UNIVERSITÀ DEGLI STUDI DI PADOVA

SISMES
SOCIETÀ ITALIANA DELLE SCIENZE MOTORIE E SPORTIVE

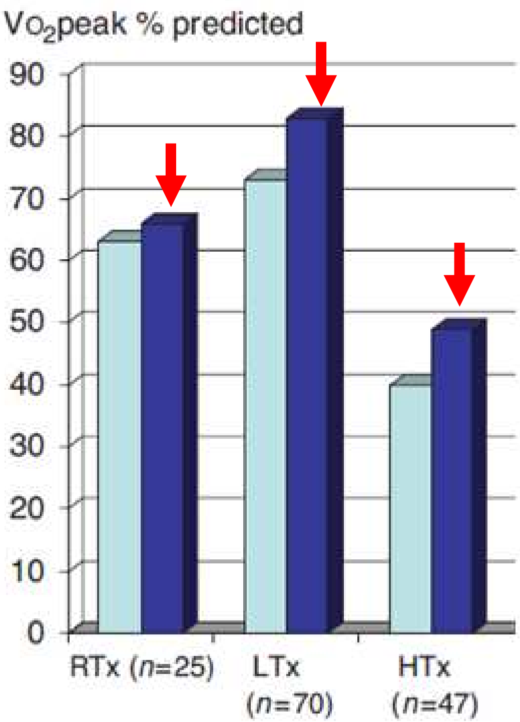
# The effect of endurance training on pulmonary $\dot{V}O_2$ kinetics in solid organs transplanted recipients

del Torto; A, Capelli; C, Peressutti, R; Di Silvestre, A; Livi, U;

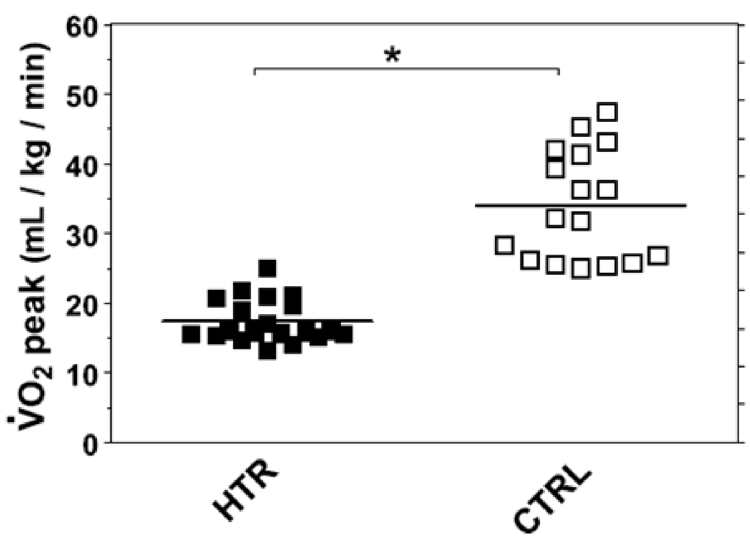
Nalli, C; Sponga, S; Amici, G; Baccarani, U; Lazzer, S

*School of Sport Sciences, University of Udine, Udine, Italy; Department of Biomedical Sciences, University of Padova, Padova, Italy*

# Heart, kidney, and liver transplant recipients (HTx, KTx, and LTx, respectively) suffer from an impaired cardiorespiratory fitness.




William and McKenna, 2012




Lanfranconi et al., 2006

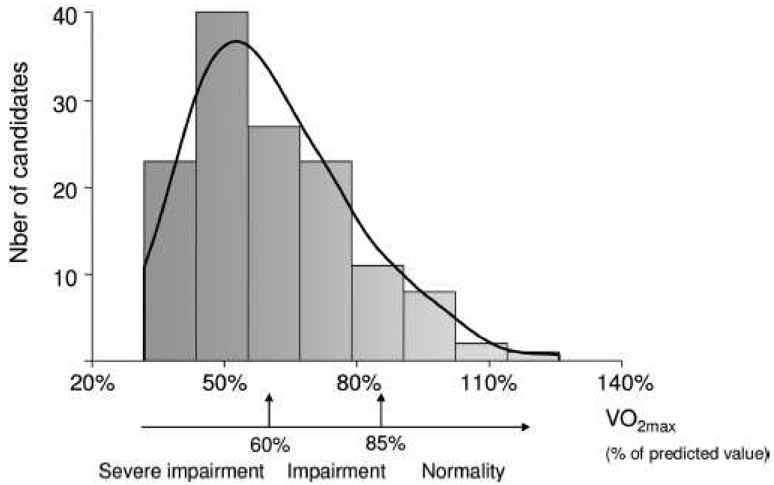
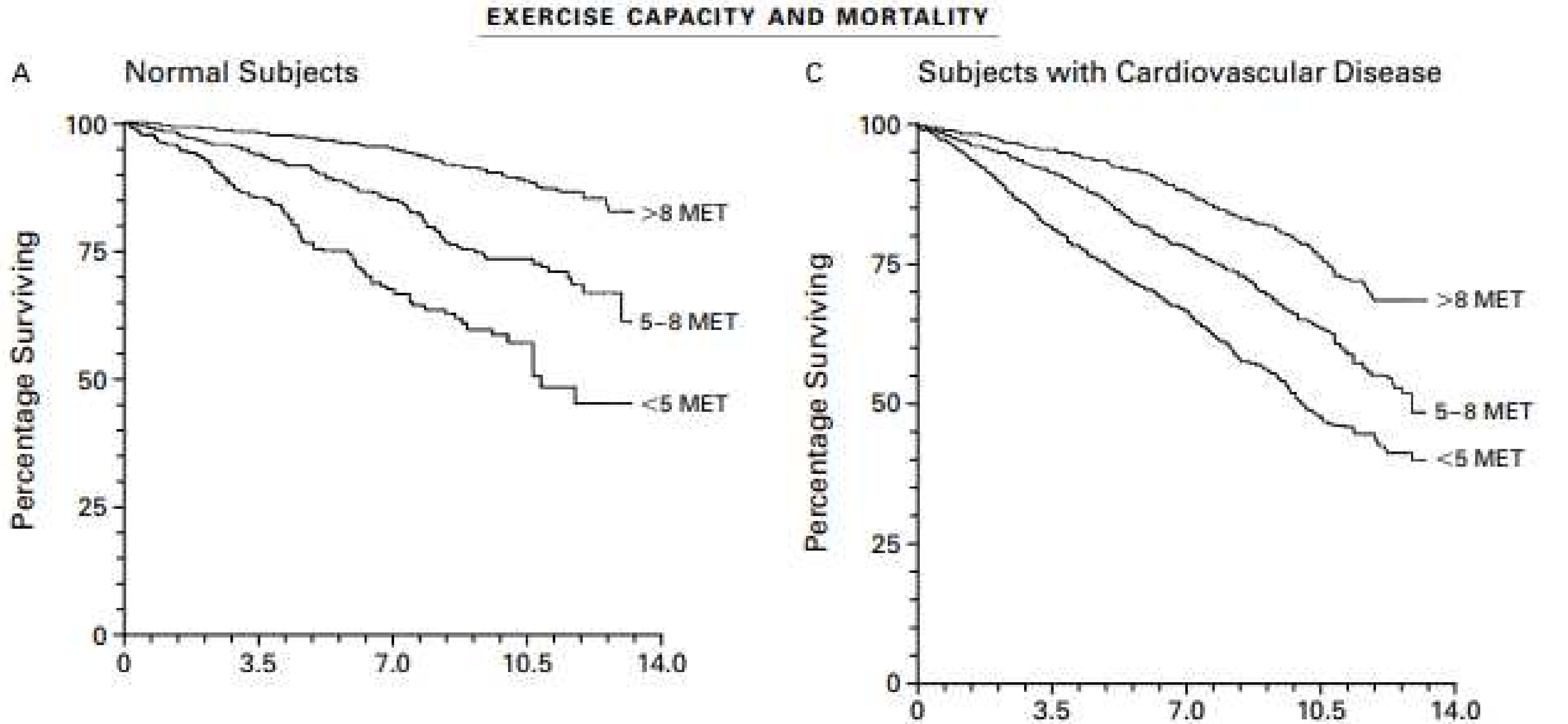



**FIGURE 1.** Distribution of peak $VO_2$ within the study population (n=135). Peak $VO_2$, expressed as percentage of predicted value, was normal (≥85%) in only 11.9% of cases and impaired in 88.1% of cases. Impairment was severe (<60%) in 54% of cases.

