at the neck are also documented in the article and did not affect the outcome of the flaps.1

We do not accept the derogatory suggestion by Pitak-Arnnop et al that we have deliberately created case selection nor do we feel a lesson in the basics of publication bias is needed. Our article describes our experience with maxillary reconstruction in, to the best of our knowledge, one of the largest cohort series that have been published. Artificially, subdividing into different groups within this cohort would lead to an overflowing production of meaningless data that would provide less valid information to the reader as well as exceed the word count of the journal. It is not unusual for academics to make claims about shortcomings of research design in the so-called era of “evidence-based practice.” The clinical reality is that the finite controls required to generate this level of evidence are seldom available and those of us who practice surgery in this demanding field will only ever be able to rely on careful, honest, and valid documentation of results.

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doi:10.1016/j.tripleo.2010.08.024

A histopathologic comparison between synchronous and single primary oral squamous cell carcinomas

To the Editor:

We have read with great interest and would like to take the opportunity to comment on the recently published article by Dissanayaka et al.,1 “A histopathologic comparison between synchronous and single primary oral squamous cell carcinomas.” It is hypothesized that synchronous oral squamous cell carcinomas (OSCCs) may present with more aggressive histologic behavior. Hence, the authors compared histologic parameters with known prognostic significance between synchronous and single primary OSCCs. The unexpected results showed that synchronous OSCCs have more aggressive histologic features than single primary OSCC.

It is a known fact that OSCCs in 2 different individuals will have different histologic features even if they are age, gender, and site matched, which in turn largely depends on biological behavior and degree of differentiation of OSCC.2 Thus, making it very obvious that the prognosis and survival of patients of the same age and sex with OSCC of the same location will also vary. The same result is expected when comparing histologic features of synchronous with single primary OSCCs. The results of the present study showed a significantly higher number of mitosis, tumor-induced stroma, lymph node metastasis, extracapsular invasion, and more tumor thickness and invasion into deeper areas in single primary OSCC as compared with synchronous OSCCs. We strongly posit that these results could be because of unintentional inclusion of control cases (selection bias) showing more aggressive histologic features. We would also like to question the authors’ selection of only 1 case of primary OSCC showing a verrucous appearance (micro and microscopic) in comparison with 6 cases of synchronous OSCCs. The verrucous appearance is known to have less aggressive histologic features and this must have further exacerbated the bias. Although the authors have made a genuine attempt to shed some light on the behavior of synchronous OSCCs, the results seem to be misleading.
as its validity is questionable along with being scientifically and statistically incorrect. Drawing attention to the fact that the authors have failed to assess the prognosis and survival rate in the present study, the question posed by the authors in discussion on “whether the synchronous OSCCs behave in a different way clinically despite their less aggressive histologic features or if some unknown factors affect the survival of these patients” seems inappropriate.

In this study, the site was not matched while selecting single primary OSCCs. The explanation offered was the presence of 2 different sites in most cases of synchronous OSCCs. However, there appears to be great variation in sitewise selection of control cases, which could have been carefully avoided (e.g., 2 tongue synchronous versus 5 tongue single primary, 2 commissural and retromolar synchronous versus 0 single primary, 0 floor of mouth synchronous versus 3 single primary, 0 alveolar synchronous versus 6 single primary OSCCs). We feel that the authors could have easily avoided this variation as the fact that prognosis and survival is site dependent cannot be overemphasized. We also would like to know the site involved in the “others” category, as there is great variation in number of cases selected (8 synchronous versus 3 single primary OSCCs). The side (same/contralateral) is also an important determinant of prognosis and survival in synchronous OSCC patients, but this important finding has been overlooked in the study except for buccal mucosa and tongue.

Lymph node metastasis is one of the important indicators for prognosis and survival of OSCC which correlates well with the tumor thickness, depth of invasion, site and to some extent, histologic grades. In the study, 1 synchronous and 7 single primary OSCCs were positive for lymph node metastasis, but the authors have failed to correlate lymph node metastasis with the tumor thickness, depth of invasion, site, and histologic grades.

In the discussion, the authors have quoted the data on 5-year survival of synchronous and single primary OSCCs, but this important statement needs a reference to state its authenticity, which unfortunately is missing. In conclusion, the authors have purportedly stated that the reason for reported unfavorable survival of synchronous OSCC patients may not be because of histologic differences. However, because the survival data were not available on synchronous OSCCs in the present study, we feel that the authors should not have taken the privilege of commenting on it.

One of the criteria to identify synchronous tumors given by Warren and Gates and Moertel et al. states that the tumor masses should be separated by at least 2 cm of normal tissue. Although rare, the possibility of undermining of single primary OSCC beneath the clinically normal-looking mucosa and its presence at the other area (simulating synchronous OSCC) cannot be ignored. Conversely, it is also possible that 2 closely associated sites in case of synchronous OSCCs can invade underneath the normal mucosa toward each other and collide. In both the situations, malignant epithelial cells will be present beneath the clinically normal oral mucosa. It is impossible to confirm whether OSCC is synchronous or single primary in such situations. Hence, we propose that the histologic examination of normal tissue is mandatory to rule out any underneath connection between the synchronous OSCCs. The cases showing presence of malignant epithelial cells beneath the normal mucosa should be excluded from the study. In the present study, there were 3 cases of lip and buccal mucosa. In such a situation where synchronous tumors are present in close proximity, it becomes important to conduct histologic examination of normal tissue and rule out the underneath tumor connection.

Other points that are minor but deemed important and yet not included in the study are

1. TNM staging and its correlation with other prognostic parameters
2. Habit and its correlation with the site of OSCC
3. Duration of lesion and its relation to tumor thickness and nodal metastasis

To summarize, we would like our suggestions to be considered, as it would have strengthened the rationale of this study thus avoiding obscurity in the study and biased results.

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doi:10.1016/j.tripleo.2010.08.026