Imaging of laryngeal cancer: what clinicians want to know

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Learning objectives

• To assess the role of CT and MRI in the evaluation of laryngeal cancer (LC), stressing the importance of a correct examination technique.
• To show a systematic method of analysis in the assessment of LC, illustrating the key findings that are necessary for staging and to help clinicians in the choice of the appropriate treatment.

Background

Diagnostic imaging (CT and MRI) is essential in the staging (deep loco-regional extension, nodal and distant metastases) and follow-up (treatment results) of LC.

However, the complex anatomy of the laryngeal district and the difficult interpretation of imaging findings require a methodical approach, both in the examination execution and in the image analysis, in order to correctly and usefully contribute to the management of LC.

Findings and procedure details

The larynx (Fig. 1 on page 7) is the organ that connects the upper (nas/o/oropharynx) and lower (trachea) airway, located in the visceral space of the infrahyoid neck. It mainly consists of cartilages:

• the thyroid "shield" superiorly (formed by two laminae joining anteriorly at the thyroid notch and extending posteriorly into two superior and two inferior cornua), connected to the hyoid bone through the thyrohyoid membrane;
• the cricoid cartilage inferiorly (the only "complete" ring formed by an anterior arch and a posterior lamina), connected to the thyroid shield through the cricothyroid membrane;
• the arytenoid cartilages, paired pyramidal structures that sit atop the posterior cricoid (with vocal processes anteriorly and muscular processes laterally) and, above these, the corniculate cartilages;
• the epiglottis, a leaf-shaped "lid" with a free margin (suprahyoid) and a fixed portion (infrahyoid), connected to the hyoid bone through the hyoepiglottic ligament (which represents a barrier for disease spread from the larynx to the oropharynx/oral cavity), covered by mucosa (the glossoepiglottic fold), and to the thyroid shield through the thyroepiglottic ligament.
The main structure to identify in the larynx is the glottis, which divides the supraglottic larynx above from the subglottic larynx below:

1. the **glottic** larynx is formed by the **true vocal cords**, soft tissue folds (vocal ligaments covered by mucosa) attached anteriorly to the thyroid shield (where they join in the **anterior commissure**) and posteriorly to the arytenoids (**posterior commissure** in the inter-arytenoid space), including the intrinsic thyroarytenoid muscle beneath (its medial fibers are called "vocalis muscle").

2. the **supraglottic** larynx contains: the **false vocal cords or ventricular folds** # mucosal folds ABOVE the true vocal cords; the **vestibule** # air-space above the false vocal cords; the **ventricle** # air-space between false and true vocal cords; the **aryepiglottic folds** # mucosal folds extending from arytenoids to infero-lateral epiglottis, forming the junction between the larynx and the hypopharynx; the **pre-epiglottic space** # fat between the epiglottis and the hyoid bone, "halved" by the hyoepiglottic ligament; the **paraglottic or paralaryngeal spaces** # fat beneath the false but also the true vocal cords (therefore extending in the glottic larynx, where it continues posteriorly in the thyro-arytenoid gap/crico-thyroid space # pathway of disease spread from the larynx to the hypopharynx), merging superiorly into the pre-epiglottic space.

3. the **subglottic** larynx consists of mucosa closely applied to the cricoid.

**LC** is a relatively rare disease, but with a high morbidity and mortality, that typically affects men over 50 years of age with a history of tobacco and alcohol use; the association with a second primary pulmonary tumor is frequent. The symptoms, often manifesting late, include hoarseness/dysphonia, sore throat, dyspnea, dysphagia/odynophagia and/or a neck mass. The symptoms, often manifesting late, include hoarseness/dysphonia, sore throat, dyspnea and a neck mass. The vast majority of LCs consists of **squamous** cell carcinomas, more frequently arising in the glottis, followed by the supraglottic and, rarely, the subglottic larynx.

The site of involvement influences differences in tumor staging (Table 1 on page 8), especially in the early stages; also, it is useful to remember that supraglottic tumors have a higher incidence of nodal metastases because the supraglottic larynx, having a different embryologic origin (primitive buccopharyngeal anlage), is richer with lymphatics compared to the glottic-subglottic larynx (derived from tracheobronchial buds).

