

This author's PDF version corresponds to the article as it appeared upon acceptance. Fully formatted PDF versions will be made available soon.

The effect of oral nutritional supplements on the nutritional status of community elderly people with malnutrition or risk of malnutrition

doi: 10.6133/apjcn.202106/PP.0004

Published online: June 2021

Running title: ONS & Malnutrition

Han Zhang MD^{1†}, Yanfang Qiu MD^{2†}, Jinping Zhang B.S.Med³, Zhengjun Ma B.S.Med⁴, Adwoa N. Amoah PhD¹, Yuan Cao MD⁵, Xiaofang Wang B.S.Med⁶, Ping Fu PhD², Quanjun Lyu PhD^{1,5}

¹Department of Nutrition and Food Hygiene, College of Public Health, Zhengzhou University, Zhengzhou, China

²Zhoukou center for disease control and prevention, Zhoukou, China

³Beijing Geriatric Hospital, Beijing, China

⁴Department of Health Care, the Third Affiliated Hospital of Zhengzhou University, Zhengzhou, China

⁵Chinese Society of Gerontology and Gerontology Nutritional Food Branch, Beijing, China

⁶Department of Nutrition, the First affiliated Hospital of Zhengzhou University, Zhengzhou, China

[†]Both authors contributed equally to this manuscript.

Authors' email addresses and contributions:

QL: lvquanjun666@163.com

Contribution: study design, manuscript revision, and funding acquisition.

HZ: 15736758268@163.com

Contribution: data collection, statistical analysis, and manuscript writing.

YQ: 18595372791@163.com

Contribution: data collection, statistical analysis.

JZ: zhangjinpings213@163.com

Contribution: ethical approval, data collection.

ZM: lnyyilm@qq.com

Contribution: ethical approval, data collection.

AN: adwoason@gmail.com

Contribution: manuscript revision, English editing

YC: 552553623@qq.com

Contribution: data collection

XW: 1442496977@qq.com

Contribution: manuscript revision

PF: pingfu0222@sina.com

Contribution: study design, manuscript revision.

Corresponding Author: Prof. Ping Fu, Chinese Society of Gerontology and Gerontology Nutritional Food Branch, 118 Wenquan Road, Beijing, 100062, China. Tel: +86 133 1117 8898. Email: pingfu0222@sina.com

ABSTRACT

Background and Objectives: To evaluate the effect of oral nutritional supplements (ONS) on community elderly people with malnutrition or risk of malnutrition. **Methods and Study Design:** A single arm intervention trial for 3 months was conducted. Whole nutrient powder was given to all the participants. Dietary intakes were measured by 3-day diet record. Nutritional status was evaluated using body weight, body mass index (BMI), calf circumference (CC), and Mini Nutritional Assessment Short-Form (MNA-SF) scores. Muscle mass was measured by bioimpedance analysis (BIA). All these parameters as well as muscle strength, physical function, and quality of life were measured at both the baseline and the end. **Results:** Compared with the baseline, ONS increased protein intake (58.32 ± 16.67 vs 41.90 ± 18.49 g/d, $p < 0.001$), body weight (57.03 ± 8.31 vs 56.68 ± 8.23 kg, $p < 0.05$), BMI (22.16 ± 2.13 vs 22.02 ± 2.08 kg/m², $p < 0.05$), CC (34.21 ± 2.53 vs 33.80 ± 2.53 cm, $p < 0.001$), MNA-SF scores (12.61 ± 1.43 vs 10.48 ± 0.99 , $p < 0.05$), hand grip strength (24.54 ± 8.05 vs 23.27 ± 7.74 kg, $p < 0.001$), and 6-m gait speed (1.11 ± 0.33 vs 0.96 ± 0.28 m/s, $p < 0.001$). Moreover, SF-36 scores of the overall subjects have been improved in all dimensions ($p < 0.05$). **Conclusions:** The study demonstrated that ONS can effectively increase protein intake and improve nutritional status, muscle strength, physical function and quality of life of the elderly with malnutrition or malnutrition risk in communities.

Key Words: oral nutritional supplements, the elderly, community, malnutrition or risk of malnutrition, nutrition supplement

INTRODUCTION

Malnutrition is widely defined and usually refers to a special state in which adverse effects can be observed in body shape or body function due to the deficiency or excess of energy, protein and/or other essential nutrients.¹ Many epidemiological studies have revealed that almost 50% of adults admitted to hospital suffer from malnutrition,² and 40% ~ 90% of older adults in both community and healthcare settings were malnourished or at risk of malnutrition.^{3,4} The elderly faces a series of inevitable health problems with age, such as chewing and swallowing difficulties caused by tooth loss, absorption and utilization disorders caused by the decline of body tissues and organ functions, and anorexia caused by taking drugs. All these can result in the lack of energy and multiple nutrients, which ultimately lead to malnutrition or risk of malnutrition in the elderly. Studies have confirmed that the elderly with malnutrition or malnutrition risk have lower immunity, poor resistance, quality of life,

treatment effect and prognosis, and a higher incidence of complications compared with those in better nutritional status, which prolongs hospitalization, increases hospitalization costs and risk of fracture.⁵⁻⁸ Furthermore, it will cause a huge economic burden on families and society.⁹ Therefore, it is necessary to manage the nutritional status of the elderly with malnutrition or malnutrition risk by means of dietary counseling and guidance, food fortification, physical exercise, or the intake of oral nutritional supplements (ONS) with soft texture, high energy and protein content.¹⁰

In 2006, the guidelines proposed by European Society for Clinical Nutrition and Metabolism (ESPEN) defined ONS as a category of food not included in daily diet. ONS is a kind of food for special medical purposes that can supply a variety of nutrients required by the body through oral intake.¹¹ ONS aims to increase the intake of nutrients for patients, including various kinds of macronutrients (proteins, fats, and carbohydrates) and micronutrients (minerals and vitamins), added to the diet in liquid, semi-solid, powdered form or as nutritional supplements taken alone. ONS has the advantages of convenient and fast operation as well as high efficiency.

