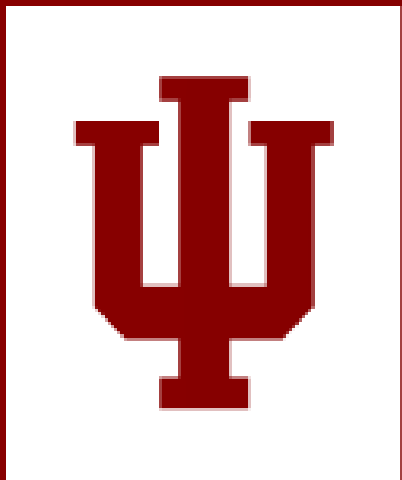
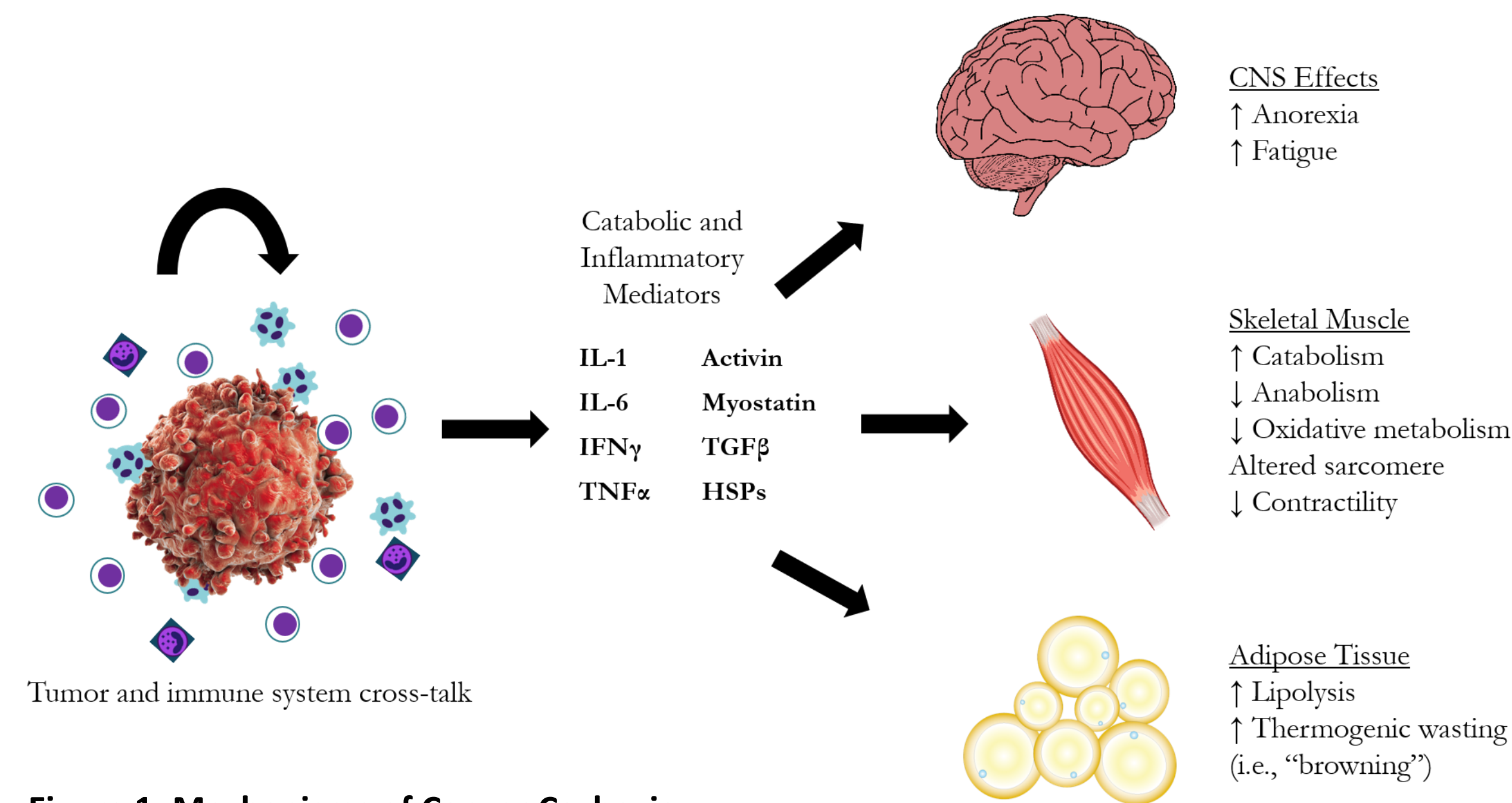




