

Treatment of Squamous Cell Carcinoma of the Larynx Involving the Anterior Commissure: Systematic Review of Literature

Thesis

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List of Abbreviations

AC	: Anterior Commissure
DL	: Direct Laryngoscopy
PDT	: Photodynamic therapy
RT	: Radiotherapy

Introduction

Tumours of the anterior commissure (AC) present a unique diagnostic and therapeutic challenge. The point of controversy and failure of primary treatment comes from the fact that cases with squamous cell carcinoma of the larynx with anterior commissure AC involvement can be staged incorrectly, usually by understaging, as proximity of the AC to the thyroid cartilage (only 2 to 3 mm) can lead to direct spread which cannot be seen with the naked eye during diagnostic sessions of direct laryngoscopy (DL). This can lead to down staging of a patient, i.e. patients are mistakenly classified as having early stage I; T1a or T1b carcinoma when in fact they are stage III or stage IV, due to unseen invasion of the thyroid cartilage. A preoperative computed tomographic scan can aid in evaluating this space (*Krespi and Meltzer, 1989 and Bradley et al., 2006*).

I. Anatomy of the Anterior Commissure

The AC of the larynx is a much contested area in the anatomical and clinical sense. Anatomically it is considered the most anterior meeting point of the two vocal cords and their insertion into the posterior surface of the thyroid cartilage. Clinically, the AC (Fig.1) includes the above anatomical definition plus its extensions in all directions, subglottically, supraglottically, as well as the anterior portions of both left and right vocal folds.

Currently, the degree of extension into these mentioned directions is the point of contention and there is no standard dimensions available in any anatomical or otorhinological reference texts nor any consensus among practising otorhinolaryngologists.

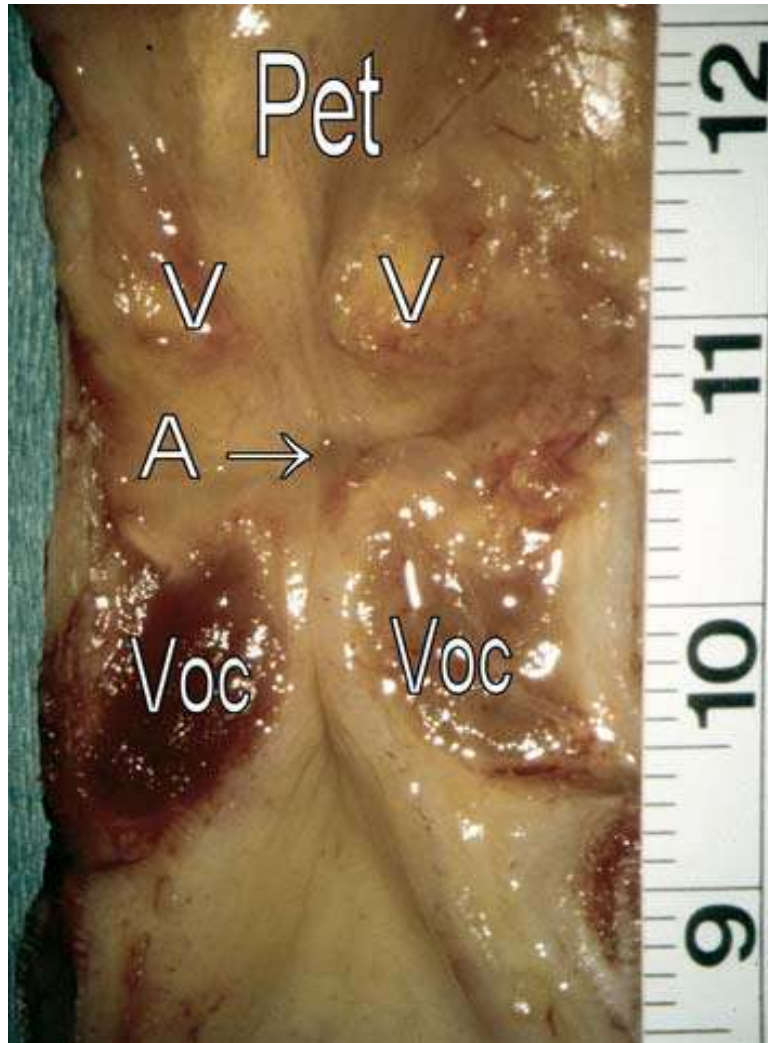


Figure (1): Gross anatomical View of the anterior commissure—frontal plane, human specimen larynx; Pet petiole, V ventricular fold, A anterior commissure, Voc vocal fold (*Remacle et al., 2007*).

