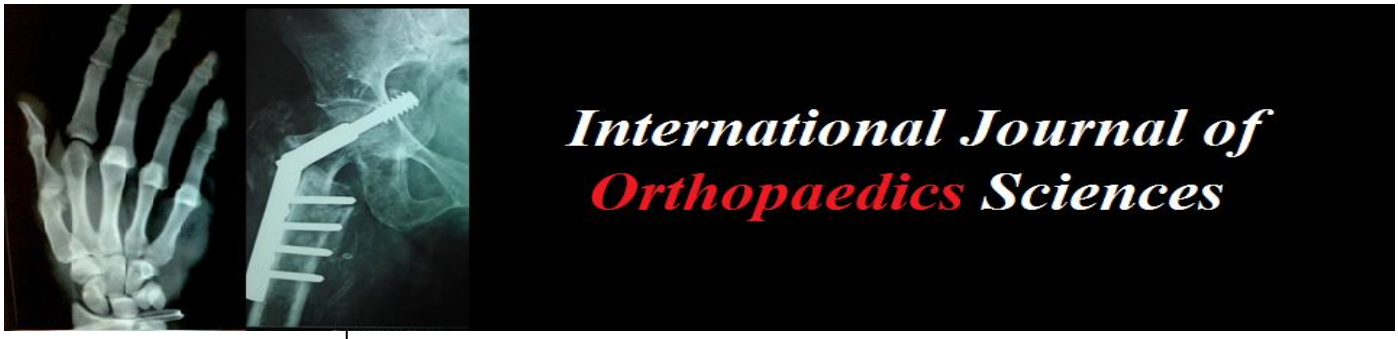

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Benefits of essential amino acid supplementation in patients following total knee arthroplasty

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Abstract
Introduction: Total knee arthroplasty is becoming a frequent procedure in the current times. Following this surgery, considerable muscle atrophy occurs which results in decreased strength and impaired functional mobility. Essential amino acids (EAAs) have shown to attenuate muscle loss during periods of reduced activity and could be beneficial for patients undergoing total knee replacements.
Methodology: We conducted a prospective study of 20 geriatric patients undergoing TKA. Patients were divided into 2 groups. The first group ingested 3 capsules of EAAs and the second group ingested 3 capsules of placebo (salt capsule) twice daily between meals for 1 week before and 6 weeks after TKA. An MRI was performed to determine mid-thigh muscle and adipose tissue volume at baseline and 6 weeks after TKA. Muscle strength and functional mobility were also checked.
Results: Significant changes in mean muscle volume for both the quadriceps and the hamstrings from baseline to 6 weeks post operatively, regardless of treatment group. Quadriceps muscle atrophy was significantly greater in the placebo group than in the EAA group in both the involved leg (-11.2% ± 1.9% compared with -8.5% ± 2.5%; p= 0.014) and the contralateral leg (-7.2% ± 1.4% compared with -4.6% ± 1.6%; p = 0.011). Similarly, hamstrings muscle atrophy was significantly greater in the placebo group than in the EAA group in both the involved leg (-10.2% ± 1.4% compared -7.4% ± 2.0%; p = 0.026) and the contralateral leg (-7.5% ± 1.5% compared with -4.8% ± 1.7%; p =0 .0014).
Conclusion: EAA treatment attenuated muscle atrophy and accelerated the return of functional mobility in older adults following TKA.

Keywords: Essential amino acids, total knee arthroplasty

Introduction
The demand for total knee replacements have been drastically increased in recent years. Muscle atrophy and weakness in the operated leg are significant clinical barriers for patients and their caregivers following TKA [1-3]. Specifically, quadriceps atrophy and weakness compromise balance [4], reduce functional mobility [5, 6], and increase the risk of falls [7]. Tests of functional mobility consistently demonstrate marginal improvements following TKA surgery [8-10]. Functional tasks such as level walking and stair climbing, which is considered a high fall-risk activity, are chronically deficient in patients following TKA as compared with age- and gender-matched adults [9, 10]. Evidence suggests that acute weakness in the non-operated limb following TKA is related to poorer functional outcomes in the long term [11], and maintaining greater muscle volume in the operated extremity is essential to maximize muscle strength [12, 15]. For older adults, acute muscle atrophy and weakness are particularly debilitating, exacerbating underlying issues related to Sarcopenia, defined as the chronic loss of muscle mass and function associated with normal aging [14, 15]. Sarcopenia is related to physical disability [16] and increased risk of home care [17], nursing home placement [18], and hospitalization [19].
Thus, mitigating quadriceps-specific muscle atrophy and weakness appears to be a prudent undertaking with the potential to improve quality of life for millions of older adults following TKA. A role for essential amino acid (EAA) treatment in mitigating muscle atrophy has previously been proposed but has not been thoroughly tested in a clinical population [20].

