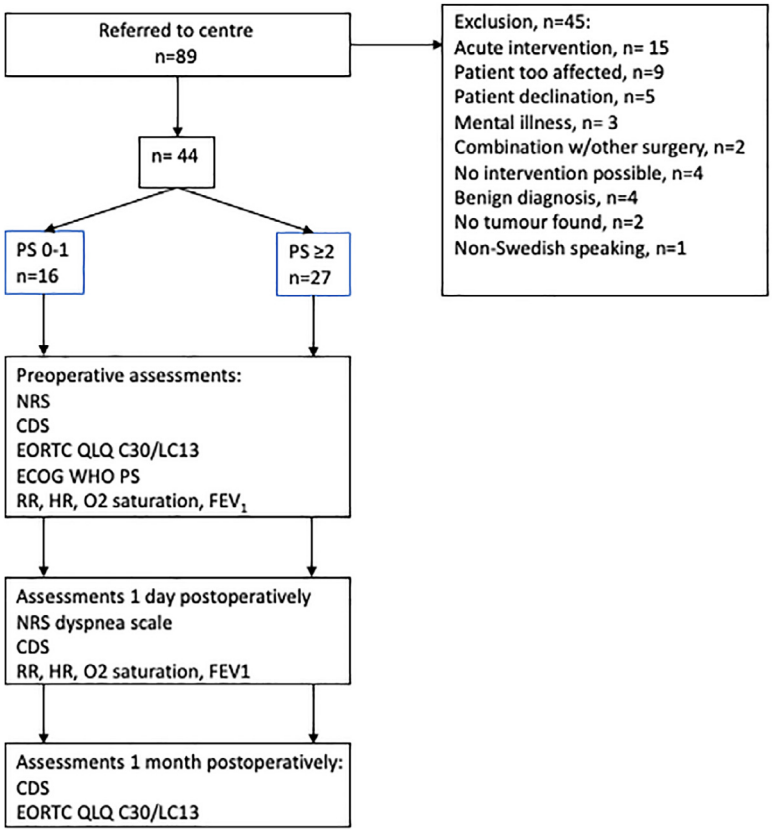

Fig. 1. Flow chart of study population. CDS = chronic disease score; ECOG WHO PS = Eastern Cooperative Oncology Group World Health Organisation Performance Status; EQRTC QLQ C30/LC13 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire/Lung Cancer Module 13; FEV1 = forced expiratory volume in one second; HR = heart rate; LC13; NRS = Numerical Rating Scale; NSCLC = non−small-cell lung cancer; QLQ-C30 = quality of life questionnaire-core 30; RR = respiratory rate; SCLC = small cell lung cancer.

Table 1
Pretreatment Baseline Data Stratified by ECOG-WHO PS Score

	PS 0-1 *N* = 16	PS 2-4 *N* = 27	Total *N* = 43	*P*-Value
Age (yrs)	69.4 (4.1)	69.2 (8.1)	69.3 (6.8)	0.93
Women (%)	10 (62%)	14 (52%)	24 (56%)	0.50
Diagnosis type				0.32
Carcinoid	1 (6%)	0 (0%)	1 (2%)	
Metastasis	3 (19%)	5 (19%)	8 (19%)	
NSCLC	9 (56%)	17 (63%)	26 (60%)	
SCLC	3 (19%)	2 (7%)	5 (12%)	
Unknown	0 (0%)	3 (11%)	3 (7%)	
Heart rate	83.4 (10.5)	92.6 (12.8)	89.3 (12.7)	0.022
Respiratory rate	18.9 (4.5)	20.4 (4.9)	19.9 (4.7)	0.36
Oxygen saturation	94.9 (2.7)	93.7 (4.6)	94.1 (4.0)	0.32
FEV1 (% of predicted)	58.9 (25.2)	43.2 (14.7)	49.2 (20.5)	0.029
Oxygen therapy	1 (6%)	8 (30%)	9 (21%)	0.069
CDS score	10.3 (6.1)	17.9 (7.1)	15.1 (7.6)	0.002
EQRTC QLQ-C30 summary score	57.8 (29.5)	84.0 (23.8)	74.2 (28.7)	0.004
LC13 dyspnea score	42.7 (24.4)	68.4 (20.4)	58.0 (25.2)	0.003
Global health status	47.6 (20.0)	20.5 (14.5)	30.5 (21.2)	< 0.001
NRS dyspnea score	4.7 (2.1)	6.0 (2.2)	5.5 (2.2)	0.072

