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Cancer Control
Volume 30: 1–2
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Letter to the Editor: Radiotherapy Increases aMMP-8 Levels and Neutrophil/Lymphocyte Ratio Rapidly in Head and Neck Cancer Patients: A Pilot Study

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Keywords
head and neck cancer, radiotherapy, neutrophil/lymphocyte ratio, aMMP-8, periodontitis

Received May 8, 2023. Accepted for publication June 21, 2023.

Dear Editor,

Brandt and colleagues' study on the diagnostic efficacy of blood neutrophil count, neutrophil-to-lymphocyte (NLR), and mouth rinse aMMP-8 levels in predicting periodontal side effects in head and neck cancer (HNC) patients undergoing radiotherapy (RT) is commendable.[1] The authors compared mouthwash aMMP-8 levels, MMP-8 molecular forms, blood neutrophil counts, and NLR in 13 patients 3 weeks before and 3 weeks after RT started (mid-RT). The results betrayed that higher NLR and aMMP-8 levels were linked to increased risk for periodontitis following RT ($P < .005$). The present results hold significant implications for assessing the likelihood of periodontitis resulting from RT as they provide insight into both local and systemic inflammation. However, given that advanced periodontitis may result in tooth extraction with the risk of severe complications, we would like to voice a few concerns regarding the interpretation of each factor considered in conjunction with the effects of RT.

First, the study cohort was small (N = 13) and heterogeneous with respect to tumor primaries, tumor and nodal stages, and presence/absence of surgery and chemotherapy, which may have unpredictably affected the outcomes, as they may have influenced the mean, maximum, and Vx (jaw volume exposed to x Gray or higher) doses of RT received by the mandible.[2] In addition, the authors did not provide any information regarding the exact location of periodontal examination procedures performed on the jawbone or the severity of periodontitis after RT. The reported mean RT dosage of 32.3 Gy pertains solely to the primary tumors and does not reflect the periodontal regions, which will determine the exact incidence and severity of periodontitis. In laryngeal cancers, which account for 46.2% of the study population, it is less likely that the whole 32.3 Gy was received by the upper or lower periodontal regions in all cases compared to their oropharyngeal cancer counterparts due to the significant differences in the radiation portal designs.[2,3] Hence, because of the dose-volume effects, it may be challenging to precisely ascertain the RT-induced periodontitis risk and establish a correlation between the periodontitis and elevation of aMMP-8 and NLR levels in every instance.

And second, the potential association between the pre-RT blood neutrophil, NLR, and aMMP-8 levels and the presence/absence of periodontitis could have yielded different rates of periodontitis if the authors had attempted to determine an optimal cutoff for the differences between the 2 measurements through the utilization of receiver operating

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curve analysis.[4] This approach could have segregated patients into 2 groups with significantly distinctive periodontitis rates. However, this may be prohibited by the small sample size. Hence, the matters discussed here ought to be acknowledged as recommendations for suitably structured future investigations that scrutinize the effectiveness of these parameters in more uniform tumor characteristics and larger study cohorts rather than particular critiques of the present study. Finally, we believe such efforts will yield valuable insights that will enhance our comprehension of the correlation between biological markers and the risk of periodontitis following RT or chemoradiotherapy.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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