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NEPHROLOGY – ORIGINAL PAPER

Anti-sarcopenic effect of leucine-enriched branched-chain amino acid supplementation among elderly chronic kidney disease patients: a double-blinded randomized controlled trial

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Abstract

Background Leucine, a branched-chain amino acid (BCAA), is an effective nutritional strategy to enhance skeletal muscle mass in aging populations. This study aimed to evaluate the effects of oral leucine-enriched BCAA supplementation on muscle mass, muscle synthesis biomarkers, and physical performance in elderly patients with chronic kidney disease (CKD).

Methods A randomized controlled trial was conducted among CKD patients aged over 65 years. The participants were randomly assigned to receive either oral mixed BCAA supplementation (60% leucine, 4.5 g/day; 20% valine, 1.5 g/day; 20% isoleucine, 1.5 g/day) ($N=29$) or a placebo ($N=26$) for 12 weeks. Muscle mass, serum insulin-like growth factor 1 (IGF-1), and myostatin levels were measured at baseline and after 12 weeks. A 3-day food record was reviewed by a dietitian, and functional capacity was assessed using handgrip and 6-min walk tests.

Results Fifty-five patients (mean age 75.4 ± 5.2 years) were enrolled. Daily protein and calorie intake were comparable between groups. At study conclusion, lean muscle mass significantly increased in the leucine group compared to placebo (0.4 kg [95% CI 0.1–0.7] vs. − 0.2 kg [95% CI − 0.6–0.2], $P=0.010$). A significant difference in the percentage change in muscle mass was also observed ($1.0 \pm 1.8\%$ vs. $-0.5 \pm 2.6\%$, $P=0.014$). No significant differences were found in muscle strength, serum myostatin, IGF-1, or adverse events.

Conclusions Leucine-enriched BCAA supplementation for 12 weeks significantly increased muscle mass but did not impact biomarkers of muscle activity or functional capacity in elderly CKD patients.

Clinical trial registration TCTR20200314003

Keywords Sarcopenia · Leucine · Chronic kidney disease · Body composition · Muscle wasting

Abbreviations

BCAA	Branched-chain amino acids
CKD	Chronic kidney disease
EAAs	Essential amino acids
ELISA	Enzyme-linked immunosorbent assay
GFR	Glomerular filtration rate
IGF-1	Insulin growth factor-1
SD	Standard deviations

Background

Sarcopenia is a common problem among elderly people with a prevalence from 5 to 13% in persons aged 60–70 years and up to 50% among individuals over 80 years of age [1]. In addition, chronic kidney disease (CKD) in older populations is a likely contributor to loss of muscle mass [2]. Muscle wasting is a common feature of the uremic phenotype among patients with CKD and increases risk of physical disability, poor quality of life, frailty and death [3]. Therefore, therapies designed to increase muscle mass and strength of patients with CKD might be expected to improve their physical function and possibly their survival rates. Treating muscle wasting poses difficulties among elderly exercise-hesitant patients and identifying effective therapies for age-related sarcopenia represents an ongoing challenge [4, 5].

The branched-chain amino acids (BCAA) especially leucine-enriched essential amino acids (EAA) have been

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thought to promote anabolic responses and basal muscle protein synthesis that might mitigate sarcopenia [6]. Leucine-enriched EAAs exert stimulatory effects on skeletal muscle protein synthesis particularly via activation of the mammalian target of rapamycin (mTOR) signaling pathway and an inhibitory effect on proteolysis mediated by branched-chain keto acids [7–9]. Clinical studies showed that L-leucine supplementation enhanced strength performance during a resistance training program of initially untrained healthy subjects [10] and leucine supplementation improved muscle protein synthesis among elderly men [11]. In addition, enriching an EAA mixture with leucine demonstrated prophylaxis against age-related sarcopenia among the elderly [12]. Increased activation of proteolysis and leucine oxidation has been reported in CKD associated with metabolic acidosis [13]. Early studies indicated that leucine-enriched BCAA supplementation significantly decreased muscle catabolism and improved muscle mass, nutritional status, and physical function in hemodialysis patients [14–16]. This study aimed to evaluate the efficacy of leucine-enriched BCAA supplementation over a 12-week period on muscle mass, biomarkers of muscle synthesis, and physical capacity among elderly patients with CKD stages 3–4.

