

Peer Review File

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Reviewer A

Good series from a single surgeon adding to the body of local Australian experience in TORS for HPVOPSCC.

My question centres around smoking, in several Australian centres current/recent smokers or a cumulative 10 year plus pack hx of smoking makes a patient intermediate risk vs low risk SCC for pure early stage HPVOPSCC, particularly in older patients. I note in your series about 1/2 of the patients are ex or current smokers - did that have an impact on:

- patient selection for TORS
- decision for adjuvant Rx
- DFS outcomes

This data should be available in your cohort and may be useful to provide KM curves for non-smokers, ex smokers, current smokers.

Reply 1:

Thank you for your review and questions. Smoking status at our institution did not influence treatment decisions (both for consideration of TORS and decision for adjuvant therapy) for patients presenting with HPV-related disease.

Please see " Materials and Methods: patient selection, and Adjuvant Therapy" sections that highlights patient selection for TORS and indications for adjuvant radiotherapy.

Stratifying patients based on number of pack years demonstrated that there was 20 patients that had never smoked, 13 patients that had <10 pack year history, 7 patients with >10 pack year history, and 1 with an unknown pack year history. Please see the revised "Table 1." that presents this information. As there were only 2 patients that died in the cohort, statistical associations based on smoking pack year history could not be made and hence not included in this study. Please see the limitations section of the "Discussion" section where this information has been included.

Changes in the text:

See the revised sentence within the "Material and Methods: Clinical and Pathological Features" on page 7/137; "Collected data included age at time of diagnosis, sex, HPV status (by both p16 staining and HPV ISH testing), smoking (defined as never, <10 pack years, or >10 pack years) and alcohol consumption (grams per day), as well as clinical and pathologic TNM classification from MDT discussions."

Please see revised smoking status section within Table 1. (page 20/461)

Smoking	
Never	20 (48.8)
<10 pack years	13 (31.7)
>10 pack years	7 (17.2)
Unknown	1 (2.4)

See revised sentence within “Discussion” section on page 14/335-336; “Disease-related mortality was rare (n=2), making meaningful associations with regards to smoking status, and recurrence on survival analysis difficult and therefore excluded from this study.”

Reviewer B

This is a single-surgeon retrospective case series of 41 patients who underwent TORS for HPV-related oropharyngeal SCC, with a good median follow-up of 51 months.

The STROBE checklist is complete.

It is a well-written paper, comparing the results with the available international literature - they are comparable. While it does not add anything new to the literature it is an Australian series of a relatively new surgical treatment that is only performed in certain high-volume centres, and reinforces the current literature on the topic.

The legend for Figure 1 would benefit from including more information for figures A and B to clearly explain what the 2 different Kaplan-Meier curves demonstrate.

Reply 2:

Thank you for your review and comment. The legend of Figure 1 has been elaborated to provide more information as suggested on page 22/489-490.

Changes in the text:

“**Figure 1.** – Kaplan-Meier graphs demonstrating disease-specific survival (A) and recurrence free survival (B) of patients with HPVOPSCC undergoing transoral robotic surgery (TORS).”