Laryngeal Neoplasms

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Abstract

Most laryngeal neoplasms are squamous cell cancers, and the larynx is a relative frequent site of head and neck malignancy. Although most laryngeal cancers are detected clinically, and their superficial extent can be well evaluated by endoscopic examination, imaging is required to evaluate the frequent submucosal spread of these tumors. Accurate staging of laryngeal cancer requires imaging, and the radiological findings affect tumor staging and treatment choice. This chapter reviews the normal anatomy of the larynx, and focuses on the imaging findings in laryngeal squamous cell cancer, both before and after treatment. The prognostic value of imaging-derived parameters is explained. The radiological findings in less common laryngeal tumor types are also reviewed.

1 Introduction

The larynx is one of the most frequent head and neck cancer sites. Nearly all laryngeal malignancies are squamous cell carcinomas. Cigarette smoking and excessive alcohol consumption are well-known risk factors. An important factor in the treatment planning of laryngeal neoplasms is the accuracy of pretherapeutic staging. As most

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laryngeal tumors are mucosal lesions, they often can be seen directly or indirectly, but the limitations of clinical and endoscopic tumor evaluation are well recognized. The clinical and radiological evaluation of laryngeal tumors are complementary; the combination of the obtained information will lead to the most accurate determination of tumor extent. Imaging may be used to monitor tumor response and to detect recurrent or persistent disease as early as possible.

2 Normal Laryngeal Anatomy

Essentially the larynx consists of a supporting skeleton, a mucosal surface, and in between a soft tissue layer containing fat, some ligaments and muscular structures (Figs. 1, 2, 3, and 4).

2.1 Laryngeal Skeleton

The laryngeal skeleton is made up of cartilage and fibrous bands. The foundation of the larynx is the cricoid cartilage. The cricoid cartilage is the only complete cartilaginous ring in the airway. Its horizontal ring-shaped part is known as the arch (arcus), while the higher posterior part is called the lamina. Two paired facets are found at the upper margin of the lamina, allowing articulation with the arytenoid cartilages.

The largest supporting cartilage is the thyroid cartilage, essentially consisting of two wings or laminae. The teardrop-shaped epiglottis extends downward and attaches to the inner side of the thyroid cartilage. Only a small part of the epiglottis extends above the hyoid bone, the suprahyoid or free margin of the epiglottis.

The vocal ligament stretches from the vocal process of the arytenoid to the inner side of the thyroid cartilage; it forms the medial support of the true vocal cord. The ventricular ligament stretches from the upper arytenoid to the thyroid cartilage, forming the medial margin of the false cord. The epiglottis is held in place by the hyoepiglottic ligament, running through the fatty preepiglottic space.

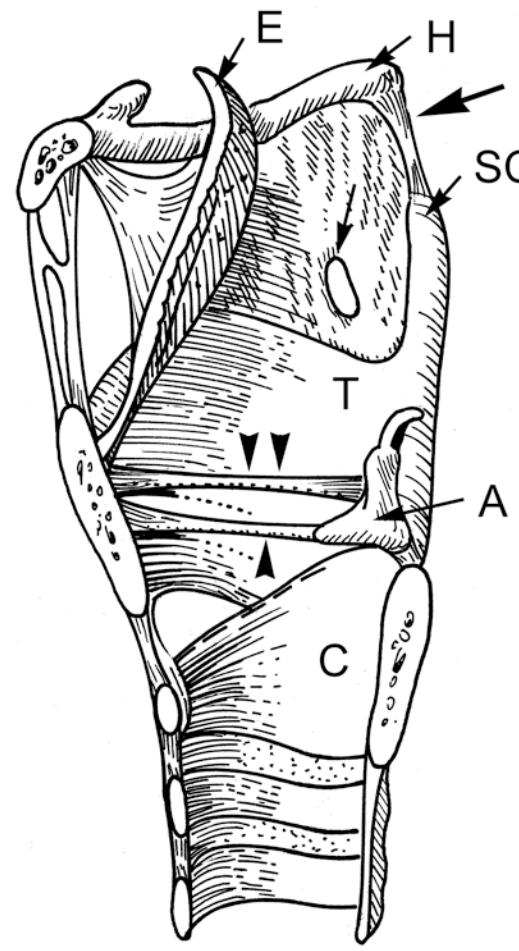

Fig. 1 Lateral diagram of the larynx showing the cartilaginous skeleton (mucosa, intrinsic laryngeal muscles, and paraglottic fat removed). The vocal ligament (single arrowhead) stretches from the vocal process of the arytenoid (A) to the anterior thyroid cartilage. The ventricular ligament (double arrowhead) runs from the upper arytenoid to the anterior thyroid cartilage. *T* thyroid lamina, *SC* superior cornu (of thyroid). The superior cornua are attached to the hyoid by the thyrohyoid ligament (unlabeled thick arrow), which forms the posterior margin of the thyrohyoid membrane. *C* cricoid cartilage, *E* epiglottis, *H* hyoid bone. Note: The small structure at the upper tip of the arytenoid is the corniculate cartilage. It has no clinical significance, but is occasionally seen on CT. The small hole (unlabeled thin arrow) in the thyrohyoid membrane transmits the internal branch of the superior laryngeal nerve that provides sensation to the laryngeal mucosa

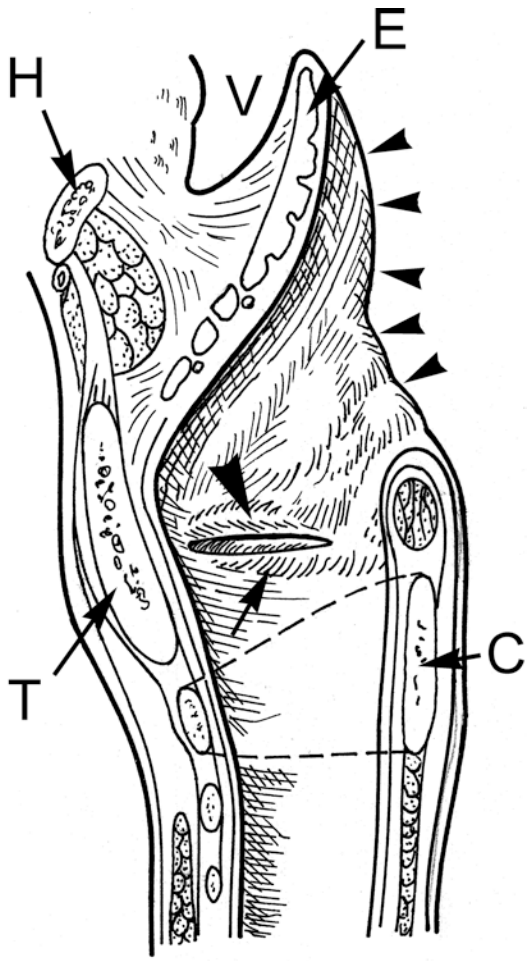

Fig. 2 Lateral diagram of the larynx sectioned sagittally in the midline. The slitlike ventricle separates true vocal cord (unlabeled arrow) and false vocal cord (large arrowhead). *Small arrowheads* aryepiglottic fold, *T* thyroid cartilage, *C* cricoid cartilage (lamina), *dashed line* projection of the arch of the cricoid cartilage, *E* epiglottis, *H* hyoid bone, *V* vallecula

2.2 Mucosal Layer and Deeper Laryngeal Spaces

All these structures are covered by mucosa; the inner larynx is dominated by two prominent parallel bands, the true and false cord, separated by a slitlike opening towards the laryngeal ventricle. The true cord largely consists of a muscle, running parallel and lateral to the vocal ligament, between the arytenoid and thyroid cartilage, hence known as the thyro-arytenoid

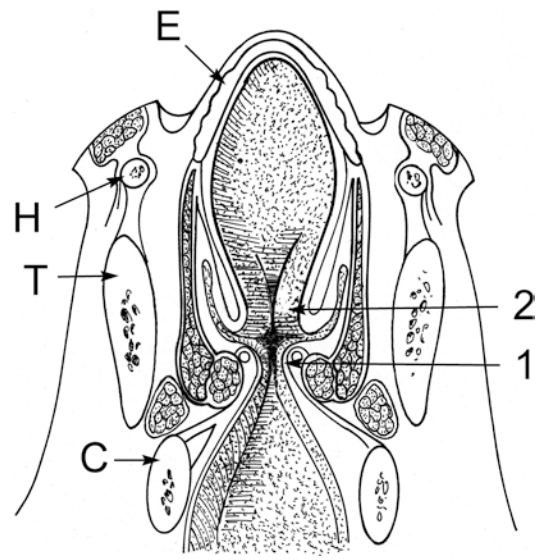

Fig. 3 Coronal diagram of the larynx showing the laryngeal subsites. (1) True vocal cord (TVC) consist mainly of the bellies of the thyroarytenoid muscle. (2) False vocal cord (FVC) consists mainly of fatty tissue. TVC and FVC are separated by the slitlike laryngeal ventricle (sinus of Morgagni), extending superolaterally as the sacculus laryngis or appendix. *E* epiglottis, *H* hyoid bone, *T* thyroid cartilage, *C* cricoid cartilage

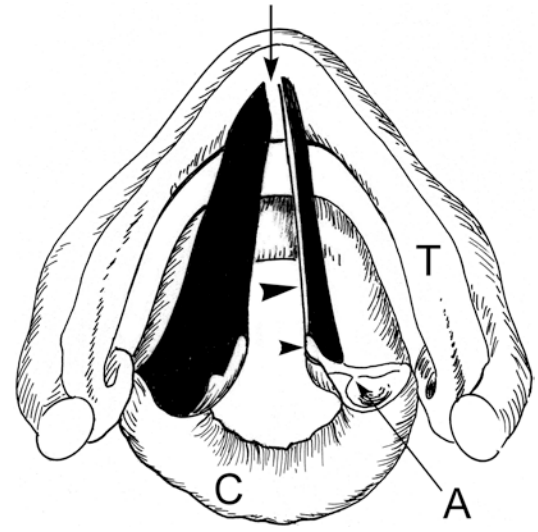

Fig. 4 Inner view of the larynx, seen from above, after removal of most soft tissues. *A* arytenoid cartilage, *C* cricoid lamina, *T* thyroid cartilage. The bulk of the TVC is made up of the thyroarytenoid muscle (in dark) running from the inner aspect of the thyroid lamina to the arytenoid cartilage, paralleling the vocal ligament (large arrowhead). The thyroarytenoid muscle can be separated in two bellies. Only the medial portion (vocalis muscle) is seen on the right. The vocal ligament extends from the vocal process (small arrowhead) to the anterior commissure (unlabeled arrow)

Table 1 Subsites within the larynx (UICC 2017)

Supraglottis
Suprahyoid epiglottis (including tip, lingual, and laryngeal surfaces)
Infrahyoid epiglottis
Aryepiglottic fold, laryngeal aspect
Arytenoid
Ventricular bands (false vocal cords)
Glottis
True vocal cords
Anterior commissure
Posterior commissure
Subglottis

muscle. The false cord largely consists of fat. In between the cords, the ventricle is rising into the laryngeal tissue space between the mucosa and supporting skeleton. The relationship of pathological conditions to these three parallel structures is significant in the evaluation of laryngeal cancer.

Above the false cords, from the arytenoid cartilages, the mucosa reflects upwards towards the epiglottis, forming the aryepiglottic folds.

The part of the larynx at the level of the true vocal cords is called the glottis. The region beneath the undersurface of the true vocal cords until the undersurface of the cricoid cartilage is the subglottis. Above the level of the true vocal cords is the supraglottis. Within these different levels, further subsites are distinguished, important for staging purposes (Table 1).

The bare area between the anterior attachment of the true vocal cords, where no or only minimal soft tissue is present against the cartilage, is known as the anterior commissure. The area between the arytenoids is known as the posterior commissure.

The fat-containing space between the mucosa and the supporting skeleton is variable in size. The part of this deep space, anterior to the epiglottis, is known as the preepiglottic space. This preepiglottic space is continuous with the more lateral submucosal spaces, extending into the aryepiglottic folds and false vocal cords. These lateral spaces are known as the paraglottic spaces. At the level of the glottis, the paraglottic spaces are reduced to a very thin stripe of fat just lateral to the thyro-arytenoidal muscles.

The paraglottic fat tissue is continuous with a thin infraglottic fat plane, bordered by the conus elasticus. The preepiglottic and paraglottic spaces together are sometimes called the paralaryngeal space.

2.3 Normal Radiological Anatomy

The normal radiological anatomy of the larynx is shown in Fig. 5.

The appearance of the laryngeal cartilages can vary considerably, depending on the degree of ossification and the amount of fatty marrow in the ossified medullar space. In children, the CT density of the laryngeal cartilages is similar to soft tissue. The (endochondral) ossification of hyaline cartilage starts early in the third decade of life. A high degree of variation exists between individuals. The thyroid cartilage shows the greatest variability in ossification; its ossification may also occur in an asymmetrical fashion. The cricoid and arytenoids show less pronounced variability in ossification. The epiglottis and vocal process of the arytenoids are composed of yellow fibrocartilage; this type of cartilage usually does not ossify.

3 Squamous Cell Carcinoma

Squamous cell carcinoma, originating from the mucosal lining, is the most common malignant tumor in the larynx. Mucosal abnormalities can be far better evaluated by the clinician than with even sophisticated imaging methods such as CT or MRI. However, these tumors have the tendency to spread submucosally, and this extension into the deeply lying tissue planes may be difficult to evaluate by clinical examination alone.

The clinical criteria used for giving a tumor a particular T-classification are site-dependent; in

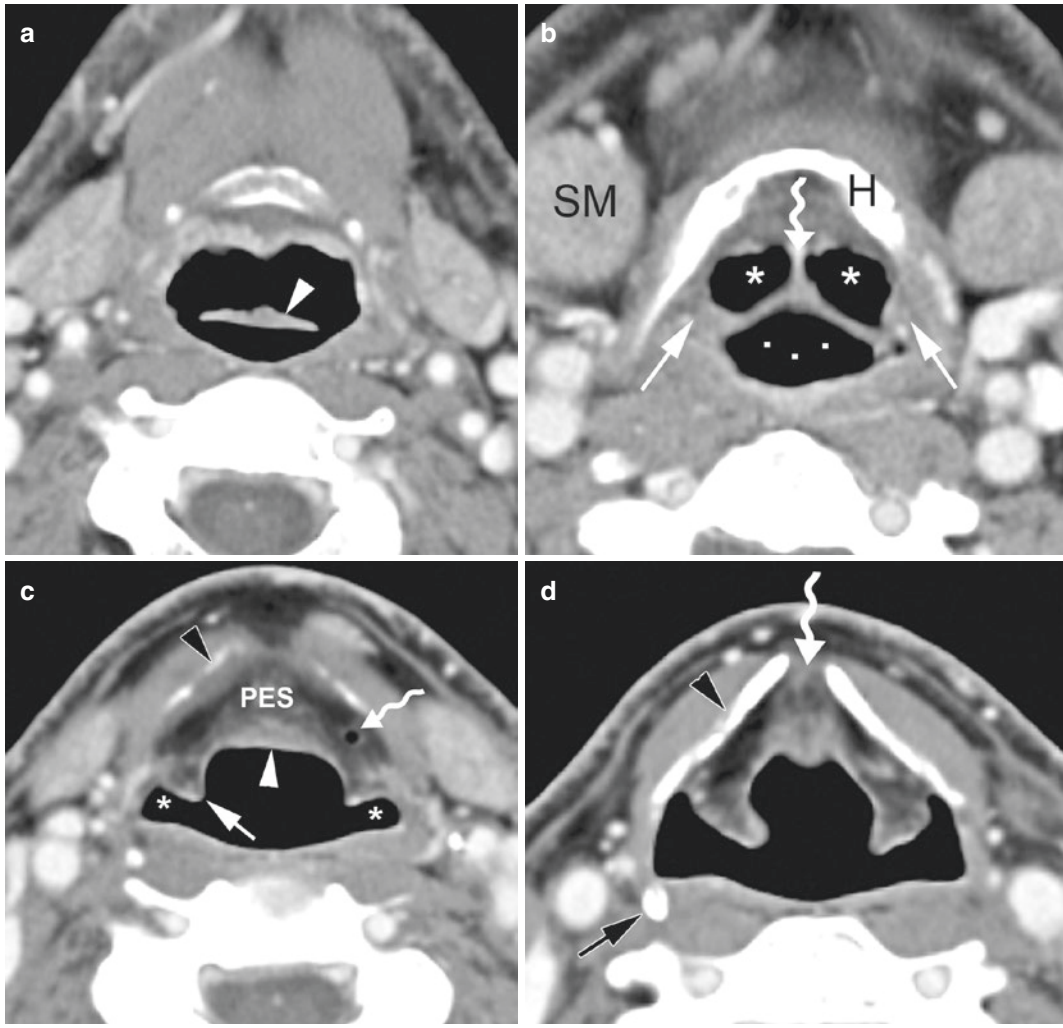

Fig. 5 Axial CT images through normal appearing larynges (different patients), from cranial to caudal, illustrating normal radiological anatomy. (**a**) Level of the free epiglottic margin (arrowhead), at the superior edge of the hyoid bone. (**b**) Level of the hyoid bone (H). The glosso-epiglottic ligament (curved arrow) separates both valleculae (asterisks). The epiglottis separates the oropharyngeal valleculae from the laryngeal vestibule (dots). The pharyngo-epiglottic folds (arrows) correspond to the anterocranial margin of the piriform sinuses. Submandibular salivary gland (SM). (**c**) Level of superior margin of thyroid cartilage (black arrowhead). Epiglottis (white arrowhead), ary-epiglottic fold (arrow), piriform sinuses (asterisks). The fatty space just in front to the epiglottis is the preepiglottic space (PES). The more lateral fatty spaces are called the paraglottic spaces; in the left paraglottic space, the air-containing tip of the laryngeal ventricle is seen (curved arrow). (**d**) Level of thyroid cartilage (black arrowhead). Thyroid notch (curved arrow). Superior thyroid cornu (arrow). (**e**) Level of false vocal cords. Within the fatty paraglottic space, some tissue with higher density can be seen, corresponding to intrinsic laryngeal muscles and the collapsed laryngeal ventricles (white arrow). The thyroid cartilage shows areas of calcification (black arrowheads), ossification (black arrows), and non-calcified cartilage (white arrowheads). (**f**) Level of true vocal cords. Arytenoid cartilage (A, partially ossified); lamina of cricoid cartilage (C). The fatty paraglottic spaces are reduced to a thin fatty line (white arrows) between the thyroid cartilage and vocal muscles. Posteriorly, the paraglottic spaces are continuous with the anterior submucosal fat plane in the retrocricoidal part of the hypopharynx (black arrowhead). Hypopharyngeal mucosa (black arrows), posterior submucosal fat plane in retrocricoidal hypopharynx (white arrowheads), pharyngeal constrictor muscle (curved arrow). (**g**) Level of subglottis. Arch of cricoid cartilage (C). The denser areas correspond to islands of non-ossified cartilage within the otherwise ossified cricoid. Inferior thyroid cornu (black arrowhead). Posterior cricoarytenoid muscle (white arrowhead)

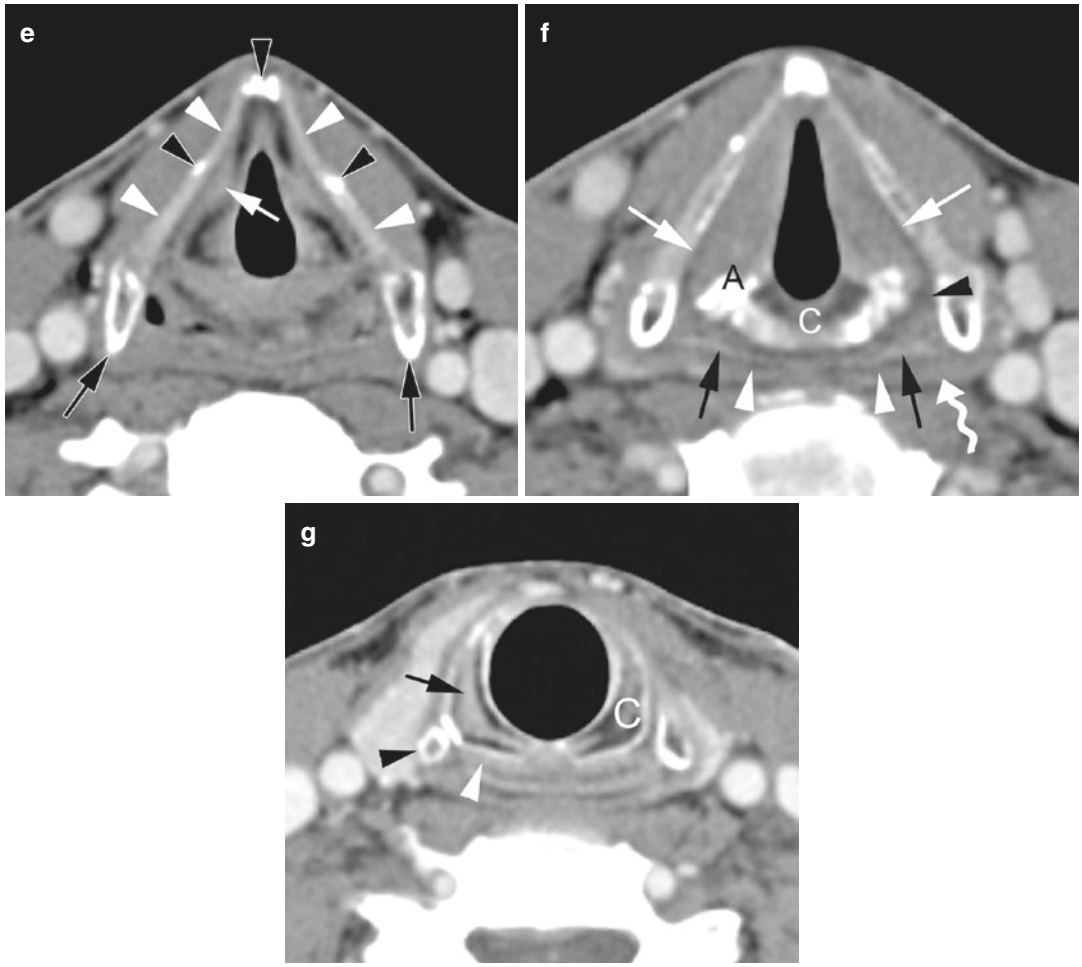

Fig. 5 (continued)

the larynx involvement of different laryngeal subsites and reduced vocal cord mobility are important criteria. The local staging criteria for glottic, supraglottic, and subglottic cancer, as well as the stage grouping, are summarized in Tables 2, 3, 4, and 5. About 65–70% of laryngeal cancers originate at the glottic level, and about 30% at the supraglottic level; laryngeal cancer originating from the subglottic region is rare.

The regional (neck) staging criteria for laryngeal cancer are similar to those for hypopharyngeal cancer and sinonasal cancer.

