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**Title:** The effect of tiotropium on lung dynamic hyperinflation and treadmill exercise capacity in mild to moderate COPD

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**Body:** RATIONALE: In previous studies tiotropium improved cycle exercise duration in GOLD II-IV COPD patients. This double-blind crossover study (NCT01072396) compared tiotropium with placebo in GOLD I and II COPD using treadmill exercise testing. METHODS: Patients were current or ex-smokers aged  $\geq 40$  y with post-bronchodilator  $FEV_1/FVC < 70\%$ ,  $FEV_1 \geq 50\%$  predicted, and dynamic hyperinflation ( $\geq 100$  mL inspiratory capacity [IC] decrease during incremental treadmill exercise). Patients received tiotropium 18  $\mu$ g qd and placebo for 6 weeks each (random order, 4-week washout). Patients performed constant work rate treadmill exercise at 80% of peak incremental test work rate before and after each treatment period. The primary endpoint was the difference in exercise isotime IC change from baseline to Week 6 between tiotropium and placebo. Secondary endpoints included change in exercise duration. RESULTS: Patients (n=126, 52% male) had mean age 61 y, post-bronchodilator  $FEV_1/FVC$  59% and  $FEV_1$  77% predicted. Baseline IC was 2.27 L and exercise duration 447 s. The difference in change in isotime IC from baseline to Week 6 between tiotropium and placebo was statistically significant (65 mL,  $P=0.009$ ). The difference in change from baseline in exercise duration between tiotropium and placebo was not significant in the combined GOLD I+II (29.3 s,  $P=0.109$ ) and GOLD I (-23.5 s,  $P=0.415$ ) groups, but was statistically significant for GOLD II (63.0 s,  $P=0.007$ ). CONCLUSIONS: Tiotropium was associated with reduced lung hyperinflation at rest and during exercise in GOLD I and II COPD patients. Significantly improved exercise duration was observed in GOLD II patients but not the combined or GOLD I groups.