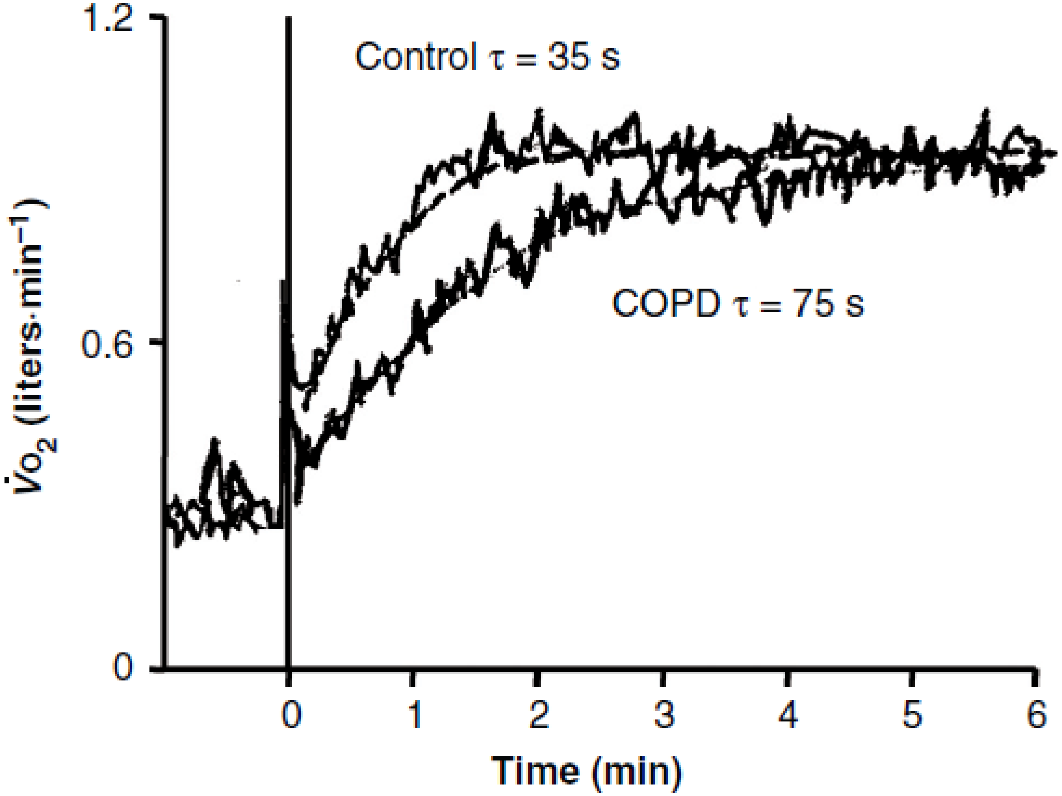
Dharanc et al., 2008

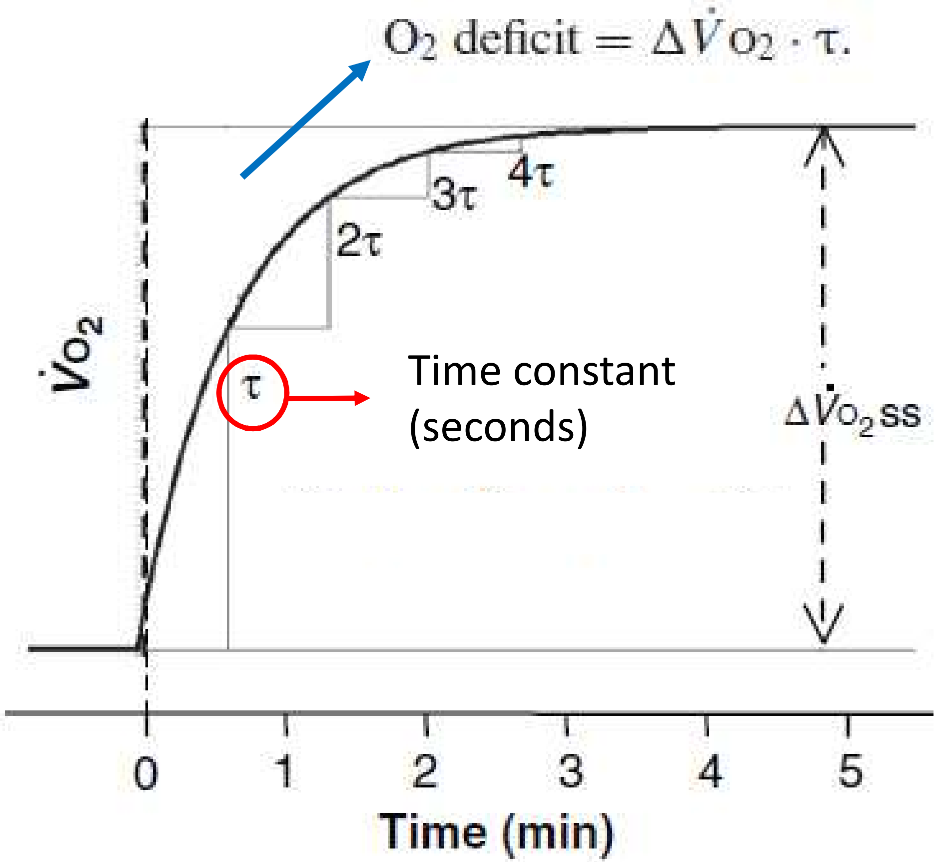
# Poor maximal exercise capacity predicts mortality




Myers et al., 2002

- Heart, kidney, and liver transplant recipients suffer from impaired (slow) $\dot{V}O_2$ kinetics
- Slow $\dot{V}O_2$ kinetics and greater $O_2$deficit, at a given workload, are a marker of poor exercise tolerance (Grassi et al., 2011)



# Prognostic value of assessing the $\dot{V}O_2$ kinetics

Canadian Journal of Cardiology
Volume 31, Issue 10, October 2015, Pages 1259-1265

Prognostic Value of Oxygen Kinetics During Recovery From Cardiopulmonary Exercise Testing in Patients With Chronic Heart Failure

› Am J Cardiol. 1999 Sep 15;84(6):741-4, A9. doi: 10.1016/s0002-9149(99)00426-9.

**Prognostic significance of oxygen uptake kinetics during low level exercise in patients with heart failure**

CHEST®
Volume 124, Issue 2, August 2003, Pages 580-586

Prolonged Oxygen Uptake Kinetics During Low-Intensity Exercise Are Related to Poor Prognosis in Patients With Mild-to-Moderate Congestive Heart Failure *

