

Inflammation and frailty measures in older people

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Introduction

- Frailty is an important concept
- Its aetiology is unknown
- Chronic inflammation may have a pathophysiological role ^(1, 2)

- C-reactive protein (CRP) and interleukin-6 (IL-6) are inversely correlated with poor physical performance and muscle weakness ⁽³⁾
- IL-6 predicts the onset of disability ⁽⁴⁾
- Tumour necrosis factor- α (TNF- α) is associated with death ^(5, 6)

- Older people defined as frail by Fried criteria ⁽⁷⁾ show increased inflammation:
 - higher levels of CRP ⁽⁸⁾
 - higher levels of IL-6 ⁽⁹⁾
- Fried's model has **strengths**
 - clinical reproducibility and coherency ⁽¹⁰⁾
 - validated against adverse outcomes ⁽¹¹⁾
- Fried's model has **weaknesses**
 - based on physical parameters only ⁽¹²⁾

- Inflammation in Fried frail subjects may be related primarily to sarcopenia
- IL-6 and disability: importance of muscle strength ⁽⁴⁾
- Low-grade inflammation → sarcopenia ⁽¹³⁾

- Defining frailty is an area of ongoing debate ⁽¹⁴⁾
- Application of different frailty criteria can give heterogenous results in clinical practice ⁽¹⁵⁾

Objectives

- The aim of this study was
 - to investigate inflammation in older patients according to varied frailty criteria

Methods

- SAMPLE

110 participants aged ≥ 75 years

Exclusion criteria: signs of infection or taking antibiotic treatment

- FRAILTY MEASURES

1. FUNCTION

INDEPENDENT: community-dwelling

INTERMEDIATE: patients attending

DH for rehabilitation

DEPENDENT: ongoing nursing and medical needs, meeting CHC criteria

2. FRIED

exhaustion, weight loss, slow walking

speed, low handgrip strength, low

physical activity

3. HANDGRIP STRENGTH

women < 17.5 kg

men < 30 kg

4. ROCKWOOD FRAILITY INDEX

30 variables

Deficits added

Index: total deficits as a proportion of those counted (e.g. $6/30 = 0.20$)