The purpose of this study was to measure changes in muscle volume and functional mobility in two groups (EAA versus placebo) of older adults before and after TKA. Our hypothesis is that twice-daily ingestion of 3 capsules of EAAs for 1 week before and 6 weeks after TKA would attenuate muscle loss and help restore functional mobility.

Materials and Methods

In the present study, patients were allocated to treatment with EAA or placebo in a 1:1 ratio. Twenty subjects ranging from 50 to 70 years of age were included in this study between January 2021 and June 2021. It was conducted at Krishna Institute of Medical Sciences KARAD. Patients between 50 and 70 years of age who were scheduled to undergo primary unilateral TKA were included. The exclusion criteria included - 1) History of lower extremity total joint replacement surgery 2) Uncontrolled endocrine disease; heart, kidney, liver, blood, or respiratory disease3) Peripheral vascular disease 4) Active malignancy; and 5) Recent treatment with anabolic steroids or oral corticosteroids for > 1 week. Patients were randomly assigned to ingest 3 capsules of EAA or placebo (Salt capsules) twice daily for 7 days preoperatively and for 6 weeks postoperatively.

Study Design

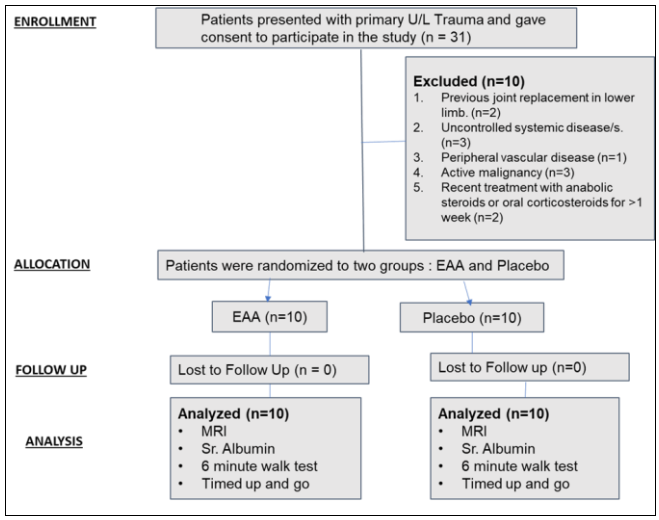

Table 1: Nutritional contents of EAA (3 capsules)

L-Leucine (mg)	1020
L-Valine (mg)	510
L-Isoleucine (mg)	510
L-Lysine (mg)	450
L-Phenylalanine (mg)	300
L-Threonine (mg)	180
L-Tryptophan (mg)	30

2 Weeks preoperative magnetic resonance imaging (MRI), serum albumin levels and functional mobility (Timed up and go test and 6 meter walk test) were assessed and repeated at 6 weeks preoperatively.

Results

The present study included 20 patients who were randomized to treatment with EAA (10 patients) or placebo (10 patients). The sample was 64% female and 36% male with a mean age (and standard error) of 64.41 ± 0.94 years

