



# Low-Dose Alcohol Consumption Throughout Chemotherapy Does Not Amplify Muscle Wasting



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## ABSTRACT

Chronically high levels of alcohol consumption leads to skeletal muscle wasting, contributing to myopathy and cachexia. Chemotherapy treatment can induce cachexia independently of the presence of cancer. Furthermore, consuming alcohol while receiving chemotherapy treatment has unknown effects but may further exacerbate muscle wasting. To determine if alcohol consumption further worsens rodent skeletal muscle loss due to chemotherapy treatment. Male BALB/c mice (n= 23), were randomized into 4 groups (n= 4-8/gr): Control-Chemo, Control-non-Chemo, EtOH-Chemo, EtOH-non-Chemo. Mice consumed 8% v/v EtOH in drinking water for 20 weeks. Control-Chemo and EtOH-Chemo mice received intraperitoneal injections of the chemotherapy treatment FOLFIRI for 3 weeks until sacrifice, while Control-non-Chemo and EtOH-non-Chemo mice received vehicle (saline). Mice were euthanized when the average weight loss of the chemotherapy-treated group was 15-20% of initial bodyweight. The gastrocnemius and quadriceps muscles, tibias, spleen, seminal vesicles, and testes, were excised. Tissue weight data were normalized to tibia length and analyzed via 2-way ANOVA. Both treatments significantly decreased body weight (p<0.05), while chemotherapy reduced seminal vesicle and teste weights. Independent samples t-test show alcohol consumption reduces spleen weight (p=0.0424) during chemotherapy. A trend for a main effect of chemotherapy treatment was detected for gastrocnemius and quadricep mass (p=0.07-0.09), but no further effects of alcohol were observed. Low-dose alcohol consumption did not exacerbate muscle atrophy due to chemotherapy. Results should be validated in follow-up work with larger sample sizes.

## INTRODUCTION

- Consuming chronically high levels of alcohol leads to skeletal muscle wasting.
- Chemotherapy treatment is known to further exacerbate muscle wasting due to cancer cachexia.
- The effect of consuming alcohol while receiving chemotherapy treatment is unknown but thought to further exacerbate the wasting.
- **Purpose:** To investigate whether low-dose alcohol consumption during chemotherapy treatment further worsens rodent muscle wasting.

## METHODS

**Tissue Harvest:** Chemotherapy (C) mice received intraperitoneal injections of chemotherapy treatment FOLFIRI, and non-chemotherapy (NON) mice were given vehicle (saline and sterile water). Sacrifice was determined when chemotherapy treated mice lost 15-20% of their initial body weight. In one group, this occurred after 3 weeks from onset of chemotherapy treatment, another was 5 weeks after.

**Tissue Harvest Cont.:** The gastrocnemius (GAS) and quadriceps (QUAD) muscles, as well as the tibias, spleen, seminal vesicles, and testes, were excised from the mice and immediately frozen.

**Statistics:** Tissue weights were normalized to tibia length and analyzed via a 2-way ANOVA. In the event of a significant interaction, Tukey's post-hoc analysis was used to identify specific differences between groups. Significance was set at  $P < 0.05$ .

## CONCLUSIONS

- Low-dose alcohol consumption did not exacerbate skeletal muscle atrophy due to chemotherapy.
- As sample sizes were small, future work should validate the current findings by increasing the sample size.
- Chemotherapy treatment significantly reduced seminal vesicle and teste weight, independent of alcohol.
- No main effect of either treatment was observed in the spleen.
- Chemotherapy and alcohol treatments were sufficient to induce detrimental effects on muscle weights and body weight.

## METHODS

**Groups:** Mice were randomized into 4 groups (n= 4-8/gr): control-chemo (CON-C), control-non-chemo (CON-NON), EtOH-chemo (EtOH-C), EtOH-non-chemo (EtOH-NON).

**Animals:** Male BALB/c mice (n= 23), were started on 10% v/v EtOH in drinking water. After 3 weeks, were switched down to 8% v/v EtOH in water where they maintained for the remaining 20 weeks of the study.

## RESULTS

- Both treatments significantly decreased body weight (p<0.05), while chemotherapy reduced seminal vesicle and teste weights.
- Independent samples t-test show alcohol consumption reduces spleen weight (p=0.0424) during chemotherapy.
- A trend for a main effect of chemotherapy treatment was detected for gastrocnemius (p= 0.09) and quadricep mass (p=0.07), but no further effects of alcohol were observed.

## REFERENCES

- Li Y, Zhang F, Modrak S, Little A, Zhang H. Chronic Alcohol Consumption Enhances Skeletal Muscle Wasting in Mice Bearing Cachectic Cancers: The Role of TNF $\alpha$ /Myostatin Axis. Alcohol Clin Exp Res. 2020 Jan;44(1):66-77. doi: 10.1111/acer.14221. Epub 2019 Nov 11. PMID: 31657476; PMCID: PMC6980877.

