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Semon Lecture: 'Laryngectomy Practice Based on Personal Research', Royal Society of Medicine, 5 November 2020, London, UK

J J Fagan

Division of Otorhinolaryngology, Faculty of Health Sciences, University of Cape Town, South Africa

Lecture

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Author for correspondence:
Prof Johannes J Fagan,
Division of Otorhinolaryngology,
Faculty of Health Sciences,
University of Cape Town,
Cape Town, South Africa
E-mail: johannes.fagan@uct.ac.za

I wish to thank the Semon Committee for inviting me to deliver the 2020 Semon lecture. This is a very special honour, as is evidenced by the list of distinguished lecturers dating back to the inaugural lecture delivered at University College London in 1913. I am not the first South African to deliver the Semon lecture, having been preceded by my previous chairman Sean Sellars in 1993, and by Jack Gluckman in 2001, who was South African raised and educated and who subsequently became the chairman of otolaryngology in Cincinnati, USA.

Mr Peter Clarke asked me to share some of my personal clinical research related to laryngeal cancer with you. Unlike the UK, South Africa is a developing country with far greater healthcare limitations than what you experience in the National Health Service. Hence, the way that we manage patients with laryngeal cancer is tailored according to our financial constraints. I am therefore hoping that by sharing our experience with you in the Global North, it fulfils Felix Semon's express wish that his lectureship be given to those from both the UK and overseas, to (presumably) provide more varied perspectives relating to patient care.

When I was a registrar in the early 1990s, tumour (T) stage T_{1-2} laryngeal cancers were treated by vertical or horizontal partial laryngectomy, or by primary radiotherapy (RT). T_1 cancers involving the anterior commissure were treated surgically with vertical partial or even total laryngectomy, because of concerns about thyroid cartilage invasion along Broyle's ligament that could not be excluded with the inferior computed tomography images of that time. Cancers staged as T_{3-4} were treated with total laryngectomy and routine thyroid lobectomy. Post-operative RT was administered for cartilage invasion, subglottic tumour extension, positive margins and when a pre-operative tracheostomy had been required for airway compromise.

Selecting treatment should, however, be more complicated. One must consider: whether the objective is to cure or to palliate; the morbidity and mortality of treatment; and patient factors, including personal objectives, what is acceptable morbidity for the patient, cultural bias, co-morbidities, socioeconomic factors, employment type, follow-up reliability (a challenge in developing countries) and cost (in many poor countries, patients pay out of their own pockets for surgery and RT). One also needs to consider institutional factors such as: the expertise, experience and bias of the multidisciplinary team; audited treatment outcomes of the institution; and the institution's capacity in relation to specialised imaging, surgery, voice prostheses and RT (only 24 out of 52 African countries have RT facilities).

Current treatment options for advanced (T_{3-4}) laryngeal cancer are: conservation laryngeal surgery (transoral endoscopic carbon dioxide laser or transoral robotic surgery, and supracricoid laryngectomy), total laryngectomy, RT and chemoradiotherapy.

At the University of Cape Town, we perform approximately 40 primary total laryngectomies per year. We have a proactive approach to the node-negative (N_0) neck; we perform selective neck dissection for most patients, and more than 90 per cent of patients undergo a primary tracheoesophageal puncture for 'fistula speech'. Reasons for the many primary laryngectomies include the following: our patients generally have advanced disease, with 51 per cent of laryngectomees requiring emergency tracheostomies compared to 11 per cent in the Netherlands;[1] pressure on specialised imaging and chemoradiotherapy services; simplified long-term management in relation to swallowing, follow up and avoiding complex salvage surgery; we have excellent fistula speech outcomes, as I shall discuss later; reported global quality of life (QoL) scores are equivalent for total laryngectomy versus chemoradiotherapy; uncertainties regarding whether chemoradiotherapy for T_3 laryngeal cancers accounts for the decline in survival reported for laryngeal cancer in the USA in the 1990s;[2] and the equal overall survival for T_3 cancers treated with chemoradiotherapy and T_4 cancers treated with total laryngectomy.[1]

Our cohort of primary laryngectomies have provided us with an opportunity to conduct several clinical studies that have informed how we manage our laryngectomy patients.[3–13] Our findings are presented in relation to the following questions and topics: (1) does tracheostomy cause peristomal recurrence?;[3–6] (2) management of the thyroid

gland with laryngectomy;[7–9] (3) is tracheoesophageal speech appropriate in a developing world community?;[10,11] (4) early oral feeding following total laryngectomy;[12,13] (5) do peri-operative proton pump inhibitors (PPIs) reduce the incidence of pharyngocutaneous fistulae following total laryngectomy?;[14] (6) are cloth stoma covers effective to control tracheal climate of laryngectomy patients?;[15,16] and (7) does socioeconomic status affect QoL after total laryngectomy?[17,18]

Does tracheostomy cause peristomal recurrence?

