

The Spectrum of Tumor Mutational Burden in a Head and Neck Cancer Cohort

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Introduction

Head and neck cancers are a varied collection of malignancies of the skin, upper aerodigestive, salivary glands and thyroid. The annual incidence worldwide of oral cavity, oropharyngeal, and laryngeal cancers are 350k, 180k, and 90k, respectively. The immune oncologic profile is variable among solid tumors and this may have future implications for treatment options and considerations. Information is evolving about the profile differences within the head and neck subsites.

Objective

Tumor mutational burden (TMB) has been shown to correlate with response to immunotherapy and is being evaluated as a potential predictive biomarker for many solid organ malignancies. There is limited data focused on the clinical landscape of TMB in head and neck cancers (HNC). We sought to evaluate TMB, microsatellite instability (MSI), and programmed death ligand-1 (PD-L1) expression across various HNSCC subsites.

Methods

Using our institutional HNSCC database, we performed a retrospective chart review on patients diagnosed with HNSCC who underwent next generation sequencing utilizing Tempus proprietary DNA and RNA sequencing technology from Sept 2018 to Nov 2020. Patients were analyzed according to primary subsite and TNM staging. TMB and the presence or absence of MSI and PD-L1 expression (PD-L1 positivity was characterized by >1% expression), were determined for each site with subsequent comparison of cohorts via a sample t-test and ANOVA analysis.

Results

A total of 170 HNSCC patients were included in this study. The average TMB of P16-positive oropharyngeal cancer (OPC) was 3.20 (± 2.62) [n=49], P16-negative (OPC) 4.33 (± 2.62) [n=14], young oral cavity (<45 years old) 3.29 (± 3.58) [n=9], advanced oral cavity (T-stage ≥ 3 &/or N-stage >0) 4.29 (± 3.45) [n=48], larynx 6.22 (± 3.95) [n=24], and cutaneous SCC (cSCC) 28.79 (± 18.73) [n=26]. As expected, the TMB of cSCC was significantly higher than those of all mucosal cancer sites ($p < 0.001$). Additionally, there was a statistically significant difference between TMB of mucosal site tumors and laryngeal tumors ($p = 0.007$). Across all subsites, MSI rate remained low (0-10%). PD-L1 positivity was highest in P16-negative OPC (100%) and lowest in laryngeal cancers (70.6%). Young oral cavity, advanced oral cavity and P16-positive OPC expressed PD-L1 in 75%, 81.5%, and 82.1% of tumors, respectively.

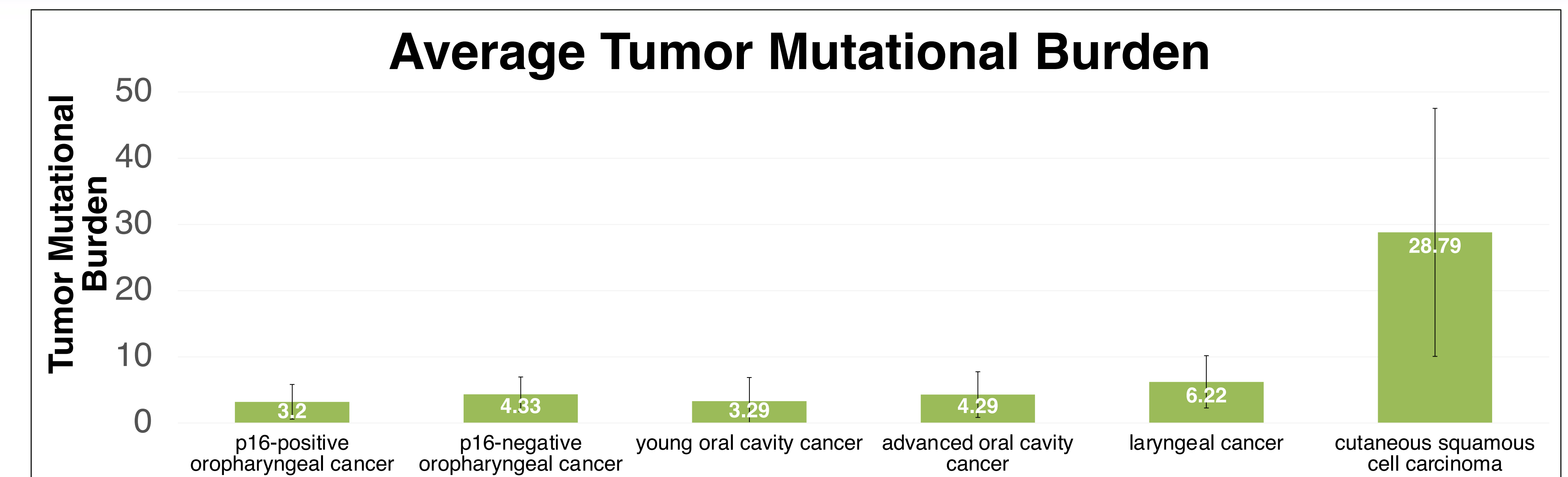


Figure 1: Bar graph showing the distribution of the average tumor mutational burden of each subtype of head and neck cancer with bars indicating the standard deviation of these averages.

