Neck dissection for advanced laryngeal cancer: Role and relevance in KwaZulu-Natal Province, South Africa

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Background. The global standard of care for advanced laryngeal squamous cell carcinoma (SCC) is total laryngectomy and neck dissection. While this approach aligns with international guidelines, there is no consensus on whether elective neck dissection (END) should be incorporated during primary surgery for clinically negative neck nodes (cN0) or as a therapeutic option after nodal relapse. It is therefore imperative to evaluate associated oncological outcomes and local contextual factors regarding END surgical approach in advanced laryngeal SCC.
Objective. To evaluate the lymph node outcomes and the rate of occult metastases (OM) of patients with advanced laryngeal cancer who underwent total laryngectomy with neck dissection.
Methods. A retrospective chart review was conducted at a South African hospital. Clinical records of 113 patients with stage III/IV laryngeal cancer who underwent total laryngectomy were retrieved from the hospital's health information system for analysis. Demographic data, postoperative care, and clinical and pathological reports were analysed.
Results. The patients were predominantly male (92.6%), of African origin (62%), with a mean age of 61.0 years and HIV seroposivity rate of 13.2%. Combined alcohol and tobacco use prevalence was 58.4%, while that of tobacco use alone was 31%. Overall histopathological tumour analyses showed that 74.3% had clear margins, 16.8% close margins and 8.0% positive margins. A total of 71.7% of the patients were initially classified as cN0, before histopathological results revealed 30.9% to have OM, with 3.75% having extranodal involvement. Substance use in the cN0 group with OM, regardless of HIV serostatus, was strongly associated with OM.
Conclusion. This study supports the importance of END in advanced laryngeal SCC and cN0 patients, aligning with global OM rates. These findings provide critical insights into the local context, supporting the continuation of END as standard of care in our institution.

Keywords: advanced laryngeal cancer, neck dissection, occult metastasis, clinically N0 necks, substance use

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Laryngeal squamous cell carcinoma (SCC) ranks as the second most prevalent primary malignant tumour of the respiratory tract and head and neck, following lung cancer.[1] The primary culprits, tobacco and alcohol, contribute significantly to its incidence.[1] Advanced cases (stage III/IV) demand rigorous treatment, typically involving total laryngectomy, neck dissection and adjuvant radiotherapy.[2-4] Cervical lymph node status emerges as a pivotal prognostic factor, significantly influencing patient outcomes.[3,5] The impact of lymph nodal metastasis on survival, reducing it by almost 50%, emphasises the critical nature of addressing this aspect in treatment.[1,2,6]

In the context of a developing country such as South Africa (SA), particularly in regions such as KwaZulu-Natal Province (KZN), unique challenges surface, including limited resources, unreliable patient follow-up and, crucially, addressing cervical lymph node status.[7] Clinically staged N0 patients with advanced laryngeal cancer exhibit an estimated 15 - 20% chance of occult metastasis (OM).[8,9] Therefore, optimising therapeutic approaches considering these limitations becomes imperative.[9,10] Despite global acceptance of total laryngectomy and neck dissection, there remains a significant gap in understanding the nuanced challenges faced in regions such as KZN. The dearth of literature addressing lymph nodal outcomes and their prognostic indicators underscores the necessity of in-depth research to bridge this gap, to enhance patient care.

Elective neck dissections (END) as standard of care for cN0 individuals who have advanced laryngeal SCC remain contentious. The debate was historically based on high postoperative mortality rates, and uncertainty in overall survival.[3,4,8] However, with advances in surgical techniques, points of contention are now around necessity, benefits and postoperative morbidity. The benefits of END use include staging for postoperative therapies.[8]

Building upon established knowledge about the significance of cervical lymph node status and its impact on treatment outcomes, the adoption of END in certain contexts may be beneficial. In exploring the intricate interplay between limited resources, unreliable follow-up and the clinical complexities of treating advanced laryngeal SCC, this study seeks to illustrate the advantages of END in cN0 individuals.

The objectives of this study were to assess the rate of occult lymph node metastases in patients with advanced laryngeal SCC undergoing total laryngectomy and neck dissection. In addressing these aspects, the study can then inform decision-making around the need for END in the management of advanced laryngeal cancer, particularly in resource-constrained settings such as KZN.

Methods

Study design

This study employed a retrospective chart review approach to analyse clinical data of patients with advanced laryngeal SCC. The research involved a thorough examination of patient records to assess various factors related to the disease and its management.