The validity of any classification is dependent on the diagnostic methods employed. It is recognized that clinical classification of laryngeal can-

Table 2 T-staging of glottic cancer (UICC 2017)

T1	Tumor limited to vocal cord(s) with normal mobility (may involve anterior or posterior commissure)
	T1a: limited to one vocal cord
	T2b: involving both vocal cords
T2	Extension into supra- and/or subglottis, and/or with impaired vocal cord mobility
T3	Vocal cord fixation and/or invasion of paraglottic space, and/or inner cortex of the thyroid cartilage
T4	Extralaryngeal tumor spread
	T4a: tumor invading through the outer cortex of the thyroid cartilage, or tissues beyond the larynx (e.g., trachea, soft tissues of the neck, deep/extrinsic muscles of the tongue,[a] strap muscles, thyroid gland, esophagus)
	T4b: tumor invading prevertebral space, mediastinum, or encasing carotid artery

[a]Genioglossus, hypoglossus, palatoglossus, and styloglossus muscle

Table 3 T-staging of supraglottic cancer (UICC 2017)

T1	Tumor limited to one subsite of supraglottis with normal vocal cord mobility
T2	Tumor invades mucosa of more than one adjacent subsite of supraglottis, glottis or region outside of supraglottis, without fixation of the larynx
T3	Vocal cord fixation or invasion of postcricoid area, preepiglottic and/or paraglottic space, and/or inner cortex of thyroid cartilage
T4	Extralaryngeal tumor spread
	T4a: tumor invading through thyroid cartilage, or tissues beyond the larynx (e.g., trachea, soft tissues of the neck, deep/extrinsic muscles of the tongue,[a] strap muscles, thyroid gland, esophagus)
	T4b: tumor invading prevertebral space, mediastinum, or encasing carotid artery

[a]Genioglossus, hypoglossus, palatoglossus, and styloglossus muscle

Table 4 T-staging of subglottic cancer (UICC 2017)

T1	Tumor limited to subglottis
T2	Tumor extends to vocal cord(s) with normal or impaired mobility
T3	Vocal cord fixation
T4	Extralaryngeal tumor spread
	T4a: tumor invades cricoid or thyroid cartilage, and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of the neck, deep/extrinsic muscles of the tongue,[a] strap muscles, thyroid gland, esophagus)
	T4b: tumor invading prevertebral space, mediastinum, or encasing carotid artery

[a]Genioglossus, hypoglossus, palatoglossus, and styloglossus muscle

Table 5 Stage grouping of laryngeal cancer (UICC 2017)

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1,T2	N1	M0
	T3	N0, N1	M0
Stage IVa	T4a	N0, N1, N2	M0
	T1, T2, T3	N2	M0
Stage IVb	T4b	Any N	M0
	Any T	N3	M0
Stage IVc	Any T	Any N	M1

cer is insufficient when compared with pathologic classification (Pillsbury and Kirchner 1979). As some criteria (such as vocal cord fixation or impaired mobility) are prone to subjective interpretation, difficulties occur to clinically determine the extension of a laryngeal tumor, or to reproduce this assessment (Takes et al. 2010). A marked improvement in accuracy is obtained when the results of CT or MRI are added to the clinical findings (Zbären et al. 1996). Imaging is mainly of benefit in detecting deep soft tissue extension, such as in the preepiglottic space, the laryngeal cartilages, and base of tongue. Findings from imaging studies frequently result in an upclassification of the disease.

3.1 General Imaging Findings

Criteria used for tumor involvement are abnormal contrast enhancement, soft tissue thickening, presence of a bulky mass, infiltration of fatty tissue (even without distortion of surrounding soft tissues), or a combination of these. Any tissue thickening between the airway and the cricoid arch is considered to represent subglottic tumor.

Several studies have compared the CT/MRI findings with the results of whole organ sectioning after total or partial laryngectomy, showing that both techniques are accurate methods to visualize laryngeal pathology (Zbären et al. 1996). These studies correlating whole organ sectioning and imaging have also revealed some pitfalls. Small foci of mucosal tumor may be difficult to detect or may be invisible, and associated inflammatory and edematous changes may cause overestimation of the tumor extent. Distortion of adjacent normal structures may mimic tumoral involvement.

Gross cartilage invasion can be detected with CT. Due to the large variability in the ossification pattern of the laryngeal cartilages, CT often fails to detect early cartilage invasion. Nonossified hyaline cartilage shows more or less the same density values as tumor on CT images. Demonstration of tumor on the extralaryngeal side of the cartilage is a reliable, but late, sign of cartilage invasion. Asymmetrical sclerosis, defined as thickening of the cortical margin and/or increased medullary density, comparing one arytenoid to the other, or one side of the cricoid

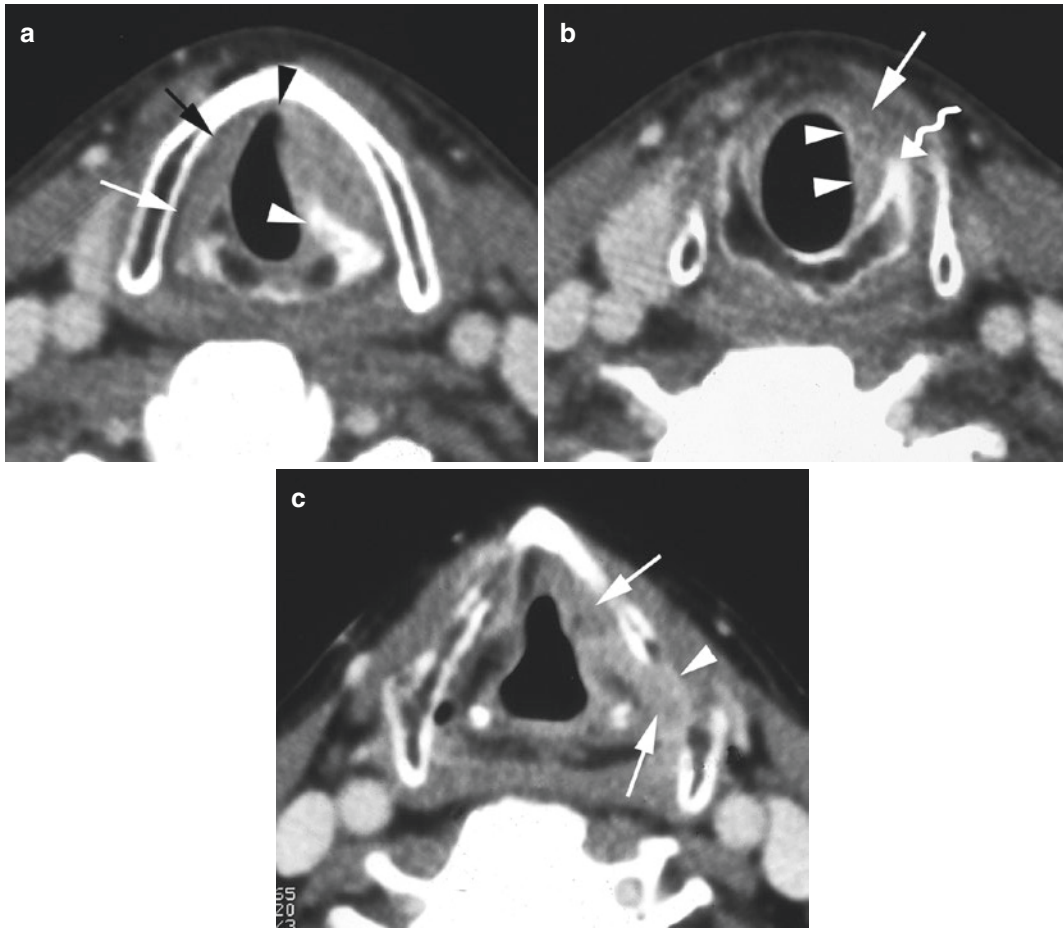

Fig. 6 Contrast-enhanced axial CT images in a patient with a clinically T3 glottic cancer on the left side. (**a**) Level of true vocal cords. The left true vocal cord appears thickened and slightly enhancing. The tumor reaches the anterior commissure (black arrowhead). The left paraglottic space is infiltrated (compared to normal opposite side (arrows)). Marked sclerosis of the left arytenoid (white arrowhead). There appears to be some sclerosis of the left thyroid lamina. (**b**) Level of subglottis. Enhancing soft tissue thickening on left side (arrowheads). Note slight sclerosis cricoid arch on the left (curved arrow). Slight enhancement is seen anteromedially to the subglottis, corresponding to subtle extralaryngeal tumor spread or peritumoral inflammation (arrow). (**c**) Level of false vocal cords. Soft tissue infiltration of the paraglottic space along the thyroid cartilage (arrows). Area of non-ossified thyroid cartilage (arrowhead); as the surrounding ossified thyroid cartilage shows no abnormalities, most likely normal variant. The patient was treated by extended hemilaryngectomy. Pathologic examination confirmed glottic squamous cell carcinoma extending in the subglottic and supraglottic region without evidence of extralaryngeal tumor extension. The arytenoid showed focal neoplastic invasion; in the other cartilages only inflammatory changes were noted

or thyroid cartilage to the other side, is a sensitive but nonspecific finding on CT (Fig. 6) (Becker et al. 1995). Erosion or lysis has been found to be a specific criterion for neoplastic invasion in all cartilages (Fig. 7). Other signs, such as cartilaginous blowout or bowing, a serpiginous contour, or obliteration of the medullary space, are not very reliable for cartilage invasion. The combination of several diagnostic CT criteria for neoplastic invasion of the

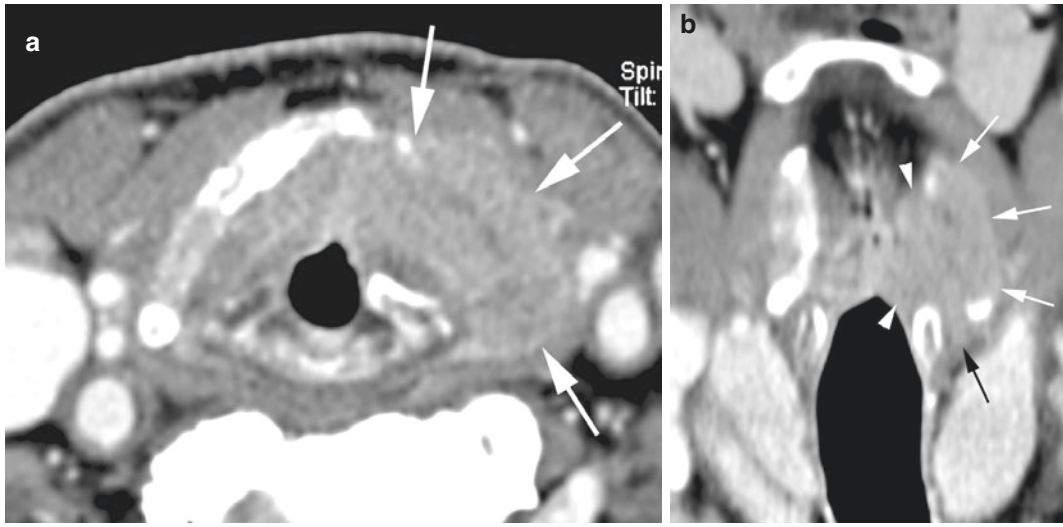

Fig. 7 Contrast-enhanced CT images in a patient with a large left-sided glottic squamous cell carcinoma. (**a**) Axial image. The tumor mass massively invades and destructs the left wing of the thyroid cartilage, growing into the extralaryngeal soft tissues (arrows). (**b**) Coronal reformatting. Involvement of the glottic and supraglottic laryngeal level (arrowheads) is seen, as well as massive destruction of left thyroid cartilage wing and extralaryngeal tumor spread (white arrows). Extralaryngeal extension also occurs through the lateral cricothyroid membrane (black arrow)

laryngeal cartilages seems to constitute a reasonable compromise: when extralaryngeal tumor and erosion or lysis in the thyroid, cricoid, and arytenoid cartilages were combined with sclerosis in the cricoid and arytenoid (but not the thyroid) cartilages, an overall sensitivity of 82%, an overall specificity of 79%, and an overall negative predictive value of 91% were obtained (Becker et al. 1995).

The controversy on which modality should be preferred to image the larynx dealt for a great part with the accuracy to detect cartilage invasion. MRI was recommended to be the best method to determine the status of the cartilages in the presence of a laryngeal tumor (Becker et al. 1997a). MRI is a more sensitive technique than CT to detect cartilage abnormalities. Areas of cartilage abnormality will result in an increase in signal intensity T2-weighted images and contrast-enhanced T1-weighted MRI images. However, due to its high sensitivity for intracartilaginous alterations, MRI causes in a considerable number of cases a false positive result, as distinction between true cartilage invasion and reactive inflammation, edema, fibrosis, or ectopic red bone marrow is not possible (Becker et al. 1995). Peritumoral inflammatory changes without tumoral invasion are common coincidental findings in laryngeal cartilages, especially in the thyroid cartilage. The positive diagnosis of neoplastic invasion of the thyroid cartilage should be made with caution on MRI; it has been suggested that one should rather talk about "abnormal signal intensity in the cartilage" instead of "invasion of cartilage" (Castelijns et al. 1996b). A later study suggests that reactive inflammatory changes and true neoplastic involvement of the laryngeal cartilages can be better distinguished by comparing the T2-weighted and postcontrast T1-weighted cartilage signal intensity with that of the adjacent tumor tissue. If the cartilage signal intensity on these sequences is higher than that of the tumor, this more likely indicates inflammation; the reported specificity of this sign is 82% (Fig. 8) (Becker et al. 2008).

A recent study suggests that dual-energy CT may have additional value compared to conventional

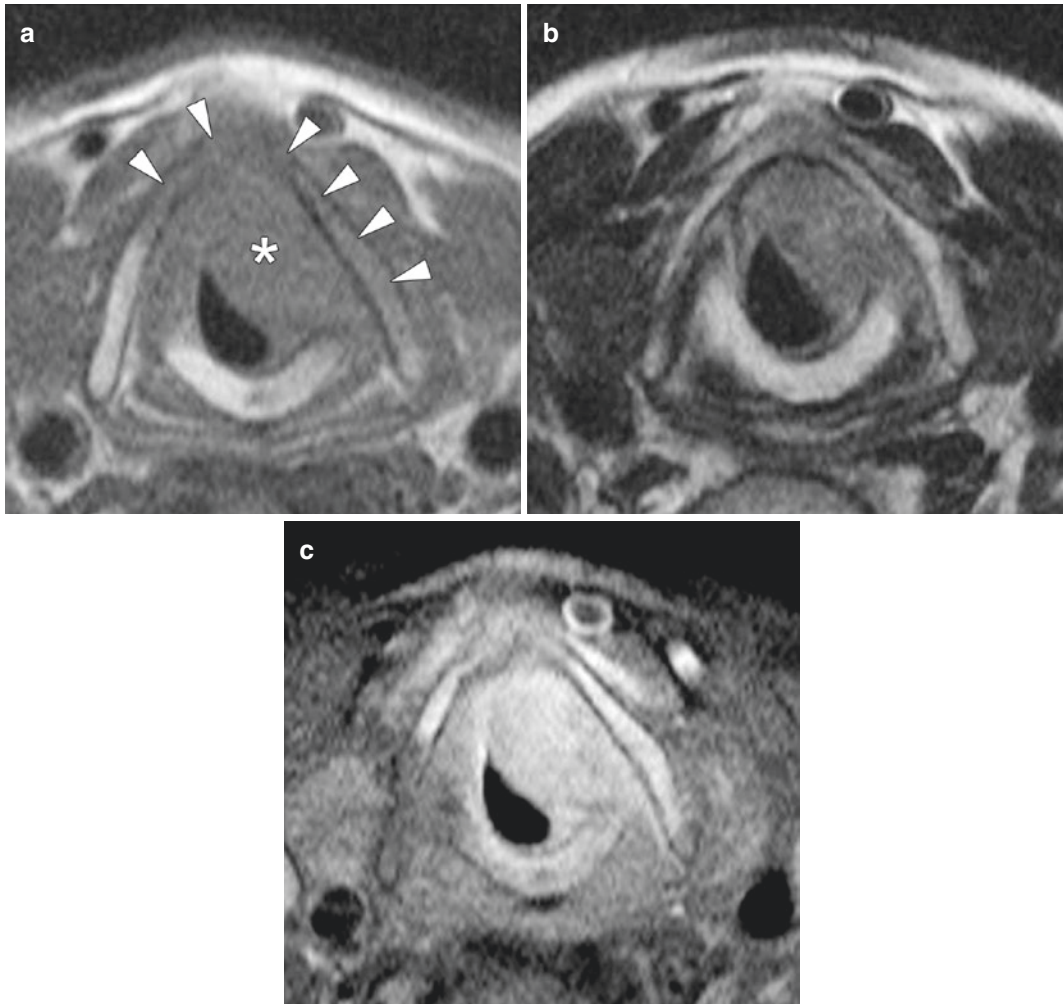

Fig. 8 Axial MR images in a patient suffering transglottic cancer. A large soft tissue mass (asterisk) is seen, centered on the left glottis/subglottis, extending over the midline. On the T1-weighted spin echo image (**a**), signal loss is seen in the adjacent part of the thyroid cartilage (arrowheads). On the T2-weighted image (**b**) the tumor shows a lower signal intensity than the thyroid cartilage. On the gadolinium-enhanced T1-weighted image (**c**) both the tumor and the cartilage show similar enhancement. This cartilage signal behavior suggests cartilaginous inflammation, rather than tumoral invasion. Total laryngectomy was performed; no neoplastic cartilage involvement was present

CT, allowing to distinguish iodine-enhancing cartilaginous tumor invasion from non-ossified cartilage, increasing study specificity (Kuno et al. 2018).

The prognostic importance of minimal cartilage involvement in laryngeal cancer, as seen on imaging studies, remains debated (Ginsberg 2018). In the absence of extralaryngeal tumor spread, cartilage infiltration does not exclude the possibility of organ preservation therapy (see also below).

3.2 Neoplastic Extension Patterns of Laryngeal Cancer

3.2.1 Glottic Cancer

3.2.1.1 Local Tumor Spread

The most common site of involvement is the anterior portion of the vocal cord, usually at the free margin or upper surface. Involvement of the anterior commissure is commonly present and such lesions may extend over the midline in the

contralateral vocal cord. As the amount of normal soft tissue visible at the level of the anterior commissure is somewhat variable (Kallmes and Phillips 1997), radiological detection of subtle tumor spread into this structure by imaging can be challenging; however, usually the anterior commissure can be well evaluated during endoscopic examination.

Lesions limited to the anterior commissure are rarely seen (<2%). Lesions involving the anterior commissure may directly invade the thyroid cartilage; involvement of the anterior subglottic region, lower preepiglottic space, as well as extralaryngeal spread through the cricothyroid ligament may occur (Fig. 9).

When the tumor arises from the posterior side of the vocal cord, posterior extension over the medial facet of the arytenoid cartilage, eventually involving the posterior commissure, may occur (Fig. 10). The redundant mucosa at the level of the posterior commissure should not be misinterpreted as evidence for tumor spread. From the region of the posterior commissure, invasion of the cricoarytenoid joint may occur.

Obstruction of the opening of the ventricular orifice may be the cause of a fluid-filled laryngocele (also called a saccular cyst) (Fig. 10). Most laryngoceles are not caused by an obstructive mass, but an underlying neoplasm has to be excluded, both clinically and radiologically.

Extension into the subglottis may occur along the mucosal surface, or submucosally after penetration of the conus elasticus. As the upper airway wall gradually slopes from the free edge of the true vocal cords towards the inner side of the cricoid ring, the precise border between the undersurface of the true vocal cord and subglottic level is difficult to define on axial cross-sectional imaging. For practical purposes, the glottis is defined as a horizontal slab, 1 cm thick, extending downwards from the superior margin of the true vocal cord. When soft tissue thickening is seen adjacent to a glottic neoplasm along the inner side of the cricoid, the lesion is extending into subglottis. Coronal images, either direct MR images or coronally reformatted CT images, may be helpful to evaluate more subtle subglottic tumor extension.

Lateral spread of the cancer causes infiltration of the vocal ligament and muscle. In a more advanced stage, the paraglottic space is infiltrated and the perichondrium of the thyroid cartilage is reached (Fig. 6). The tumor is diverted by the thyroid cartilage to grow further in the paraglottic

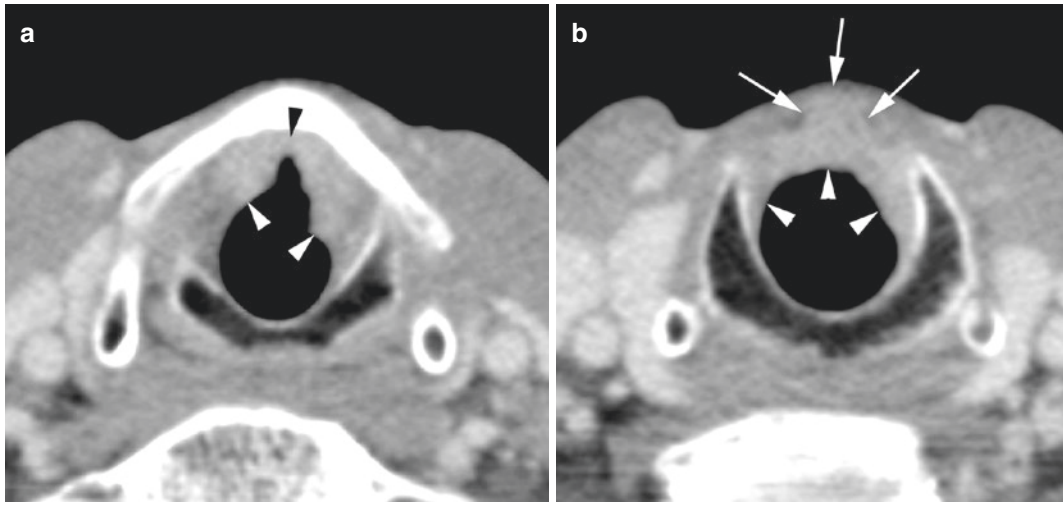

Fig. 9 Axial contrast-enhanced CT images in a patient with squamous cell carcinoma of the anterior glottic region. (**a**) Thickening and slightly increased enhancement of lower surface of true vocal cords (white arrowheads) and anterior commissure (black arrowhead) is seen. (**b**) Soft tissue thickening at the subglottic level (arrowhead); extralaryngeal extension (arrows) occurred, through the cricothyroid membrane

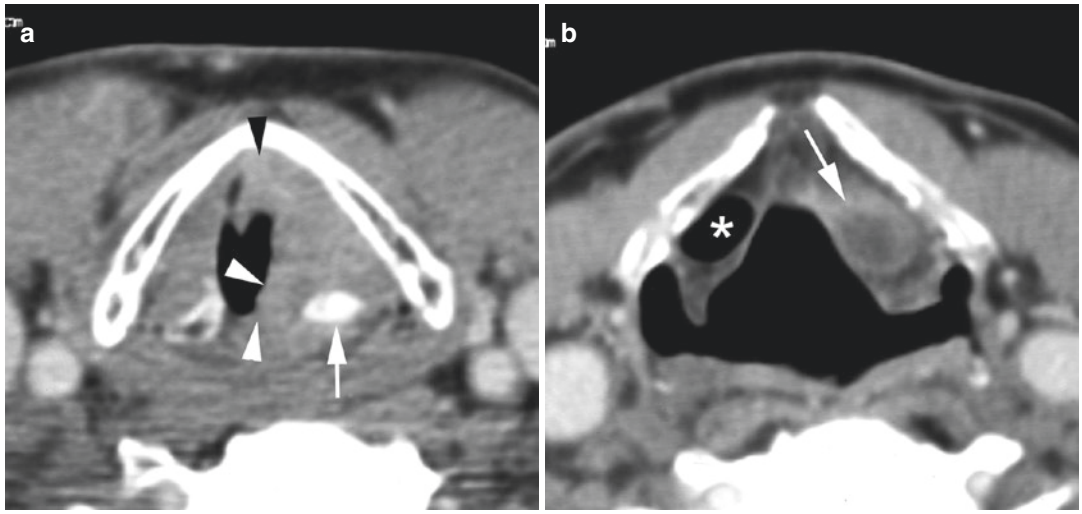

Fig. 10 Axial contrast-enhanced CT images in a patient with a clinically T3 glottic cancer on the left side. (**a**) Level of true vocal cords. The left true vocal cord is markedly thickened. The lesion extends into the anterior commissure (black arrowhead), and grows over the medial facet of the arytenoid into the posterior commissure (white arrowheads). The left paraglottic space is infiltrated. The left arytenoid cartilage appears sclerotic (arrow). (**b**) Level of the aryepiglottic folds. Secondary fluid-filled laryngocele (arrow). Air-filled ventricle in the right paraglottic space (asterisk). The patient was treated by total laryngectomy. Pathologic examination confirmed squamous cell carcinoma, invading the anterior commissure and spreading to the right true vocal cord. The left arytenoid cartilage was invaded by the neoplasm

space, extending cranially into the supraglottic region of the larynx, or caudally into the subglottic region. A glottic cancer growing inferiorly may be diverted by the conus elasticus, laterally and extralaryngeally, to grow through the opening between the thyroid and cricoid cartilage (Fig. 7).

