

Article

Not peer-reviewed version

# Different Effects of Functional Food and Music Aerobic Exercise on Complete Blood Counts, Blood Biochemistry and Frailty of the Elderly

Shu-Hui Yeh , Chia-Hua Lee , [Ming-Tsung Lee](#) , [Jeng-Hwan Wang](#) , Mu-Hsuan Pan , [Wen-Chien Sung](#) , [Kuender D Yang](#) \*

Posted Date: 13 July 2023

doi: 10.20944/preprints202307.0893.v1

Keywords: functional food, music aerobic exercise, complete blood counts, biochemistry, frailty



Preprints.org is a free multidiscipline platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This is an open access article distributed under the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

## Article

# Different Effects of Functional Food and Music Aerobic Exercise on Complete Blood Counts, Blood Biochemistry and Frailty of the Elderly

Shu-Hui Yeh <sup>1</sup>, Chia-Hua Lee <sup>2</sup>, Ming-Tsung Lee <sup>3</sup>, Jeng-Hwan Wang <sup>4</sup>, Mu-Hsuan Pan <sup>1</sup>, Wen-Chien Sung <sup>5</sup> and Kuender D. Yang <sup>6,\*</sup>

<sup>1</sup> Institute of Long-term Care, Mackay Medical College, New Taipei City, Taiwan; yehshuhui@mmc.edu.tw

<sup>2</sup> Department of Nursing, Suang-Lien Elderly Center, New Taipei City, Taiwan; hau0831@yahoo.com.tw

<sup>3</sup> National Center for Geriatrics and Welfare Research, National Health Research Center, Yunlin County, Taiwan; lee6717kimo@yahoo.com.tw

<sup>4</sup> Department of Food Beverage Management, MacKay Junior College of Medicine, Nursing and Management, Taipei, Taiwan; s319@mail.mkc.edu.tw

<sup>5</sup> Department of Food Science, National Taiwan Ocean University; sungwill@mail.ntou.edu.tw

<sup>6</sup> Department of Medical Research, MacKay Memorial Hospital, Taipei, Taiwan; yangkd.yeh@hotmail.com

\* Correspondence: yangkd.yeh@hotmail.com; Tel.: +886-905239268

**Abstract:** (1) Background: The elderly who have chewing difficulty (CD) are prone to malnutrition, frailty, and sarcopenia, and those with insufficient physical activity (IPA) are also prone to frailty, overweight, and high blood cholesterol. There is an urgent need to prepare functional foods and to promote healthy physical activity for the elderly over 70 years of age to prevent poor nutrition and frailty. (2) Methods: This study prepared functional foods (FF) with softened chicken moose and milkfish without fin for the elderly and compared the different effects of FF from those of music aerobic exercise (MAE) on the complete blood counts, blood biochemistry, including nutrition index of albumin, and cholesterol levels, and frailty scores before and after institution of FF and MAE among residents of long-term care institutes. (3) Results: The FF significantly increased the high-density lipoprotein cholesterol and albumin levels. In contrast, MAE significantly increased red blood cells (RBC), and decreased the rates of frailty items on fatigue feeling and low physical activity. In comparison between FF and MAE groups, we found that the FF for 5 weeks significantly improved better on HDL-C and MCV while the MAE for 10 weeks improved significantly better on hematopoiesis as increases in red blood cells and platelets. (4) Conclusions: Results from this study suggest that FF and MAE for the elderly have different effects on nutrition status, blood biochemistry and frailty. A combination of both FF and MAE might provide better benefits of nutrition status, physical function, and frailty for the elderly.

**Keywords:** functional food; music aerobic exercise; complete blood counts; biochemistry; frailty

## 1. Introduction

Older adults with chewing difficulty (CD) are prone to insufficient intake of meat and plant fibers. They are more likely to cause many health problems, such as malnutrition, frailty, and sarcopenia [1,2]. Similarly, the elderly with insufficient physical activity (IPA) are prone to frailty, sarcopenia, and anabolic resistance to muscle metabolism [3]. The prevalence of CD and IPA in the elderly with sarcopenia has increased by over 30% and 50%, respectively [4–7].

