Effects of Alcohol Consumption on Cancer Cachexia

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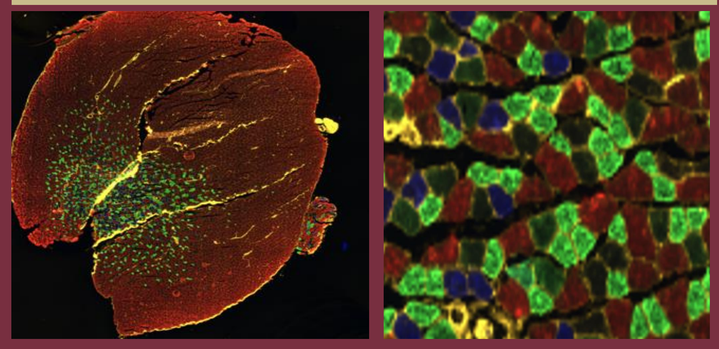
Background:

Cancer cachexia is a deteriorating syndrome designated by a gradual loss of body weight that commonly affects adipose tissue and skeletal muscle (Li et al., 2020). Chronic alcohol use is one factor that can contribute to the onset of cancer cachexia in cancer patients, but this syndrome is not always characterized by alcohol use. Suppressed protein synthesis and enhanced protein degradation are some of the major indicators of cancer cachexia (Li et al., 2020). Chronic alcohol use incites atrophy in the skeletal muscles and tissues of mice. In this research, we are testing how the effects of alcohol consumption in mice influences cancer cachexia by measuring changes in body weight. Further, we are looking at changes in fat mass as well as specifically in the skeletal muscle at changes in its weight and size of the individual skeletal muscle fibers. This research will help doctors know the possible impacts of alcohol consumption on cancer cachexia to help guide patients with cancer as to whether it is safe to drink alcohol or not. We believe that cancer patients that have had a history of chronic alcohol use will experience a larger loss in body weight due to a larger loss of adipose tissue and skeletal muscle than a patient who has cancer that did not have a history of alcohol abuse.

Methods:

CD2F1 mice were divided into the following groups: control diet non-cancer (CON), control diet with cancer (Cancer), Prior EtOH diet- non-cancer (PRIOR), Prior EtOH diet- cancer (PRIOR-cancer); EtOH diet non-cancer (EtOH), and EtOH diet with cancer (EtOH-Cancer). Mice were then acclimated to a non-alcohol control liquid diet for 1-week, after which the EtOH groups transitioned to an isocaloric Lieber DeCarli EtOH diet at 12% kcal for 1-week, then finally to 20% kcal EtOH for 6 weeks. After 6 weeks of alcohol diet, mice in the PRIOR groups transitioned back to consuming the alcohol-free control diet. C26 colon cancer cells were then injected into the right flank of cancer groups and allowed to develop for two weeks. On the day of sacrifice, body weight was measured and the muscles and epididymal fat were removed and frozen. Muscles and fat were then weighed. Gastrocnemius muscles were then sectioned onto slides using a cryostat. Immunohistochemical procedures were used to stain the membranes of muscle fibers. Pictures of muscle cross sections were taken on a Leica microscope and then analyzed for cross sectional area using Image J software.



The figure to the left is an image of the cross section of the gastrocnemius muscle of a mouse. This mouse was in the EtOH diet with cancer treatment group. The image to the right is a zoomed in version of the muscle fiber where you can see the type 1 fibers (blue), type 2A fibers (green) and the type 2B fibers (red).