Erosion and eventually breakthrough of the thyroid cartilage with extralaryngeal tumor spread are not commonly seen, being usually late phenomenons in advanced lesions (Figs. 7 and 11). Neoplastic cartilage involvement usually occurs in ossified parts of the laryngeal framework, most frequently at the inferior margin of the thyroid cartilage, upper margin of the cricoid cartilage, or at the level of the anterior commissure (Kurita et al. 1985). These sites correspond to the attachment site of ligaments and membranes to the cartilages.

With extralaryngeal growth, tumor extension into nonfatty soft tissue structures surrounding the larynx may be present. Neoplastic invasion of the thyroid gland mostly occurs in glottic cancer

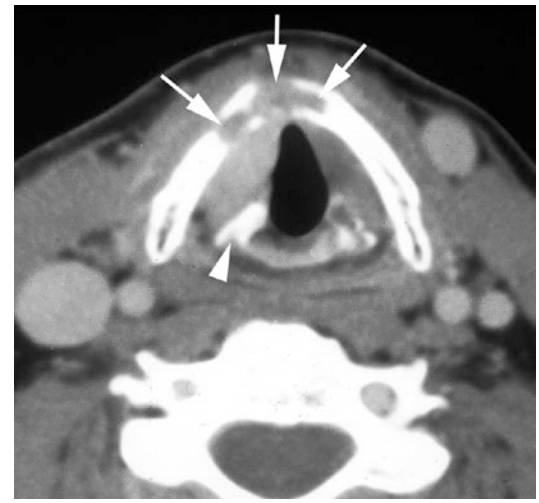

Fig. 11 Axial contrast-enhanced CT image in a patient with a clinically T3 glottic cancer on the right side. Thickening and increased enhancement of the right true vocal cord. Sclerosis of the right arytenoid cartilage (arrowhead) and lysis of the anterior part of the thyroid cartilage, containing enhancing tissue (arrows). The patient was treated by definitive radiotherapy; long-term local tumor control was achieved

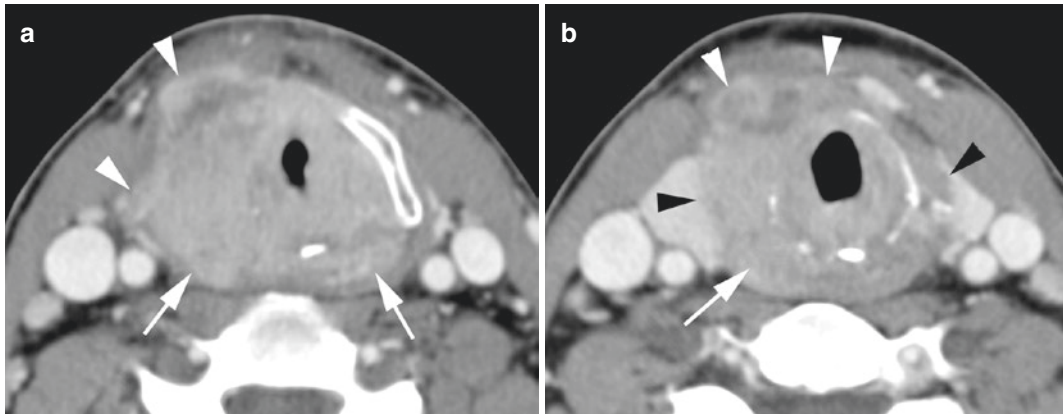

Fig. 12 Axial contrast-enhanced CT images in a patient with extensive glottic squamous cell carcinoma. (**a**) Level of true vocal cords. Circumferential neoplastic involvement of the glottis, with massive destruction of the thyroid cartilage and extralaryngeal spread into the soft tissue anterolateral to the larynx (white arrowheads). Posterior tumor spread into the hypopharynx is at this level visible on both sides (arrows). (**b**) Circumferential involvement of the subglottis, including massive lysis of cricoid cartilage. Extralaryngeal spread into the prelaryngeal soft tissues (white arrowheads), as well as in both lobes of thyroid gland (black arrowheads). Involvement of retrocricoidal part of hypopharynx on the right side (arrow)

showing subglottic extension or invading the thyroid cartilage (Dadas et al. 2001). Invasion of the subcutaneous layers and eventually skin may be seen in anteriorly spreading cancer. Posterior spread to the retrocricoid hypopharynx and eventually esophagus may occur (Fig. 12).

Rarely, a cancer originating at the level of the anterior commissure grows predominantly into the thyroid cartilage, without causing clear tumoral abnormalities at endoscopic examination. In such cases, imaging studies show an irregularly shaped, lytic expansion of the anterior part of the thyroid cartilage (Fig. 13). In the absence of mucosal changes, it may be difficult to prove the presence of cancer by routine biopsy. A deep, surgical biopsy may be required. In selected cases, an image-guided fine needle aspiration or tru-cut biopsy can be an alternative method to obtain representative cytological or histological material (Preda et al. 2010).

A prelaryngeal abscess is another rare presentation of a glottic squamous cell carcinoma invading the anterior part of the thyroid. Presumably the neoplasm, or a combination of the neoplasm and an associated locally aggressive infection, erodes through the thyroid cartilage and offers bacteria a pathway to the prelaryngeal soft tissues (Fig. 14) (Op de beeck et al. 2001). The main differential diagnosis in such cases is infected

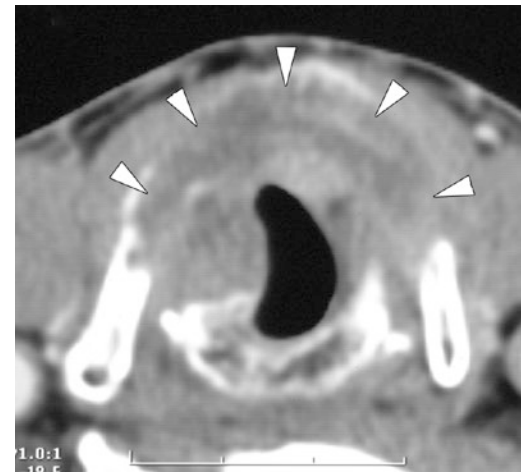

Fig. 13 Patient presenting with history of chronic laryngitis since 2 years. Endoscopic examination shows edema of the anterior commissure, and scarring of the vocal cords. The axial CT image shows thickening and distortion of the laryngeal soft tissues, as well as osteolysis and expansion of a large part of the thyroid cartilage (arrowheads). These findings are very suspect for a malignant lesion. Deep biopsy revealed squamous cell cancer

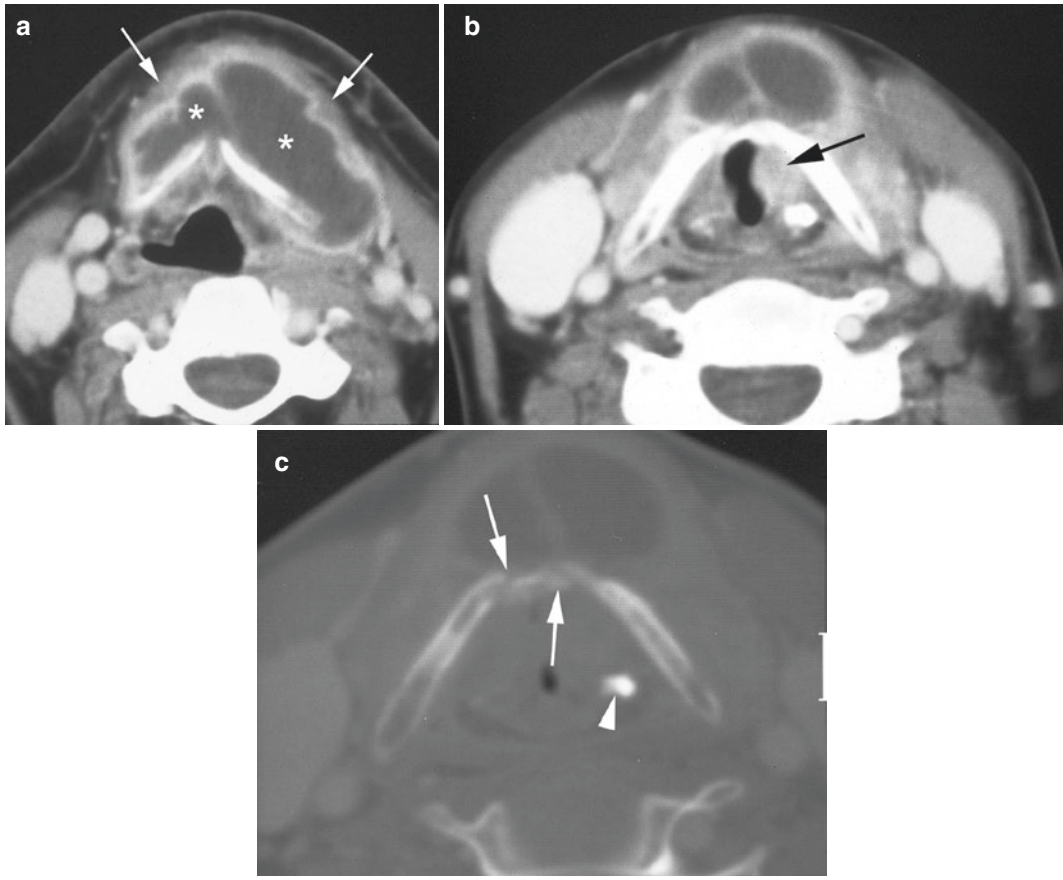

Fig. 14 Axial contrast-enhanced CT images. (**a**) Supraglottic level. Large fluid collection (stars) with rim enhancement is seen in the prelaryngeal soft tissues, displacing the strap muscles (arrows) anteriorly. (**b**) Glottic level. The large fluid collection extends downwards to this level. Thickening and enhancement of the left true vocal cord (arrow). (**c**) Same level as (**b**), bone window. Fragmentation of the anterior part of the thyroid cartilage (arrows). Sclerosis of left arytenoid cartilage (arrowhead)

thyroglossal duct cyst. Infection coexisting with malignancy complicates the clinical picture and may lead to a delayed diagnosis of malignancy. Therefore, careful follow-up after the initial treatment should be initiated if the etiology of the prelaryngeal infection remains obscure, especially in patients with an increased risk of developing head and neck cancer (alcohol and/or tobacco abusers). Repeated imaging studies may be helpful in coming to a correct diagnosis.

Cancer involving the glottic and supraglottic region is also called transglottic cancer. However, the definition of transglottic cancer varies from author to author. Usually, tumors crossing the laryngeal ventricle involving both the false and true vocal cord are called transglottic cancer; most agree that the use of this term also implies that the subglottic region is involved, with fixation of the true vocal cord (Mancuso et al. 1989).

Verrucous carcinoma is a variant of squamous cell carcinoma, occurring in 1–2% of patients with glottic cancer. The histologic diagnosis of this type of cancer is difficult, and must be correlated with the gross appearance of the tumor. Clinically, it appears as an accretion or papillary mass with a warty surface or filiform projections, and it may extend over a large area. It is often

"underdiagnosed" as a benign hyperplasia. Repeated and deep biopsy may be necessary to confirm the diagnosis. On CT and MR studies, verrucous carcinoma is difficult to differentiate from other types of squamous cell carcinoma, although an exophytic soft tissue mass originating from the true vocal cords, displaying an irregular surface and no or minimal submucosal extension, may suggest the diagnosis (Becker et al. 1998).

3.2.1.2 Lymphatic Spread

Usually, glottic cancer only metastasizes to the neck lymph nodes when growing beyond the glottic region. Level III is the most commonly affected level. Neck adenopathies are very uncommonly encountered in small (T1) lesions, but the risk increases to about 8% and 30% in, respectively, T2 and T3 lesions. Imaging studies may detect these adenopathies at an earlier stage than clinical examination alone.

3.2.2 Supraglottic Cancer

Essentially, the radiological signs are similar to those in glottic cancer, but supraglottic cancers often show a larger tumor volume at first presentation.

Clinically visible tumor extension and radiological tumor volume are not always correlated, because of submucosal spread in the preepiglottic space and/or paraglottic space. Laryngeal cartilage invasion is rarely seen in supraglottic cancer.

3.2.2.1 Suprahyoid Epiglottis

Lesions of the suprahyoid epiglottis may grow exophytically. Others invade the epiglottic tip and spread to adjacent structures, such as the valleculae, tongue base, and preepiglottic space; soft tissue ulceration and amputation of the epiglottic tip may be present (Fig. 15).

3.2.2.2 Infrahyoid Epiglottis

As the infrahyoid epiglottis contains tiny perforations, such lesions easily infiltrate the preepiglottic space; from this space, they may spread upwards towards the valleculae and tongue base, or downwards to the epiglottic petiolus. Invasion of the anterior commissure or subglottic spread is rare, but may be seen in advanced cases.

Extension into the aryepiglottic folds and false vocal cords may be seen; extension to the true vocal cords mostly occurs in advanced cases (Fig. 16).

3.2.2.3 Aryepiglottic Fold and Arytenoid

Aryepiglottic fold tumors may present as exophytic lesions, or infiltrative masses invading the paraglottic space. Along the paraglottic space, they may spread towards the false and eventually true vocal cord. Invasion of the cricoarytenoid joint may be seen. Extension towards the piriform sinus commonly occurs, and it may be difficult to distinguish between a primary piriform sinus cancer and supraglottic cancer.

3.2.2.4 False Vocal Cords

Submucosal tumor spread is commonly present in these lesions, with involvement of the paraglottic space at the level of the infrahyoid epiglottis/aryepiglottic fold and/or at the level of the true vocal cord (Fig. 17). Subglottic tumor spread is seen in advanced cases.

3.2.2.5 Lymphatic Spread

As the supraglottic region has a rich network of lymphatic channels, lymphadenopathy is frequently present in supraglottic cancer. At presentation, about 50–60% of patients with supraglottic cancer have clinically manifest lymphadenopathy. The incidence of neck metastasis is about 30% in T1 and T2 lesions, and about 70% in T3 and T4 lesions. Neck level II is most commonly affected, to a lesser extent level III.

3.2.3 Subglottic Cancer

Subglottic cancer is a rare malignant lesion. Apart from squamous cell carcinoma, also adenoid cystic carcinoma is frequently located at this level (Marchiano et al. 2016). By the time of diagnosis, subglottic cancer has usually invaded

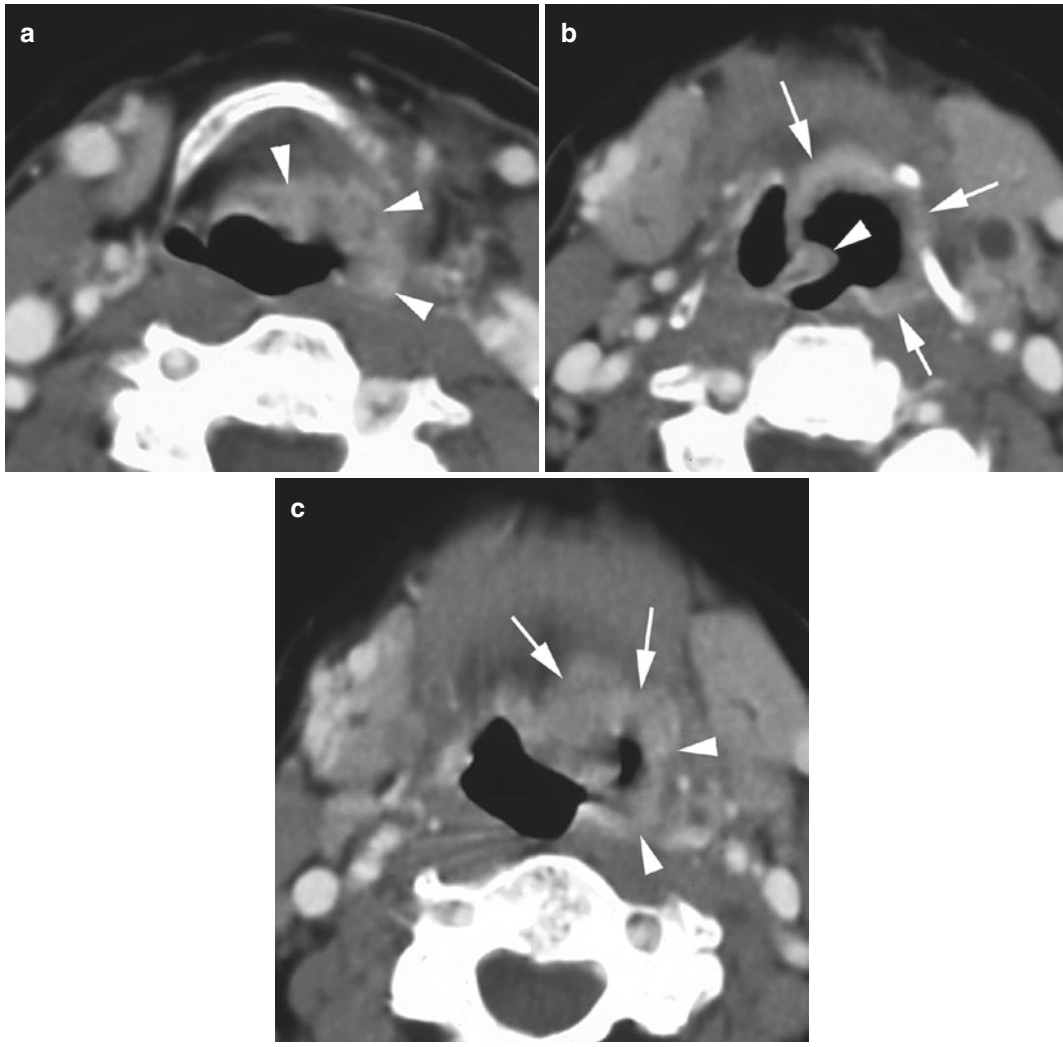

Fig. 15 Contrast-enhanced axial CT images in a patient with a supraglottic squamous cell carcinoma. (**a**) Level of hyoid bone. Thickening and increased enhancement of the epiglottis, as well as infiltration of the preepiglottic and paraglottic space, with extension into the left aryepiglottic fold, is seen. Involvement of the upper part of the left piriform sinus cannot be excluded. (**b**) Level of free epiglottic margin. The epiglottic tip (arrowhead) is amputated on the left side. The margins of the left vallecula are occupied by tumoral tissue, and there is extension into the posterolateral wall of the oropharynx. (**c**) At a slightly higher level, invasion of the tongue base (arrows), as well as posterolateral oropharyngeal wall (arrowheads), is seen. Pathological neck lymph nodes are ipsilaterally present

the true vocal cords, and it may be difficult to distinguish between a cancer originating in the glottis or subglottis. Subglottic cancer is commonly bilateral or even circumferential at presentation. Cricoid cartilage invasion occurs early; extralaryngeal extension, anteriorly through the cricothyroid membrane or inferiorly into the trachea, is also commonly present.

Lymphatic dissemination is seen in about 10% of cases; among the lymph nodes which may become involved are the Delphian node and paratracheal lymph nodes.

Imaging shows a subglottic soft tissue mass (normally no soft tissue is seen between the subglottic air column and the cricoid cartilage), more or less with circumferential extension along the cricoid cartilage. The findings may include cricoid cartilage alterations (sclerosis, lysis), intratracheal soft tissue thickening, and infiltration of the glottic and prelaryngeal soft tissues (Fig. 18).

