1. No.
   2022Y008

2. Title
   Chronic Obstructive Pulmonary Disease (COPD) Progression Mechanisms: Testosterone Deficiency Exacerbates COPD and Comorbidity with Vascular Dysfunction

3. Period
   2022-2024

4. Summary
   [Background] Chronic obstructive pulmonary disease (COPD) is often accompanied by comorbidities such as cardiovascular disease, depression, anxiety and muscle weakness, leading to reduce the quality of life in COPD patients. Our previous study showed testosterone deficiency aggravated pulmonary emphysema in orchiectomized (ORX) mice exposed to porcine pancreatic elastase (PPE). However, it is unclear whether testosterone deficiency influences comorbidities in COPD mouse model with testosterone deficiency.
   [Methods] After the acclimatization period, C57BL6/J mice were randomly assigned to one of four groups (sham/PBS, sham/PPE, ORX/PBS and ORX/PPE). Two weeks after orchiectomy, the mice were intratracheally inhaled by porcine pancreas elastase (PPE). Open field test and Morris's water maze mask were conducted to evaluate behavioral performance. Pulmonary expressions of claudin-5, occludin and ZO1 proteins were detected using western blotting. The weights of soles and gastrocnemius muscles were measured and the mRNA expression of IGF-1, MuRF-1, claudin-5, occludin and ZO-1 in gastrocnemius muscles were analyzed by RT-PCR.
   [Results] There was no significant change of locomotor activity among each group from 14 weeks old to 26 weeks old. Morris water maze task showed that ORX mouse significantly increased escape latency compared to sham mouse at 27 weeks of age. Pulmonary expression of claudin-5 protein in ORX mice was significantly decreased compared to sham mice. In skeletal muscles, the weight of the gastrocnemius muscle of ORX mice was decreased. IGF-1 mRNA expression in the ORX/PBS group was significantly decreased compared to the sham/PBS group. The levels of claudin-5 mRNA expression in sham/PPE, ORX/PBS and ORX/PPE group were significantly lower than that of sham/PBS group.
   [Conclusions] These results suggest that decreased levels of testosterone may contribute to a decline in cognitive function, muscle atrophy and the decrease of claudin-5 expression independent of pulmonary emphysematous pathology.