Healthy subjects (at sea level) during dynamic exercise with large muscle mass

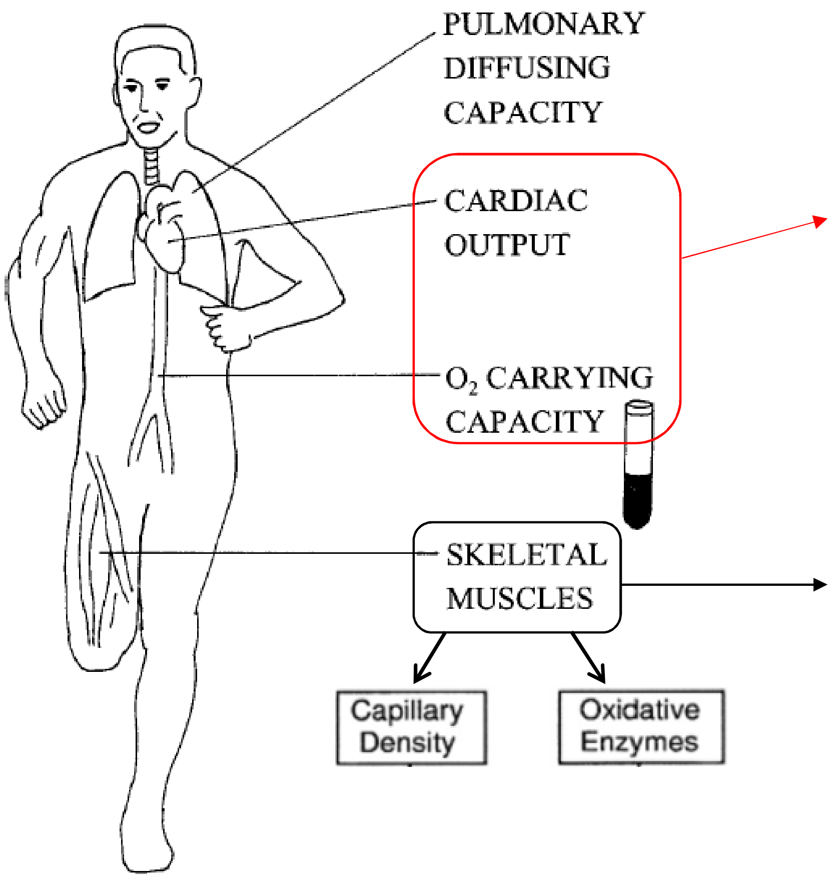
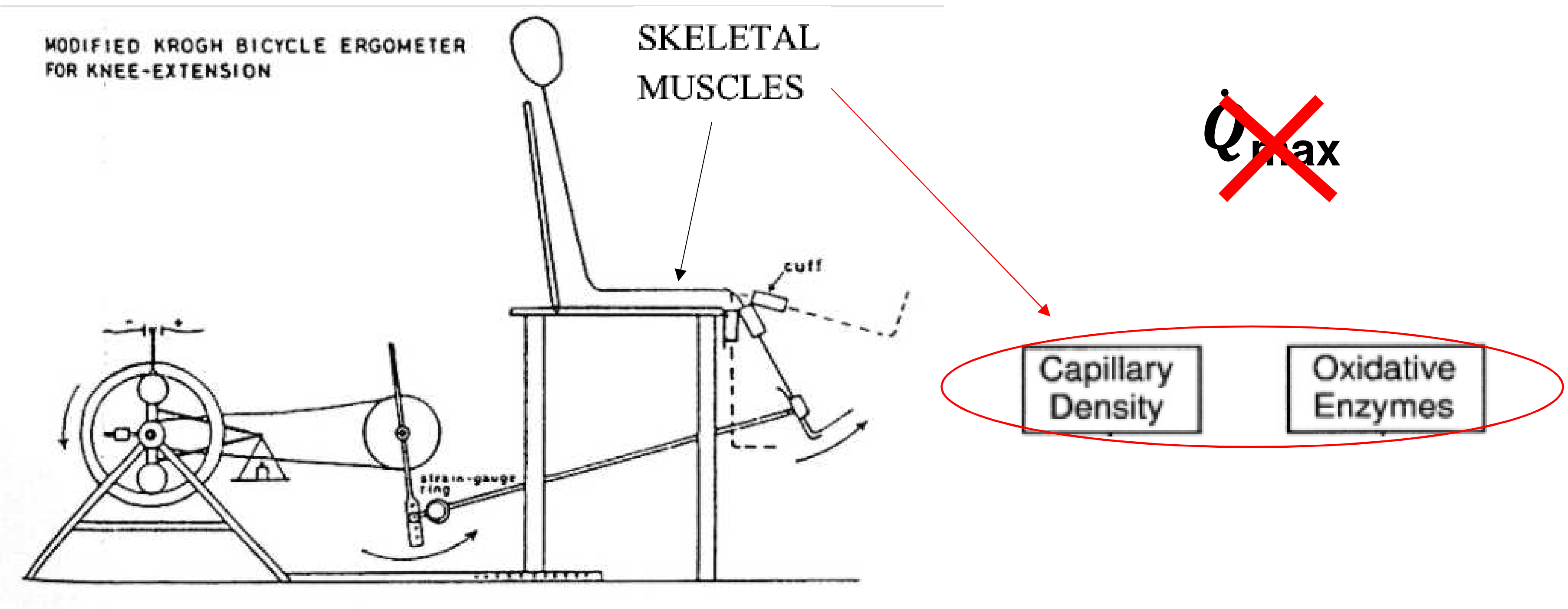



Figure 4—Physiological factors that potentially limit maximum oxygen uptake ($\dot{V}O_{2max}$) in the exercising human.

- $\dot{V}O_{2max}$ is mainly limited by the maximal $O_2$ delivery ($\dot{Q}_aO_{2max}$)
- 75% of the total fractional limitation of $\dot{V}O_{2max}$
- The peripheral factors account for the remaining part (~ 25%)

(di Prampero and Ferretti, 1990; Basset and Howley et al., 2000)

Healthy subjects (at sea level) during dynamic exercise with small muscle mass



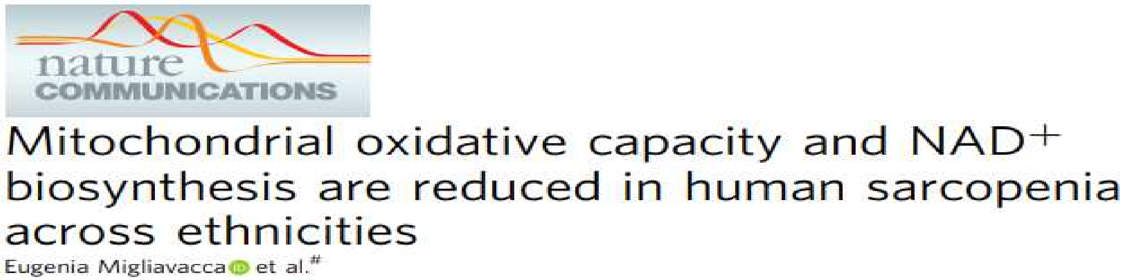

Muscle $\dot{V}O_2$ is limited by the peripheral factors (i.e. muscle oxidative capacity and capillary density)

(Saltin B, 1985; Am J Cardiol)

Transplanted recipients make a **long-life use of immunosuppressive drugs** and usually are deconditioned and inactive.

Immunosuppressive drugs and disuse/deconditioning affect skeletal muscles (Hokanson et al., 1995; Mercier et al., 1995; Ferretti *et al.*, 1997; Capelli *et al.*, 2006):

- **Oxidative enzymes defects** (Braith et al., 2005; Kempeneers et al., 1990)
- **Reduced capillary density** and endothelial dysfunction (Herman et al., 2011; Lampert et al., 1998)
- **Sarcopenia** (Kallwitz, 2015), recently linked to oxidative enzymes defects (Migliavacca et al., 2019)

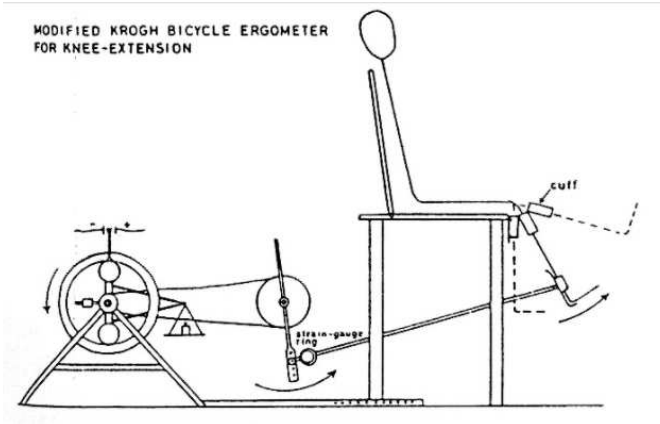

nature COMMUNICATIONS

Mitochondrial oxidative capacity and NAD+ biosynthesis are reduced in human sarcopenia across ethnicities

Eugenia Migliavacca et al.#

Peripheral $O_2$ delivery and $O_2$ utilization are both impaired

- **Small muscle mass endurance training:** greater adaptations of the factors responsible for the peripheral gas exchanges when compared to large muscle mass endurance training (i.e. double leg cycling).
- **Transplanted recipients:** muscular abnormalities affecting peripheral gas exchanges are commonly present.


**VS**

**Is small muscle mass endurance training more effective then large muscle mass endurance training to improve exercise capacity in solid organ transplanted patients?**

(Abbiss et al., 2011; Klausen et al., 1981; Braith et al, 2000; Rud et al., 2012; Esposito et al, 2010)

Solid organ transplanted recipients (n = 38), 5 drop outs (n = 33).