INTRODUCTION

- Head and neck cancer (HNC) is often accompanied by cachexia
 - Involuntary weight loss
- Sarcopenia (low muscle strength, quantity, and performance)
- Malnutrition
- Diagnostic criteria for cancer cachexia
 - Unintentional weight loss of > 5% over 6 months *OR*
 - > 2% weight loss with BMI < 20kg/m² *OR*
 - > 2% weight loss with sarcopenia

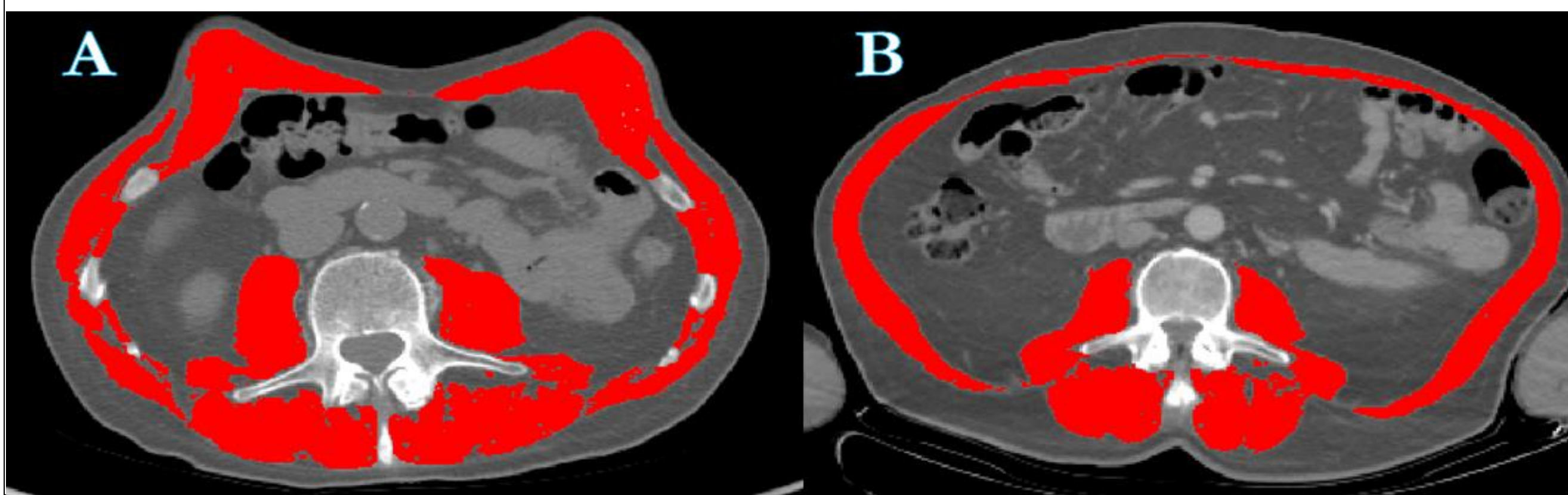
HYPOTHESIS: Larger, more aggressive tumors impose greater cachexia severity in HNC patients



METHODS

- Single-institution, retrospective study from 2014-2019
- Adult patients receiving ablative surgery and free flap reconstruction for active, non-HPV, mucosal head & neck squamous cell carcinoma were included
- Patients without 30-day preoperative abdominal CT imaging for measuring skeletal muscle index (SMI) were excluded
- Patient demographics, comorbidities, SMI, weight and nutrition data, and cancer pathology reports collected
- Cachexia severity categorized as none, low (5-14.9% weight loss), and high (≥15% weight loss)
- 2-sided one-way Welch's ANOVA with Tukey's post-hoc analyses, Kruskal-Wallis ANOVA, Pearson's χ^2 . Significant at $p < 0.05$.

Figure 2. Axial CT comparison of a non-sarcopenic 47-year-old male with BMI of 21.0 kg/m² and SMI of 60.1 cm²/m² (A) and a sarcopenic 54-year-old male with BMI of 20.2 kg/m² and SMI of 38.2 cm²/m² (B). The highlighted areas indicate the isolated abdominal skeletal muscles at L3.



