Skeletal muscle oxygenation and blood volume during incremental loading in interstitial lung disease

L. Wickerson,[1-3] S. Mathur, [1,2] D. Brooks, [1,2] L. Bonetti, [1] LG. Singer, [3] J. Granton, [3] WD. Reid [1,2]

[1]Department of Physical Therapy, Faculty of Medicine, University of Toronto, Toronto, ON, [2] Rehabilitation Sciences Institute, Faculty of Medicine, University of Toronto, Toronto, ON

[3] Toronto Lung Transplant Program, University Health Network, Toronto, ON

Introduction

- Individuals with interstitial lung disease (ILD) often exhibit exertional hypoxemia that impairs oxygen transport, delivery and utilization.
- Exercise prescription if often guided by pulse oximetry, however this does not provide information about regional oxygenation of exercising muscle.
- SpO_2 reflects global rather than local muscle oxygenation (SmO_2).
- Near infrared spectroscopy (NIRS) is a non-invasive optical technique to measure muscle oxygen saturation (SmO_2) and blood volume (tHb). [1]

Aim and Objectives

Aim Examine muscle oxygenation and regional blood volume during incremental limb loading in non-oxygen dependent mild ILD, oxygen-dependent lung transplant candidates with severe ILD and healthy people

Objectives

During incremental elbow flexor loading (EFL) and knee extensor loading (KEL) examine:

1. If active muscles deoxygenate
2. If blood volume is preferentially redistributed to active muscles
3. If whole body oxygenation (SpO_2) is associated with muscle oxygen saturation (SmO_2)

Methods

Design: Cross-sectional study with repeated measures

Exclusion criteria: 1) adipose tissue thickness > 10mm at NIRS monitoring sites, 2) < 45 or > 75 years, 3) active myositis, 4) muscle or joint issues 5) lung transplant candidates listed as rapidly deteriorating, hospitalized or listed for a re-transplant.

Statistical analysis: Muscle oxygenation and blood volume were examined at end exercise (task failure) using one-way ANOVA and during incremental loading by dividing the task duration into quintiles and using a repeated measures ANOVA. Within and between group differences were examined and post-hoc testing was performed if significant. A Spearman rank correlation analysis examined the relationship between SmO_2 and SpO_2.

BASELINE MEASURES

- Adipose and muscle layer thickness using B-mode ultrasound imaging
- Resting muscle oxygenation and blood volume using spatially resolved NIRS

Exercise Protocol: on Biodex dynamometer

- Five 5-second maximal isometric voluntary contractions (highest= 100% MIVC)
- Isotonic contractions (10 reps/min for 2 mins) starting at 10% MIVC and increasing by 10% MIVC until task failure
- Duty cycle 1 second contraction: 5 seconds relaxation

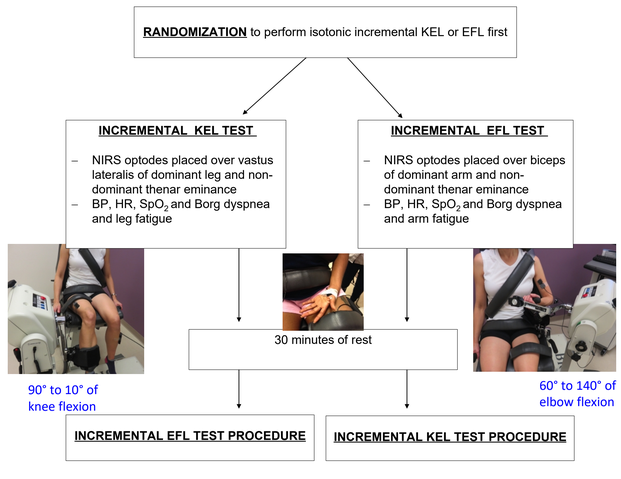

Figure 1: **Incremental loading protocol**

Results

Tables 1: Participant characteristics (n=36), mean (SD)

	Healthy (n=13)	Mild ILD (n=10)	Severe ILD (n=13)
Male: female (% female)	8:5	6:4	8:5
Age (years)	60 (9)	60 (9)	65 (5)
BMI (kg/m^2)	25 (3)	27 (4)	26 (3)
FVC (% predicted)	101 (14)	81 (17)	59 (20) *
D_{LCO} (% predicted)		69 (14)	48 (15) *
GAP index		1.5 (1)	4.2 (1) *
6MWD (m)		558 (107)	397 (71) *
6MWD (% predicted)		83 (15)	62 (13) *
Estimated FiO_2			0.45 (0.1)
Diagnosis*			
IPF		3	4
IPF/COPD			2
Other IIP		3	3
NYD		1	1
Hypersensitivity pneumonia			2
LAM			1
Sjogren's		2	
RA-ILD		1	

