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Ratio of dietary ω -3 and ω -6 fatty acids—independent determinants of muscle mass—in hemodialysis patients with diabetes



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ABSTRACT

Objective: ω-3 and ω-6 polyunsaturated fatty acids (PUFAs) are essential nutrients in the human diet and possibly affect muscle mass. We evaluated the association between the dietary ratios of ω-3 and ω-6 PUFAs and muscle mass, indicated as skeletal muscle mass (SMM) and appendicular skeletal muscle mass (ASM), in patients with diabetes undergoing hemodialysis (HD).

Methods: In this cross-sectional study, data on 69 patients with diabetes who underwent standard HD therapy were analyzed. For estimating muscle mass, anthropometric and bioelectrical impedance analyses were conducted following dialysis. In addition, routine laboratory and 3-d dietary data were obtained. The adequate intake (AI) cut-off for ω -3 PUFAs was 1.6 g/d and 1.1 g/d for male and female patients, respectively.

Results: The average age of the participants was 63.0 ± 10.4 y. The mean ratios of ω-3/ω-6 PUFA intake, ω-6/ω-3 PUFA intake, SMM, and ASM of the patients were $0.13 \pm 0.07, 9.4 \pm 6.4, 24.6 \pm 5.4$ kg, and 18.3 ± 4.6 kg, respectively. Patients who had AI of ω-3 PUFAs had significantly higher SMM and ASM than did their counterparts. Linear and stepwise multivariable adjustment analyses revealed that insulin resistance and the ω-6/ω-3 PUFA ratio were the independent deleterious determinants of ASM normalized to height in HD patients.

Conclusions: Patients with AI of ω -3 PUFAs had total-body SMM and ASM that were more appropriate. A higher dietary ratio of ω -6/ ω -3 PUFAs was associated with reduced muscle mass in HD patients.

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Introduction

Diabetes mellitus (DM), the most common cause of end-stage renal disease (ESRD), has been a major risk factor for body protein loss and muscle wasting, which are associated with increased morbidity and mortality in patients undergoing hemodialysis (HD) [1,2]. In 1970 [3], Thage reported that patients with diabetes undergoing dialysis have a higher prevalence and forms of uremic-induced skeletal myopathy that are more severe. Pupim et al. demonstrated that patients with diabetic ESRD exhibited higher loss of lean body mass than did their age-, sex-,

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and race-matched counterparts without diabetes [4]. Identifying an approachable treatment for maintaining muscle mass or mitigate the consequences associated with muscle wasting in HD patients is expected to improve patient function, because the coexistence of DM and potential stressful conditions result in protein-energy wasting, which may synergistically increase the death risk in patients undergoing HD [5].

A large body of evidence now shows that unbalanced ratio of ω -3 and ω -6 polyunsaturated fatty acids (PUFAs), as is found in today's Western diets, leads to the pathogenesis of many diseases [6-9], including vascular disease, cancer, osteoporosis, autoimmune diseases, cognitive decline, and incidence of dementia; however, studies investigated the ratio between these two PUFAs in muscle science is less well known. Both ω -3 and ω -6 PUFAs are essential fatty acids for human body. These two PUFAs not only play critical roles in cell membrane integrity, but potentially contribute to muscle hypertrophy and atrophy; they also have catabolic and anabolic effects on muscle cells [10]. Helge et al. demonstrated that participants with improved leg muscle functioning had significantly lower ω -6/ ω -3 ratio of muscle phospholipid fatty acid composition [11]. In a population-based study on older Italians [12], a higher plasma ω -6/ ω -3 ratio was associated with age-related decline in physical performance. If the ratios between ω -3 and ω -6 PUFAs were associated with indices of muscle mass, the effective nutrition therapy strategies for patients with diabetes undergoing dialysis are warranted.

