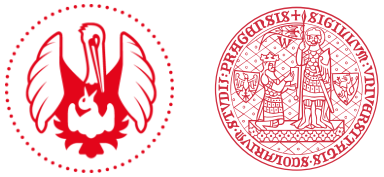
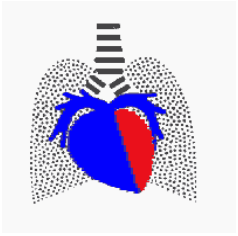
SILDENAFIL ABOLISHES PULMONARY HYPERTENSION INDUCED BY THE LEFT HEART PRESSURE OVERLOAD IN RATS

Milan **Chovanec**[1,2] Jana **Ďurišová**[1], Barbora **Kaftanová**[1], Václav Hamp[1]l and Jan **Herget**[1]

1.) Department of Physiology, Second Faculty of Medicine, Charles University, Prague, Czech Republic
2.) Department of Cardiology, Na Homolce Hospital, Prague, Czech Republic

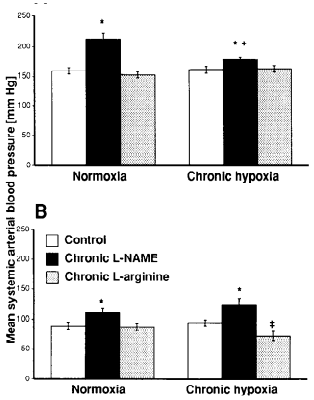




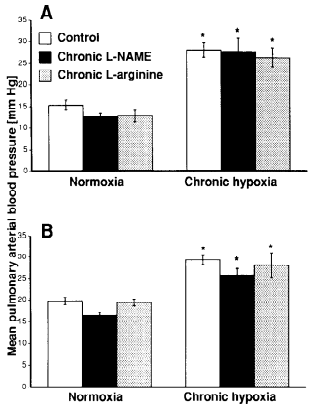
Introduction

- The most common cause of pulmonary hypertension in clinical practice are the left heart diseases.
- Unfortunately, there is no specific treatment for this group of patients.
- Nitric oxide (NO) plays important role in pulmonary circulation mainly in the development or developed pulmonary hypertension.
- New rodent model of reactive pulmonary hypertension induced by the left heart pressure overload.

