Effect of Phrenic Nerve Palsy on Early Postoperative Lung Function After Pneumonectomy: A Prospective Study

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Background. **The issue of phrenic nerve preservation during pneumonectomy is still an unanswered question. So far, its direct effect on immediate postoperative pulmonary lung function has never been evaluated in a prospective trial.**

Methods. **We conducted a prospective crossover study including 10 patients undergoing pneumonectomy for lung cancer between July 2011 and July 2012. After written informed consent, all consecutive patients who agreed to take part in the study and in whom preservation of the phrenic nerve during operation was possible, were included in the study. Upon completion of lung resection, a catheter was placed in the proximal paraphrenic tissue on the pericardial surface. After an initial phase of recovery of 5 days all patients underwent ultrasonographic assessment of diaphragmatic motion followed by lung function testing with and without induced phrenic nerve palsy. The controlled, temporary paralysis of the ipsilateral hemidiaphragm was achieved by local administration of lidocaine 1% at a rate of 3 mL/h (30 mg/h) via the above-mentioned catheter.**

Results. **Temporary phrenic nerve palsy was accomplished in all but 1 patient with suspected catheter dislocation. Spirometry showed a significant decrease in dynamic lung volumes (forced expiratory volume in 1 second and forced vital capacity; $p < 0.05$) with the paralyzed hemidiaphragm. Blood oxygen saturation levels did not change significantly.**

Conclusions. **Our results show that phrenic nerve palsy causes a significant impairment of dynamic lung volumes during the early postoperative period after pneumonectomy. Therefore, in these already compromised patients, intraoperative phrenic nerve injury should be avoided whenever possible.**

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In some patients, pneumonectomy is the only curative treatment option for centrally located or advanced stage lung tumors, despite a higher perioperative mortality and worse functional outcome compared with lobectomy. As expected, a substantial loss of dynamic lung volumes is observed in clinical practice after the operative procedure, and the degree of lung function attenuation in patients after pneumonectomy has been described to be in the range of a 30% functional loss at 5 and more years after the operation [1]. In the early days of pneumonectomy, it was thought that patients would benefit from phrenic nerve crushing or even resection because of the resulting elevation of the hemidiaphragm and thus timely obliteration of the pneumonectomy space. In addition, phrenic palsy and the subsequently elevated diaphragm were considered to have beneficial effects due to prevention of a hyperinflation of the residual lung, which was thought to be associated with worse functional results.

In the meantime, the effects of phrenic nerve discontinuation have been questioned, and some authors started debating this issue, mostly by comparing postpneumonectomy patients with preserved diaphragmatic motion to patients with phrenic nerve palsy [2, 3]. So far, no prospective study has been performed to demonstrate the direct effect of phrenic nerve injury on the immediate postoperative lung function in patients who have undergone pneumonectomy. Thus, the possible importance of ipsilateral phrenic nerve preservation and its effect on postpneumonectomy lung function still remains unclear, even after almost 80 years since the first successfully performed pneumonectomy by Graham and Singer in 1933 [4].

Therefore, our goal was to prospectively investigate this issue by evaluating the direct intraindividual effects on postoperative lung function of a temporarily iatrogenically induced ipsilateral phrenic nerve paralysis in patients after pneumonectomy.

Patients and Methods

From July 2011 to July 2012, a total of 10 patients with an indication for pneumonectomy were included in the study, if preservation of the phrenic nerve during operation was technically possible. For the lung resection, a

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Abbreviations and Acronyms

DLCOcorr = diffusing lung capacity for carbon monoxide, corrected for hemoglobin
FEV1 = forced expiratory volume in 1 second
FVC = forced vital capacity
MRI = magnetic resonance imaging

standard anterolateral thoracotomy was performed and, upon completion of the resection, a chest tube that was connected to a Heimlich valve and a bag was placed in the thoracic cavity. The chest tube was removed from all patients in the morning of the first postoperative day.

The study protocol was approved by the local ethics committee and written consent was obtained from all patients prior to study inclusion.

Induction of Phrenic Nerve Palsy

Our group has previously demonstrated the feasibility and reproducibility of a controlled induction of paralysis of the diaphragm after lung resection by paraphrenic lidocaine application [5]. The same technique was used for this study: upon completion of lung resection a standard epidural catheter (Braun Perifix; B. Braun Medical Ltd, Melsungen, Germany) was placed in the paraphrenic tissue on the pericardial surface and fixed with an absorbable suture (4-0) and externalized through a separate parasternal incision where the catheter was fixed to the skin with a nonabsorbable suture (3-0). For details see Figure 1.