The anatomy of the AC was investigated in several studies (*Rödel et al., 2009 and Zouhair et al., 2003 and Steiner et al., 2004*) and is still the subject of controversy. The vocal ligament inserts at the AC by two characteristic structures: the noduli elastici and the vocal ligament tendon (Broyle's ligament). These structures fulfil biomechanical function by equalizing the different elastic moduli of tendon, cartilage, or bone.

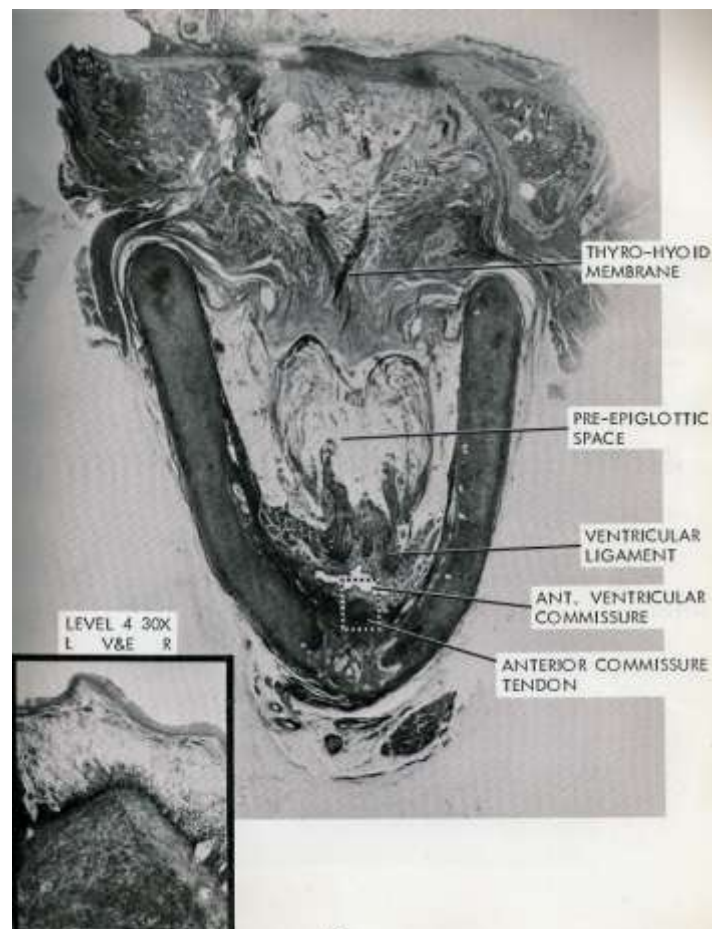


Figure (2): Microscopic anatomy of the larynx; Coronal section of a larynx of a 44 year old male showing the microscopic anatomy at the level of the anterior commissure (*Tucker, 1971*).

Some authors consider the fibrous tissue of the AC tendon (as seen in Fig. 2) to act as a tumour barrier preventing tumour spread anteriorly to the glottic plane or invasion of the adjacent thyroid cartilage (*Rödel et al., 2009 and Zouhair et al., 2003 and Steiner et al., 2004*). In contrast, other investigators assume the AC to represent a weak point with regard to tumour spread because it is here that Broyle's ligament inserts into the thyroid cartilage, and penetration might induce susceptibility to tumour invasion (*Rödel et al., 2009 and Zouhair et al., 2003 and Steiner et al., 2004*).



Figure (3): Radiographic anatomy of the larynx; Axial CT scan with contrast of the neck, level of the glottis (*Remacle et al., 2007*).

II. Staging of Laryngeal carcinomas

Carcinomas involving the AC represent a heterogeneous group of lesions that cannot be accurately classified by the TNM system alone but requires additional description (*Sachse et al., 2009*). The American Joint committee on Cancer (AJCC) in their classification of malignant tumours of the larynx include in the anatomical sites of glottis the subsites: vocal cords, AC and posterior commissure, *without* defining their anatomic boundaries (*Bradley et al., 2006*). This system while useful in determining possible treatment options based on clinical stage of patients, ignores all controversy around the AC and barely mentions it. Currently the seventh edition of this classification system is in use (*Edge et al., 2009*).

Much of the controversy about staging of AC tumours is because only a few millimetres separate the AC mucosa from the thyroid cartilage especially below the AC tendon. Therefore a small tumour on the surface actually may penetrate the cartilage changing the stage from early (T1) to advanced (T3 or T4) glottic cancer only within a few millimetres of growth (*Rödel et al., 2009 and Zouhair et al., 2003 and Steiner et al., 2004*).