- LABORATORY MEASURES

- Total WBC count
- Albumin
- CRP
- IL-6
- TNF- α

- LREC APPROVAL

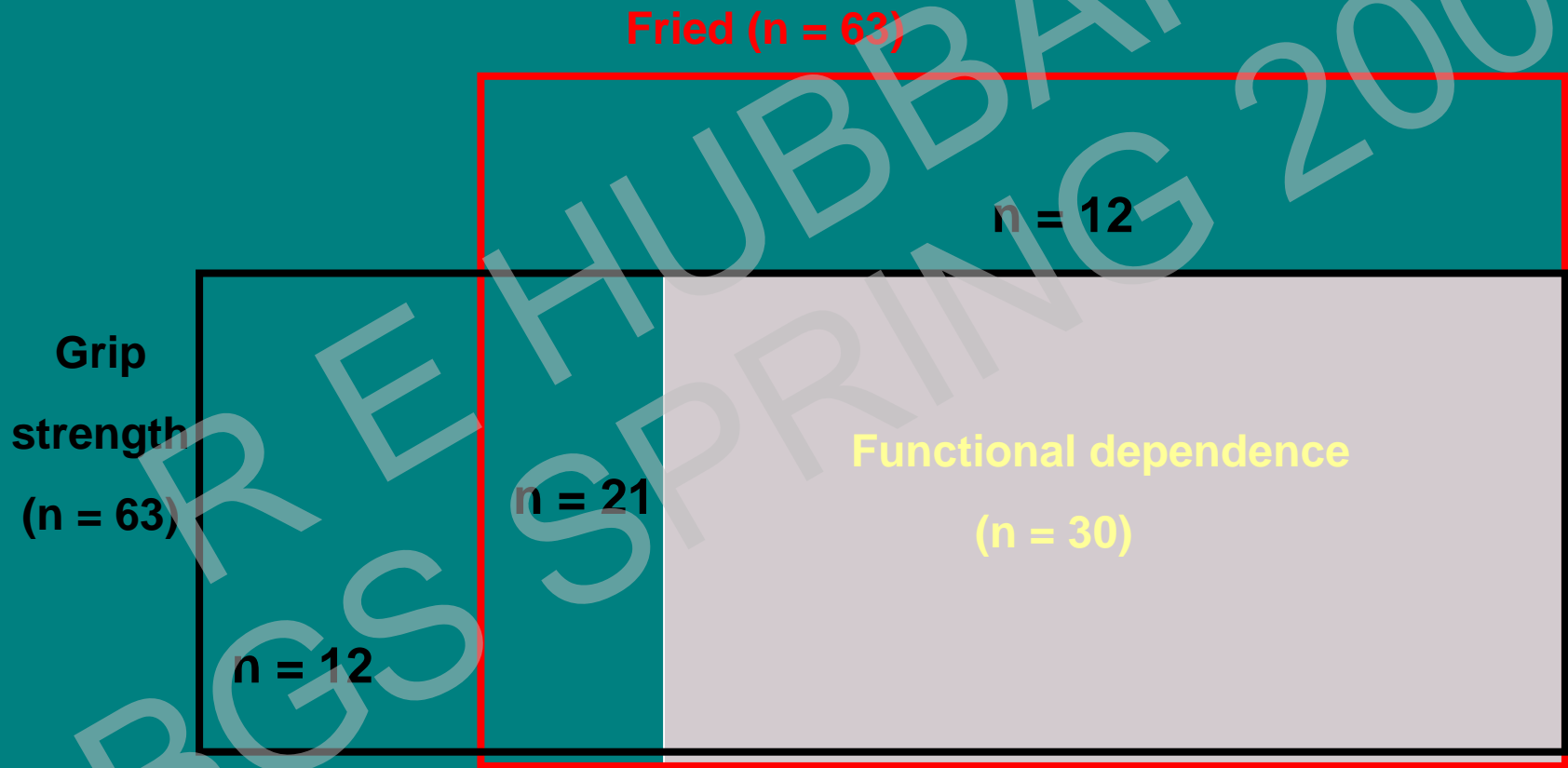
- STATISTICAL ANALYSIS

Results

- 110 subjects
- Age range 75 to 97 years, mean 83.9 (5.5)
- Forty four men (40%)
- All were Caucasian

- Prevalence of frailty varied from 27% (functional definition) to 57% (Fried and handgrip strength)
- Populations identified as frail by each measure overlapped partially

Figure 1: Distribution of subjects identified as frail according to different frailty criteria

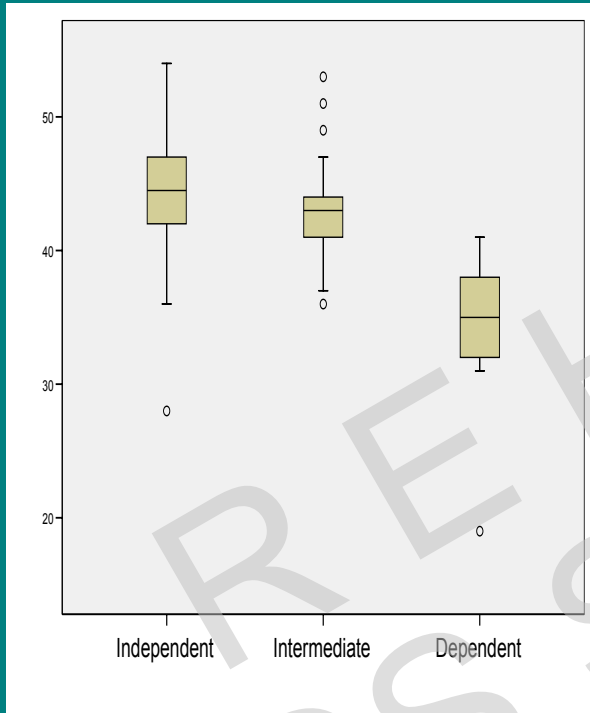


- The Rockwood Frailty Index showed mathematical properties previously described in larger cohorts ⁽¹⁶⁾
- Normally distributed, reached a maximal value approximating 0.67 (0.63 in this study)

- Venesection
 - 4 subjects declined
 - One extreme CRP, one high lymphocyte count excluded
- With increasing patient frailty as defined by all 3 categorical criteria,
 - albumin significantly decreased
 - TNF- α significantly increased