Participant were 13 HTx, 9 LTx, 11 KTx

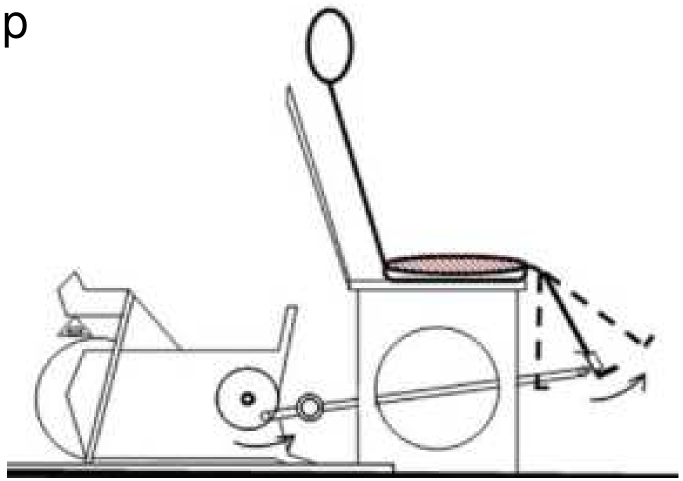
Double leg training group

($DL\text{-}ET_{GRP}$; n = 16):

7 heart,

4 liver,

5 kindey



Single leg training group

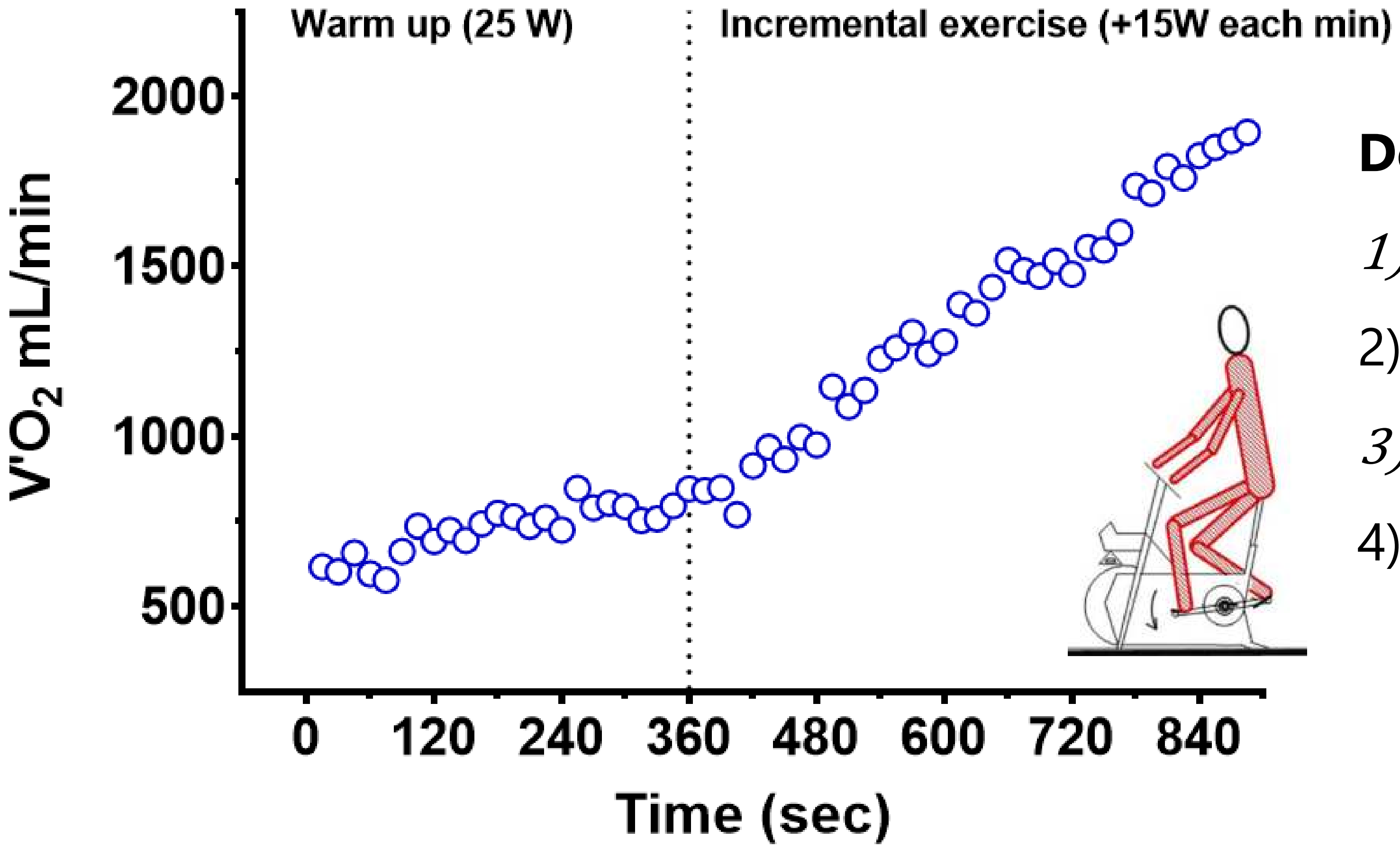
($SL\text{-}ET_{GRP}$; n = 17):

6 heart

5 liver

6 kideny

# Testing phase: day 1

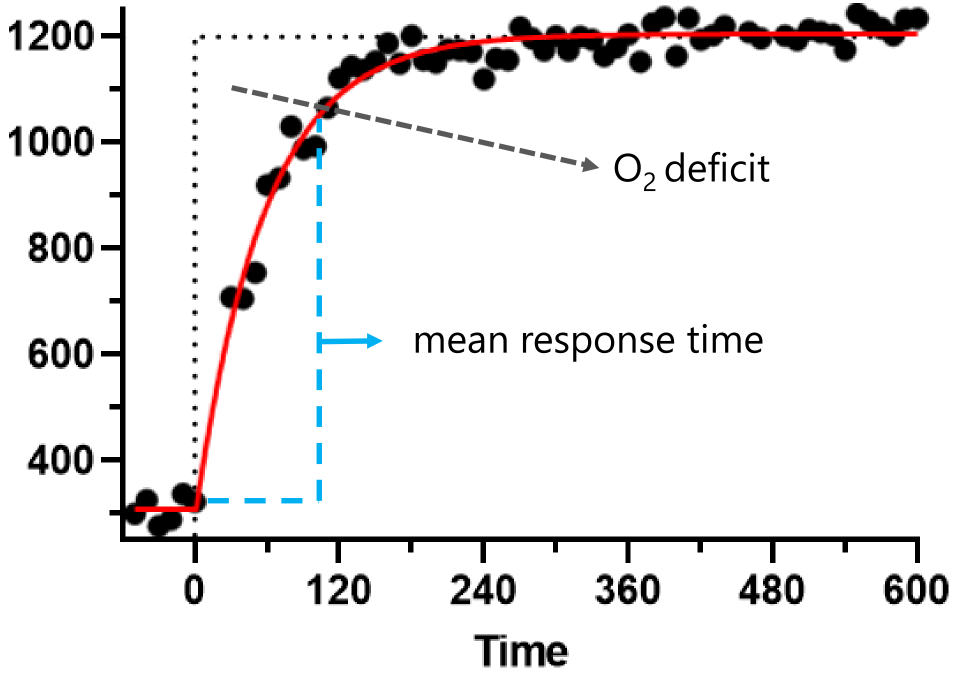



**Determined parameters:**

1) $\dot{V}O_2$max
2) Gas exchange threshold
3) $\dot{Q}$max
4) Hemoglobin

# Testing phase: day 2

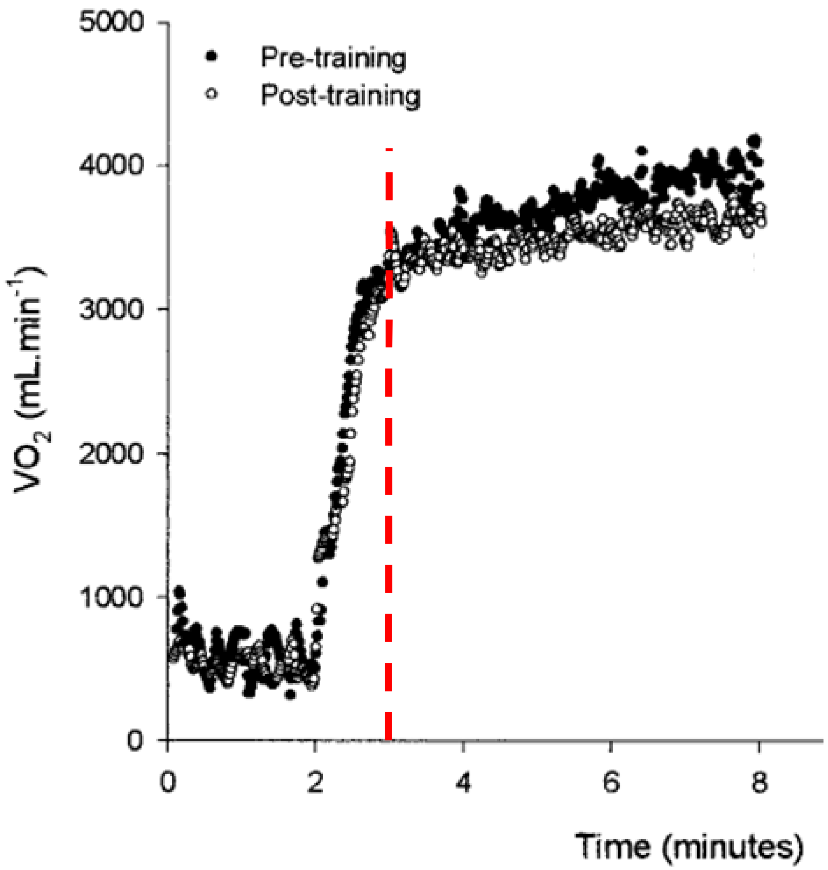
**Moderate** intensity constant load exercise




