# *Frailty Index Study: A Challenge Study to Quantify Fatigue*

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**Abstract**
*Background:* Frailty indices have been assessed worldwide using Index by the Fried et al. (2001). The index consists of five indicators: (1) unintentional weight loss, (2) self-reported fatigue, (3) weakness (grip strength), (4) slow walking speed, and (5) low physical activity. Of these, the self-reported fatigue index is a subjective assessment and may differ from objective assessments of physical and mental fatigue. There is a need to investigate whether subjective fatigue can be replaced by an objective measure. *Purpose:* We examine the relationship between subjective fatigue and indicators of chronic fatigue syndrome and to investigate factors that influence subjective fatigue. *Methods:* We measured a measure of autonomic nervous system activity in 1258 people. *Result:* Results Study 1: TP, ccvTP, LF and HF decrease with age; LF/HF (stress index) is independent of age. Study2-1: Fatigue, muscle mass and lean body mass are strongly negatively correlated. In relation to age and body composition, age and body fat percentage and fat mass, total body muscle score, muscle mass, estimated bone mass, and body water content showed a non-significant negative correlation. Study 2-2: There was a non-significant negative correlation between subjective fatigue and HF, LF/HF, TP and ccvTP. Study 2-3: There were correlations between subjective fatigue and muscle mass, lean body mass, bone mass, and body water content. *Conclusions:* Autonomic nervous system indices may be associated with subjective fatigue in Japanese older adults. The results suggest that subjective fatigue may be associated with body composition.

Keywords: Frailty Index, Subjective Fatigue, Autonomic Nervous System, Body Composition, Older Adults

## Introduction

In our research projects, we have investigated the early detection of frailty and provide guidelines to improve health promotion and quality of life for individual older adults. The global assessment of frailty is based on the Frid Frailty Index with 5 indicators. The Japanese Geriatrics Society also proposes the J-CHS with 5 indicators to assess frailty in older adults (Satake & Arai, 2020). The index consists of five indicators, which are (1) unintentional weight loss, (2) self-reported fatigue, (3) weakness (grip strength), (4) slow walking speed, and (5) low physical activity.

In our previous study, we examined the relationship between expiratory pressure and grip strength in 232 community-dwelling older adults. The results showed a moderate positive correlation between grip strength and brachial muscle area, and a weak significant positive correlation between grip strength and expiratory pressure (Kariya, et al., 2019).

Subsequent studies have focused on indicators that are effective in the early detection of pre-frailty (Kariya, et al., 2021). Twenty-nine middle-aged and older community-dwelling adults participated in the study. Frailty was measured using the Revised Japanese Cardiovascular Health Study Standards (Revised J-CHS Standards), as well as expiratory pressure and brachial muscle circumference as indicators.  Since there was a correlation between grip strength, arm circumference (AC), arm muscle circumference (AMC), and expiratory pressure, frailty was assessed using expiratory pressure measurements as an indicator for the older adults who could not measure grip strength. In particular, expiratory pressure has a high contribution to the upper body pre-frailty index and a high correlation with the level of assistance and care required.

The above review suggests that the use of expiratory pressure as an alternative index of grip strength is effective for older adults with dementia, rheumatism, and diseases of the bones and nerves in the fingers who have difficulty receiving instruction.

In the course of daily management and teaching of health promotion classes and various experiences, we were confronted with a new research question.

The problems are that the self-reported fatigue indicator is either yes or no. It is subjective and does not accurately capture the feeling of fatigue because it is a questionnaire that asks about the feeling of fatigue over the past two weeks, although the feeling of fatigue changes daily and has diurnal fluctuations.

Even when data are collected prospectively and the life backgrounds of older adults are understood, the question "I don't feel tired." and immediately after that we see cases where they have car accidents or fall and break bones.

The purpose of this study is to examine the relationship between subjective fatigue and (1) autonomic indices and (2) body composition, and to investigate whether physiological indices can be used to assess the relationship between subjective fatigue and (1) autonomic indices.

## Literature Review

We reviewed the literature that focused on the measurement of fatigue, the relationship between fatigue and the autonomic nervous system.

A variety of fatigue measures existed. It is important to select an appropriate frailty scale depending on the type of fatigue of interest (Knoop, 2019). Fatigue is a multidimensional symptom and that individual dimensions of fatigue can be measured by validated clinical measures (Billones, 2021). Garis et al. reported that fatigue and heart rate variability (HRV) may have relationships and may be an indicator.

Vreijling, et al (2021) reported that lower HF HRV was found in patients with medically unexplained physical symptoms (MUPS) compared to healthy population. These results explain the potentiality of using HRV in the analysis of diagnosis and treatment of MUPS related symptoms. Differences in autonomic response between patients with CFS and healthy population (Van Cauwenbergh, et al. 2014).

Functional Somatic Syndromes (FSSs) and Somatic Symptom Disorders (SSDs) patients have significantly lower Heart Rate Variability (HRV) compared to healthy individuals (Ying-Chih, et al., 2020). Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) patients have altered autonomic cardiac regulation compared to healthy controls (Nelson, et al., 2019). Lower HF-HRV in patients with medically unexplained physical symptoms (MUPS) indicates autonomic nervous system dysregulation, particularly lower parasympathetic activity (Vreijling, et. al. 2021).