NO in pulmonary circulation



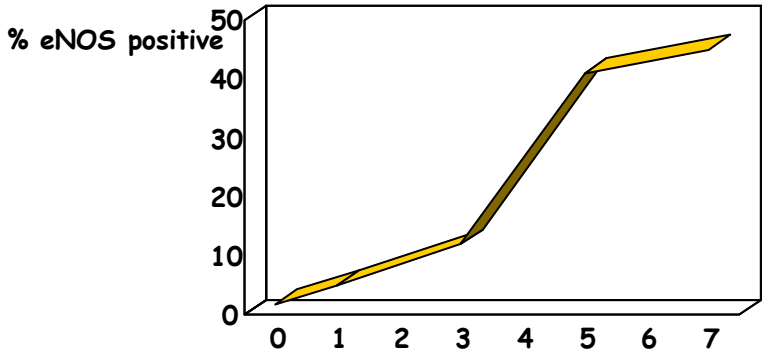
Systemic vessels



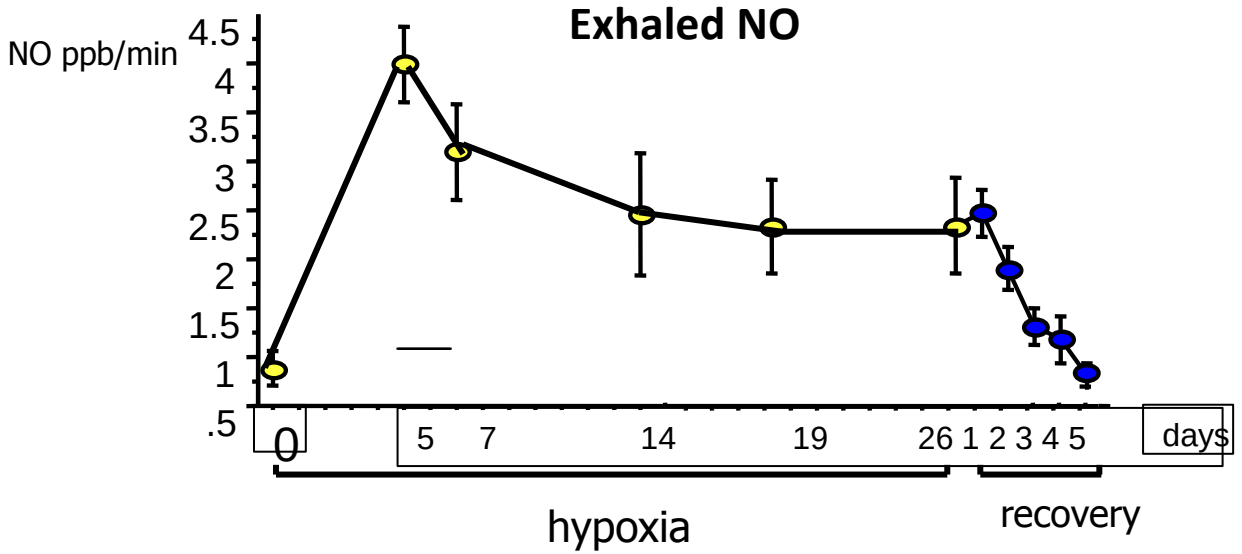
Pulmonary vessels

Hampl et al, J. Appl. Physiol., 1993

eNOS expression in the walls of pulmonary arteries

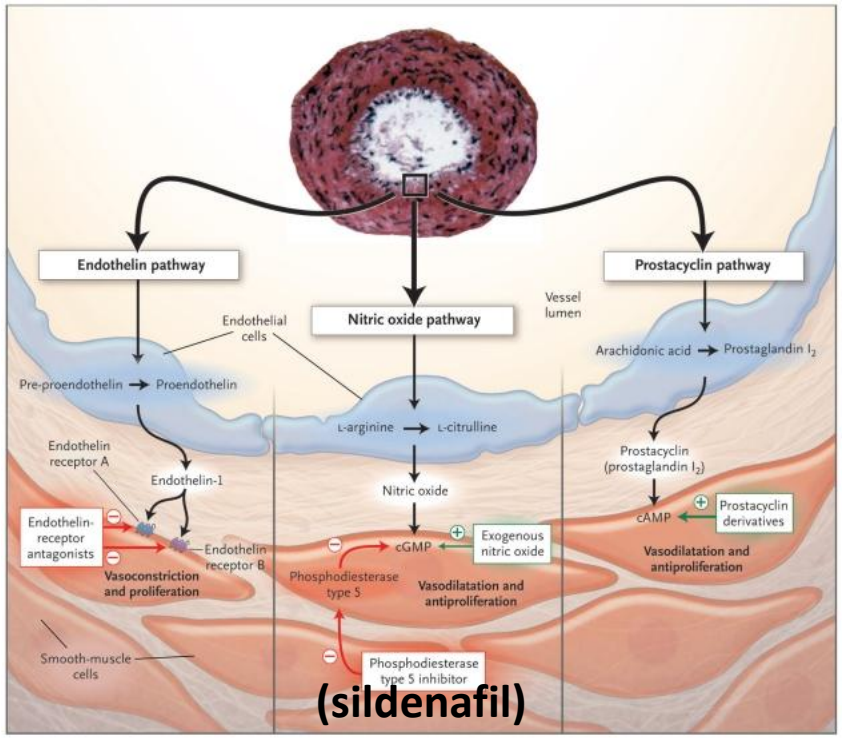


Xue et al, *Am J Physiol* 1996



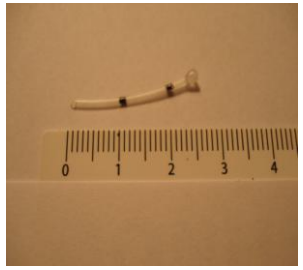
Hampl et al. AJP 2006

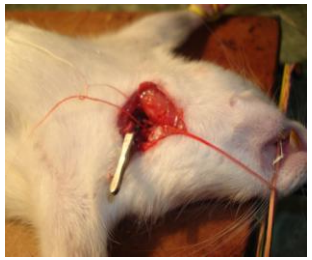
NO metabolism and the role of PDE-5 inhibition

