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Decrease in pulmonary function and oxygenation after lung resection

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ABSTRACT Respiratory deficits are common following curative intent lung cancer surgery and may reduce the patient's ability to be physically active. We evaluated the influence of surgery on pulmonary function, respiratory muscle strength and physical performance after lung resection.

Pulmonary function, respiratory muscle strength (maximal inspiratory/expiratory pressure) and 6-min walk test (6MWT) were assessed pre-operatively, 2 weeks post-operatively and 6 months post-operatively in 80 patients (age 68±9 years).

Video-assisted thoracoscopic surgery was performed in 58% of cases. Two weeks post-operatively, we found a significant decline in pulmonary function (forced vital capacity −0.6±0.6 L and forced expiratory volume in 1 s −0.43±0.4 L; both $p<0.0001$), 6MWT (−37.6±74.8 m; $p<0.0001$) and oxygenation (−2.9±4.7 units; $p<0.001$), while maximal inspiratory and maximal expiratory pressure were unaffected. At 6 months post-operatively, pulmonary function and oxygenation remained significantly decreased ($p<0.001$), whereas 6MWT was recovered.

We conclude that lung resection has a significant short- and long-term impact on pulmonary function and oxygenation, but not on respiratory muscle strength. Future research should focus on mechanisms negatively influencing post-operative pulmonary function other than impaired respiratory muscle strength.

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Introduction

Lung resection remains the main curative treatment for early-stage lung cancer. However, surgery results in persistent reduction in post-operative pulmonary function of 10–40% [1, 2], which may contribute to functional impairments [3]. The cause of impaired pulmonary function following lung resection is multifactorial, including the removal of lung tissue and alterations in chest wall mechanics due to the surgical incision [4]. A significant decrease in respiratory muscle strength (RMS) 4 and 12 weeks after thoracotomy has been reported [5–7], while another study describes spontaneous recovery 30 days post-operatively [8]. There is inconsistency in the literature regarding the influence of the surgical approach on RMS. Video-assisted thoracoscopic surgery (VATS) may induce a smaller decrease in RMS compared with thoracotomy [9–11].

After major lung resection, a decline in ambulatory daily activity has been reported, despite recovery of the functional exercise capacity 1 month post-operatively [12, 13]. Whereas respiratory muscle dysfunction following surgery has been suggested to negatively influence post-operative pulmonary function [14], the influence of respiratory muscle dysfunction on functional outcomes has not been subject to studies. Thus, the aim of this study was to describe pulmonary function, RMS and physical performance within a period of up to 6 months after surgery.

Materials and methods

Subjects and design

Eligible were patients aged ⩾18 years, scheduled for lung resection on the suspicion of or confirmed lung cancer at the Dept of Cardiothoracic Surgery, Aalborg University Hospital, Denmark, between November 2012 and April 2014. Approximately 100 surgeries for confirmed lung cancer are performed in this centre annually. The exclusion criteria were physical or mental deficits adversely influencing walking ability, inability to understand written and spoken Danish, previous ipsilateral lung resection, disseminated or nonresectable lung cancer, pancoast tumour, and thoracic or abdominal surgery within 1 year pre-operatively. The extent of expected or resected lung tissue is not routinely calculated in all patients. The majority of patients (n=59) participated in a randomised controlled trial designed to evaluate the effects of post-operative inspiratory muscle training on RMS [15]. The study was approved by the Research Ethics Committee (N-20120027) and the Danish Data Protection Agency (N-2008-58-0028). Written informed consent was obtained prior to inclusion.

Perioperative management

All patients received pre-medication and general anaesthesia (propofol/remifentanil). Lung resections were performed either by conventional three-port VATS or by muscle-sparing lateral or postero-lateral thoracotomy (preserving the musculus latissimus dorsi and musculus serratus anterior). The choice of the surgical approach and the use of a rib retractor were at the discretion of the surgeon. In general, thoracotomy is used for major resections, while VATS is used for minor resections or resection in patients with compromised lung function. At the end of the surgery a single chest tube connected to a suction system with negative pressure of 5–10 cmH_2O (Thopaz Chest Drainage System; Medela, Baar, Switzerland) was placed in the pleural space. No drainage was used after pneumonectomy. Pain management was primarily achieved by continuous epidural infusion over a period of 1–5 days, supplemented with *per os* nonsteroidal anti-inflammatory drugs and paracetamol. All patients received post-operative respiratory physiotherapy consisting of breathing exercises and instructions in coughing and huffing and early mobilisation [15].