**Research Methods**

*Study Design:* Observational study
*Study period:* December 2014 - June 2023
*Research Index:* the J-CHS index recommended by the Japan Geriatrics Society as our research index.
*Study Location:* Several cities in Shiga, Hiroshima, and Okayama prefectures in Japan
*Study participants:*

Study 1: 1258 participants in the research program (age *M*=39.47, *SD*=17.37).
Study 2: 12 participants (age *M*=72.75, *SD*=5.53) in the frailty prevention program were selected from Study 1.

The following measures were administered: (1) presence/absence of fatigue, (2) fatigue level (assessed on 6 levels: 0, 1, 2, 3, 4, and 5), (3) autonomic nervous system index, and (4) body composition.

This project is approved by the Institutional Review Board at the Prefectural University of Hiroshima.

**Measurement**

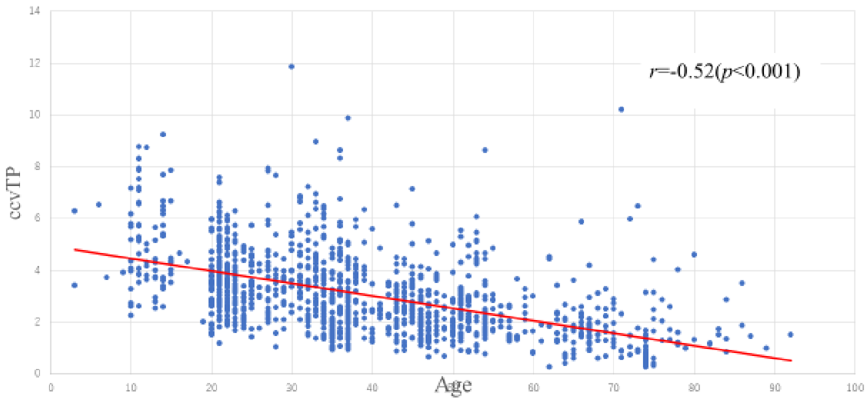
Gender, age, HRV (Murata Manufacturing Co., Ltd.), body composition analyzer (Tanita), blood pressure, SpO2, fatigue, expiratory pressure, grip strength, height, weight.

## Results

### *Study1: 1,258 Participants in the Research Program*

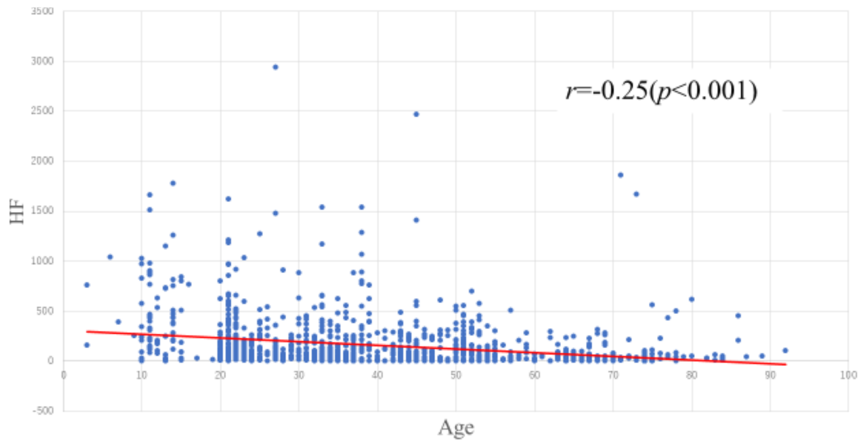
1) The higher the ccvTP, the lower the age (Figure 1)

Figure 1: Scatter Plot of Age and ccvTP($n$=1258)



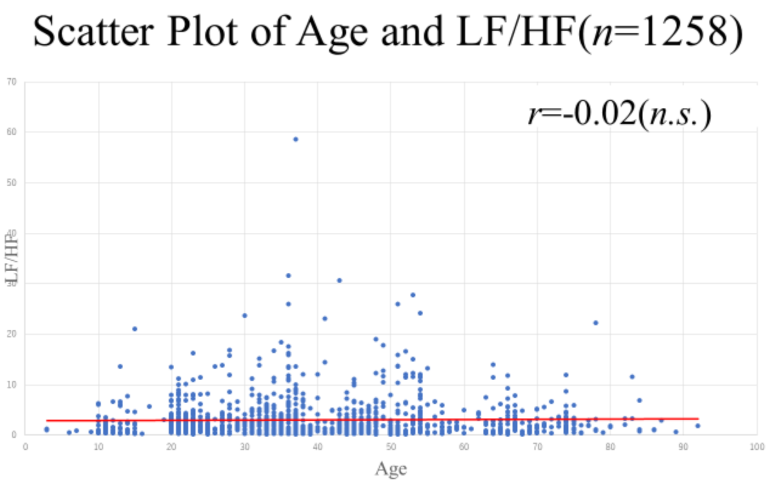

2) HF and age have a weak negative correlation ($r$=-0.25, $p < 0.00$) (Figure 2)

Figure 2: Scatter Plot of Age and HF($n$=1258)



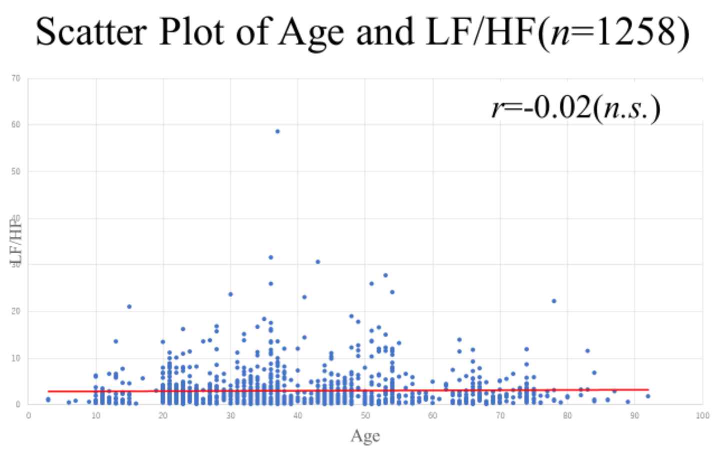
3) Weak negative correlation between LF and age ($r$=-0.25, $p$＜0.001) (Figure 3)