Data are presented as mean (SD) for continuous measures, and n (%) for categorical measures.
CDS = chronic disease score; ECOG WHO PS = Eastern Cooperative Oncology Group World Health Organisation Performance Status; EQRTC QLQ C30 = European Organisation for Research and Treatment of Cancer Quality of life Questionnaire; FEV1 = forced expiratory volume in one second; LC13 = lung cancer module 13; NRS = numerical rating scale; NSCLC = non−small-cell lung cancer; QLQ-C30 = quality of life questionnaire-core 30; SCLC = small cell lung cancer.

missing. There were no differences in age or gender between patients with ECOG PS 0-1 (n = 16) and patients with ECOG-WHO PS ≥2 (n = 27). Patients with worse ECOG-WHO PS had higher baseline heart rate, and scored higher on the CDS scale, the dyspnea items in the QLQ-C30 and QLQ-LC-13 scale, and lower on the global health score (GHS) in the QLQ-C30 questionnaire. The FEV1 was lower in the ECOG-WHO PS 2-4 group. The majority of patients (60%) had a diagnosis of non−small-cell lung cancer.

Treatment Results

A majority of patients improved in FEV1, NRS dyspnea and CDS score at postoperative day 1 (Table 2). The results were stable after 1 month for CDS. The QLQ-C30 dyspnea score, LC-13 dyspnea score and GHS were improved after 1 month compared to baseline in evaluable patients. Notably, significant improvements were only observed in patients with a baseline ECOG PS of ≥2 for respiratory rate (20.4 ± 5.0 vs. 17.1 ± 2.7, P = 0.002), FEV1 (1.1 ± 0.4 l vs. 1 ± 0.6, P = 0.0010), CDS (16.7 ± 6.7 vs. 5.3 ± 2.9, P = 0.0002). In contrast, numerical changes were not significant in patients with baseline ECOG-WHO PS 0-1 for RR (18.9 ± 4.5 vs. 17.1 ± 5.4, P = 0.31), FEV1 (1.4 ± 0.5 l vs. 1.5 ± 0.5 l, P = 0.3913), and CDS (9.7 ± 5.9 vs. 6.4 ± 6.7, P = 0.23).

Individual results are depicted in Fig. 2a-d. Improvement in FEV1 was associated with improvements in CDS and NRS dyspnea scores (Fig. 3a-c).

Mortality

No procedure-related deaths occurred. The median follow-up time was 3.5 (95% CI 1.1−16.3) months. The median survival time after intervention was 105 (95% CI 72−105) days and 1 year survival was 27% (95% CI 15%−41%). The overall survival after inclusion is illustrated in Fig. 4 with patients grouped according to ECOG-WHO PS, showing a significantly shorter survival time for patients with ECOG-WHO PS 2-4.

Discussion

This prospective, single-center study found that signs of breathing distress, including subjective (dyspnea scores) and objective (FEV1, RR) indicators, were likely to improve after endoscopic treatment of malignant central airway obstruction. Most patients with MCAO have advanced cancer beyond treatment with curative intent, which makes palliation the goal of the intervention. Whereas a few retrospective studies have shown an improvement in dyspnea in response to endoscopic intervention,[2,22] Stratakos et al.[23] presented a series of