- **$O_2$ deficit ($O_2$Def)**
- **Mean response time (MRT)**
- **HR kinetics**

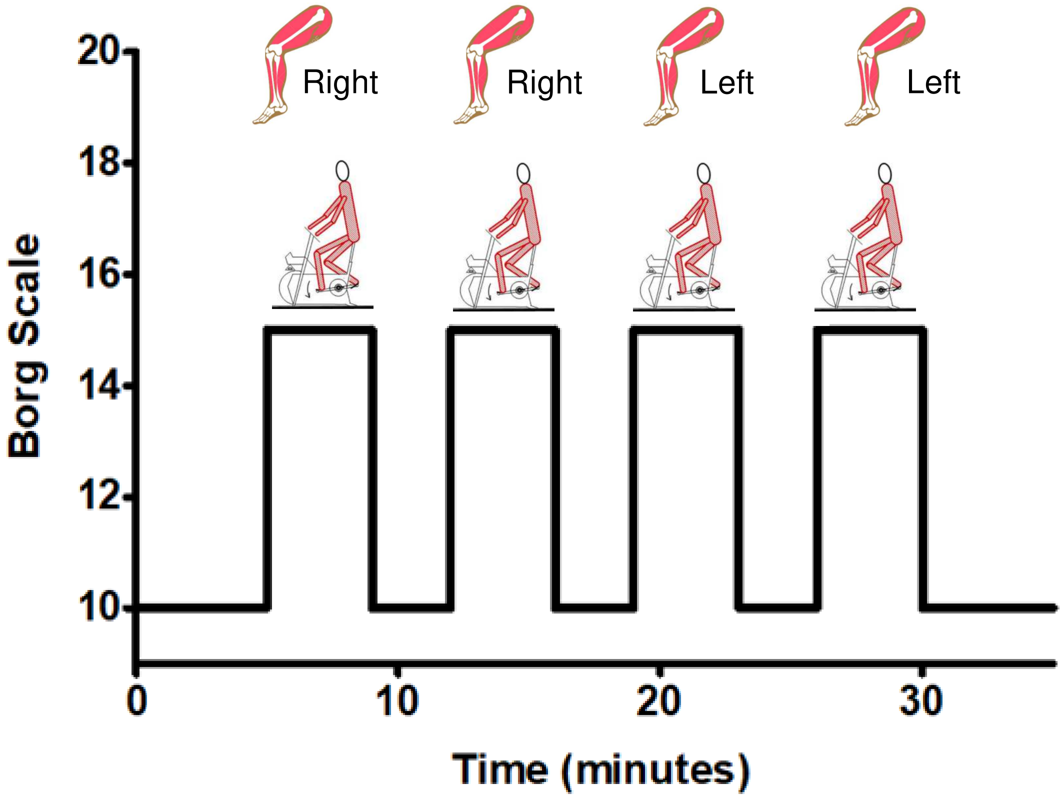
# Testing phase: day 3

Moderate + **Heavy** intensity constant load




- **Indexes of $\dot{V}O_2$ slow component**

# Endurance training: 3 **supervised** sessions per 8 weeks




- *Warm up:*

  5-10 min of light pedaling
- ***Main sets:***

  4x (4min at high intensity + 3min of active recovery)
- *Cool down:*

  5 min of light pedaling

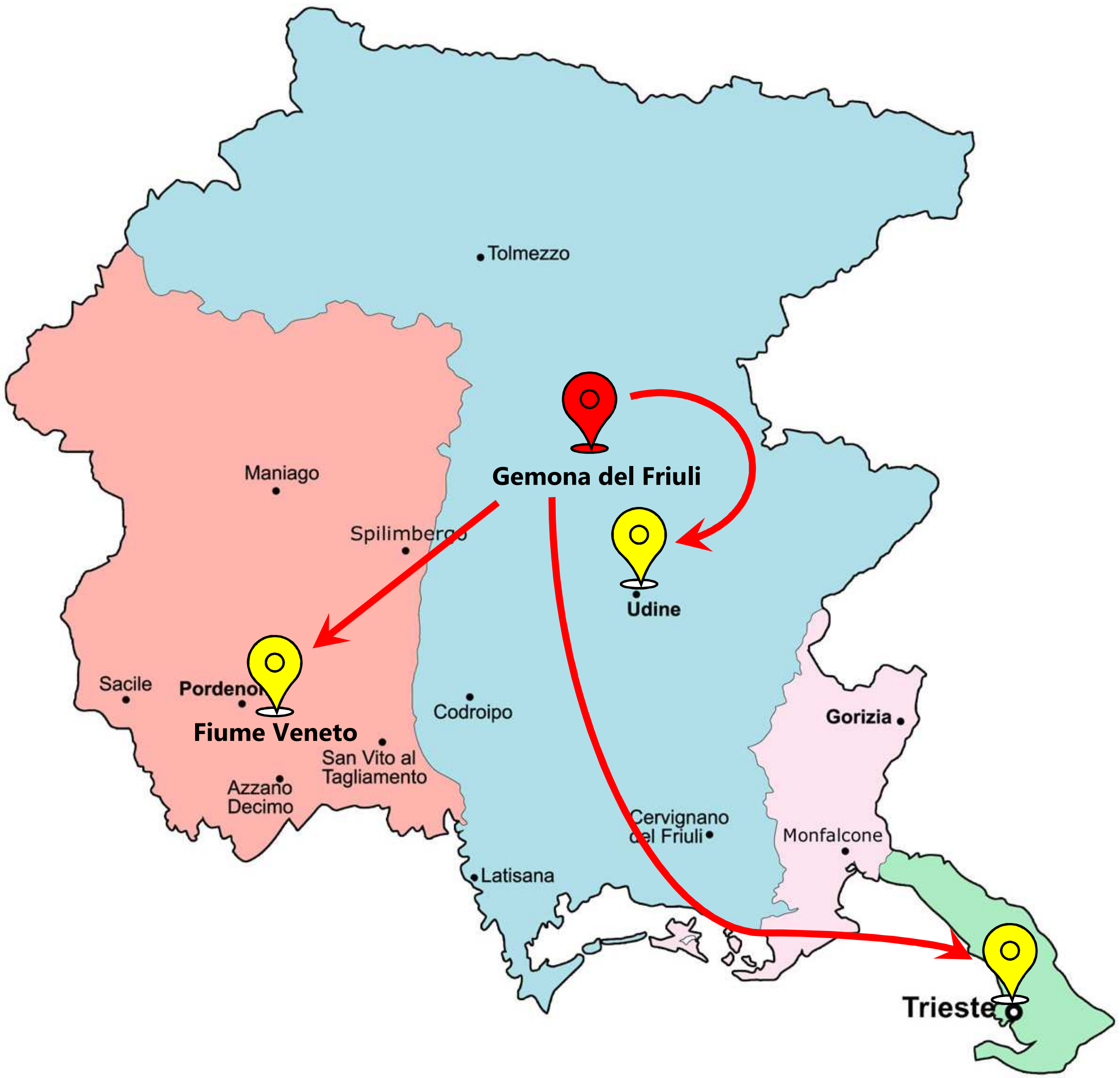
High intensity intervals had to elicit a value of the Borg's scale = or > than 15 for the DL-$ET_{GRP}$ and = or >than 5 for the SL-$ET_{GRP}$