Setting

The study was conducted at a tertiary hospital in KZN, SA.

Study population and sampling strategy

Clinical records of 113 patients with stage III/IV laryngeal carcinoma who underwent total laryngectomy and various types of neck dissection were retrieved from the tertiary hospital's health information system for analysis. Inclusion criteria encompassed patients with advanced laryngeal SCC who received total laryngectomy and any form of neck dissection. Exclusion criteria comprised patients who failed chemoradiotherapy or radiation, and subsequently required salvage surgery. Non-SCC cases of the larynx were also excluded. The data collection sheet comprised demographic information such as age, gender, race, risk factors, HIV status/comorbidities, clinical staging and pathological staging, including histological details and the number of positive nodes.

Data collection

Data from January 2010 to December 2020 were selected for analysis. Patient records were systematically reviewed using a standardised data collection sheet.

Data analysis

Statistical analysis was performed using R statistical software (R Core Team, Austria). Both univariate and multivariate analyses were conducted to explore the collected data comprehensively. Statistical significance was set at $p<0.05$.

Ethical considerations

Ethical approval for this study was obtained from the University of KwaZulu-Natal Biomedical Research Ethics Administration (ref. no. BREC/00004282/2022).

Results

Demographics

The cohort of patients was predominantly male (92.9%, *n*=105); with 7.1% (*n*=8) female. The majority were of black African descent (61.9%, *n*=70), followed by white (14.2%, *n*=16), Indian/Asian (13.3%, *n*=15), coloured (6.2%, *n*=7) and other (4.4%, *n*=5). The mean age was 61.0 years, and the HIV seroposivity rate was 13.2%.

Substance use

Fig. 1 illustrates the levels of substance use in this study's patient population.

Primary tumour histopathological results

Histopathological analysis of the primary laryngeal tumour specimens, i.e. where the larynx that was surgically removed, showed that 74.3% (*n*=84) had clear surgical margins, 16.8% (*n*=20) had close margins and 8.0% (*n*=9) had positive margins.

Overall occult metastasis

When comparing the preoperative clinical nodal status (cN) to the postoperative pathological nodal status, 81 out of 113 (71.7%) patients were staged as cN0 preoperatively. However, 30.9% (*n*=25) of these clinically node-negative patients were found to have occult lymph node metastases on pathological evaluation (Fig. 2).

Nodal metastasis

Out of 113 patients included in this study, 21 were clinically staged as N1, 9 were clinically staged as N2 and 2 were clinically staged as N3. In the N1 patient group, 38.1% (*n*=8) were found to have lymph node metastases on pathological evaluation. Among the N2 patients, 33.3% (*n*=3) were found to have lymph node metastases. Additionally, both of the N3 patients (100%) were confirmed to have lymph node metastases on pathological examination (Fig. 3).

Analysis of the interplay between substance use, HIV serostatus and histopathological results showed higher incidence of OM in patients who used a combination of alcohol and tobacco, regardless of serostatus. The results also showed that 3.7% (*n*=3) of cN0 patients had extranodal extensions (Table 1).

Discussion

The majority of patients were male, with an average age of 61 years. These findings are consistent with the established epidemiological profile of advanced laryngeal cancer.[1,11-13] The literature indicates that advanced laryngeal SCC primarily affects older males, particularly those with a history of smoking and alcohol use. Laryngeal cancer is significantly more prevalent in men, occurring 4 - 5 times more often in males than females. The average age of laryngeal cancer diagnosis is ~66 years, with most cases occurring in individuals aged ≥55 years. A combined alcohol and tobacco use history was present in 58.4% (*n*=66) of patients. These results were not surprising, as the evidence from literature also shows that the combined use of alcohol and tobacco plays a critical role in increasing the risk of laryngeal cancer.[1,12] For instance, the odds for supraglottic cancers were notably higher compared with glottic cancers when both substances were consumed.[14] This indicates a possible biological interaction between smoking and drinking that increases the risk of laryngeal cancer, especially in the supraglottic area of the larynx. KZN has high HIV rates; however, it appears that HIV status does not seem to be a contributing factor to laryngeal cancer and OM.