Pre-operative tracheostomy is required in 51 per cent of our laryngectomees, predominantly in those with subglottic cancers and advanced tumours. In the 1990s, post-operative RT or emergency laryngectomy was advocated for emergency tracheostomy patients, even though the evidence for tumour seeding causing peristomal recurrence was questionable and the tracheostomy tract is completely resected at the time of laryngectomy.

The question we tried to address was whether seeding of cancer cells into the tracheostomy tract causes peristomal recurrence. We conducted a retrospective review of 43 clinically staged T_3 glottic cancers treated with primary total laryngectomy and post-operative RT, and found no difference in peristomal recurrence between tracheostomy and non-tracheostomy patients.[3] Though not conclusive (as all patients received RT), the results did question whether tracheostomy caused peristomal recurrence. Given supportive evidence from studies by Rubin *et al.*,[4] Pezier *et al.*[5] and Mei *et al.*,[6] we do not consider pre-operative tracheostomy to be an independent indication for post-operative radiation therapy, unless the tracheostomy tract passed through a tumour, or the tracheostomy was necessitated by subglottic extension or advanced cancer.

Management of thyroid gland with laryngectomy

Joseph Ogura (1955) and Sir Donald Harrison (1973) advocated routine thyroid lobectomy with total laryngectomy, as do the current National Comprehensive Cancer Network guidelines (2020).[9] The reasoning is to clear occult neck level VI nodal metastases as might occur with subglottic and hypopharyngeal cancers, or to resect possible direct cancer extension to the thyroid gland. However, the thyroid gland is located some distance from the glottis, making direct extension unlikely unless there is subglottic tumour extension.

Compared to an incidence of clinical or subclinical hypothyroidism of 5–10 per cent in the general population, the pooled risk of hypothyroidism following total laryngectomy with thyroid lobectomy is approximately 32 per cent, and, following laryngectomy, thyroid lobectomy and RT, the risk is approximately 89 per cent.[9] There is also an attendant risk of hypoparathyroidism. In developing countries, this can be problematic, as patients may not have access to or be able to afford thyroid hormone and calcium replacement or monitoring.

In order to determine whether routine thyroidectomy is oncologically indicated, we conducted a retrospective clinicopathological study of 102 total laryngectomies performed for clinically staged T_3 glottic squamous cell carcinoma.[7] We found that the thyroid gland was involved in only two cases, both with subglottic extension. Hence, we changed our practice to preserve the thyroid, unless there was subglottic or hypopharyngeal cancer, or intra-operative evidence of direct tumour extension to the thyroid.

Table 1. Impact of thyroid preservation on thyroid function

Treatment	Hypothyroidism (%)	*P*-value
Without RT		0.05
– Thyroid-sparing total laryngectomy	9	
– Thyroid lobectomy	50	
With RT		0.58
– Thyroid-sparing total laryngectomy	55	
– Thyroid lobectomy	65	
With or without RT		0.04
– Thyroid-sparing total laryngectomy	36	
– Thyroid lobectomy	62	

RT = radiotherapy

We subsequently assessed the oncological safety of the above practice in a retrospective review of 142 total laryngectomy patients, of which 69 had thyroid-preserving laryngectomy and 73 had thyroid lobectomies.[8] We found that there were no significant differences in local tumour recurrence or survival.

In a recent retrospective review of 84 total laryngectomy patients, we investigated whether thyroid-sparing total laryngectomy does indeed decrease the risk of hypothyroidism.[9] As is summarised in Table 1, preserving both thyroid lobes was significantly associated with preservation of thyroid function, although this advantage was lost in patients receiving post-operative radiation therapy.

Based on these three studies, it is our practice to reflect the thyroid and inspect the larynx, and to preserve the thyroid, unless there is direct tumour extension to the thyroid, or there are concerns about paratracheal nodes in patients with subglottic extension or cancer of the hypopharynx (Figure 1).

Is tracheoesophageal speech appropriate in a developing world community?