* p < 0.05

Abbreviations: BMI: body mass index; FVC: forced vital capacity; D_{LCO}: diffusing capacity for carbon monoxide; GAP index: gender, age and pulmonary physiology index for mortality in idiopathic pulmonary fibrosis; 6MWD: six-minute walk distance; FiO_2: fraction of inspired oxygen, IPF: idiopathic pulmonary fibrosis; NSIP: non-specific interstitial pneumonia; IPF/COPD: idiopathic pulmonary fibrosis/ chronic obstructive pulmonary disease; DIP: desquamative interstitial pneumonia; COP: cryptogenic organizing pneumonia; NYD; not yet diagnosed; LAM: lymphangioleiomyomatosis; RA-ILD: rheumatoid arthritis –associated interstitial lung disease

	Healthy (n=13)	Mild ILD (n=10)	Severe ILD (n=13)
Muscle layer thickness (mm)			
Vastus lateralis and intermedius	36.3 (6)	36.9 (5)	32.5 (5)
Biceps	30.5 (6)	28 (4)	24 (8)
Skin and adipose thickness (mm)			
Over vastus lateralis	7.9 (3)	7.2 (3)	7.1 (3)
Over biceps	5.1 (2)	6.7 (2)	6.6 (1)

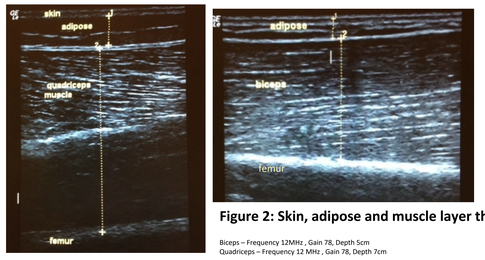

Figure 2: Skin, adipose and muscle layer thickness

Biceps – Frequency 12MHz , Gain 78, Depth 5cm
Quadriceps – Frequency 12 MHz , Gain 78, Depth 7cm

Table 2: Incremental isotonic loading characteristics (n=36), mean (SD)

	Healthy (n=13)	Mild ILD (n=10)	Severe ILD (n=13)	p value
Knee extensor loading				
Knee extensor peak torque (Nm)	162 (50)	137 (44)	104 (32)	N.S
Protocol length (minutes)	11.7 (2)	10 (3)	10 (2)	N.S
Total work performed (J)	6328 (2515)	4911 (2211)	3368 (1330)	0.006
Elbow flexor loading				
Elbow flexor peak torque (Nm)	60 (19)	57 (18)	40 (18)	N.S
Maximal MIVC achieved	52 (7)	44 (10)	36 (10)	N.S
Protocol length (minutes)	10.5 (1)	8.8 (2)	7.2 (2)	0.0003
Total work performed (J)	3003 (1212)	2514 (911)	1446 (811)	0.001

Abbreviations: Nm: newton-metres; MVC: maximal isometric voluntary contraction; J: joules

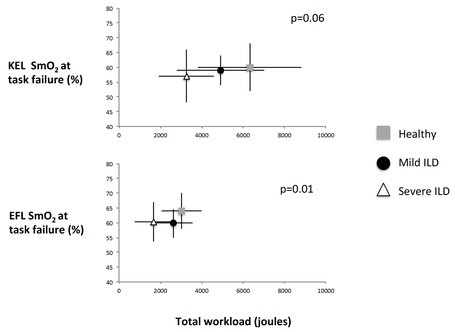

Figure 3: End exercise (task failure) SmO_2 over total workload (n=36)

Abbreviations: SmO_2: muscle oxygenation; ILD: interstitial lung disease

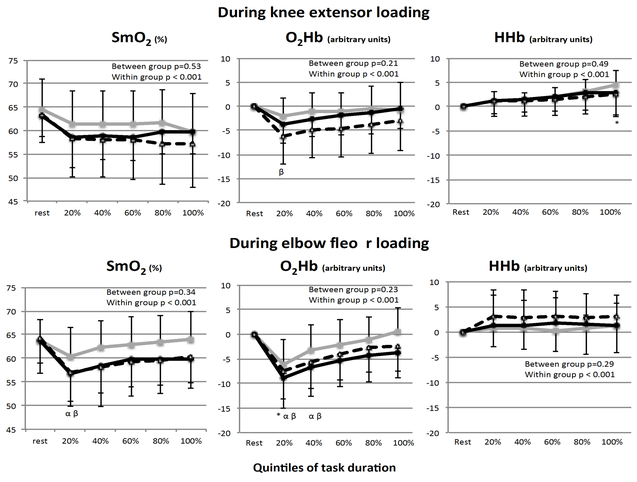

Figure 4: Change in muscle oxygenation during exercise (n=36)