The study revealed a 30.9% OM rate in cN0 patients with advanced laryngeal cancer. These findings highlight the need to adopt changes in therapeutic interventions. Given the challenges associated with follow-up in environments with limited resources, the adoption of END regardless of clinical nodal staging seems necessary.[7]

The high rates of OM observed in this patient population support the END use approach. These findings contribute to the longstanding clinical controversy surrounding the necessity of END for cN0 patients. However, the debate continues as to whether the potential benefits of END outweigh the additional surgical morbidity, especially for early-stage laryngeal tumours. Stokes *et al.*[6]'s findings in the USA resonate with the current study, emphasising the importance of bilateral level II - IV neck dissection for T4N0 laryngeal cancer. Sharbel *et al.*[8]'s review supports the need for END in advanced T staging (T3/4), especially in supraglottic and transglottic tumours.[8] The authors propose a selective, risk-adapted approach to END in laryngeal cancer, tailoring the extent of dissection to the primary tumour subsite and stage. This strategy is said to minimise unnecessary surgical morbidity while effectively addressing high-risk areas for occult disease.[9] Hence we advocate for END in all T3 and T4 laryngeal SCC, based on our findings.

The findings from this study, which drew on historical data over a 10-year period, shed light on the challenges faced in cancer treatment in this region. These data inform the ongoing debate regarding the optimal management approach for advanced

laryngeal cancer. Some studies recommend tailored treatment based on the specific subsite involved (glottic, supraglottic or subglottic), while others advocate for END regardless of tumour location.[5,8,9,11,15] In early-stage glottic cancers, some surgeons argue that END may not be necessary owing to the relatively low rate of neck metastases.[15] However, with advanced laryngeal cancers, the tumour may involve multiple subsites, making it difficult to reliably determine whether the disease is limited to the glottis alone.[5,11] Therefore many experts recommend performing END for all patients with advanced laryngeal cancer, as the risk of occult nodal disease is significant. These findings underscore the importance of END approaches. Healthcare policies should consider integrating these insights, especially in resource-limited settings, to optimise patient outcomes.

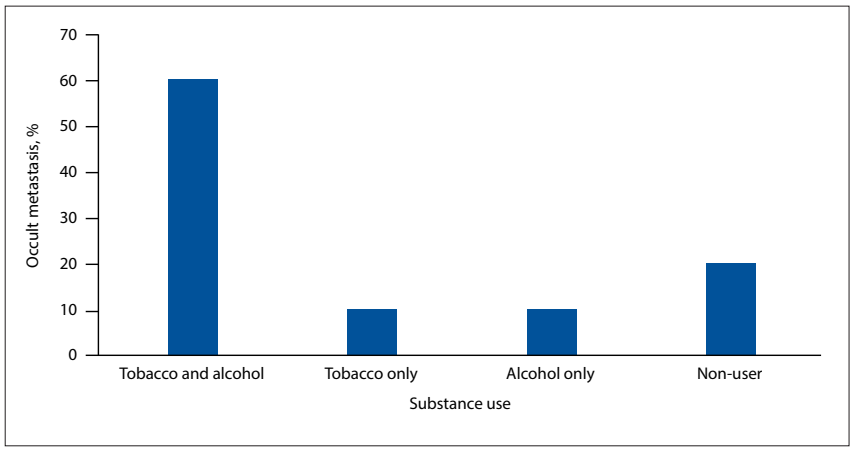

Fig. 1. The prevalence of substance use in the study population (N=113).