Methods

Subjects

This study was a randomized controlled trial conducted among elderly patients with CKD treated at Phramongkutklao Hospital between 1 June 2019 and 30 April 2020. The inclusion criteria included age over 65 years and CKD stages 3–4 with stable kidney function for 12 weeks. The exclusion criteria comprised hypercatabolic stages such as sepsis, malignancy, liver disease, inflammatory myopathy, autoimmune diseases or recent hospitalization within 12 weeks, history of steroids, immunosuppressive agents and chemotherapy and history of hypersensitivity to EAAs. The study was registered at Thai Clinical Trials Registry (TCTR) (TCTR20200314003, date of registration: 11/03/2020). The study complies with the Declaration of Helsinki (1964). The Ethical Review board in Phramongkutklao Hospital and College of Medicine, Bangkok, Thailand approved the study protocol. All subjects provided written informed consent.

Study design and protocol

The subjects were randomly assigned by block of four randomizations based on a computerized random-number generator and allocation concealment, then divided in two groups as shown in Fig. 1. Assuming similar standard deviations (SD) from related studies, a t test comparison using a

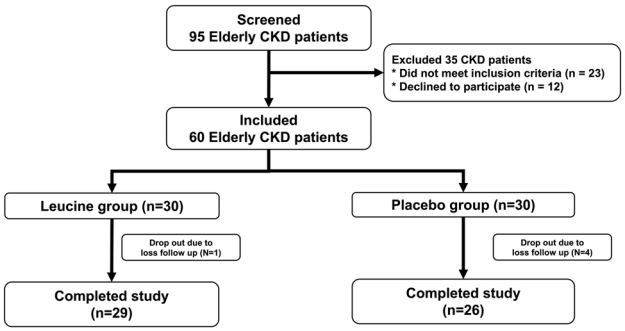

Fig. 1 Flow chart of study

two-sided α of 0.05 was estimated to detect a difference in lean muscle mass with 80% power in a sample of 54 participants (30 per group) [6]. One group consisted of 29 patients treated with oral 4.5 g/day of 60% leucine, 1.5 g/day of 20% valine and 1.5 g/day of 20% isoleucine supplement, while the other group comprised 28 patients treated with placebo containing maltose in equal weight with isocaloric supplements in similarly identical gelatin capsules (size 500 mg/capsule), 5 capsules three time daily in the same manner for 12 weeks. Pill count and telephone reminders were used to check drug compliance by nutritionists every mouth and at every follow-up of all patients in both groups. Renal function and adverse events related to leucine using Naranjo's algorithm were monitored in every four weeks.

Data relating to demographics, medical and psychiatric history and CKD treatment were collected before and after the study. All subjects received nutritional counseling from dietitians for target daily energy intake of 30 – 35 kcal/kg/day and protein intake of 0.8 – 1 g/kg/day. Every 4 weeks, all patients maintained a 3-day food record and underwent dietary interviews by a registered dietitian. Nutrient composition of the diets was analyzed using the Inmucal National Food Database Program. All subjects typically continued their normal daily life activities and exercise during treatment.

Body composition measurement and muscle synthesis biomarkers

The subjects were measured wearing light-weight clothing. Height was determined using a stadiometer and body weight was recorded using electronic scales. At baseline and week 12, whole body composition was assessed using a dual energy X-ray absorptiometry scan (Lunar iDXA, GE Healthcare, Madison, WI, USA) with calibration checked daily using the GE Lunar calibration. The mean change of lean muscle mass between the leucine and placebo groups at 12 weeks constituted the primary outcome of study.

All subjects underwent routine blood chemistry, serum insulin growth factor-1 (IGF-1), serum myostatin by enzyme-linked immunosorbent assay (*ELISA*) at baseline and 12 weeks at the end of the study. Serum biomarkers (IGF-1, myostatin level) were compared between the leucine and the control groups. The coefficients of variation for serum biomarkers assays were < 10%, for intra-assay and inter-assay variation.