We fit over 90 per cent of patients with voice prostheses. However, voice prostheses are expensive and are unaffordable for many public hospitals and patients. Our speech therapists are responsible for patient selection, pre-operative counselling and long-term management of fistula speech.

We surgically optimise fistulae for speech by performing pharyngo-oesophageal myotomy, creating a capacious pharynx by closing the pharynx transversely, having liberal indications for augmenting the pharyngeal repair with a pectoralis major flap, and dividing the sternal heads of the sternocleidomastoid muscles to create a flat peristomal profile.

We first conducted a study to determine whether fistula speech was appropriate in a developing world setting given its expense, and whether to include socioeconomic status, literacy levels and proximity to the hospital as selection criteria for fistula speech.[10] Fistula speech was the primary mode of communication in 81 per cent of patients, and was unaffected by employment status or proximity to specialist services. Even though it was affected by literacy level and type of housing, several illiterate shack dwellers acquired good speech.

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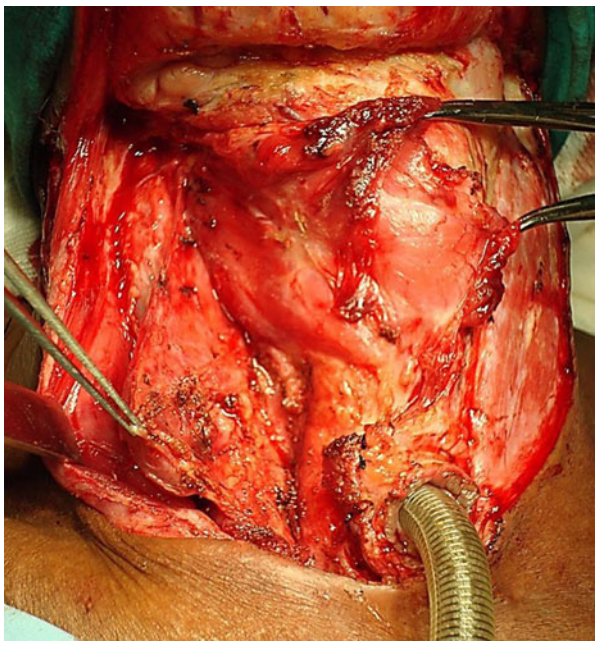

Fig. 1. It is our practice to reflect the thyroid and inspect the larynx for extralaryngeal cancer extension.

A more recent study of ours revealed that 93 per cent of patients fitted with a voice prosthesis used fistula speech as their primary mode of communication.[11] This improvement was attributed to: improved selection criteria that focused on manual dexterity and cognitive function; more rigorous education relating to valve maintenance and dealing with valve extrusion; and fitting indwelling as opposed to removable prostheses, to reduce extrusion rates in patients living far from the hospital.

Our current practice to optimise the use of expensive voice prostheses, therefore, is: careful patient selection in terms of manual dexterity and cognitive function; not excluding patients based on educational or socioeconomic status, or distance from the hospital; rigorous education relating to valve maintenance and dealing with valve extrusion; and fitting indwelling prostheses to prevent extrusion.

Early oral feeding following total laryngectomy

Despite oral feeding traditionally being withheld for 7–10 days, pharyngocutaneous fistulae occur in 3–65 per cent of primary laryngectomies. Medina (2001) (cited in Aswani *et al.*[12]) reported no difference in pharyngocutaneous fistula rates between early and delayed feeding. The question we posed was whether the same applied in a developing world setting with our more advanced tumours, more frequent neck dissections and poorly nourished patients.

We compared the pharyngocutaneous fistula rates in 40 primary laryngectomy patients fed according to the early feeding protocol (outlined in Table 2) with 39 historical control cases in whom feeding had been delayed for 7–10 days, and found no significant difference in fistula rates.

In a subsequent systematic review that compared early versus delayed feeding, I also reported that none of 11 studies found an association between early feeding and pharyngocutaneous fistulae with primary laryngectomy.[13] It is therefore our current practice to introduce early feeding for primary laryngectomy patients given its psychological benefits, reduced nursing care and cost savings. Delayed feeding is still employed for patients in whom a flap has been used to reconstruct the pharynx, or in those who have undergone salvage surgery following radiation therapy.