Outcome measurements

The assessments were performed pre-operatively, 2 weeks post-operatively and 6 months post-operatively.

Assessment of RMS measured at the mouth was performed according to American Thoracic Society/European Respiratory Society guidelines [16]. We used a hand-held electronic pressure transducer (Micro RPM; MicroMedical/CareFusion, Chatham, UK) with a flanged mouthpiece and the patient sitting in a chair. Measurements were performed from total lung capacity for maximal expiratory pressure (MEP) and from residual volume for maximal inspiratory pressure (MIP). The highest plateau pressure (1-s average) obtained after at least five attempts, with three attempts lying within 10 cmH_2O of each other, was used. The percentage of predicted normal values was also calculated [17]. Patients rated their wound pain during the assessment of RMS on a 0–10 numerical rating scale. Higher ratings corresponded to higher levels of pain.

Forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) were measured using a calibrated portable spirometer (Spirovit SP-2; Schiller, Baar, Switzerland). The best of three measurements was

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recorded [18] and the FEV1/FVC ratio was calculated. Predicted values were related to age, sex and height [19].

The 6-min walk test (6MWT) was used to assess physical performance. The test was performed twice, according to American Thoracic Society guidelines [20], in a 20-m corridor. Results were related to reference values [21]. Peripheral oxygen saturation measured by pulse oximetry (S_{pO_2}) (ri-fox N; Riester, Jungingen, Germany) and patient's experienced dyspnoea (Borg CR10 scale) [22] were assessed before and after the test. The perceived exertion post-6MWT was assessed using a modified 0–10 Borg scale. Higher ratings corresponded to higher levels of dyspnoea or exertion.

Statistical analysis

Data were reported as mean±standard deviation and median (minimum–maximum range) for ordinal or continuous variables, and as number and percentages for categorical variables. Nonparametric tests were used for analysis: the Wilcoxon signed-rank test for within-groups comparisons, the Mann–Whitney U-test for between-groups comparisons and the Kruskal–Wallis test for comparisons in categorical variables. For calculation of relative changes we used: (value at 2 weeks−value at baseline)/value at baseline) and likewise for values at the 6-month follow-up. All statistical tests were performed two-sided and conducted at the 5% significance level with SAS version 9 (SAS Institute, Cary, NC, USA).

Results

The study flowchart is provided as supplementary figure S1. 121 out of 232 screened patients were eligible, 88 were recruited and 80 completed the assessments 2 weeks post-operatively. 65 patients completed the assessments 6 months post-operatively. Demographic and post-operative data for the study sample are summarised in tables 1 and 2, which also present characteristics of the participants who completed all assessments and those not available after 6 months. At baseline, as a group, participants did not present impairments in RMS or 6MWT (both >100%). Chronic obstructive pulmonary disease (COPD) was diagnosed in 36% of cases. All patients underwent lung resection and radical surgery was performed in case of a malignant diagnosis. Two patients died between 2 and 6 months post-operatively. Nonmalignancy was the main reason for dropouts (n=7) 6 months post-operatively (no need for medical follow-up, according to hospital routines).