## RESULTS

### 1. Body Weights

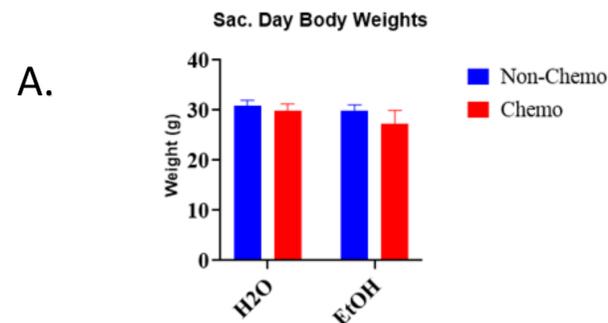


Figure 1. (A) Body weights at sacrifice (g).  
Main effect of chemotherapy and alcohol to reduce body weights.

## RESULTS

### 2. Quadriceps Weight

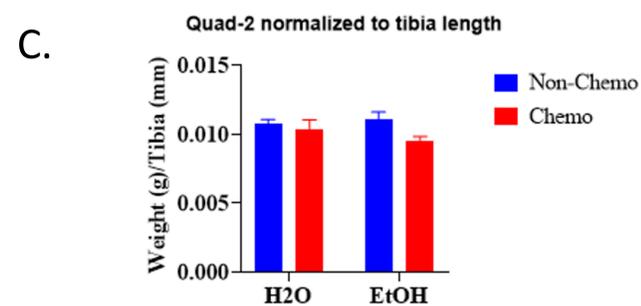


Figure 2. (C) Quad-2 weight (g) normalized to tibia length (mm).  
Trend for main effect chemotherapy, but no effects from alcohol.

## RESULTS

### 3. Various Organ Weights Cont.

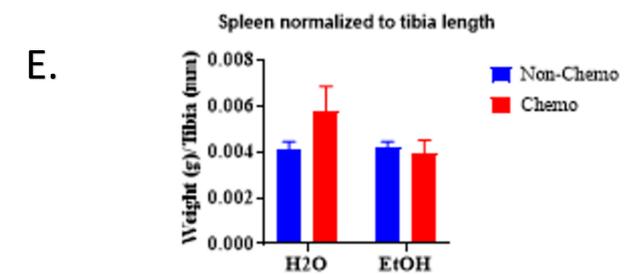


Figure 3. (E) Spleen weight (g) normalized to tibia length (mm).  
No effects of treatment.

### 2. Gastrocnemius Weight

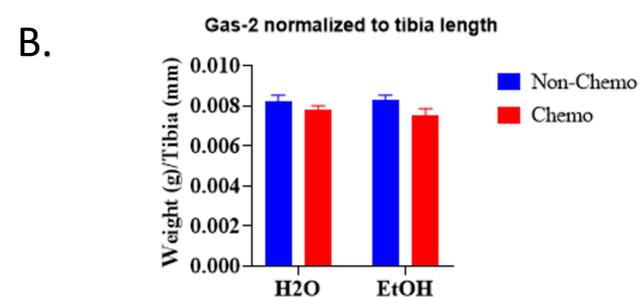


Figure 1. (B) Gas-2 weight (g) normalized to tibia length (mm).  
Trend for main effect chemotherapy, but no effects from alcohol.

### 3. Various Organ Weights

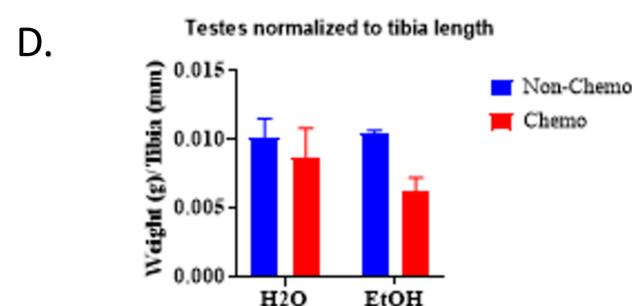


Figure 3. (D) Teste weight (g) normalized to tibia length (mm).  
Main effect of chemotherapy.

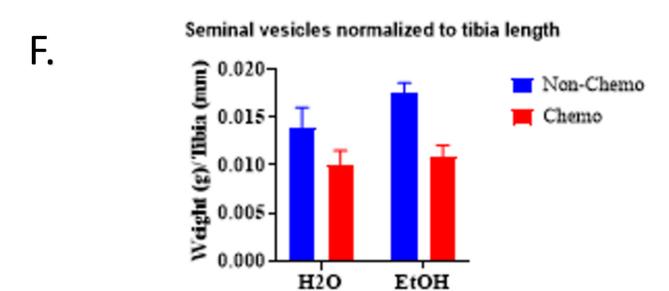


Figure 3. (F) Seminal vesicle weight (g) normalized to tibia length (mm).  
Main effect of chemotherapy.