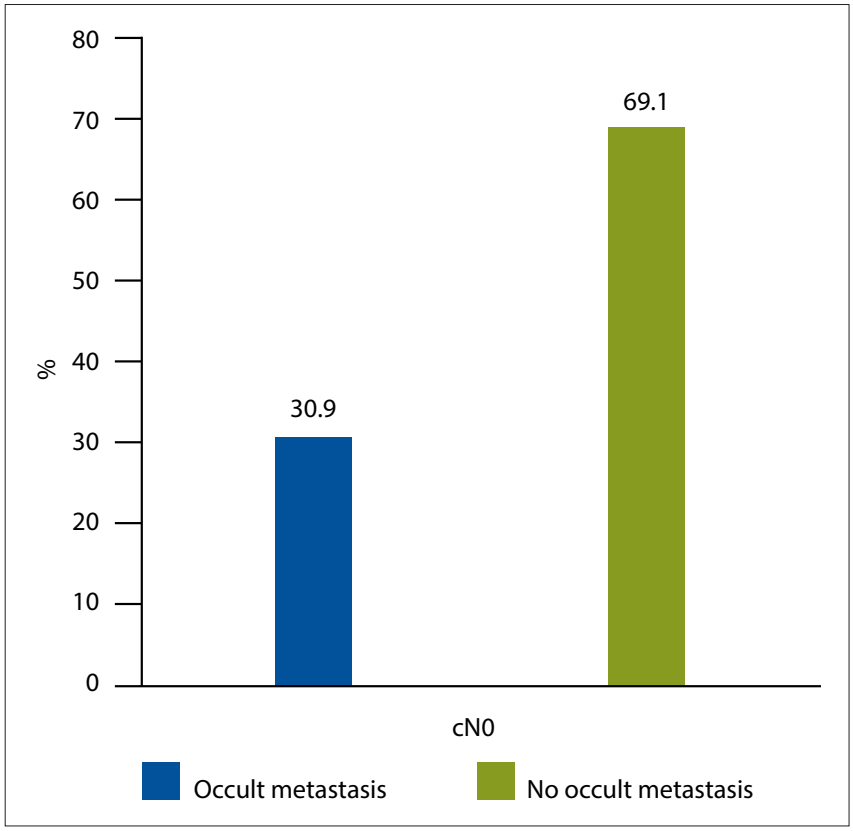

Fig. 2. Occult metastasis in patients with clinically negative neck nodes (cN0) (N=81).

Future research should focus on expanding the study's scope to encompass a broader demographic, providing a more comprehensive understanding of laryngeal cancer and OM, and potentially uncovering factors previously overlooked. For instance, future studies could include patients from other parts of the country, or different countries, to provide a more diverse and globally representative sample. The demographic expansion efforts should also include under-represented sex and age groups. Socioeconomic status and a list of comorbidities could also be incorporated and investigated.

This study demonstrated a similar prevalence of OM for all subsites of the larynx to those in other studies. T3/T4 had a 30.9% rate of OM in this study, which is comparable with what is reported globally.[3,8,9] The surgical margins of the primary laryngeal tumour excision are also an important prognostic factor. Clear margins indicate successful resection of the primary disease, which is crucial for improving survival rates and reducing locoregional recurrence. In this study, KZN demonstrated a low prevalence (8.0%) of positive margins compared with the literature, where the estimated prevalence of positive margins is 9.3% - 45.4%.[15,16]

Stokes *et al.*[6] analysed patients in the US National Cancer Database diagnosed from 2004 to 2012 with T4N0 laryngeal cancer, and showed that the overall survival rate for those undergoing surgery with

Table 1. Prevalence of substance use, HIV serostatus and histopathological results in cN0 patients with occult metastasis (*N*=25)

Alcohol use	Tobacco use	HIV serostatus	Pathological nodes	cN0, *n* (%)
Yes	Yes	Negative	>1	10 (12.3)
No	Yes	Negative	>1	9 (11.1)
Yes	Yes	Negative	>1; extra extension	2 (2.5)
No	Yes	Positive	>1; extra extension	1 (1.2)
Yes	Yes	Positive	>1	1 (1.2)
No	Yes	Positive	>1	1 (1.2)
No	No	Negative	>1	1 (1.2)

cN0 = clinically negative neck nodes.