The elderly with CD and/or IPA are closely correlated to frailty [8] and linked with geriatric syndrome [9]. There is an urgent need to promote healthy physical activity and prepare functional foods for the elderly to prevent malnutrition and frailty. We have previously shown that moderate exercise such as Tai Chi Chuan, Yoga, and music aerobic exercise (MAE) could enhance immune function, stress adaptation, and neural function [10–14]. Tai Chi Chuan exercise for 12 weeks improved immune regulation and neuropathy [10,11], Yoga exercise could improve stress adaptation [12], and MAE could enhance immune function [13], decrease depression, and increase brain-derived neurotrophic factor levels [14]. We also found that CD is prevalent in nursing homes and correlated

to the institution of gastric tube feeding and frailty [5,15]. Here, we postulated that the FF made in softened meat and jelly fruit juice for the elderly could be comparable to or different from the effects of the MAE on frailty and blood biochemistry.

This study aimed to compare the different effects between the moderate exercise of music (MAE) and functional food (FF) made in softened chicken meat or fish with antioxidant herbs and fresh jelly fruit juices on complete blood counts, blood biochemistry including nutrition index of albumin, and cholesterol levels, and rates of the frailty items among residents of long-term care institutes.

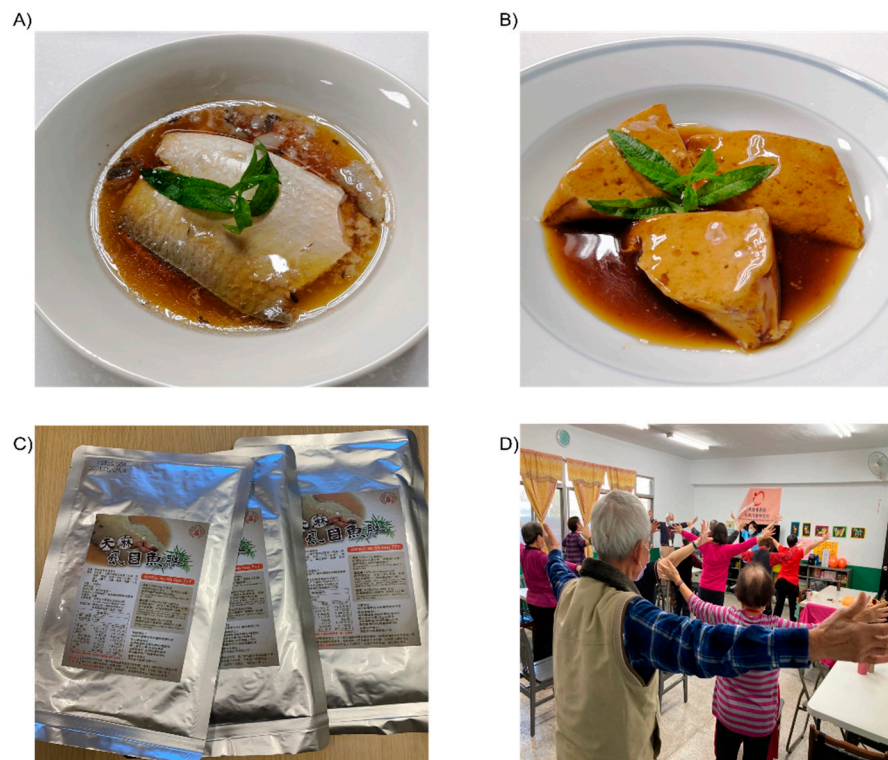
## 2. Materials and Methods

### 2.1. Study Design

This quasi-experimental research was conducted in communities around the northeastern coast of Taiwan. Eighty-five older adults in eight long-term care institutes were recruited to participate in the FF group (n = 36 in 4 institutes) or MAE group (n = 49 in 4 institutes) after obtaining informed consent for the participation agreement from the institutes and residents. This comparative study was initially designed to do a parallel comparison between FF and MAE groups for ten weeks. During the COVID-19 pandemic, the quarantine policy for group meals at long-term care facilities was changed to prohibit extramural preparation of group meals so that the study period of the FF group was cut off at five weeks. The MAE group performed the study as scheduled three times a week, each for 50 minutes of performance for ten weeks. Inclusion criteria are the elderly over 65, who signed the participation agreement and moved independently. Exclusion criteria for participation are those who were bedridden, unable to move or eat softened food.