At 2 weeks post-operatively, RMS remained unchanged. Reductions in 6MWT (mean −37.6±74.8 m; p<0.001), S_{pO_2} post-6MWT (−2.9±4.7 units; p<0.0001) (table 3), and FVC and FEV1 (both p<0.001) were detected (table 4). We also found that dyspnoea and exertion post-6MWT were significantly increased

TABLE 1 Demographics and patient characteristics stratified by compliance to the 6-month follow-up protocol

	Baseline	Completed 6-month follow-up	Dropout at 6 months
Patients	80	65	15
Age years	68±9	68±9	68±11
	69 (46–82)	67 (51–82)	0 (46–81)
Males	46 (58)	39 (60)	7 (47)
COPD#			
Mild: FEV1 ⩾80% pred	8 (10)	8 (12)	0
Moderate: FEV1 50–80% pred	15 (15)	9 (14)	6 (8)
Severe: FEV1 30–50% pred	6 (8)	6 (9)	0
Previous cancer diagnosis	31 (40)	24 (37)	7 (44)
Pack-years¶	35 (30)	33 (28)	47 (36)
D_{LCO} % pred	67 (17)	67 (16)	67 (17)
ASA physical status			
2	64 (80)	52 (80)	12 (80)
3	16 (20)	13 (20)	3 (20)
ECOG performance status			
0	51 (64)	44 (68)	7 (47)
1	29 (36)	21 (33)	8 (53)

Values are presented as n, mean±SD, median (minimum–maximum range) or n (%). COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 s; D_{LCO}: diffusing capacity of the lung for carbon monoxide; ASA: American Society of Anaesthesiologists; ECOG: Eastern Cooperative Oncology Group. #: n=29; ¶: n=72.

TABLE 2 Surgical and cancer characteristics of the study population stratified by compliance to the 6-month follow-up protocol

	Baseline	Completed 6-month follow-up	Dropout at 6 months
Patients	80	65	15
VATS	46 (58)	34 (52)	12 (80)
Resection degree			
Wedge resection/segmentectomy	26 (33)	17 (26)	9 (60)
Lobectomy	45 (56)	39 (60)	6 (33)
Bilobectomy	3 (4)	3 (5)	0
Pneumonectomy	6 (7)	6 (9)	0
Duration of surgery min	132±60	136±58	99±47
	120 (30–320)	120 (45–320)	95 (30–150)
Duration of chest tubes h	68±77	74±83	44±48
	29 (8–360)	33 (8–360)	24 (11–172)
Length of hospital stay[#] days	8±5	8±5	7±7
	6 (3–30)	6 (3–25)	5 (3–30)
Post-operative chemotherapy	20 (25)	19 (29)	1 (7)
Cancer characteristics			
NSCLC	54 (67)	47 (72)	7 (47)
Stage IA/IB[¶]	13/18 (24/34)	11/15 (23.5/32)	2/3 (28.5/43)
Stage IIA/IIB[¶]	1/11 (2/20)	1/9 (2/19)	0/2 (0/28.5)
Stage IIIA[¶]	11 (20)	11 (23.5)	0
Metastatic tumour	11 (14)	10 (16)	1 (6)
Nonmalignancy	15 (19)	8 (12)	7 (47)

Values are presented as n, n (%), mean±SD or median (minimum–maximum range). VATS: video-assisted thoracoscopic surgery; NSCLC: nonsmall cell lung cancer. #: length of hospital stay includes transfer to other units; ¶: data refer only to NSCLC.

(both p<0.0001). The relative changes in pulmonary function, 6MWT and S_{pO_2} for wedge resection/segmentectomy, lobectomy, bilobectomy and pneumonectomy were, respectively: FVC −14±10%, −16±15%, −27±5% and −47±5% (p=0.000); FEV1 −13±13%, −19±13%, −29±5% and −47±5% (p=0.000); 6MWT −2±11%, −0.8±14%, −25±8% and −16±14% (p=0.005); S_{pO_2} −1±4%, −5±6%, −2±1% and −4±7% (p=0.123). The relative change in RMS was similar across the different resection degrees (MIP: p=0.499; MEP: p=0.134) (not illustrated).