In addition, relevant studies have shown that the compliance of ONS in medical institutions and community population is relatively high and it can effectively save medical expenses and greatly shorten hospital stay.^{12,13} A large number of clinical trials have been conducted to provide ONS nutritional support to patients who were undergoing surgery, radiotherapy, chemotherapy or other treatments to maintain or improve their nutritional status, increase their tolerance to treatment, enhance their quality of life, and extend their survival time.^{5,8,14,15} However, the studies to improve the nutritional status of the elderly with malnutrition or malnutrition risk in communities through nutrition intervention are few in China. This study aims to explore the effect of ONS on the elderly with malnutrition or malnutrition risk in communities, prevent malnutrition in the elderly and provide a scientific basis for intervention strategy to improve the nutritional status of the old people.

MATERIALS AND METHODS

Subjects

From April 2017 to July 2017, 192 urban elderly people over 60 years old were recruited from four large communities in Beijing for risk screening of malnutrition and 174 people were finally included for further research. Elderly people with malnutrition or at risk of malnutrition who signed the informed consent and were willing to participate in the

experiment were given an oral nutritional supplement intervention from August 2017 to November 2017.

The inclusion criteria were: 1) Age ≥ 60 years old; 2) Subjects could walk independently; 3) Subjects were malnourished or at risk of malnutrition (MNA-SF scores < 12); 4) BMI < 24 kg/m²; 5) Subjects voluntarily signed the informed consent form and indicated the date. Subjects who suffered from metabolic or chronic diseases (diabetes mellitus, heart disease, kidney disease, malignant tumors, active tuberculosis, hepatitis, AIDS, dementia, etc.), allergies, dysphagia, digestive and absorption disorders, disabilities and other conditions that affect the intake of the intervention and the measurement of indicators; with drug or alcohol abuse; took other ONS during the study; were participating in other clinical trials; and refused to participate were excluded.

Study design

This study was designed as a single arm intervention trial for three months. The baseline data of the research subjects was used as the control, and each measurement indexes at the end of the trial were compared with the baseline to evaluate the effect of oral nutritional supplements on nutritional status, muscle strength, motor function, body composition, and quality of life. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the ethical committee of Beijing Geriatric Hospital. The study was registered under the Chinese Clinical Trial Registry with the identifier: ChiCTR1900026784. Written/verbal informed consent was obtained from all subjects/patients. Verbal consent was witnessed and formally recorded.

Intervention

The whole nutrient powder used in our study was provided by Abbott Nutrition China R & D Center. It is a kind of ONS product which is suitable for the elderly, and its nutrient content was shown in Table 1. The whole nutrient powder (53.8g, 6 teaspoons each time) was dissolved in 190 ml water and taken orally. In order not to affect the subjects' normal diet, the intervention preparation should be consumed two hours before or after a meal. The subjects took the intervention preparations once every morning and evening. Four cans of intervention preparations were distributed to each subject by the staff every month.

Outcome measurement

The following outcomes were measured by trained researchers during designated visits at the beginning and the end of the intervention. Body composition, including body water, muscle mass, skeletal muscle, body fat rate, was assessed by bioelectric impedance analysis (BIA, Inbody 770). In order to make the measurement results more accurate, participants were required to empty their bowels, take off heavy clothes, shoes, hats and socks, and remove metal jewelry (such as necklaces, earrings, bracelets, etc.). Then the subjects stood barefoot on the instrument pedal as instructed, with the palms, fingers, soles and toes of both hands closed to the corresponding electrodes. At the same time, the subjects kept their hands drooping naturally, with the arms and body at an angle of 30 degrees, until the numbers on the instrument display no longer changed. Finally, the body composition test results were printed by researchers.

Hand grip strength was assessed with an electronic hand dynamometer (CAMRY-EH101; Nantong Qijun Company, China) when the participant was in a sitting position. Two consecutive hand grip strength (kg) were measured to the nearest 0.1 kg for both hands, and the averaged value was taken for further analysis.

Six-m gait speed (6-m walk at the usual pace) was assessed twice and all values were averaged.¹⁶

Self-reported quality of life was measured by the MOS item short form health survey (SF-36),¹⁷ including 8 dimensions, namely physical function, role function, physical pain, overall health, energy, social function, emotional function and mental health, and the scoring principle refers to the previous literature.¹⁸ Mini Nutritional Assessment Short-Form (MNA-SF) was used to measure the nutritional status.¹⁹ This scale includes 6 aspects such as eating status, activity ability, recent weight change, BMI (or calf circumference), disease and stress. Evaluation criteria: a total score of 12 to 14 indicates good nutritional status, a total score of 8 to 11 indicates the risk of malnutrition, and a total score of 0 to 7 indicates malnutrition. The SF-36 and MNA-SF data were collected by specially trained investigators. Dietary intake was assessed prospectively by 3-day diet records. During the trial period, the subjects were asked to record the types and quantities of all foods and beverages they ingested for 3 consecutive days (1 weekend day and 2 week-days), the time and place of meals (including meals at home and out). When retracting the questionnaire, the researchers carefully reviewed all the contents filled in, and promptly inquired about the unclear parts to ensure the accuracy of the filled contents.

