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The importance of phrenic nerve preservation and its effect on long-term postoperative lung function after pneumonectomy

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Abstract

OBJECTIVES: The importance of phrenic nerve preservation during pneumonectomy remains controversial. We previously demonstrated that preservation of the phrenic nerve in the immediate postoperative period preserved lung function by 3–5% but little is known about its long-term effects. We, therefore, decided to investigate the effect of temporary ipsilateral cervical phrenic nerve block on dynamic lung volumes in mid- to long-term pneumonectomy patients.

METHODS: We investigated 14 patients after a median of 9 years post pneumonectomy (range: 1–15 years). Lung function testing (spirometry) and fluoroscopic and/or sonographic assessment of diaphragmatic motion on the pneumonectomy side were performed before and after ultrasonographic-guided ipsilateral cervical phrenic nerve block by infiltration with lidocaine.

RESULTS: Ipsilateral phrenic nerve block was successfully achieved in 12 patients (86%). In the remaining 2 patients, diaphragmatic motion was already paradoxical before the nerve block. We found no significant difference on dynamic lung function values (FEV1 'before' 1.39 ± 0.44 vs FEV1 'after' 1.38 ± 0.40; *P* = 0.81).

CONCLUSIONS: Induction of a temporary diaphragmatic palsy did not significantly influence dynamic lung volumes in mid- to long-term pneumonectomy patients, suggesting that preservation of the phrenic nerve is of greater importance in the immediate postoperative period after pneumonectomy.

Keywords: Pneumonectomy • Phrenic nerve • Diaphragm • Pulmonary function • Lung cancer

INTRODUCTION

Even nowadays, more than 80 years after the first successfully performed pneumonectomy by Graham and Singer in 1933 [1], the importance of phrenic nerve preservation during pneumonectomy is unclear. While some authors described adverse outcomes after phrenic nerve sacrifice in pneumonectomy patients [2], others are not concerned at all whether the nerve should be preserved or not.

Ugalde *et al.* [3] investigated the effect of ipsilateral diaphragmatic motion on lung function in long-term pneumonectomy patients and described significantly better dynamic lung values in patients with a functional diaphragm years after the procedure. They did, however, compare two different groups of patients with a working and a non-working diaphragm, respectively, rather than investigate the effect of diaphragmatic palsy in the same cohort. This was recently done by Kocher *et al*. [4] but only in the early postoperative course following pneumonectomy where a modest but significant deterioration of dynamic lung volumes was observed when the ipsilateral diaphragm was paralysed by lidocaine. In order to elucidate whether the impact of phrenic nerve palsy increases further with time after the operation, as the results of the Canadian study suggest [3], we decided to investigate the effect of ipsilateral phrenic nerve palsy induction on diaphragmatic motion and lung function in mid- to long-term pneumonectomy patients.

MATERIALS AND METHODS

This study was approved by the local ethics committee (S-20130105) and written consent was obtained from all patients. All patients from the southern region of Denmark who were alive at least 12 months after pneumonectomy at the Department of Cardiothoracic Surgery, Odense University Hospital, Denmark, were identified from the hospital database and invited by letter to take part in the study. Patients with intentional resection of the phrenic nerve during pneumonectomy due to mediastinal tumour infiltration were excluded from our study. Likewise, patients with the need for supplemental oxygen or an oxygen saturation of ≤90% at room air at the time of the study were also excluded.

In all patients, lung function testing (spirometry) and fluoroscopic and/or sonographic assessment of diaphragmatic motion on the pneumonectomy side were performed before and 30 min after ultrasonographic-guided ipsilateral cervical phrenic nerve block.

Evaluation of diaphragmatic motion

Diaphragmatic motion was assessed by a sniff-test during fluoroscopy [5] before and after induction of phrenic nerve palsy. If the diaphragm could not be accurately identified by radiography, the evaluation was supplemented by ultrasonography. All investigations were performed and evaluated by the same radiologist. Diaphragmatic motion was recorded and later categorized as normal, without movement or with paradoxical movement. Normal motion was defined as synchronous diaphragmatic motion compared with the healthy contralateral side. If the diaphragm was moving upwards during inspiration, the movement pattern was categorized as paradoxical.