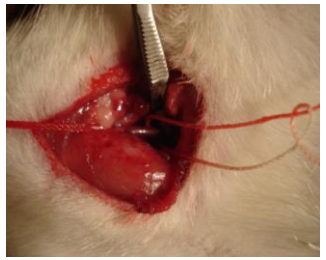


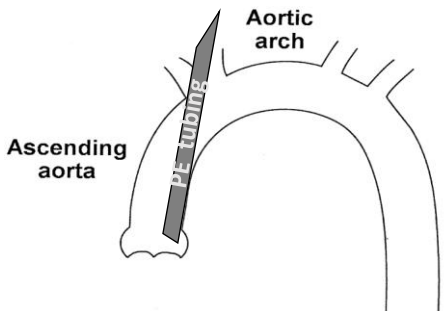
http://dx.doi.org/10.2147/DDDT.S6208

New model of reactive pulmonary hypertension

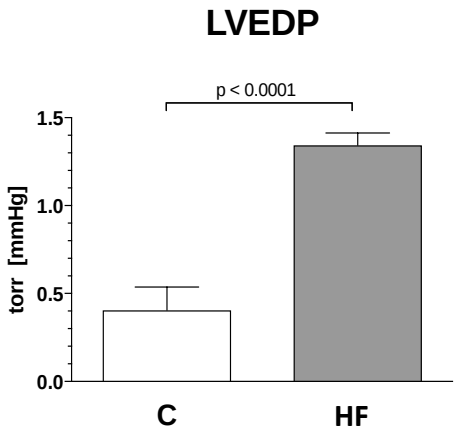


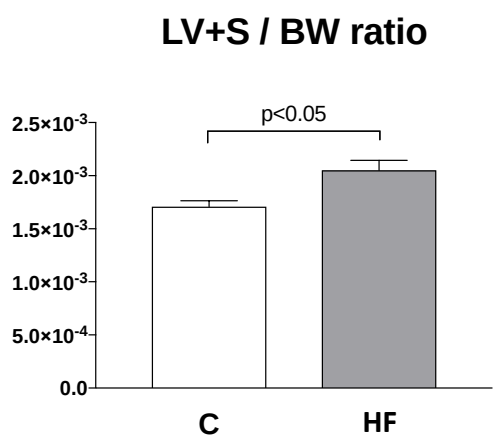




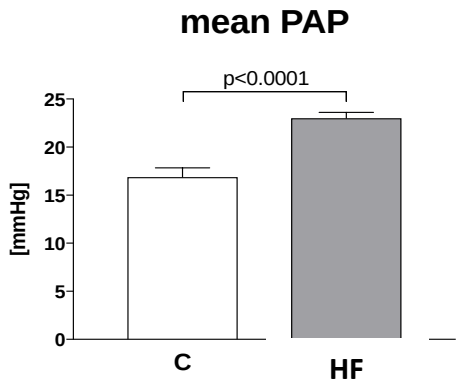


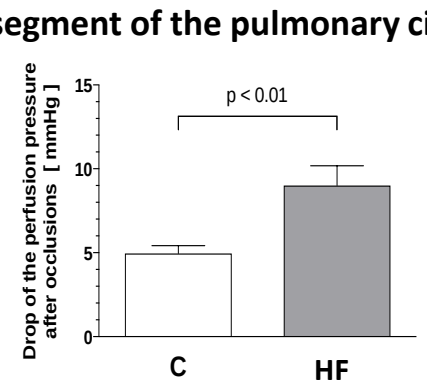
Scheme of the procedure





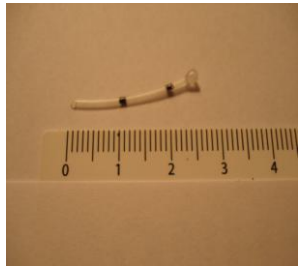
Left ventricle failure with hypertrophy after left ventricle pressure overload for 3 weeks