Figure




4) LF/HF as a stress index is independent. ($r$=-0.02, *n.s.*) (Figure4)

Figure



***Study 2-1: Age-Related Changes in Body Composition***

1) Total body muscle mass decreases with age ($r$=0.57,$p$=0.049) (Figure 5)

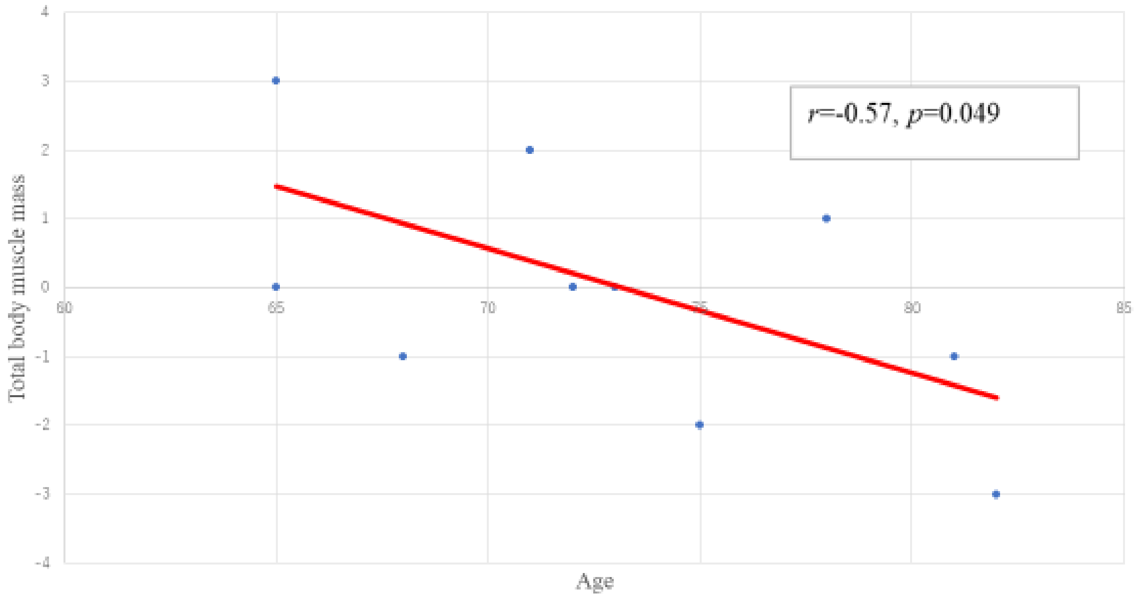



Figure 5 Scatter Plot of Age and Total Body Muscle Score($n$=12)

2) Fat mass decreased with age ($r$=0.44, $p$=0.14) (Figure 6)

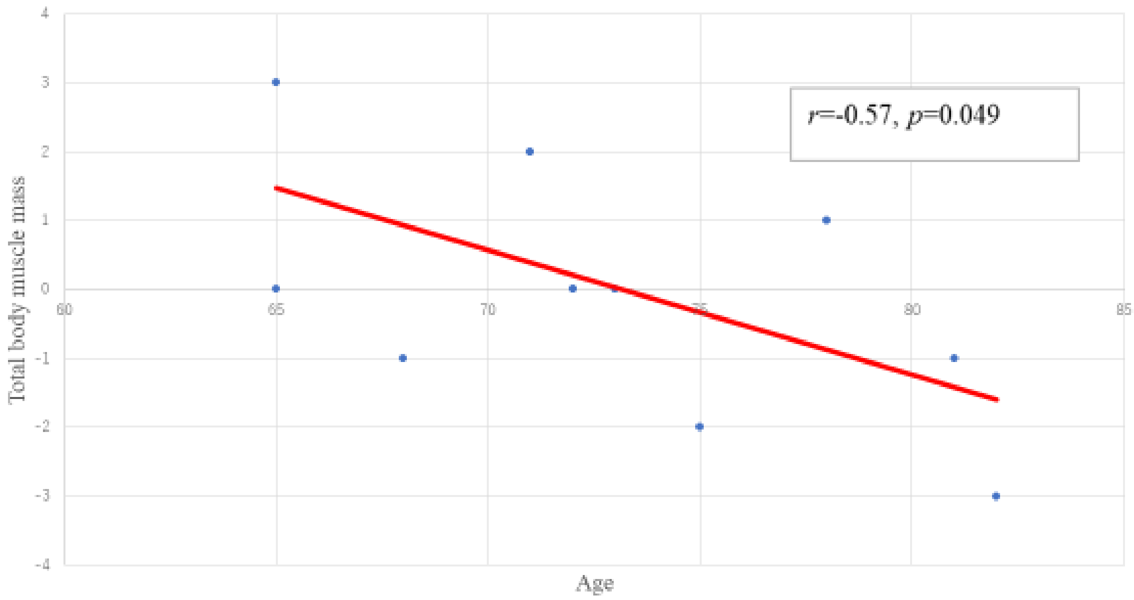



Figure 5 Scatter Plot of Age and Total Body Muscle Score($n$=12)

