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Comment on 'Human papillomavirus association is the most important predictor for surgically treated patients with oropharyngeal cancer'

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Sir,

We read with great interest the article by Wagner *et al* (2017), which aimed to test the previously proposed risk stratification of oropharyngeal cancer (OPC) (Ang *et al*, 2010) in a setting of patients receiving different treatments. However, we believe that their findings should be interpreted with caution, according to the following considerations:

The authors evaluated all the patients diagnosed with OPC in a 10-year time frame and treated with different approaches (radiotherapy or surgery alone, or surgery with adjuvant radiation or concurrent chemoradiation). They observed better survival for patients in the low- and intermediate-risk groups when treated with upfront surgery. However, the treated population cannot be defined as an 'unselected cohort', as the authors stated, as unresectable tumours were included and patients receiving surgery were younger and with lower stage and better performance status. Moreover, the treatment selection bias is undisputable as the choice of surgical *vs* non-surgical approach was left to the patient's decision. As the patients were included after diagnosis at the Head and Neck Surgery department, it is possible that the so-called 'anchoring bias' could have guided patients to prefer surgery (Jang *et al*, 2010).

As the study was conducted over a long time frame, the treatment approach selected by the patients should also be specified according to the time period.

The study population was composed of a mix of radiologically and pathologically staged cancers. This implies a stage migration, by possibly upstaging the latter. In this scenario the comparison of risks group among nonsurgical and surgical patients will expose the analysis to the Will Rogers phenomenon. To avoid this, we may consider the global survival of the two groups. In Figure 1 the global survival of the surgical group seems to be better than that of the nonsurgical group; however, we cannot exclude that these figures result from a clinical selection as previously discussed.

The authors tried to test a prognostic model originally built on a population of stage III–IV OPC patients on a wider population including patients with stages I and II. As they wanted to test the performance of a previously built prognostic model, they should have limited the analysis to a population with a homogenous stage of disease. Moreover, the authors arbitrarily grouped stage I and II with stage III (the so-called 'less advanced disease'), in comparison with 'advanced disease' consisting of stage IV disease.

The inclusion of metastatic patients in such an analysis is not appropriate; this group of patients receive a treatment with a completely different intent in respect to the nonmetastatic one (palliative *vs* curative).

The smoking history of the patients has been calculated according to pack-year consumption in the past 16 years. We wonder whether using a more standardised measurement of lifetime tobacco exposure could better help in interpreting these data.

It is not clear whether the authors considered as variable the performance status (PS), which reflects the patient's level of functioning (care for themselves, daily activity, physical ability) or the comorbidities, as they stated. The two parameters are not interchangeable, as patients with moderate or severe comorbidities, if compensated, may retain a good PS.

Finally, we would be very interested by the results of a new analysis done by Wagner *et al* (2017) that adopts the new AJCC cancer (Amin *et al*, 2017) staging to provide a validation of the prognostic model by Ang *et al* (2010) with this novel classification.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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