(Buchheit & Laursen, 2013; Ciolac et al., 2015; Gordon et al., 2019, Arney et al., 2019)


Example of single leg cycling

(do not try at home…)

# The net behind the project…




Headquarters

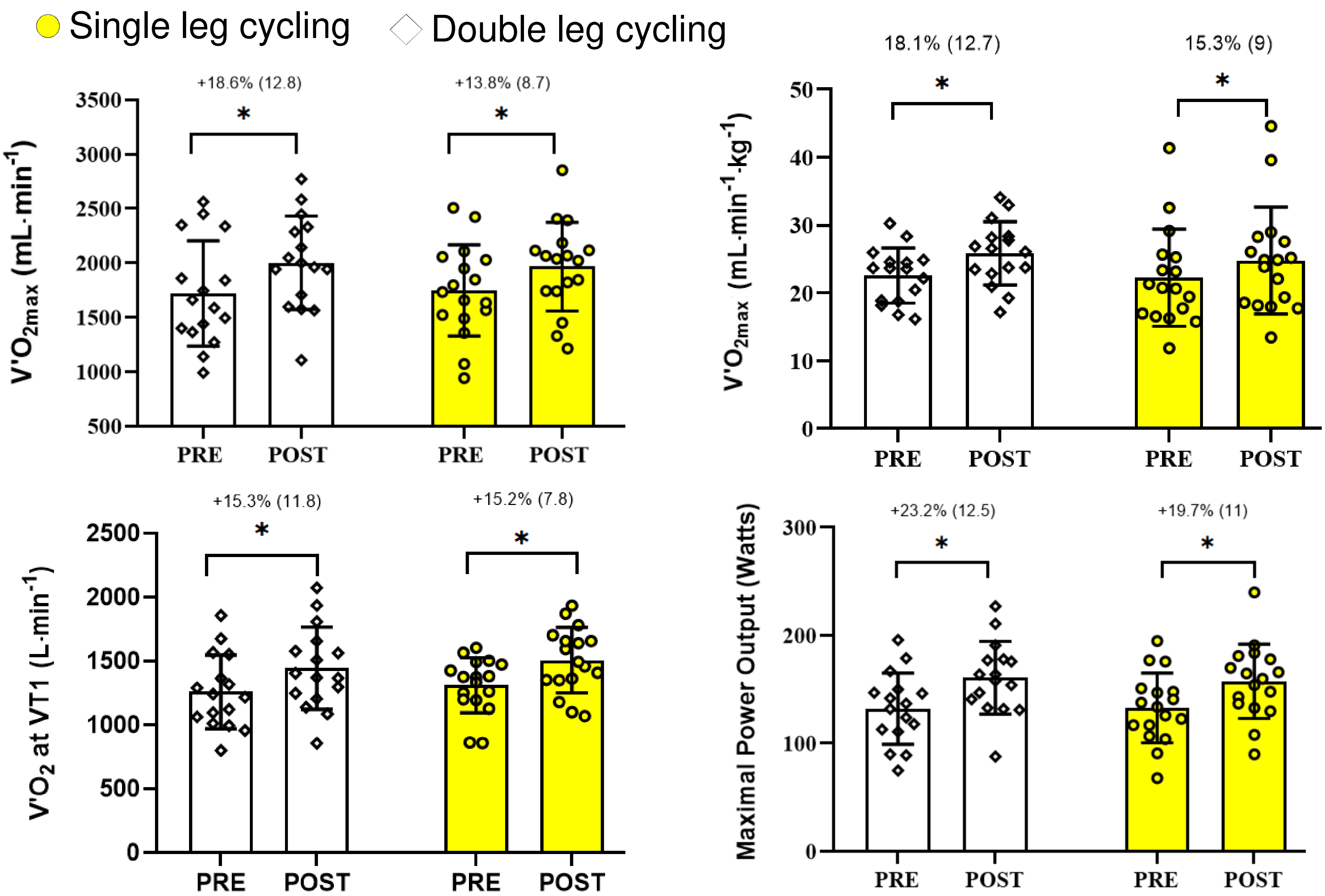
Associated Gym

**Logistics**

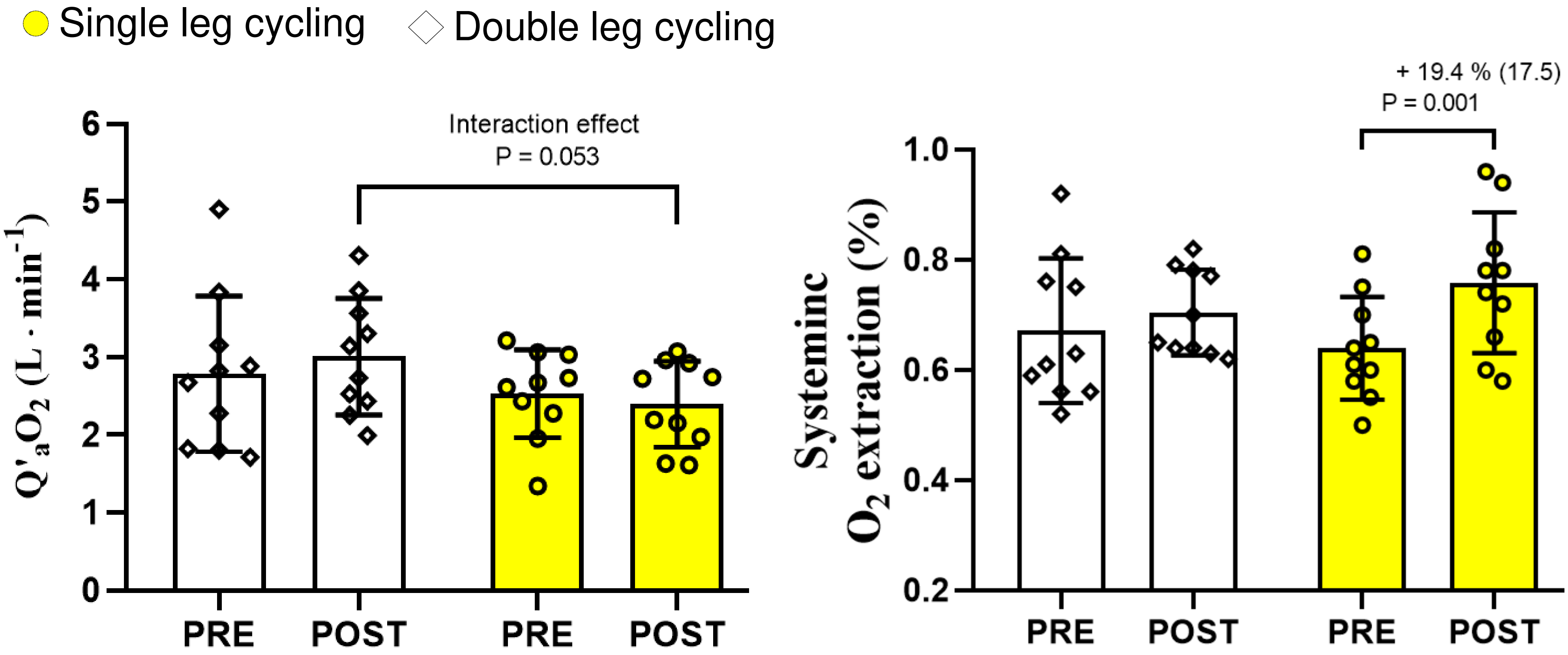
- Participants detection and enrollment through transplanted associations. University of Udine. Udine's Hospital and Gemona's Hospital
- Experimental sessions at the Gemona's Hospital