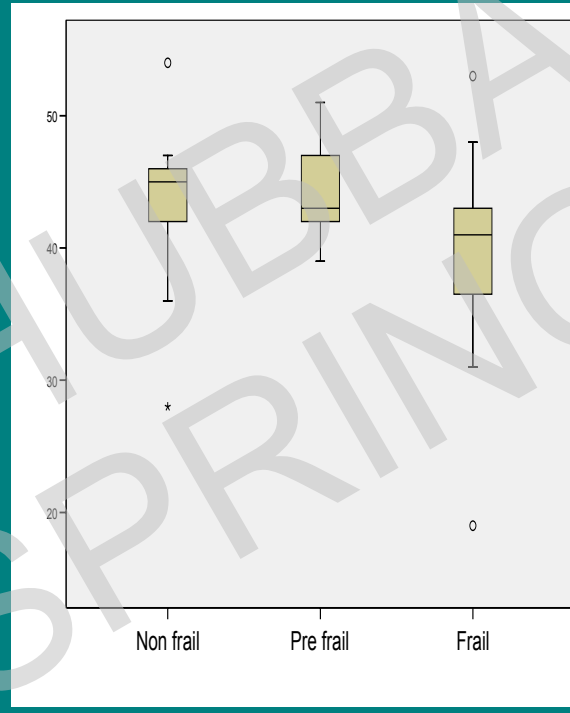
Albumin

FUNCTION



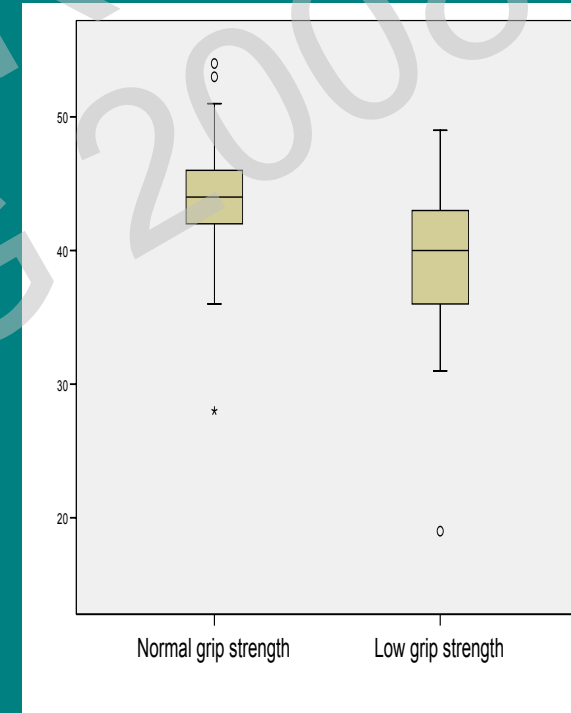
$p < 0.005$

FRIED



$p < 0.005$

GRIP STRENGTH



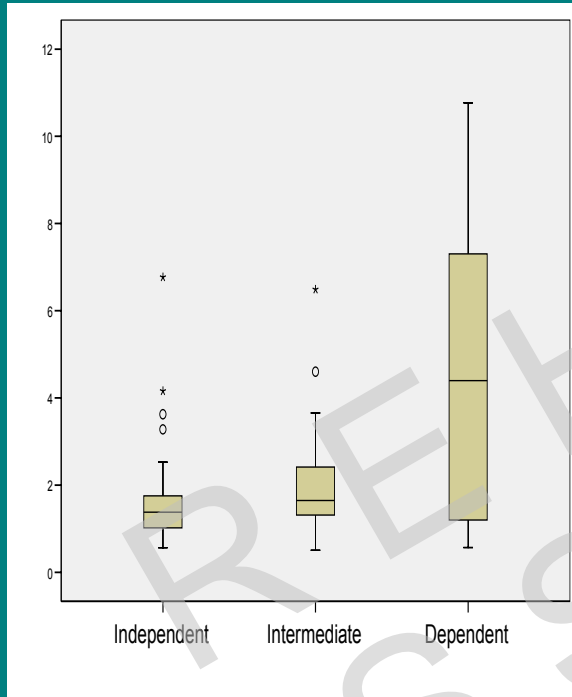
$p < 0.005$

Albumin g/dl

BR E HUBBARD 2008
BGS SPRING

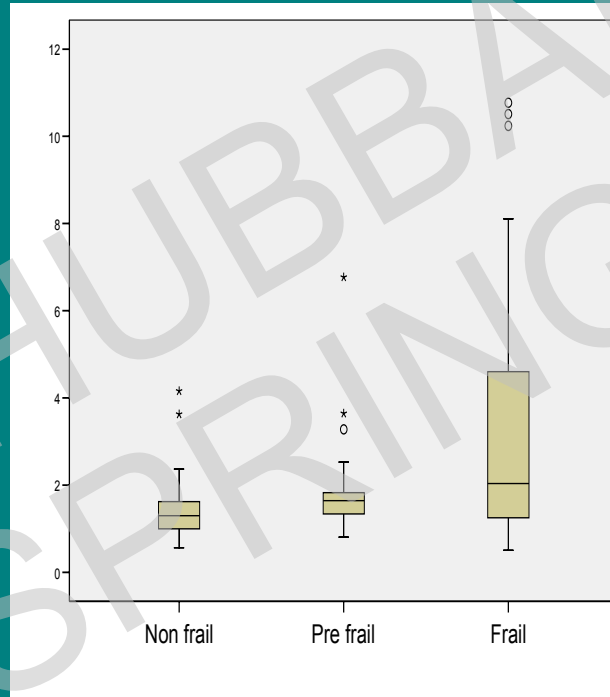
TNF - α

FUNCTION



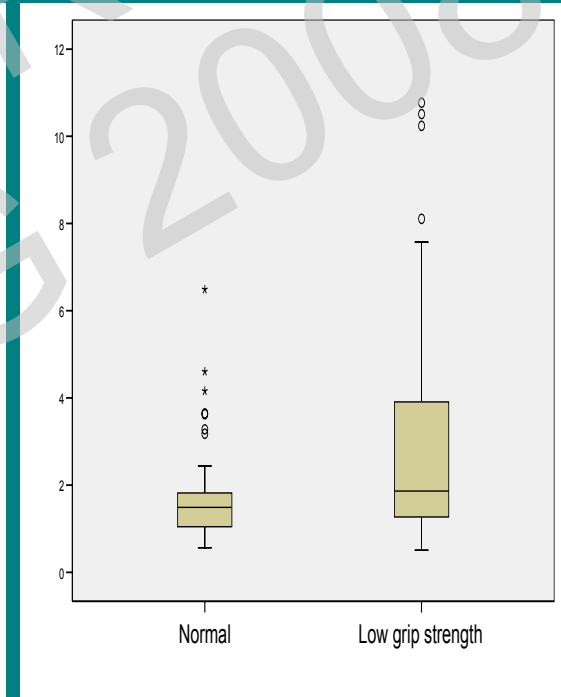
$p < 0.005$

FRIED



$p < 0.005$

GRIP STRENGTH



$p < 0.005$

TNF- α pg/ml

BCS
HUBBARD
SPRING 2008

- CRP increased significantly according to functional criteria only
- IL-6 significantly increased according to function and grip strength
- There were no significant differences in WBC count between frailty groups