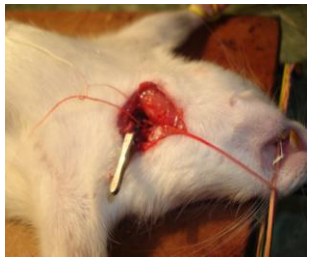


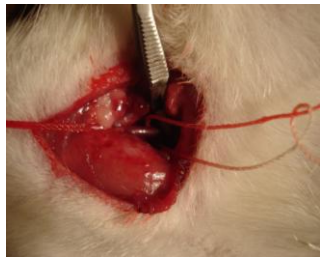


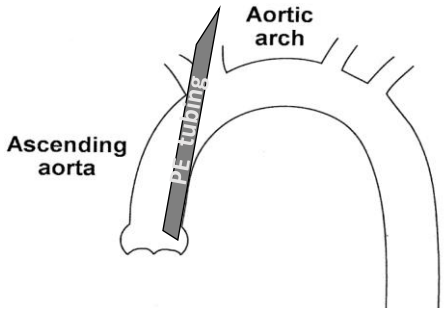
The development of pulmonary hypertension with participation of the arterial segment of the pulmonary circulation on elevated PAP after left ventricle pressure overload for 3 weeks – reactive pulmonary hypertension

New model of reactive pulmonary hypertension

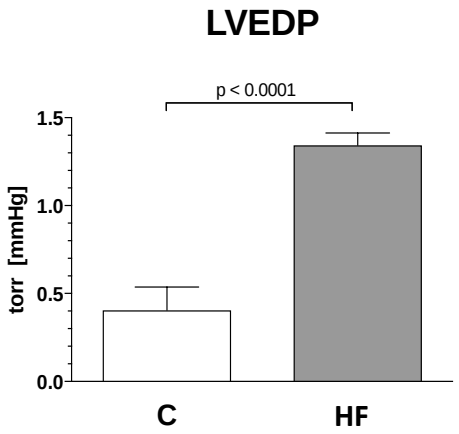


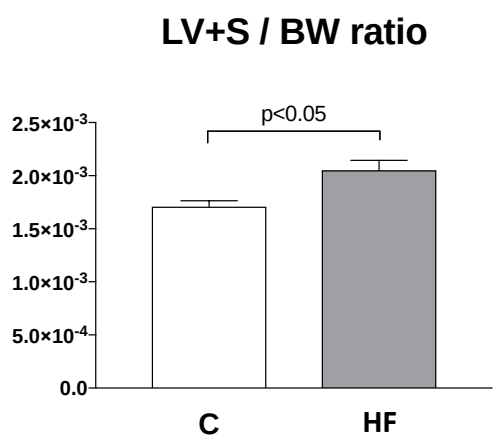




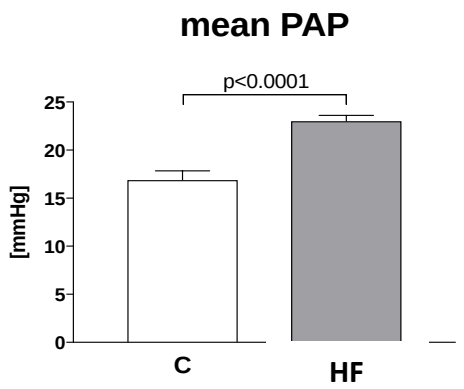


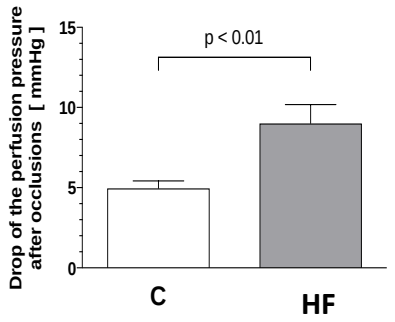
Scheme of the procedure

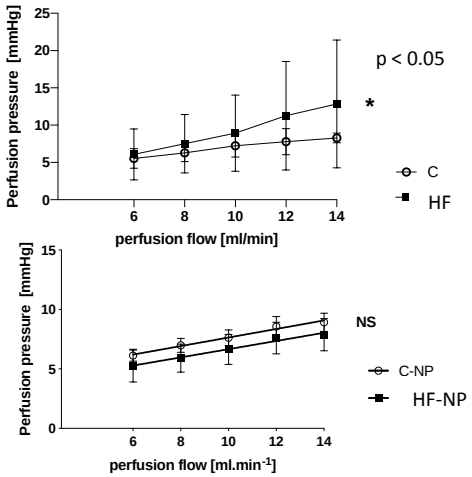




Left ventricle failure with hypertrophy after left ventricle pressure overload for 3 week