Table 2
Pretreatment Data Compared to Postoperative Data

	Baseline Values	Postoperative Day 1	n	*P*-Value	Follow-up at 1 Month	n	*P*-Value
Heart rate (beats per min)	89.1 (12.9)	86.8 (18.8)	40	0.398			
Respiratory rate (breath per min)	19.9 (4.9)	17.1 (3.8)	39	0.003			
Oxygen saturation (%)	94.5 (3.4)	94.6 (5.3)	40	0.88			
FEV1 (% of predicted)	50.7 (21.0)	61.7 (24.8)	30	0.002			
NRS dyspnea score	5.6 (2.2)	2.3 (2.4)	41	< 0.001			
CDS score	13.6 (7.2)	5.8 (4.1)	25	< 0.001	5.2 (4.1)	17	< 0.001
QLQ-C30 dyspnea score	76.5 (25.7)				41.2(27.7)	17	0.001
QLQ-C30 GHS score	33.9 (4.9)				47.0 (18.7)	14	0.012
QLQ-LC-13 dyspnea score	62.5 (6.4)				32.3 (5.5)	16	0.003

CDS = chronic disease score; FEV1 = forced expiratory volume in one second; LC13 = lung cancer module 13; n = number of participants; NRS = numerical rating scale; QLQ-C30 = quality of life questionnaire-core 30.

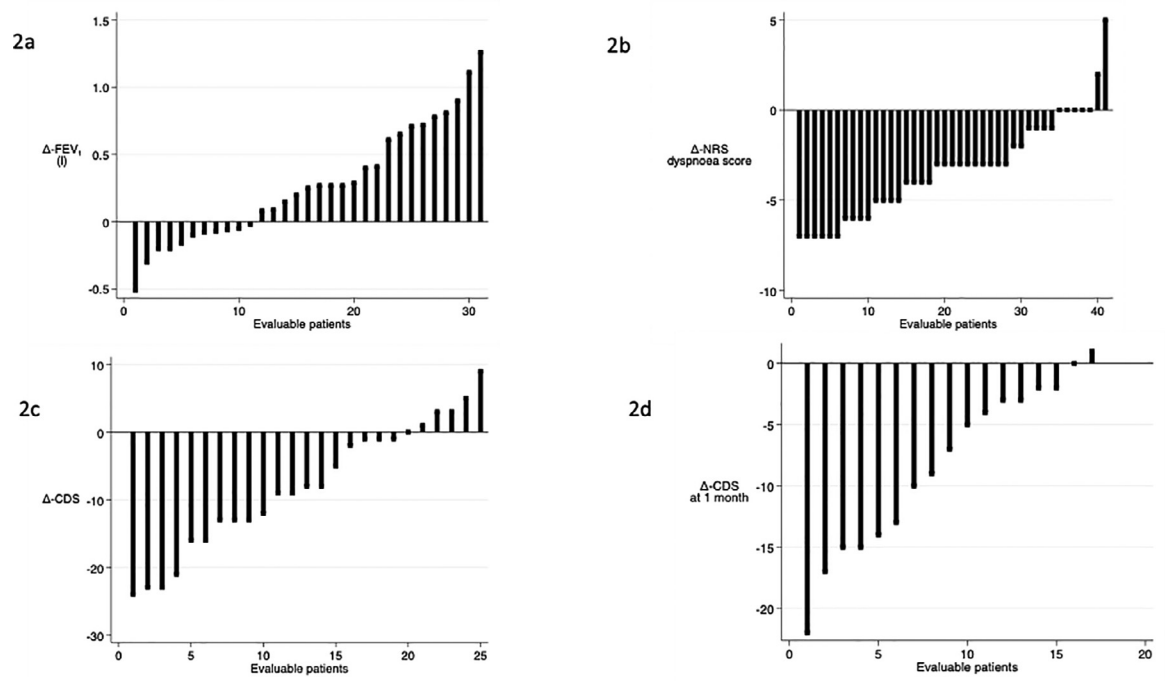

Fig. 2. (a-d) Waterfall diagrams illustrating individual changes in FEV1, NRS and CDS scores postoperative day 1 and after 1 month after bronchial intervention. CDS = chronic disease score; FEV1 = forced expiratory volume in one second; NRS = numerical rating scale.