Statistical analyses

Two independent samples *t* test (for continuous variables) and chi square test (for categorical variables) were used to compare the differences between male and female at the baseline characters. To compare the differences between the subjects and the gender groups before and after the intervention, paired sample *t* test and paired chi-square test were used for continuous and categorical variables, respectively. All statistical analyses were performed with SPSS 25.0 for Windows software (IBM). A two-sided significant level was $\alpha=0.05$.

RESULTS

Baseline information

A total of 192 subjects were screened in this study. Eighteen participants were excluded because: 8 were in good nutrition, 6 were using nutritional supplements, and 4 refused to participate. Among the remaining 174 people, 12 people were lost to follow-up and 2 refused to continue to participate during the intervention, 160 subjects (50 men and 110 women) were included in the final analysis (Figure 1). The information of baseline demographic and nutritional status was shown in Table 2.

Daily energy and nutrient intake

Table 3 showed that there were no significant differences in daily energy, protein, fat, carbohydrate and dietary fiber consumed by all subjects only through the diet between before and after the intervention, that is, there was no significant change in the diet of the subjects during the intervention (all $p>0.05$). However, because the intervention agents were rich in various nutrients, the intake of energy, protein, fat, carbohydrate and dietary fiber through the diet and intervention agents were increased after the intervention ($p<0.05$).

Daily dietary energy source

Due to abundant protein in the intervention preparations, the intake of energy and energy ratio from protein after intervention were significantly higher than that before ($p<0.05$) (Table 4).

Changes in nutritional status

As presented in Table 5, body weight, BMI, calf circumference and MNA-SF scores were significantly increased after intervention among the overall subjects. The same results were obtained in female when we conducted a hierarchical analysis based on gender ($p<0.001$). In the male study subjects, the calf circumference and MNA-SF indicators were significantly

improved after the intervention ($p<0.05$), but there was no difference in body weight and BMI ($p>0.05$).

Changes in muscular strength, physical function and body composition

The grip strength, 6-m gait speed, extracellular water, body fat, body fat rate and trunk fat removal rate of all subjects had significant differences between baseline and follow-up ($p<0.05$). The grip strength and 6-m gait speed index were significantly improved in males after intervention ($p<0.05$). Significant differences were observed in grip strength, 6-m gait speed, extracellular water, body fat and body fat rate among females after intervention ($p<0.05$) (Table 5).

Changes in quality of life

Physical function, role function, body pain, overall health, energy, social function, emotional function and mental health were enhanced in all subjects after the intervention ($p<0.05$). Among male subjects, role function, physical pain, overall health, energy, social function, emotional function and mental health were significantly improved after the intervention ($p<0.05$). Role function, body pain, overall health, and vigor were also increased after the intervention in the females ($p<0.05$) (Table 5).

DISCUSSION

The current study found that ONS can not only increase the intake of energy and nutrients among the elderly people who were malnourished or at risk of malnutrition, but also improve the grip strength, 6-m gait speed, nutritional status and the quality of life.

The prevalence of malnutrition is associated with increasing age, multiple comorbidities and inadequate care, so malnutrition is increasingly regarded as a geriatric syndrome.^{10,20} Malnutrition includes both nutritional deficiencies and overnutrition, among which, poor nutrition is most common among the elderly. Nevertheless, the gastrointestinal tract of most elderly people in the community is complete and well-functioning. Malnutrition in these older adults is mainly caused by insufficient energy and nutrients. Therefore, it is strongly reasonable to choose ONS for such elderly people. Our study showed that ONS can increase the intake of energy, protein and other nutrients of the elderly. This is good news for improving the nutritional status of the elderly.

Weight, BMI and calf circumference are always adopted as indicators to evaluate the nutritional status and they are easy to measure. One meta-analysis specifically focused on

older adults aged 65 years and above found a U-shaped association between BMI and mortality, and the lowest risk was among those with BMI between 24.0 and 30.9.²¹ However, the review included 32 studies conducted only in Europe, North America, Canada and Australia. Excitingly, in a meta-analysis among older people living in nursing homes in Europe, America, Canada, and Asia (including China), it has been shown that there was an inverse association between BMI and all-cause mortality.²² According to the BMI standard of Chinese population, overweight is defined as BMI ≥ 24 kg/m², while malnutrition is more likely to occur in people with low BMI. Therefore, BMI < 24 kg/m² was taken as an inclusion standard. Numerous studies have shown that ONS is beneficial for increasing weight, BMI and calf circumference of the elderly.^{23,24} A meta-analysis including 17 studies indicated that non-meat and high-protein supplements can significantly improve weight and BMI of elderly people in nursing homes.²⁵ Lee et al. conducted a randomized controlled trial (RCT) on elderly people in a nursing home for 6 months of intervention with soy protein supplementation, which showed that weight, BMI and calf circumference of the elderly were significantly increased after the intervention.²⁶ Another meta-analysis of 15 RCT, including 589 subjects showed that short-term oral energy or protein/amino acid supplements could improve the nutritional status of patients who were receiving maintenance dialysis by increasing their body weight and BMI.²⁷ Studies on Chinese older adults aged 65 years and above suggest that being overweight/obese was not associated with an increased all-cause mortality.^{28,29} Besides, another study found that underweight was associated with an increased risk of all-cause mortality but overweight was associated with a reduced risk among the oldest old Chinese.³⁰ In this study, after three-month intervention, there was statistically significant improvement in body weight, BMI and calf circumference among the overall subjects and women, respectively, which was consistent with the previous studies.