At 6 months, MEP remained unchanged while MIP was significantly improved compared with baseline values (6.2±16 cmH_2O; p=0.0009); 6MWT improved from 2 weeks post-operatively and was comparable to pre-operative values. S_{pO_2}, dyspnoea and exertion post-6MWT remained significantly lower compared with pre-operative values (table 3). In addition, pulmonary function remained significantly decreased (FVC: p<0.0001; FEV1: p<0.001) (table 4). The relative changes in pulmonary function, 6MWT and S_{pO_2} for wedge resection/segmentectomy, lobectomy, bilobectomy and pneumonectomy were, respectively: FVC −7±11%, −4±13%, −15±15% and −35±5% (p=0.001); FEV1 −7±7%, −8±10%, −20±14% and −32±8% (p=0.001); 6MWT −7±3%, −1±11%, −13±14% and −16±12% (p=0.251); S_{pO_2} −1±4%, −2±4%, −3±2% and −2±6% (p=0.919). The relative change in RMS was similar across the different resection degrees (MIP: p=0.797; MEP: p=0.327) (not illustrated).

Individual characteristics of subjects with S_{pO_2} ⩽90% at 2 weeks post-operatively are shown in supplementary table S1. Supplementary table S2 shows outcome measures 2 weeks post-operatively for the whole sample and stratified by desaturators and nondesaturators.

Discussion

This study was aimed at describing pulmonary function, RMS and physical performance within a period of up to 6 months after curative intent lung cancer surgery. We found that 1) both pulmonary function and physical performance decreased significantly 2 weeks post-operatively, 2) S_{pO_2} after the 6MWT was significantly decreased at 2 weeks and 6 months post-operatively, and 3) RMS was not affected 2 weeks post-operatively. Thus, the post-operative decrease in oxygenation post-6MWT is not likely related to impaired RMS, since the latter was already recovered 2 weeks after the surgery.

TABLE 3 Respiratory muscle strength and physical performance: changes from baseline to 2 weeks and 6 months after surgery

	Baseline	2 weeks	Change		6 months	Change	
			Baseline to 2 weeks	p-value		Baseline to 6 months	p-value
Patients	80	80			65		
MIP cmH_2O	85±30 86 (23–152)	84±32 78 (18–181)	−0.8±18.1 1.5 (−44–60)	1.00	94±31 94 (19–183)	6.2±16 5.0 (−57–40)	0.0009
MIP % pred	104±30 106 (40–165)	101±34 100 (30–184)	−6.6±20 −6.0 (−49–61)	0.43	114±31 117 (32–196)	9.2±22 6.0 (−59–68)	0.011
MEP cmH_2O	102±33 101 (37–185)	99±34 96 (36–203)	−3.3±18.4 0.00 (−95–44)	0.23	108±37 108 (37–247)	3.1±17.8 4.0 (−36–62)	0.14
MEP % pred	106±25 103 (49–168)	102±28 102 (41–171)	−3.2±20.5 −3 (−61–50)	0.52	110±30 103 (46–207)	4.2±18 4.6 (−38–54)	0.14
6MWT m[#,¶]	506±125 519 (120–751)	467±135 472 (119–726)	−137.6±74.8 −28 (−304–116)	<0.0001	519±127 527 (231–793)	−5.6±60.1 −3.0 (−132–224)	0.52
6MWT % pred	100±20 102 (32–136)	92±22 94 (24–148)	−7.4±14.9 −5.0 (−61–23)	<0.0001	101±20 104 (52–146)	−1.6±12.5 0.0 (−33–38)	0.32
Oxygen saturation at rest, before 6MWT %[#,¶]	96±1.9 97 (87–99)	96±1.6 97 (91–98)	0.1±1.5 0.0 (−3.0–6.0)	0.57	97±1.2 97 (93–99)	0.4±1.8 0.0 (−2–9.0)	0.21
Oxygen saturation post-6MWT %[#,¶]	95±3.7 96 (80–100)	92±5 93 (77–98)	−2.9±4.7 −2 (−19–8)	<0.0001	93±3.9 94 (80–98)	−2.1±3.7 −2 (−12–7)	<0.0001
Dyspnoea units[#,¶,+]	2±1.5 2 (0–7)	3±1.9 3 (−0.8–8.5)	1.1±1.7 1 (−3–6)	<0.0001	3±1.8 3 (−1–7)	0.8±1.5 0.5 (−2–5)	0.0001
Exertion units	3.2±2.1 3 (0–10)	4.3±1.9 4 (1–9)	1.1±1.9 1 (−6–5)	<0.0001	3.92±2.2 3 (0–10)	0.86±2 1 (−5–6)	0.0014

Data are presented as n, mean±SD or median (minimum–maximum range), unless otherwise stated. MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; 6MWT: 6-minute walk test. #: n=79 at 2 weeks; ¶: n=61 at 6 months; +: difference after–before the 6MWT. Statistical analysis by Wilcoxon signed-rank test.