3) Body fat percentage decreased with age ($r$=0.42, $p$=0.16) (Figure 7)

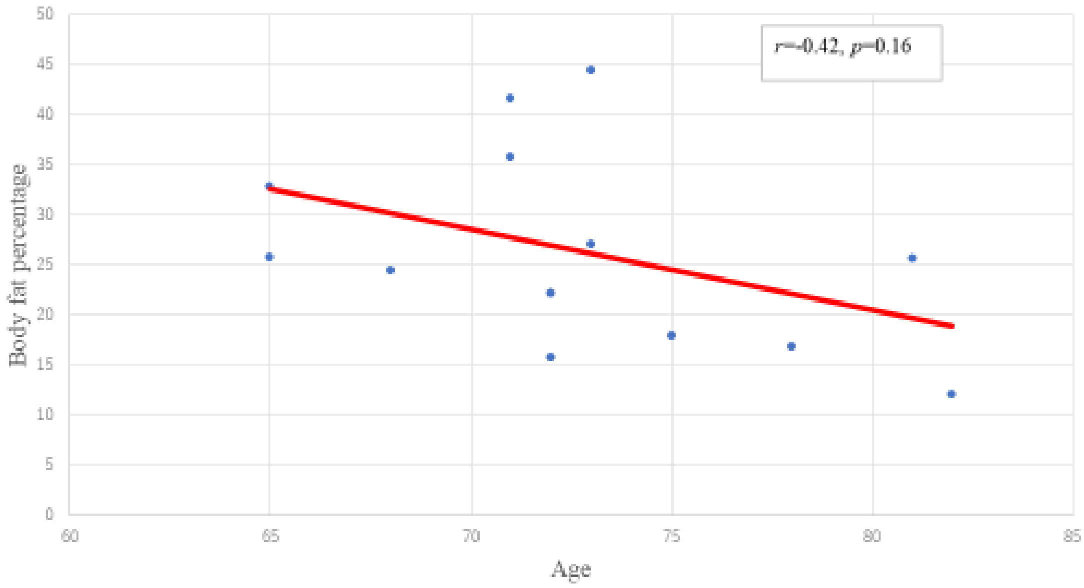



Figure 7 Scatter Plot of Age and Body fat percentage ($n$=12)

4) Bone mass decreased with age ($r$=0.31, $p$=0.32) (Figure 8)

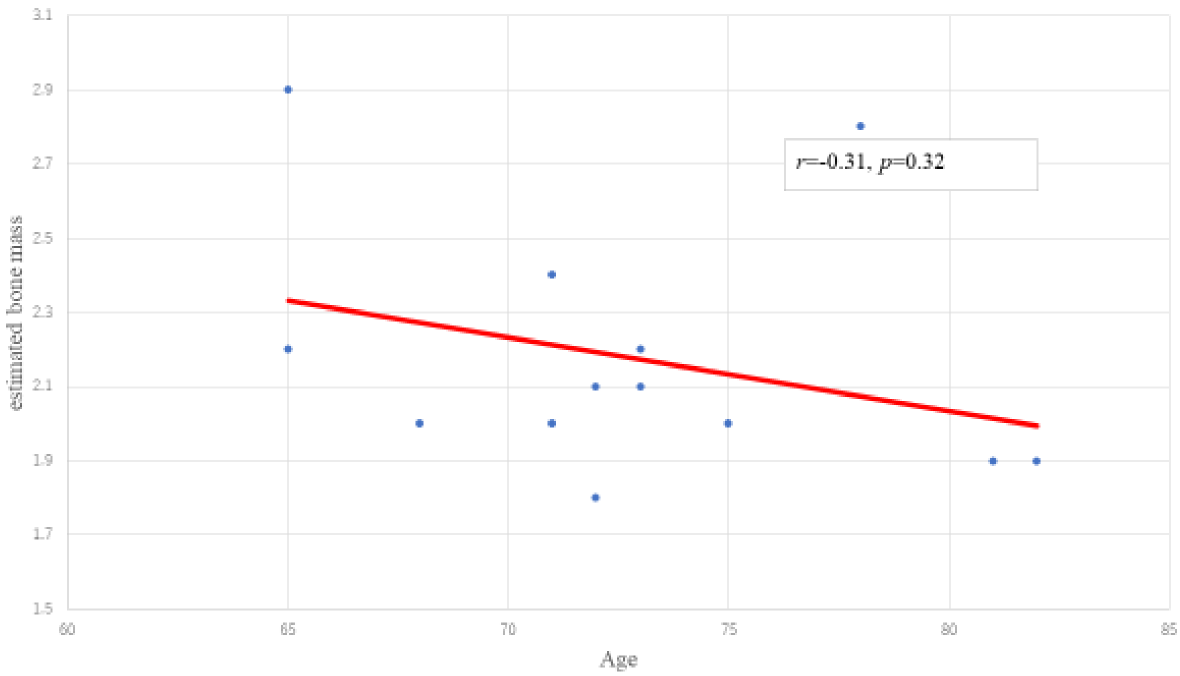



Figure 8 Scatter Plot of Age and estimated bone mass($n$=12)

5) Body water content decreased with age ($r$=0.30, $p$=0.34) (Figure 9)