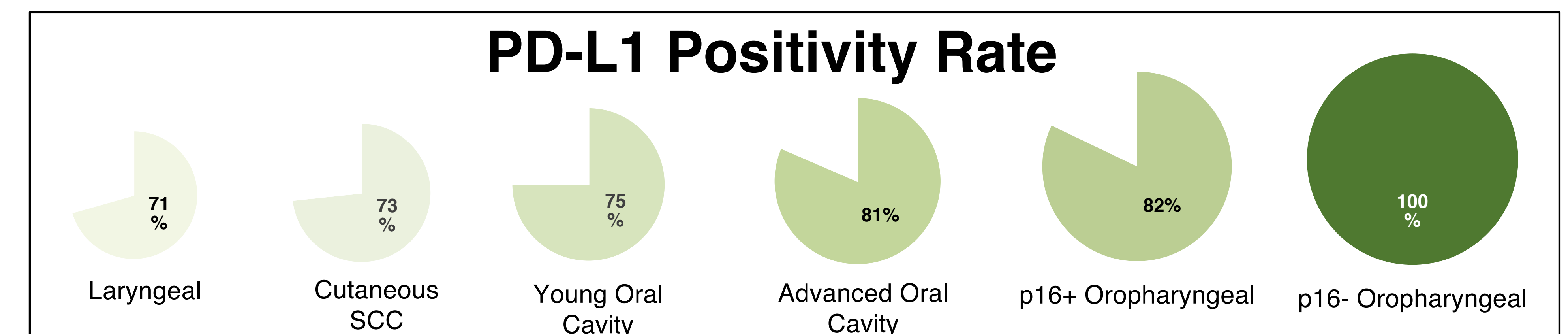


Figure 2: Pie charts showing the increasing prevalence of in PD-L1 expression across each head and neck cancer subtype.

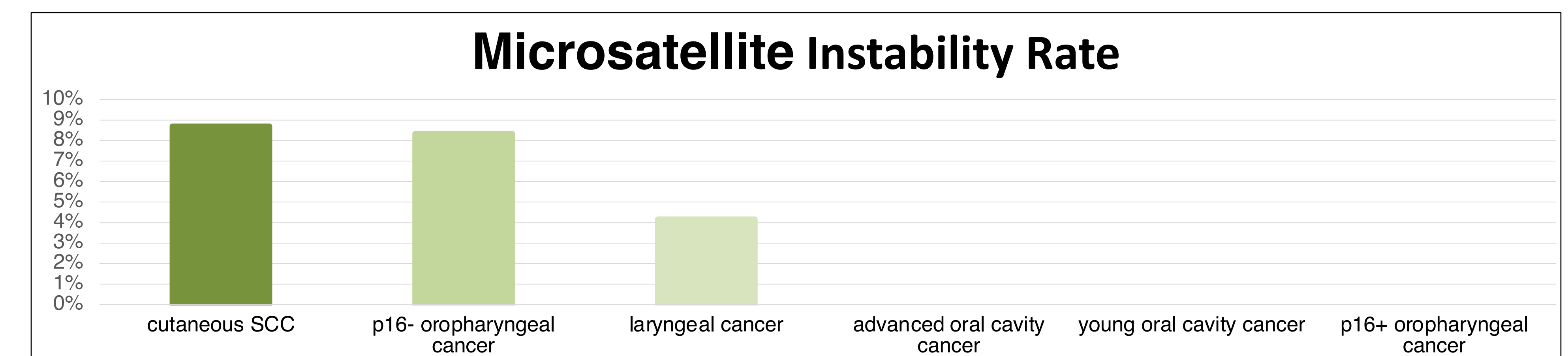


Figure 3: Plot showing the rate of microsatellite instability across each head and neck cancer subtype.

Conclusion

Patients with mucosal HNSCC demonstrated a low TMB. Within these patients, larynx cancer patients demonstrated a higher TMB compared to the other mucosal sites. Cutaneous SCC demonstrated the highest TMB. Across all head and neck cancer sites the frequency of MSI remained low, while the majority of tumors were positive for PD-L1. This data provides a foundation to understand the impact of TMB on HNC treatment sensitivity.