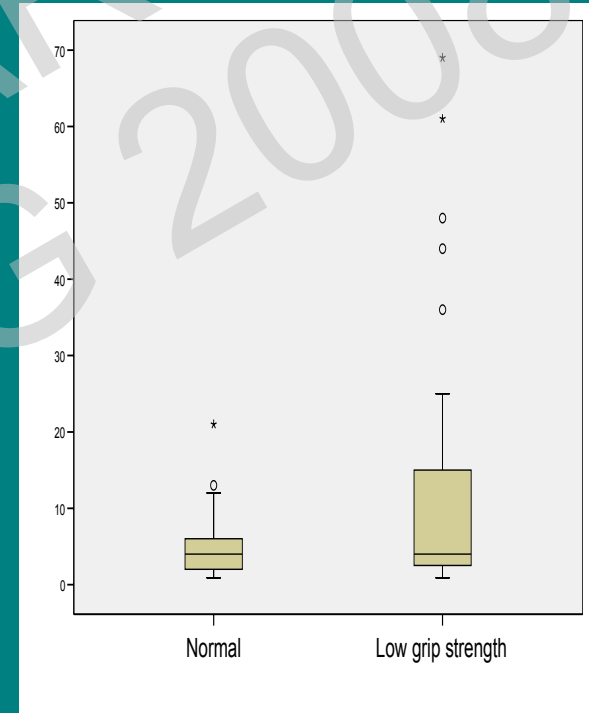
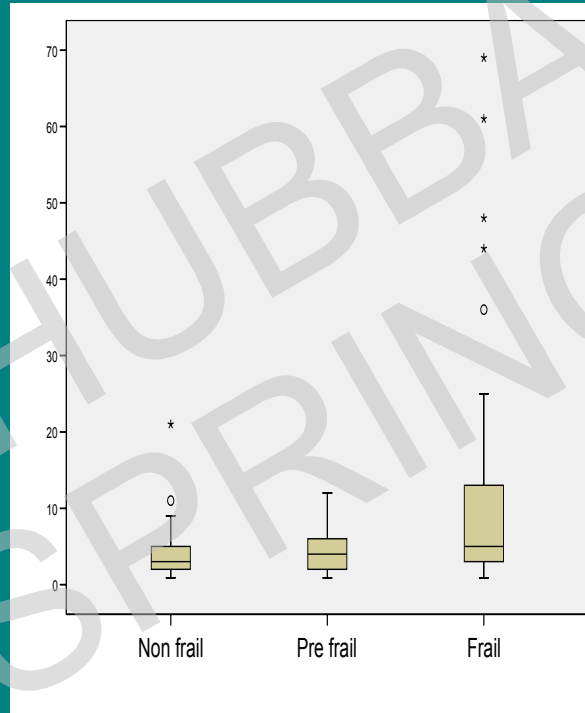
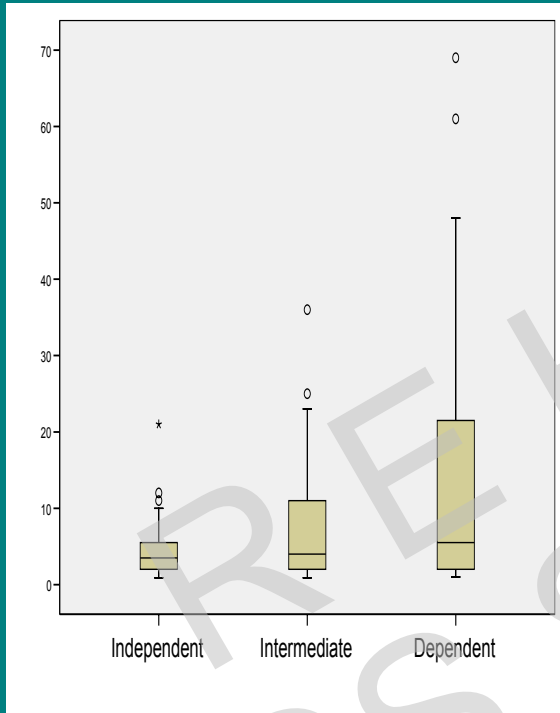
C-Reactive Protein

