**Longitudinal analysis of exercise performance in patients after TOF repair**

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**Introduction:** With the increase in survival of Tetralogy of Fallot patients (TOF), treatment strategies may shift their focus from preventing mortality towards improvement of quality of life. A diagnostic tool to early recognize deterioration is the cardiopulmonary exercise test (CPET). Serial CPETs in these patients have been an emerging strategy for therapeutic interventions and monitoring their health status. The purpose of this study is to show the change in exercise performance over time in TOF patients.

**Methods:** This retrospective cohort study included all TOF patients followed in the German Heart Center of Munich, who underwent a CPET between September 2001 and June 2015. CPETs were included when the respiratory exchange ratio was above 1.00. There were no restrictions concerning the interval between the CPETs. Predictive values were calculated based on Bongers 2014 for children, extrapolated to the age of 25, and Gläser 2010 for adults. The main outcome was peak oxygen uptake as percentage of predicted (peak VO2). Statistical analyses were based on time-dependent growth models.

**Results:** A total of 1133 CPETs were included, corresponding to 451 individual patients. Serial testing of at least 3 follow-up moments was completed in 178 patients. The average age at the first visit was 25.7 ± 11.5, ranging from 6.4 to 63.8 years of age. The interval between CPETs varied from 1 day to 135 months. The peak VO2 at the first visit was 27.7 ± 8.6 ml/min/kg, corresponding to 74 ± 19 %.

The time-dependent growth model showed a decrease in peak VO2 predicted early in the 2nd decade and an upsloping pattern towards 40 years-of-age (Graph A). This might be in part an effect of the increase of the reference values during puberty, that was not observed in patients with TOF (Graph B). The second decline in exercise performance might be a supra-physiological decline while aging.

**Conclusions:** These results of serial CPETs in a large cohort of patients with repaired TOF show a pattern of continuous deterioration, whereas the reference population is increasing their exercise capacity during adolescence. Further analyses are warranted to identify modifiers of exercise performance such as interventions, medication use, and comorbidities.

![Graph A: Exercise capacity over time in 451 individual patients with 1133 measurements expressed as percentage of predicted (A) and as oxygen uptake indexed for body weight (B).](image)