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#### Applied nutritional investigation

# Glomerular filtration rate after a 12-wk resistance exercise program with post-exercise protein ingestion in community dwelling elderly

Alfons Ramel Ph.D.<sup>a,\*</sup>, Atli Arnarson M.Sc.<sup>a</sup>, Olof G. Geirsdottir Ph.D.<sup>a,b</sup>, Palmi V. Jonsson M.D.<sup>b,c</sup>, Inga Thorsdottir Ph.D.<sup>a</sup>

<sup>a</sup> Unit for Nutrition Research, National University Hospital and Faculty of Food Science and Nutrition, University of Iceland, Reykjavik, Iceland <sup>b</sup> The Icelandic Gerontological Research Center, National University Hospital and Faculty of Medicine, University of Iceland, Reykjavik, Iceland <sup>c</sup> Department of Geriatrics, National University Hospital and Faculty of Medicine, University of Iceland, Reykjavik, Iceland

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#### ABSTRACT

*Objective:* Increased protein intake and resistance exercise can be beneficial for maintenance of lean body mass (LBM) in older adults. However, these factors could also negatively affect renal function. We investigated changes in renal function after a 12-wk resistance exercise program combined with protein supplementation in community dwelling older adults.

*Methods*: Patients (N = 237, 73.7  $\pm$  5.7 y, 58.2% female) participated in a 12-wk resistance exercise program (3 times/wk) designed to increase strength and muscle mass of major muscle groups. Participants were randomly assigned to one of three dietary supplements consumed directly after training: whey protein drink (20 g whey protein, 20 g carbohydrates), milk protein drink (20 g milk protein, 20 g carbohydrates), or carbohydrate drink (40 g carbohydrates). Renal function was estimated as glomerular filtration rate (GFR, Cockcroft-Gault formula), and dietary intake was measured as 3-d-weighed food record at baseline and endpoint.

*Results:* During the intervention, energy intake did not increase. Carbohydrate intake increased in the carbohydrate group and protein intake increased in the milk group, both approximately in accordance with the supplementation. In the whey group, protein intake did not increase, but carbohydrate intake did. GFR increased after the intervention (+4.4 mL/min/1.73 m<sup>2</sup>; P < 0.001), and the changes were similar in men and women or in the age quartiles. Changes in GFR at endpoint were not associated with LBM, dietary supplements, or total protein intake.

*Conclusions:* A 12-wk resistance exercise program combined with protein supplementation in community dwelling older adults does not negatively affect GFR. The supplementation had only minor effects on total dietary intake.

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#### Introduction

Aging is associated with changes in body composition, i.e., decreased lean body mass (LBM), increased fat mass, and a more central distribution of adipose tissue [1]. The loss of LBM accelerates after the age of 60 and is a contributor to disability, frailty, and functional impairments [2,3]. Higher LBM has also been reported to be a predictor of lower mortality in older adults [4]. There is a large variation between individuals in the changes of LBM during aging partly explained by physical activity, in particular resistance exercise [5,6].

Inadequate dietary intake, especially protein intake, has been associated with decreased LBM [7]. Dietary protein affects muscle mass by the stimulation of muscle protein synthesis after the absorption of amino acids into muscle cells. It has been questioned whether optimal intake for older adults should be higher, e.g., 1.2 g/kg to 1.5 g/kg body weight, [7,8] than the current RDA of 0.8 g/kg body weight [9].

Concerns have been raised about potential detrimental effects of increased protein intake on renal function, as reflected by reduced glomerular filtration [7]. Usually, the glomerular filtration rate (GFR), a parameter of renal function, declines by 1 mL/min per 1.73 m<sup>2</sup> after the age of 50 y [10]. And there is a general agreement that protein intake should be limited in individuals with renal disease because it can contribute to the deterioration of kidney function [11]. However, according to a recent review on protein

<sup>\*</sup> Corresponding author. Tel.: +354 543 8417; fax: +354 543 4824. *E-mail address:* alfonsra@hi.is (A. Ramel).

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intake in older adults, there is no evidence that a low protein diet is beneficial to individuals without pre-existent renal disease [7].

Another factor that can affect LBM is physical activity. In general, 150 min/wk of physical activity are recommended for older adults by the American College of Sports Medicine and by the American Heart Association, as physical activity can reduce the development and progression of chronic diseases and disabling conditions [12]. In particular, resistance exercise at least twice a wk is recommended for older adults as it has been shown to delay the loss of LBM and strength associated with aging [12].

However, strenuous exercise, as done during a resistance exercise program, can result in muscle damage, evidenced by delayed-onset muscle soreness, strength loss, weakness, tenderness, and increased blood levels of muscle proteins, e.g., myoglobin. High blood myoglobin levels can "spill over" into the urine, resulting in myoglobinuria, and also can precipitate in the kidney tubules, potentially resulting in acute renal failure [13–15]. A negative correlation between muscle damage and renal function 3 d after resistance exercise has been reported in women [16].

Taken together, both increased protein intake and resistance exercise training can be beneficial for LBM, strength, and physical function in older adults. However, there is also the potential that these factors negatively affect renal function in this group. To investigate this issue, a secondary analysis of a recent dietary intervention trial in older adults was conducted [17,18]. The aim of the current paper was to investigate the changes in renal function after a 12-wk resistance exercise program combined with post-exercise protein ingestion in community dwelling older adults.