A two-month RCT with amino acid supplementation to the older adults in nursing homes showed that there was a statistical difference in the MNA-SF scores of the elderly in the intervention group between before and after the intervention.³¹ MNA-SF is a simple and convenient tool for evaluating the nutritional status of the elderly with high sensitivity and specificity. ESPEN strongly recommends it as the preferred tool for nutritional risk screening of inpatients.^{19,32} Interestingly, the MNA-SF scores among the overall subjects, men and women were statistically increased after the intervention ($p < 0.05$) in our study. This indicates that ONS can indeed improve the nutritional status of the old people with malnutrition or at risk of malnutrition in the community.

Studies have shown that a large amount of protein supplementation in the diet is closely related to maintain the muscle mass of the limbs of middle-aged and elderly population.³³ Proteins are rich in substances required by the body such as glutamine and leucine, among which glutamine has the function of inhibiting protein decomposition, increasing muscle cell volume and promoting muscle growth. Leucine can promote the synthesis of skeletal muscle protein. Rondanelli et al. concluded that oral essential amino acid could enhance the grip strength of the elderly hospitalized patients.³⁴ Grip strength is an indicator to reflect the development level of human upper limb strength by measuring the strength of the forearm and hand muscles of the subjects. Haruki conducted a 28-day supportive amino acid supplement intervention test on 82 patients with liver cirrhosis, and the grip strength were significantly improved after the intervention ($p < 0.001$).³³ Previous study has also shown that oral whey protein combined with multivitamins can enhance the grip strength and 6-m gait speed of the sarcopenic elderly.³⁵ This indicates that protein and nutrients supplementation can not only increase muscle strength, but also improve motor function. The intervention preparations we used in this study are rich in protein and other nutrients (including vitamin D) and the protein intake through the daily diet combined with ONS was as high as 58.32 ± 16.67 g, which basically reached the recommended daily protein intake level. When sufficient protein was absorbed by the body, it can help to maintain the mass and function of muscles in elderly people. Therefore, the improvement of grip strength and 6-m gait speed of the elderly after the intervention was not unexpected.

Recent studies have revealed that muscles in older people are generally resistant to strong anabolic stimuli after protein intake when compared with those in younger people.^{36,37} It has been reported that after the intervention of dietary supplemented whey protein combined with vitamin D and E, the muscle tissue of the limbs of the sarcopenic elderly increased by 0.23 ± 1.07 g, but the difference was not significant.²³ In current study, after 3-month intervention with whole nutrition powder (rich in high-quality protein), the weight gain and fat gain of the elderly were significant, but the muscle tissue (including muscle mass and skeletal muscle) change showed no significant difference among the overall subjects and also both sexes, which was consistent with the former findings found by Bo et al. The reasons for this phenomenon situation may be as follows: 1) There is a certain resistance in the elderly when ingesting protein for body synthesis; 2) The intervention period of our study was not long enough; 3) Nutritional powder combined with exercise is more beneficial to improve the muscle mass of the elderly,³⁷ but this study did not explore this joint effect.

The SF-36 questionnaire is an effective and general measurement method for scoring health-related quality of life in multiple research fields. The validity, internal consistency and retest reliability of the scale are credible, so it is widely used to assess the quality of life of the elderly.³⁸ A lot of studies have shown that an appropriate increased intake of high-quality protein can effectively improve the quality of life of elderly subjects.^{23,39} A cross-sectional study showed that the quality of life scores of the elderly with poor nutritional status were significantly lower than those with good nutritional status after adjusting socio-demographic and health-related covariables.⁴⁰ Moreover, a cohort study documented that the occurrence of fractures in the elderly is significantly related to low quality of life.⁴¹ Interestingly, malnutrition can increase the risk of fractures in older adults.^{42,43} Our study found that the supplementation of whole nutrition powder can effectively improve the quality of life of the elderly with malnutrition or malnutrition risk in community. The reason is probably that ONS increases their energy and nutrient intake, and further improves their nutritional status and physical function, thereby enhancing their confidence, vitality, life experience and living ability.

There are some strengths in this study. Firstly, this is one of the few nutritional intervention studies on the elderly who are malnourished or at risk of malnutrition in Chinese communities. Secondly, the assessment of outcome parameters in present study is wide, and this study enables good comparability with other studies, and the compliance of this study is excellent. Thirdly, all measurements are highly standardized and performed by professionally trained researchers. Furthermore, it is a realistic study which has a high practicality, the results can provide reference and basis for Chinese government to formulate policies and strategies for the nutritional supplementation to community elderly.

At the same time, the study is not without limitations. The main limitation of this study is that there is no control group in which the elderly did not receive the nutritional supplementation. When planning the study, an ethical issue was proposed that it was not ethical for not using supplements in old people with established malnutrition, so we compared the intake of energy and nutrient only through diet with that through diet plus ONS to clarify the effect of ONS. There may be observational bias in this study, because during the dietary survey, the amount of cooking oil ingested by all subjects was calculated as 30g. Meanwhile, compliance was determined based on the empty canister which was brought when distributing the intervention preparation, it was actually unknown whether it was in accordance with the intervention consumption. Finally, serological indicators were not designed in this study, so

the effect of ONS on micronutrient level could not be observed. These issues need more attention in future researches.

Conclusion

In conclusion, the study demonstrated that ONS can effectively increase protein intake, maintain or increase body weight and BMI, and improve nutritional status, muscle strength and quality of life among the old people with malnutrition or malnutrition risk in the community. Whole nutritional powder may be an applicable strategy to improve the nutritional status of the elderly. Further larger well-designed studies are warranted to explore the impact of nutritional interventions on the serological indicators of elderly people with malnutrition or risk of malnutrition.

