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## Evaluation of laryngeal cartilage calcification in computed tomography

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### Summary

**Background:**

Computed tomography (CT) is one of the basic methods used for laryngeal carcinoma diagnostics. Osteosclerotic and osteolytic changes of the cartilages are considered as a common radiologic symptom of laryngeal neoplasms. The aim of this paper was to evaluate the prevalence of both osteosclerotic changes and focal calcification defects, which may be suggestive of osteolysis. Calcification was assessed in the thyroid, the cricoid and the arytenoids cartilages on CT images of the neck.

**Material/Methods:**

We have retrospectively analyzed neck CT examinations of 50 patients without any laryngeal pathology in anamnesis. The grade and symmetry of calcifications was assessed in the thyroid, the cricoid and the arytenoids cartilages.

**Results:**

Calcification of the laryngeal cartilages was present in 83% of the patients. Osteosclerotic lesions of the thyroid cartilage were seen in 70% of the patients (asymmetric in 60% of them), of the cricoid cartilage in 50% (asymmetric in 60%), and of the arytenoid cartilages in 24% (asymmetric in 67%). Focal calcification defects were present in the thyroid cartilage in 56% of the patients (asymmetric in 67% of them), in the cricoid cartilage in 8% (asymmetric in all cases), and in the arytenoid cartilages in 20% (asymmetric in 90%).

**Conclusions:**

Osteosclerotic changes and focal calcification defects, which may suggest osteolysis, were found in most of the patients. Therefore, they cannot be used as crucial radiological criteria of neoplastic invasion of laryngeal cartilages.

**Key words:**

**larynx • computed tomography • calcification**

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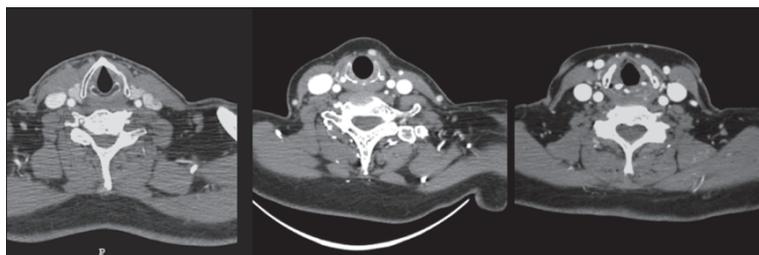
### Background

The larynx is an organ composed of cartilage, fibrous and muscular tissue. Its cartilaginous framework is formed by 9 cartilages: paired (arytenoid, corniculate and cuneiform) and unpaired (thyroid, cricoid and epiglottic). The structure of thyroid, cricoid and arytenoid cartilages is hyaline, surrounded by the cortical layer [1]. The physiological calcification process taking place in the laryngeal cartilages is subject to individual variations. In women, it usually begins around 15 years of age, and in men at the age of 18–20 years, progressing from the posterior region towards the

anterior portion of the larynx. Calcification of the thyroid cartilage starts in its posteroinferior part and progresses upwards and towards the front, causing complete ossification in man around 50, and in women around 76 years of age. Mineralization of the cricoid cartilage begins at the same time from a focus in the region of cricothyroid and cricoarytenoid junctions. However, complete mineralization of the cricoid cartilage is infrequent. Calcification of the arytenoid cartilages starts later: in men around 20 and in women around 23 years of age with the initial calcification focus at the base, whereas the vocal process and the apex of the cartilages are never calcified. It has been assumed that



**Figure 1.** Homogeneous osteosclerotization of the laryngeal cartilages: thyroid, cricoid and arytenoid.



**Figure 2.** Asymmetric focal calcification defects of the laryngeal cartilages: thyroid, cricoid and arytenoid.



**Figure 3.** Non-calcified cartilages of the larynx: thyroid, cricoid and arytenoid.

there is no close correlation between the subject's age and the extent of calcification of the laryngeal cartilages [2].

The most common changes in the structure of laryngeal cartilages are caused by neoplastic invasion, inflammatory processes (specific and non-specific), as well as injuries and iatrogenic conditions. The aim of the study was to assess the prevalence of osteosclerotic changes and focal calcification defects suggestive of osteolytic processes in the thyroid, cricoid and arytenoid cartilages in CT of the neck performed in patients without any laryngeal pathology in anamnesis.

### Material and Method

The results of neck CT scans performed in 50 patients (13 women, 37 men; mean age  $62 \pm 12.8$  years) were analyzed retrospectively. None of the subjects reported any laryngeal pathology in anamnesis and no pathologic involvement of the larynx was found on CT.