Table 2. Early feeding protocol

Day 1	Intravenous general maintenance solution & stomagastric feeds
Day 2	Clear oral fluids & stomagastric feeds
Day 3	Free oral fluids
Day 4	Soft diet
Day 5	Normal diet

Fig. 2. Cloth stoma cover (bib).

Do proton pump inhibitors reduce pharyngocutaneous fistulae?

In this study, we conducted a prospective, placebo-controlled, double-blind, randomised, controlled trial to determine whether peri-operative PPIs reduce the incidence of pharyngocutaneous fistulae following primary total laryngectomies.[14] Forty patients were randomised to either receive 14 days' PPI treatment (20 mg enteral omeprazole) or a placebo. There was a statistically significant difference ($p = 0.04$) in pharyngocutaneous fistulae in the omeprazole group (1 out of 21 (5 per cent)) versus the placebo group (6 out of 19 (32 per cent)). Hence, our current practice is to administer prophylactic PPIs for all total laryngectomy patients.

Are cloth stoma covers effective?

This section addresses the question: are cloth stoma covers effective to control the tracheal climate of laryngectomy patients? Neither our patients nor our public hospital can afford heat and moisture exchanger devices. Hence, we have cloth stoma covers made by a local seamstress for 35p, to humidify and warm the inspired air of laryngectomy patients (Figure 2).

We conducted a study to determine whether our inexpensive stoma cover was effective, and how it compared with the commercial Buchanan® Bib and heat and moisture exchanger devices. A thermocouple temperature sensor and a relative humidity sensor were incorporated into a housing that permitted us to record the temperature and humidity of the expired

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Table 3. Summary of how our clinical studies have impacted management of primary total laryngectomy cases

Parameter	Practice & considerations prior to clinical study	Current practice
Emergency tracheostomy	Post-operative radiation	No radiation
Thyroid gland	Routine thyroid lobectomy	Selected thyroid lobectomy
Fistula speech	Developing world criteria?	Consider dexterity & cognitive function, not socioeconomics, education, or distance from hospital
Oral feeding after total laryngectomy	7–10 days	Early feeding
PPI for pharyngocutaneous fistulae	PPI not used	PPI routinely used
Cloth stoma cover or HME	Cloth stoma cover effective?	Cloth stoma cover more effective than high-resistance or high-humidification HME
Socioeconomic status & QoL	Should patients be counselled differently?	Not a consideration, except for voice expectations

PPI = proton pump inhibitor; HME = heat and moisture exchanger; QoL = quality of life

air at the tracheostoma. The inexpensive stoma cover and Buchanan Bib both significantly improved humidity and temperature ($p < 0.05$), and were more effective than heat and moisture exchanger devices ($p < 0.05$).[15]

These findings were corroborated by Lansaat *et al.* in an *ex vivo* experimental setting.[16] We therefore recommend that cloth stoma covers be encouraged when heat and moisture exchangers are unavailable, unaffordable or inappropriate.

Does socioeconomic status affect quality of life after total laryngectomy?

South Africa is the most unequal society in the world in terms of the Gini Index. We conducted a study to examine whether QoL after laryngectomy is affected by socioeconomic status, and whether potential laryngectomy patients should be counselled differently depending on their socioeconomic status.[17]

Specifically, we carried out a cross-sectional, observational QoL assessment of public (Groote Schuur Hospital) versus private patients, more than two years after laryngectomy. Quality of life was measured using the Updated University of Washington Quality of Life questionnaire, the Voice-Related Quality of Life questionnaire and the Brief Illness Perception questionnaire. The private and public patient cohorts differed significantly in terms of: levels of education ($p < 0.001$), income ($p < 0.001$), permanent employment ($p < 0.001$), social welfare grant recipient ($p < 0.001$), distance to the hospital ($p = 0.008$) and poorer living conditions ($p = 0.001$). Thirty-five per cent of the public patients lived in informal settlements or low-cost government housing.[17]

The results of the study revealed that socioeconomic status did not significantly affect QoL.[17] However, lower socioeconomic status was associated with better voice-related QoL, which concurs with a study by Agarwal *et al.*[18] We therefore concluded that socioeconomic status should not affect indications for total laryngectomy, but that it should be considered when reporting voice outcomes of total laryngectomy patients.

Conclusion

I wish to conclude by again thanking the Semon Committee for this special opportunity to share our management perspectives of advanced laryngeal cancer based on our own clinical research (Table 3). Such crosspollination between the Global South and the Global North can only enrich our thinking and our practices, and ultimately improve patient care.

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