The development of pulmonary hypertension with participation of the arterial segment of the pulmonary circulation on elevated PAP after left ventricle pressure overload for 3 weeks – reactive pulmonary hypertension

Summary

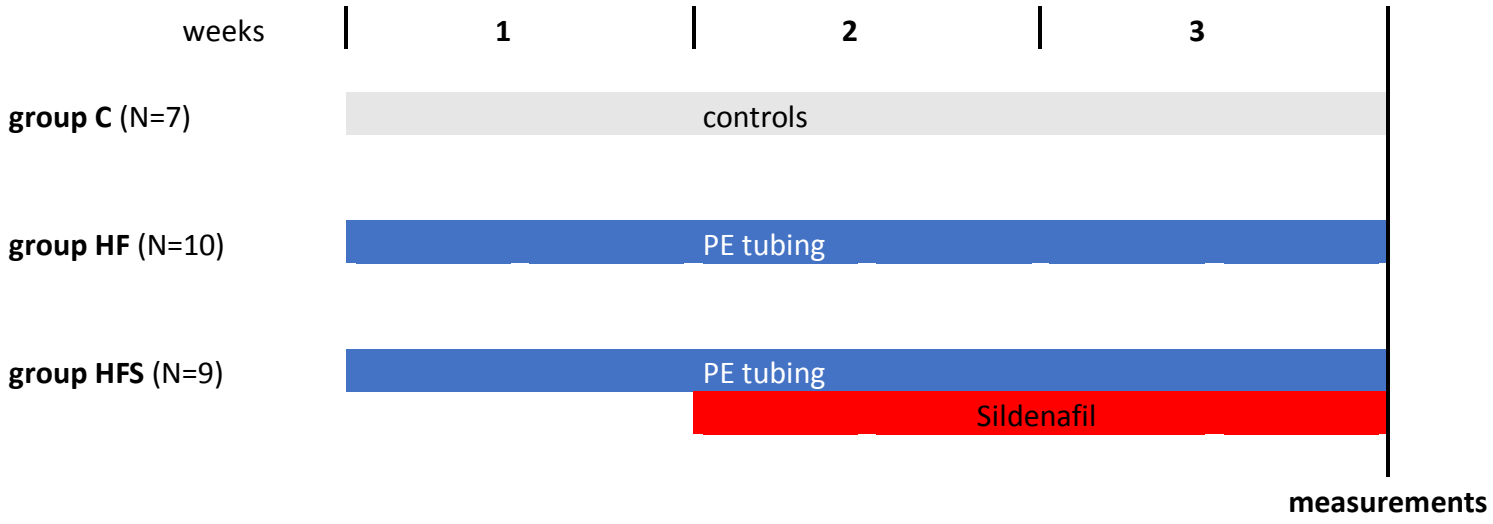
- A simple, well tolerated experimental method of inducing left heart failure by pressure overload leading to the development of reactive pulmonary hypertension

Aim

To confirm whether sildenafil can be beneficial in this type of pulmonary arterial hypertension.