The indication for CT was assessment of stenosis of the carotid arteries due to atherosclerosis. The scans were performed according to the angio-CT protocol: helical acquisition  $4 \times 1.3$  mm, increment 0.6 mm, pitch 1.0, FOV 250, voltage 120 kV, current intensity 190 mAs. The mean radiation dose expressed as CTDI vol. was 16.6 mGy. The data were initially reconstructed using 800 HU windows of 2000 HU. The obtained angio-Ct images were then processed using multislice reconstructions for soft tissue and bone windows.

The extent of laryngeal cartilage calcification was assessed: osteosclerotic changes (Figure 1), focal calcification defects

which might suggest osteolytic changes (Figure 2) as well as symmetry or asymmetry of these changes. Differences in prevalence of calcification variants in the particular cartilages were assessed using chi2 test with significance level of  $p < 0.05$ .

### Results

Inhomogeneous calcification of the laryngeal cartilages was found in 41 patients (82%), whereas in the remaining 9 subjects the cartilages were non-calcified (Figure 3). The distribution of osteosclerotic changes and focal calcification defects in the particular cartilages are presented in Table 1.

Osteosclerotic changes and focal calcification defects were seen most frequently in the thyroid cartilage ( $p < 0.02$ ).

Focal calcification defects were the least frequent in the cricoid cartilage ( $p < 0.05$ ). Both osteosclerotic changes and focal calcification defects were significantly more frequent in men than in women ( $p < 0.05$ ), except for osteosclerotic changes in arytenoid cartilages (Table 2).

### Discussion

Qualification of patients with tumors of the larynx for surgery and/or radiotherapy is based on laryngological examination and microlaryngoscopy (with collection of the specimens for histopathological investigation) as well as imaging modalities, such as CT and, less frequently, MR. Laryngovideostroboscopy, which is a non-invasive, reproducible and simple, but not widely available method, is also very useful [3]. Stage T1 and T2 laryngeal tumors involving

**Table 1.** Prevalence of osteosclerotic changes and focal calcification defects in the study group.

	Osteosclerotic changes			Focal calcification defects		
	Present	Symmetric	Asymmetric	Present	Symmetric	Asymmetric
Thyroid cartilage	70%	40%	60%	56%	36%	64%
Cricoid cartilage	50%	40%	60%	8%	0%	100%
Arytenoid cartilages	24%	33%	67%	20%	10%	90%

**Table 2.** Prevalence of osteosclerotic changes and focal calcification defects in women (F) and men (M).

	Osteosclerotic changes		Focal calcification defects	
	F	M	F	M
Thyroid cartilage	18%	52%*	16%	40%*
Cricoid cartilage	15%	35%*	2%	6%*
Arytenoid cartilages	12%	12%	8%	12%*

\* p&lt;0.05.

the glottis are treated with laser microsurgery or conventional partial laryngectomy – to preserve the voice. Stage T3 and T4 tumors qualify the patients for radical surgery – total laryngectomy with cervical lymph node resection, followed by radiotherapy [4,5]. If a well-delineated tumor lesion involves the anterior commissure, accurate T staging may be difficult. In this region of the glottis, the mucous membrane adheres closely to the thyroid cartilage, and its involvement is associated with a qualification change from voice-sparing surgical treatment to radical laryngectomy [6]. Neoplastic invasion within the laryngeal cartilages results in poorer response to radiotherapy and increases considerably the risk of relapses [7]. Infiltration of the cartilages excludes partial laryngectomy and provides a contraindication for radiotherapy, which is the only alternative method of treatment. Therefore, assessment of neoplastic infiltration within the laryngeal cartilages is an important element of imaging diagnostics in the cases of larynx and laryngopharynx tumors [5], and the abnormalities in chondrous structure, including also osteosclerotic and osteolytic lesions, are the basis for detection of tumor invasion involving the cartilages in CT images [8]. On the other hand, according to some authors, there are no significant differences in the prevalence of local relapses, distant metastases and survival time between patients without the signs of laryngeal cartilage infiltration (stage T3) and with laryngeal cartilage infiltration present (stage T4) [9].