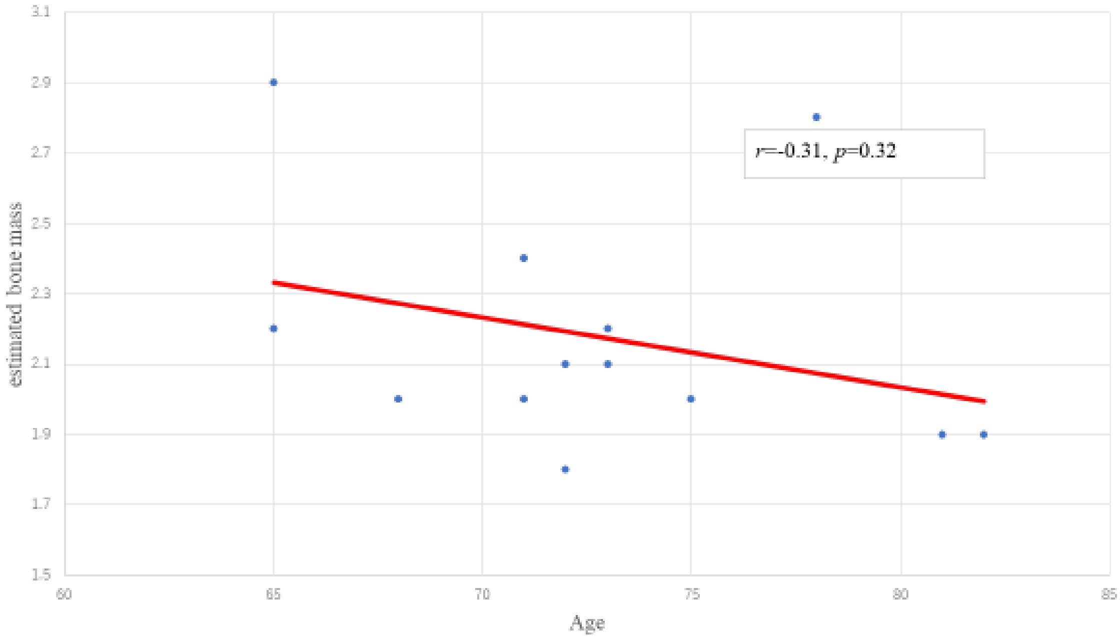



Figure 8 Scatter Plot of Age and estimated bone mass($n$=12)

6) Total Body Muscle Score decreases with age ($r$=-0.57, $p$=0.049) (Figure 10)

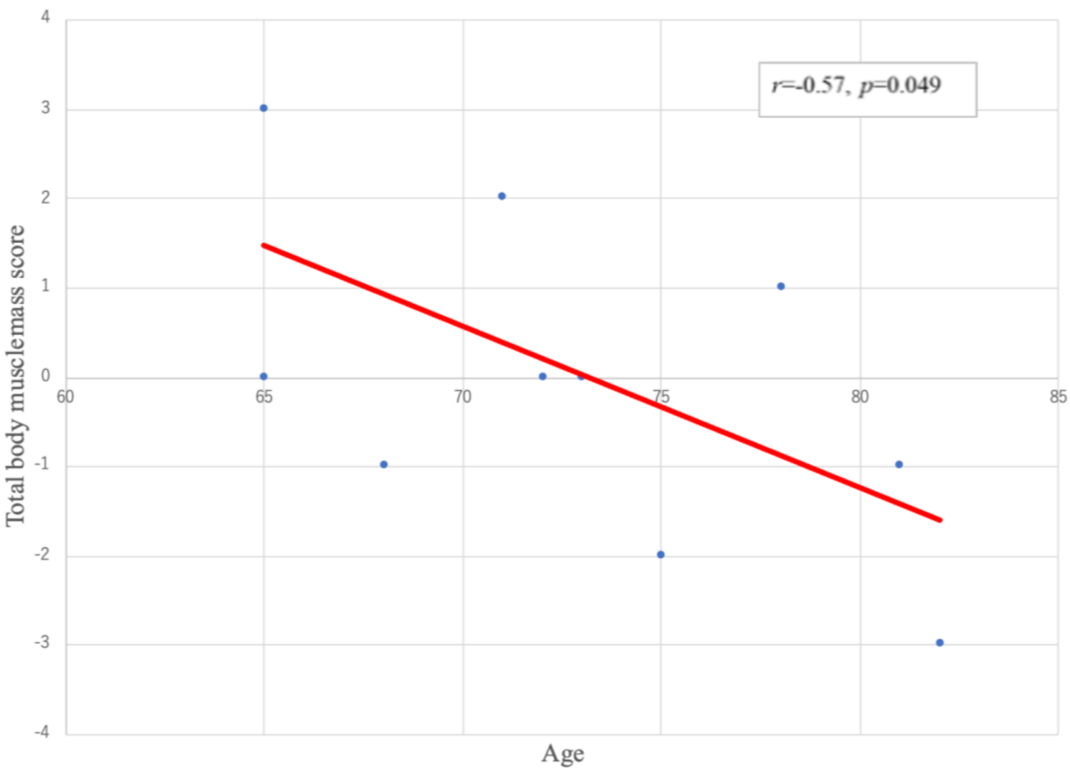



Figure 10 Scatter Plot of Age andTotal body musclemass score ($n$=12)

***Study 2-2: Relationship Between Fatigue and Autonomic Nervous System (Figure6)***

1) There was a positive correlation between fatigue level and age of autonomic function (*r*=0.33, *p*=0.32).(Figure11)