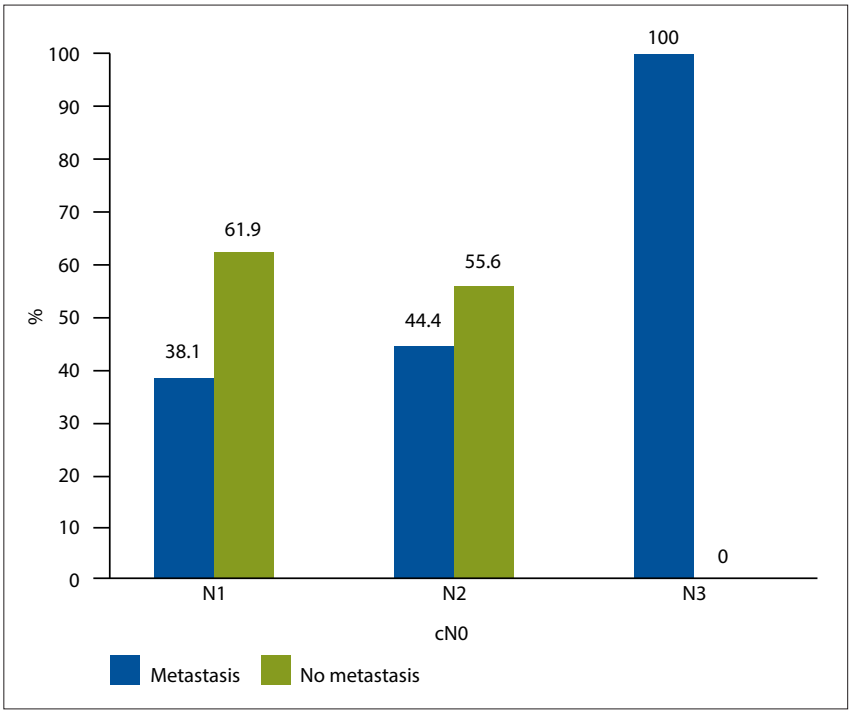

Fig. 3. Rate of nodal metastasis (N=21).

adjuvant radiation therapy was superior to that of the patients treated with concurrent chemoradiotherapy. All these patients needed treatment of the neck, and the N0 neck needed bilateral level II - IV neck dissection.[6] Indications for elective neck treatment entail a 15 - 20% chance of occult neck metastasis, given that vigilant follow-up is not possible, and clinical evaluation of the neck and access to the neck for reconstruction are difficult.[10] This further supports the use of END in our province, because of the existing high burden to the healthcare services.

Sharbel *et al.*[8] found that the overall OM rates were 20.5%, and in terms of T staging, they found that T1/2 had a 13% rate of OM, and T3/4 had a 25% rate, covering all subsites. These findings suggest that patients with advanced T stage laryngeal cancer (T3/4) should receive END despite having cN0 neck.

In patients with cN0 laryngeal cancer, Sanabria *et al.*[9] advise against END in T1/2 glottic tumours, but for T1/2 supraglottic tumours, END should omit levels I, IIB and V, while T3/4 tumours (glottic or supraglottic) warrant exclusion of levels I, IIB and V.

Riviere *et al.*[3] report distribution of occult nodal metastasis by level: level IIB (1.3%), level IIA (11.5%), level III (11.5%) and level IV (1.3%) in cN0 necks. They argue that elective neck treatment of level IIB and level IV can be omitted in patients with cN0 laryngeal cancer. Chone *et al.*[4] also argue that dissection of level IV is not mandatory in patients with cN0 laryngeal cancer.

Overall, it is clear that accurate staging is crucial in guiding treatment decisions for advanced laryngeal cancer. Ultrasound-guided fine-needle aspiration (US-FNA) has emerged as a valuable diagnostic tool, particularly for T3 and T4 stage tumours. This minimally invasive technique allows for targeted sampling of suspicious masses, providing critical information to ensure appropriate, tailored therapy.[1,17-21] The high success rates, rapid diagnosis and outpatient feasibility of US-FNA make it an essential component of modern head and neck oncology practices.

However, US-FNA does have certain limitations. In cases of inconclusive or false negative results, additional diagnostic modalities such as core needle biopsy may be required. Furthermore, inherent limitations of ultrasound examination in the laryngeal and pharyngeal regions underscore the need for a comprehensive approach to staging.

In the context of END, the staging information provided by US-FNA and other diagnostic tools is crucial to guide treatment decision-making for the cN0. The ongoing debate surrounding the necessity of END in advanced laryngeal cancer highlights the importance of considering both oncological outcomes and local contextual factors when determining the optimal management approach for this patient population.

Conclusion

The high rates of occult lymph node metastases and extranodal extension identified in this study support the use of END for all advanced laryngeal cancer patients, regardless of clinical staging. However, improving patient follow-up systems, particularly in the SA and broader sub-Saharan African context, will be crucial to optimising outcomes. We recommend strengthening collaborations between healthcare providers, governmental bodies and non-governmental organisations to enable earlier detection of recurrence, and timely intervention. Ongoing monitoring and analysis of this patient population will be essential to refining the management of advanced laryngeal carcinoma in this region. Overall, these insights can inform surgical planning and improve outcomes for this challenging patient group.

Data availability. The data that support the findings of this study are available from the corresponding author upon request.

Declaration. This research formed part of SSG's MMed training in Otolaryngology – Head and Neck Surgery at the University of KwaZulu-Natal, South Africa.

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