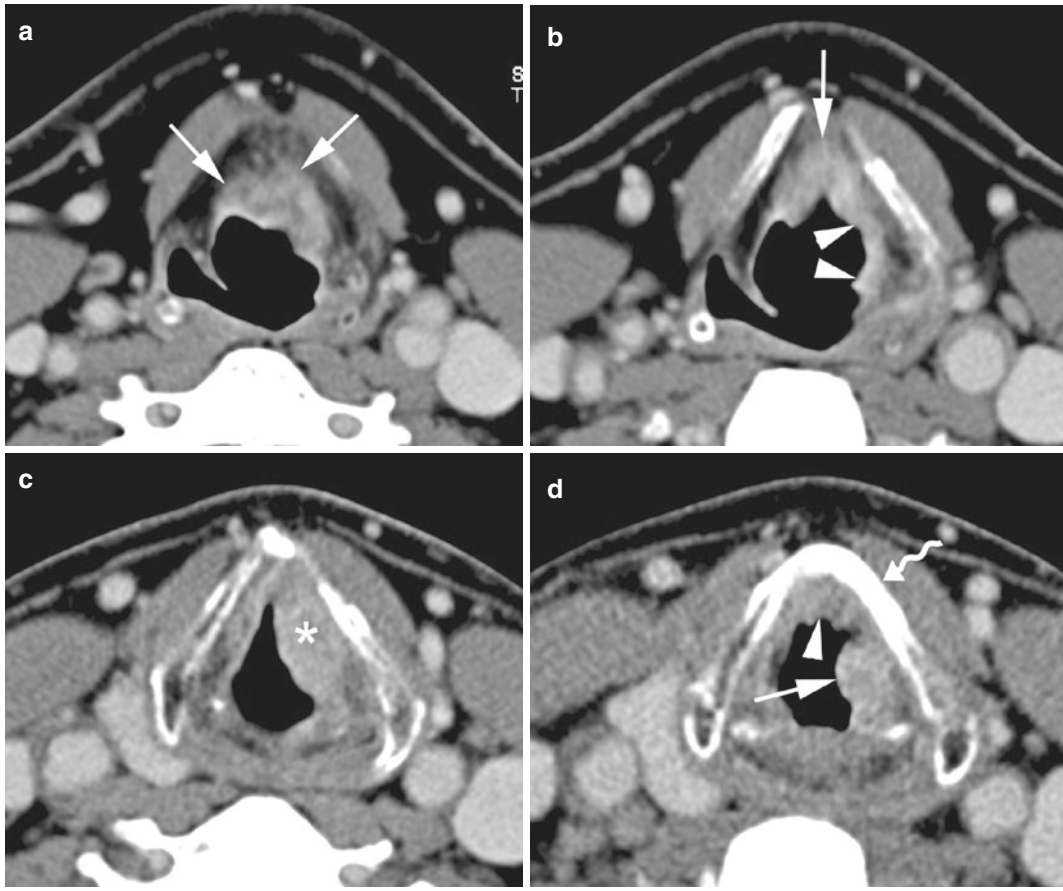

Fig. 16 Contrast-enhanced CT images in a patient with supraglottic squamous cell carcinoma. (**a**) Axial image. Thickening and increased enhancement of the infrahyoid epiglottis, with infiltration of the preepiglottic space (arrows). (**b**) Axial image, more inferiorly, shows downwards tumor extension along the epiglottis and preepiglottic space (arrow), as well as posterolateral growth into the aryepiglottic fold. (**c**) Axial image, more inferiorly, shows tumoral infiltration of the left false vocal cord. (**d**) Axial image, level of ventricle entrance. Tumoral soft tissue thickening just above the level of the anterior commissure (arrowhead), as well as just above the level of the true vocal cord (arrow). Sclerosis of left thyroid cartilage wing (curved arrow). (**e**) Axial image, level of true vocal cords. Apart from sclerosis of left arytenoid cartilage (arrowhead), no abnormalities are seen. (**f**) Coronal image. The tumor mass (arrows) extends throughout the left paraglottic space, abutting and slightly displacing downwards the upper margin of the true vocal cord. Normal right true vocal cord (asterisk), right laryngeal ventricle (arrowhead). (**g**) Sagittal image. Tumoral thickening of the infrahyoid epiglottis (arrowheads), extending down to the level just above the anterior commissure. True vocal cord (arrow)

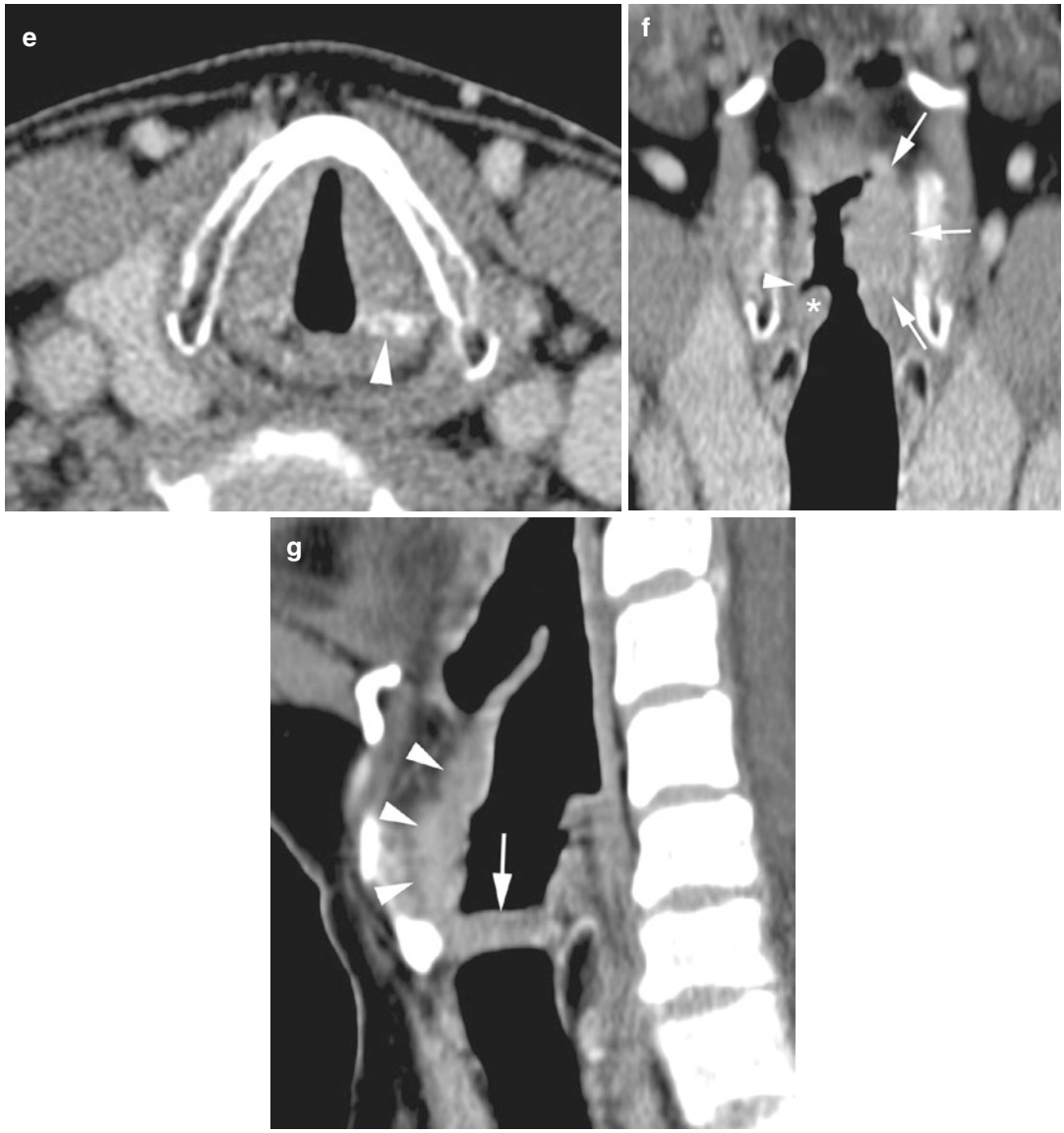

Fig. 16 (continued)

4 Prognostic Factors for Local Outcome of Laryngeal Cancer

4.1 Treatment Options

4.1.1 Glottic Cancer

Carcinoma in situ can often be controlled by stripping the cord or laser treatment; radiotherapy is used after rapid or multiple recurrences of such superficial cancer (Million 1992).

In T1 and T2 tumors radiation treatment is usually preferred, as the voice quality is better than after partial laryngectomy, and fewer complications are encountered. Patients with well-defined lesions suitable for transoral laser excision with a good functional outcome can be treated with either laser or radiotherapy (Mendenhall et al. 2004).

Patients with advanced laryngeal cancer (stage III and IV) are offered concurrent

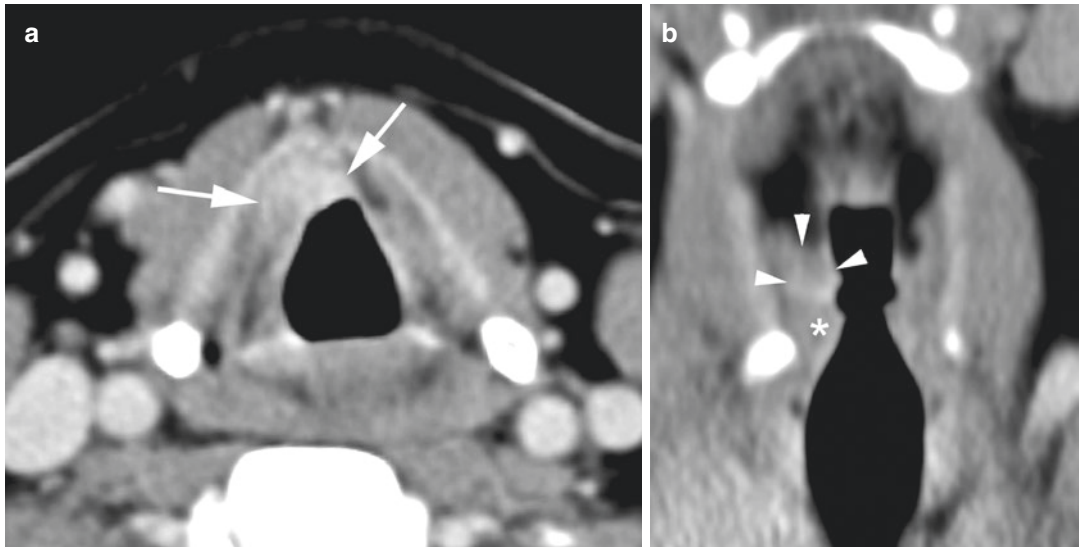

Fig. 17 Patient presenting with hoarseness. Squamous cell carcinoma of the left false vocal cord. (**a**) Axial contrast-enhanced CT image shows small infiltrating lesion (arrows) in the right paraglottic space, at the level of the false vocal cords; the lesion extends into the anterior midline (lower part of preepiglottic space, level of epiglottic petiole). (**b**) Coronal reformatting. Enhancing soft tissue lesion in the right false vocal cord (arrowheads), just above the normal true vocal cord (asterisk)

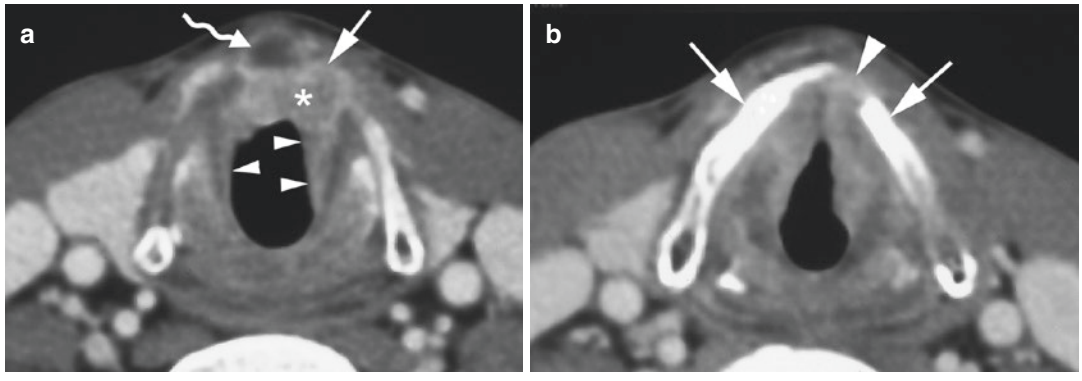

Fig. 18 Patient suffering from subglottic squamous cell carcinoma. Axial contrast-enhanced CT images. (**a**) Anterior subglottic soft tissue thickening (asterisk), with bilateral posterior spread along the subglottic wall (arrowheads). Extralaryngeal spread through the cricothyroid membrane (arrow). Centrally hypodense nodule (curved arrow), presumably corresponding to necrotic prelaryngeal ("Delphian") lymph node. (**b**) Section 9 mm cranial to (**a**). The soft tissue mass extends into the anterior commissure and both true vocal cords. Some sclerosis (arrows) of the thyroid cartilage is visible; the adjacent area of absent cartilage ossification (arrowhead) may correspond to lysis of previously ossified cartilage

chemoradiotherapy, with further surgery reserved for salvage, as treatment option. Platinum-based concomitant chemoradiotherapy improves the likelihood of organ preservation, with locoregional control rates of about 75% (Forastiere et al. 2003, 2013). The drawback of this approach are the acute and late toxic side effects, which are more frequent than after radiotherapy alone.

Treatment complications, such as treatment-induced severe dysphagia, chronic lung aspiration, laryngeal radionecrosis, and others, may occur, reducing the benefit of larynx preservation in a number of patients (Lambert et al. 2010). Although the survival after concurrent radiotherapy is somewhat improved, the probability of developing distant metastases later on is estimated to be around 15–20%, less good than initially expected.

In selected patients with advanced glottic cancer, extended partial laryngectomy may still be feasible. Extended hemilaryngectomy with tracheal autotransplantation allows to remove half of the larynx, including the full height of the cricoid; the resection can be extended to include the apex of the piriform sinus. This allows to perform a partial laryngectomy in patients with arytenoid cartilage fixation and subglottic tumor extension reaching the upper border of the cricoid cartilage (Delaere et al. 2000, 2007; Delaere and Hermans 2003) (see below).

Verrucous carcinoma is not consistently responsive to irradiation; although debated, an anaplastic transformation may follow such a treatment (Ferlito et al. 1998). Therefore, in patients with this type of tumor, surgery is usually recommended as treatment of choice.

4.1.2 Supraglottic Cancer

Patients with a T1, T2, or a "favorable" T3 lesion can be treated with either irradiation or supraglottic laryngectomy (Robbins et al. 1987; Lee et al. 1990; Million 1992). The selection is at the preference of the patient and the physician in charge. A "favorable" T3 tumor is classified as T3 due to preepiglottic space involvement (visible on CT) or limited extension to the medial wall of the piriform sinus or postcricoid area, not due to vocal cord fixation which precludes supraglottic laryngectomy (Million 1992). Supraglottic laryngectomy probably produces a higher initial local control rate but, based on anatomic and coexisting medical considerations, is suitable for a smaller subset of patients and has a higher risk of complications compared with radiotherapy (Hinerman et al. 2002). Patients with pulmonary or cardiac disease are not good candidates for this procedure, as essentially all patients aspirate to some degree after the operation. The proportion of patients suitable for conservative surgery in an unselected population with supraglottic cancer is estimated to be about 15–20%.

Fifty percent or more of patients who undergo a supraglottic laryngectomy will have a combined treatment with radiotherapy (Weems et al. 1987; Lee et al. 1990). Radiotherapy increases the morbidity of supraglottic laryngectomy (Steiniger et al. 1997). If such a combined treatment can be anticipated (clinically positive neck nodes), or the likelihood of conversion of partial to total laryngectomy during surgery is high, radical radiotherapy is preferred over surgery (Weems et al. 1987).

T3 cancers with a fixed vocal cord have lower local control rates after radiotherapy than those with normal mobility (Mendenhall et al. 1996).

Bulky, endophytic T3 lesions and most T4 lesions are considered unfavorable for radiotherapy; often they will show vocal cord fixation and/or airway compromise. Partial (if feasible) or total laryngectomy, with or without postoperative radiotherapy, is an option in these patients, as the local control rates are better for the surgically treated patients than for those treated by radiotherapy alone (Weems et al. 1987). Patients who are medically unfit for total laryngectomy or refuse this procedure are treated with chemoradiotherapy; in T3 and T4 tumors anatomically unsuitable for conservation surgery, local control can be achieved by radiotherapy in 40–63% of patients (Mendenhall et al. 1996).

There is a need for better selection of patients with a T3 lesion, medically suitable for partial laryngectomy, into the favorable group for chemoradiotherapy; in this way a more informed treatment choice can be made. Imaging findings can be helpful to select patients in which radiotherapy has a good chance of success (see below).

Some selected T4 lesions may also be not as unfavorable for (chemo)radiotherapy as is suggested by their staging: minimal cartilage

invasion or minimal neck soft tissue extension may not influence the local outcome when treated by RT (Million 1992; Parsons et al. 1998).

As for glottic cancers, chemotherapy is useful as concurrent therapy in patients with advanced tumors (see above). CT-determined parameters, such as tumor volume, are helpful to select patients likely to benefit from such combined treatment (Mendenhall et al. 2003).

4.2 Impact of Imaging on Treatment Choice and Prognostic Accuracy

Very few studies are available on the impact of imaging on treatment choice and the accuracy of predicting treatment outcome in laryngeal cancer. Such an impact depends on the treatment policy of laryngeal cancer in a given center (Barbera et al. 2001). Charlin et al. (1989) studied the impact of CT on management, working in an institution where at that time all cancers with a small to moderate tumor volume and no sign of deep infiltration were treated by radiotherapy alone, larger cancers and those with signs of deep infiltration by conservation surgery when local extension allowing it, and total laryngectomy with postoperative radiotherapy was performed for tumors with vocal cord fixation, cartilage destruction, and other signs of deep major infiltration. Charlin et al. (1989) observed a change in therapeutic attitude with CT in 10 out of 66 consecutive patients (15.1%). In all 10 patients radiotherapy was thought to be the best treatment after endoscopic evaluation; this was changed to conservative surgery in 7 and total laryngectomy with postoperative irradiation in 3 patients.

In other centers, nearly all laryngeal cancers are treated by radical radiotherapy with or without chemotherapy, and surgery being used as a salvage procedure. In such institutions the impact of laryngeal imaging on initial treatment selection can be anticipated to be of less importance. However, the radiological findings may influence the definition of radiation portals, which require an exact knowledge of the local extension of the tumor, the status of the neck lymph nodes, and the location of metastatic neck adenopathies.

In a retrospective multicenter study, the incorporation of CT information did not improve the ability of the T-classification for predicting local failure or cause-specific survival (Barbera et al. 2001). However, as noted by these authors, the ability of CT to improve the predictive value of the T-classification is constrained by the definitions of the T-classifications, which do not take into account other prognostic information provided by CT.

Archer et al. (1984) have proposed a classification system of laryngeal cancer based on CT findings. This classification used the localization of the tumor mass relative to the arytenoid cartilage, as visible on CT studies. The rationale was that tumors with their plane of maximal size at or below the mid-body of the arytenoid cartilage have a much higher likelihood of cartilage invasion. In more than half of their cases such cartilage invasion was only detectable by microscopic study of the resection specimen. This alternative classification system has not been adopted.

4.3 Use of Imaging Parameters as Prognostic Factors for Local Outcome Independently from the TN-Classification

4.3.1 Predicting Local Outcome After Radiotherapy

4.3.1.1 Tumor Volume and Deep Tissue Infiltration

Success in controlling a tumor by radiotherapy depends on killing all clonogenic cells. The probability of cure depends, among other factors, on the initial number of clonogenic cells. There are indications that the clonogen number increases linearly with tumor volume (Johnson et al. 1995).

Large primary tumor volume is already for a long time known to be a reason for poor local outcome of laryngeal cancer after definitive radiation treatment (Fletcher et al. 1975). Clinical estimation of tumor volume in various advanced

head and neck cancers treated in a multicenter EORTC trial correlated with survival and locoregional control after radiation treatment (Van den Bogaert et al. 1995), but the volume classes defined in this study (<10 cc, 10–30 cc, 30–100 cc, >100 cc) are too rough to be applicable to less advanced head and neck cancers. Overgaard et al. (1986) reported laryngeal tumor diameter (<2 cm, 2–3.9 cm, >4 cm) to be of significant importance to both probability of local control and survival in glottic and supraglottic tumors. However, tumor diameters are a rough and potentially inaccurate estimation of tumor volume due to invisible deep tumor extension (Van den Bogaert et al. 1983).

Three-dimensional tumor visualization, as offered by modern cross-sectional imaging techniques, allows more accurate estimation of the tumor volume. To determine the volume of a particular structure, its borders are traced on consecutive images, either manually or with some (semi-)automated method. The segmented surface on each image is then calculated. The obtained surfaces are then multiplied by the slice interval. The summation of all these obtained volumes represents the total volume of the structure of interest. This technique is called the summation-of-areas technique (Breiman et al. 1982).

Gilbert et al. (1987) have been the first to report the prognostic value of CT-determined laryngeal tumor volume for outcome after definitive radiation therapy. Their study consisted of 37 patients with T2-T4 laryngeal cancer (both from glottic and supraglottic origin). The mean tumor volume for patients failing radiotherapy in their study was 21.8 ml, and for patients primarily controlled this was 8,86 ml; tumor volume significantly predicted disease-free interval and outcome with radiotherapy.

Glottic and supraglottic tumors should be considered separately in such studies, as the anatomic situation, and correlated extension pattern, is very different for glottic versus supraglottic tumors. Freeman et al. (1990) and Mancuso et al. (1999) were able to identify those patients with T1–T4 supraglottic carcinomas who had a higher likelihood of local control based on pretreatment CT volumetric analysis (tumors <6 ml had a probability of 89% of local control, while tumors >6 ml had only a control rate of 40%). In another study, a significant difference in local outcome after radiotherapy was found in supraglottic cancer, with local control rates for tumors with volumes greater than or less than 8 ml being 20% and 70%, respectively (Kraas et al. 2001).

Lee et al. (1993) and Pameijer et al. (1997) could stratify in a similar way patients with T3 glottic carcinoma into groups with different likelihood of local control (tumors of ≤3.5 ml had a local control probability of 85%, while tumors of >3.5 ml had only a local control rate of 22%).

The results of the studies by Hermans et al. (1999a, b) corroborate well these previous findings. Both for glottic and supraglottic cancer, tumor volume was found to be a significant prognostic indicator of local control. In glottic cancer, failure probability analysis showed a clear relation between larger tumor volume and increasing risk for local failure (Fig. 19); a tumor volume of 3.5 ml correlated with a risk for local failure of approximately 50%. From the graph published by Pameijer et al. (1997), an approximately 40% chance of local failure in T3 glottic cancer with a similar tumor volume can be inferred. Also for supraglottic cancer, Hermans et al. (1999a) found a significant relation between tumor volume and risk for local failure (Fig. 20). Compared to glottic cancer, larger supraglottic tumor volumes were found for similar local control rates; similar results can be inferred from other publications (Mancuso et al. 1999). The reason for this different critical tumor volume between glottic and supraglottic cancer is not clear; it might be related to a different local environment in the glottic and supraglottic region, but also (and maybe predominantly) to the more exophytic growth pattern exhibited by supraglottic tumors.