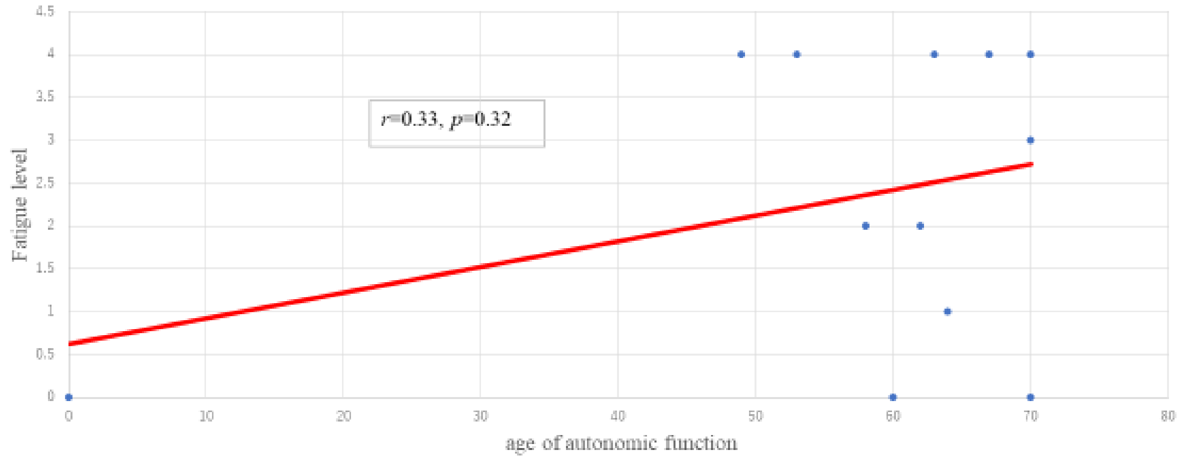



Figure 11 Scatter Plot of fatigue and age of autonomic function (*n*=11)

2) There was a negative correlation between fatigue level and HF (parasympathetic index) (*r*=-0.23, *p*=0.47) (Figure12)

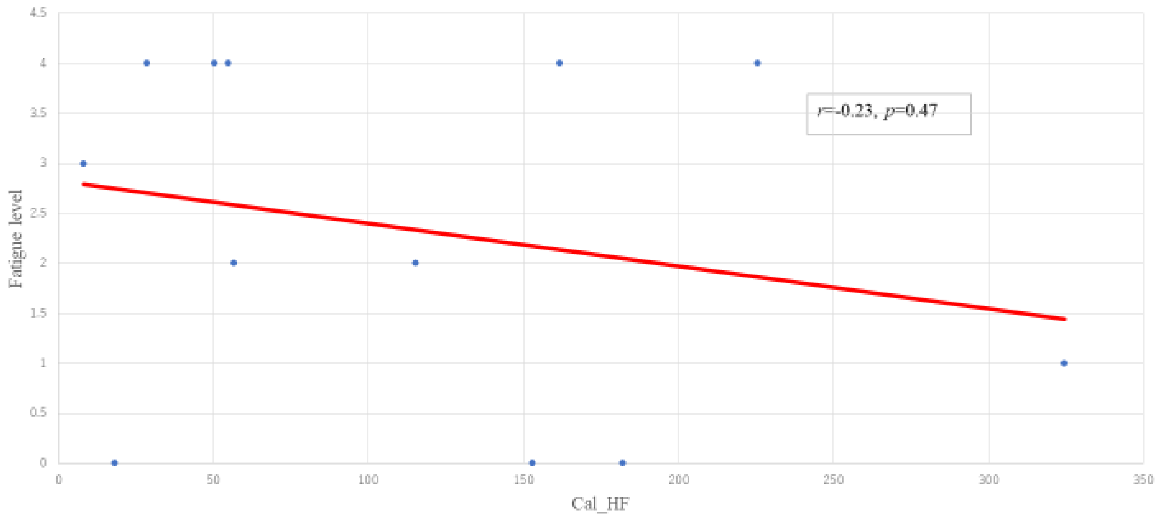



Figure 12 Scatter Plot of fatigue and Cal_HF(*n*=11)

***Study 2-3 Relationship Between Subjective Fatigue (Assessed on 6 Levels: 0, 1, 2, 3, 4, and 5) and Body Composition***

1) A t-test was performed with the degree of fatigue as the independent variable and the autonomic index and body composition as the dependent variables, all of which were not significant. (Table 1 and Table 2)

Table1:Result of t-test1; Binary subjective fatigue index and autonomic nervous index

| | **Group*** | ***n*** | ***M*** | ***SD*** | ***t*** | ***df*** | ***p*** |
|---|---|---|---|---|---|---|---|
| LH/HF | 1 | 6 | 3.29 | 2.43 | -0.40 | 10 | 0.70 |
| | 2 | 6 | 4.05 | 4.05 | | | |
| TP | 1 | 6 | 416.53 | 480.45 | 0.34 | 10 | 0.74 |
| | 2 | 6 | 343.06 | 238.82 | | | |
| ccvTP | 1 | 6 | 2.17 | 1.16 | 0.52 | 10 | 0.62 |
| | 2 | 6 | 1.89 | 0.64 | | | |
| LF | 1 | 6 | 320.32 | 438.04 | 0.56 | 10 | 0.59 |
| | 2 | 6 | 209.58 | 198.52 | | | |
| HF | 1 | 6 | 96.21 | 78.67 | -0.65 | 10 | 0.53 |
| | 2 | 6 | 133.49 | 117.06 | | | |