Our data show a significant decline in S_{pO_2} post-6MWT: from 95% to 92% 2 weeks post-operatively and to 93% after 6 months. At the same time, patients experienced greater dyspnoea and exertion after the 6MWT (~1 unit) at both follow-ups, despite recovery of walked distance by 6 months post-operatively. Similar findings of decreased oxygenation following the 6MWT have been described 2 [23] and 6–10

TABLE 4 Lung volumes: changes from baseline to 2 weeks and 6 months after surgery

	Baseline	2 weeks	Change		6 months	Change	
			Baseline to 2 weeks	p-value		Baseline to 6 months	p-value
Patients	80	80			65		
FVC L	3.4±0.9 3.4 (1.5–5.6)	2.8±0.9 2.8 (1–5)	−0.6±0.6 −0.6 (−2.5–0.7)	<0.0001	3.2±0.1 3.1 (1.3–5.7)	−0.29±0.5 −0.29 (−1.7–0.8)	<0.0001
FVC % pred	101±21 98 (59–170)	83±21 83 (35–131)	−17.6±17.6 −16 (−7.6–17)	<0.0001	94±21.9 91 (56–150)	−8.9±17.7 −7 (−6.6–30)	<0.0001
FEV_1 L	2.3±0.8 2.2 (0.7–4.2)	1.8±0.7 1.8 (0.6–3.6)	−0.43±0. 4 −0.43 (−1.6–0.3)	<0.0001	2.1±0.7 2.1 (0.8–4)	−0.27±0.3 −0.2 (−0.9–0.5)	<0.001
FEV_1 % pred	83±21.4 86 (28–134)	68±20.3 66 (20–118)	−15.2±14.1 −16 (−55–16)	<0.0001	76±18.5 75 (28–120)	−9.6±11.4 −9 (−42–19)	<0.0001
FEV_1/FVC	66±12.9 68.4 (21.6–85)	65±12.5 65.5 (39–88.6)	−0.92±7.69 12 (−18.6–20.5)	0.17	65±11.5 65.1 (32.5–87.6)	−2.12±7.12 −2.5 (−16.7–17.9)	0.002
FEV_1/FVC % pred	87±17.3 91 (29–111)	86±16 87 (52–119)	−0.9±1 −0.1 (−25–29)	0.28	86±15 87 (43–114)	−2±1 −3 (−21–24)	0.017

Data are presented as n, mean±SD or median (minimum–maximum range), unless otherwise stated. FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 s. Statistical analysis by Wilcoxon signed-rank test.

weeks [24] following lobectomy. Our data indicate that impaired oxygenation after the 6MWT is present not only after lobectomy and major resections, but also following minor resections. The impaired oxygenation may be explained by a degree of ventilatory inefficiency on a given workload, *i.e.* a combination of ventilatory and gas exchange impairments, secondary to the removal of lung tissue [14], which might result in a persistent mismatch in the oxygen delivery capacity during exercise. Patients with S_{pO_2} ⩽90% 2 weeks post-operatively had lower pre-operative values of diffusing capacity of the lung for carbon monoxide (D_{LCO}) when compared with nondesaturators, despite a relatively more preserved post-operative FEV1. CAVALHERI *et al.* [24] also suggested that the increased sensation of dyspnoea after lung resections might be related to the development of lung hyperinflation during exercise, similar to those with COPD [25]. Monitoring tidal volumes during the 6MWT and changes in inspiratory capacity before and after the 6MWT, in particular in patients with impaired D_{LCO}, could provide important information regarding the mechanisms involved in the ventilatory limitations during exercise in this population.