However, tumor volume was not found to be an independent predictor of local outcome when a multivariate analysis was performed. In glottic carcinoma, involvement of the paraglottic space at the level of the true vocal cord and involvement of the preepiglottic space were found to be independent predictors of local outcome (Hermans et al. 1999b). Deep involvement of the paraglottic space at the glottic level, as seen on imaging

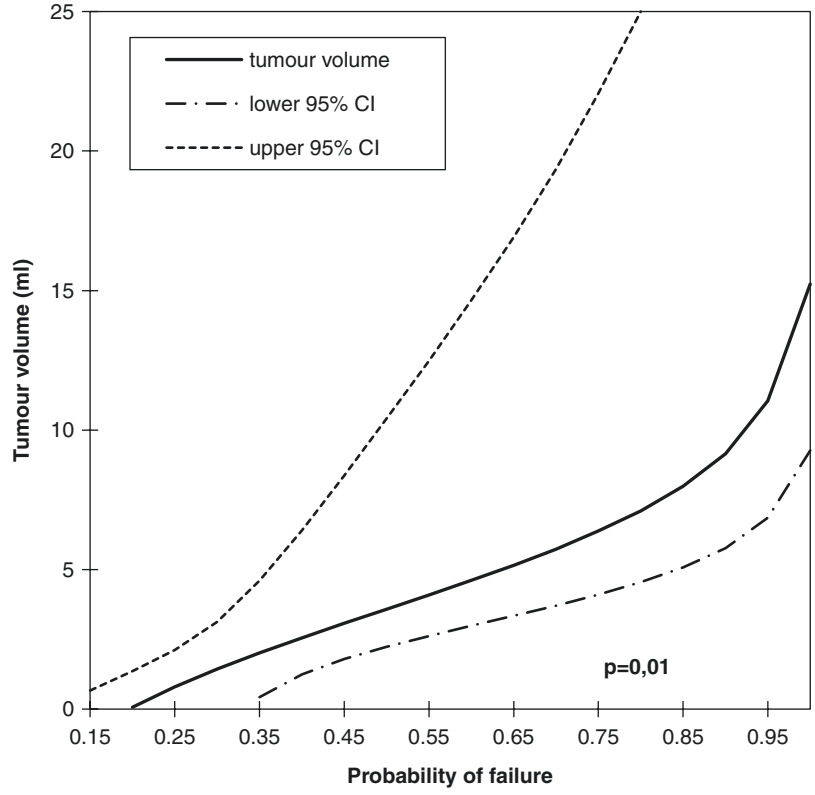

Fig. 19 Glottic cancer: probability of local failure after definitive radiation therapy versus CT-determined primary tumor volume. Local failure rate is significantly higher with larger primary tumor volume. The 95% confidence intervals for tumor volume are indicated. (From Hermans et al. (1999b) with permission)

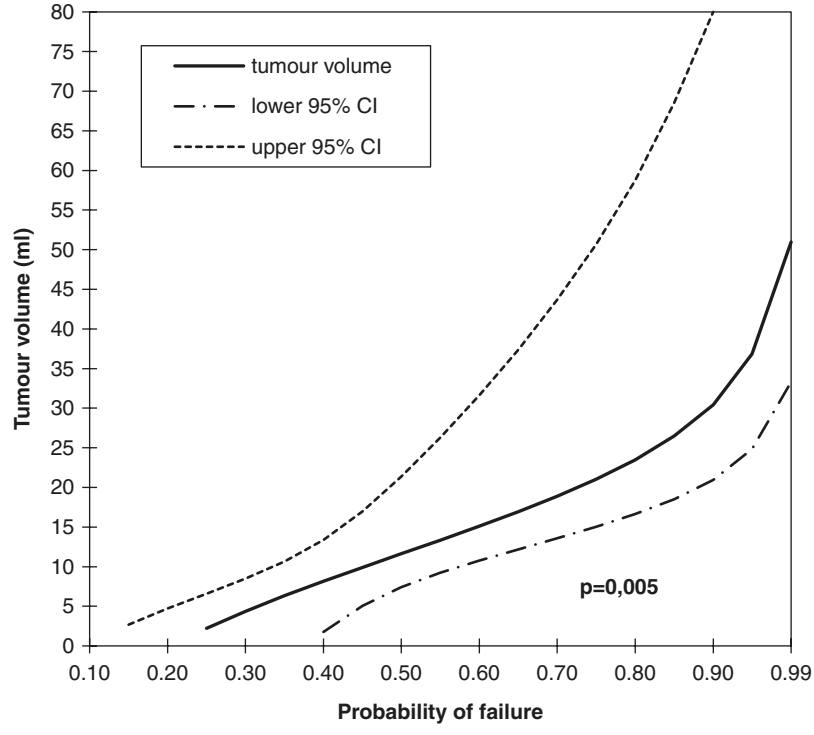

Fig. 20 Supraglottic cancer: probability of local failure after definitive radiation therapy versus CT-determined primary tumor volume. As for glottic cancer, local failure rate is significantly higher with larger primary tumor volume. The 95% confidence intervals for tumor volume are indicated. (From Hermans et al. (1999a) with permission)

studies, is also called the "adjacent sign." This sign was found to be the only independent predictor of local outcome and survival in a series of 130 patients suffering T1–T2 glottic cancer (Murakami et al. 2005). In a study where MRI was used as imaging method, intermediate signal in the thyroid cartilage on a T2-weighted sequence and hypopharyngeal extension were found as independent predictors of local control (Ljumanovic et al. 2007). However, these authors did not include involvement of the paraglottic space in their analysis; as mentioned below, cartilage signal alterations can be regarded as an indirect parameter reflecting tumor spread in the deep tissues. An association between tumor volume and thyroid cartilage penetration was demonstrated in a study on laryngectomy specimens (Kats et al. 2013).

In supraglottic carcinoma, involvement of the preepiglottic space and subglottic extension were the strongest independent predictors of local control (Hermans et al. 1999a). Also in a study using MRI as imaging tool, preepiglottic space involvement as well as abnormal signal intensities in the thyroid cartilage adjacent to the anterior commissure and /or cricoid cartilage were the independent predictors of local control (Ljumanovic et al. 2004). Again, these cartilage abnormalities can be regarded as reflecting extensive invasion of the deep laryngeal tissues (see below).

Tumor volume and degree of involvement of the laryngeal deep tissues are correlated to some extent. However, these descriptive CT parameters may also reflect a more aggressive tumoral behavior, which could explain their stronger association with local recurrence. Fletcher and Hamberger (1974) stated that the preepiglottic space is poorly vascularized; they suggested that the anoxic compartment of tumors invading this space must be significant, and thus relatively radioresistant.

Imaging-determined tumor volume was also found to predict the local outcome in patients suffering advanced head and neck cancer, including laryngeal cancer, when treated by chemoradiotherapy (Hoebers et al. 2008; Shiao et al. 2017). In another study, including patients with T3-laryngeal tumors, not tumor volume but deep tumor extension was found to independently predict local outcome (Kamal et al. 2018).

4.3.1.2 Cartilage Involvement

Laryngeal cartilage invasion is often considered to predict a low probability of radiation therapy alone to control the primary tumor site, and to indicate an increased risk of late complications, such as severe edema or necrosis (Lloyd et al. 1981; Castelijns et al. 1990).

Before the era of computer-assisted cross-sectional imaging only gross cartilage destruction, usually occurring in large volume laryngeal tumors, could be detected clinically or by conventional radiography. More limited laryngeal cartilage invasion can be detected with modern cross-sectional imaging methods (Becker et al. 1995). Earlier studies described an association between CT-depicted cartilage involvement in laryngeal carcinoma and poor outcome after radiation therapy (Silverman 1985; Isaacs et al. 1988). However, according to others involvement of laryngeal cartilage is not necessarily associated with a reduced success rate of radiation therapy (Million 1989). More recent studies correlating laryngeal cartilage abnormalities, detected on CT, with local outcome after RT seem to corroborate this last point of view.

The cartilage most often showing abnormalities is the arytenoid cartilage; usually this cartilage appears sclerotic. An abnormal appearance of this cartilage was not found to be associated with poorer local control, and may be unimportant in terms of prognosis (Tart et al. 1994; Hermans et al. 1999b). The majority of sclerotic arytenoid cartilages do not contain tumor within ossified bone marrow, which can help to explain why radiation therapy is efficient in a large percentage of patients with isolated arytenoid sclerosis on CT (Becker et al. 1997a, b).

Pameijer et al. (1997) found a lower probability of local control in patients with T3 glottic carcinoma, when both arytenoid and cricoid showed sclerosis. These authors assume that if both the arytenoid and cricoid cartilage are sclerotic, the probability of microscopic cartilage invasion will increase. Hermans et al. (1999a) did also find that cricoid cartilage abnormalities in glottic

carcinoma yielded a statistically significant lower control rate. Ten out of the 13 patients with sclerosis of the cricoid in this study had also sclerosis of the arytenoid cartilage, corresponding with the "double sclerosis" situation described by Pameijer et al. (1997). However, the multivariate analysis performed in the study by Hermans et al. (1999b) showed that an abnormal appearing cricoid cartilage is not an independent predictor of poor local control in glottic carcinoma: it lost significance when paraglottic and preepiglottic space involvement were entered in the statistical model. Even relatively subtle cartilage abnormalities, as detected in this study population (sclerosis of the cartilage being the most frequent alteration seen), seem to be correlated with deep tumor extension. More destructive cartilage changes are associated with very bulky tumors, which are not selected for radiation therapy.

There are only few data available on the correlation between thyroid cartilage abnormalities as seen on CT and local outcome of glottic cancer after definitive radiation therapy. Some studies explicitly excluded patients showing evidence of thyroid cartilage involvement (Mukherji et al. 1995; Pameijer et al. 1997). In the study by Hermans et al. (1999b), where tumor visible on both sides of the cartilage and lysis of ossified cartilage were used as signs of thyroid cartilage invasion, only a limited number of patients with glottic carcinoma had an abnormal appearance of this cartilage. No evidence was found that thyroidal cartilage involvement on itself as seen on CT is associated with a poorer local outcome after definitive radiation therapy but, as said, the number of patients in this study with signs of neoplastic involvement of this cartilage was small.

In a study including patients suffering laryngeal cancer, regardless of the site of origin and tumor stage, all treated with primary radiation therapy (with or without chemotherapy), cartilage sclerosis as seen on CT was not associated with a different outcome compared to patients without such cartilage sclerosis (Moubayed et al. 2012).

On MRI, cartilage involvement in patients with small sized tumors (under 5 cc) is not correlated with tumor recurrence; abnormal MR signal pattern in cartilage combined with large tumor volume (above 5 cc) worsens the prognosis significantly (Castelijns et al. 1996a). Consequently abnormal MR signal pattern in laryngeal cartilage should not automatically imply laryngectomy, especially in lesions with smaller volumes. It is incorrect to postulate that radiotherapy cannot cure a substantial number of lesions with cartilage involvement on MRI. Castelijns et al. agree with Million (1989) that minimal cartilage involvement in patients with low staged tumors does not imply a bad prognosis (Castelijns et al. 1995, 1996b). Similar to CT, the presence of cartilage abnormalities on MRI studies may be just reflecting a large tumor volume and deep tumor spread, and as such being only indirectly correlated with local outcome after radiotherapy (Ljumanovic et al. 2004, 2007; Kats et al. 2013).

Recent experience shows that organ preservation after chemoradiotherapy is possible in advanced laryngeal cancer invading the cartilage, or even spreading through the cartilage, as visible on imaging studies (Knab et al. 2008; Worden et al. 2009; Wagner et al. 2012). However, the use of organ preservation as end point in such studies may be questioned; in patients with pretreatment gross cartilage destruction, a poor functional outcome may be expected, because of breakdown of a significant part of the larynx during tumor regression (Wolf 2010). As discussed above, quantification of tumor bulk may be a more reliable way to predict success of therapy.

4.3.1.3 Imaging of the Tumoral Micro-Environment

Multiple factors determine the resistance of tumors against radiation treatment and chemotherapy. Tumors may show an intrinsic, genetically determined inherent resistance. However, extrinsic physiological (environmental) factors are also important. Most critical is the presence of less or inadequate and heterogeneous vascular networks leading to chronic "diffusion-limited" tumor hypoxia.

There is strong evidence that for some human tumors treatment may fail due to the presence of hypoxia (Overgaard and Horsman 1996).

Identification and quantification of tumor hypoxia is useful as predictor of outcome, but also to select patients for concomitant radiosensitizing therapy to overcome the hypoxia effect. Treatments such as hyperbaric oxygen or carbogen (95–98% O_2 with 2–5% CO_2) breathing during RT have been extensively investigated and initiated in clinics (Kaanders et al. 2002). The adequate appreciation of tumor hypoxia may also lead to the efficient use of hypoxia-directed treatments such as bioreductive drugs or gene therapy.

Until now one has to rely on invasive methods, e.g., biopsy-based immunohistochemistry techniques, or the use of Eppendorf oxygen-sensitive electrodes to screen tumors for hypoxia. However, oxygen-sensitive needle electrodes can only to a certain extent be used, as some primary tumors (such as laryngeal cancers) are deeply seated and difficult to reach.

There is a clear need for noninvasive methods to investigate the tumoral micro-environment. Nuclear imaging methods (such as PET imaging) may provide important information on tumor physiology. There is evidence that CT and MR studies, classically used to demonstrate the anatomic position and extent of tumors, are able to provide additional, biological information (Rijpkema et al. 2001, 2002; Hermans et al. 2003; Bisdas et al. 2010).

4.3.2 Predicting Local Outcome After Surgery

One study addressed the correlation between volume of supraglottic cancer, as assessed on imaging studies, and outcome after surgical therapy. This study examined a small population with few local recurrences; patients with a tumor volume over 16 ml were found to have a significantly worse local outcome than those with smaller volumes (Mukherji et al. 2000). The threshold tumor volume in this surgical series is greater than threshold tumor volumes reported for supraglottic cancer treated by radiotherapy (see above). This can be expected as during laryngectomy the tumor is resected *en bloc*. The endolaryngeal soft tissues of the larynx are contained within a cartilaginous framework; the primary tumor should therefore be completely contained within the resected specimen in a successfully performed laryngectomy. Large tumors are more likely invading the laryngeal framework and grow extralaryngeally (Mukherji et al. 2000).

It is often suggested that cartilage involvement precludes voice-sparing partial laryngectomy (Tart et al. 1994; Becker et al. 1995; Castelijns et al. 1996b). However, one study indicated that cartilage alterations, as seen on preoperative CT, are not correlated with the local outcome of patients treated by a speech-preserving surgical technique: no increased local failure rate was observed in the patients with cartilage alterations (1 of 11) over those without cartilage abnormalities (1 of 5) (Thoeny et al. 2005). The used surgical technique in this study (extended hemilaryngectomy with tracheal autotransplantation) allows resection of the hemilarynx, including half of the cricoid cartilage. Therefore, areas of possible neoplastic cartilage involvement are very likely to be included in the resection specimen. The inability of other speech-preserving surgical techniques to adequately resect areas of laryngeal framework invasion may falsely lead to the belief that cartilage involvement, in itself, is a contraindication for partial laryngectomy (Thoeny et al. 2005).

4.3.3 Towards Risk Profiles Incorporating Imaging Findings

As staging procedure, CT and MRI have an important function in corroborating clinical findings and ruling out more extensive disease. Accurate staging is critical in decision-making in oncology (Barbera et al. 2001). However, to what extent CT or MRI influence treatment decisions in laryngeal cancer is currently not very clear, and likely varies from institute to institute. This influence depends on the conducted treatment policy, more precisely on the relative role of radiotherapy and surgery as primary treatment modality in more advanced laryngeal cancer.

The parameters defined in the T-classification are mainly based on clinical examination; the addition of modern imaging methods in staging

laryngeal cancer may change the prognostic information of the T-classification itself, by causing stage migration (Piccirillo and Lacy 2000; Champion and Piccirillo 2004). Furthermore, imaging-derived parameters such as tumor volume and depth of invasion in the deep tissues are stronger related to local outcome than the T-categories.

Pure morphologic criteria cannot explain entirely the biologic behavior of a tumor and its response to treatment. Ongoing research focuses on the evaluation with radiological methods of tumor microvascularization, perfusion and oxygenation, factors known to be of important prognostic value.

New classification systems should be conceived, incorporating not only morphologic tumor extent as within the present TNM system, but also including other variables with independent prognostic significance (Takes et al. 2010).

5 Posttreatment Imaging in Laryngeal Cancer

5.1 Expected Findings After Treatment

After treatment of a head and neck cancer, a number of tissue changes become visible on CT and MR images of the neck. These expected alterations should be known, so that they are not misinterpreted as evidence of persistent or recurrent tumor.

Imaging may be used to monitor tumor response and to try to detect recurrent or persistent disease before it becomes clinically evident, possibly with a better chance for successful salvage.

Treatment complications, such as soft tissue or cartilage/bone necrosis, are less frequent than tumor recurrences, but these conditions may be clinically sometimes difficult to distinguish. Although definitive distinction between necrosis and recurrent tumor may also radiologically be difficult, imaging findings may be helpful in guiding further patient management (Hermans 2004).

5.1.1 Expected Tissue Changes After Radiotherapy

Within the first 2 weeks after radiotherapy, there is an acute inflammatory reaction within the deep tissues. Increased permeability, due to detachment of the lining endothelial cells within small blood and lymphatic vessels, results in interstitial edema. After this initial period of a few weeks, there is progressive thickening of the connective tissue. Endothelial proliferation is also seen, eventually resulting in complete obstruction of the vessels. The reduction in venous and lymphatic drainage results in further accumulation of interstitial fluid. Then the fibrosis becomes progressively more advanced, but the interstitial edema may be reduced by formation of collateral capillary and lymphatic channels.The changes visible on posttreatment CT and MR images depend on the radiation dose and rate, the irradiated tissue volume, and the time elapsed since the end of radiation therapy (Mukherji et al. 1994a; Nömayr et al. 2001). Changes which may be seen include (Fig. 21):

- Thickening of the skin and platysma muscle.
- Reticulation of the subcutaneous fat and the deep tissue fat layers.
- Edema in the retropharyngeal space.
- Increased enhancement of the major salivary glands, followed by size reduction of these glands: postirradiation sialadenitis.
- Atrophy of lymphatic tissue, in both the lymph nodes and Waldeyer's ring.
- Thickening and increased enhancement of the pharyngeal walls.
- Thickening of the laryngeal structures, with increased density of the fat in the preepiglottic and paraglottic spaces.

These tissue changes are most pronounced during the first few months after the end of radiation therapy, and diminish or even resolve with time. It is important to note that the expected tissue changes after radiation therapy appear symmetrical, unless the neck was irradiated using asymmetric radiation portals.

The laryngeal cartilages do not show changes after irradiation. Reduction in the degree of cartilage sclerosis in the neighborhood of the tumor

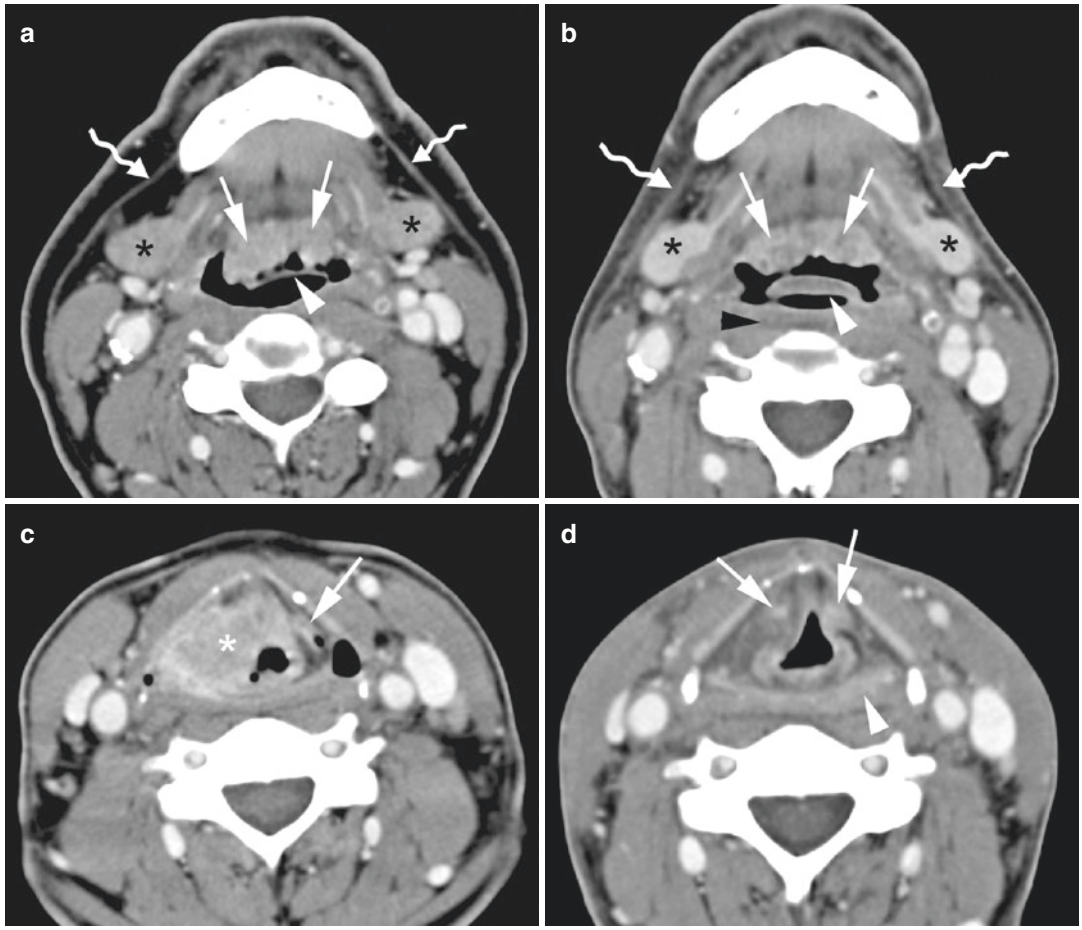

Fig. 21 Patient with supraglottic squamous cell carcinoma, staged T3N0, treated by definitive radiotherapy. Axial contrast-enhanced CT images are shown, obtained just before and 3 months after completion of radiation treatment. (**a**, **b**). Level of lingual tonsil. After radiotherapy (**b**), apart from diffuse increased attenuation of the neck fatty tissue, thickening of the free edge of the epiglottis (white arrowhead), platysma muscles (curved arrows), and oropharyngeal walls is seen. Slight amount of retropharyngeal edema is present (black arrowhead). Note also increased enhancement of the submandibular salivary glands (asterisks), corresponding to radiation sialadenitis, and volume reduction of lingual tonsil (arrows). (**c**, **d**) Level of supraglottis. Before radiotherapy (**c**), a large supraglottic tumor mass (asterisk) is seen, infiltrating the preepiglottic and right paraglottic space; normal left ventricle, containing air bubble, in left paraglottic space (arrow). After radiotherapy (**d**), the tumor mass disappeared; increased attenuation of the paraglottic fat spaces, somewhat more pronounced in former tumor bed; no mass lesion can be recognized. Laryngeal ventricle is now visible on both sides (arrows). Thickening and increased enhancement of the hypopharyngeal walls (arrowhead)

has been described, and this appears to correlate with local control (Pameijer et al. 1999).

5.1.2 Expected Findings After Laryngeal Surgery

The limits of surgical therapy are determined by the balance between obtaining cure by radical resection of the tumor, and leaving the patient in a functionally and esthetically acceptable situation. More extensive resections are possible by the introduction of various reconstructive materials, such as pedicled or free soft tissue flaps, grafts, and protheses.

