Role of Skeletal Muscle Mitochondrial Energetics in Fatigue Among Older Cancer Survivors

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Introduction

- Fatigue is one of the most common and distressing conditions reported by cancer survivors that lead to physical inactivity, reduction in daily productivity, and physical impairment.
- Skeletal muscle mitochondrial oxidative capacity affects muscle function and that inefficiency in skeletal muscle bioenergetics explains physical function impairments in older adults.
- The link between complaints of fatigue, physical inactivity, and skeletal muscle mitochondrial energetics has never been shown.

Objectives

- Explore skeletal muscle energetics correlates with reports of fatigue and inactivity among older cancer survivors.

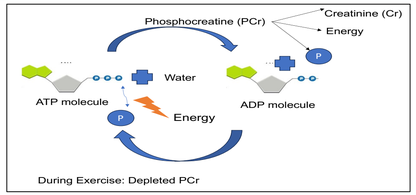
Methods

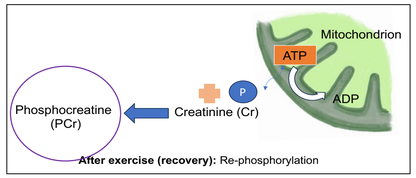
- **Design:** Cross sectional exploratory study
- **Sample:** Adults aged 18 and older, diagnosed with solid tumor cancer receiving either immunotherapy or hormonal therapy for 3 months or longer, and self reported average fatigue level within the past 7 days at the level of 3/10
- The participants were divided into 2 groups, young adults (ages younger than 65) and older adults (age 65 and older).

variables	Measures
Skeletal muscle mitochondrial oxidative capacity	in vivo phosphorus magnetic resonance spectroscopy (MRS), measuring the time phosphocreatine (PCr) recovery (τPCr)
Fatigue	• Patient-Reported Outcomes Measurement Information System® (PROMIS-F): high score indicate high fatigue • The Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F):low score indicate greater fatigue
Physical Activity	A commercial physical activity tracker (Fitbit) for 7 days.

Table 1: variables and measures

Magnetic Resonance Spectroscopy





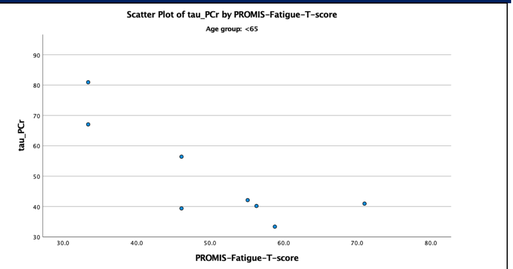
- Non-invasive analytical chemistry technique that allow us to see the tissue biochemistry in vivo and measure the rate of phosphocreatine (PCr) recovery (τ_{PCr})
- The rate of PCr resynthesis depends on the rate of ATP produced by mitochondria so it can be used to measure of the rate of oxidative ATP synthesis as a representation of **mitochondrial function.**
- **Procedure:**
  - Individual perform a knee extension exercise (fast kicking on kicking pads) inside the magnetic scanner
  - Change in energy metabolites concentration was measured by a 31P-tuned surface coil fastened on an individual thigh
  - τPCr represents the time necessary to reach full recovery of PCr.

Result

Variables	Category	< 65 year (n = 8)	≥ 65 year (n = 3)	p
Age		47.88 ± 10.37	67.67 ± 12.73	.014
Gender	Male	3 (37.5%)	2 (66.7%)	.545
	Female	5 (62.5%)	1 (33.3%)	
Year diagnosed with cancer		5.75 ± 3.73	6.33 ± 4.51	1.000
τPCr		50.06 ± 16.55	59.49 ± 16.54	.307
PROMIS-F		50.03 ± 12.90	55.77 ± 8.56	.352
FACIT-F		115.22 ± 31.71	102.22 ± 27.64	.307
Steps/day		7,479 ±3,917	5,583 ± 1,830	.405
Activity levels (based on step/day)	Sedentary (≤ 5K step/day)	2 (25%)	2 (66.7%)	
	Active (> 5K step/day)	6 (75%)	1 (33.3%)	

Table 2: Characteristics and outcomes differences between age groups

- Older cancer survivors have lower muscular oxidative capacity(τPCr = 59.49 secs), higher self- report fatigue (PROMIS-F =55.77) and lower average step count/day compared to younger cancer survivors



Age group	Variables	1	2	3	4
< 65 year old	1.τPCr	-	-.711*	.619	.107
	2.PROMIS-F		-	-.916**	-.523
	3. FACIT-F			-	.607
	4. Steps/day				-

* p <.05, ** p < .01

Table 3: Correlation (Spearman's rho) among variables

- τPCr was negatively associated with the self-report fatigue measured by PROMIS-F

Discussion

- This preliminary finding provide evidence that aging play role in
  - mitochondrial bioenergetics. Older individuals showed slower rate of PCr resynthesis after exercise compared to younger individuals
  - self report fatigue measured by PROMIS-F and FACIT-F. Older individuals reported higher fatigue compared to younger individuals
  - activity levels as measured by a commercially available physical activity tracking device. Older individuals had lower average steps/day compared to young individuals
- The finding showed that among participants age younger than 65, the low self-report fatigue was significantly associated with the poor mitochondrial function (prolong τPCr time). This finding warren further investigation by including other factors such as cancer staging, type of treatment, current medication that may influence the ATP synthesis.
- The result of this study is limited due to a small sample size and cross-section design nature. Further study of the mechanisms of fatigue and physical inactivity in cancer patients to confirm the role of mitochondrial function in self-report fatigue is needed.

Acknowledgement

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