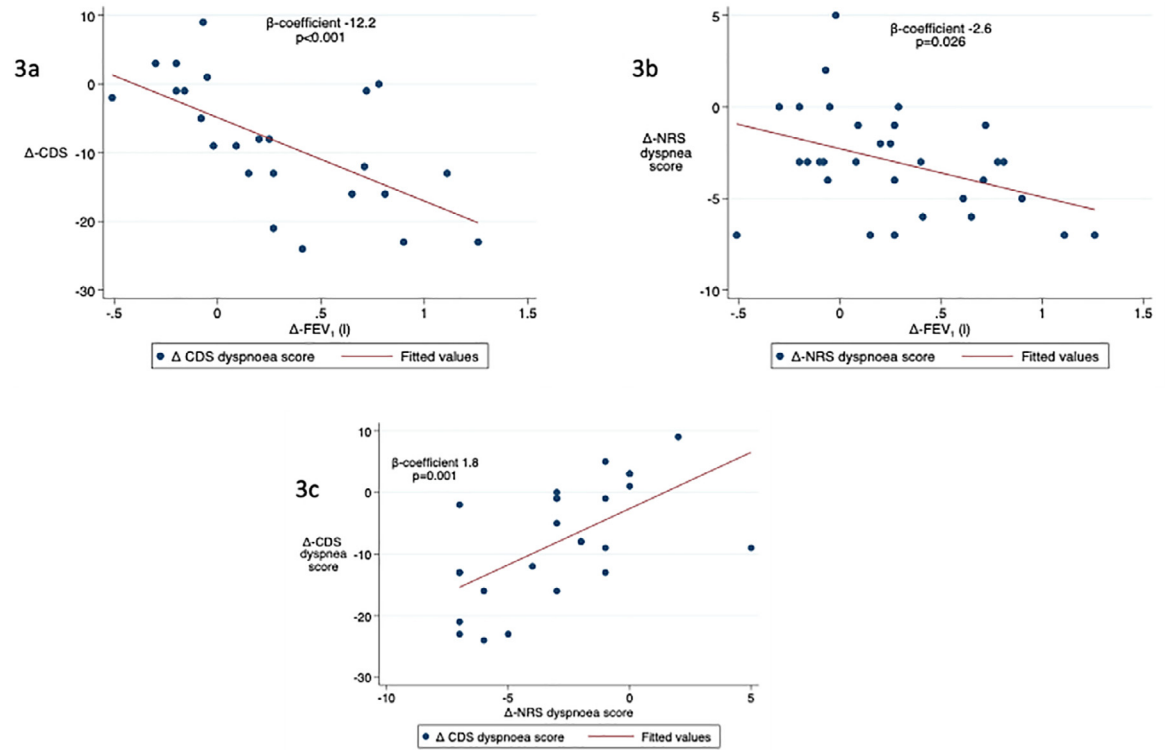

Fig. 3. (a-c) Correlations between change in CDS, NRS dyspnea and FEV1. CDS = chronic disease score; FEV1 = forced expiratory volume in one second; NRS = numerical rating scale.

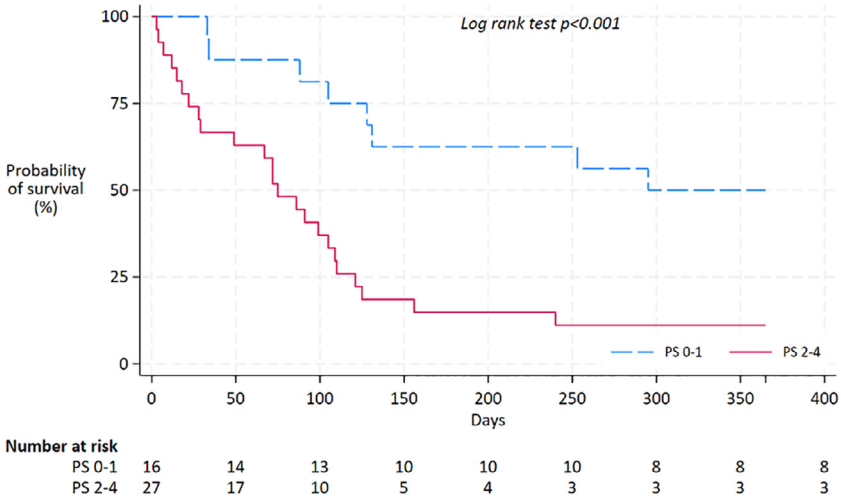

Fig. 4. Overall survival according to ECOG-WHO PS. ECOG WHO PS = Eastern Cooperative Oncology Group World Health Organisation Performance Status.

