Nutrition supplementation can reduce the risk of complications and loss of muscle mass after trauma, but what subgroups benefit the most?

John Davison, Gretchen Ann Jones, Nathan Hendrickson[1], Emiko Hasegawa, Natalie Ann Glass, J Lawrence Marsh[2], Michael C Willey[3]
[1]University Of Minnesota, [2]Dept Of Orthopaedics, [3]University Of Iowa Hospitals

INTRODUCTION:
Muscle atrophy after trauma is a direct result of poor nutritional intake and catabolic response to meet the demands for healing. Nutrition supplementation is a low-cost intervention with potential to limit muscle loss and associated complications. However, it is unclear which populations would benefit most from nutrition supplementation. This is a secondary analysis of a randomized controlled clinical trial designed to evaluate the influence of perioperative conditionally essential amino acid (CEAA) supplementation on changes in body composition and complication rates after orthopedic trauma, stratified by injury type. We hypothesized that geriatric patients and those sustaining high-energy trauma would experience the greater loss of muscle mass and higher complication rates and thus, potentially benefit most from nutrition intervention.

METHODS:
The previously published RCT used for this secondary analysis evaluated changes in body composition and complication rates among patients receiving CEAA supplementation (Intervention) vs. Standard Diet (Control). Eligible subjects were adults indicated for operative fixation of acute long bone, and pelvis fractures. Randomization was stratified by injury type (open fracture/polytrauma (OF/PT), fragility fracture (FFx), and isolated fractures (IFx)). Body composition (fat-free mass [FFM]) was measured at baseline, 2, 6, and 12 weeks postoperatively. Complications were prospectively collected up to 1 year. Body composition was determined using A-mode ultrasound. CEAA supplement was taken twice daily for 14 days postoperatively.

RESULTS:
Enrollment took place from March 2018 - November 2019. 394/400 enrolled subjects were included in the final analysis (OF/PT n=161, FFx n=80, IFx n= 153). There were no differences in baseline demographics (age, sex, BMI, baseline FFM) between CEAA and Control patients within each stratification group.

Assessing FFM changes, regardless of randomization, demonstrated significant decreases at 6 weeks among OF/PT patients (-1.08±0.39kg, p=0.006), and at 12 weeks in the FFx patients (-1.68±0.68kg, p=0.015). FFM increased in IFx subjects at 12 weeks (1.21±0.40kg, p=0.003). Changes at all other time points for each group were non-significant (p>0.05). (**Figure 1.**) Comparatively, the OF/PT subjects lost significantly more FFM at 6 weeks compared to IFx subjects (diff=1.11±0.55kg, p=0.04). The 12-week FFM increase in the IFx group was also significant compared to both OF/PT (diff=1.73±0.56, p=0.002) and FFx (diff=2.89±0.80kg, p<0.001).

Among only control subjects, FFM decreased in OF/PT subjects at 6 weeks (-1.82±0.6kg, p=0.003) and increased in IFx subjects at 12 weeks (1.37±0.58kg, p=0.18). The FFM decrease in the OF/PT group at 6 weeks was significant compared to the IFx group (diff=1.89±0.83kg, p=0.023). The 12-week FFM increase in IFx subjects was significant compared to changes in both the OF/PT (diff=2.21±0.81kg, p=0.007) and FFx (diff=3.07±1.16kg, p=0.009) groups.

Assessing body comp changes within each stratification group (CEAA vs. Control), in the OF/PT group, FFM decreased at 6 weeks among controls (-1.81±0.66kg, p=0.007) but not among CEAA subjects (-0.52±0.58kg, p=0.37). In the FFx Group, FFM decreased at 12 weeks among controls (-1.69±0.81kg, p=0.040) and CEAA subjects (-1.6±0.78kg, p=0.043). In the IFx group, FFM increased at 12 weeks among both control (1.29±0.53kg, p=0.02) and CEAA (1.04±0.51kg, p=0.042) subjects. FFM changes between study arms were not significantly different at any timepoint during follow-up (all p>0.05).

Overall complication risks between groups, regardless of randomization, were compared using IFx subjects as the reference group. OF/PT subjects had significantly higher risk of surgical site infections (SSI) (RR=2.91 (95% CI: 1.49-5.67), p=0.002), unplanned re-operation (RR=3.02 (1.45-6.32) p=0.003), and total complications (RR=1.67 (1.19-2.33) p=0.003). FFx subjects had higher risk of medical complications (RR=2.35 (1.47-3.74) p<0.001), mortality (RR=4.88 (1.03-23.17) p= 0.046), and total complications (RR= 1.78 (1.24-2.55) p=0.002).

Among only control subjects, OF/PT subjects had greater risk of SSI (RR=2.21 (1.04-4.70) p= 0.039) and re-operation (RR=3.30 (1.31-8.31) p= 0.011) compared to the IFx group. FFx subjects had significantly higher risk of mortality (RR=9.32 (1.20-72.14) p=0.033).

Within stratification analysis, demonstrated lower risk of non-union among CEAA subjects vs. Controls in the OF/PT group (RR=0.42 (0.18-0.98) p=0.044). GFx CEAA subjects had lower risk of mortality (RR=0.86 (0.77-0.97) p=0.027). IFx CEAA subjects had lower risk of total complications (RR=0.45 (0.24-0.83) p=0.010).

DISCUSSION AND CONCLUSION:

This secondary analysis found significant loss of muscle mass in young adults that sustained high-energy trauma (OF/PT) and in older adults with fragility fractures (FFx). This early loss of muscle mass was not seen in young adults with isolated injuries. Stratification analysis demonstrated a protective effect of supplementation against FFM loss among patients that sustained high-energy trauma (OF/PT) and older adults with fragility fracture (FFx). As expected, patients that sustained high-energy trauma and older adults with fragility fractures also had more complications that young adults with isolated injuries. Subjects randomized to CEAA supplementation had lower rates of complications compared to controls across injury stratification groups. Overall, younger patients with high-energy trauma and older adults with fragility fractures may benefit most from supplementation. Future multi-center studies are needed to determine optimal dosing and duration of supplementation to prevent muscle loss and complications after musculoskeletal trauma.

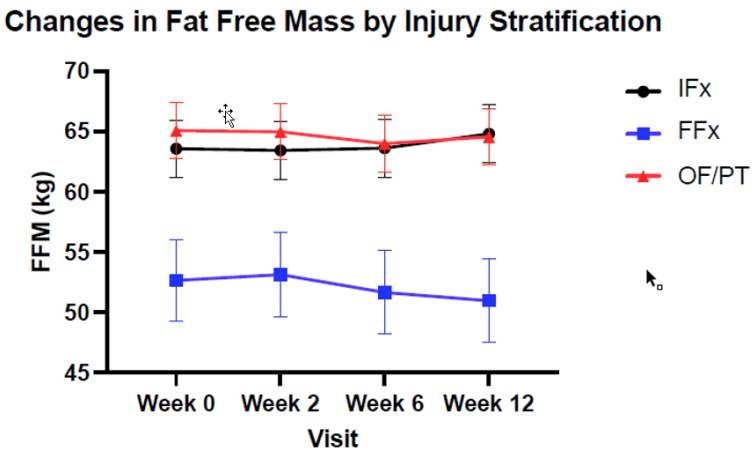

Figure 1. Postoperative changes in Fat Free Mass (FFM) in each stratification group regardless of study arm randomization (CEAA vs. Control). (IFx = isolated fractures, FFx = fragility fractures, OF/PT = open fractures/polytraumas)