FUNCTION

FRIED

GRIP STRENGTH

C-reactive protein mg/l



$p < 0.005$

$p = 0.022$

$p = 0.072$

BCS
HUBBARD
SPRING 2008

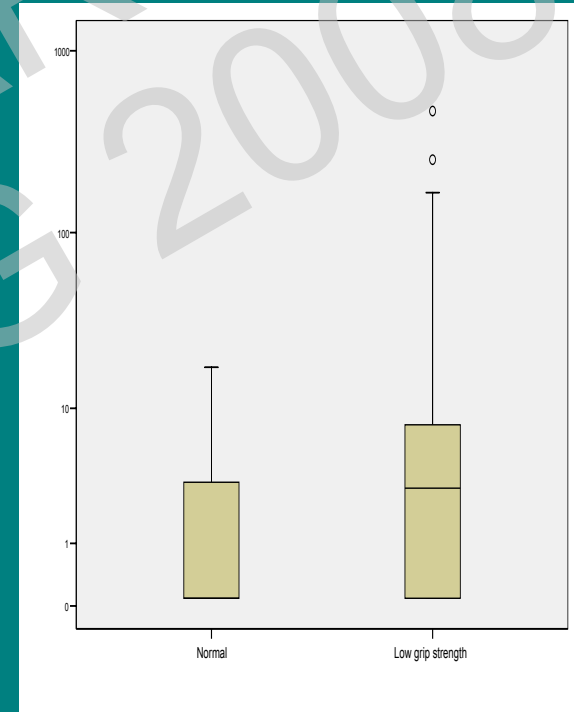
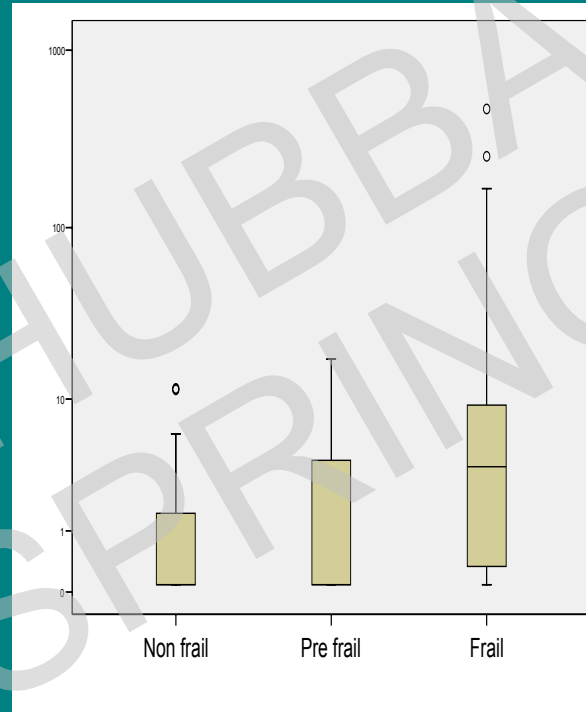
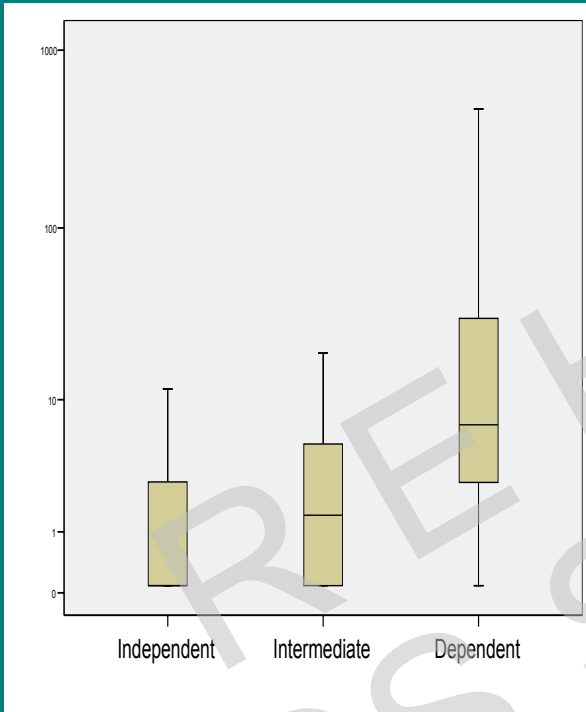
Interleukin-6