Functional capacity

All participants were monitored for functional capacity using the handgrip and 6-min walk tests during the study. A digital handheld dynamometer (Takei® Kigi Kogyo Hand Analog Grip Dynamometer) was used to record the isometric muscle strength of both arms and the three-time repetition test. The average values of the isometric muscle strength for both arms and the three-time repetition test were then calculated. The results are reported relative to body weight. Regarding the 6-min walk test, subjects attained their maximal distance in 6 min then reported in meters. Concerning physical activity recall, we used an electronic step count watch to monitor steps in daily life activities.

Statistical analyses

Using the intention-to-treat principle, participants were analyzed in the groups to which they were randomized. Data were presented as percentages and means ± SD. Categorical variables were compared using Chi-square or Fisher's exact tests, and continuous variables were compared using Independent *t*-test, paired-sample *t* test, Mann–Whitney *U* test and repeated measures two-way analysis of variance (ANOVA) test. All results were considered significant when *P* was < 0.05.

Results

Ninety-five elderly patients with CKD were screened determining 60 subjects eligible according to the inclusion criteria. In all, 30 patients were assigned to the leucine and 30 patients to the placebo groups. Fifty-five (91.7%) patients completed the study: 29 (96.7%) in the leucine and 26 (86.7%) in the placebo groups. The mean age was 75.4 ± 5.2 years, mean estimated glomerular filtration rate (GFR) was 42.2 ± 9.5 mL/min/1.73 m^2 and 60% of patients were male. Over 85% had at least one comorbidity, with hypertension and type 2 diabetes being the most common. The baseline characteristics of the study population are shown in Table 1. No significant differences were observed in baseline clinical data including age, body weight, body mass index, dietary intake, biochemistry, serum IGF-1 level, myostatin level, muscle mass, and functional capacity.

Body weight and body compositions

Body weight and body compositions throughout the study are shown in Table 2. Over 12 weeks, no significant difference was observed in changes of body weight and fat mass between the leucine and placebo groups. However, lean muscle mass was significantly increased at 0.4 kg (95% CI 0.1 to 0.7, $P = 0.006$) from baseline in the leucine group, but did not significantly change from baseline in the placebo group (− 0.2 kg; 95% CI − 0.6 to 0.2, $P = 0.283$). A significant difference was observed in the increased lean muscle mass between the leucine and placebo groups. (0.8 kg; 95% CI (0.2–1.3), $P = 0.010$) (Fig. 2). Moreover, percentage of changes in muscle mass at 12 weeks of treatment were significantly higher among patients receiving leucine compared with those receiving placebo (1.0 ± 1.8 vs. − 0.4 ± 2.6%, $P = 0.014$).

Serum IGF-1 and myostatin levels

Serum IGF-1 and myostatin level throughout the study are shown in Table 3. Serum IGF-1 levels decreased from baseline in the leucine group (− 19.6 ng/mL, 95% CI − 35.2 to − 3.9, $P = 0.017$), whereas they did not change in the placebo group (13.7 ng/mL (95% CI − 30.2 to 2.9, $P = 0.100$). No significant difference was observed in the changes of serum IGF-1 and myostatin levels between the leucine and placebo groups.

Biochemistry, nutrient intake and functional capacity

Over 12 weeks, no significant differences were found in change in energy and protein intake, serum albumin, prealbumin, blood urea nitrogen, estimated GFR, bicarbonate and functional capacity including distance of the 6-min walk test, hand grip test and walking distance in 1 day between the leucine and placebo groups (Table 4). The percentage of medication adherence ascertained by pill count was 95% in the leucine and 98% in the placebo groups.

Adverse events

At the end of the study, no drug-related serious adverse events or anaphylaxis was reported in both groups. Nausea related to treatment occurred 3.4% in the leucine and 3.8% in the placebo groups. These results indicated that leucine supplement was well-tolerated in the study.