Tumor staging is the most relevant prognostic factor and is essential to decide the appropriate **treatment**:

- **early stages (0-II)** usually undergo radiation therapy or surgery only;
• advanced stages (III-IV) are generally treated with a combination of radiation therapy (with concurrent chemotherapy) and surgery (typically including selective or radical neck dissection).

Surgical resection of the larynx (laryngectomy) may be:

• partial (laser/endoscopic or "open"), especially for early (T1-T2) supraglottic/glottic tumors (e.g. cordectomy, vertical laryngectomy or hemilaryngectomy, horizontal or supraglottic laryngectomy, supracricoid laryngectomy with crico-hyoido(epiglottopotexy, near-total laryngectomy # preservation of one true vocal cord/crico-arytenoid unit);

• total with tracheostomy, particularly for advanced (T3-T4 or N+) stages/subglottic tumors # in detail, indications include: advanced tumors with cartilage destruction and anterior extra-laryngeal spread; subglottic disease (with cricoid cartilage involvement); circumferential submucosal disease with/without bilateral vocal cord paralysis; posterior commissure or bilateral arytenoid/crico-arytenoid joint involvement; radiotherapy/chemoradiation and/or partial laryngectomy failures/complications (e.g. radiation necrosis, severe aspiration); uncommon non-radiosenstive histology (e.g adenocarcinoma); massive nodal metastases; advanced extra-laryngeal tumors (pos-cricoid hypopharyngeal neoplasms) invading the larynx.

LC diagnosis includes various procedures:

1. endoscopy (laryngoscopy) # indirect (with an angled mirror) and direct (with an endoscope/laryngoscope). It is usually the first step in the workup of LC, as it provides the best visualization of laryngeal mucosa/airway, giving an excellent view of mucosal neoplastic extent, and it allows to perform biopsies to analyze the histologic features of the tumor; however, laryngoscopy cannot accurately define bulky tumors, subglottic and deep submucosal loco-regional extent of LC, nor nodal/distant metastases, for which CT/MRI (and sometimes, in advanced stages and post-laryngectomy recurrent tumors, PET) must be used.

2. CT is generally chosen because it is less susceptible to motion artifacts, common in the larynx (unless intravenous contrast injection is contraindicated, in which case MRI should be preferred). CT relies on contrast-enhanced spiral multislice scanning with high-resolution images: this is obtained by using a small Field Of View (FOV) (18 cm), thin overlapping sections (0.5-1 mm), a low pitch (about 1) and adequate mAs/kVp (around 500/120, respectively). Patients are examined in the supine position, with the neck slightly hyperextended (the imaging plane should be parallel to the vocal cords) and the shoulders lowered as much as possible, preventing any asymmetry; they should be instructed to
breathe shallowly (to keep the vocal cords open) and to avoid swallowing/coughing. E-phonation or modified Valsalva maneuver can (additionally) be employed to improve the evaluation of vocal cord mobility (especially for glottic tumors) or the piriform sinuses, respectively. Good vascular enhancement/lymph node delineation can be obtained in the arterial or venous/"early" interstitial phase (the latter being more often used), but adequate tumor enhancement requires a longer waiting period because it relies on both hypervascularization and interstitial leakage of contrast ("late" interstitial phase). Therefore, different protocols can be used to study these two elements together or separately: a monophasic injection (around 100 ml of contrast medium at a flow rate of about 2-3 ml/s) followed by a monophasic (circa 90 s) or biphasic scanning (circa 60 s and 120 s, one of which using E-phonation/modified Valsalva maneuver); a biphasic injection (two injections of around 50 ml at a flow rate of about 2-3 ml/s, separated by a pause of 20-30 s) followed by a monophasic scanning (circa 90-120 s) # a monophasic scanning implies a single evaluation but also a lower radiation dose, whereas a biphasic scanning allows a double evaluation but with a higher radiation dose. Imaging processing is essential for a complete and thorough analysis of the tumor: MultiPlanar Reformations (MPR) can be used to obtain optimally symmetric/angulated (parallel to the vocal cords) axial sections (especially when acquisition is suboptimal) or coronal/sagittal sections for cranio-caudal tumor extension; Volume Rendering Techniques (VRT) can provide "fluoroscopic-like" images of the airways or virtual laryngoscopic images to demonstrate subtle irregularities/asymmetries of the larynx and to create a roadmap for surgery or for sites that are difficult to assess by conventional laryngoscopy.