### 2.2. Preparation of functional foods

Functional foods, including softened chicken meat, softened milkfish, and jelly fruit juice for the elderly with CD, were made in tongue-crushed food with a physical property tester of less than  $2.0 \times 10^4$  N/m<sup>2</sup> [16]. Choosing a technique of vacuum low-temperature cooking of the meat and fish with phytochemical-rich herbs makes meat sufficiently soft to be broken up by the tongue and gives a good taste of herbs' fragrance. The FF included softened milkfish (Figure 1A) and chicken moose (Figure 1B) with herbs containing ginseng and wolfberry, and the jelly fruit juice was made from golden and green fruits (apple, pineapple, kiwi, and strawberry) prepared by a central kitchen. The low-temperature cooking foods were put into the vacuum packaging of aluminum foil for better storage for six months (Figure 1C). The two FF products fulfilled the Microbiological Standards for Frozen Foods requirement at less than ten colony-forming units of *E. coli*. The FF group consumed original meals plus chicken moose and milkfish five packs and two bottles of fresh fruit jelly per week for five weeks.



**Figure 1.** Presentation of functional food (FF) and music aerobic exercise (MAE). A) The FF of softened milkfish without fin; B) The FF of chicken moose with herbs fragrance prepared by a central kitchen; and C) The low-temperature cooking foods were put into the vacuum packaging of aluminum foil for better storage of 6 months. D) The MAE practice with musical rhythm in a long-term care center.

### 2.3. Moderate exercise of music aerobic exercise (MAE)

The physical activity for the elderly with IPA should be moderate exercise and harmonious balance without cardiopulmonary exacerbation. Previous studies [13,14] showed that the MAE was a moderate exercise for community adults, effectively improving stress adaptation and immune regulatory function. The MAE included rhythmic exercise for 50 minutes (10 minutes of warm-up, 30 minutes of musical exercise, and 10 minutes of cool-down exercise) 3 times a week for ten consecutive weeks. Before and after the program, the participants received tests on frailty, biochemistry, and complete blood counts.

### 2.4. Assessment of complete blood counts and biochemistry

Blood samples (5 ml) were subject to measurement of CBC and biochemistry. The biochemistry, including high-density lipoprotein cholesterol (HDL-C, mg/dl), low-density lipoprotein cholesterol (LDL-C, mg/dl), and albumin (gm/dl), were measured by Roche c702 (Roche Diagnostics, Indianapolis, USA). The complete blood counts including WBC (cells/ul), RBC ( $\times 10^6$ /ul), Hemoglobin (gm/dl), Hematocrit (%), MCV (pl/cell), MCH (pg/cell), MCHC (gm/dl), Platelet ( $\times 10^3$ /ul), Neutrophil (cells/ul), Lymphocyte (cells/ul), Monocyte (cells/ul), Basophil (cells/ul) and Eosinophil (cells/ul) were measured by Sysmex XP300 (Sysmex Diagnostics, Seattle, USA).

### 2.5. Measurement of the rate changes of the frailty items

Employing Fried's frailty assessment scales, including body weight loss, fatigue feeling, low physical activity, decreased muscle strength, and slowed walking speed [17], we assessed the rate changes of the frailty items before and after the FF or MAE program. The cut-off values for the frailty items were defined as 1) Weight loss: less than 20% of peers; 2) Fatigue feeling: tired 3 or more days a week; 3) Decreased muscle strength: grip strength test in male (female)  $< 26$  (18) kg determined by a digital hand dynamometer (Handexer Inc., Sacramento, CA); 4) Slowly walking speed less than 0.8



m/s (6 minutes < 288 m); and 5) Low physical activity: less than 20% of peers. The rates (percentages) of the five frailty items were assessed before and after the FF and MAE programs.

## 2.6. Data Analyses and Statistics

This study recruited the elderly in eight long-term care facilities, where the institutes and residents were willing to participate in moderate exercise or function food study. The sample size was estimated based on the effect size on the changes in cholesterol levels or blood counts at 0.2 before and after MAE or FF intake, study power of 0.8, and alpha level of 0.05. The estimated number of effective samples was calculated as 40. Statistical analyses are performed using SPSS version 22 (IBM, Inc., Armonk, NY, USA). The Chi-square test was applied to compare the difference of rates (percentages), paired t-test was applied to test the normally distributed changes before and after the FF or MAE program, and the Generalized Estimating Equation (GEE) statistics were used to compare the differences between the effects of FF and MAE.