Table 1 Baseline characteristics

	Leucine group($N=29$)	Placebo group($N=26$)
Age (years)	75.8 ± 5.3	75.0 ± 5.1
Male (*N*, %)	17 (58.6%)	16 (61.5%)
Body weight (kg)	64.0 ± 9.7	60.6 ± 10.6
Body mass index (kg/m^2)	24.7 ± 2.8	24.7 ± 2.8
Energy intake (kcal/kg/day)	23.5 ± 5.7	26.7 ± 7.0
Protein intake (g/kg/day)	0.8 ± 0.2	0.9 ± 0.3
Underlying diseases (*N*, %)		
Hypertension	28 (96.6%)	25 (96.2%)
Dyslipidemia	26 (89.7%)	22 (84.6%)
Ischemic heart disease	4 (13.8%)	4 (15.4%)
Gout	4 (13.8%)	3 (11.5%)
Fasting plasma glucose (mg/dL)	95.8 ± 11.4	94.5 ± 7.4
Blood urea nitrogen (mg/dL)	19.1 ± 6.3	20.3 ± 6.7
Serum creatinine (mg/dL)	1.5 ± 0.4	1.5 ± 0.4
Estimated GFR (mL/min/1.73m^2)	42.2 ± 9.5	41.5 ± 11.1
Serum prealbumin (mg/dL)	28.6 ± 7.8	28.3 ± 7.2
Serum albumin (g/dL)	4.4 ± 0.2	4.5 ± 0.3
Serum bicarbonate (mEq/L)	25.6 ± 2.7	25.5 ± 2.0
Serum IGF-1 (ng/mL)	124.6 ± 46.2	110.6 ± 25.9
Serum myostatin (pg/mL)	3987.2 ± 1769.6	4136.1 ± 1326.7
6-min walk test (m)	315.1 ± 85.8	345.5 ± 64.9
Right hand grip test (kg)	25.9 ± 7.7	23.9 ± 5.9
Left hand grip test (kg)	24.3 ± 7.6	21.7 ± 6.5
Walking distance in a day (km)	2.0 ± 1.1	2.3 ± 1.3

Data are expressed as mean ± SD and percentage

All parameters were not significant difference ($P>0.05$)

Table 2 Changes in body weight and body composition by dual energy X-ray absorptiometry

	Leucine group($n=29$)	Placebo group($n=26$)	*P*-value between group
Body weight (kg)			
Baseline	63.9 ± 9.7	60.6 ± 10.6	0.231[a]
At 12 weeks	64.1 ± 9.4	60.4 ± 10.4	0.166[a]
Change from baseline (95% CI)	0.2 (−0.3, 0.6)	−0.3 (−0.6, 0.1)	0.120[b]
Lean muscle mass (kg)			
Baseline	39.6 ± 7.3	38.5 ± 6.7	0.572[a]
At 12 weeks	39.9 ± 7.4	38.3 ± 6.5	0.373[a]
Change from baseline (95% CI)	0.4 (0.1, 0.7)[*]	−0.2 (−0.6, 0.2)	0.010[b]
Fat mass (kg)			
Baseline	22.0 ± 5.7	20.0 ± 6.2	0.222[a]
At 12 weeks	22.0 ± 5.8	20.2 ± 6.2	0.257[a]
Change from baseline (95% CI)	−0.01 (−2.4, 1.8)	0.1 (−1.0, 1.7)	0.574[b]

Data are expressed as mean ± SD and mean with 95% CI

[*] *P*-value < 0.05 obtained by paired *t* test

[a] *P*-value obtained by independent *t* test

[b] *P*-value for the interaction effect of treatment and time by repeated measure ANOVA analysis

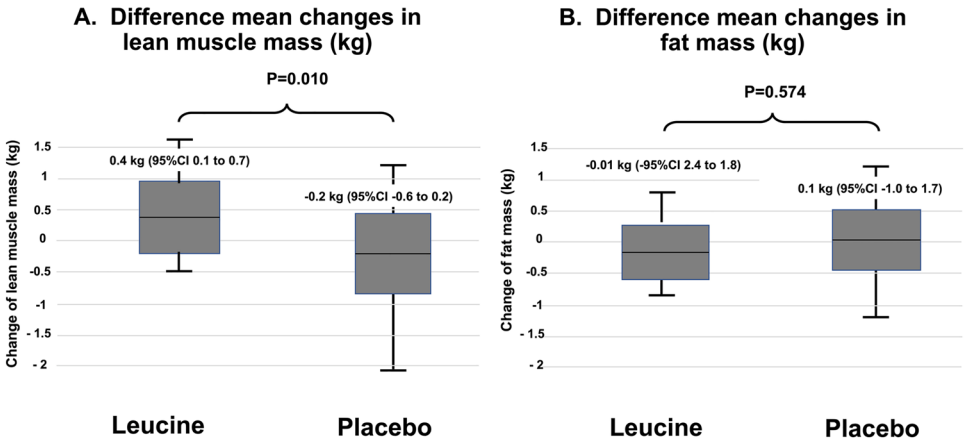

Fig. 2 Mean change of lean muscle mass and fat mass over 12 weeks of treatment. Significant between-group differences were noted in the mean change of lean muscle mass ($P < 0.001$)