III. Treatment Choices and Controversies

Treatment for early AC laryngeal cancer can consist of radiotherapy or surgery. First and foremost of the controversies is whether to use radiotherapy or surgery as the line of treatment for such cases. Surgery has been the preferred method of treatment, since studies previously indicated early tumour

invasion of the thyroid cartilage at the AC, thereby assuming less curability by radiotherapy (*Patrick et al., 2006*).

Kirchner in 1970 stated “that radiotherapy is not the treatment of choice for glottic cancer which crosses from one vocal cord to the other at the AC”; this was because of difficulty with evaluation and follow-up as well as predisposing to under-treatment or radionecrosis. He theorized that these poor results were related to the presence of radiation “coldspots” receiving less radiation dosage, with ortho-voltage irradiation techniques. Since then the debate has raged on, with a review of the more recent publications on using curative radiotherapy for AC carcinoma rebuffing and proving this statement false (*Kirchner 1970 and Bradley et al., 2007*).

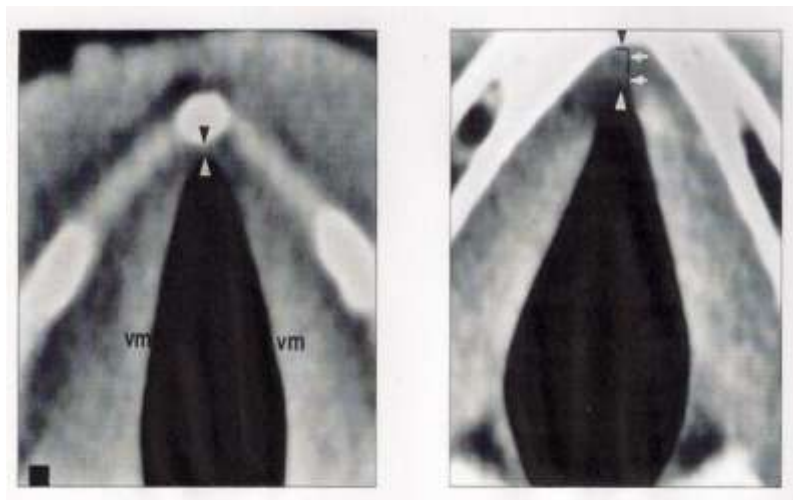


Figure (4): Anatomic variations in size of the AC (Left) Axial CT neck with normal AC in 55 year old woman. Width of AC shown by Arrowheads; 1.0mm (Right) Axial CT neck with normal AC in 45 year old man. Width of AC by Arrowheads 2.2mm (*Kallmes et al., 1997*).

Subsequent laryngeal anatomic studies and refinement of radiotherapy techniques have brought into question the ineffectiveness of curative irradiation in early glottic tumours (*Persky et al., 2000*).

That said other technical difficulties in the actual administration of radiotherapy have been mentioned as pitfalls that result in poor cure rates despite the improvements and advanced that have been made over the years. The local radiotherapy centre cure rates are one of the most paramount factors to be considered when referring a patient for treatment (*Bradley et al., 2007*).

Despite the fact that radiotherapy is the current accepted treatment for early laryngeal carcinoma in most oncology centres, it is not without its risks and complications. The most severe but thankfully uncommon complication is radionecrosis of the thyroid and other laryngeal cartilages. This has no definitive curative treatment and in worst case scenarios may necessitate total laryngectomy. This defeats the purpose of treating early laryngeal carcinomas with radiotherapy as opposed to radical non-conservative surgery. It should be noted that radionecrosis can occur any time after finishing radiotherapy with some cases occurring even 50 years after initial treatment. Other complications include laryngeal oedema, skin damage, and perichondritis (*Oppenheimer et al., 1989 and Cukurova, 2010*).

It should be noted that most authors have reported lower rates of success for radiotherapy at the AC, especially for lesions classified as stage T2 or a more advanced stage. Special techniques may help, such as larger fraction sizes, more frequent doses (“hyperfractionation”), or a higher overall dosage (at least 70 Gy). However, no reports have duplicated the success reported for surgery of T2 cases (*Pearson et al., 2003*).



Figure (5): Endoscopic view of the glottis post excision of AC tumour with CO2 laser (*Remacle et al., 2007*).

The other main alternative to radiotherapy is transoral endoscopic approach for excision of laryngeal carcinomas. This dates back to Lynch during the 1920s. Lynch and his group or researchers started out performing excision using cold instruments however, since Strong and Jako first introduced the carbon dioxide (CO2) laser for laryngeal carcinoma in 1972, its use for treating early stage laryngeal malignancies has been advocated by many physicians and researchers. Werner et al in