RESULTS

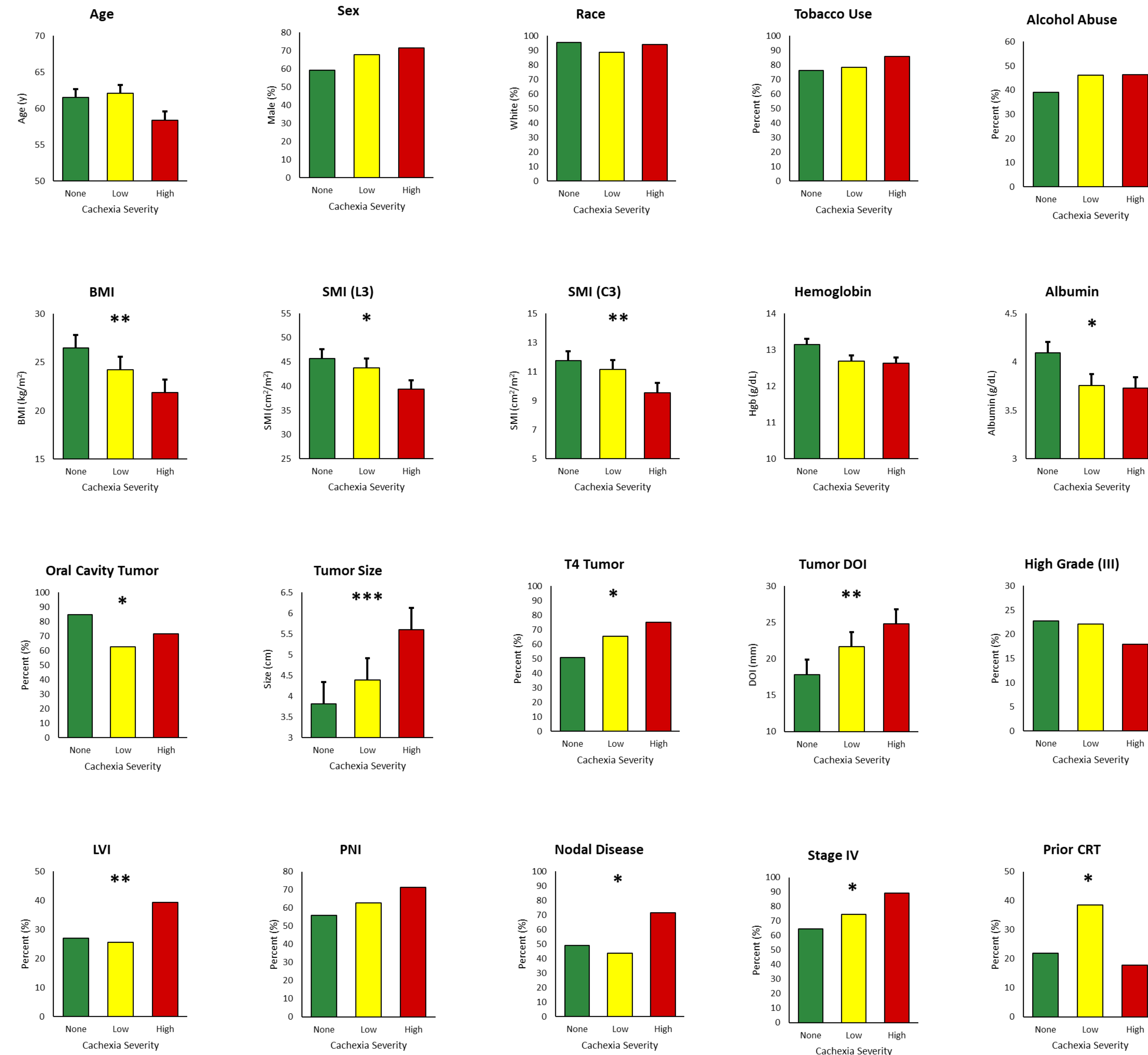


Figure 3. Analyses comparing patients with no cachexia vs. low-severity cachexia vs. high-severity cachexia. A total of n=165 patients were included with n=106 (64.2%) patients having varying degrees of cachexia. Increased cachexia severity was associated with lower BMI, lower SMI at C3 and L3, lower serum albumin, larger tumor size, greater DOI, higher T, N, and overall stage, LVI, and. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Abbreviations: BMI, body mass index; CRT, chemoradiation therapy; DOI, depth of invasion; Hgb, hemoglobin; LVI, lymphovascular invasion; PNI, perineural invasion; SMI, skeletal muscle index.