## 3. Results

### 3.1. Demographic data of the FF and MAE groups

This study was designed to do a parallel 10-week comparison between FF and MAE groups for the different effects on nutrition biochemistry, CBC, and frailty rates. The FF study was cut off to a 5-week study due to the change of quarantine policy in the COVID-19 periodic outbreaks. Forty-nine participants in four long-term care institutes completed the 10-week MAE study, and thirty-six completed the 5-week FF study. The demographic data of the two studies are shown in Table 1. More female residents participated in the MAE group, and more male residents participated in the FF group. The population studied had an average of 76 years old. Neither group significantly differed in age, weight, height, or blood pressure.

Table 1. Demographic data of participants between FF and MAE groups

Variables	MAE (n = 49)		FF (n = 36)		Total (n = 85)	
	Mean	SD	Mean	SD	Mean	SD
Gender						
Male/female	15/34		21/15		36/49	
Age, year	78.2	5.7	73.1	7.8	76.0	7.1
Height, cm	157.0	8.4	160.1	8.8	158.3	8.7
Weight, Kg	60.3	10.1	66.3	11.5	62.8	11.0
Blood pressure						
Systolic	129.9	15.2	138.5	20.0	134.1	18.1
Diastolic	70.8	10.9	73.4	12.7	72.0	11.8

Notes: MAE, music aerobic exercise; FF functional food; SD, standard deviation.

### 3.2. Effects of the FF on Biochemistry, CBC, and frailty

As shown in Table 2, we found that the intake of FF increased the HDL-C from 48.8±12.7mg/dl to 50.8±14.6mg/dl ( $p = 0.049$ ). The albumin levels increased from 4.13±0.32g/dl to 4.25±0.27g/dl ( $p = 0.027$ ) after the intake of FF for five weeks. Total white blood cells (WBC) and red blood cells (RBC) were not significant difference before and after the intake of FF. Differential counts of WBC were not significantly different, except basophils increased significantly from 0.69 to 0.76 cells/ul. Hemoglobin (Hb) and hematocrit (Hct) levels were not significant differences, but mean corpuscular volume

(MCV) significantly increased from 91.9 to 92.4 (pl/cells ) after the intake of FF. As shown in Table 3, we found that the frailty rate in the study population was 35% ( $\geq 3$  of 5 items). The intake of FF improved the frailty at slow walking speed ( $p = 0.021$ ) but not weight loss, fatigue feeling, low physical activity, or grip strength (Table 3).

Parameters	Pre-test		Post-test		t	p
	Mean	SD	Mean	SD		
HDL-C (mg/dl)	48.8	12.7	50.8	14.6	-2.043	0.049
LDL-C (mg/dl)	99.0	33.8	96.2	34.9	0.969	0.339
Albumin (gm/dl)	4.13	0.32	4.25	0.27	-2.477	0.027
WBC (cells/ul)	6230.6	1238.3	6027.5	932.4	1.280	0.209
RBC ( $\times 10^6$ cells/ul)	4.53	0.48	4.51	0.44	0.601	0.552
Hemoglobin (gm/dl)	14.1	1.4	14.0	1.3	0.164	0.870
Hematocrit (%)	41.6	4.0	41.7	3.8	-0.231	0.819
MCV (pl/cell)	91.9	3.6	92.4	4.2	-2.218	0.033
MCH (pg/cell)	31.1	1.6	31.2	1.5	-1.245	0.221
MCHC (gm/dl)	33.8	1.1	33.7	0.9	0.879	0.386
Platelet ( $\times 10^3$ /ul)	218.0	57.4	210.6	55.7	1.748	0.089
Neutrophil (cells/ul)	60.2	10.3	60.9	8.2	-0.783	0.439
Lymphocyte (cells/ul)	29.4	9.2	29.1	7.8	0.449	0.656
Monocyte (cells/ul)	6.28	1.53	6.23	1.37	0.246	0.807
Basophil (cells/ul)	0.69	0.28	0.76	0.23	-2.236	0.032
Eosinophil (cells/ul)	3.48	2.86	3.09	1.91	1.226	0.229

Notes: *p* values are calculated by paired t-test

Parameters	MAE (n = 49)			FF (n = 36)		
	Pretest	Post-test	<i>p</i>	Pretest	Post-test	<i>p</i>
Weight loss	5.3%	0.0%	-	15.4%	10.3%	0.687
Fatigue feeling	34.2%	5.3%	0.001	20.5%	23.1%	1.000
Low physical activity	40.0%	11.4%	0.006	41.0%	30.8%	0.454
Grip strength	36.4%	27.3%	0.500	38.5%	43.6%	0.754
Slow walking	52.2%	56.5%	1.000	53.8%	28.2%	0.021

Notes: MAE, music aerobic exercise; FF, functional food. *P* values are calculated by Chi-square test.