Table 2: EAA and Placebo

	EAA	Placebo
Male	6	5
Female	4	5
Total	10	10

Table 3: Age (in years), EAA and Placebo

Age (in years)	EAA	Placebo
50-60	4	5
61-70	5	3
71-80	1	2
Total	10	10

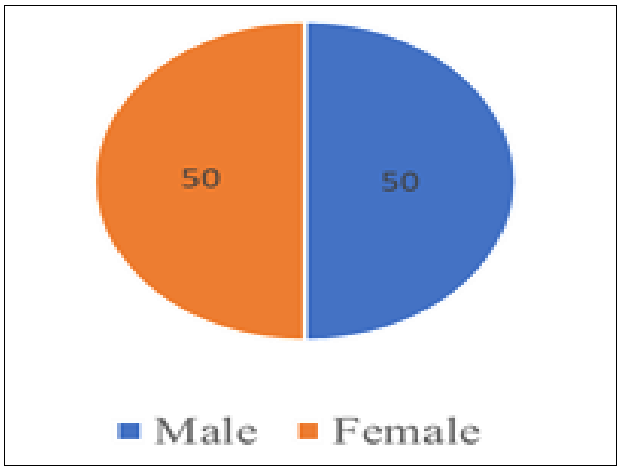

Fig 1: Gender Distribution Placebo

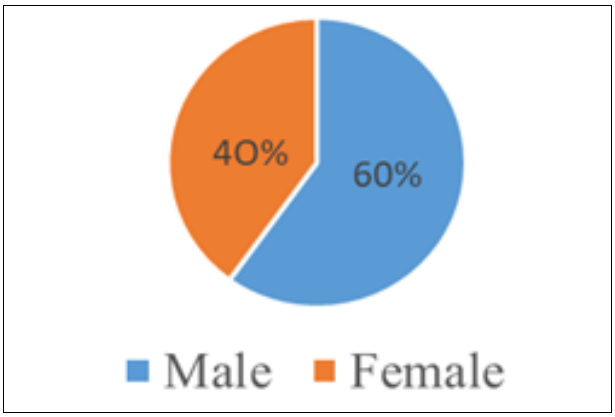

Fig 2: Gender Distribution EAA

This study demonstrated significant changes in mean muscle volume for both the quadriceps and the hamstrings from baseline to 6 weeks postoperatively, regardless of treatment group. Quadriceps muscle atrophy was significantly greater in the placebo group than in the EAA group in both the involved leg (-13.4% ± 1.9% compared with -8.5% ± 2.5%; p = 0.033) and the contralateral leg (-7.2% ± 1.4% compared with -1.5% ± 1.6%; p = 0.014). Similarly, hamstrings muscle atrophy was significantly greater in the placebo group than in the EAA group in both the involved leg (-12.2% ± 1.4% compared with -7.4% ± 2.0%; p = 0.036) and the contralateral leg (-7.5% ± 1.5% compared with -2.1% ± 1.3%; p = 0.005).

Table 5: Change in muscle thickness at 6 weeks post-operative from baseline in operated limb

	EAA	PLACEBO	P value
Quadriceps	-8.5% ± 2.5	-11.2% ± 1.9	0.0141
Hamstrings	-7.4% ± 2.0	-10.1% ± 1.4	0.0026

Table 6: Change in muscle thickness at 6 weeks post-operative from baseline in non-operated limb

	EAA	Placebo	P Value
Quadriceps	-4.6%± 1.6	-7.2% ± 1.4	0.0011
Hamstrings	-4.8% ± 1.7	-7.5% 1.5	0.0014

MRI

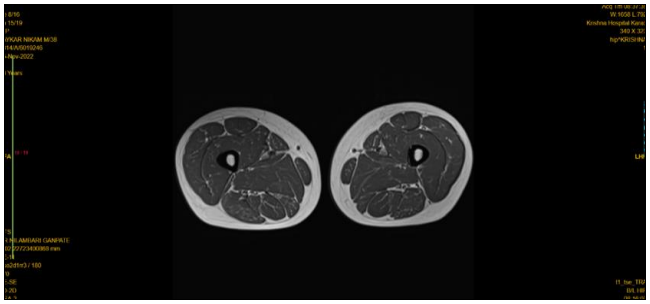

Fig 3: 2 Weeks pre-op (placebo)

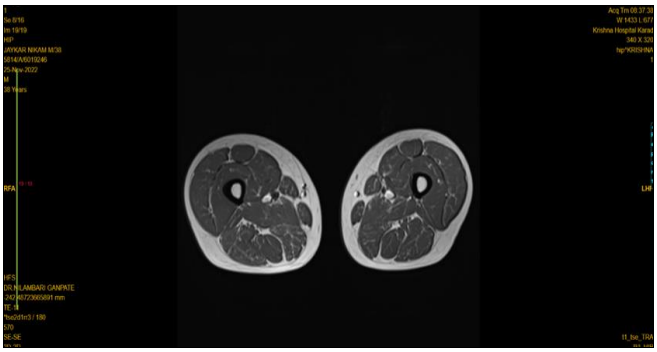

Fig 4: 6 Weeks post-op (placebo)