Induction of phrenic nerve palsy

We targeted the phrenic nerve in the neck region where it was accessible for ultrasonographic-guided periphrenic infiltration. We used the technique described by Renes *et al*. [6] and the phrenic nerve on the side of pneumonectomy was identified with a curvilinear 3–6 MHz sonography probe (BK Medical, Herlev, Denmark) and infiltrated with 5 ml of 1% lidocaine at the level of the vertebral body C6 where the nerve passes along the anterior scalene muscle.

Pulmonary function testing

Dynamic lung volumes were measured before and after phrenic nerve block by digital spirometry (Schiller Spirovit SP-2), which was performed according to the European Respiratory Society recommendations [7]. The same study nurse performed all spirometry examinations and the best test result from three consecutive measurements before and after infiltration of the phrenic nerve was used.

Statistical analysis

We used a paired *t*-test to compare lung function values before and after phrenic nerve block. Quantitative data were expressed as mean ± standard deviation or as median including range when appropriate. Exact two-tailed *P*-values were reported and *P*-values of <0.05 were considered significant. Statistical analysis was performed using the IBM SPSS software package (Version 22, IBM SPSS, Chicago, IL, USA).

RESULTS

From the hospital database, we identified 84 patients who were alive more than 12 months after pneumonectomy. The majority declined our invitation to participate because they did not want to travel up to 160 km to and from the hospital for our 1-day investigatory trial, but 14 patients accepted our invitation and were enrolled in the study. They were investigated between December 2013 and April 2014 after a median of 110 months following pneumonectomy (range: 15–185 months). Median age at the time of surgery was 61 years (range: 34–72 years). Eight (57%) of the 14 patients were males. The indication for pneumonectomy was non-small-cell lung cancer in all patients. Four patients underwent a right-sided, and 10 patients a left-sided pneumonectomy. Oxygen saturation was ≥90% at room air in all patients at follow-up. Diaphragmatic evaluation by a sniff-test under fluoroscopic or ultrasonography revealed that 7 patients had normal movement, 5 patients showed no movement and 2 patients had paradoxical diaphragmatic motion. Following phrenic nerve block, paradoxical movement was seen in all patients (Fig. 1). The lung function values before and after phrenic nerve block are presented in Table 1 and there was no difference between the two sides of pneumonectomy.

None of our patients experienced any subjective respiratory deterioration during induction of the phrenic nerve block. In fact, 1 patient reported that he felt subjective improvement with less strenuous respiration after the block. Side effects of the infiltration were seen in 5 patients (35%): Temporary Horner's syndrome in 3 patients who also reported temporary hoarseness and 2 had additional temporary sensomotory impairment of the shoulder. Isolated temporary hoarseness was seen in one patient and isolated temporary sensomotory impairment was observed in another patient. At this point, it has to be stated that the described side effects are rather common findings when performing an infiltration near the anterior scalene muscle, since all the corresponding nerves lie in close proximity to the target region. All patients were monitored for at least 4 h after nerve infiltration. All side effects described above resolved spontaneously ~2 h after the injection.

DISCUSSION

The two major findings of our study are that the ipsilateral hemidiaphragm remains surprisingly mobile even years after pneumonectomy and that temporary induction of phrenic nerve paralysis did not significantly influence dynamic lung volumes in our patients. Our results, therefore, contribute information to the ongoing controversial debate, even nowadays more than 8 decades after the first pneumonectomy [1], whether preserving the phrenic nerve during pneumonectomy is important. Although most surgeons preserve the phrenic nerve, some routinely sacrifice it during pneumonectomy because it leads to faster filling of the chest cavity due to elevation of the paralysed diaphragm, which in turn may lead to faster mechanical stability of the mediastinum. Nevertheless, most surgeons prefer preservation of the phrenic nerve because the diaphragm is assumed to be an entity where both hemidiaphragms contribute positively to the remaining postoperative lung function. Little human data have been published to verify this assumption [2] but Takeda *et al*. were also able to demonstrate a beneficial effect of diaphragmatic plication on respiratory mechanics in dogs with unilateral phrenic nerve palsy [8]. Furthermore, as reported by Welvaart *et al*. [9] phrenic nerve sacrifice during right pneumonectomy can lead to compression of the right ventricle, resulting in right–left shunt through an open foramen ovale.