Methods

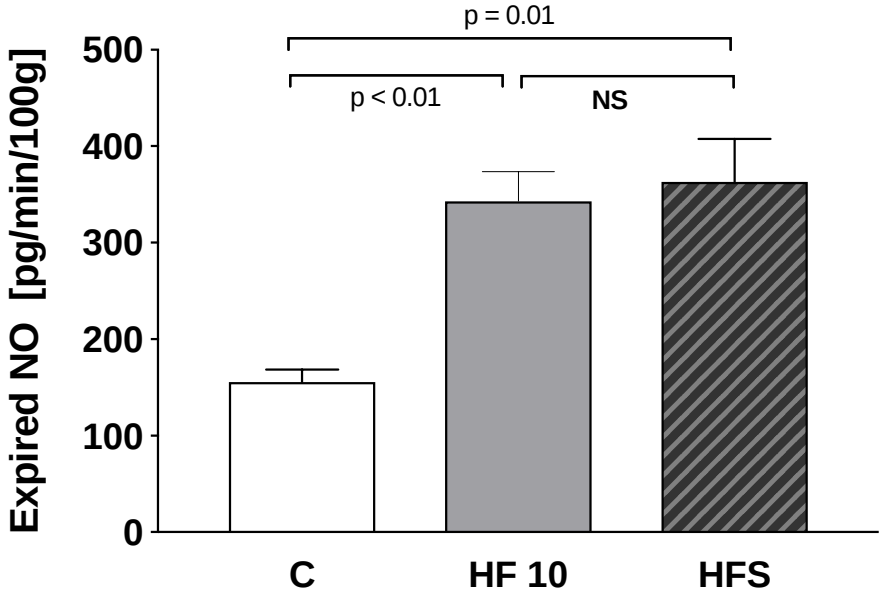
- Adult male Wistar rats
- Left heart pressure overload for 3 weeks
- **Sildenafil** (25 mg.kg^{-1} by gavage once a day) for last 2 weeks