The MAE for ten weeks did not significantly increase blood albumin or cholesterol levels (Table 4). The MAE did increase the RBC significantly from 4.26 to 4.33 ( $\times 10^6$  cells/ul), but decreased the MCV from 94.8 to 94.2 pl/cell. The platelet counts increased from 203.1 to 212.6 ( $\times 10^3$ /ul), which did not reach a significant increase ( $p = 0.085$ ). The MAE for ten weeks had no significant effects on differential counts of WBC. The MAE improved the frailty at fatigue feeling ( $p = 0.001$ ) and low physical activity ( $p = 0.006$ ) but not at slowly walking speed, weight loss, or grip strength (Table 3).

We used Generalized Estimating Equation (GEE) statistics to compare the effects of the FF and MAE on CBC and biochemistry (Table 5). We found that the participants in the FF group revealed a significantly better impact on the HDL-C level (Wald  $X^2 = 4.32$ ,  $p = 0.038$ ). In contrast, participants in the MAE group compared to the FF group significantly increased RBC (Wald  $X^2 = 3.86$ ,  $p = 0.049$ ) and platelets (Wald  $X^2 = 6.69$ ,  $p = 0.01$ ), suggesting that MAE for 10 weeks tends to enhance hematopoiesis on RBC and platelets.

Parameters	Pre-test		Post-test		t	p
	Mean	SD	Mean	SD		
HDL-C (mg/dl)	57.0	15.0	55.5	16.3	1.393	0.173
LDL-C (mg/dl)	91.9	27.2	92.8	27.2	-0.214	0.832
Albumin (gm/dl)	4.42	0.26	4.46	0.22	-1.104	0.278
WBC (cells/ul)	6142.3	1482.6	6246.6	1438.8	-0.675	0.504
RBC (x10 <sup>6</sup> cells/ul)	4.26	0.48	4.33	0.52	-2.141	0.038
Hemoglobin (gm/dl)	13.1	1.4	13.3	1.5	-1.589	0.119
Hematocrit (%)	40.3	4.0	40.7	4.4	-1.207	0.234
MCV (pl/cell)	94.8	5.3	94.2	5.0	2.702	0.010
MCH (pg/cell)	30.9	2.0	30.8	1.9	1.966	0.056
MCHC (gm/dl)	32.6	0.9	32.6	0.8	-0.633	0.530
Platelet (x10 <sup>3</sup> /ul)	203.1	65.4	212.6	63.8	-1.766	0.085
Neutrophil (cells/ul)	63.9	8.6	64.4	6.6	-0.543	0.590
Lymphocyte (cells/ul)	26.7	7.7	26.4	6.5	0.496	0.622
Monocyte (cells/ul)	6.44	1.85	6.20	1.47	1.140	0.261
Basophil (cells/ul)	0.62	0.35	0.60	0.35	0.296	0.769
Eosinophil (cells/ul)	2.33	1.81	2.45	1.86	-0.529	0.600

Notes:  $p$  values are calculated by paired t-test.

Table 5. Changes of blood biochemistry and complete blood counts between MAE and FF group participants

Groups Parameters	MAE Changes	FF Changes	Wald X <sup>2</sup>	p*
HDL-C (mg/dl)	-1.56	2.03	4.316	0.038
LDL-C (mg/dl)	0.97	-2.86	2.327	0.127
Albumin (gm/dl)	0.04	0.13	0.058	0.810
WBC (cells/ul)	104.32	-203.06	0.846	0.358
RBC (x 10 <sup>6</sup> cells/ul)	0.07	-0.02	3.861	0.049
Hemoglobin (gm/dl)	0.15	-0.01	1.700	0.192
Hematocrit (%)	0.38	0.07	0.426	0.514
MCV (pl/cell)	-0.64	0.54	14.120	<0.001
MCH (pg/cell)	-0.13	0.09	5.130	0.024
MCHC (gm/dl)	0.06	-0.09	1.336	0.248
Platelet (x10 <sup>3</sup> /ul)	9.50	-7.39	6.689	0.010
Neutrophil (cells/ul)	0.49	0.69	0.152	0.697
Lymphocyte (cells/ul)	-0.35	-0.33	0.005	0.944
Monocyte (cells/ul)	-0.25	-0.05	0.525	0.469
Basophil (cells/ul)	-0.01	0.07	1.437	0.231
Eosinophil (cells/ul)	0.12	-0.39	3.373	0.066

Notes: p\* values are calculated by Generalized Estimating Equation (GEE) analysis adjusted for gender, age and body weight.

