



Failure of Compensatory Vasodilation Correlates with Blunted Post-Pneumonectomy Lung Growth in eNOS^{-/-} Mice



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Background

We have previously demonstrated significant impairment of compensatory lung growth following pneumonectomy in endothelial nitric oxide synthase deficient (eNOS^{-/-}) mice¹. We believe this observation may be due, in part, to the inability of the pulmonary vasculature to vasodilate and handle increased pulmonary artery volumes following pneumonectomy in these mice.

Hypothesis

eNOS is required for vasodilatory compensation following pneumonectomy, and lack of this compensation correlates with impaired compensatory lung growth in eNOS^{-/-} mice.

Methods

Animals:

C57BL6 adult male mice were used for wild-type (WT) group (n=8/group).

eNOS gene knockout mice (on C57BL6 background) were used for eNOS^{-/-} group (n=8/group).

Surgery:

Mice were anesthetized with ketamine and xylazine followed by tracheotomy and intubation, and ventilated with room air.

Left pneumonectomy was performed through a small left anterior thoracotomy. The hilum was isolated and ligated with a silk suture. The chest was closed in layers and animals were recovered under normoxic conditions.

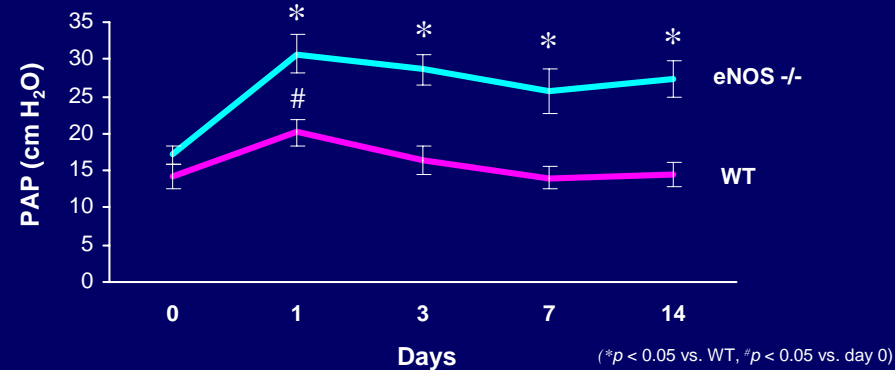
Pulmonary artery pressures were measured preoperatively (day 0) and postoperative days (POD) 1,3,7, and 14 by right ventricular cannulation.

A separate study (n=6/group) was undertaken as described above except that animals were recovered in a closed chamber with either inhaled NO (INO, 10 ppm) or room air (RA) for 7 days following pneumonectomy.

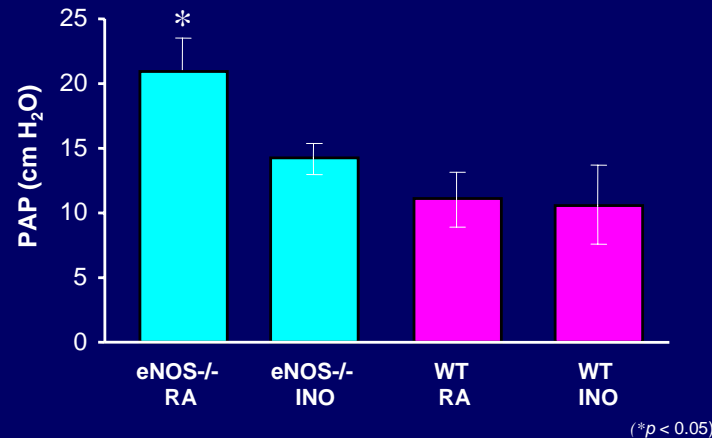
Pulmonary artery pressures of these mice were measured at POD 7.

Results

Pulmonary Artery Pressure (PAP) in WT mice was significantly elevated at POD 1, which resolved by POD 3. PAP was significantly elevated in eNOS^{-/-} mice at POD 1 versus day 0 and also versus WT at POD 1. PAP in eNOS^{-/-} mice remained significantly elevated throughout the 14 day post-pneumonectomy period without resolving.



Pulmonary Artery Pressure (PAP) 7 days after pneumonectomy with inhaled NO (INO) recovery or room air (RA) recovery. eNOS^{-/-} mice demonstrated significantly reduced PAP when recovered in INO compared to RA. No difference was observed in WT animals recovered with RA or INO.



Conclusions

- Under normal circumstances, pneumonectomy results in a transient increase in pulmonary artery and RV pressure. These pressures return to normal by POD 3.
- This compensatory vasodilation to reduce PAP fails to occur in eNOS^{-/-} mice but can be “rescued” with inhaled NO.
- This compensatory vasodilation may be an important component in post-pneumonectomy compensatory lung growth.
- Future studies will measure post-pneumonectomy compensatory lung growth in an inhaled nitric-oxide environment.

1. Leuwerke SM, Kaza AK, Tribble CG, Kron IL, Laubach VE. Inhibition of Compensatory Lung Growth in Endothelial Nitric Oxide Synthase-Deficient Mice. *Am J Physiol Lung Cell Mol Physiol* 282: L1272-8, 2002.