Our findings that RMS was not reduced 2 weeks after lung resection are contradictory to previous studies, as impairments in both inspiratory and expiratory muscle strength have been reported after major [5–8, 10] and minor [11] lung resections, evaluated at different time-points: 1 [9, 11], 4 [11] and 12 weeks post-operatively [5–7]. A single study performed by BORGES-SANTOS *et al.* [8] reported on normalisation of MIP and MEP between days 10 and 15 following thoracotomy. A smaller decrease in RMS has been reported following VATS compared with non-muscle-sparing thoracotomy [6, 9, 10]. The surgeons in our institution perform thoracotomy with muscle-sparing techniques for major resections, while VATS is mostly used in patients with limited pulmonary function or for minor resections. This practice is in accordance with other authors, who describe better outcomes following VATS compared with traditional open techniques [26]. As a result of the reduced damage to the chest wall, less invasive techniques may ameliorate the negative impact of the surgery on pulmonary function and reduce the risk of post-operative pulmonary complications [5, 14].

Two major issues may explain the diverging reports in the literature on the negative effect of surgery on RMS and support our findings of no reduction in RMS 2 weeks after surgery. First, comparisons with older studies can be difficult, because there have been major changes over the last decade in the clinical pathway following lung resection. Factors such as the increasing use of VATS, improvements in pain management and the incorporation of structured early mobilisation may enhance the overall recovery [27], including the recovery of RMS. Second, because measurement of RMS is effort dependent [17], impaired RMS, especially early after the surgery, may reflect higher levels of pain in the surgical site, in particular following standard thoracotomy [28], which could explain the decrease in RMS reported in some studies [5, 6, 9]. Our data do not support that pain has an impact in the assessment of RMS, considering that the mean pain rating 2 weeks post-operatively was low (score of 1 on the numerical rating scale).

In a previous study from our group we evaluated the effects of 2 weeks of post-operative inspiratory muscle training on RMS in high-risk patients following lung cancer surgery in a randomised controlled setting [15]. We reported on a significant decrease in RMS by post-operative day 5 with recovery 2 weeks post-operatively. The study included 73% of the present study's cohort, of which 33 patients received the active intervention. Considering that we found no differences between the groups in RMS at 5 days and 2 weeks post-operatively [15], we cannot endorse that inspiratory muscle training as the active intervention could have enhanced recovery of RMS to a degree that influenced the results of the present study. Meanwhile, as we did not assess RMS by post-operative day 5 in all patients, we cannot exclude the presence of a transient decline in RMS early after the surgery. In the present study we report on a significant increase in MIP of 6.2 cmH_2O 6 months post-operatively. An increase in MIP of 13 cmH_2O has been reported as clinically relevant in the COPD population [29], but there is no definition of a clinically relevant change in MIP following lung resection. Although statistically significant, we do not consider the increase in MIP at 6 months to be of clinical relevance, considering that S_{pO_2}, dyspnoea and exertion at this time-point were higher compared with baseline values.

Strengths and limitations

The dropout percentage in our study was 17% at the 6-month follow-up and this is consistent with previous reporting [13, 30]. This was a single-centre study with a heterogeneous group regarding the degree of resection of lung tissue and included patients with different diagnoses (nonsmall cell lung cancer, metastatic tumour and nonmalignant disease). Surgeons perform segmentectomies and wedge resections in patients with compromised cardiorespiratory function/early-stage nonsmall cell lung cancer in order to preserve as much of the parenchyma as possible [31]. We present results on relative changes in outcome measures 2 weeks and 6 months post-operatively stratified by the resection degree, since our results suggest that short- and long-term desaturation post-6MWT may occur regardless of the resection degree. Meanwhile, due to the small sample size and subsequent large standard deviations, the stratified results we present should not be interpreted conclusively. Also, we could not assess the influence of the surgical approach (VATS *versus* thoracotomy) on RMS as a sample of 70 patients in each group would be necessary to detect a difference in MIP of 15±32 cmH_2O [32], considering 80% power and a significance level of <0.05. Furthermore, the reliability of measurement of S_{pO_2} can be questioned, since arterial blood gas analysis is the gold standard in accuracy for the detection of hypoxaemia. We chose to use S_{pO_2} because it is a noninvasive method widely used in the clinical and rehabilitation setting. Furthermore, its accuracy is within ±2–3 units from the results obtained from the arterial blood gas analysis [33]. It also is important to consider that the 6MWT is a submaximal test and may not induce higher levels of dyspnoea compared with an incremental test. Meanwhile, the 6MWT has been shown to detect a greater decline in S_{pO_2} compared with an incremental, cycle-based test [24], supposedly related to the use of larger muscle mass involved in walking. Finally, comparison between measurement of RMS by mouth pressure, as performed in our study, with an effort-independent technique that measures diaphragm contractility (twitch transdiaphragmatic pressure) [20, 34] is warranted in the surgical setting as it may provide useful diagnostic data on respiratory muscle weakness.