1. Mass (mg) of Several Muscles of the Lower Limb:

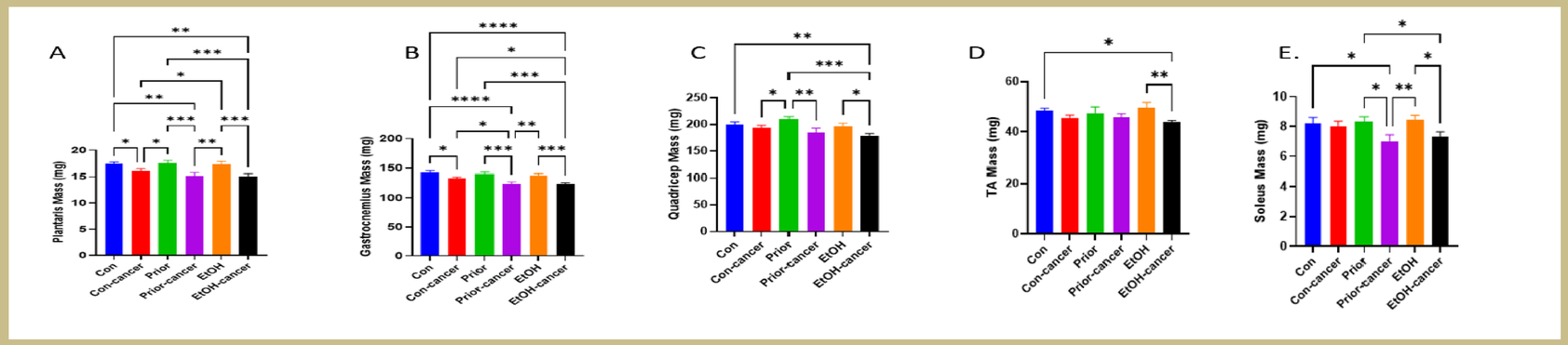


Figure 1: The mass of the (A) Plantaris (mg), (B) Gastrocnemius (mg), (C) Quadricep (mg), (D) Tibialis Anterior (mg), and (E) Soleus (mg) muscle across all six of the treatment groups. Asterisks (*) represent significance between the two treatment groups connected by the line when their P-value is less than 0.05. Greater number of asterisks indicates more significant differences.

2. Body Weight and Epididymal Fat of the Mice

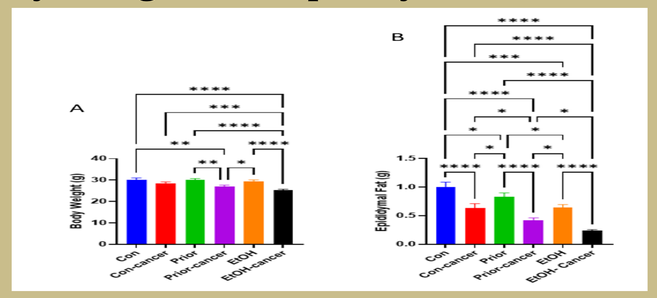


Figure 2: (A) Body Weight (g) and (B) Epididymal Fat (g) across all six of the treatment groups. Asterisks (*) represent significance between the two treatment groups connected by the line when their P-value is less than 0.05. Greater number of asterisks indicates more significant differences.

3. Measurements of Muscle Fiber Size:

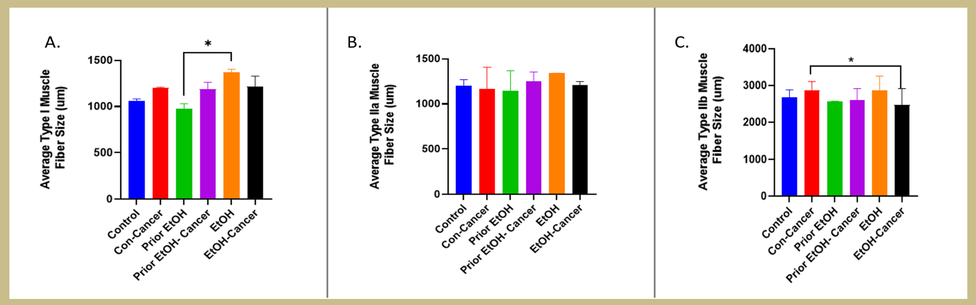


Figure 3: (A) Average Type 1 Muscle Fiber Size (um), (B) Average Type 2A Muscle Fiber Size (um), and (C) Average Type 2B Muscle Fiber Size (um) across all six of the treatment groups. Asterisks (*) represent significance between the two treatment groups when their P-value are less than 0.05.

Conclusion:

Data show that alcohol significantly decreased soleus mass in prior-alcohol and alcohol-consuming mice indicating that alcohol enhanced the effects of cancer cachexia. Within each diet group (control or alcohol), tumor-bearing mice had decreased plantaris and gastrocnemius mass compared to non-cancer mice indicating that the presence of a tumor negatively affected the plantaris and gastrocnemius mass. Tumor-bearing mice in prior and continuous-alcohol groups showed decreased quadricep mass compared to non-cancer mice. Overall, this data shows that alcohol increases the rate of cancer cachexia by decreasing the mass of the soleus, plantaris, gastrocnemius, and quadricep muscles. This data is essential because it shows that alcohol consumption enhances cancer cachexia in several muscles of the lower limb. Therefore, in patients with cancer alcohol may worsen the effects of cancer cachexia compared to somebody who has cancer and stops drinking or never drank alcohol.

Future Directions:

After concluding that alcohol increases the rate of cancer cachexia in several muscles of the lower limbs, the lab aims to further test how the incorporation of a new variable: chemotherapy, influences chronic alcohol consumption during cancer cachexia. Chemotherapy is a method of combating the progression of a tumor, and mice that were tumor-bearing, in both the prior alcohol and continuous alcohol treatments, displayed decreased plantaris, gastrocnemius, and quadricep mass compared to the non-cancer mice. Therefore, future research should aim to identify the influence of chemotherapy in a model of chronic alcohol consumption during cancer cachexia.

References/Acknowledgements:

- Li, Yuanfei, et al. “Chronic Alcohol Consumption Enhances Skeletal Muscle Wasting in Mice Bearing Cachectic Cancers: The Role of TNFA/Myostatin Axis.” *Alcoholism: Clinical and Experimental Research*, vol. 44, no. 1, 2019, pp. 66–77., https://doi.org/10.1111/acer.14221.

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