ACKNOWLEDGEMENTS

We gratefully acknowledge the Abbott Laboratories for the kind provision of the whole nutrition powder. Special thanks also go to researchers and volunteers for their active participation.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

There is no conflict of interest. The present study was supported by Abbott fund (No. ANCH1602), the National Natural Science Foundation of China under grant number [81673165], and Chinese Nutrition Society (CNS) Nutrition Science Foundation-Feihe Tizhi, nutrition and health research fund (No. CNS-Feihe2019A34).

REFERENCES

1. Agarwalla R, Saikia AM, Baruah R. Assessment of the nutritional status of the elderly and its correlates. *J Family Community Med.* 2015;22:39-43.
2. Correia MI, Hegazi RA, Diaz-Pizarro Graf JI, Gomez-Morales G, Fuentes Gutiérrez C, Goldin MF, Navas A, Pinzón Espitia OL, Tavares GM. Addressing disease-related malnutrition in healthcare: a Latin American perspective. *JPEN J Parenter Enteral Nutr.* 2016;40:319-25.
3. Salvador M, Fernandez O, Murillo S. Malnutrition and factors that influence the food intake in hospitalized patients: a report. *J Hum Nutr Diet.* 2014;15:187-90.
4. van Zwienen-Pot JI, Visser M, Kuijpers M, Grimmerink MFA, Kruizenga HM. Undernutrition in nursing home rehabilitation patients. *Clin Nutr.* 2017;36:755-9.
5. Avenell A, Smith T, Curtain J, Mak J, Myint PK. Nutritional supplementation for hip fracture aftercare in older people. *Cochrane Database Syst Rev.* 2016;11:1-168.

6. Goates S, Du K, Braunschweig CA, Arensberg MB. Economic Burden of Disease-Associated Malnutrition at the State Level. *PLoS One*. 2016;11:1-15.
7. Kostka J, Borowiak E, Kostka T. Nutritional status and quality of life in different populations of older people in Poland. *Eur J Clin Nutr*. 2014;68:1210-5.
8. Zeraatkar D, Petrisor B. Cochrane in CORR(R): Nutritional supplementation for hip fracture aftercare in older people. *Clin Orthop Relat Res*. 2019;477:491-3.
9. Snider JT, Linthicum MT, Wu Y, LaVallee C, Lakdawalla DN, Hegazi R, Matarese L. Economic burden of community-based disease-associated malnutrition in the United States. *JPEN J Parenter Enteral Nutr*. 2014;38(2 Suppl):77s-85s.
10. Guyonnet S, Rolland Y. Screening for malnutrition in older people. *Clin Geriatr Med*. 2015;31:429-37.
11. Lochs H, Allison S, Meier R, Pirlich M, Kondrup J, Schneider S, van den Berghe G, Pichard C. Introductory to the ESPEN Guidelines on Enteral Nutrition: Terminology, definitions and general topics. *Clin Nutr*. 2006;25:180-6.
12. Hubbard GP, Elia M, Holdoway A, Stratton RJ. A systematic review of compliance to oral nutritional supplements. *Clin Nutr*. 2012;31:293-312.
13. Philipson T, Snider J, Lakdawalla D, Stryckman B, Goldman DP. Impact of oral nutritional supplementation on hospital outcomes. *Am J Manage Care*. 2013;19:121-8.
14. Lewis S, Egger M, Sylvester P, Thomas S. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. *BMJ*. 2001;323(7316):773-6.
15. Stratton RJ, Elia M. A review of reviews: A new look at the evidence for oral nutritional supplements in clinical practice. *Syst Rev*. 2007;2:5-23.
16. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, Scherr PA, Wallace RB. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol*. 1994;49:M85-94.
17. Wan C, Fang J, Shi M, L MC, M HS. MOS sf-36 scale was used to measure the quality of life of drug addicts. *Psychol Addict Behav*. 1998;7:260-2.
18. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30:473-83.
19. Kaiser M, Bauer J, Ramsch C, Uter W, Guigoz Y, Cederholm T et al. Validation of the Mini Nutritional Assessment short-form (MNA-SF): a practical tool for identification of nutritional status. *J Nutr Health Aging*. 2009;13:782-8.
20. Saka B, Kaya O, Ozturk G, Erten N, Karan MA. Malnutrition in the elderly and its relationship with other geriatric syndromes. *Clin Nutr*. 2010;29:745-8.
21. Winter JE, MacInnis RJ, Wattanapenpaiboon N, Nowson CA. BMI and all-cause mortality in older adults: a meta-analysis. *Am J Clin Nutr*. 2014;99:875-90.