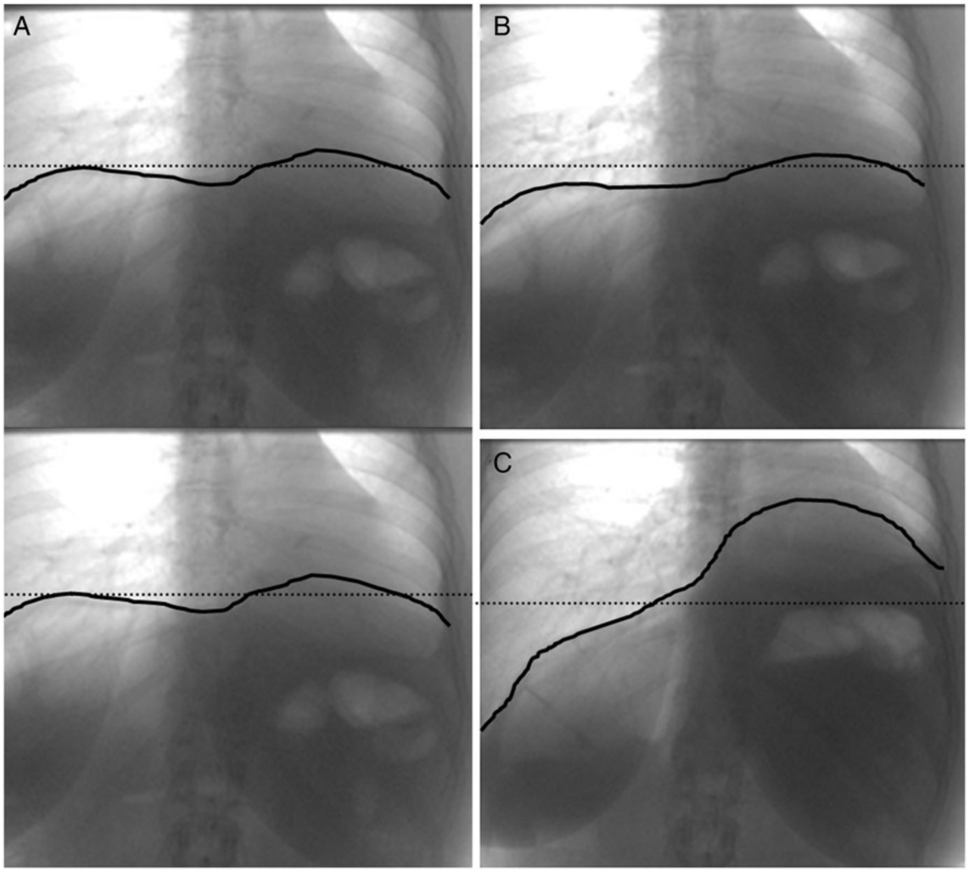

Figure 1: (**A**) Normal diaphragmatic position in a 79-year old female patient 9 years after left pneumonectomy. Diaphragmatic inspiratory movement before (**B**) and after (**C**) phrenic nerve block showing absent movement on the left side before, and paradoxic motion after phrenic nerve block.

Table 1: Main study results

Factor	Before phrenic nerve block	After phrenic nerve block	*P*-value
Diaphragmatic motion (*n*)			
Normal (symmetric)	7		
No movement	5		
Paradoxical	2	14	
FEV1 (l)[a]	1.39 ± 0.44	1.38 ± 0.4	0.808
FVC (l)[a]	2.20 ± 0.72	2.13 ± 0.56	0.849
Blood oxygen saturation (%)[a]	96.83 ± 1.95	96.75 ± 1.22	0.801

[a]Two patients were excluded because of paradoxical movement before the induction of phrenic nerve block.