Table2:Result of t-test2; Binary subjective fatigue index and body composition

| | **Group*** | ***n*** | ***M*** | ***SD*** | ***t*** | ***df*** | ***p*** |
|---|---|---|---|---|---|---|---|
| Autonimic Nurves Age | 1 | 6 | 60.67 | 8.12 | 0.61 | 10 | 0.55 |
| | 2 | 6 | 53.67 | 26.76 | | | |
| Body Fat rate | 1 | 6 | 26.13 | 7.25 | -0.06 | 10 | 0.96 |
| | 2 | 6 | 26.50 | 13.62 | | | |
| Fat Mass | 1 | 6 | 13.60 | 5.78 | -0.60 | 10 | 0.56 |
| | 2 | 6 | 16.50 | 10.25 | | | |
| Mass except Fat | 1 | 6 | 36.68 | 2.37 | -1.50 | 10 | 0.17 |
| | 2 | 6 | 42.37 | 8.98 | | | |
| Muscle Mass | 1 | 6 | 34.62 | 2.15 | -1.52 | 10 | 0.16 |
| | 2 | 6 | 40.08 | 8.54 | | | |
| Total Body Muscle Score | 1 | 6 | 0.00 | 1.10 | -0.16 | 10 | 0.88 |
| | 2 | 6 | 0.17 | 2.32 | | | |
| Estimated Bone Mass | 1 | 6 | 2.07 | 0.22 | -1.07 | 10 | 0.31 |
| | 2 | 6 | 2.28 | 0.45 | | | |
| Body Water Content | 1 | 6 | 27.15 | 2.84 | -1.44 | 10 | 0.18 |
| | 2 | 6 | 32.23 | 8.17 | | | |
| Standard Weight | 1 | 6 | 51.43 | 2.04 | -1.56 | 10 | 0.15 |
| | 2 | 6 | 54.25 | 3.91 | | | |
| Degree of Obesity | 1 | 6 | -2.32 | 13.80 | -0.94 | 10 | 0.37 |
| | 2 | 6 | 9.23 | 26.72 | | | |
| Visceral Fat Level | 1 | 6 | 4.50 | 2.17 | -1.84 | 10 | 0.10 |
| | 2 | 6 | 8.83 | 5.35 | | | |
| Footing Point | 1 | 6 | 95.33 | 4.63 | 1.55 | 10 | 0.15 |
| | 2 | 6 | 87.83 | 10.94 | | | |
| Basal Metabolism | 1 | 6 | 1038.17 | 88.93 | -1.45 | 10 | 0.18 |
| | 2 | 6 | 1182.83 | 227.01 | | | |
| Determination of Basal Metabolism | 1 | 6 | 12.50 | 3.56 | 0.67 | 10 | 0.52 |
| | 2 | 6 | 10.67 | 5.65 | | | |

*Group1: Fatigue, Group2: Not Fatigue

2) There is a negative correlation ($r$=-0.63, $p$=0.04) between subjective fatigue and muscle mass. (Figure13)

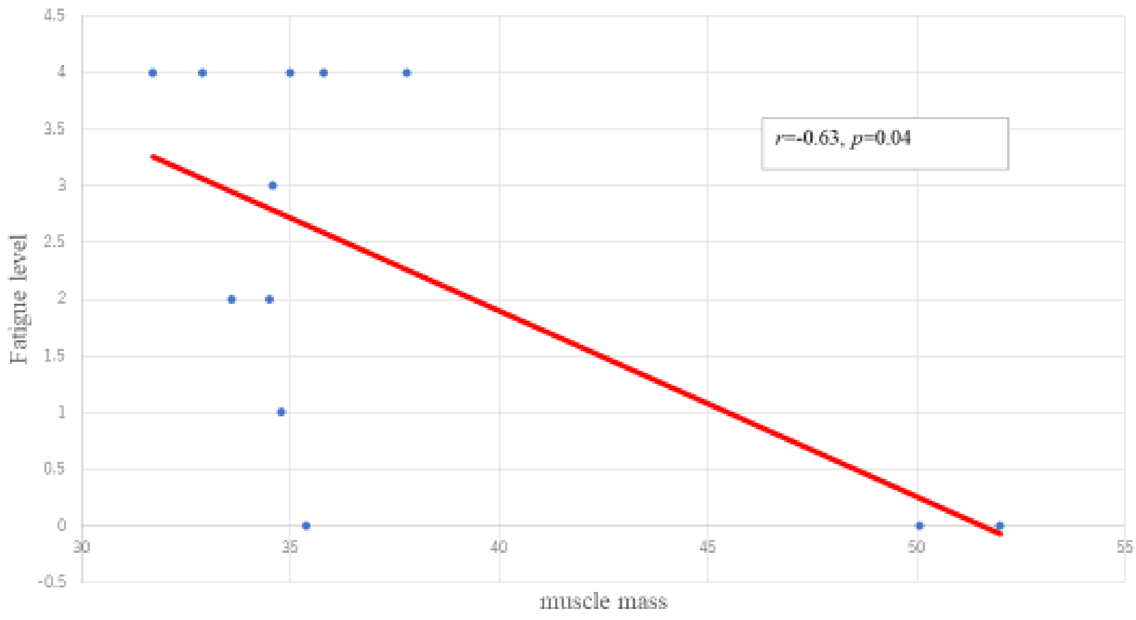



Figure 13 Scatter Plot of fatigue level and muscle mass($n$=11)

3) There was a negative correlation ($r$=-0.62, $p$=0.04) between subjective fatigue and lean body mass. (Figure14)