#### Methods

#### Participants

Participants (N = 236) were 65 y and older (range 65–92 y old) and were recruited by advertisements posted in the Reykjavik area. Exclusion criteria were low cognitive function (Mini-Mental State Examination (MMSE)  $\leq$ 19 points) [19], major orthopedic disease, and pharmacological interventions with exogenous testosterone or other drugs known to influence muscle mass. Furthermore, participants had to be free of any musculoskeletal disorders or other disorders that could affect their muscle mass. Enrolled participants were apparently healthy, although some had hypertension, hyperlipidemia, or type 2 diabetes. The study was approved by the Icelandic National Bioethics Committee (VSNb2008060007/03-15), and informed written consent was obtained from all participants.

#### Study design and intervention

The main purpose of this intervention study [17,18] was to investigate whether post-exercise ingestion of whey protein, milk protein, or carbohydrate drinks in combination with a resistance exercise program affects lean body mass, muscle strength, or physical function in older adults. The participants participated in a 12-wk resistance exercise intervention program, which was designed to increase strength and muscle mass of all major muscle groups. All data were obtained at baseline and again at the end of the study period.

Participants exercised for three nonconsecutive d per wk for 12 wk in groups of 20 to 30 individuals. The first week was used to teach correct exercise techniques at lower loads (60% of 1-repetition maximum [RM]). Thereafter, resistance training involved 3 sets, for which each exercise was repeated 6 to 8 times, at 75% to 80% of their 1-RM. The training load was systematically increased by 5% to 10% each week in order to keep the number of repetitions per set between 6 and 8. Each exercise session started with a 10 min to 15 min warm up, after which resistance training with weights on all major muscle groups was performed. Stretching exercises were performed at the end of each session. Each session was supervised by study staff, an athletic trainer, and occasionally, a physical therapist.

Participants were randomly assigned to one of three different dietary supplements that were consumed after each training session. The dietary supplements were (1) a whey protein drink (20 g whey protein isolate + 20 g

carbohydrates), (2) a milk protein drink (20 g milk protein isolate + 20 g carbohydrates), or (3) a carbohydrate drink (40 g carbohydrates).

#### Dietary intake

Participants weighed and recorded their food intake for three consecutive d before the 12-wk training program (baseline) and during the last week of the program (endpoint), including two weekdays and either a Saturday or a Sunday. One of the three days was a training day. The food records were analyzed using an online program (www.hvaderimatnum.is) based on the Icelandic food composition database (ISGEM). ISGEM is based on 1148 food items from the National Nutritional Database [20].

#### Body composition

Body composition was assessed by dual energy x-ray absorptiometer (DXA) with Hologic QDR-2000 plus (Hologic Inc., Waltham, MA, USA). The DXA measurements were conducted at the Icelandic Heart Association, Kopavogur, Iceland. Body weight (BW) was measured in light underwear on a calibrated scale (model no. 708, Seca, Hamburg, Germany), and height was measured with a calibrated stadiometer (model no. 206; Seca, Hamburg, Germany). Body mass index (BMI) was calculated from the recorded height and weight (kg/m<sup>2</sup>). Waist circumference was measured halfway between the top of the lateral iliac crest and the lowest rib. All measures were performed twice using a tape measure and recorded to the nearest centimeter.

#### Physical function

#### Timed up and go (TUG) test

During the TUG test, the participant was instructed to rise from a chair with a seat height of 43 cm, walk 3 m, turn around, return, and sit down again, wearing ordinary footwear and using customary walking aids if necessary [21].

#### Six min walk for distance (6MWD)

The 6MWD was performed indoors, in a spacious gym hall, and conducted according to the guidelines from the American Thoracic Society [22].

#### Leisure time physical activity

Leisure time physical activity was assessed by self-reports. It is shown either as kcal/wk by multiplying the appropriate kcal score (based on metabolic equivalent of the task values) for each of the activities by the amount of time spent during the week doing the activity [23]. Total physical activity was defined as the sum of the activity reported on the questionnaire for non-exercise walking (e.g., walking the dog), walking for exercise, and other moderate and vigorous exercise activities.

#### Biochemical measurements

Participants were instructed to avoid strenuous exercise and alcohol consumption the day before the drawing of fasting blood samples at baseline and endpoint. The blood samples were centrifuged, and the serum was stored at  $-80^{\circ}$ C for subsequent analyses. Serum creatinine (µmol/L) was measured by standard dry chemistry methodology on a Vitros 750 XRC 700 analyzer (Johnson & Johnson) at the laboratory of the Landspitalinn University Hospital in Reykjavik.

#### Calculation of glomerular filtration rate (GFR)

GFR was calculated using the Cockcroft-Gault formula [24]:

 $\label{eq:GFR} GFR \ = \ ([140-age]\times\ weight\ \times\ 1.23\ \times\ [0.85\ for\ women])/serum\ creatinine;$ 

GFR is shown as GFR/1.73 m<sup>2</sup>. Body surface area (BSA) was calculated using the formula from DuBois and DuBois:  $0.007184 \times \text{height}^{0.725} \times \text{weight}^{0.425}$ 

Adjustment for the Cockcroft-Gault formula was done as follows: GFR/BSA  $\times$  1.73.

We decided to use Cockcroft-Gault formula, because it has been reported to be robust against variations in training regimen [25].

#### Statistical analysis

The data were entered into the SPSS statistical package, version 18.0 (SPSS, Chicago, IL, USA) and checked for normality using the Kolmogorov-Smirnov test. Data are described as mean  $\pm$  standard deviation (SD). The paired samples *t* test was used to assess differences in GFR and dietary intake before and after the 12-wk intervention; Mann-Whitney test was used to assess these differences in

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