**Personnel**

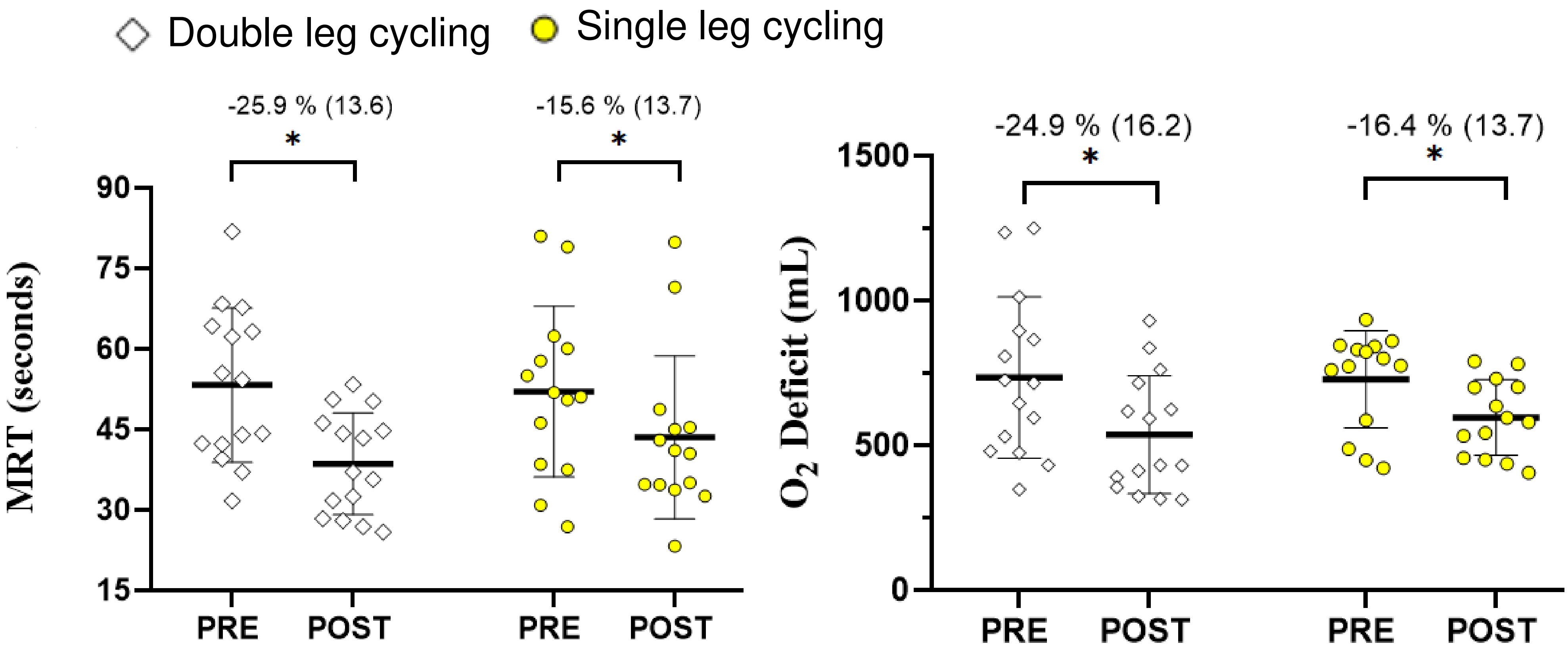
- Testing and training: 9 students from Sport Science degree


Single leg cycling
Double leg cycling
+18.6% (12.8)
+13.8% (8.7)
V'O2max (mL·min-1)
3500
3000
2500
2000
1500
1000
500
PRE
POST
PRE
POST
18.1% (12.7)
15.3% (9)
V'O2max (mL·min-1·kg-1)
50
40
30
20
10
0
PRE
POST
PRE
POST
+15.3% (11.8)
+15.2% (7.8)
V'O2 at VT1 (L·min-1)
2500
2000
1500
1000
500
0
PRE
POST
PRE
POST
+23.2% (12.5)
+19.7% (11)
Maximal Power Output (Watts)
300
200
100
0
PRE
POST
PRE
POST

# Study 1 – Results: incremental exercise

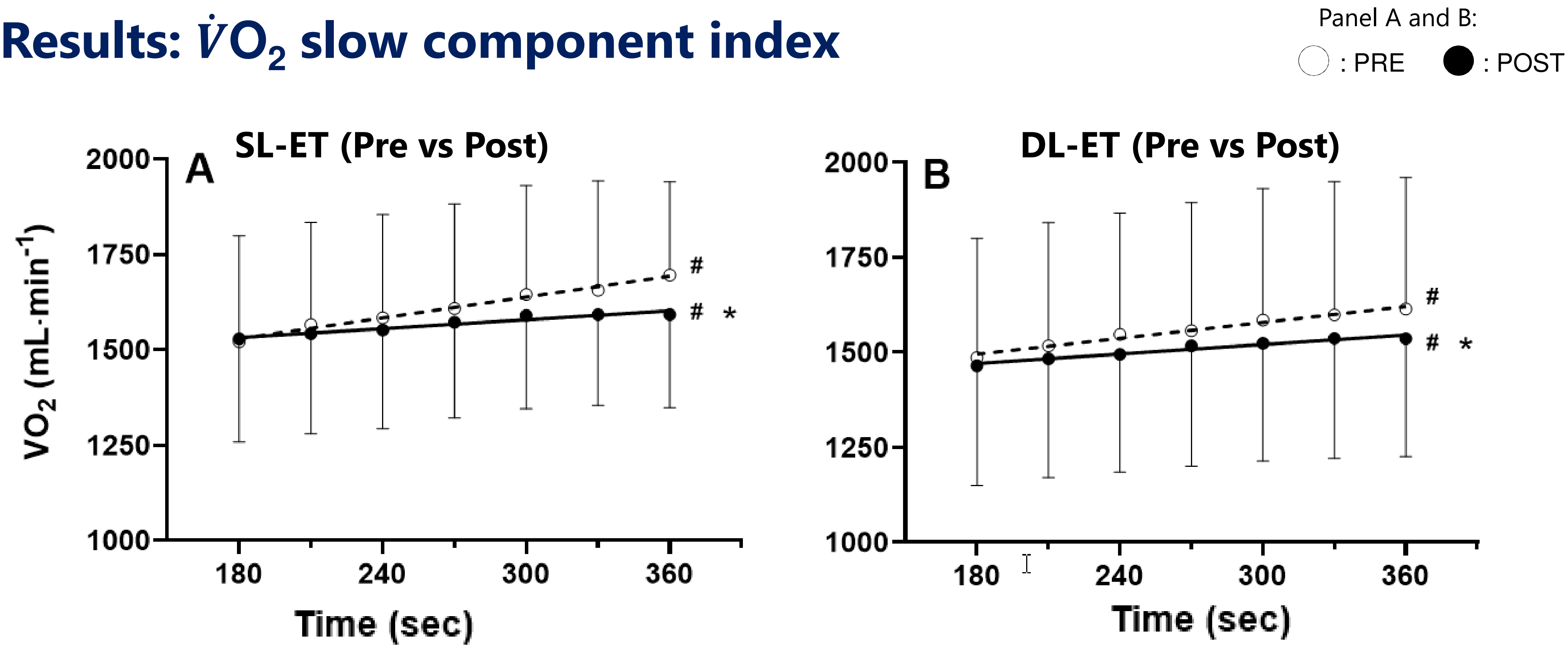


# Results: Moderate constant load exercise




**Improved $O_2$Def and MRT are indexes of better exercise tolerance**

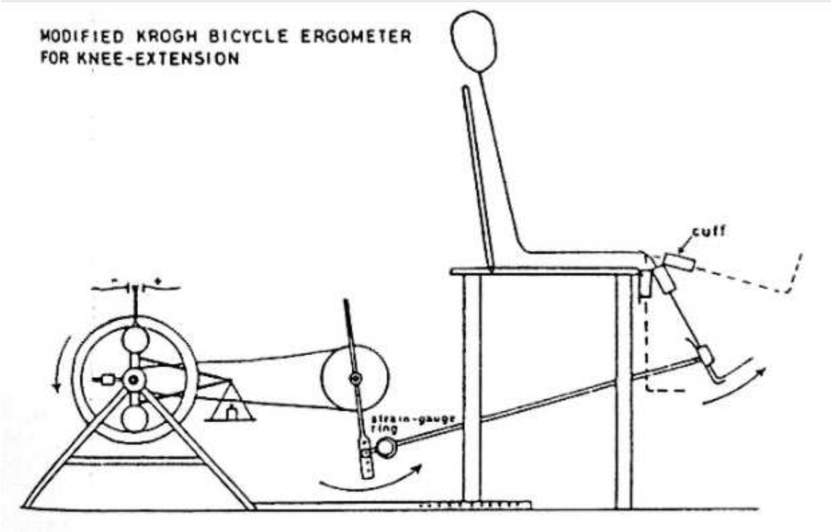
# Results: $\dot{V}O_2$ slow component index




#: angular coefficient of the regression line is significantly different from zero; *: angular coefficient of the regression line is significantly different from PRE.

