



Differential Vascular Growth Following Left Pneumonectomy

Lucas G. Fernandez¹, Timothy D. Le Cras², Irving L. Kron¹, and Victor E. Laubach¹

¹Department of Surgery, University of Virginia Health System, Charlottesville, VA, USA

²Cincinnati Children's Hospital Medical Center, Division of Pulmonary Biology, Cincinnati, OH, USA



Background

- Following pneumonectomy (PNX), a rapid compensatory growth occurs in the remaining lung. The vascular response during this growth is not known, nor is it well understood how individual lobes of the lung respond.
- Left PNX changes the distribution of pulmonary blood flow in that the entire cardiac output is diverted to the right lung, and blood flow to the remaining lung increases by 65-70%. Increased pulmonary blood flow following PNX might modify compensatory lung growth.
- It is possible that relative changes in blood flow and lung expansion might be different among individual lobes of the remaining lung after PNX.

Hypothesis

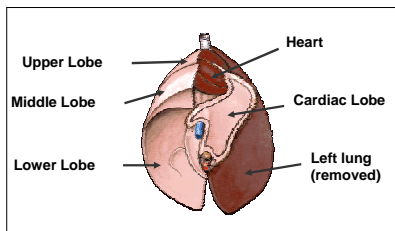
We hypothesized that vascular growth correlates with lobe growth during compensatory lung growth.

Study

The four lobes of the right lung were studied up to 21 days after PNX in the following two groups of rats (n=6/group/time):

PNX Group: Left pneumonectomy.

Sham Group: Sham left thoracotomy.

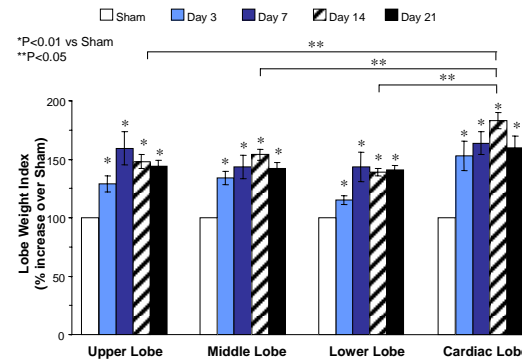


Methods

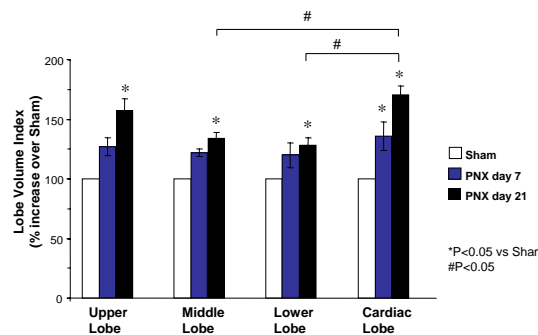
- Surgical Procedure:** Left PNX was performed through a small posterolateral thoracotomy (Kaza, AK et al. *Ann Thorac Surg* 71: 1645-1650, 2001). Animals in the sham group underwent a left thoracotomy.
- Lung and lobe weight index:** Animals were recovered for 3, 7, 14 and 21 days after surgery and the lung weight (g) of each lobe was expressed as a ratio to the final body weight of the animal.
- Lung and lobe volume index:** A second group of rats was euthanized 7 and 21 days post-PNX. The lungs were fixed by intratracheal instillation of 4% paraformaldehyde at a constant pressure of 20 cm H₂O. Following fixation, total lung volume and individual lobe volumes (ml) were measured by the volume displacement technique, and expressed as ratio to the body weight (g).
- Vascular area measurements:** Lungs were infused with a barium sulfate solution through the pulmonary artery at constant pressure (74mmHg) prior to fixation by tracheal installation of fixative. The arterial structure in the right lobes was imaged by high resolution radiography, scanned and quantitated using Imagequant software. The arterial area was indexed to body weight to derive vascular area index for each right lobe.
- Arterial density:** Lobes were paraffin embedded, sectioned and stained with H & E. Lobar arterial density was measured by counting barium-filled arteries per high-power field in 10 fields per section of each lobe.
- Relative blood flow distribution:** Up to four radiolabeled microspheres (Ce-141, Sr-85, Nb-95 or Sc-46) were injected via tail vein in 2 groups: acute (10 min after surgery, and 3, 24 and 48 hrs later) or chronic (3 hrs after surgery, and 3, 10 and 21 days later). The ratio between counts per minute (CPM) in each lobe and CPM in the whole right lung was used as an index to determine the relative distribution of blood flow between the lobes.