5.1.2.1 Laser Resection

The expected findings after transoral laser excision of a laryngeal cancer depend on the amount of tissue resected. The laryngeal soft tissues may appear normal, or show a focal tissue defect (Fig. 22). After a more extensive resection, the

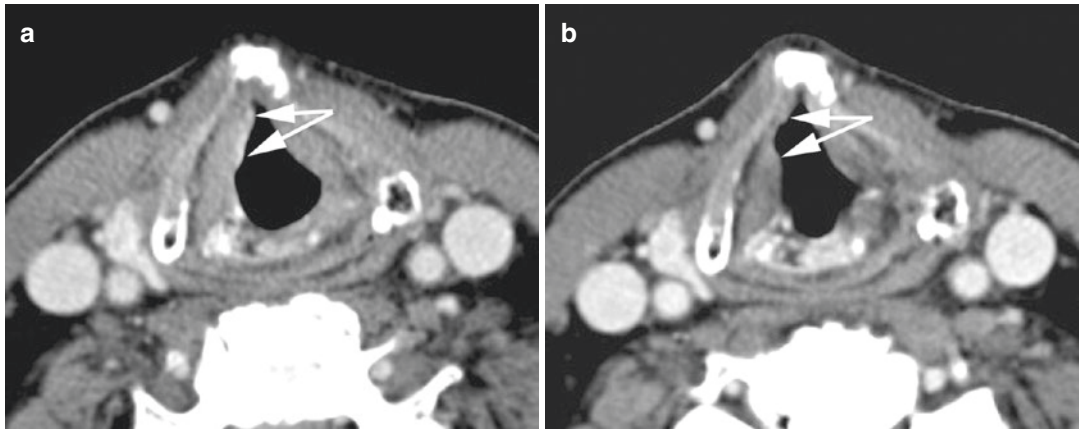

Fig. 22 (**a**) Recurrent glottic squamous cell cancer, presenting as soft tissue thickening (arrows), 2 years after radiotherapy for a right-sided glottic cancer (T2N0). (**b**) Situation 7 months after partial cordectomy by transoral laser resection: a soft tissue defect is seen in the anterior half of the right true vocal cord (arrows); no evidence for recurrent cancer

laryngeal soft tissue may be replaced by scar, appearing as homogenous but relatively dense tissue with a straighter inner border (Maroldi et al. 2001); in such cases, differentiation with recurrent tumor may be difficult and correlation with endoscopic findings is necessary. In case of doubt, biopsy is warranted.

5.1.2.2 Partial Laryngectomy

The aim of partial laryngectomy is to combine radical tumor resection with preservation of laryngeal function. This requires continuity and patency of the airway, separation of the airway and digestive tract, and sparing or reconstruction of the glottic phonation function.

Traditional partial laryngectomies include horizontal supraglottic laryngectomy and vertical hemilaryngectomy, but more complex surgical techniques are also being employed (Maroldi et al. 1997; Delaere et al. 2007; Ferreiro-Argüelles et al. 2008). The postoperative radiological findings depend on the technique employed. Changes in the laryngeal framework offer landmarks for interpreting postoperative findings. However, a somewhat different appearance for the same technique may be encountered among different patients, depending on technical adaptations needed for adequate tumor resection. The postoperative soft tissue changes are less predictable, depending on individual differences in healing, and variations in amount of edema and scarring (Maroldi et al. 2001). The differentiation between redundant or hypertrophic mucosa, as well as scar tissue, from recurrent cancer, may be difficult.

Horizontal supraglottic laryngectomy can be performed in supraglottic cancer staying above the level of the ventricles; this procedure is not performed when the tumor infiltrates both arytenoids (one arytenoid can be resected), the posterior commissure, the postcricoid area, the apex of the sinus piriformis, the glottis, or the thyroid cartilage. Minimal tongue base invasion is not a contraindication. Almost all of the larynx above the level of the ventricles is removed. The residual thyroid cartilage is pulled upwards and sutured to the hyoid bone.

Limited glottic cancer can be treated by vertical hemilaryngectomy. The most limited variant of this procedure is a cordectomy, where the entire vocal cord is removed from the anterior commissure to the vocal process of the arytenoid. In a frontolateral laryngectomy, the true and false vocal cord is removed, as well as the greatest part of the ipsilateral thyroid cartilage, including the angle to encompass the anterior commissure; the vocal process of the arytenoid can also be included. In a frontal laryngectomy, the anterior portion of both vocal cords is removed, together with the anterior commissure; a modified frontal laryngectomy is Tucker's, near-total technique, using the epiglottis as reconstructive tissue (Fig. 23).

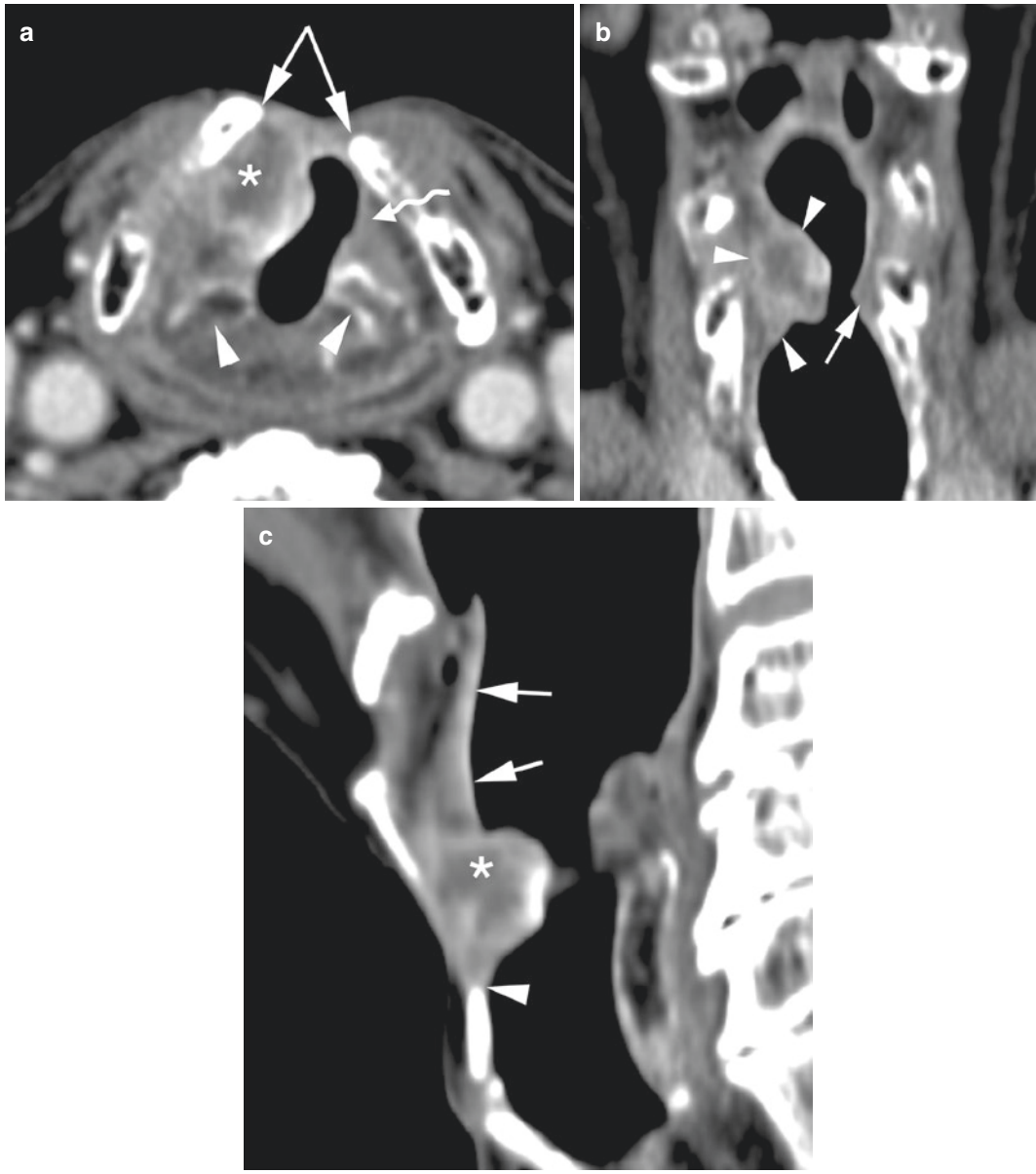

Fig. 23 Contrast-enhanced CT images in a patient who was treated by a frontal laryngectomy (according to Tucker) for a carcinoma in the anterior commissure. Three years later, the patient presents with increasing dysphonia. Clinically, swelling of the right false vocal cord is noted with an intact mucosa. (**a**) Axial section at the level of the arytenoid cartilages (arrowheads). Defect in the anterior part of the thyroid cartilage (arrows); the anterior part of the left true vocal cord (curved arrow) has been resected. On the right side, a centrally necrotic soft tissue mass is seen (asterisk), indicating tumor recurrence. (**b**) Coronal reformatting. Level of true vocal cord is indicated on left side by arrow. The recurrent tumor on the right (arrowheads) grows from the false vocal cord region into the true vocal cord; early subglottic extension may be present (lower arrowhead). (**c**) Sagittal reformatting. The upper part of the epiglottis (arrows) has a more anterior course as normally expected, as this structure was used to close the thyroid cartilage defect. The recurrent tumor (asterisk) abuts the upper margin of the arch of the cricoid cartilage, appearing sclerotic (arrowhead). No neoplastic cartilage invasion was present histologically

If more extensive involvement of the arytenoid is present (possibly with involvement of the cricoarytenoid joint) and/or subglottic extension is present, these procedures are not performed. Extended hemilaryngectomy may than be an alternative. During this procedure, half of the larynx, including half of the cricoid cartilage, is removed. The large defect in the larynx is reconstructed with a tracheal patch, revascularized by a freely transplanted radial forearm soft tissue flap. Full height cricoid defects can be closed using this patch in a position comparable to unilateral laryngeal paralysis. This is a functional reconstruction, allowing the patient to breathe and speak through his larynx, and swallow without aspiration (Delaere et al. 2007) (Fig. 24).

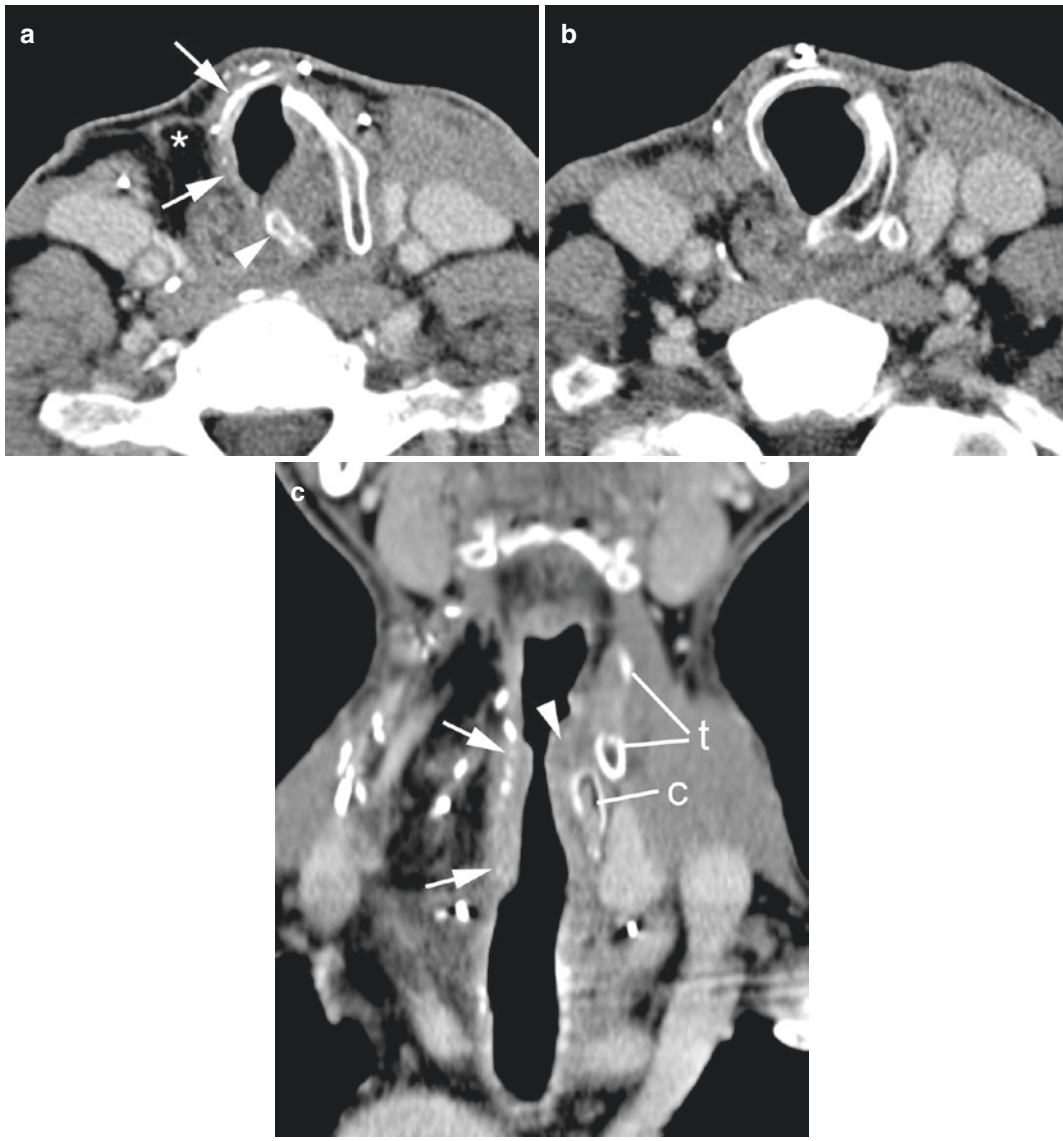

Fig. 24 Contrast-enhanced CT images in a patient treated by extended hemilaryngectomy for a right-sided true vocal cord carcinoma. (**a**) Axial section at the level of the left true vocal cord. Left arytenoid (arrowhead). The right hemilarynx was resected, and the defect closed by a tracheal patch (arrows). The fatty structure along the tracheal patch (asterisk) corresponds to the radial forearm fascial flap. (**b**) Axial section at the level of the subglottis. The subglottic airway is reconstructed by the tracheal transplant. (**c**) Coronal reformatting shows restoration of the laryngeal airway by the tracheal transplant (arrows). Left true vocal cord (arrowhead); cricoid cartilage (c); thyroid cartilage (t)

Some advanced glottic and supraglottic cancer can be treated by supracricoid partial laryngectomy (SPL), entailing en bloc resection of all tissues between the upper margin of the cricoid cartilage and the inferior margin of the hyoid bone, including the true and false vocal cords. Only the arytenoid on the less involved site is left in place. For glottic cancers without involvement of the supraglottis, the upper two thirds of the epiglottis can be preserved; this variant is known as SPL with cricohyoidoepiglottopexy (CHEP) (Gavilan 2000).

5.1.2.3 Total Laryngectomy

Complete removal of the larynx may be required as primary treatment of extensive laryngeal cancer or for salvage of tumor recurrence after radiation treatment or failed partial laryngectomy.

When the larynx is removed, the airway and upper digestive tract become completely separated. The airway will then end at a tracheostomy in the base of the neck. If, following the laryngectomy, not sufficient hypopharyngeal tissue is left for creating a neopharyngeal lumen of acceptable diameter, a soft tissue flap is used to create a wider lumen. A pedicled pectoralis major musculocutaneous flap is commonly used for this purpose (Fig. 25). The pectoralis major flap has an excellent blood supply. The skin of the flap borders the lumen, while the bulk of the flap fills the soft tissue neck defect, creating a more acceptable aesthetic appearance. On imaging studies, the pectoralis major flap appears initially as a bulky soft tissue structure, showing the characteristics of muscle; gradually, denervation atrophy appears, causing volume loss and fatty replacement of the muscle. At the time of imaging, the muscle denervation may be incomplete; fiber-like structures with muscle density within the flap should not be confused with tumor recurrence. Sometimes a radial forearm flap is used to create a neopharynx (Fig. 26), or an intestinal structure is transplanted to function as neopharynx.

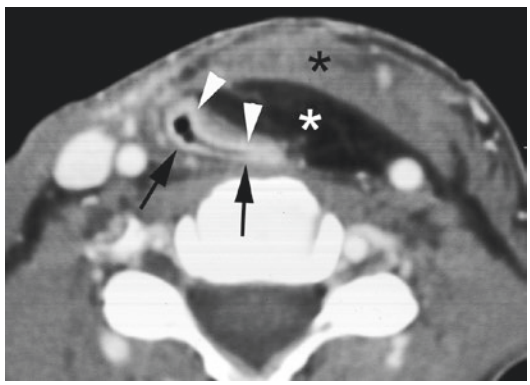

Fig. 25 Axial contrast-enhanced CT image. Situation after total laryngectomy. The neopharynx is reconstructed by residual pharyngeal tissue (arrows) and a musculocutaneous soft tissue flap (pectoral major flap), containing skin (arrowheads), subcutaneous fat (black asterisk), and muscle (white asterisk)

Between the proximal trachea and esophagus, a small one-way valve (such as a Provox voice prothesis) is placed, allowing escape of air from the proximal trachea to the esophagus if the tracheostome is closed by the patient. In this way the patient has a lot of air available for producing pharyngeal speech, allowing more rapid speech rehabilitation. Such a valve is visible on imaging studies as a small tube, situated in the wall between the proximal trachea and upper esophagus (Fig. 27).

Commonly during laryngectomy, tissue of the thyroid gland is removed. Unilateral thyroidectomy may be performed, to facilitate surgical access to the larynx and to remove at the same time a site of potential direct spread of the cancer. Another option is to remove the isthmus of the thyroid gland, leaving the two thyroid lobes. This remnant thyroid tissue is usually easy to recognize because it shows a high density, related to the high iodine concentration in the gland and its strong vascularization. However, as the normal shape of the thyroid gland is lost, these remnants usually show a rounded or oval appearance. Thyroid tissue may appear inhomogeneous due to the presence of nodular hyperplasia, adenomas, or cysts. It is important that these thyroid remnants are not confused with recurrent cancer; unlike recurrent cancer, these have well-defined borders (Fig. 28).

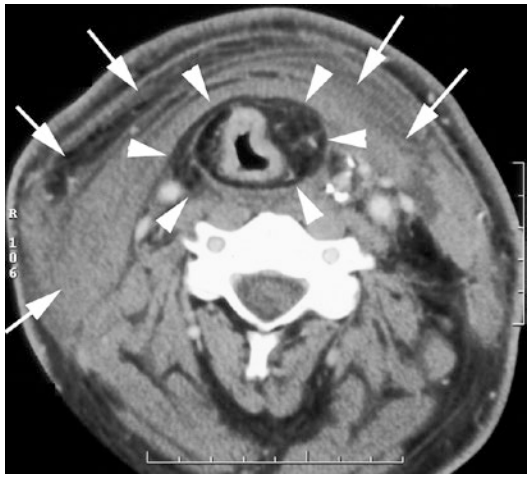

Fig. 26 Axial contrast-enhanced CT image, in a patient treated by total laryngectomy. The neopharynx is reconstructed by a free radial forearm flap (arrowheads; inner enhancing rim is skin); the soft tissues are anteriorly covered by a pedicled pectoralis major flap (arrows)

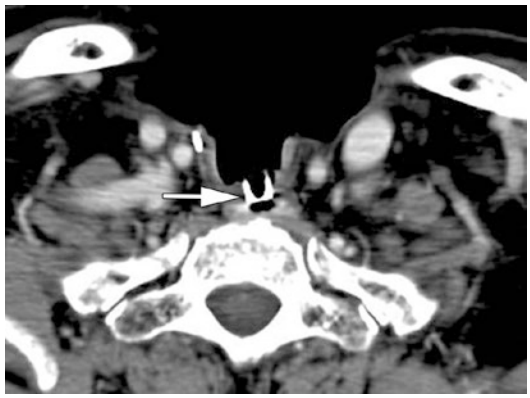

Fig. 27 Axial CT image at the level of the tracheostomy, in a patient who underwent total laryngectomy. Normal appearance of a voice prothesis (arrow), placed through the tracheo-esophageal septum

5.2 Persistent or Recurrent Cancer

5.2.1 Imaging Strategies and Findings

Posttreatment imaging is useful to confirm the presence of clinically suspected tumor recurrence.

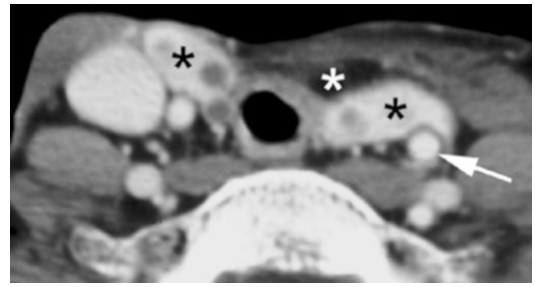

Fig. 28 Axial contrast-enhanced CT image. The neopharynx is seen lying between both thyroid lobes (black asterisks). The thyroid isthmus was resected during the laryngectomy. The inhomogeneous appearance of the thyroid lobes is caused by nodular hyperplasia. Absence of left internal jugular vein along the common carotid artery (arrow), resected during radical neck dissection. Soft tissue flap (white asterisk)

On CT or MRI, tumor recurrence appears after radiation therapy as a soft tissue mass at the primary site and/or as an enlarged (and/or centrally liquefied) neck adenopathy. After surgical treatment, the most reliable imaging finding in recurrent tumor is an enhancing soft tissue mass (Figs. 23 and 29); after partial laryngectomy, destruction of residual laryngeal cartilage may be seen.

Early tumor recurrence may be difficult to distinguish from tissue changes induced by therapy. Therefore, it is recommended to obtain a follow-up CT or MR study after surgical, radiation, or combined treatment for a laryngeal neoplasm with high-risk profile (Hermans et al. 2000; Schwartz et al. 2003). Probably the best time to obtain such a baseline study is about 3–6 months after the end of treatment. Such a baseline study allows treatment-caused changes in the head and neck tissues to be documented. By comparing subsequent studies with the baseline study, it becomes possible to detect with more confidence tumor recurrences or treatment complications, and this at an earlier stage than is possible with clinical follow-up alone (Fig. 30). In patients with laryngeal cancer, CT is an adequate imaging modality for pre- and posttreatment imaging, but similar results can be obtained using MRI (Ljumanovic et al. 2008).

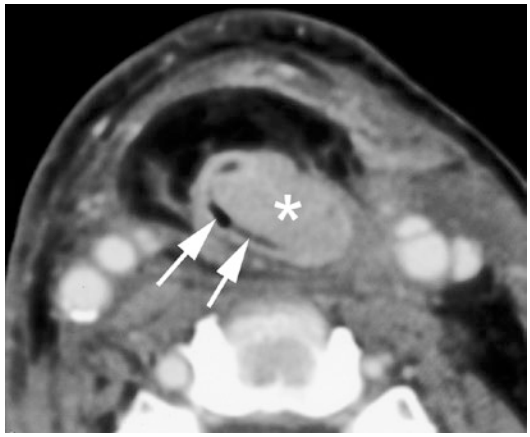

Fig. 29 Axial contrast-enhanced CT image, after total laryngectomy for squamous cell carcinoma. Enhancing soft tissue mass (asterisk) at the anterolateral side of the neopharyngeal lumen (arrows): recurrent cancer

There is evidence that the baseline study after radiotherapy carries important predictive information regarding the eventual local outcome: several studies show that CT may be useful in the early differentiation of treatment responders from nonresponders in irradiated laryngeal and hypopharyngeal cancer (Hermans et al. 2000; Mukherji et al. 1994b).

Based on the appearance of the larynx/hypopharynx on an early post-radiotherapy CT study, a prediction of long-term local outcome can be made according to the following scores: 1 = expected post-radiotherapy changes, i.e., complete resolution of the tumor at the primary site and symmetrically appearing laryngeal and hypopharyngeal tissues, as described above; 2 = focal mass with a maximal diameter of <1 cm and/or asymmetric obliteration of laryngeal tissue planes; 3 = focal mass with a maximal diameter of >1 cm, or <50% estimated tumor volume reduction (Pameijer et al. 1999; Hermans et al. 2000).