#### 4. Discussion

Results from this study showed that the intake of FF increased the HDL-C and albumin levels, suggesting improvement in metabolism and nutrition. In contrast, the MAE appeared to increase RBC and platelets, suggesting the MAE might enhance erythropoiesis and thrombopoiesis in the elderly with age over 70 in this study.

Frailty is closely associated with IPA and nutritional status. Inappropriate nutrient intake has been shown to cause a risk of malnourishment and frailty in the elderly [18]. Poor appetite, low protein, and low vitamin D intake correlate to frailty [19,20]. A clinical trial with higher protein intake for 12 weeks has increased muscle mass and physical activity in frail elders [21]. Proper supplementation of functional food may be applied to improve nutrition and functional activity. We showed in this study that additional supplementation of chicken moose and milkfish in softened texture with herbs fragrance five times a week for five weeks did improve the blood albumin level, HDL-C level, and better walking speed. Although this short-term administration of higher protein intake did not improve fatigue feeling, weight gain, or muscle strength, a more prolonged supplementation or a combination with physical exercise may improve both nutrition and physical activity.

Different exercises have been shown to prevent physical dysfunctions and reverse frailty in the elderly [22,23]. However, the elderly with different ages and comorbidities may require different styles of exercises, aerobic, resistance, or balanced training. Combined training on strength, endurance, and balance has been shown the best to prevent falls and improve balance and physical performance in the frailty elderly [24]. The problem is encouraging the elderly to exercise regularly



and practice moderate exercise without falls or cardiopulmonary exacerbation safely. Employing the MAE, which is a moderate exercise with harmonious posture in musical rhythm [13,14], we showed that the MAE exercise 3 times (50 minutes a session) a week for 12 weeks, increased erythropoiesis and thrombopoiesis in addition to improving fatigue feeling and physical activity. The MAE alone did not improve nutrition status on blood albumin levels or blood cholesterol levels in the study population with an average of 76 years of age.

Limitations of the study include 1) this study was not a randomized control trial, 2) the FF group completed only 5 weeks of additional high protein FF, and 3) the participants in the MAE group had a high rate of female participants. Moreover, the outcome measurements were limited to blood biochemistry and frailty scales but not biomarkers of senescence or aging. We recently identified that the elderly had a significantly higher senescence-associated secretory phenotype (SASP) in urinary extracellular vesicles than young adults [25]. We thus propose that a combination of active aging exercise and functional food might improve nutrition, immunity, and frailty based on the pre-and post-interventional monitoring of aging biomarkers by non-invasive point-of-care tests of SASP in urinary extracellular vesicles.

## 5. Conclusions

Results from this study suggest that FF and MAE for the elderly have different effects on nutrition status, hematopoiesis, biochemistry, and frailty. Further studies will investigate whether a combination of both FF and MAE for the elderly improves physical function, nutrition, frailty, and mental health scales.

## 6. Conference presentation

This study was partly presented in the American Geriatric Society 2023 (AGS23) annual scientific meeting at Long Beach, Los Angeles, as a poster with ID: 3863755.

**Supplementary Materials:** All the data of this study have been input into Tables 1-5.

**Author Contributions:** Conceptualization, S.Y., and K.Y.; methodology, C.L., and J.W.; software, M.L.; validation, C.L., M.L., and S.Y.; formal analysis, M.L.; investigation, C.L., and S.Y.; resources, S.Y.; data curation, M.L., and K.Y.; writing-original draft preparation, S.Y.; writing-review and editing, K.Y.; project administration, S.Y.; funding acquisition, S.Y., and J.W. All authors have read and agreed to the published version of the manuscript.

**Funding:** This work was supported by grants MOST 110-2314-B-715-008 (for SY) and MOST 109-2811-B-195 -503 -MY3 (for KY) from the National Sciences Technology Council, Taiwan, and by grants MMC-RD-109-1C-04, and MMC-RD-109-1B-16 from Mackay Medical College.

**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of MacKay Memorial Hospital for studies involving humans (code 19MMHIS019e and 2019/01/21 of approval).

**Informed Consent Statement:** Informed consent was obtained from all participants involved in the study.

**Data Availability Statement:** All the study data are input into an Excel file and summarized in Tables 1-5.

**Acknowledgments:** The authors would like to thank the participants and staff from eight long-term care institutes involved in this study.