After the operation, a window of 5 days was maintained to all patients for recovery. Patients were then reassessed for the absence of signs of infection (no fever, no increasing leucocyte count, and C-reactive protein level) and good pain control (visual analog scale $\leq$2, with 0 points indicating absence of pain and 10 points indicating maximum pain); intact phrenic nerve function was ascertained by sonographic evaluation. On postoperative day 6, patients were randomly allocated to sonographic assessment of ipsilateral diaphragmatic motion followed by pulmonary function testing, either with or without induction of phrenic nerve palsy. On the following day (day 7) groups were switched to obtain an evaluation of each patient with and without paralyzed hemidiaphragm (crossover design). A detailed description of the study plan is given in Figure 2.

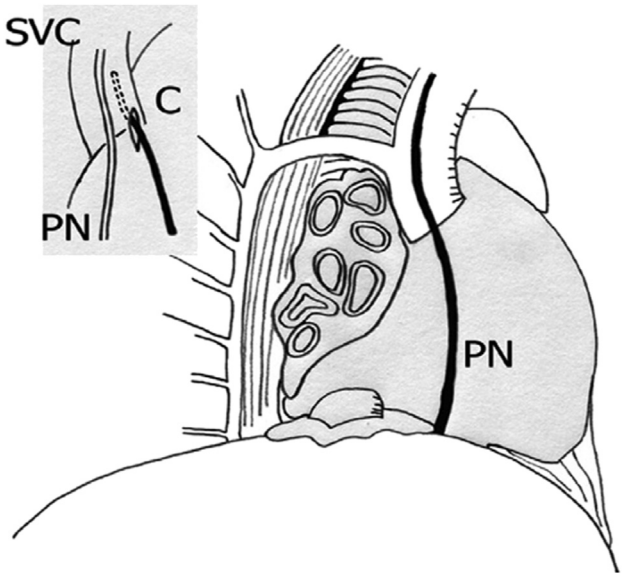

Fig 1. The epidural catheter (C) for the lidocaine administration is placed on the apical pericardial surface adjacent to the phrenic nerve (PN); SVC = superior vena cava.

For induction of phrenic nerve palsy, the previously placed catheter was connected to a perfusion system injecting a 1% lidocaine solution at a rate of 3 mL/h (30 mg/h). After 1 hour, induction of paralysis of the ipsilateral hemidiaphragm was assessed by pleural sonography, followed by spirometric assessment. Shortly after spirometry the lidocaine administration was stopped and the catheter removed. If the patient was first randomized to induction of phrenic nerve palsy, a minimum time of at least 12 hours was required before the second evaluation without phrenic nerve palsy was done. This window was chosen to guarantee a sufficient washout time for lidocaine, based on an elimination half-life of the drug of 1.5 to 2 hours and the assumption of a certain amount of drug accumulation in the pneumonectomy space during application.

Evaluation of Diaphragmatic Motion

The postoperative evaluation of diaphragmatic motion was performed by independent and blinded radiologists from the in-house department of radiology, performing a standard pleural ultrasonography (Acuson Sequoia; Siemens Medical Solution, Malvern, PA). Diaphragmatic motion was categorized into normal motion or paralyzed. Normal motion was defined as synchronous diaphragmatic motion compared with the healthy contralateral side, including slightly attenuated movement patterns. If diaphragmatic motion was absent, hardly noticeable, or paradoxical, it was categorized as paralyzed.

Pulmonary Function Testing

Dynamic lung volumes were measured preoperatively and postoperatively by spirometry (Viasys/SensorMedics, Yorba Linda, CA) performed according to European Respiratory Society recommendations [6]. All examinations were performed by independent staff members of the in-house department of pulmonology and evaluated by a blinded board-certified chest physician, who was not aware of the results of the sonographic evaluation.

During the entire study period arterial oxygen saturation levels were repeatedly measured by pulse oximetry. After lidocaine administration, measurement intervals were shortened to an hourly recording of data to assure patient safety. For comparison of oxygen saturation levels with and without phrenic nerve palsy, the values were used that were recorded at the time of pulmonary