FUNCTION

FRIED

GRIP STRENGTH

Log transformed IL-6



$p < 0.005$

$p = 0.128$

$p < 0.005$

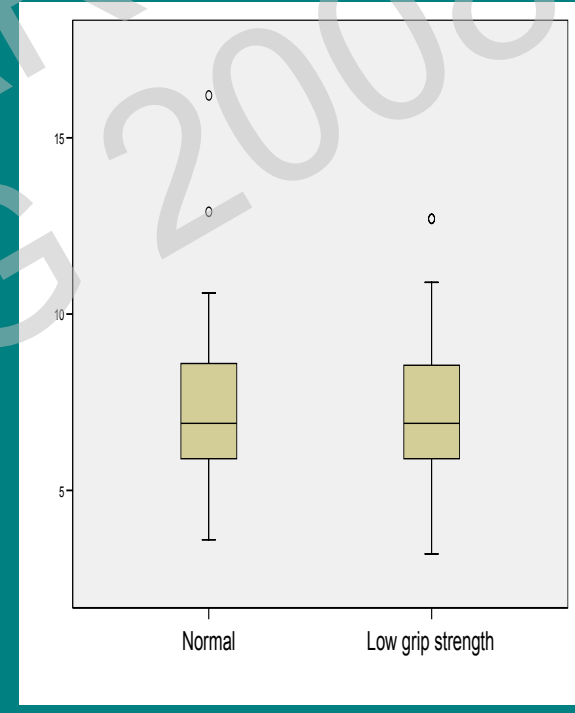
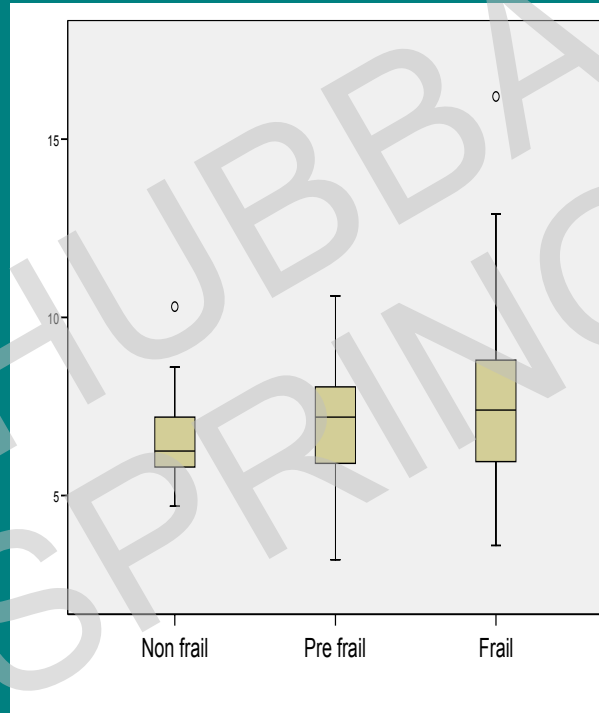
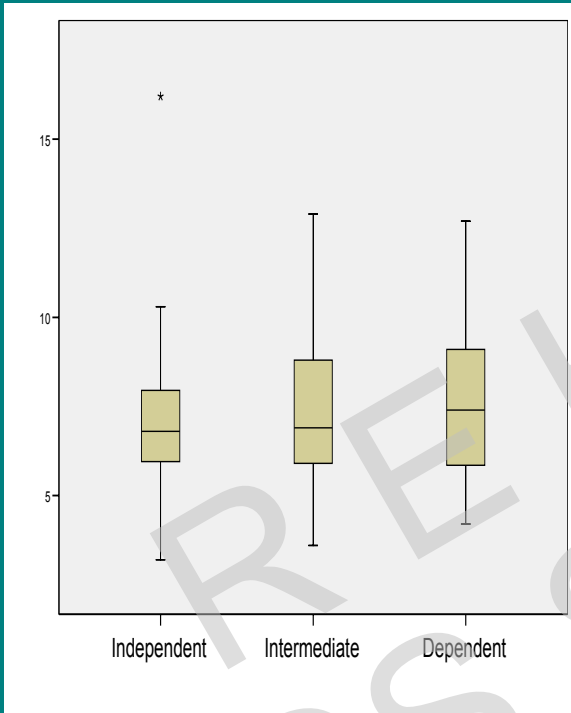
White Cell Count

FUNCTION

FRIED

GRIP STRENGTH

White cell count



$p = 0.450$

$p = 0.095$

$p = 0.757$

- Frailty Index correlated significantly with
 - log transformed CRP ($r = 0.221$, $p < 0.05$)
 - log transformed IL-6 ($r = 0.369$, $p < 0.01$)
 - TNF- α ($r = 0.379$, $p < 0.01$)
 - albumin ($r = -0.545$, $p < 0.01$)
- No correlation with WBC count ($r = 0.176$, $p = 0.072$)

Discussion

- High IL-6 levels may
 - be part of the driving force toward disability
 - anti-inflammatory strategies desirable
 - reflect a compensatory response
 - anti-inflammatory strategies undesirable
 - be an epiphenomenon ⁽¹⁸⁾
 - anti-inflammatory strategies irrelevant

Conclusions

- Frailty prevalence varies according to criteria used
- The association between frailty status and markers of inflammation is consistent

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