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## Incidence of Breast Cancer and Enterococcus Infection: A Retrospective Analysis

Authors: Matthew Cardeiro, Amalia D. Ardelian, Lexi Frankel, Dianela Prado Escobar, Catalina Molnar, Omar M. Rashid Abstract: Introduction: Enterococci comprise the natural flora of nearly all animals and are ubiquitous in food manufacturing and probiotics. However, its role in the microbiome remains controversial. The gut microbiome has shown to play an important role in immunology and cancer. Further, recent data has suggested a relationship between gut microbiota and breast cancer. These studies have shown that the gut microbiome of patients with breast cancer differs from that of healthy patients. Research regarding enterococcus infection and its sequala is limited, and further research is needed in order to understand the relationship between infection and cancer. Enterococcus may prevent the development of breast cancer (BC) through complex immunologic and microbiotic adaptations following an enterococcus infection. This study investigated the effect of enterococcus infection and the incidence of BC. Methods: A retrospective study (January 2010- December 2019) was provided by a Health Insurance Portability and Accountability Act (HIPAA) compliant national database and conducted using a Humans Health Insurance Database. International Classification of Disease (ICD) 9th and 10th codes, Current Procedural Terminology (CPT), and National Drug Codes were used to identify BC diagnosis and enterococcus infection. Patients were matched for age, sex, Charlson Comorbidity Index (CCI), antibiotic treatment, and region of residence. Chi-squared, logistic regression, and odds ratio were implemented to assess the significance and estimate relative risk. Results: 671 out of 28,518 (2.35%) patients with a prior enterococcus infection and 1,459 out of 28,518 (5.12%) patients without enterococcus infection subsequently developed BC, and the difference was statistically significant ( $p < 2.2 \times 10^{-16}$ ). Logistic regression also indicated enterococcus infection was associated with a decreased incidence of BC (RR=0.60, 95% CI [0.57, 0.63]). Treatment for enterococcus infection was analyzed and controlled for in both enterococcus infected and noninfected populations. 398 out of 11,523 (3.34%) patients with a prior enterococcus infection and treated with antibiotics were compared to 624 out of 11,523 (5.41%) patients with no history of enterococcus infection (control) and received antibiotic treatment. Both populations subsequently developed BC. Results remained statistically significant (p<2.2x10-16) with a relative risk of 0.57 (95% CI [0.54, 0.60]). Conclusion & Discussion: This study shows a statistically significant correlation between enterococcus infection and a decrease incidence of breast cancer. Further exploration is needed to identify and understand not only the role of enterococcus in the microbiome but also the protective mechanism(s) and impact enterococcus infection may have on breast cancer development. Ultimately, further research is needed in order to understand the complex and intricate relationship between the microbiome, immunology, bacterial infections, and carcinogenesis.

Keywords: breast cancer, enterococcus, immunology, infection, microbiome

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