Conclusions

Lung resection has a significant short- and long-term impact on pulmonary function as well as on oxygenation levels and symptoms following the 6MWT, but not on RMS. Future research should focus on mechanisms other than post-operative impairments in RMS, which may explain the respiratory deficits influencing physical performance in this population.

References

1 Brunelli A, Xiume F, Refai M, *et al.* Evaluation of expiratory volume, diffusion capacity, and exercise tolerance following major lung resection: a prospective follow-up analysis. *Chest* 2007; 131: 141–147.

2 Cukic V. Reduction of pulmonary function after surgical lung resections of different volume. *Med Arch* 2014; 68: 231–235.

3 Poghosyan H, Sheldon LK, Leveille SG, *et al.* Health-related quality of life after surgical treatment in patients with non-small cell lung cancer: a systematic review. *Lung Cancer* 2013; 81: 11–26.

4 Miserocchi G, Beretta E, Rivolta I. Respiratory mechanics and fluid dynamics after lung resection surgery. *Thorac Surg Clin* 2010; 20: 345–357.

5 Nomori H, Kobayashi R, Fuyuno G, *et al.* Preoperative respiratory muscle training. Assessment in thoracic surgery patients with special reference to postoperative pulmonary complications. *Chest* 1994; 105: 1782–1788.

6 Weiner P, Man A, Weiner M, *et al.* The effect of incentive spirometry and inspiratory muscle training on pulmonary function after lung resection. *J Thorac Cardiovasc Surg* 1997; 113: 552–557.

7 Ziyade S, Baskent A, Tanju S, *et al.* Isokinetic muscle strength after thoracotomy: standard vs. muscle-sparing posterolateral thoracotomy. *Thorac Cardiovasc Surg* 2010; 58: 295–298.

8 Borges-Santos E, Genz IC, Longo AF, *et al.* Pulmonary function, respiratory muscle strength and quality of life in patients submitted to elective thoracotomies. *Rev Col Bras Cir* 2012; 39: 4–9.

9 Nomori H, Horio H, Fuyuno G, *et al.* Respiratory muscle strength after lung resection with special reference to age and procedures of thoracotomy. *Eur J Cardiothorac Surg* 1996; 10: 352–358.

10 Nomori H, Horio H, Naruke T, *et al.* What is the advantage of a thoracoscopic lobectomy over a limited thoracotomy procedure for lung cancer surgery? *Ann Thorac Surg* 2001; 72: 879–884.

11 Bernard A, Brondel L, Arnal E, *et al.* Evaluation of respiratory muscle strength by randomized controlled trial comparing thoracoscopy, transaxillary thoracotomy, and posterolateral thoracotomy for lung biopsy. *Eur J Cardiothorac Surg* 2006; 29: 596–600.

12 Novoa N, Varela G, Jimenez MF, *et al.* Influence of major pulmonary resection on postoperative daily ambulatory activity of the patients. *Interact Cardiovasc Thorac Surg* 2009; 9: 934–938.