Results

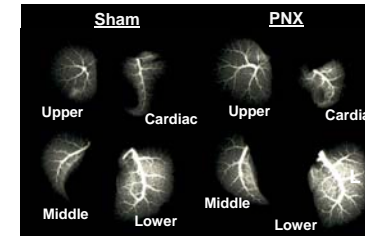
Lobe weight index increased in all lobes at 3, 7, 14 and 21 days after PNX versus Sham controls. At day 14, the cardiac lobe was significantly increased compared to the rest, but was not different at other time-points.



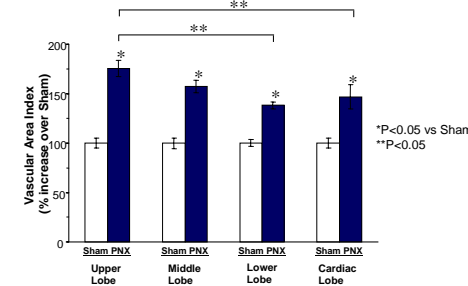
Lobe volume index was significantly increased in all lobes at 21 days after PNX and was significantly increased at day 7 only in the cardiac lobe. In addition, the cardiac lobe reached a significant increase over the middle and lower lobes.



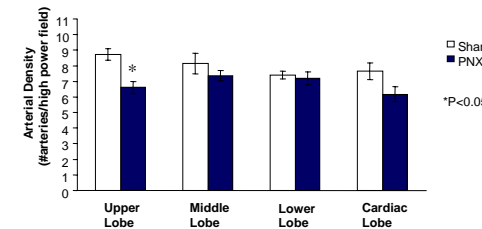
Arteriograms. Representative arteriograms of the four right lung lobes after PNX and sham surgery showed an increase in overall arterial area.



Lobe vascular area index was significantly increased in all lobes at 21 days after PNX versus sham. In addition, the upper lobe displayed a significant increase compared to lower and cardiac lobes.

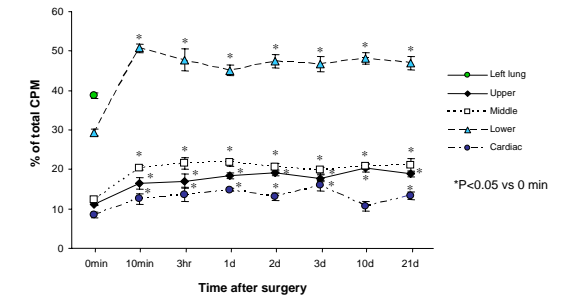


Arterial density was similar in the middle, lower and cardiac lobes between groups. However, the upper lobe showed a reduction in the arterial density after PNX compared with the sham controls.



Pulmonary blood flow.

- In unoperated animals, the right lower lobe received the highest portion of flow (30%); followed by middle (12%), upper (11%) and finally, the cardiac lobe (8%). The left lung accounted for 39% of the total pulmonary blood flow.
- After left PNX, a large increase in blood flow to the right lung was observed. The lower lobe showed the highest increase in blood flow (73%) which was followed by the middle (66%), cardiac (49%) and upper (46%) lobes, and no evidence of further change was observed for each lobe at later time-points.
- These increases in blood flow experienced by each lobe resulted in a final blood flow distribution in the lobes after 21 days: lower lobe (47%), middle lobe (21%), the upper lobe (19%) and cardiac lobe (13%). These post-PNX blood flow distributions were in very close ratio to unoperated rats, with each lobe experiencing an increase in blood flow ranging from 1.63- to 1.75-fold.



Summary

- Left-PNX induced compensatory growth in each of the four lobes of the right lung as illustrated by elevated weight and volume indices, and also vascular area indices.
- These elevations in growth and vascularization were not uniform. However, measurements of relative lobar blood flow could not explain the disproportionate changes in lobar growth.
- Further studies of the relative changes in lung ventilation and distension may help understand the disproportionate lobar growth after PNX.