3. MRI usually has a complementary role, but is more sensitive for a number of issues including cartilage invasion and recurrence; it is worth knowing that MRI tends to overestimate tumor extension (because of edema/inflammation), while CT tends to underestimate it. MRI involves the use of a neck dedicated surface phased-array coil with a small FOV (18 cm), thin (3-4 mm with 0-1 mm gap) and multiplanar (axial, coronal and sagittal) sections and/or gapless volumetric scans. Patient position/instructions are similar to CT. Localizer sequences are initially obtained to define the planes and limits of the region to be examined; then, fast sequences (typically Fast-Spin Echo, FSE) are employed, both T1- and T2- weighted. T1-weighted images have a high anatomical detail and are acquired before and after contrast injection; T2-weighted images better identify pathologic tissue. Both fat-saturated and non fat-saturated acquisitions should be performed: fat-saturation is crucial on post-contrast T1-weighted images (but it could also be of some use on unenhanced T1-weighted images for comparison) and can be helpful on T2-weighted images (to distinguish pathologic tissue from fat, both hyperintense without saturation). Diffusion-Weighted Imaging (DWI) and Apparent Diffusion Coefficient (ADC) are increasingly important techniques for tumor and node evaluation; Perfusion-Weighted Imaging (PWI) and spectroscopy still have a limited/under investigation role.
Before discussing the characteristics of LC on CT/MRI, it is critical to remember that an accurate radiologic interpretation requires the knowledge of the results of endoscopy, assessing the mucosal extent of the primary tumor: rendering a report without this knowledge will lead to significant errors in radiologic staging.

LC generally presents on imaging with the following features:

- **exophytic and/or infiltrating mass of variable size** (typically smaller in the glottis and larger in the supraglottis) centered in one site/subsite of the larynx: special care must be taken in looking for soft tissue and/or airway asymmetries, which could represent neoplastic tissue (especially with small tumors); also, an anterior commissure > 1 mm thick is strongly suspicious for glottic tumor;
- on unenhanced scans, LC frequently appears isodense on CT (not being clearly distinguishable # unenhanced CT acquisitions are NOT routinely used) whereas, on MRI, it shows a low to intermediate signal intensity on T1-weighted images and a moderately increased signal intensity on T2-weighted images and on DWI (with hypointensity and low ADC values on ADC maps); after contrast administration, relative homogenous (small lesions) or heterogeneous (large lesions) enhancement can usually be appreciated;
- once the "core" of the mass has been identified, the next step is to evaluate adjacent structures and organs for invasion # particular attention must be paid to the obliteration of fat spaces, namely pre-epiglottic (sagittal scans are very useful) and paraglottic, especially with supraglottic and glottic tumors, which are endoscopic blind spots. Cartilage involvement is another point not to miss # destruction or trans-cartilage extension of the tumor (e.g. "strap" muscles enhancement) is a clear sign of invasion on CT, while sclerosis may be related to invasion but also to tumor-induced periostitis (moreover, cartilage calcification, despite being typically symmetric, can mimic tumor involvement); in this instance, an altered signal intensity on MRI (hyperintensity on T2-weighted and on post-contrast T1-weighted images) is a more accurate sign, and DWI can be helpful to distinguish cartilage edema/inflammation (hyperintense on both DWI images and ADC maps) versus invasion (hyperintense on DWI images but hypointense on ADC maps);
- finally, cord mobility should be examined when possible (e.g. E-phonation scans): a "prominent" cord compared to the contralateral (adducted and of unchanged aspect on both free breathing and E-phonation scans) has a reduced motion.
- after evaluating the primary tumor, nodal metastases must be sought # this is particularly true with supraglottic tumors, which more often present with nodal involvement (level II-III); however, while this is less common with glottic/subglottic tumors, it is important to know that it may be found in
"infrequent" sites (level VI, to which the so-called "delphian" or pre-laryngeal node of glottic tumors belongs). CT/MRI cannot accurately assess lymph nodes as metastatic if they are not of **round morphology, increased dimension (short axis > 1 cm) and/or heterogeneously enhancing (with internal necrotic areas)**; DWI and ADC could be useful in this setting, but their role is still controversial # PET is currently preferred, as it can also evaluate distant metastases.