22. Veronese N, Cereda E, Solmi M, Fowler SA, Manzato E, Maggi S et al. Inverse relationship between body mass index and mortality in older nursing home residents: a meta-analysis of 19,538 elderly subjects. *Obes Rev.* 2015;16:1001-15.
23. Bo Y, Liu C, Ji Z, Yang R, An Q, Zhang X et al. A high whey protein, vitamin D and E supplement preserves muscle mass, strength, and quality of life in sarcopenic older adults: A double-blind randomized controlled trial. *Clin Nutr.* 2019;38:159-64.
24. Stow R, Ives N, Smith C, Rick C, Rushton A. A cluster randomised feasibility trial evaluating nutritional interventions in the treatment of malnutrition in care home adult residents. *Trials.* 2015;16:1-21.
25. Donaldson AIC, Smith TO, Alder S, Johnstone AM, De Roos B, Aucott LS, Gordon AL, Myint PK. Effect of nonmeat, high-protein supplementation on quality of life and clinical outcomes in older residents of care homes: a systematic review and meta-analysis. *Nutr Rev.* 2019;77:116-27.
26. Lee LC, Tsai AC, Wang JY, Hurng BS, Hsu HC, Tsai HJ. Need-based intervention is an effective strategy for improving the nutritional status of older people living in a nursing home: a randomized controlled trial. *Int J Nurs Stud.* 2013;50:1580-8.
27. Liu P, Ma F, Wang Q, He SL. The effects of oral nutritional supplements in patients with maintenance dialysis therapy: A systematic review and meta-analysis of randomized clinical trials. *PLoS One.* 2018;13:e0203706.
28. Gao S, Jin Y, Unverzagt FW, Cheng Y, Su L, Wang C et al. Cognitive function, body mass index and mortality in a rural elderly Chinese cohort. *Arch Public Health.* 2014;72:9.
29. Sun H, Ren X, Chen Z, Li C, Chen S, Wu S, Chen Y, Yang X. Association between body mass index and mortality in a prospective cohort of Chinese adults. *Medicine (Baltimore).* 2016;95:e4327.
30. Wang J, Taylor AW, Zhang T, Appleton S, Shi Z. Association between Body Mass Index and All-Cause Mortality among Oldest Old Chinese. *J Nutr Health Aging.* 2018;22:262-8.
31. Rondanelli M, Opizzi A, Antonielli N, Boschi F, Iadarola P, Pasini E, Aquilani R, Dioguardi FS. Effect of essential amino acid supplementation on quality of life, amino acid profile and strength in institutionalized elderly patients. *Clin Nutr.* 2011;30:571-7.
32. Group PC, Nutrition SoPaE, Association CM. Guidelines for pediatric clinical application of enteral and parenteral nutritional support in China. *Chinese Journal of Pediatrics.* 2010;48:436-41.
33. Uojima H, Sakurai S, Hidaka H, Kinbara T, Sung JH, Ichita C et al. Effect of branched-chain amino acid supplements on muscle strength and muscle mass in patients with liver cirrhosis. *Eur J Gastroenterol Hepatol.* 2017;29:1402-7.
34. Dangin M, Guillet C, Garcia-Rodenas C, Gachon P, Bouteloup-Demange C, Reiffers-Magnani K, Fauquant J, Ballèvre O, Beaufrère B. The rate of protein digestion affects protein gain differently during aging in humans. *J Physiol.* 2003;549:635-44.
35. Borsheim E, Bui Q, Tissier S, Kobayashi H, Ferrando AA, Wolfe RR. Effect of amino acid supplementation on muscle mass, strength and physical function in elderly. *Clin Nutr.* 2008;27:189-95.

36. Burd NA, Yang Y, Moore DR, Tang JE, Tarnopolsky MA, Phillips SM. Greater stimulation of myofibrillar protein synthesis with ingestion of whey protein isolate v. micellar casein at rest and after resistance exercise in elderly men. *Br J Nutr.* 2012;108:958-62.
37. Kim H, Suzuki T, Saito K, Yoshida H, Kobayashi H, Kato H, Katayama M. Effects of exercise and amino acid supplementation on body composition and physical function in community-dwelling elderly Japanese sarcopenic women: a randomized controlled trial. *J Am Geriatr Soc.* 2012;60:16-23.
38. Newnham E, Harwood K, Page A. Evaluating the clinical significance of responses by psychiatric inpatients to the mental health subscales of the SF-36. *J Affect Disord.* 2007;98:91-7.
39. Smoliner C, Norman K, Scheufele R, Hartig W, Pirlich M, Lochs H. Effects of food fortification on nutritional and functional status in frail elderly nursing home residents at risk of malnutrition. *Nutrition.* 2008;24:1139-44.
40. Masel MC, Graham JE, Reistetter TA, Markides KS, Ottenbacher KJ. Frailty and health related quality of life in older Mexican Americans. *Health Qual Life Outcomes.* 2009;7:1-7.
41. Gobbens R, van Assen M, Luijkx K, Schols JM. The predictive validity of the Tilburg Frailty Indicator: disability, health care utilization, and quality of life in a population at risk. *Gerontologist.* 2012;52:619-31.
42. Drevet S, Bioteau C, Maziere S, Couturier P, Merloz P, Tonetti J, Gavazzi G. Prevalence of protein-energy malnutrition in hospital patients over 75 years of age admitted for hip fracture. *Orthop Traumatol Surg Res.* 2014;100:669-74.
43. Goisser S, Schrader E, Singler K, Bertsch T, Gefeller O, Biber R, Bail HJ, Sieber CC, Volkert D. Malnutrition according to mini nutritional assessment is associated with severe functional impairment in geriatric patients before and up to 6 months after hip fracture. *J Am Med Dir Assoc.* 2015;16:661-7.

Table 1. Nutrient composition of the whole nutrient powder[†]

Composition	Contents/100 g
Energy, kcal	430.0
Protein, g	15.9
Fat, g	14.0
Alpha-linolenic acid, mg	310.0
Linoleic acid, g	2.5
Carbohydrate, g	57.4
Dietary fiber, g	4.3
Vitamin A, µg RE	450.0
Vitamin D, µg	4.5
Vitamin C, mg	54.0
Calcium, mg	405.0
Phosphorus, mg	270.0
Magnesium, mg	88.0
Potassium, mg	603.0
Iron, mg	4.5
Zinc, mg	4.7

[†]Only nutrients with higher content were shown in the table.

