IMPACT OF EPSTEIN-BARR VIRUS INFECTION AND MICROSATELLITE INSTABILITY STATUS ON THE PROGNOSIS OF PATIENTS WITH GASTRIC ADENOCARCINOMAS

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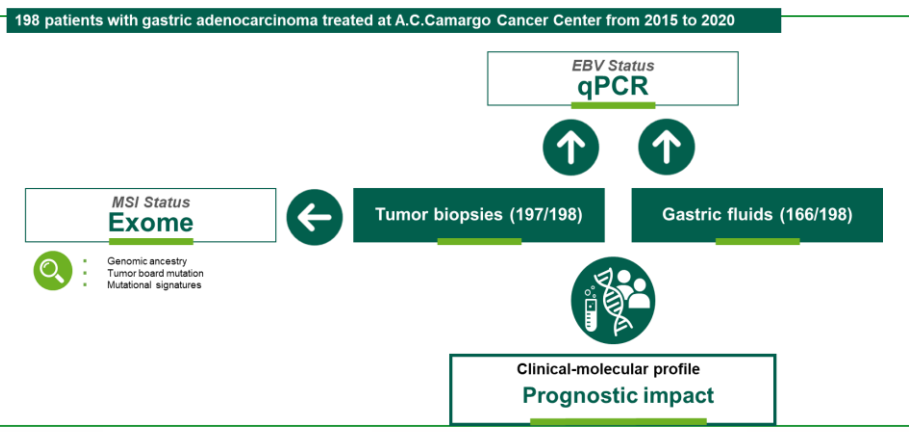
Introduction

The accurate determination of tumor prognosis is still a challenge in cancer treatment. Among gastric adenocarcinomas (GACs), two molecular subtypes seem to have a better prognosis when compared to the others, in addition to being candidates for immunotherapy. Such subtypes are characterized by the presence of Epstein-Barr virus (GAC-EBV) or by DNA Microsatellite Instability (GAC-MSI) (TCGA, 2014; PULIGA et al, 2021). In Brazil, the factors involved in the development and outcomes of GAC-EBV and GAC-MSI cases need further investigation, especially when considering the epidemiological and ethnical admixture characteristics of this population. Our main goal is to determine the prevalence of EBV, MSI and their prognostic relevances in the GACs in Brazil.

Patients and Methods



Results and Discussion

We identified precisely the same prevalence of EBV+ and MSI+, found in 14/198 (7.1%) GACs. A single subject was positive for both EBV and MSI, suggesting that the co-occurence of these subtypes to be rare. The values observed here are similar to those reported in the literature. The mean age and predominant gender for EBV+ and MSI+ were, respectively, 60 years (78.6% > 45 years) and male (85.7%); 74.3 (0 ≤ 45) and female (71.4 % p=0.016). The distribution of EBV+ and MSI+ cases regarding Lauren's subtypes was respectively, 28.6 and 69.2% intestinal, 57.1 and 15.4% diffuse, and 14.3 and 15.4% mixed. With a significant relationship between this classification and the MSI status (p=0.017). As for the presence of EBV, this was not observed. Preliminary analyses of the inference of genomic ancestry indicate an elevated prevalence of GAC-cases descending from European lineages. However, also observe that subjects with a more relevant Asian ancestry component appear to cluster a higher frequency of EBV-infection. While 29% (5/17) of subjects with stronger Asian ancestry were EBV+, only 4.9% (9/181) of subjects with other ancestries showed the presence of EBV DNA (p =0.009) (**Figure 1**).

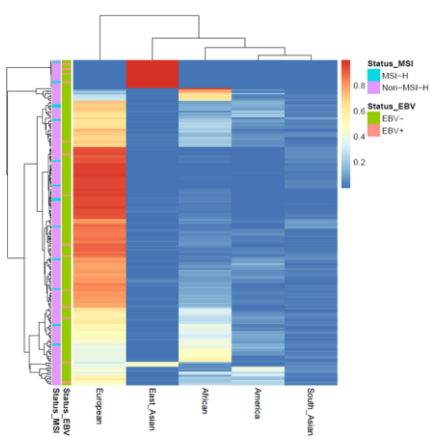


Figure 1. Heatmap of genomic ancenstry inference. EBV+= presence of EBV infection, EBV- = without EBV presence. MSI-H= Microsatellite Instability (MSI) positivity, MSI+, and Non-MSI-H= MSI negative, MSI-.

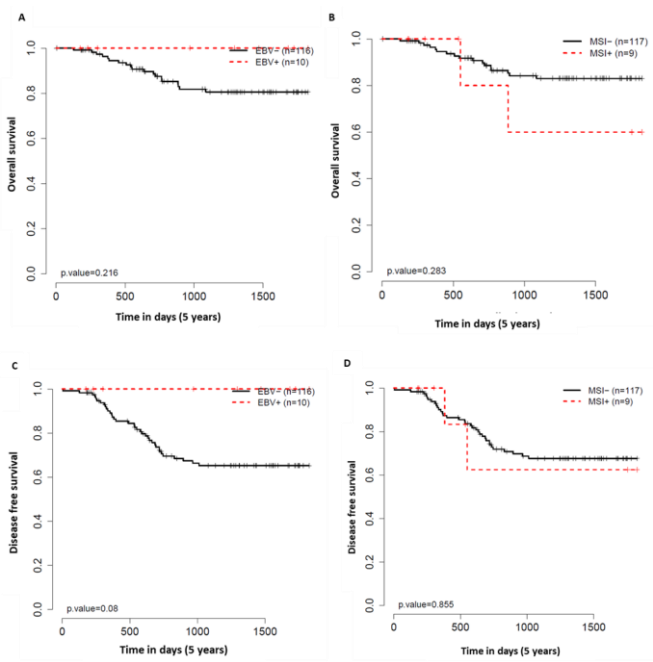


Figure 2. Prognostic impact of EBV and MSI in GAC subjects. Overall (A/B) and Disease free (C/D) survivals in 05 years, according to EBV (A/C) and MSI (B/D) status.

The prognostic impacts of EBV and MSI positivity were evaluated by the overall and disease-free survival in 05 years, excluding cases that were metastatic at diagnosis and those with TNM class IV. We found no statistical differences between the groups, which may be an impact of our still limited cohort. The findings with the highest statistical trend suggest that a longer disease-free survival more frequent in EBV+ cases (p=0.08) **(Figure 2)**. In this scenario, the presence of EBV and MSI in GAC patients has been investigated and correlated with the response to different treatment strategies in several studies, which demonstrates its importance (STANEK et al, 2022).

Conclusions

The prevalence of the GAC-MSI and GAC-EBV subtypes found in this study is low, but is in agreement with the frequency reported in the literature (TCGA, 2014). Despite the small fraction of positive cases, our study preliminarily suggests a positive impact of the presence of EBV in protecting the occurrence of relapses in AdG. These data are still being analyzed to deepen the understanding of these CAG subtypes, as well as the preliminary results of ancestry and molecular profiling, which will be further investigated in our cohort. Thus, we seek to understand the role of these markers and contribute to a better understanding of their role in the malignancy of gastric cancer, with emphasis on the Brazilian population.

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