**Conflicts of Interest:** The authors declare no conflict of interest.

## References

1. Özsürekci, C.; Kara, M.; Güngör, A.E.; Ayçiçek, G.Ş.; Çalışkan, H.; Doğu, B.B.; Cankurtaran, M.; Halil, M.G. Relationship between Chewing Ability and Malnutrition, Sarcopenia, and Frailty in Older Adults. *Nutr Clin Pract.* **2022**, *37*, 1409-1417.
2. Woo, J.; Tong, C.; Yu, R. Chewing Difficulty Should be Included as a Geriatric Syndrome. *Nutrients.* **2018**, *10*, 1997.

3. Breen, L.; Stokes, K.A.; Chirchward-Venne, T.A.; Moore, D.R.; Baker, K.S.; Smith, K.; Atherton, P.J.; Phillips, S.M. Two Weeks of Reduced Activity Decreases Leg Lean Mass and Induces "Anabolic Resistance" of Myofibrillar Protein Synthesis in Healthy Elderly. *J. Clin. Endocrinol. Metab.* **2013**, *98*, 2604–2612.
4. Abreu, M.H.D.; da Silva, A.P.L.; Cavalcanti, R.V.A.; Cecilio Hallak Regalo, S.; Siéssere, S.; Gonçalves, F.M.; de Araujo, C.M.; Taveira, K.V.M. Prevalence of Chewing Difficulty in Older People in Long-term Care: A systematic review and meta-analysis. *Gerodontology*. **2023**, *40*, 10-25.
5. Yeh, S.H.; Pan, M.H. Chewing Screen and Interventions for Older Adults. *Hu Li Za Zhi*. **2020**, *67*, 6-13. doi: 10.6224/JN.202008\_67(4).02.
6. Lübs, L.; Peplies, J.; Drell, C.; Bammann, K. Cross-sectional, and Longitudinal Factors Influencing Physical Activity of 65 to 75-year-olds: A Pan European Cohort Study Based on the Survey of Health, Ageing and Retirement in Europe (SHARE). *BMC Geriatr.* **2018**, *18*, 94. doi: 10.1186/s12877-018-0781-8.
7. Ohtsubo, T.; Nozoe, M.; Kanai, M.; Yasumoto, I.; Ueno, K. Association of Sarcopenia and Physical Activity with Functional Outcome in Older Asian Patients Hospitalized for Rehabilitation. *Aging Clin. Exp. Res.* **2022**, *34*, 391-397.
8. Hiltunen, K.; Saarela, R.K.T.; Kautiainen, H.; Roitto, H.M.; Pitkälä, K.H.; Mäntylä, P. Relationship between Fried's Frailty Phenotype and Oral Frailty in Long-term Care Residents. *Age Ageing*. **2021**, *50*, 2133-2139.
9. Woo, J.; Tong, C.; Yu, R. Chewing Difficulty Should be Included as a Geriatric Syndrome. *Nutrients*. **2018**, *10*, 1997.
10. Yeh, S.H.; Chuang, H.; Lin, L.W.; Hsiao, C.Y.; Eng, H.L. Regular Tai Chi Chuan Exercise Enhances Functional Mobility and CD4CD25 Regulatory T Cells. *Br. J. Sports Med.* **2006**, *40*, 239-43.
11. Hung, J.W.; Liou, C.W.; Wang, P.W.; Yeh, S.H.; Lin, L.W.; Lo, S.K.; Tsai, F.M. Effect of 12-week Tai Chi Chuan Exercise on Peripheral Nerve Modulation in Patients with Type 2 Diabetes Mellitus. *J. Rehabil. Med.* **2009**, *41*, 924-929.
12. Lin, S.L.; Huang, C.Y.; Shiu, S.P.; Yeh, S.H. Effects of Yoga on Stress, Stress Adaption, and Heart Rate Variability Among Mental Health Professionals--A Randomized Controlled Trial. *Worldviews Evid. Based Nurs.* **2015**, *12*, 236-245.
13. Yeh, S.H.; Lai, H.L.; Hsiao, C.Y.; Lin, L.W.; Chuang, Y.K.; Yang, Y.Y.; Yang, K.D. Moderate Physical Activity of Music Aerobic Exercise Increases Lymphocyte Counts, Specific Subsets, and Differentiation. *J. Phys. Act. Health.* **2014**, *1*, 1386-1392.