Table 2. Baseline demographic and nutritional status

Characteristic	Total (n=160)	Male (n=50)	Female (n=110)
Characteristic			
Age (y), n (%)			
~69	111 (69.4)	29 (58.0)	82 (74.5)
70~79	26 (16.3)	11 (22.0)	15 (13.6)
80~89	22 (13.8)	9 (18.0)	13 (11.8)
90~	1 (0.6)	1 (2.0)	0 (0)
Height, cm	160.18±8.24	167.37±6.55	156.91±6.72
Weight, kg	56.68±8.23	62.06±8.38	54.23±6.93
BMI, kg/m ²	22.02±2.08	22.11±2.36	21.98±1.95
CC, cm	33.80±2.56	34.41±2.72	33.53±2.45
Micro nutrition status			
MNA-SF, points	10.48±0.99	10.34±1.00	10.54±0.98
MNA-SF, n (%)			
At risk of malnutrition	157 (98.1)	49 (98.0)	108 (98.2)
Malnutrition	3 (1.9)	1 (2.0)	2 (1.8)
Handgrip strength, kg	23.27±7.74	28.44±8.71	20.92±5.96
6-m gait speed, m/s	0.96±0.28	0.89±0.30	1.00±0.26
Body composition			
Total body water, L	29.71±5.23	34.91±4.76	27.35±3.42
Intracellular water, L	18.10±3.26	21.29±3.01	16.66±2.16
Extracellular water, L	11.61±1.99	13.62±1.79	10.69±1.27
Protein, kg	7.83±1.41	9.19±1.31	7.21±0.94
Minerals, kg	2.80±0.42	3.17±0.42	2.64±0.29
Body fat, kg	16.46±4.23	15.06±4.78	17.09±3.81
Body fat percentage, %	28.98±6.39	23.92±6.46	31.27±4.88
Muscle mass, kg	38.02±6.72	44.68±6.13	35.00±4.40
Fat free weight, kg	40.35±7.03	47.28±6.46	37.20±4.62
Skeletal muscle, kg	21.62±4.25	25.77±3.93	19.73±2.81
Body fat removal weight, kg	17.86±3.21	21.03±2.89	16.42±2.14
Body fat removal rate, %	94.44±5.97	92.19±7.16	95.46±5.06
Sleeping status			
Sleep well all night, n (%)			
Yes	105 (65.6)	34 (68.0)	71 (64.5)
No	55 (34.4)	16 (32.0)	39 (35.5)
Dream, n (%)			
Yes	32 (20.0)	9 (18.0)	23 (20.9)
No	128 (80.0)	41 (82.0)	87 (79.1)
Sleeping time, h	6.28±1.19	6.55±1.13	6.16±1.21
Stool situation			
Difficulty defecating, n (%)			
Yes	32 (20.0)	11 (22.0)	21 (19.1)
No	128 (80.0)	39 (78.0)	89 (80.9)
Stool problem, n (%)			
Diarrhea or constipation	21 (65.6)	8 (72.7)	13 (61.9)
irregular	11 (34.4)	3 (27.3)	8 (38.1)

BMI: body mass index; CC: Calf circumference; MNA-SF: short-form mini nutritional assessment.

Table 3. The daily energy and nutrient intake before and after the intervention

Variable	Diet (n=160)		<i>p</i>	Diet + ONS (n=160)		<i>p</i>
	Baseline	End		Baseline	End	
Energy, kcal/d	1330.77±479.64	1314.33±404.47	0.657	1330.77±479.64	1765.39±404.47	<0.001*
Protein, g/d	41.90±18.49	41.21±16.67	0.673	41.90±18.49	58.32±16.67	< 0.001*
Fat, g/d	58.19±20.47	62.41±21.75	0.050	58.19±20.47	77.47±21.75	< 0.001*
Carbohydrate, g/d	160.78±87.56	148.61±71.08	0.053	160.78±87.56	210.37±71.08	< 0.001*
Dietary fiber, g/d	6.85±4.48	6.64±6.60	0.728	6.85±4.48	11.26±6.60	< 0.001*

p* < 0.05Table 4.** Changes in energy supply ratio of three productive nutrients

Variable	N=160		<i>t</i>	<i>p</i>
	Baseline	End		
Energy, kcal/d	1330.77±479.64	1765.39±404.47	- 11.755	<0.001*
Protein, %	12.47±3.37	13.22±2.16	- 2.593	0.010*
Fat, %	41.11±10.47	39.86±7.74	1.373	0.172
Carbohydrate, %	46.70±10.94	47.23±8.30	- 0.591	0.556

**p* < 0.05

Table 5. Changes in nutritional status, muscle mass and strength, motor function, body composition and quality of life