Table 3 Changes in serum myostatin and IGF-1 level

	Leucine group($n = 29$)	Placebo group($n = 26$)	*P*-value between group
Serum myostatin (pg/mL)			
Baseline	3987.2 ± 1769.6	4136.1 ± 1326.7	0.773[a]
At 12 weeks	4564.0 ± 2348.8	3935.0 ± 742.3	0.290[a]
Change from baseline (95% CI)	576.8 (− 124.8,1278.4)	− 201.1 (− 715.7, 313.5)	0.066[b]
Serum IGF-1 (ng/mL)			
Baseline	124.6 ± 46.2	110.6 ± 25.9	0.259[a]
At 12 weeks	105.1 ± 39.9	96.9 ± 34.8	0.513[a]
Change from baseline (95% CI)	− 19.6 (− 35.2, − 3.9)[*]	− 13.7 (− 30.2, 2.9)	0.591[b]

Data are expressed as mean ± SD and mean with 95% CI

[*] *P*-value < 0.05 obtained by paired *t* test

[a] *P*-value obtained by independent *t* test

[b] *P*-value for the interaction effect of treatment and time by repeated measure ANOVA analysis

Discussion

The present study constitutes the first randomized, placebo-controlled trial of oral leucine-enriched BCAA supplement among elderly patients with CKD. Leucine-enriched BCAA supplement promotes a significant increased lean muscle mass among elderly patients with CKD, but the supplement did not demonstrate benefits concerning biomarkers of muscle activity and functional capacity. The risk of serious adverse event was not higher among patients receiving leucine-enriched BCAA supplement. From the result of the study, the clinical trial provided evidence concerning leucine-enriched BCAA supplement among elderly patients with CKD compared with standard treatment on improving lean muscle mass.

Sarcopenia is common among elderly patients with CKD, particularly in those with more advanced stages of the disease [17]. CKD is characterized by abnormal amino acid metabolism [18], and reduced blood BCAA levels and peripheral release of leucine in patients with uremia suggest increased leucine degradation [19, 20]. Data on the benefits and risks of oral EAAs enriched with leucine in this setting remain limited. Two studies reported that leucine supplementation increased muscle mass and restored the attenuated muscle protein synthesis response among healthy elderly individuals [6, 12]. Similarly, early studies demonstrated that leucine-enriched BCAA supplementation significantly reduced muscle catabolism and improved muscle mass, nutritional status, and physical function in hemodialysis patients [14–16]. Recently, a systematic review showed that leucine supplementation improved muscle mass in elderly adults [21]. Additionally, amino acid supplementation has been shown to acutely stimulate muscle protein synthesis in elderly individuals [22]. Mechanistically, an oral EAA formulation containing approximately 35% leucine has been demonstrated to reduce muscle proteolysis and stimulate mTOR activation, thereby enhancing protein synthesis [7, 8]. Our study further supports that EAAs enriched with leucine