14. Yeh, S.H.; Lin, L.W.; Chuang, Y.K.; Liu, C.L.; Tsai, L.J.; Tsuei, F.S.; Lee, M.T.; Hsiao, C.Y.; Yang, K.D. Effects of Music Aerobic Exercise on Depression and Brain-derived Neurotrophic Factor Levels in Community-Dwelling Women. *Biomed. Res. Int.* **2015**, *2015*, 135893.
15. Hsiao, Y.S.; Yeh, S.H. Current Status and Prospects for Nutritional Care of Patients with Dysphagia. *VGH Nursing*. **2018**, *35*, 2-9.
16. Matsuo, K.; Fujishima, I. Textural Changes by Mastication and Proper Food Texture for Patients with Oropharyngeal Dysphagia. *Nutrients*. **2020**, *12*, 1613.
17. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G.; McBurnie, M.A.; Cardiovascular Health Study Collaborative Research Group. Frailty in Older Adults: Evidence for A Phenotype. *J. Gerontol. A Biol. Sci. Med. Sci.* **2001**, *56*, M146-56. doi: 10.1093/gerona/56.3.m146.
18. Groessl, E.J.; Kaplan, R.M.; Rejeski, W.J.; Katula, J.A.; Glynn, N.W.; King, A.C.; Anton, S.D.; Walkup, M.; Lu, C.J.; Reid, K., et al. Physical Activity and Performance Impact Long-term Quality of Life in Older Adults at Risk for Major Mobility Disability. *Am. J. Prev. Med.* **2019**, *56*, 141-146.
19. Moradell, A.; Fernández-García, Á.I.; Navarrete-Villanueva, D.; Sagarra-Romero, L.; Gesteiro, E.; Pérez-Gómez, J.; Rodríguez-Gómez, I.; Ara, I.; Casajús, J.A.; Vicente-Rodríguez, G.; Gómez-Cabello, A. Functional Frailty, Dietary Intake, and Risk of Malnutrition. Are Nutrients Involved in Muscle Synthesis the Key for Frailty Prevention? *Nutrients*. **2021**, *13*, 1231. doi: 10.3390/nu13041231.
20. Hernández Morante, J.J.; Gómez Martínez, C.; Morillas-Ruiz, J.M. Dietary Factors Associated with Frailty in Old Adults: A Review of Nutritional Interventions to Prevent Frailty Development. *Nutrients*. **2019**, *11*, 102. doi: 10.3390/nu11010102.
21. Park, Y.; Choi, J.E.; Hwang, H.S. Protein Supplementation Improves Muscle Mass and Physical Performance in Undernourished Pre frail and Frail Elderly Subjects: A Randomized, Double-blind, Placebo-controlled Trial. *Am. J. Clin. Nutr.* **2018**, *108*, 1026-1033. doi: 10.1093/ajcn/nqy214.
22. de Labra C, Guimaraes-Pinheiro C, Maseda A, Lorenzo T, Millán-Calenti JC. Effects of Physical Exercise Interventions in Frail Older Adults: A Systematic Review of Randomized Controlled Trials. *BMC Geriatr.* **2015**, *15*, 154. doi: 10.1186/s12877-015-0155-4.
23. García Díaz, E.; Alonso Ramírez, J.; Herrera Fernández, N.; Peinado Gallego, C.; Pérez Hernández, D.G. Effect of Strength Exercise with Elastic Bands and Aerobic Exercise in the Treatment of Frailty of the Elderly

- Patient with type 2 Diabetes Mellitus. *Endocrinol. Diabetes Nutr. (Engl Ed)*. **2019**, 66, 563-570. doi: 10.1016/j.endinu.2019.01.010.
24. Cadore, E.L.; Rodríguez-Mañas, L.; Sinclair, A.; Izquierdo, M. Effects of Different Exercise Interventions on Risk of Falls, Gait Ability, and Balance in Physically Frail Older Adults: A Systematic Review. *Rejuvenation Res.* **2013**, 16, 105-114. doi: 10.1089/rej.2012.1397.
  25. Yeh, S.H.; Lin, C.H.; Yang, Y.J.; Lin, L.W.; Tseng, C.W.; Yang, K.D. Higher Senescence Associated Secretory Phenotype and Lower Defense Mediator in Urinary Extracellular Vesicles of Elders with and Without Parkinson's Disease. *Sci. Rep.* **2021**, 11, 15783.

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.