Variable	Total (n=160)		<i>p</i>	Male (n=50)		<i>p</i>	Female (n=110)		<i>p</i>
	Baseline	End		Baseline	End		Baseline	End	
Weight, kg	56.68±8.23	57.03±8.31	<0.001*	62.06±8.38	62.23±8.75	0.402	54.23±6.93	54.67±6.94	<0.001*
BMI, kg/m ²	22.02±2.08	22.16±2.13	<0.001*	22.11±2.36	22.18±2.46	0.331	21.98±1.95	22.15±1.97	<0.001*
CC, cm	33.80±2.56	34.21±2.53	<0.001*	34.41±2.72	34.76±2.73	0.023*	33.53±2.45	33.97±2.40	<0.001*
MNA-SF	10.50±1.03	12.62±1.41	<0.001*	10.34±1.00	12.52±1.39	<0.001*	10.57±1.04	12.66±1.43	<0.001*
Handgrip strength, kg	23.27±7.74	24.53±8.05	<0.001*	28.44±8.71	30.26±9.03	0.008*	20.92±5.96	21.93±5.99	0.001*
6-m gait speed, m/s	0.96±0.28	1.11±0.33	<0.001*	0.89±0.30	1.04±0.35	<0.001*	1.00±0.26	1.13±0.31	<0.001*
Total body water, L	29.71±5.23	29.57±5.21	0.060	34.91±4.76	34.73±4.80	0.278	27.35±3.42	27.22±3.39	0.124
Intracellular water, L	18.10±3.26	18.04±3.23	0.161	21.29±3.01	21.17±3.03	0.268	16.66±2.16	16.61±2.14	0.384
Extracellular water, L	11.61±1.99	11.53±2.00	0.019*	13.62±1.79	13.56±1.82	0.367	10.69±1.27	10.61±1.27	0.020*
Protein, kg	7.83±1.41	7.79±1.40	0.121	9.19±1.31	9.15±1.32	0.370	7.21±0.94	7.18±0.92	0.200
Minerals, kg	2.80±0.42	2.80±0.43	0.435	3.17±0.42	3.17±0.43	0.974	2.64±0.29	2.63±0.30	0.340
Body fat, kg	16.46±4.23	16.87±4.36	0.001*	15.06±4.78	15.17±5.17	0.628	17.09±3.81	17.64±3.71	<0.001*
Body fat percentage, %	28.98±6.39	29.57±6.42	0.001*	23.92±6.46	24.09±6.68	0.581	31.27±4.88	32.07±4.47	<0.001*
Fat free weight, kg	40.35±7.03	40.16±7.01	0.078	47.28±6.46	47.06±6.52	0.317	37.20±4.62	37.03±4.57	0.145
Body fat removal weight, kg	17.86±3.21	17.82±3.20	0.404	21.03±2.89	20.92±2.94	0.279	16.42±2.14	16.42±2.15	0.885
Body fat removal rate, %	94.44±5.97	94.00±5.60	0.047*	92.19±7.16	91.95±6.63	0.536	95.46±5.06	94.93±4.81	0.050
Muscle mass, kg	38.02±6.72	37.84±6.69	0.070	44.68±6.13	44.45±6.19	0.282	35.00±4.40	34.84±4.36	0.144
Skeletal muscle, kg	21.62±4.25	21.53±4.22	0.136	25.77±3.93	25.61±3.95	0.247	19.73±2.81	19.67±2.79	0.347
Somatic function	87.66±16.98	89.75±15.23	0.049*	87.70±18.44	91.10±10.56	0.066	87.64±16.36	89.14±16.94	0.250
Role function	82.66±33.88	92.66±25.02	0.001*	79.50±34.14	94.00±22.34	0.004*	84.09±33.82	92.05±26.22	0.036*
Body pain	80.01±19.18	87.58±18.50	<0.001*	80.30±19.59	89.38±16.92	0.002*	79.88±19.08	86.76±19.19	<0.001*
Overall health	62.73±15.25	72.24±16.30	<0.001*	60.88±14.41	72.42±15.09	<0.001*	63.56±15.61	72.16±16.89	<0.001*
Vigor	79.75±12.26	83.66±13.58	0.001*	77.60±13.90	82.80±13.33	0.007*	80.73±11.37	84.05±13.74	0.019*
Social function	89.10±17.29	92.85±16.55	0.003*	86.44±19.99	91.78±16.16	0.012*	90.30±15.86	93.33±16.77	0.051
Emotional function	86.67±29.72	93.75±22.49	0.004*	82.67±31.04	94.00±20.96	0.010*	88.49±29.07	93.64±23.24	0.088
Mental Health	80.55±15.00	83.38±13.08	0.036*	77.92±16.41	84.32±11.40	0.013*	81.75±14.24	82.95±13.80	0.445

BMI: body mass index; CC: Calf circumference; MNA-SF: short-form mini nutritional assessment.

**p*<0.05.

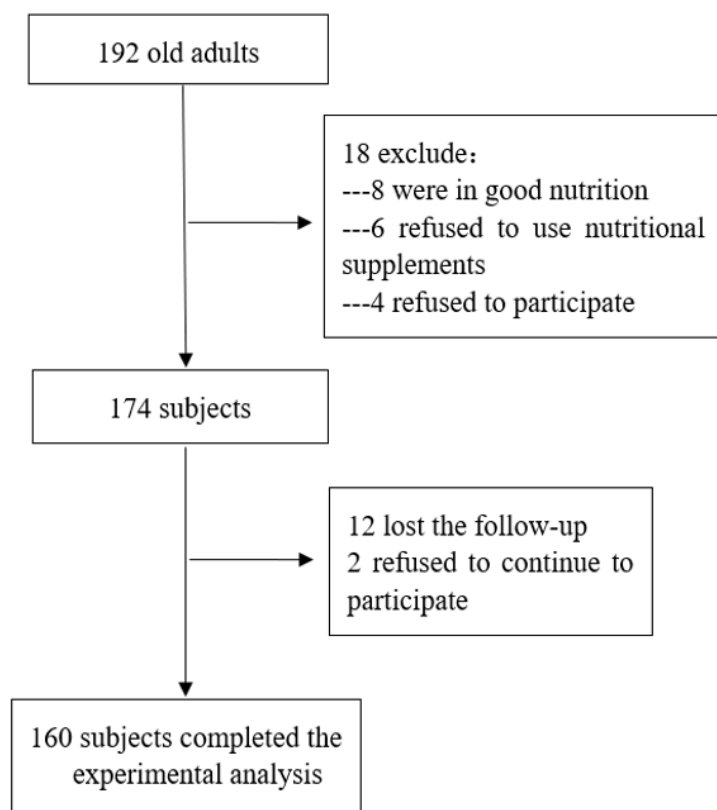


Figure 1. The selection process of research subjects.