SUMMARY & CONCLUSION

- First study to examine histopathologic features correlated to HNC cachexia.
- Cancer cachexia is highly prevalent in head & neck cancer cachexia and correlated to tumor size, staging, and adverse features.
- Cachexia severity not correlated to:
 - Age
 - Sex
 - Race
 - Tobacco use
 - Alcohol abuse
 - Hemoglobin
 - Tumor grade
 - PNI

Worsening cancer cachexia severity is associated with:

- ↓BMI
- ↓SMI
- ↓Albumin
- ↓Oral cavity tumor
- ↑Tumor size
- ↑Tumor DOI
- ↑T-stage
- ↑N-stage
- ↑Overall Stage
- ↑LVI
- ↑Prior CRT

- Hypothetical etiologies for findings
 - Larger tumor and nodal burden → More pro-cachectic and inflammatory cytokine released by cancer cells
 - Greater DOI and LVI → More interaction surface with immune system to release cytokines
 - Lower BMI, SMI, and albumin → More degradation of skeletal muscle and adipose due to catabolic imbalance
 - Higher incidence of CRT → chemotherapy can produce similar wasting effects as cancer

- Limitations of study
 - Single institution and retrospective
 - Sample size limited by availability of 30-day preoperative abdominal CT imaging
 - Cannot determine contribution of malnutrition vs. tumor effects
 - Only includes mucosal squamous cell carcinoma and does not include other HNC locations or histologists

- CONCLUSION:** Cancer cachexia severity in mucosal head & neck squamous cell carcinoma is correlated to larger, more advanced, and more aggressive tumor features.

REFERENCES

- Baracos VE, Martin L, Korc M, Guttridge DC, Fearon KCH. Cancer-associated cachexia. *Nat Rev Dis Prim*. 2018;4:17105. doi:10.1038/nrdp.2017.106
- Couch ME, Dittus K, Toth MJ, et al. Cancer cachexia update in head and neck cancer: Definitions and diagnostic features. *Head Neck*. 2015;37(4):594-604. doi:10.1002/hed.23599
- Yang W, Huang J, Wu H, et al. Molecular mechanisms of cancer cachexia-induced muscle atrophy (Review). *Mol Med Rep*. 2020;22(6):4967-4980. doi:10.3892/mmr.2020.11608
- Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol*. 2011;12(5):489-495. doi:10.1016/S1470-2045(10)70218-7
- Gorenc M, Kozjek NR, Strojjan P. Malnutrition and cachexia in patients with head and neck cancer treated with (chemo)radiotherapy. *Reports Pract Oncol Radiother*. 2015;20(4):249-258. doi:10.1016/j.rpor.2015.03.001
- Hua X, Liu S, Liao J-F, et al. When the loss costs too much: a systematic review and meta-analysis of sarcopenia in head and neck cancer. *Front Oncol*. 2020;9. doi:10.3389/fonc.2019.01561
- Richey LM, George JR, Couch ME, et al. Defining cancer cachexia in head and neck squamous cell carcinoma. *Clin Cancer Res*. 2007;13(22 Pt 1):6561-6567. doi:10.1158/1078-0432.CCR-07-0001
- Orell-Kotikangas H, Österlund P, Mäkitie O, et al. Cachexia at diagnosis is associated with poor survival in head and neck cancer patients. *Acta Otolaryngol*. 2017;137(7):778-785. doi:10.1080/00016489.2016.1277263
- Couch ME, Dittus K, Toth MJ, et al. Cancer cachexia update in head and neck cancer: Pathophysiology and treatment. *Head Neck*. 2015;37(7):1057-1072. doi:10.1002/hed.23696
- Cruz-Jentoft AJ, Bahat GG, Bauer JJ, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(1):16-31. doi:10.1093/ageing/afy169
- Jager-Wittenaar H, Dijkstra PU, Dijkstra G, et al. High prevalence of cachexia in newly diagnosed head and neck cancer patients: An exploratory study. *Nutrition*. 2017;35:114-118. doi:10.1016/j.nut.2016.11.008
- Kwon M, Kim RB, Roh J-L, et al. Prevalence and clinical significance of cancer cachexia based on time from treatment in advanced-stage head and neck squamous cell carcinoma. *Head Neck*. 2017;39(4):716-723. doi:10.1002/hed.24672
- Solis-Martinez O, Alvarez-Altamirano K, Cardenas D, Trujillo-Cabrera Y, Fuchs-Tarlovsky V. Cancer Cachexia Affects Patients with Head and Neck Cancer in All Stages of Disease: A Prospective Cross-Sectional Study. *Nutr Cancer*. Published online January 2021;1-8. doi:10.1080/01635581.2020.1869792
- Jager-Wittenaar H, Dijkstra PU, Vissink A, van der Laan BFAM, van Oort RP, Roodenburg JLN. Critical weight loss in head and neck cancer—prevalence and risk factors at diagnosis: an explorative study. *Support Care Cancer*. 2007;15(9):1045-1050. doi:10.1007/s00520-006-0212-9