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Title: Out of proportion PH in COPD: Report of a small case series

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Body: Recent interest has focused on the subset of COPD patients with severe pulmonary hypertension despite a mild to moderate airflow obstruction, named out of proportion (OoP) PH in COPD. Despite a lack of specific guidelines, a general consensus on a cut off of mPAP≥ 40-45 mmHg has been reached. Here we describe a case series of 11 naïve patients screened at the center for PH and lung transplant of S. Matteo Hospital, from jan 2011 to dec 2012. Overall we screened with RHC 25 COPD patients on the basis of Echocardiographic signs of PH. Among them 8 had normal hemodynamics while 19 had mPAP >25 mmHg. 11 of these pts met the following criteria: previous diagnosis of COPD, emphysema at CT without fibrosis, mPAP≥ 40 mmHg, FEV1 > 50% of predicted, thus were defined OoP-PH in COPD. All of these patients were males (mean age70 ± 6) and characterized by: history of severe hypoxemia lasting >2ys, significant decrease of DLCO (mean 27 ± 10 %) with severely impaired exercise capacity (6MWT 187 ±142mt.), despite preserved lung volumes (mean FEV1 91 ±21%). At RHC all patients had pre-capillary PH (mean PCWP 11.2 ± 2.82 mmHg, mean mPAP 48.91 ± 5,6 mmHg) with reduced cardiac index (2.08 ± 0.44 l/min/m^2). 9/11 pts were submitted to compassionate treatment with sildenafil (+ inhaled Iloprost in 3), 1 was enrolled in a clinical trial and 1 had criteria for double lung transplant and was transplanted in 2 months. After 6 month treatment no significant change in hemodynamics was found. During treatment, 2 pts manifested signs of an associated collagen disease, 3 pts died after 0.5, 10 and 11 months follow-up. In conclusion OoP- PH in COPD is a rare but severe condition that is probably still underestimated and overlooked.