There are only few studies on pulmonary function after pneumonectomy and the influence of phrenic nerve preservation. Ugalde *et al.* [3] reported the first larger study on ipsilateral diaphragmatic motion and lung function in pneumonectomy patients. The authors compared two cohorts with a total of 88 long-term pneumonectomy patients with functional or dysfunctional diaphragmatic motion assessed by MRI after more than 5 years following pneumonectomy. In their series, patients with abnormal diaphragmatic motion had significantly impaired dynamic lung function compared with those with normal diaphragmatic motion, with a mean difference in FVC of 27% and in FEV1 of 15%, respectively. Their study, however, evaluated diaphragmatic motion only and phrenic nerve function itself was not investigated. Additional limitations were its retrospective nature and that they investigated two different cohorts of patients, which consequently leads to bias.

Recently, Kocher *et al.* [4] were the first to prospectively investigate the effect of induced phrenic nerve palsy in the early postoperative course after pneumonectomy. Despite a relatively small number of only 10 patients, they found a small but significant decrease in dynamic lung volumes: after induction of diaphragmatic palsy on postoperative day 6 or 7 by injection of lidocaine in a periphrenically placed catheter during pneumonectomy, they observed a mean decrease in FEV1 of 5% and in FVC of 3.4%. Although statistically significant, the changes were dramatically less than those reported by Ugalde *et al.* [3] and the question remains whether changes in dynamic lung volumes would increase with time following pneumonectomy. The present study demonstrates that it was not the case because we found no difference in lung function before and after phrenic nerve palsy. Unlike the Canadian study, we used a paired design in pneumonectomized patients, as was done in the Swiss study [4], to detect intraindividual changes in lung function thereby eliminating selection bias.

We decided to infiltrate the phrenic nerve in the neck region because an approach in its intrathoracic course would have required surgical access, which was considered unethical. Phrenic nerve palsy was achieved in 86% (12 of 14) of patients, but we were not able to detect any effect of the lidocaine injection in 2 remaining patients because they both presented with paradoxical diaphragmatic movement before infiltration, and this did not change after the phrenic nerve block. We suspect that they had pre-existing phrenic nerve palsy as a surgical complication although there was no mentioning of phrenic nerve damage in the surgical notes. Another interesting finding was that the time elapsed after surgery did not influence the fact whether there was normal or no diaphragmatic movement before the infiltration.

When comparing the results from the present study and the previous trial [4], we conclude that the direct effect of diaphragmatic motion on dynamic lung function values is more important in the early postoperative period and that, on the long term, this direct effect seems to decrease. However, when taking into account the better long-term lung function values shown by Ugalde *et al*. and combining these findings with the mouse model data presented by Ysasi *et al*. [10], suggesting that a cyclic stretch associated with diaphragmatic muscle contraction is a factor that has a positive influence on post-pneumonectomy growth/hyperinflation of the remaining lung, we suspect that phrenic nerve function may be more important than our study was able to capture. It can be speculated that over time an intact phrenic nerve is particularly important for the gradual hyperinflation of the remaining lung after pneumonectomy, thus resulting in better lung function values in the end. This would also explain why the only short-lasting effect of the phrenic nerve palsy in our trial was well compensated by the patients.

Limitations of our study include the relatively small sample size but it proved difficult to persuade patients to participate in the study because of geographical reasons. Obviously, selection bias could also be a problem in this study if only patients in good health and respiratory status were willing to participate. On the other hand, patients with limited respiratory function (i.e. need of supplemental oxygen) would have been excluded from the study. Furthermore, with our study approach, phrenic nerve palsy was only temporary and short lasting (~2–3 h) and the question remains whether a more long-lasting nerve palsy would have resulted in a different result.

In conclusion, our data suggest that ipsilateral phrenic nerve function years after pneumonectomy is of minor importance on dynamic lung values compared with the immediate effect following pneumonectomy. However, because preservation of the phrenic nerve is beneficial in the early postoperative period, we suggest that it should be preserved, whenever possible, during pneumonectomy. After all, there are no reported negative side effects of nerve preservation.

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Conflict of interest: none declared.

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