Mediation Relationship between Components of Frailty Syndrome

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ABSTRACT

Frailty is a condition associated with, but not an inevitable consequence of aging. It is characterized by worsening of several physiological component syndromes, such as reduction of physical activity, weakness, slowness and weight loss.

Several studies have reported a complex loop mechanism among physio-logical systems associated with these components. However, evidence of mediation between them, while hypothesized, is not yet available.

Here we present first evidence of a mediation relationship between certain components of frailty (body composition, strength, physical performance) through statistical mediation analysis of a cohort data measured from aging adults followed over decades, as they begin to develop frailty.

BACKGROUND

Topic Overview

- Understanding frailty may lead to prevention, treatment or reversal of frailty.

Prior Studies

- A feed-forward loop relationship was found between body composition, strength and physical performance (RoyChoudhury et al. 2014, 2019, 2020).

The Dataset

- A dataset on physical measurements of 1,466 older adults (Rancho Bernardo Study)
- recorded at four visits at four year intervals (Visits 7-10)
- All variables categorized into three levels: low, medium, and high.

	Visit 7	Visit 8	Visit 9	Visit 10
Body Performance				
timed Up-and-go test time		✓	✓	✓
Strength				
Grip Strength	✓	✓	✓	✓
Body Composition				
Appendicular lean mass ratio	✓	✓	✓	✓
Subtotal lean fat ratio	✓	✓	✓	✓
Log2 lean mass/ fat ratio	✓	✓	✓	✓

RESULTS

Red Outer Circle: The left-variable influences itself through mediation of the right-variable.
Red inner Circle: The right-variable influences itself through mediation of the left-variable.

Fig.1 Grip Strength & Up-and-go Test

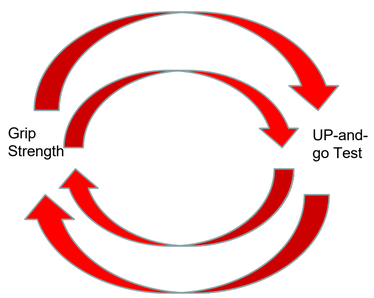


Fig.2 Subtotal Lean Fat Ratio & Up-and-go Test

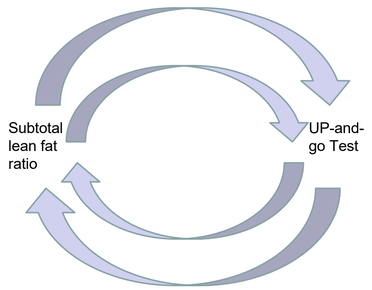


Fig.3 Subtotal Lean Fat Ratio & Grip Strength

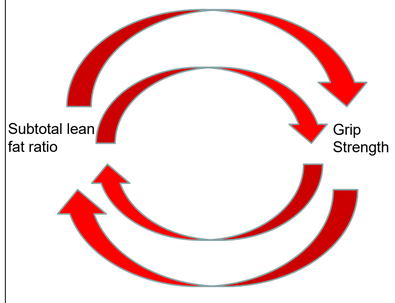


Fig.4 Log2 Lean Mass/Fat Ratio & Up-and-go Test

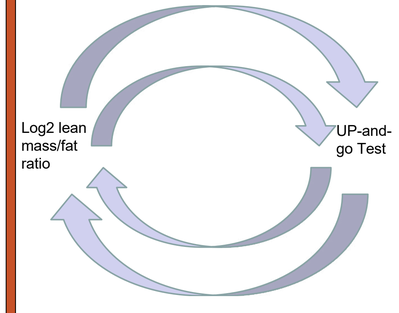


Fig.5 Appendicular Lean Fat Ratio & Grip Strength

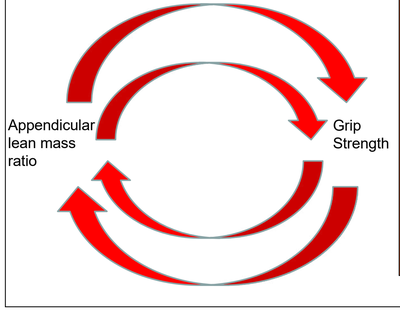
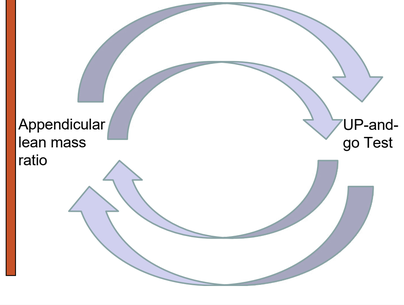


Fig.6 Appendicular Lean Fat Ratio & Up-and-go Test



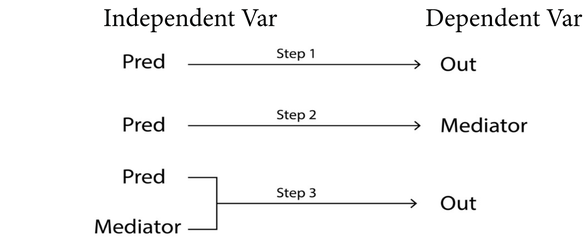
METHODS

Proportional Odds Model

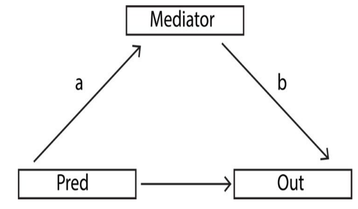
Assume the outcome variable has K levels:

$$\log\left(\frac{P(Y \le k)}{P(Y > K)}\right) = \beta_{k0} + \beta_1 x_1 + \cdots + \beta_p x_p,$$
$$k = 1, \ldots, K-1$$

Baron and Kenny's Method (three step regression)



Sobel's Test



$$se = b^2 se_a{}^2 + a^2 se_b{}^2$$
$$t\ statistics = \frac{ab}{se}$$

CONCLUSIONS

Significant Mediation Between

- Grip Strength and Up-and-Go Test
- Appendicular Lean Mass Ratio and Grip Strength
- Subtotal Lean Fat Ratio and Grip Strength

Limitations

- A considerable number of incomplete observations were removed

Further Study

- The ordinal data could be further evaluated through Causal Mediation Analysis (R package "mediation").
- Indirect effects could be evaluated by bootstrapping and the Monte Carlo Method.