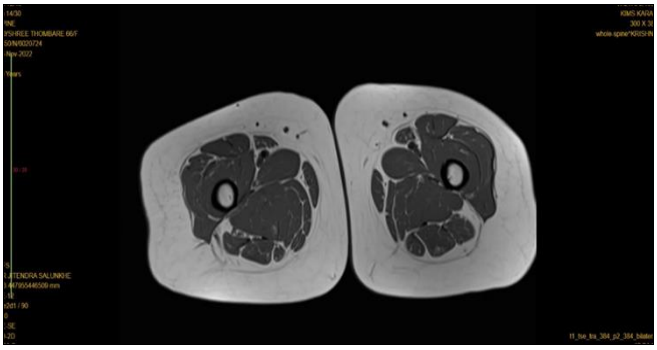

Fig 5: 2 Weeks pre-op EAA

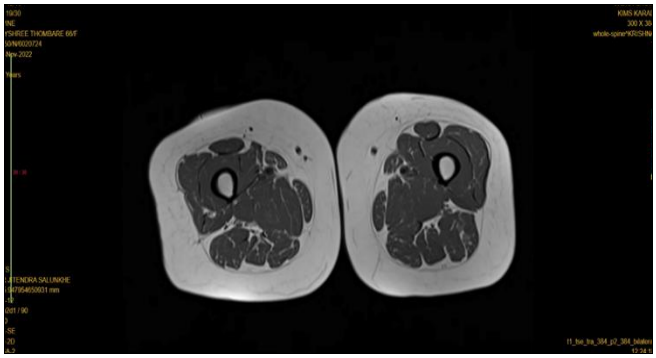

Fig 6: 6 Weeks post-op EAA

Serum albumin levels were also measured in this study at baseline (2 weeks pre-op) and at 6 weeks post -operatively. The table below depicts the mean albumin levels.

Serum Albumin levels	EAA	Placebo
Pre- op	4.4	4.5
6 weeks post-op	4.2	3.9

Functional mobility was assessed using timed up-and-go (TUG) and 6 meter walk test at 6 weeks after TKA.

	EAA	Placebo
6 Meter walk (sec) (without aid)		
Baseline (2 weeks pre-op)	8.9 ± 1.7	8.7 ± 1.24
6 weeks post-op	6.9 ± 1.5	7.5 ± 1.34
P value	0.0121	0.0522
Timed up and go (sec)		
Baseline (2 weeks pre-op)	11.40 ± 1.540	10.36 ± 1.32
6 weeks post-op	8.89 ± 1.470	9.23 ± 1.56
P value	0.0015	0.0974

Discussion

This clinical trial tested the hypothesis that EAA supplementation would mitigate muscle atrophy and mobility impairments in a patient population of older adults (60-80 years of age) following TKA. However we did not asses the influence of protein intervention on the organic and functional outcome. Results showed that twice-daily ingestion of 3capsules of EAAs for 1 week before and 6 weeks after TKA limited bilateral quadriceps and hamstring atrophy at 6 weeks after TKA and may explain the earlier recovery of functional mobility versus placebo. This results are comparable to a study conducted by Dreyer *et al*.

The mechanisms underlying the drop in muscle atrophy in the EAA group are unclear but may be due to the timing of supplement ingestion. Prior to surgery, the subjects were instructed to ingest the supplement at 10 am and again at 2 pm for 7 days, ending the day before TKA. During inpatient physical therapy, which occurred at approximately 9 am and 1 pm each day, the subjects ingested the supplement within 1 hour of physiotherapy. Upon discharge, the subjects were instructed to continue their normal schedule. The rationale for this approach was based on prior work showing that EAA ingestion 1 hour after a single bout of resistance exercise [21] was superior to EAA ingestion 1 hour before resistance exercise [21] in stimulating muscle protein synthesis. Further support comes from a recent study by Jordan *et al*. [22] showing that in older adults on an iso-caloric, iso-nitrogenous diet and having controlled levels of activity, the nitrogen balance increased 57% when protein was consumed immediately after daily exercise as opposed to at rest.

Serum albumin levels usually decrease post-operatively [23] due to catabolic effects of surgery. Post-operative levels of albumin show levels similar to pre-operative levels which could indicated slowed postoperative catabolism, which could be the reason for decreased muscle atrophy. Similar outcomes have been seen by. This study showed better outcomes for functional mobility in the group which was given EAA as compared to placebo. This could be attributed to muscle preservation seen in patients with EAA supplementation. Similar data has been published in a study by Dreyer et el. This study did not assess the effects of EAA without a physiotherapy regimen. Therefore, a combination of EAA supplementation and a good physiotherapy regimen may be important to prevent muscle atrophy.

The surgical technique of proper alignment of extensor mechanism, implant used, experience of surgeon were kept constant in this study making sure quadriceps function regained to normal, patellar tracking adequate with no extensor lag and patellar resurfacing done where required. Post-operative physiotherapy was well controlled in this study. However, there are certain drawbacks to this study. The amount and maximal duration of supplementation for maximal improvement needs to be identified. This study only identifies short term effects of EAA and long term effects of EAA need further evaluation. The nutritional intake of each patient was not assessed in this study and administration of EAA was not monitored after discharge of patients and could have affected the outcome.

Conclusion

Peri-operative administration of EAA can mitigate muscle atrophy and accelerate early functional recovery when administered in combination with a good physiotherapy regimen after TKR. However further evaluation need to be made with a larger study sample.

Conflict of Interest

Not available

Financial Support

Not available

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