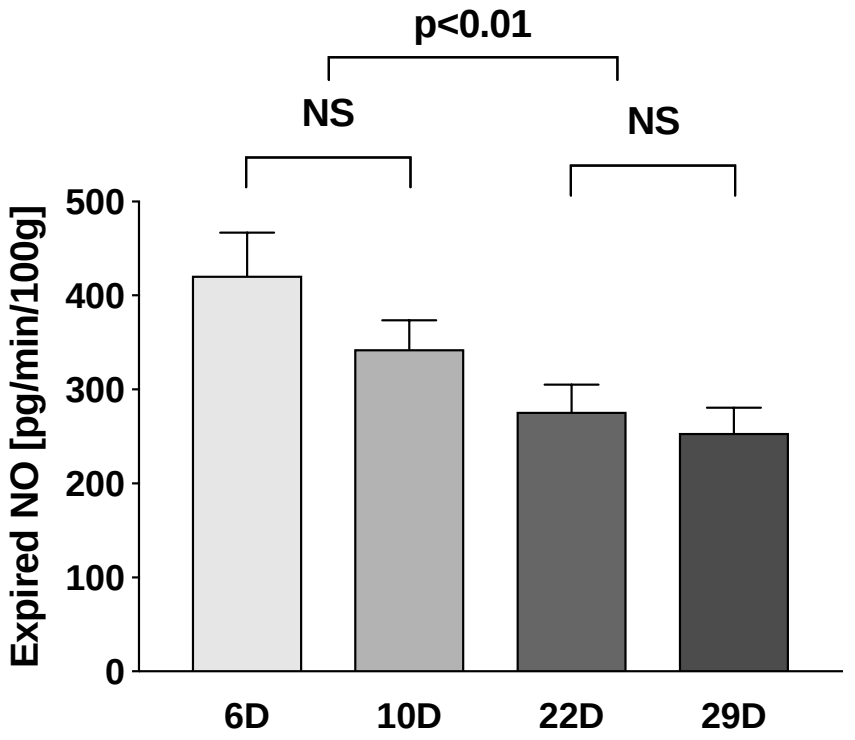


Measurements

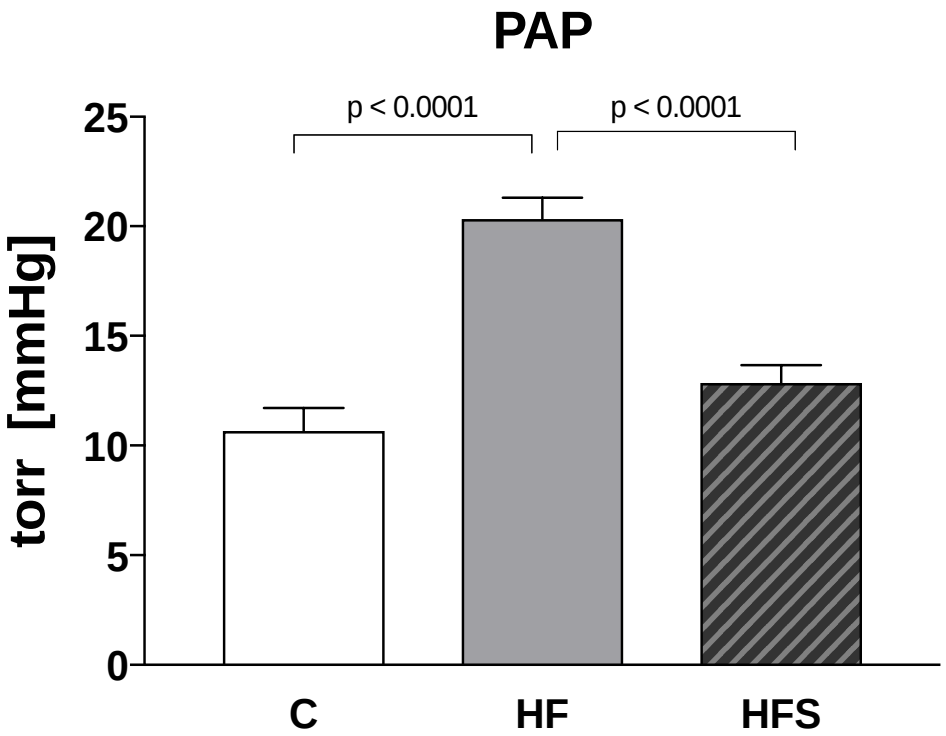
- Amount of exhaled nitric oxide, chemiluminescent method
- Mean PAP in closed-chest animals, catheterization
- Heart weights – markers of pressure overload

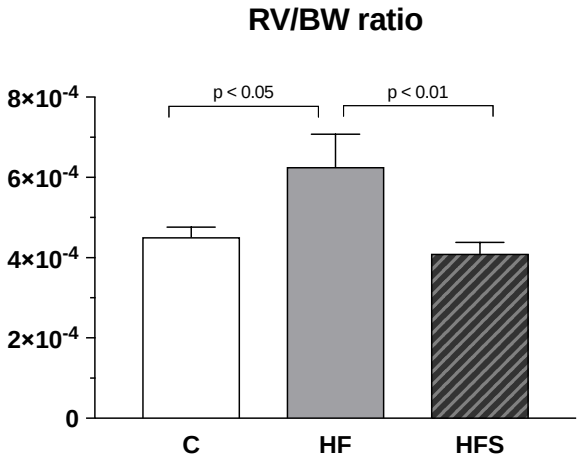
Results

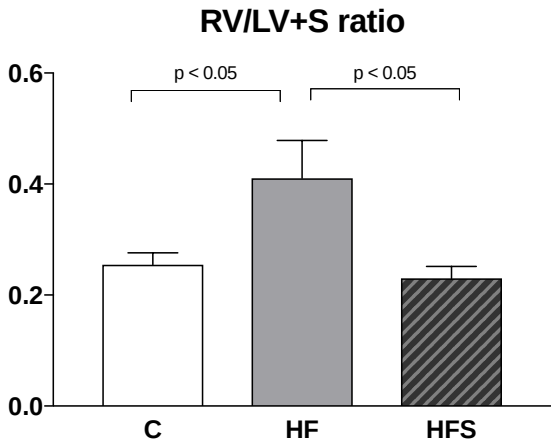

p = 0.01
p < 0.01
NS
Expired NO [pg/min/100g]
500
400
300
200
100
0
C
HF 10
HFS


p<0.01
NS
NS
Expired NO [pg/min/100g]
500
400
300
200
100
0
6D
10D
22D
29D

Results


PAP
p < 0.0001
p < 0.0001
torr [mmHg]
25
20
15
10
5
0
C
HF
HFS


RV/BW ratio
p < 0.05
p < 0.01
8×10-4
6×10-4
4×10-4
2×10-4
0
C
HF
HFS


RV/LV+S ratio
p < 0.05
p < 0.05
0.6
0.4
0.2
0.0
C
HF
HFS

Conclusion

- A simple, well tolerated experimental method of inducing left heart failure by pressure overload leading to the development of reactive pulmonary hypertension

- **Sildenafil abolishes the developed reactive pulmonary hypertension caused by the left heart pressure overload in rats.**