Objective
The aim of this study was to comprehensively study the pulmonary vasculature in baseline conditions and after maternal hyperoxygenation in growth restricted fetuses (FGR).

Methods
Prospective cohort study of singleton pregnancies including 99 FGR (defined as birthweight below 10th centile) and 110 normally grown fetuses matched with cases by gestational age at ultrasound. Fetal pulmonary vasculature was assessed at 24-37 weeks of gestation using ultrasound including main pulmonary artery and intrapulmonary artery. Ultrasound was performed in baseline conditions (women breathing room air) and repeated after the administration of oxygen 100% at a rate of 15 L/min for 10 min. Fetal Doppler waveforms were analyzed using a simplified computational model of the fetal circulation in order to estimate pulmonary vascular resistance. Unsupervised Multiple Kernel Learning was used on the pulmonary Doppler curves to find a simplified space where subjects were positioned based on waveform similarity in order to classify individuals into similarity clusters according to their displacement towards normality after maternal hyperoxygenation.

Results
FGR showed significant lower peak velocities in main (FGR mean 68.6 cm/s ± SD 12.4 vs controls 78.4 ± 22, p<0.001) and intrapulmonary arteries in baseline conditions as compared to controls. After 10 min of maternal hyperoxygenation, fetal lung Doppler traces significantly change (increase peak velocity and pulsatility indices) in FGR while not changing in controls. The computational model enabled to estimate a significant change in pulmonary vascular resistance after maternal hyperoxygenation in FGR, with no significant changes in controls (delta change FGR 0.82 ± 0.06 vs control 1.1 ±0.04, p=0.006). Machine learning identified two clusters: cluster 1 with no significant changes (where 55% of cases are FGR) and 2 with pronounced changes after maternal hyperoxygenation (where 76% of cases are FGR).

Conclusion
Pulmonary vascular reactivity to Doppler ultrasound enables to detect significant changes in pulmonary vasculature in FGR. Future studies are warranted to assess the potential clinical applicability of these measures in the diagnosis and prediction of respiratory complications in FGR.