Abbreviations: SmO_2: muscle oxygenation, O_2Hb: oxygenated hemoglobin, HHb: deoxygenated hemoglobin

post-hoc within-group differences from resting time-point * Healthy, α Mild ILD, β Severe ILD

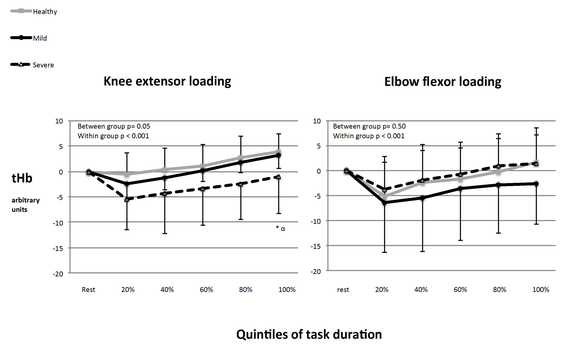

Figure 5: Change in total hemoglobin (tHb) during exercise (n=36)

post-hoc within-group differences from resting time-point * Healthy, α Mild ILD, β Severe ILD

Muscle oxygenation and blood volume during incremental loading

Within-group differences During KEL and EFL SmO_2, O_2Hb, HHb and tHb changed over time. The severe ILD group had a lower O_2Hb at the 20th percentile compared to rest during KEL. The healthy group had a higher HHb at the task failure time point compared to rest during KEL. During EFL both the mild and severe ILD groups had a lower SmO_2 at the 20th percentile compared to rest. O_2Hb was lower during EFL at 20th percentile in all groups compared to rest, and also at the 40th percentile in both ILD groups. **Figure 4** During KEL the healthy and mild ILD groups had a higher tHb at the task failure time point compared to rest. **Figure 5**

Between-group differences During KEL the severe ILD group had a lower tHb compared to the healthy group. **Figure 5**

Results

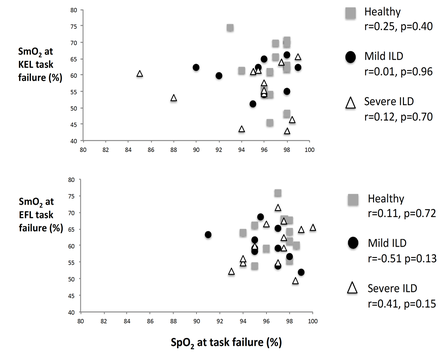

Figure 6: Relationship between SmO_2 and SpO_2 at KEL and EFL task failure (n=36)

Abbreviations: SmO_2: muscle oxygenation; ILD: interstitial lung disease

There was no relationship between SmO_2 and SpO_2 in any of the groups at KEL and EFL task failure. **Figure 6**

Discussion

- A preserved SpO_2 suggests that systemic oxygen delivery was adequate. Individuals with ILD may have been less able to extract the available oxygen due to peripheral muscle oxidative capacity [2] which may have contributed to earlier termination of exercise.
- Lower blood volume in the active muscle in severe ILD compared with healthy participants at KEL task failure may indicate less blood redistribution during exercise which may have impaired the total workload achieved. The higher workloads during KEL may have resulted in greater redistribution to respiratory muscles.

Limitations:

- There is no strict criteria to differentiate mild and severe ILD.
- The mild ILD group was heterogeneous in terms of pulmonary function and gas exchange measures.
- Only superficial muscles can be sampled using NIRS, and the vastus lateralis is only one muscle involved in knee extension.
- The variability of muscle oxygenation and blood volume was large, and post-hoc testing revealed a lack of power based on the sample size.
- As the isotonic workloads were based on an individual's MIVC and not matched for workload, we were unable to examine changes at isowork.

Conclusions:

- SmO_2 provides additional information on tissue oxygen status and may be useful to examine the effect and response to exercise training.

Acknowledgements

This study was supported by a research grant from the Ontario Respiratory Care Society.

Lisa Wickerson was supported by Canadian and Ontario Lung Association fellowships and University of Toronto Scholarships.

Dina Brooks is a Tier 2 Canada Research Chair.

Stacey Butler for patient recruitment and Marcella Adair for data entry

References

1. Ferrari et al. The use of near infrared spectroscopy in understanding skeletal muscle physiology: recent developments. Phil Trans. R. Soc A 2011;369:4577-4590.
2. Wickerson et al. Peripheral muscle dysfunction in interstitial lung disease: a scoping study. J Physio Phys Rehab 2016;1:1-11.