Table 4 Change in laboratory biochemistry and functional capacity

	Leucine group($n=29$)	Placebo group($n=26$)	*P*-value between group
Energy intake (kcal/kg/day)			
Baseline	23.5 ± 5.7	26.7 ± 7	0.079[a]
At 12 weeks	24.1 ± 5.3	25.3 ± 7.8	0.544[a]
Change from baseline (95% CI)	0.6 (− 0.9, 2.1)	− 1.5 (− 3.6, 0.6)	0.102[b]
Protein intake (g/kg/day)			
Baseline	0.8 ± 0.2	1 ± 0.3	0.105[a]
At 12 weeks	0.9 ± 0.3	0.9 ± 0.3	0.899[a]
Change from baseline (95% CI)	0.1 (− 0.03, 0.2)	− 0.1 (− 0.2, 0.04)	0.073[b]
Fasting plasma glucose (mg/dL)			
Baseline	95.8 ± 11.4	94.5 ± 7.4	0.605[a]
At 12 weeks	94.1 ± 8.9	91.5 ± 6.1	0.218[a]
Change from baseline (95% CI)	− 1.8 (− 5.5, 2.0)	− 2.9 (− 5.8, − 0.1)*	0.605[b]
Blood urea nitrogen (mg/dL)			
Baseline	19.1 ± 6.3	20.3 ± 6.7	0.462[a]
At 12 weeks	20 ± 6	20.6 ± 6	0.694[a]
Change from baseline (95% CI)	0.9 (− 0.4, 2.3)	0.3 (− 1.6, 2.1)	0.557[b]
Serum creatinine (mg/dL)			
Baseline	1.5 ± 0.4	1.5 ± 0.4	0.830[a]
At 12 weeks	1.5 ± 0.4	1.5 ± 0.4	0.685[a]
Change from baseline (95% CI)	− 0.01 (− 0.1, 0.1)	0.01 (− 0.04, 0.1)	0.574[b]
Estimated GFR (mL/min/1.73m2)			
Baseline	42.2 ± 9.5	41.5 ± 11.1	0.803[a]
At 12 weeks	42.5 ± 9.7	40.9 ± 10.2	0.556[a]
Change from baseline (95% CI)	0.3 (− 1.5, 2.1)	− 0.6 (− 2.4, 1.2)	0.469[b]
Serum albumin (g/dL)			
Baseline	4.4 ± 0.2	4.5 ± 0.3	0.380[a]
At 12 weeks	4.5 ± 0.2	4.4 ± 0.2	0.719[a]
Change from baseline (95% CI)	0.05 (− 0.03, 0.1)	− 0.04 (− 0.1, 0.1)	0.177[b]
Serum prealbumin (mg/dL)			
Baseline	28.6 ± 7.8	28.3 ± 7.2	0.902[a]
At 12 weeks	16.9 ± 2.8	17.1 ± 2.9	0.895[a]
Change from baseline (95% CI)	− 11.7 (− 15.4, − 7.9)*	− 11.2 (− 14.4, − 8.1)*	0.854[b]
6-min walk test (m)			
Baseline	315.1 ± 85.8	345.5 ± 64.9	0.147[a]
At 12 weeks	335.2 ± 101.9	370.5 ± 70.2	0.146[a]
Change from baseline (95% CI)	20.1 (1.0, 39.3)*	24.9 (10.9, 38.9)*	0.685[b]
Right hand grip test (kg)			
Baseline	25.9 ± 7.7	23.9 ± 5.9	0.282[a]
At 12 weeks	26.4 ± 8.2	24.2 ± 7.1	0.302[a]
Change from baseline (95% CI)	0.4 (− 0.6, 1.4)	0.3 (− 0.8, 1.3)	0.849[b]
Left hand grip test (kg)			
Baseline	24.3 ± 7.6	21.7 ± 6.5	0.178[a]
At 12 weeks	24.6 ± 8.4	22.1 ± 6.8	0.224[a]
Change from baseline (95% CI)	0.4 (− 0.5, 1.2)	0.4 (− 0.4, 1.2)	0.938[b]
Walking distance in a day (km)			
Baseline	2.0 ± 1.1	2.3 ± 1.3	0.375[a]
At 12 weeks	2.1 ± 1.3	2.5 ± 1.3	0.340[a]
Change from baseline (95% CI)	0.2 (− 0.01, 0.3)	0.2 (0.03, 0.4)*	0.643[b]

Data are expressed as mean ± SD and mean with 95% CI

*P-value < 0.05 obtained by paired t test

A hand grip test was used to record the isometric muscle strength of both arms and the three-time repetition test. The average values of the isometric muscle strength for both arms and the three-time repetition test were then calculated. The results are reported relative to body weight

Table 4 (continued)

[a]*P*-value obtained by independent *t* test

[b]*P*-value for the interaction effect of treatment and time by repeated measure ANOVA analysis

(containing 60% leucine) improved muscle mass among elderly patients with CKD. These findings suggest that EAAs enriched with leucine may have therapeutic potential due to their proven protein anabolic effects in this population.