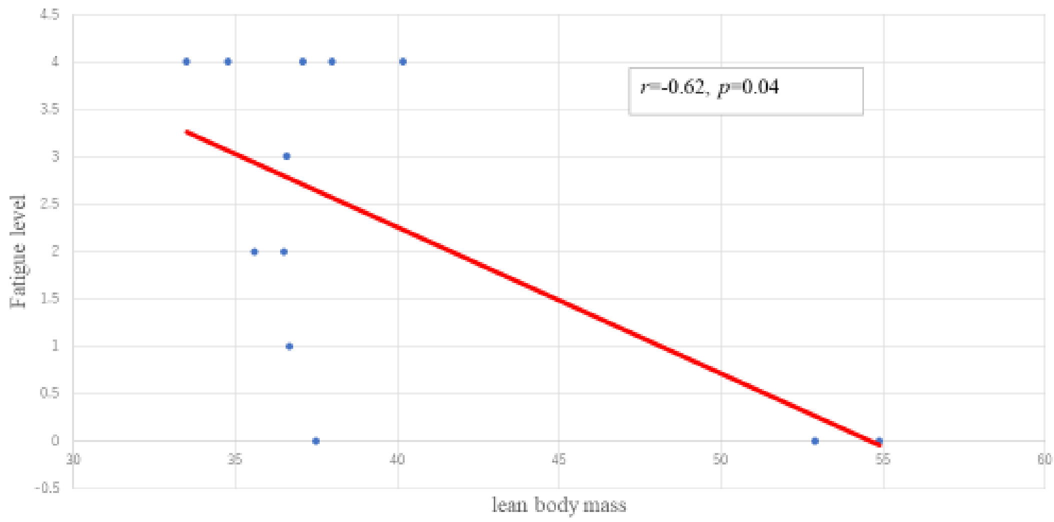



Figure 14 Scatter Plot of fatigue level and lean body mass ($n$=11)

4) Negative correlation ($r$=-0.57, $p$=0.065) between subjective fatigue level and body water content. (Figure15)

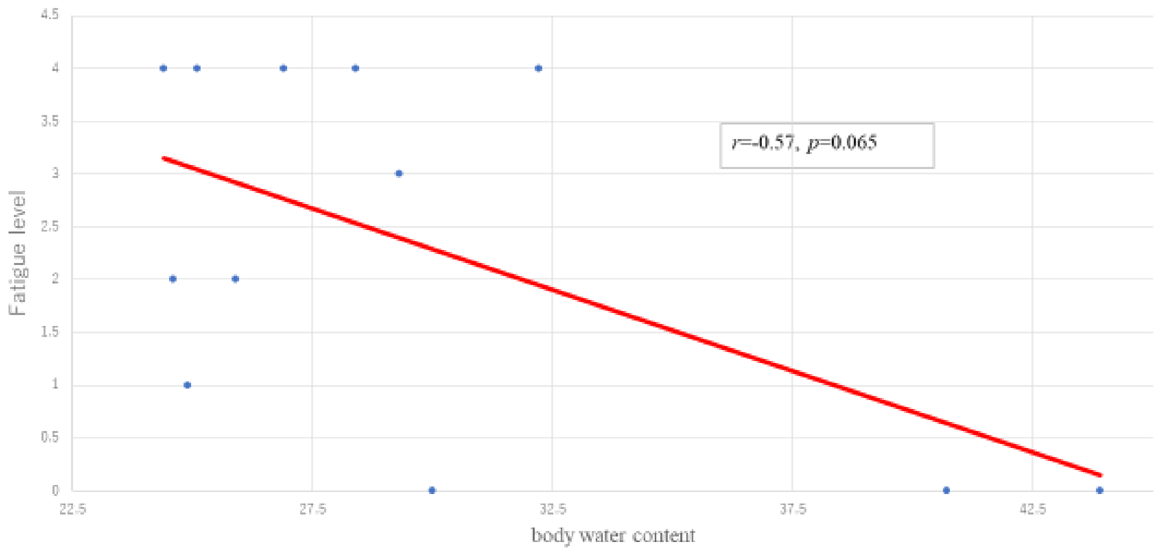



Figure 15 Scatter Plot of fatigue level and body water content ($n$=11)

## Discussion

- The finding that fatigue can be assessed by objective measures of the autonomic nervous system supports previous studies.
- The relationship between fatigue and HF in the elderly needs to be investigated.
- In this study, body composition was investigated among the factors affecting subjective fatigue in the elderly, but psychological anxiety and activity should also be investigated.

## Conclusions and Implication

- The results suggest that a two-choice "yes/no" fatigue index may not reflect an objective assessment.
- Autonomic nervous system indices may be associated with fatigue in the elderly in Japan. In particular, the association with HF (parasympathetic index) supported previous studies.
- The results suggest that body composition may be associated with fatigue. In particular, it may be related to muscle mass, bone mass, and body water content.

Further studies are needed to examine the relationship with psychological factors such as activity, sleep duration, and anxiety.

## Notes

About Autonomic Nervous System Indicators (Fatigue Science Laboratory, n.d.) translated by authors:

(1) LF: Power values obtained from spectral analysis of heart rate variability are integrated in the frequency band of 0.04 to 0.15 Hz. Power values obtained from spectral analysis of heart rate variability are called LF (Low Frequency) and mainly include sympathetic components.
(2) HF: The power value integrated in the frequency band of 0.15 to 0.4 Hz is called HF (High Frequency) and mainly includes the sympathetic component.

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