Because of the health benefits of ω-3 PUFAs in the general population, the American Heart Association recommends the consumption of fish at least twice a week [13]. Sakuma and Yamaguchi (2012) affirmed that adequate intake (AI) of ω-3 PUFAs is 1.6 g/d for men and 1.1 g/d for women [14]. Nevertheless, no specific recommendations currently exist regarding the dietary intake of ω-3 PUFAs for patients with ESRD. Friedman et al. found that 67% of HD patients who did not follow the American Heart Association fish-consumption guidelines had low plasma ω-3 PUFA concentrations [15]; therefore, they considered patients undergoing HD to be ideal for exemplifying the effects of ω-3 PUFAs [16].

According to our review of relevant literature, few studies have investigated how muscle mass is affected by dietary ω -3 and ω -6 PUFAs, particularly in HD patients. We hypothesized that patients with diabetic ESRD having a higher dietary ratio of ω -3/ ω -6 PUFAs have a lower risk of muscle mass decline. The broad aims of this study were 1) to investigate the relationship between dietary PUFAs and muscle mass; and 2) to evaluate the possible univariate significant and nonsignificant relevant predictors of muscle mass in patients with diabetes undergoing HD.

Materials and methods

Study subjects

This study used cross-sectional data in a completed study design for investigating the association between improved nutritional care and the prognosis of cardiovascular disease (CVD) in HD populations. In brief, participants ages 20 and older undergoing HD for at least 3 mo were recruited from three hospital-based HD centers of Taipei Medical University (TMU) during September 2013 to January 2015. Dialysis patients regularly underwent a thrice weekly HD regimen, for achieving an equilibrated Kt/V (eKt/V) of 1.2 in the initial 3 mo. Patients with severe edema, amputation, hyper- and hypothyroidism, <500 kcal/d or >3500 kcal/d of reported energy intake, known malignancies, infection, hospitalization 1 mo before the study, or missing data in their assessments were excluded. The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from each participant. The Research Ethics Committee of TMU approved the study protocol (201302024).

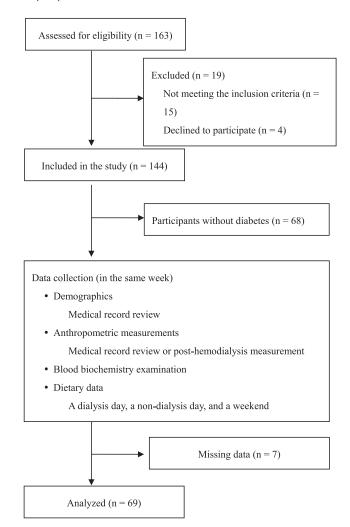


Fig. 1. Flow chart indicating patient enrolment and the study procedure.

We investigated all consecutive patients with type 2 diabetes undergoing HD by reviewing their medical charts. Among the 163 HD participants, 69 patients with diabetes were identified (Fig. 1).

Demographic characteristics and anthropometric measurements

Well-trained staff censored the medical records of the participants according to standardized methods and procedures. Demographic data comprising age, sex, dialysis vintage and dose, history of diabetes, hypertension, and CVD were retrieved. In addition, anthropometric information, comprising height, dry weight, and interdialytic weight gain, was retrieved through chart review. Body mass index (BMI) was calculated as dry weight (in kg) divided by the square of the height (in m). Skeletal muscle mass (SMM) and appendicular skeletal muscle mass (ASM) were measured using InBody S10 Biospace (a multifrequency bioelectrical impedance analyzer [BIA], InBody, Seoul, Korea), according to manufacturer guidelines. The eight surface electrodes of the BIA were placed on the thumbs, middle fingers, and either side of the ankles of the patients, who rested in a sitting position after the HD session. In total, 30 impedance measurements were obtained at six frequencies (1 kHz, 5 kHz, 50 kHz, 250 kHz, 500 kHz, and 1000 kHz). SMM and ASM were estimated as the sum of the total body and four-limb muscle mass, respectively, and normalized to the square of the height (in m), thus yielding the body composition-defining SMM and ASM indices.

Biochemical assays

Standard laboratory tests were performed during monthly routine examinations at the clinical laboratories of each hospital through automated and standardized methods. The predialysis albumin (bromocresol green), creatinine,

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