- A positive slope, significantly different from zero indicates $\dot{V}O_2$ slow component development
- Slope reduction from PRE to POST indicates a reduced $\dot{V}O_2$ slow component

# General conclusions



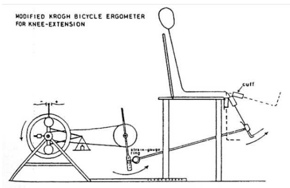

- **endurance training by exercising with a small muscle mass may represents an effective and useful modality** for improving exercise capacity in transplant recipients;

- **suggest that the limitation to exercise capacity is equally distributed between central and peripheral factors in HTx, KTx, and LTx**, and that impaired peripheral gas exchanges might play a more relevant role in decreasing exercise capacity in this type of patients.

These findings may pave the path leading to develop effective and criterion-based training protocols for post transplantation patients.

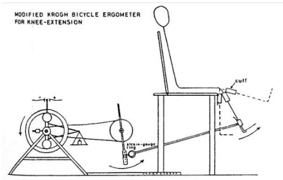
# Grazie per l’attenzione

# Conclusions




- 8 weeks of SL-ET are effective to speed $\dot{V}O_2$ kinetics (decrease $O_2$Def and faster MRT) at moderate intensity exercise and to reduce the $\dot{V}O_2$ slow component in Tx

vs



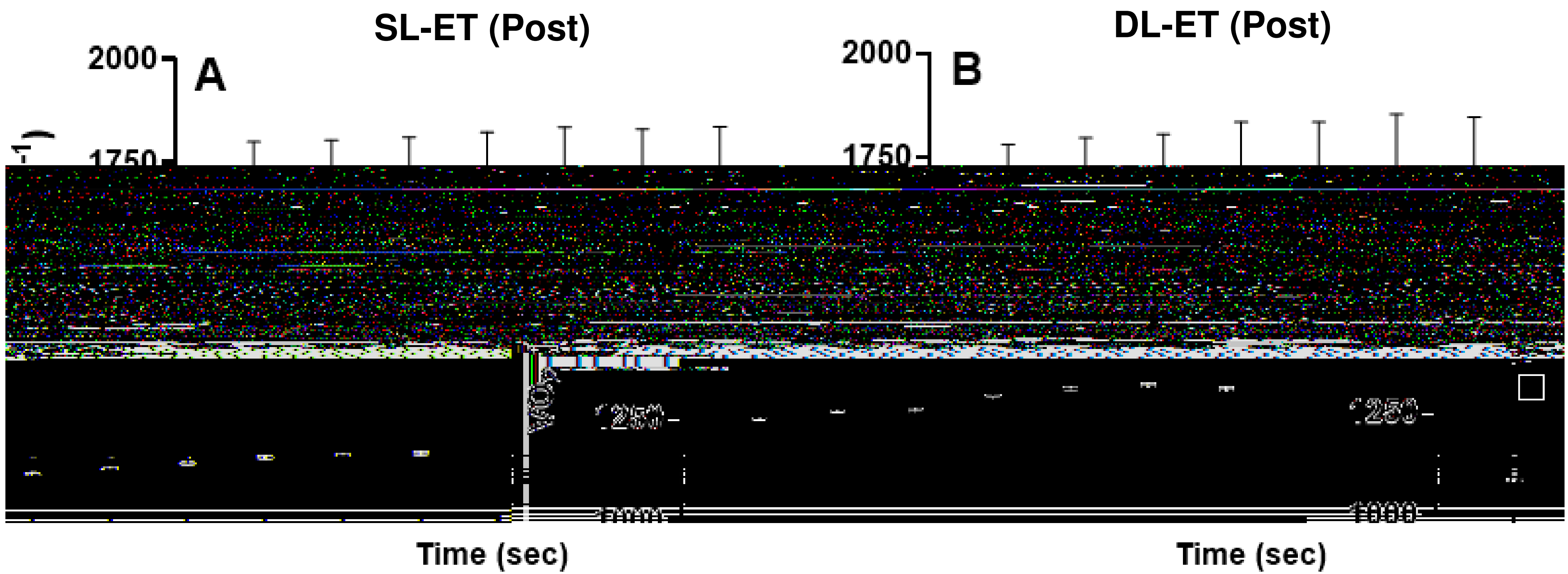

- 8 weeks of SL-ET were as effective as DL-ET to speed $\dot{V}O_2$ kinetics (reduced and to decrease $O_2$Def and faster MRT) at moderate intensity exercise and to attenuate the $\dot{V}O_2$ slow component in Tx


- The concomitant acceleration of the HR and $\dot{V}O_2$ kinetics kinetics suggests that this amelioration was induced by both improved $O_2$ delivery and $O_2$ utilisation to the working muscles

- the results suggest that the role of the factors responsible for peripheral gas exchange may be as important as the cardiovascular factors in determining the exercise capacity in transplant patients.

Briefly, B-by-B $\dot{V}O_{2p}$ values of each DL-MOD repetition were interpolated to 1-s intervals (Lamarra et al., 1987), time aligned with the onset of the exercise test, and treated by subtracting the $\dot{V}O_{2p}$ at rest. The two repetitions' data were then combined to obtain a single data file for each subject and condition. $O_2$Def was calculated as the difference between the $O_2$ that would have been consumed if $\dot{V}O_{2p\text{-}ss}$ had been attained immediately at the beginning of the exercise and the volume of $O_2$ taken up during exercise. The first quantity was calculated by multiplying $\dot{V}O_{2p\text{-}ss}$ in ml $O_2$ $s^{-1}$ by the exercise duration (600 s). The $O_2$ volume consumed during exercise was calculated by summing progressively the $\dot{V}O_{2p}$ values expressed in ml $O_2 \cdot s^{-1}$ from the trial's onset to 600 s. MRT was then computed as the ratio between $O_2$Def and the corresponding $\dot{V}O_{2p\text{-}ss}$.

$$WB = -0.430 + 0.050 \cdot (\dot{V}_E) + 0.00161 \cdot (\dot{V}_E)^2$$
$$\dot{V}O_{2\text{-}RM} = (34.9 + 7.45 \cdot WB)$$




Panel A and B

□ : $\dot{V}O_{2p}$ diminished by the estimated $O_2$ cost of breathing as a function of time at POST

● : gross $\dot{V}O_{2p}$ as a function of time at POST;

**$\dot{V}O_2$ slow component amplitude was not affected by $O_2$ cost of breathing in these patients**

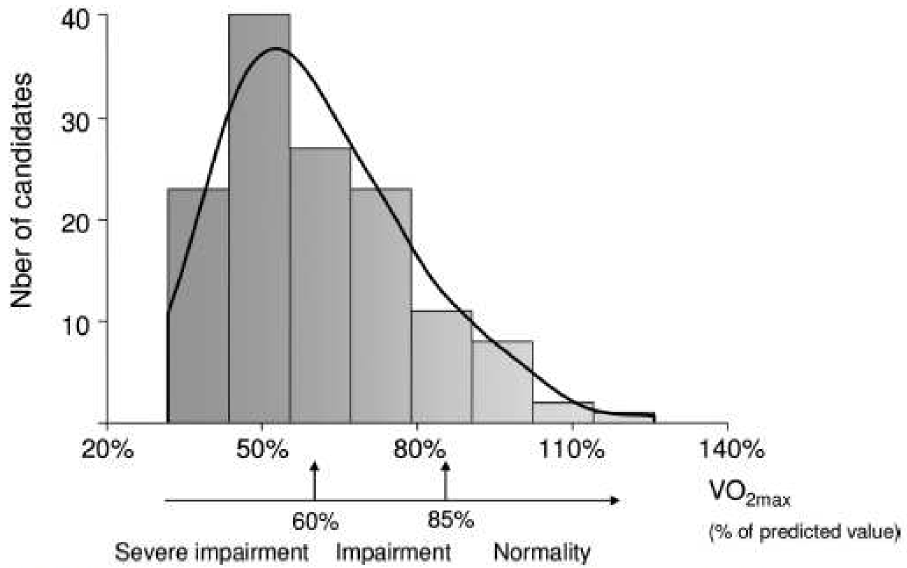



**FIGURE 1.** Distribution of peak $VO_2$ within the study population (n=135). Peak $VO_2$, expressed as percentage of predicted value, was normal (≥85%) in only 11.9% of cases and impaired in 88.1% of cases. Impairment was severe (<60%) in 54% of cases.