Computed tomography (CT) and magnetic resonance (MR) are considered to be the best methods of imaging of the larynx [10–12]. CT is preferable because of shorter duration of the examination, which is important especially in the group of patients who have problems with holding breath, which leads to movement-related artifacts [13]. The diagnostic accuracy of both methods with respect to laryngeal carti-

lage infiltration is similar, but CT is more specific and less sensitive than MR [4,13]. The only radiological criterion of laryngeal cartilage infiltration is considered to be the presence of the neoplastic process on both sides of the cartilage: internal and external [5,13,14], although also this criterion is not applicable in all patients. Becker et al. describe the cases of false-positive diagnoses of extralaryngeal progression of the neoplastic process: in one patient it was due to focal contrast enhancement of the subhyoid muscles and the thyro-arytenoid muscle, in another – enhancement of a lymph node in the vicinity of the larynx [5].

The thyroid, arytenoid (except the vocal process and the apex) and cricoid cartilage are hyaline cartilages which are calcified with age. In adults, these cartilages consist of three components: non-mineralized hyaline, the cortical layer and the marrow cavity containing adipose tissue. In young subjects, the hyaline component predominates, and the cortical layer begins to develop in the third decade of life with the gradual calcification process. Calcification proceeds according to a specific algorithm, individual for each type of cartilage, usually from the posterior part towards the front of the cartilaginous framework of the larynx. In CT the calcification process corresponds with the hyperdense areas, whereas the marrow cavity and the hyaline component are seen as hypodense (like soft tissue) [15]. The sclerotized laryngeal cartilage is presumed to be more susceptible to neoplastic infiltration than the non-calcified areas. The latter are capable of secretion of proteins inhibiting collagenases and tumor angiogenesis factors [5]. A two-stage mechanism of laryngeal tissue infiltration, including the osteoblastic phase and the osteoclastic activity phase, has been proposed [5,8]. The first one involves transformation of hyaline cartilage into osseous tissue, which is represented radiologically as sclerotization, and the second one osteolytic process.

In the studied population, osteosclerotic changes corresponding to the calcification process, were most frequent in the thyroid cartilage (in 70% of patients) and in the cricoid cartilage (50%), and were usually asymmetric. The arytenoid cartilages were characterized by the most homogeneous structure; no changes were found in 75% of cases. Schmalfluss et al. observed sclerotic changes in the arytenoid cartilages only in 16% of patients, with women predominant in the group (80%) and significantly more often they were left-sided [16]. Osteosclerotic changes in laryngeal cartilages of tumor patients can be the calcification foci formed as a result of normal mineralization process, inflammatory lesions (response of the cartilage to the neoplastic process), or the symptoms of neoplastic infiltration. In the material analyzed by Becker et al, tumor cells were

found only in 45% of thyroid and cricoid cartilages and in 16% of arytenoid cartilages with sclerotic foci in patients with a neoplastic process. Therefore, in view of the impossibility of verification of the finding by biopsy, detection of neoplastic infiltration with radiological methods is important.

In a study by Becker et al. [5], application of different combinations of diagnostic criteria for laryngeal cartilage infiltration in CT (involvement of the cartilage by the tumor, sclerotization, a tumor adjacent to non-calcified cartilage, uneven outlines of the cartilage, focal calcification defects and involvement of the marrow cavity) allowed to detect neoplastic infiltrations with 7–83% sensitivity and 40–100% specificity in comparison with histopathological investigation. The most sensitive criterion (63–83% depending on the assessed cartilage) was sclerotization, defined as thickening of the calcified layer or increased calcification within the marrow cavity, although, because of its specificity, the authors recommend to apply this parameter only in the assessment of the cricoid and arytenoid cartilages. However, the highest specificity was seen in the case coincidence of a tumor-like lesion involving the cartilage and demineralization foci (83–99%). It should be emphasized here that non-calcified laryngeal cartilages present on CT

a density similar to that of tumor tissue, which can lead to incorrect diagnosis of neoplastic infiltration within these cartilages [13].

Our results confirm the doubts associated with the possibility of neoplastic process detection in the laryngeal cartilage on the basis of extent and pattern of their calcification. In the population analyzed in this study, the structure of the laryngeal cartilages was altered in the majority of cases (82%) and were usually asymmetric. Tumors of the larynx usually occur in elderly patients, and coincide with calcifications of laryngeal cartilages, advanced at this age, which can result in false-positive and false-negative results of assessment of neoplastic infiltration and limited value of CT as a method helpful in staging of laryngeal tumors according to TNM classification [17,18].

## Conclusions

Osteosclerotic changes and focal calcification defects were present in most of the patients without any signs of laryngeal tumors. Therefore, they cannot be used as crucial radiological criteria for the diagnosis of pathologic processes, and especially neoplastic invasion, of laryngeal cartilages.

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