13 Arbane G, Douiri A, Hart N, *et al.* Effect of postoperative physical training on activity after curative surgery for non-small cell lung cancer: a multicentre randomised controlled trial. *Physiotherapy* 2014; 100: 100–107.

14 Siafakas NM, Mitrouska I, Argiana E, *et al.* Effects of surgery on the function of the respiratory muscles. *Monaldi Arch Chest Dis* 1999; 54: 526–531.

15 Brocki BC, Andreasen JJ, Langer D, *et al.* Postoperative inspiratory muscle training in addition to breathing exercises and early mobilization improves oxygenation in high-risk patients after lung cancer surgery: a randomized controlled trial. *Eur J Cardiothorac Surg* 2016; 49: 1483–1491.

16 American Thoracic Society, European Respiratory Society. ATS/ERS statement on respiratory muscle testing. *Am J Respir Crit Care Med* 2002; 166: 518–624.

17 Evans JA, Whitelaw WA. The assessment of maximal respiratory mouth pressures in adults. *Respir Care* 2009; 54: 1348–1359.

18 Miller MR, Hankinson J, Brusasco V, *et al.* Standardisation of spirometry. *Eur Respir J* 2005; 26: 319–338.

19 Quanjer PH, Tammeling GJ, Cotes JE, *et al.* Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J* 1993; 6: Suppl. 16, 5–40.

20 American Thoracic Society. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002; 166: 111–117.

21 Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med* 1998; 158: 1384–1387.

22 Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982; 14: 377–381.

23 Nomori H, Ohtsuka T, Horio H, *et al.* Difference in the impairment of vital capacity and 6-minute walking after a lobectomy performed by thoracoscopic surgery, an anterior limited thoracotomy, an anteroaxillary thoracotomy, and a posterolateral thoracotomy. *Surg Today* 2003; 33: 7–12.
24 Cavalheri V, Jenkins S, Cecins N, *et al.* Comparison of the six-minute walk test with a cycle-based cardiopulmonary exercise test in people following curative intent treatment for non-small cell lung cancer. *Chron Respir Dis* 2016; 13: 118–127.
25 Ofir D, Laveneziana P, Webb KA, *et al.* Mechanisms of dyspnea during cycle exercise in symptomatic patients with GOLD stage I chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2008; 177: 622–629.
26 Zhang R, Ferguson MK. Video-assisted versus open lobectomy in patients with compromised lung function: a literature review and meta-analysis. *PLoS One* 2015; 10: e0124512.
27 Granger CL. Physiotherapy management of lung cancer. *J Physiother* 2016; 62: 60–67.
28 Demmy TL, Nwogu C. Is video-assisted thoracic surgery lobectomy better? Quality of life considerations. *Ann Thorac Surg* 2008; 85: S719–S728.
29 Gosselink R, De VJ, van den Heuvel SP, *et al.* Impact of inspiratory muscle training in patients with COPD: what is the evidence? *Eur Respir J* 2011; 37: 416–425.
30 Arbane G, Tropman D, Jackson D, *et al.* Evaluation of an early exercise intervention after thoracotomy for non-small cell lung cancer (NSCLC), effects on quality of life, muscle strength and exercise tolerance: randomised controlled trial. *Lung Cancer* 2011; 71: 229–234.
31 Bedetti B, Bertolaccini L, Rocco R, *et al.* Segmentectomy versus lobectomy for stage I non-small cell lung cancer: a systematic review and meta-analysis. *J Thorac Dis* 2017; 9: 1615–1623.
32 Mans CM, Reeve JC, Elkins MR. Postoperative outcomes following preoperative inspiratory muscle training in patients undergoing cardiothoracic or upper abdominal surgery: a systematic review and meta analysis. *Clin Rehabil* 2015; 29: 426–38.
33 Pretto JJ, Roebuck T, Beckert L, *et al.* Clinical use of pulse oximetry: official guidelines from the Thoracic Society of Australia and New Zealand. *Respirology* 2014; 19: 38–46.
34 Steier J, Kaul S, Seymour J, *et al.* The value of multiple tests of respiratory muscle strength. *Thorax* 2007; 62: 975–980.