36 patients in a prospective clinical trial of endoscopic interventions in MCAO with QoL and dyspnea, measured by the EORTC QLQ-C30, improving after treatment. An early study performed in Japan in the late 90s demonstrated an improvement in dyspnea index up to 60 days postoperatively in 16 patients.[24] A large multicenter registry study (AQuIRE) including 947 patients undergoing therapeutic bronchoscopy showed improvement in dyspnea by the Borg scale in 48% of 147 evaluable patients and better health-related QoL postoperatively in 42%.[25] More pronounced changes occurred in patients with the worst dyspnea at baseline and in patients with a high ASA score. This aligns with our current findings, where patients with an ECOG-WHO PS ≥2 showed the most pronounced symptomatic improvement.

In the aforementioned studies, only one measurement of perceived dyspnea was used, which might be problematic when quantifying a subjective feeling such as dyspnea.[23,25] The Borg scale used in the AQuIRE study is not developed for cancer patients but constitutes an interval scale rating perceived exertion.[26,27] Also, the primary outcome in the AQuIRE study was technical success, defined as the anatomical reopening of the airways, and dyspnea and QoL were only assessed in a subset of patients.[25] In the study by Stratakos the results of the QoL questionnaire were not correlated with objective respiratory functional tests.[23] However, a prospective study of 37 patients described an amelioration of QoL (EORTC QLQ-C-30/LC-13) and dyspnea (6 minutes walking test (6MWT) and FEV1).[28]

When comparing the correlation between change in CDS and NRS dyspnea scales respectively, with change in change in FEV1 the CDS seems to correlate better to FEV1 change than the NRS dyspnea scale (Fig. 2). This might imply that the CDS is better suited to evaluate dyspnea in cancer patients than a simple, one-dimensional scale as NRS.

We found survival to be significantly lower in the group of patients who recieved a stent compared to patients who only underwent intraluminal debulking of tumor. This is likley explained by inclusion bias, since patients who had oncological treatment options postoperatively most often were not treated with a stent. This finding is in line with other studies.[29,30]

As expected, we found survival to be significantly lower in patients with worse ECOG-WHO PS.

Strength and Limitations

This is one of the few prospective studies investigating respiratory distress changes in real-life patients with MCAO in response to bronchoscopic intervention. To our knowledge, this is the first study to compare effects using several different validated instruments of dyspnea and correlate these to objective findings. The fact that most patients experienced a rapid improvement, in particular, if the performance status was affected preoperatively, provides data to substantiate the aim as expressed by the American College of Chest Physicians that *"In lung cancer patients with the inoperable disease and symptomatic airway obstruction, therapeutic bronchoscopy employing mechanical debridement, brachytherapy, tumor ablation or airway stent placement is recommended for improvement in dyspnea. . . ".*[31]

Only half of the potential study candidates could be included in this trial, an obvious limitation that illustrates the complexity of clinical reality. The relatively small study population may limit the generalizability of our results. For the same reason, the subgroup analyses should be cautiously interpreted, albeit useful for hypothesis generation. Larger studies exploring the effect of broncoscopic intervention in patients with MCAO are warranted.

The exclusion of nine patients who were deemed too affected by the airway obstruction to be able to comply with the study procedures or who needed immediate intervention inevitably introduces some degree of selection bias. Follow-up time was limited, which was inherent to the severe nature of MCAO. We had to change the study protocol due to low reporting of long-term QoL data. Hence, we cannot know how the bronchoscopic intervention affected the long-term quality of life and the experience of dyspnea.

Conclusion

Most patients with MCAO benefit from bronchoscopic intervention and those with worse ECOG-WHO PS may benefit even more in terms of symptom relief even though survival in those patients was worse.

Disclosure and Acknowledgments

The authors do not report any conflicts of interest related to this work. Outside the topic of the current study, AP reports lecturing activities for ResMed. The study was funded by a grant from Uppsala University, FoU LUL-351831.

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