The mechanisms for muscle wasting among patients with CKD indicated decreased synthesis of muscle mitochondrial proteins [23] and IGF-1 resistance play a role in decreasing muscle protein synthesis [24]. In addition, uremic toxins accelerate muscle atrophy by inducing myostatin expression, a negative regulator of skeletal muscle [25]. A previous study reported that EAA supplementation improved the postabsorptive muscle protein fractional synthesis rate and enhanced IGF-1 muscle protein expression, thereby augmenting protein synthesis in muscle tissue [6], and also significantly reduced inflammatory markers such as interleukin-10 in dialysis patients [26]. Our study also found that serum IGF-1 levels decreased from baseline after EAAs, enriched with leucine supplement, but no significant difference was observed in the changes of serum IGF-1 and myostatin levels between groups. Physiological responses to stimuli frequently cite upregulation of muscle IGF-I messenger RNA; whereas, the circulatory results may have distinct effects on muscle mass regulation [27]. Myostatin, in different disease conditions, produced conflicting results to muscle mass or muscle wasting and serum myostatin as a potential biomarker for muscle wasting. Thus, the relationship between serum and skeletal muscle mass remains unclear [28, 29]. Further studies need to measure tissue IGF-1 and myostatin after EAAs, enriched with leucine intervention.

The synergistic effects of protein supplementation and resistance exercise to increase muscle mass and strength gains have been explored among elderly subjects [30]. Similarly, combined exercise and BCAA stimulated cell signaling to promote muscle protein synthesis in CKD model rat [31] and combined exercise with oral nutritional supplementation produced larger effects concerning physical functions among patients undergoing dialysis [32]. Conflicting evidence was noted regarding the benefits of dietary EAA supplementation on increased muscle strength during resistance exercise training [33, 34]. In a systemic review, leucine-enriched protein supplementation was found to exert beneficial effects on lean body mass but not muscle strength among older individuals [35]. Our study did not provide evidence for muscle strength benefits of leucine-enriched BCAA supplementation among elderly patients with CKD. The apparent discrepancy may be attributed to inadequate exercise intensity and short duration of EAAs enriched with leucine supplement in settings of advanced age, more comorbidities and CKD. Long-term use of leucine-enriched BCAA supplement combined with physical resistance exercise may provide a significant change of physical strength among elderly patients with CKD.

The limitations of this study include a relatively small sample size for a clinical trial and the fact that most outcome measurements were obtained only at baseline and at the end of the 12-week study period. Muscle biopsy and tissue biomarkers, such as tissue IGF-1 and myostatin levels considered standard and accurate measures for evaluating muscle wasting were not used to assess the study outcomes. Another limitation is the short duration of the intervention, which may not fully capture the long-term effects of leucine-enriched BCAA supplementation on muscle mass and functional outcomes. The strength of the study lies in the use of dual-energy X-ray absorptiometry, the reference standard for measuring lean muscle mass among elderly patients with CKD [36]. In addition, all participants were monitored by nutritionists for dietary intake and exercise throughout the study. Adherence to the study medication, assessed by pill count, was adequate in both groups (90–95%). However, long-term efficacy and safety of leucine-enriched BCAA supplementation among elderly patients with CKD could not be evaluated in this study.

Conclusion

Leucine-enriched BCAA supplement improves lean muscle mass among elderly patients with CKD, but did not further augment increased muscle strength among elderly patients with CKD. Leucine-enriched BCAA supplement requires future long term studies in larger CKD populations.

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Author Contributions NS: Conceptualization, Writing-original draft, Formal analysis. PT: Conceptualization, Writing-original draft. BS: Conceptualization, Formal analysis, Writing-original draft. OS: Writing-review & editing, Supervision, Funding acquisition. All authors made final approval of the submitted version.

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Data availability Data supporting this study are available upon request.

Declarations

Conflict of interest The authors declare that they have no competing interests.

Ethics approval The study was approved by the Ethics Committee of the Institute Review Board at the Royal Thai Army Medical Department and was conducted according to the Declaration of Helsinki.

Informed consent Informed consent was obtained from all participants.

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