The post-radiotherapy CT-score 1 was shown to be a very strong predictor of long-term local control; patients with such findings on post-radiotherapy CT will probably not benefit from further follow-up imaging studies. Conversely, patients with a first follow-up examination classified as CT-score 3 do very poorly; almost all these patients will develop a local failure (Pameijer et al. 1999). Further exploration in such post-radiotherapy CT-score 3 patients is warranted. PET-CT imaging may prove to be a useful intermediate step in cases where biopsy is considered too risky, or if a biopsy result is returned as negative (Fig. 31). Indeed, the predictive value of a negative biopsy for local control is reported to be only 70% (Keane et al. 1993); this is likely due to sampling error, as tumor recurrences initially develop submucosally and can therefore not be accurately targeted. In cases of contradiction between the clinical findings, CT findings, results of radionuclide studies and/or biopsy, close clinical follow-up and repeat imaging studies are needed.

The local outcome of patients initially classified as post-radiotherapy CT-score 2 is indeterminate. Unless clinical examination is already suspect for local failure, further follow-up CT studies are needed in these patients; a time interval of 3 to 4 months is recommended, to be continued up to 2 years after completion of radiation treatment.

Another strategy is to use PET-CT as the initial baseline study, in patients treated with advanced disease with low clinical suspicion of recurrence, and in patients with nonspecific symptoms that could indicate recurrence but without a clinically obvious mass. PET-CT has a high negative predictive value; however, false positive results are not uncommon (Purohit et al. 2014); cross-sectional imaging should then be performed for an equivocal or positive PET study (Aiken et al. 2018).

False positive findings are frequent if CT, MRI (using conventional sequences), as well as PET is used earlier than 3 months after the end of radiotherapy. This is caused by radiotherapy-induced tissue changes. These tissue changes, such as edema, inflammation, fibrosis, and necrosis, are expected to show low cellularity on histological examination, in contrast with recurrent or persistent tumor. Diffusion-weighted MRI takes advantage of this completely different microstructure, which will be reflected by a different signal intensity and ADC value. Based

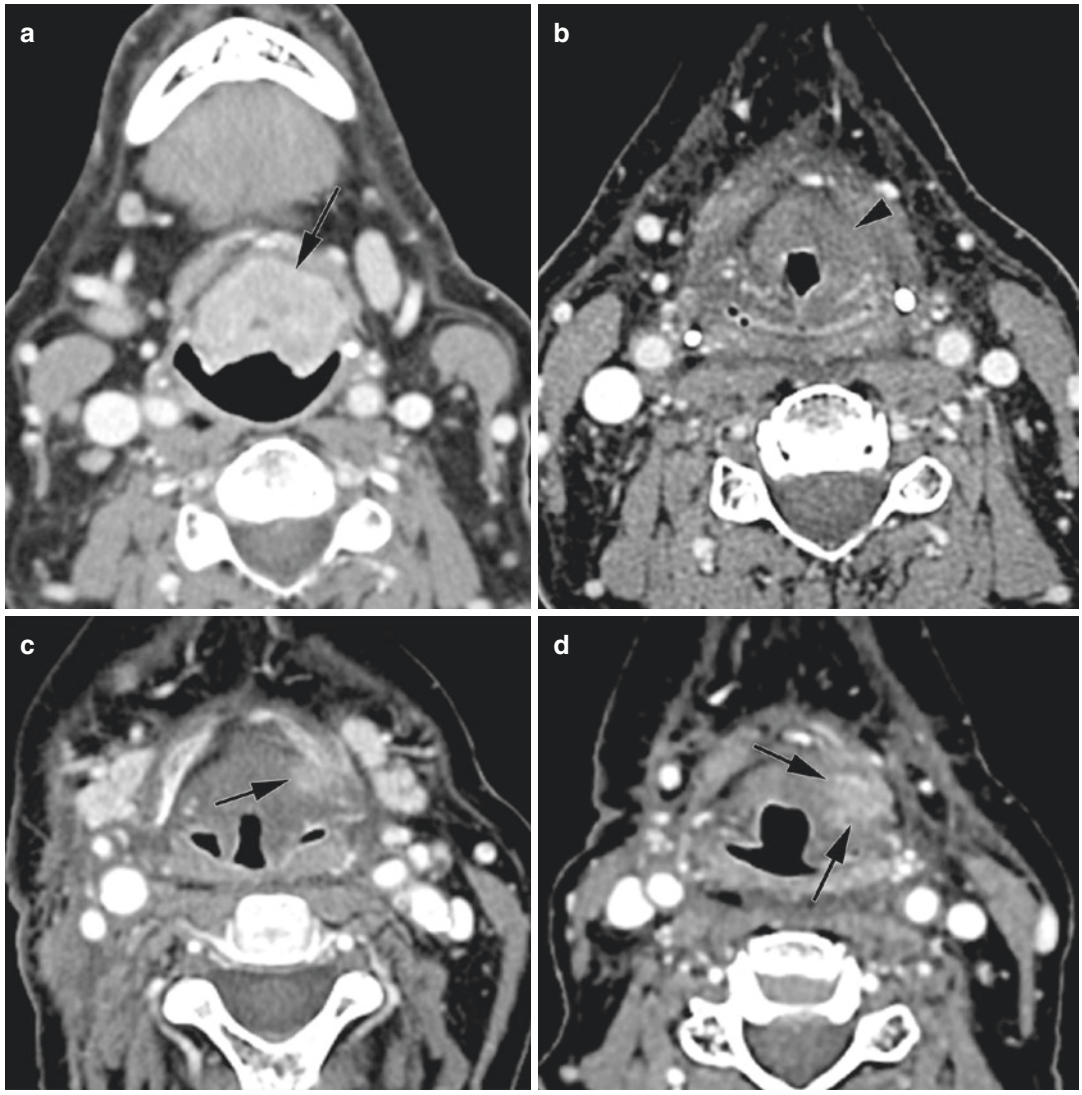

Fig. 30 (**a**) Patient suffering from a large supraglottic cancer, invading the preepiglottic space (arrow), staged as a T3N2c cancer. It was decided to treat with concomitant chemoradiotherapy. (**b**) First follow-up CT, 4 months after treatment. The patient responded well to treatment, the tumor and adenopathies disappeared. Diffuse edema of the supraglottic larynx is seen, appearing slightly asymmetric (arrowhead). Therefore, further follow-up with intermittent CT scanning was recommended. (**c**) Follow-up CT study obtained 17 months after treatment shows appearance of a small contrast-enhancing lesion (arrowhead), close to the hyoid bone. This new finding is suspect for recurrent tumor. Clinical examination did not show any suspect finding, the patient was asymptomatic, and as the lesion was considered unreachable for biopsy, it was decided to adopt a wait-and-see policy. (**d**) Three months later, CT shows clear growth of the lesion (arrows). (**e**) Same time (20 months after treatment), the abnormality was confirmed on PET-CT (arrow). A surgical exploration was done, but not tumoral tissue could be found and histology was negative. The patient refused further exploration at that time. (**f**) CT study 26 months after treatment: the lesion again has grown, and now starts extending outside the larynx (arrowhead). The patient was advised to undergo a total laryngectomy, as the imaging findings are very suggestive for progressive tumor. However, as she still was asymptomatic, she did not agree unless a histological proof of recurrence was obtained. (**g**) An ultrasound study was performed, visualizing the pathological region through the thyrohyoid membrane (arrows); fine needle aspiration was done and did confirm squamous cell cancer, and total laryngectomy was performed. The patient remained free of disease later on

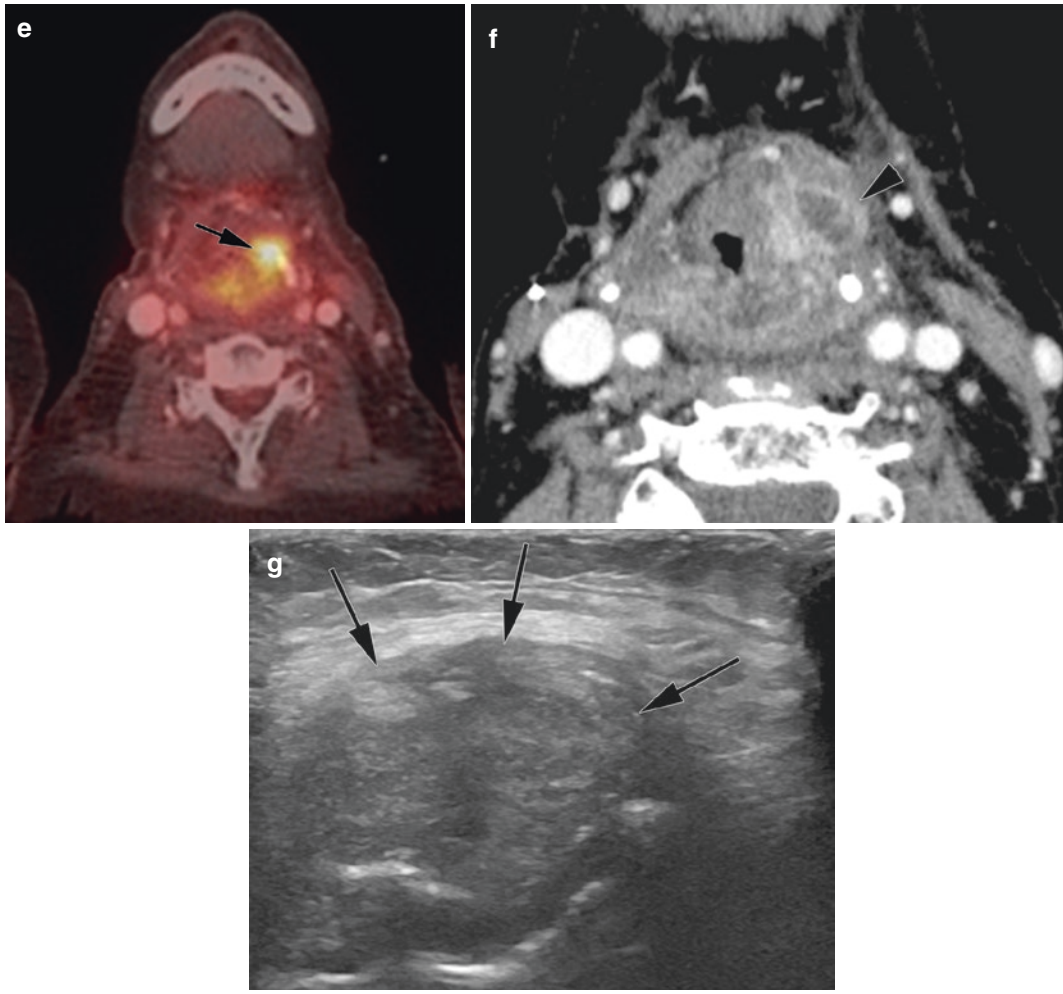

Fig. 30 (continued)

on ADC values, diffusion-weighted MRI allows differentiation of tumoral tissue from post-radiotherapy alterations and tissue necrosis with high accuracy, and this both in early and late tumor recurrences. In the head and neck, sensitivities in the range of 84–93% and specificities in the range of 90–96% were reported (Vandecaveye et al. 2007; Abdel Razek et al. 2007, 2008). Also in the larynx, diffusion-weighted MRI allows to differentiate tumor recurrence from inflammation and necrosis (Vandecaveye et al. 2007). However, further validation and standardization of this imaging technique is needed.

5.2.2 Potential Value of Imaging Surveillance

Use of this imaging-based information could lead to more prompt salvage surgery and potentially improve the survival of these patients (Hermans et al. 2000). However, few data regarding the value of posttreatment surveillance in patients with head and neck cancer are available. Some authors argue that routine follow-up is indispensable, as patients with asymptomatic locoregional recurrences, discovered during surveillance, have a significant better postrecurrence survival than those patients where recurrent disease was found by symptoms (De Visscher and Manni 1994).

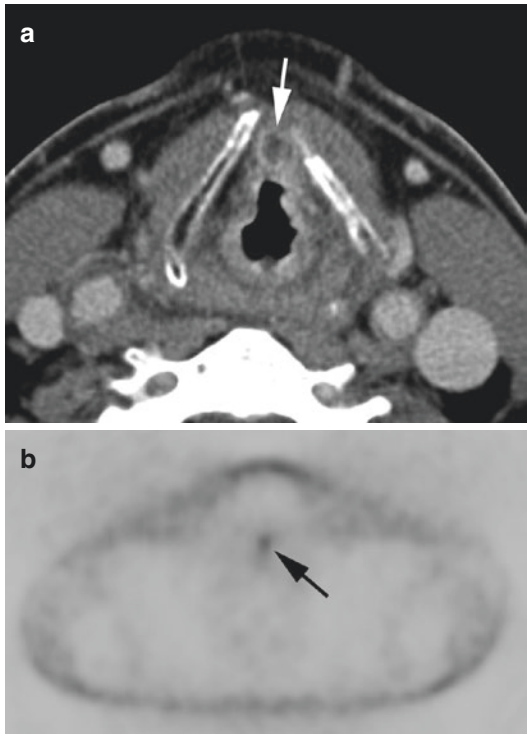

Fig. 31 Same patient as in Fig. 16. Six months after radiotherapy, clinical suspicion of tumor recurrence. (**a**) Axial contrast-enhanced CT image shows centrally hypodense nodular lesion in the preepiglottic space (arrow) suggesting necrotic tumor. Biopsies were negative. (**b**) FDG-PET image shows faint tracer accumulation at the level of the supraglottis. Total laryngectomy was performed; histological analysis of the resection specimen confirmed the presence of squamous cell carcinoma

Other authors point out that the apparently longer survival of patients with recurrent tumor diagnosed by testing may be due to lead time bias (i.e., early diagnosis falsely appears to prolong survival) (Schwartz et al. 2003). This statement probably is true for patients treated by combined-modality therapy for advanced head and neck cancer, who are known to do extremely poorly after relapse and rarely have an effective treatment option available (Cooney and Poulsen 1999). However, in single modality treated patients, where a reasonable chance of salvage exists after locoregional recurrence (e.g., 35–60% surgical salvage rate for irradiated laryngeal cancer), imaging surveillance may be worthwhile to add to the clinical follow-up in order to further improve the salvage rate. More studies are required to elucidate this question.

5.3 Treatment Complications

5.3.1 Complications After Surgery

Most surgical complications occur early after treatment, and are dealt with on a clinical basis. Imaging may be required in the detection and follow-up of a fistula after partial or total laryngectomy. Many of these fistulas will close spontaneously, but some may need reintervention.

After conservative surgery, swallowing coordination may be impaired. The postoperative swallowing function can be analyzed by videofluoroscopy or videofluorography, providing information allowing the planning of rehabilitation (Maroldi et al. 2001). In some cases, surgical intervention may be required; in case of severe aspiration, total laryngectomy may be necessary.

Imaging may also be of use in the confirmation of flap failure due to necrosis (Fig. 32).

A voice prosthesis may cause an inflammatory reaction in the surrounding tissues, and infections may also occur. Clinically, the differentiation

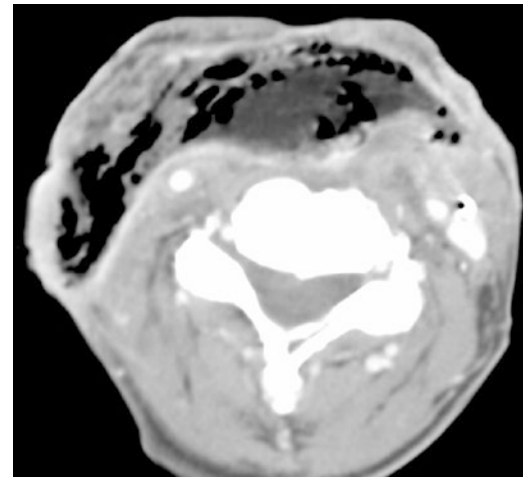

Fig. 32 Axial contrast-enhanced CT image. A few weeks before this CT study, total laryngectomy was performed, with neopharyngeal reconstruction by a pectoralis major flap. The patient suffers now from persistent fistulization. Throughout the pectoralis major flap, large, confluent gas bubbles are visible, indicating flap necrosis. Flap necrosis was surgically confirmed

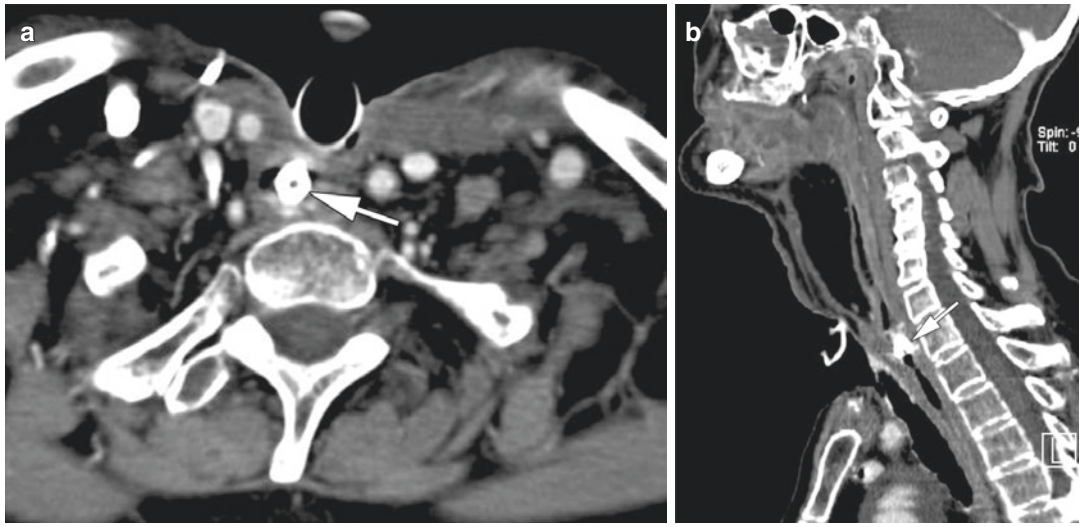

Fig. 33 Axial (**a**) and coronal (**b**) CT image in a patient presenting with dysphagia after total laryngectomy; no evidence for tumor recurrence was seen, but the voice prosthesis (arrow) was seen to be dislodged into the neopharynx, explaining the patient's complaints. At endoscopy, the prothesis was found completely embedded within the neopharyngeal mucosa

with tumor recurrence is not always obvious, and also on imaging, such inflammation causes a soft tissue thickening which may be difficult to differentiate from tumor recurrence. More severe cases of infection complicating a voice prosthesis have been reported, including cervical osteomyelitis and mediastinitis. The presentation may be insidious, with symptoms such as dysphagia, swollen neck, and reduced cervical mobility (Malik et al. 2007).

Another complication that may be seen after total laryngectomy is dislocation of the voice prosthesis, causing dysphagia (Fig. 33).

5.3.2 Complications After Radiotherapy

5.3.2.1 Laryngeal Necrosis

Acute effects of radiotherapy (skin and mucosal reactions) occur during or immediately after treatment, and usually settle spontaneously.

Persisting severe edema and radionecrosis of the larynx are uncommon treatment complications, with an incidence of about 1%. The occurrence of laryngeal necrosis peaks during the 12 months following treatment, which is more or less contemporaneous with the peak incidence of tumor recurrence. However, cases of laryngeal necrosis more than 10 years after radiation treatment do occur (O'Brien 1996). These late effects after radiation treatment are largely due to impaired vascular and lymphatic flow, caused by endothelial damage and fibrosis (Alexander 1963). Cartilage itself is resistant to the effect of irradiation (see above). Cartilage changes usually occur when the perichondrium is broached by trauma or tumor, exposing the underlying irradiated cartilage to microorganisms in the airway (Keene et al. 1982); this may lead to infectious perichondritis, possibly resulting in necrosis and laryngeal collapse.

Patients with laryngeal necrosis often have neck and/or ear pain, some degree of dysphagia, and anterior neck swelling. Hoarseness and dyspnea are caused by increasing edema with impairment of vocal cord mobility, resulting in cord fixation. Inflammatory changes in the overlying skin or cutaneous fistulae may be present.

Palpation of the laryngeal region usually is painful. On imaging studies, a variable degree of laryngeal soft tissue swelling is seen (Hermans et al. 1998). These soft tissue changes surrounding the necrotic cartilage can be very pronounced and may be the only visible abnormality, making the differentiation with recurrent tumor very difficult. Furthermore, laryngeal necrosis and tumor recurrence may occur simultaneously. In laryngeal necrosis, some fluid may be seen surrounding the cartilages (Fig. 34). Cartilaginous abnormalities are often visible, but in some patients they may only become apparent on follow-up CT studies.

Necrosis of the thyroid cartilage may cause fragmentation and collapse of this cartilage with or without gas bubbles visible adjacent to or in it. Patients with arytenoid cartilage necrosis may show anterior dislocation of this cartilage; this could be due to cricoarytenoidal joint effusion, secondary to inflammation or infection. Progressive lysis of the arytenoid is possible, showing a crumbly aspect evolving to complete disappearance (De Vuysere et al. 1999). Also, sloughing of the arytenoid cartilage into the airway has been described (Hermans et al. 1998). The adjacent part of the cricoid cartilage may appear sclerotic. Cricoidal sclerosis or destruction may be also seen in association with lysis of the thyroid cartilage (Fig. 35).

On MR studies, laryngeal necrosis may appear as focal swelling of the laryngeal soft tissues, loss of the normal high signal in the medullary space of ossified laryngeal cartilage on T1-weighted images, and enhancement of the affected cartilage after injection of gadolinium (Bousson et al. 1995).

