Title: Reduction of peak oxygen consumption in patients with non-small cell lung cancer treated with neoadjuvant chemotherapy

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Body: Background Fitness is best assessed with cardiopulmonary exercise testing (CPET) in patients with non-small cell lung cancer (NSCLC) eligible for lung resection surgery. Peak oxygen consumption (VO2 peak) is predictive of short-term complications after elective thoracic surgery. Anti-neoplastic drugs have toxic effects on cellular metabolism and therefore on VO2 peak. Effect of neoadjuvant chemotherapy on cardiopulmonary fitness has received little attention. Method We compared CPET results in patients with (n=12) or without (n=89) neoadjuvant chemotherapy before elective surgery for NSCLC. We performed linear regression to compare CPET results in patients with or without neoadjuvant chemotherapy with adjustment for anthropomorphic variables and comorbidities. Results Overall, VO2 was low in both groups (VO2 peak 1424 ml/min, SD 444 ml/min; 20.3 ml/min/kg, SD 5.7). After adjustment for age, sex, height, weight, hematocrit, FEV1% and comorbid conditions, peak VO2 was lower in patients with neoadjuvant chemotherapy (-290 ml/min/kg [CI95% -509; -70] p=0.010). Adjusted peak VO2/kg was reduced by 23% (-4.7 ml/min/kg [CI95% -8.0; -1.3]) compared to patients without chemotherapy. Heart rate VEO2 and VECO2 at anaerobic threshold were similar. Conclusion Pre-operative oxygen consumption was markedly reduced in NSCLC patients with neoadjuvant chemotherapy after adjustment for confounders. CPET pattern might be explained by a complex toxic effect of anti-neoplastic drugs on lung interstitium, muscle metabolism and heart function. Because of low VO2 peak, patients with neoadjuvant chemotherapy may thus be at risk of being denied surgery.