A **radiologic report** should describe **in a structured and sequential manner all of the above information**, which must be summarized at the end by indicating the **radiologic clinical staging**, keeping in mind that this is the most important thing that clinicians want to know.

**Images for this section:**
Fig. 1: Anatomy of the larynx.
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**Table 1:** TNM Staging of LC (adapted from AJCC, 7th edition 2010).
**Fig. 2:** Glottic LC. CT (a-c). Post-contrast coronal (soft tissues window) (a), axial (bone window) (b) and virtual laryngoscopic (c) images: the tumor involves the left true vocal cord, extending to the ipsilateral false vocal cord, laryngeal ventricle and paraglottic space (arrow) (a); the thyroid cartilage is sclerotic (b); reduction of the lower airway on the left side is visible (c). MRI (d-e). Axial fat-saturated T2-weighted (d) and post-contrast T1-weighted (e) images: the left true vocal cord and the ipsilateral thyroid shield lamina show signal alteration (arrow) (d, e). Stage cT3.
**Fig. 3:** Supraglottic LC. CT (a-b). Post-contrast axial (a) and coronal (c) images: the tumor involves the right aryepiglottic fold, false cord, laryngeal ventricle and medial wall of the hypopharynx, reaching the ipsilateral arytenoid cartilage (sclerotic). MRI (c-f). Axial fat-saturated T2-weighted (c), post-contrast T1-weighted (d), diffusion-weighted (e) images and ADC map (f): the lesion shows moderately increased signal intensity on T2-weighted (c) images, with heterogeneous enhancement after contrast injection (d); hyperintensity on diffusion-weighted images (e), with corresponding hypointensity on ADC map (f), is also visible. Stage cT2.

**Fig. 4:** Supraglottic LC. CT (a-c). Post-contrast axial (a, b) and sagittal (c) images: exophytic-infiltrating tumor involving the aryepiglottic folds, the right aspect of the epiglottis and the ipsilateral pharyngo-epiglottic fold (a). Single ipsilateral necrotic
lymphadenopathy (3.4 cm in greatest dimension) at level IIa, in contact with the right internal jugular vein (thick arrow), sternocleidomastoid muscle (arrow) and posterior belly of digastric muscle (curved arrow) (b, c). MRI (d-f). Post-contrast fat-saturated axial T1-weighted images: CT findings for the tumor (d) and the lymphadenopathy, including the contact with the right sternocleidomastoid muscle (arrow) and posterior belly of digastric muscle (curved arrow) (b, c), are confirmed. PET (g-i). Axial images with 18FDG and CT-coregistration: the tumor (g, arrow) and the lymphadenopathy (h, arrow) are clearly visible as hyperaccumulating areas; two hyperaccumulating pulmonary lesions (i, arrows) are also discovered in the right and left inferior lobe, respectively, suspicious for distant metastases. Stage IVc (cT2N2aM1).
**Fig. 5:** Subglottic LC. CT (a-b). Post-contrast axial images with soft tissue (a) and bone (b) window: small asymmetric mucosal thickening of the subglottic larynx on the right side, representing a tumor (a, arrow); the cricoid cartilage is not sclerotic (b). MRI (c-d). Axial T1-weighted images before (c) and after (d) contrast injection: the tumor is better visualized (heterogeneously enhancing) after contrast administration (d, arrow); the cricoid cartilage shows minor post-contrast signal alteration (d, arrow head), but this finding is not evident on unenhanced scans (c) and is more likely related to inflammation than invasion. Stage cT1.
Conclusion

LC is a **challenging disease**, which requires radiologists to have an **informed and structured knowledge of all imaging aspects** in order to be able to effectively communicate with and be helpful to clinicians.

Personal information

References