In some cases, the imaging findings allow better differentiation between tumor recurrence and chondronecrosis than clinical examination alone. Studies on post-radiotherapy surveillance of laryngeal and hypopharyngeal cancer (Mukherji

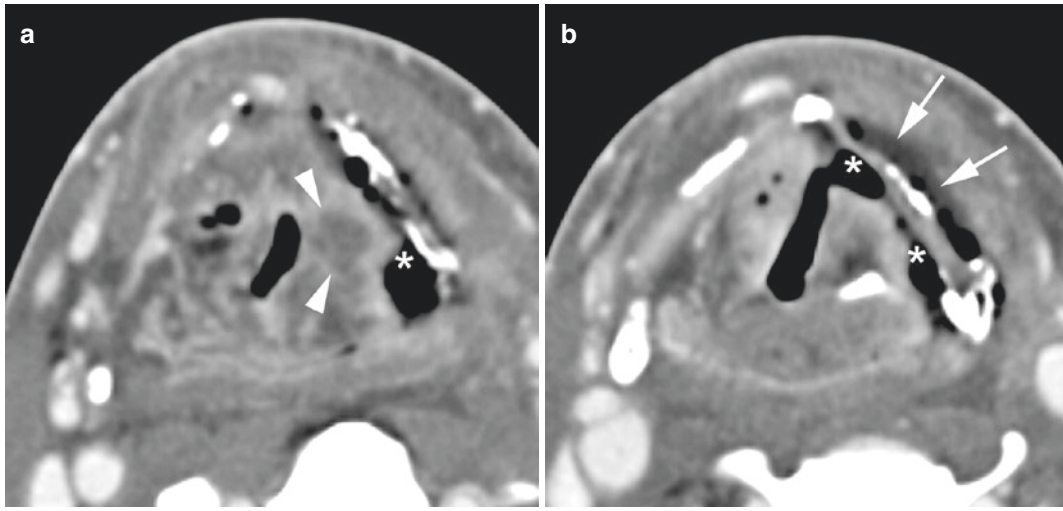

Fig. 34 Axial contrast-enhanced CT images. Patient treated 5 months earlier by irradiation for T3 supraglottic cancer, suffering from progressive dysphagia. Laryngoscopy showed a fixed left vocal cord, suspect for tumor recurrence. (**a**) On a background of expected changes after radiation therapy, a centrally hypodense nodular area of soft tissue thickening is seen in the left aryepiglottic fold (arrowheads). Furthermore, a large soft tissue defect (asterisk), connecting the left piriform sinus with the denuded thyroid cartilage lamina, is seen. The thyroid lamina appears slightly irregular, and is abutted by air. (**b**) At a lower level, soft tissue defects are seen to connect to the left piriform sinus, as well as to the laryngeal ventricle (asterisks). Fluid layer at the outer side of the thyroid cartilage (arrows). A FDG-PET study was strongly positive at the level of the supraglottis. Because of a rapidly deteriorating clinical situation, total laryngectomy was performed. Histologic examination revealed extensive tissue necrosis, but no laryngeal tumor recurrence

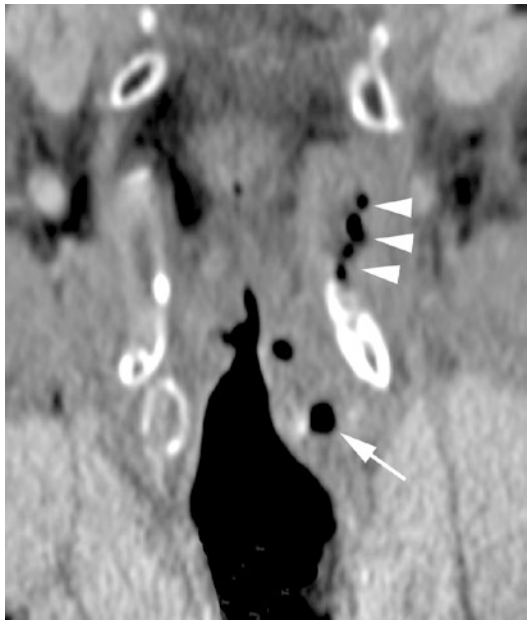

Fig. 35 Coronal reformatting of contrast-enhanced laryngeal CT study. The patient was treated 2 years earlier with radiotherapy for a T2 glottic carcinoma, and now present with increasing breathing and swallowing difficulties. Laryngeal soft tissue thickening is seen, more pronounced on the left side. Lysis of the left part of the cricoid arcus, with presence of an intracartilaginous gas bubble (arrow); also the upper part of the left thyroid cartilage wing appears lytic and contains several gas bubbles (arrowheads). The image is suggestive for extensive laryngeal necrosis. Total laryngectomy was performed; histopathologic study confirmed extensive radionecrosis, without evidence of tumor recurrence

et al. 1994b; Pameijer et al. 1999) showed that progressive cartilage alterations on post-radiotherapy CT studies predicted poor local outcome, due to either tumor recurrence or chondroradionecrosis. In these studies gas bubbles in the vicinity of cartilage and cartilage collapse were not observed in cases of tumor recurrence. Such findings can be regarded as suggestive of radionecrosis; nevertheless, a coexistent tumor recurrence may be difficult to exclude, depending on the associated tissue alterations (Fig. 34).

It has been suggested that FDG-PET may allow differentiation between tumor recurrence and tissue necrosis as complication of therapy (Anzai et al. 1996; McGuirt et al. 1998). However, false positive results may occur as tissue necrosis may be associated with an important inflammatory reaction, increased metabolism, and thus increased uptake of the tracer, suggesting tumor recurrence (Purohit et al. 2014).

As already mentioned above, diffusion-weighted MRI may be a useful complementary method to differentiate between tissue necrosis and persistent or recurrent cancer.

5.3.2.2 Other Complications After Radiotherapy

Fibrosis after radiotherapy may lead to contraction and hardening of the cervical tissues. Fibrosis-induced laryngeal dysfunction may lead to aspiration due to immobilization of the epiglottis and/or delayed closure of the laryngeal vestibulum and glottis; secondary aspiration may be caused by ineffective clearance of the pharynx. Dysphagia may be caused by pharyngeal or upper esophageal stenosis, occurring in 3–4% of patients irradiated for head and neck cancer; rarely, this may evolve to complete obstruction of the upper digestive tract (Laurell et al. 2003; Maple et al. 2006).

Fibrosis of the masticatory muscles may occur, particularly if they were involved by the cancer. The MRI-signal characteristics of fibrosis are variable; often, follow-up studies are needed to rule out tumor recurrence with a sufficient degree of confidence.

Other long-term complications of radiotherapy include arteriopathy, delayed central nervous system reaction, radiation myelopathy, cranial nerve palsy, and secondary tumors (Becker et al. 1997a).

6 Non-squamous Cell Laryngeal Neoplasms

The vast majority of laryngeal mass lesions are squamous cell carcinomas, and most of them clinically show mucosal alterations. Non-squamous cell carcinomas typically grow beneath

an intact mucosal layer. Clinical and endoscopical diagnosis of a submucosal laryngeal mass lesion is more difficult, and the initial biopsy results of such lesions may be returned as inconclusive or negative.

CT and MR studies demonstrate the presence and extension of such submucosal mass lesion. However, the radiological differentiation between a benign and malignant submucosal mass may be difficult. Signs suggesting malignancy include cartilage destruction, the presence of adenopathies, and a multifocal appearance and/or widely infiltrating behavior.

A variety of epithelial non-squamous neoplasms, and non-epithelial neoplasms can be encountered within the larynx (De Foer et al. 1996). The following discussion is limited to malignant lesions.

6.1 Minor Salivary Gland Neoplasms

Minor salivary glands are found throughout the mucosa of the oral and upper respiratory tract. In the larynx, these glands are located in the supra- and subglottic region; the glottis is devoid of minor salivary glands. The incidence of malignant tumors is considerably higher in minor salivary glands than in the large salivary glands; adenoid cystic carcinoma is the most frequent neoplasm of the minor salivary glands, but also adenocarcinoma and muco-epidermoid carcinoma arise from these glands.

Adenoid cystic carcinoma is a misleading name as macroscopic cystic structures are unusual in this tumor. It is sometimes called cylindroma, an old name which is better abandoned as it includes several nonrelated types of neoplasms.

About 25–35% of minor salivary gland tumors are adenoid cystic carcinomas. This tumor is mainly seen in the fourth, fifth, and sixth decade of life.

The radiographic characteristics of adenoid cystic carcinoma are nonspecific. In the larynx, these tumors usually present as a submucosal soft tissue mass in the subglottis (Fig. 36). As they grow submucosally, they are often locally more extensive than clinically suspected.

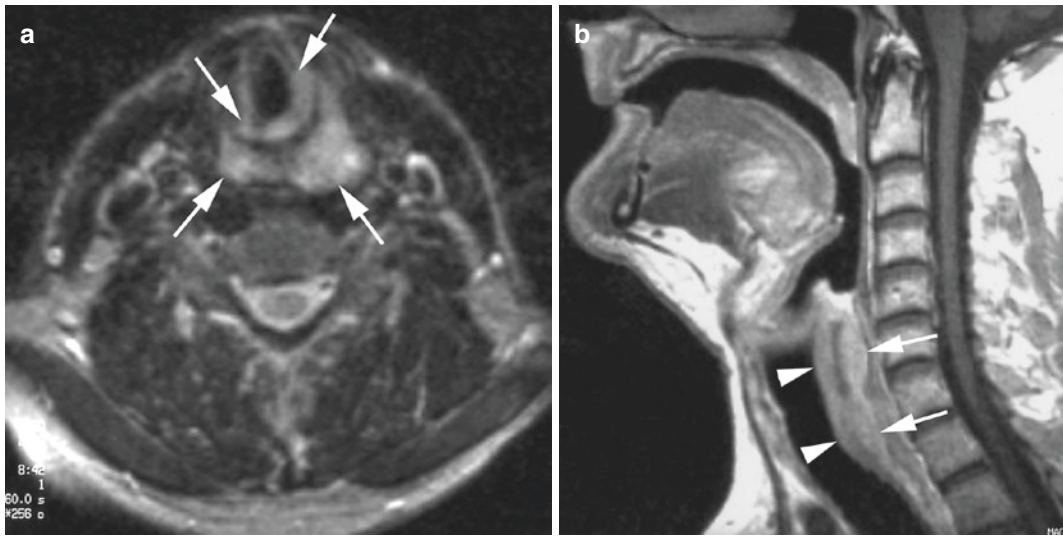

Fig. 36 Patient presenting with hoarseness; endoscopically, a submucosal mass lesion is suspected. The axial T2-weighted MR image (**a**) shows a hyperintense mass lesion (arrows) in the subglottis and distal hypopharynx. On the sagittal gadolinium-enhanced T1-weighted image (**b**), the mass is seen to infiltrate the larynx (upper arrowhead), proximal trachea (lower arrowhead), distal hypopharynx (upper arrow), and proximal esophagus (lower arrow)

6.2 Mesenchymal Malignancies

6.2.1 Chondrosarcoma

Chondrosarcomas are the most frequent laryngeal sarcomas. Cartilaginous tumors of the larynx account for less than 1% of all laryngeal tumors. Both chondroma and chondrosarcoma are encountered in the larynx, with 70% arising from the cricoid cartilage, and the thyroid cartilage being the next most common site of origin.

These cartilaginous tumors may be asymptomatic, or present with hoarseness, dyspnea, or dysphagia. At presentation, the lesion is usually less than 2–3 cm in diameter. On pathological examination, a lobular growth pattern with low cellularity is seen; nuclear atypia and mitoses are not encountered (Devaney et al. 1995).

True chondromas of the larynx are probably very rare. It is difficult to firmly establish the diagnosis of benign laryngeal chondroma on a small amount of tissue obtained by biopsy. Low-grade chondrosarcoma may also show a lobular growth pattern. Compared to chondroma, low-grade chondrosarcoma may display only minimally increased cellularity and nuclear atypia, a pattern overlapping with benign chondromas; there is also no appreciable degree of mitotic activity in such lesions (Devaney et al. 1995).

On CT studies, cartilaginous tumors of the larynx appear as hypodense, well-circumscribed masses centered within the laryngeal cartilage, with coarse or stippled calcification within the lesion (Fig. 37). The imaging findings do not allow to distinguish between a benign and malignant chondroid tumor, although in high-grade chondrosarcomas nodal metastasis in the head and neck may rarely be seen. MRI is less specific for diagnosing such a lesion as it does not depict the intratumoral calcifications as well as CT; on MRI, the tumor matrix shows a relative high signal intensity on T2-weighted images; the tumor enhancement after injection of gadolinium is variable (Fig. 38).

Cystic-appearing chondrosarcomas have been reported, and may mimic a fluid-filled laryngocele when originating from the thyroid cartilage (De Foer et al. 1996).

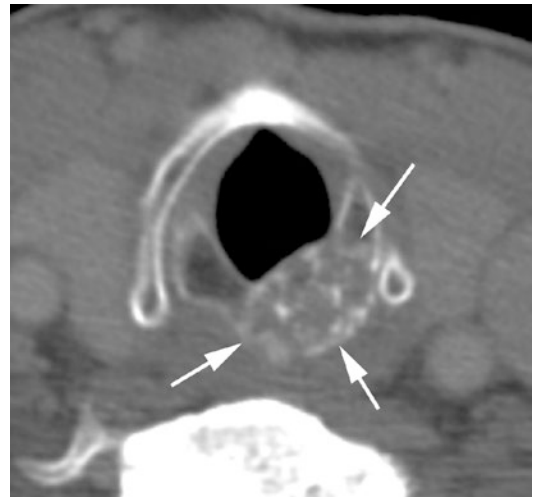

Fig. 37 Coincidently discovered mass lesion in cricoid cartilage, on occasion of a MR study of the cervical spine. Clinical examination showed submucosal swelling underneath the left true vocal cord. Axial CT image (bone window) confirms an expansile lesion in the left posterolateral part of the cricoid arch; the lesion contains punctiform calcifications. The patient was treated by extended hemilaryngectomy; histological examination showed low-grade chondrosarcoma

Surgery is the only curative modality in laryngeal cartilaginous tumors. Low-grade chondrosarcomas may locally recur if incompletely resected, but have only limited risk of metastatic disease. Therefore, in all laryngeal cartilaginous tumors a conservative approach is followed whenever possible, directed towards voice-sparing partial laryngectomy. However, total laryngectomy may be the appropriate treatment in lesions involving larger portions of the cricoid cartilage, interfering with surgical reconstruction of a functional larynx, or when the diagnosis of high-grade chondrosarcoma is established (Chin et al. 2017).

6.2.2 Other Mesenchymal Malignancies

Other types of laryngeal sarcomas are extremely rare. These include osteosarcoma, malignant fibrous

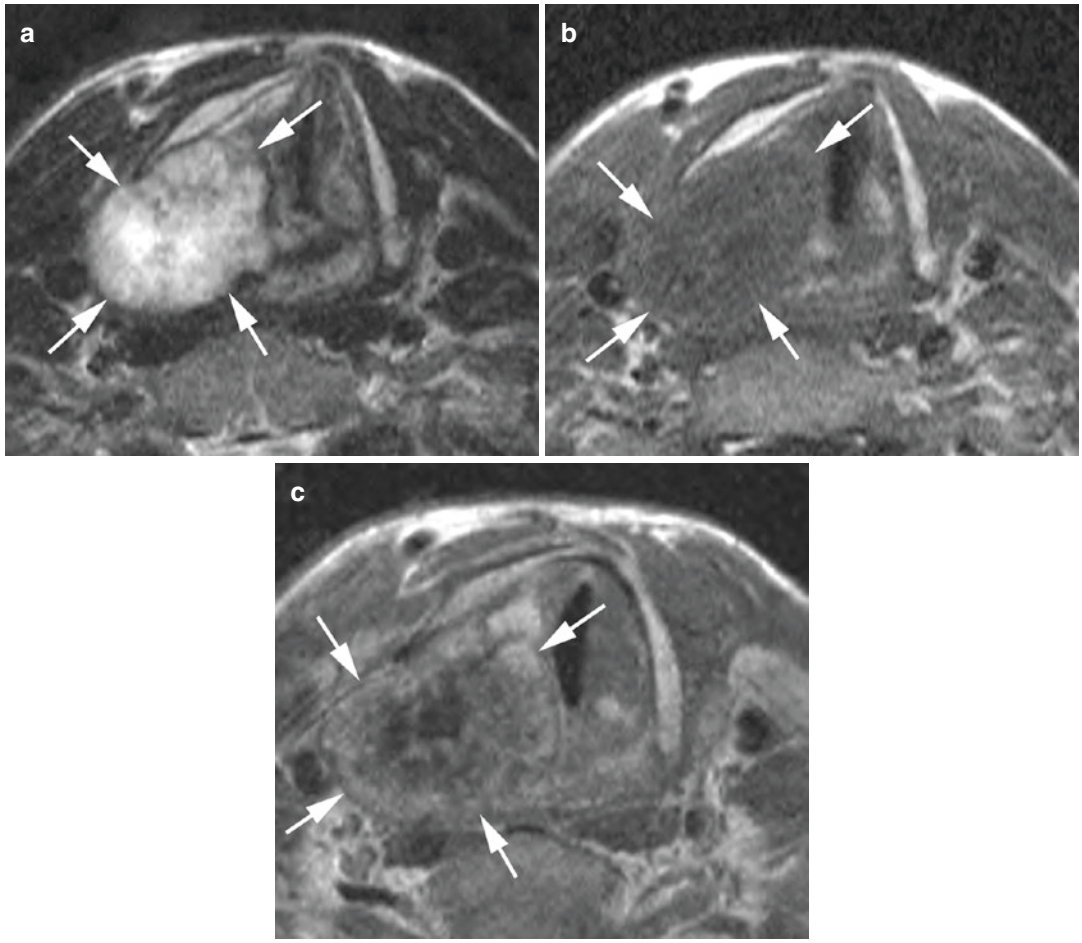

Fig. 38 MR appearance of a large low-grade chondrosarcoma originating from the cricoid cartilage. (**a**) Axial T2-weighted spin echo image shows a lobulated mass (arrows) with high signal intensity. (**b**) Axial T1-weighted spin echo image. (**c**) Gadolinium-enhanced axial T1-weighted spin echo image shows irregular enhancement of the mass lesion

histiocytoma, fibrosarcoma, liposarcoma (Fig. 39), angiosarcoma, synovial sarcoma, rhabdomyosarcoma, leiomyosarcoma, and Kaposi's sarcoma. These tumors usually appear radiologically as a huge and infiltrating supraglottic mass lesion.

6.3 Hematopoietic Malignancies

6.3.1 Lymphoma

Non-Hodgkin lymphoma is a heterogeneous group of neoplasms originating from lymphocytes or their derivatives. Non-Hodgkin lymphoma has varying clinical presentations and different courses and prognoses (see chapter on Neck Lymphoma).

Non-Hodgkin lymphoma is a disease of the middle-aged and elderly, with only few cases occurring before the age of 40. It represents about 5% of head and neck malignancies. About 11% of non-Hodgkin lymphomas present with lesions in this region, and about 50% of patients with head and neck disease have systemic disease.

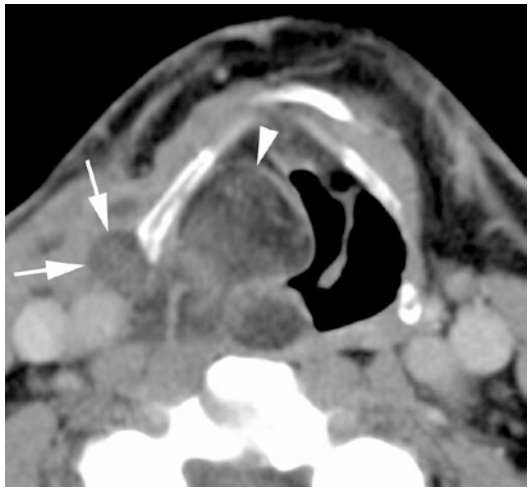

Fig. 39 Axial contrast-enhanced CT image. Soft tissue mass centered in the right paraglottic space (arrowhead), extending into the hypopharynx as well as extrapharyngeally (arrows). The tumor appears inhomogeneously, consisting of tissue with negative and positive density values. Liposarcoma

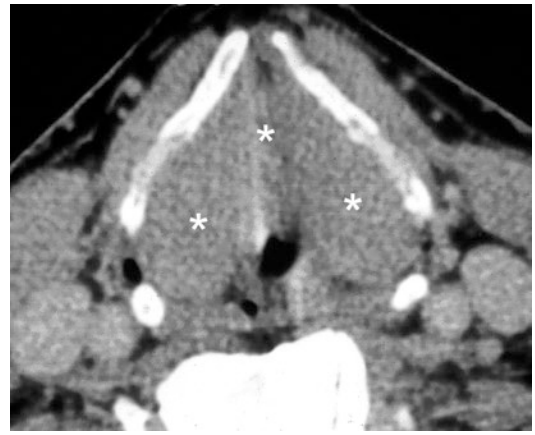

Fig. 40 Axial contrast-enhanced CT image shows diffuse soft tissue infiltration of the deep fatty laryngeal spaces (paraglottic and preepiglottic space), corresponding to non-Hodgkin lymphoma

Non-Hodgkin lymphoma can involve virtually any site in the extracranial head and neck. Nodal involvement is common, but in several studies extranodal spread is reported to occur more frequently than nodal enlargement. In the head and neck, two distinct extranodal sites are recognized: extranodal lymphatic spread or involvement of Waldeyer's ring, and extranodal extralymphatic spread. Extranodal extralymphatic non-Hodgkin lymphoma occurs most commonly in the sinonasal cavities and orbits, but it may infiltrate any tissue of the head and neck, such as the deep spaces, skeletal structures, larynx, and thyroid gland. Laryngeal non-Hodgkin lymphoma often shows on imaging studies a large submucosal mass lesion in the supraglottic region; extension to the glottis, subglottis, laryngeal cartilage, and strap muscles is less frequent (King et al. 2004) (Fig. 40).

Whenever an infiltrating mass is present in the extracranial head and neck region, lymphoma is a possible cause (Hermans et al. 1994).

6.3.2 Plasma Cell Neoplasms

Plasma cell neoplasms are unusual malignancies of the head and neck region. Multiple myeloma, solitary plasmacytoma of bone, and extramedullary plasmacytoma are plasma cell neoplasms.

The incidence of laryngeal plasmacytoma with respect to all malignant tumors of the larynx is small (Maniglia and Xue 1983). Approximately 6–18% of extramedullary plasmacytomas in the head and neck region occur in the larynx. The most common laryngeal sites are the epiglottis, followed by the vocal cords, false cords, ventricles, and subglottis. Laryngeal plasmacytomas are generally submucosal lesions, but can also be polypoid and may involve multiple contiguous sites of the larynx (Nofsinger et al. 1997).

The imaging findings of extramedullary plasmacytoma in the larynx are nonspecific. The major role of imaging is to confirm the presence of a tumor mass and show the extent of the lesion.

6.3.3 Metastasis

The larynx is a rare site for metastasis. In most cases, such a metastasis involves the supra- or subglottic submucosa, or the ossified laryngeal framework. The most common primary tumors are malignant melanoma, renal cell carcinoma, gastro-intestinal cancer, breast cancer, and pulmonary cancer (Batsakis et al. 1985; Nicolai et al. 1996). Laryngeal metastasis may be asymptomatic, or cause symptoms similar to primary laryngeal tumors (Fig. 41).

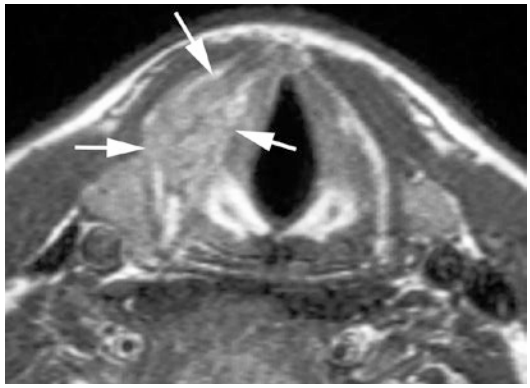

Fig. 41 Patient known with localized bladder cancer, treated by endoscopic resection. Because of pain during swallowing, an imaging study of the neck was performed. Gadolinium-enhanced axial T1-weighted spin echo image shows enhancing and expansile mass lesion (arrows) in the right thyroid cartilage wing. Resection was performed; pathologic examination revealed urothelial cancer, histologically similar to the previously removed bladder tumor: metastasis. The patient died a few months later due to widespread and rapidly progressive metastatic disease

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