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Potential pitfalls of computed tomography in advanced laryngeal cancer

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Abstract

Objective: In laryngeal cancer the most suspected regions of invasion are preepiglottic space (PES), anterior commissure (AC), thyroid cartilage (TC), subglottic region (SR) and extralaryngeal spread (ELS). The objective of this study is to compare the results of preoperative computed tomography (CT) with postoperative histopathologic analysis in these critical regions for the total or partial laryngectomy.

Methods: Eighty-nine patients, who had undergone total laryngectomy with a diagnosis of laryngeal cancer reported that squamous cell cancer (SCC) between 2005 and 2013, were reviewed retrospectively. All the patients, after the first application done total laryngectomy before flexible laryngoscopy, computed tomography for the neck and endoscopic biopsy with direct laryngoscopy. Histopathological results of PES, AC, TC, ELS and SR invasion are compared to preoperative CT findings and determined of specificity, sensitivity, false negative and false positive results and rate of accuracy.

Results: All the patients were male, median age was 67 (range: 48 to 81) years. Fifty-six patients were in T4 and 33 patients in T3 stage. Compared to results between positive CT findings and negative histopathological examination; PES invasion in 41 patients/ 5 patients, AC invasion was found in 38/ 15 patients, TC invasion in 28/16 patients, SR invasion in 49/ 9 patients and ELS invasion in 25 /7 patients. Accuracy rate of computed tomography in these regions are 85%, 64%, 76%, 79%, and 83%, respectively. All the results especially thyroid cartilage invasion were statistically significant.

Conclusion: In all regions invasion, CT has a low diagnostic reliability in high-grade laryngeal cancer in our study. We suggested that histopathological results are the gold standard intraoperatively for determining total or partial laryngectomy.

Keywords: Computed tomography, larynx carcinoma, accuracy.

Özet: İleri evre larenks kanserinde bilgisayarlı tomografideki potansiyel tuzaklar

Amaç: Larenks kanserinde invazyonda en şüpheli alanlar preepiglottik boşluk (PEB), ön komissür (ÖK), tiroid kıkırdak (TK), subglottik bölge (SB) ve ekstralarengeal invazyon (ELY) varlığıdır. Çalışmadaki amacımız total ya da parsiyel larenjektomi için bu kritik bölgelerin preoperatif bilgisayarlı tomografi (BT) incelemesi ve postoperatif histopatolojik analizinin karşılaştırılmasıdır.

Yöntem: 2005–2013 yılları arasında raporda skuamöz hücreli kanser tanısı nedeniyle total larenjektomi uygulanan 89 larenks kanseri hastası retrospektif olarak incelendi. Hastaların hepsine başvuru sonrası fleksibl laringoskopi, boyuna yönelik bilgisayarlı tomografi ve sonrasında direkt larengoskopi eşliğinde endoskopik biyopsi yapılarak total larenjektomi uygulandı. Histopatolojik sonuçlar PEB, ÖK, TK, ELY ve SB invazyonları operasyon öncesi BT raporlarındaki invazyon sonuçlarıyla karşılaştırıldı, spesifite, sensitivite, yalancı negatif ve yalancı pozitif sonuçlar ile doğruluk oranları belirlendi.

Bulgular: Hastaların tümü erkekti ve yaş aralığı 48 ile 81 arasında olup ortalama yaş 67 bulundu. Elli altı hasta T4 evre, 33 hasta T3 evre larenks kanseri idi. BT'de pozitif, histopatolojik olarak negatif saptanan hastalar karşılaştırıldığında; PEB invazyonu 41/5 hasta, ÖK invazyonu 38/15 hasta, TK invazyonu 28/16 hasta, SB invazyonu 49/9 hasta ve ELY 25/7 hastada görüldü. BT'nin bu bölgelerdeki doğruluk oranları sırasıyla; %85, %64, %76, %79, %83 olarak bulundu. Özellikle tiroid kartilaj invazyonunda olmak üzere tüm sonuçlar istatistiksel olarak anlamlıydı.

Sonuç: Çalışmamızda ileri evre larenks kanserinde BT'nin tüm bahsedilen bölgelerde tanısal değerinin düşük olduğunu gördük. Total ya da parsiyel kararı vermede intraoperatif olarak histopatolojik değerlendirmenin altın standart olduğu kanaatindeyiz.

Anahtar sözcükler: Bilgisayarlı tomografi, larenks kanseri, doğruluk.

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Laryngeal cancer is the second most common head and neck cancer after thyroid cancer. The 5-year survival rate exceeds 90% if the patient is diagnosed at an early stage and 60% to 70% otherwise.[1] The aim of surgery is to achieve local control while preserving the functions of speech and swallowing without a permanent tracheostomy. Conservative surgery with radiotherapy (RT) is a good option if possible.[2] However, total laryngectomy is required if there is extralaryngeal spread (ELS) or invasion of the pre-epiglottic space (PES), thyroid cartilage (TC), arytenoid cartilage (AC), SR, or interarytenoid region.[3]

Before planning cancer surgery, staging is important and might necessitate indirect laryngoscopy, imaging, and biopsy under direct laryngoscopy.[4] However, submucosal and deep invasion cannot be identified with indirect or direct laryngoscopy. Sagittal or coronal radiological imaging should be performed to detect ELS and deep invasion, especially of the PES, AC, SR, and TC.[5] This report compares computed tomography (CT) findings with surgical and histopathological findings to determine the reliability of CT in advanced laryngeal cancer.

Materials and Methods

The study retrospectively reviewed 89 patients (stage T4, n=56; stage T3, n=33) who underwent total laryngectomy for treatment of high-grade laryngeal cancer from 2005 to 2013. The study was approved by the local institutional review board. All tumors were reported as squamous cell carcinoma (SCC). Patients with history of preoperative laryngeal surgery or RT were excluded from the study. All of the patients were male with an average age of 67 (range: 48 to 81) years. After a detailed inspection using flexible nasopharyngolaryngoscopy, CT imaging was performed using an Aquilion 64 system (Toshiba, Tokyo, Japan), and 64 sections of the larynx were obtained. Transverse images were obtained (120 kV, 200 mAS, 2-mm section thickness) during normal inspiration after injecting ionizing contrast fluid. All CT images were inspected by a radiologist with 10 years of experience in head and neck radiology, and any suspicion of invasion was accepted as a site of invasion. A pathologist with 10 years of experience in head and neck pathology examined the specimens histopathologically. The total laryngectomy specimens were fixed in formalin and paraffin, cut into 3- to 4-Ìm-thick slices, stained with hematoxylin and eosin, and inspected under light microscopy.

The histopathological results of ELS and invasion of the PES, AC, TC, and SR were compared with the preoperative CT findings (Figs. 1–5). The McNemar test and Z-test were used for the statistical analysis. Data were analyzed sing SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA). A p value of <0.05 was accepted as statistically significant.

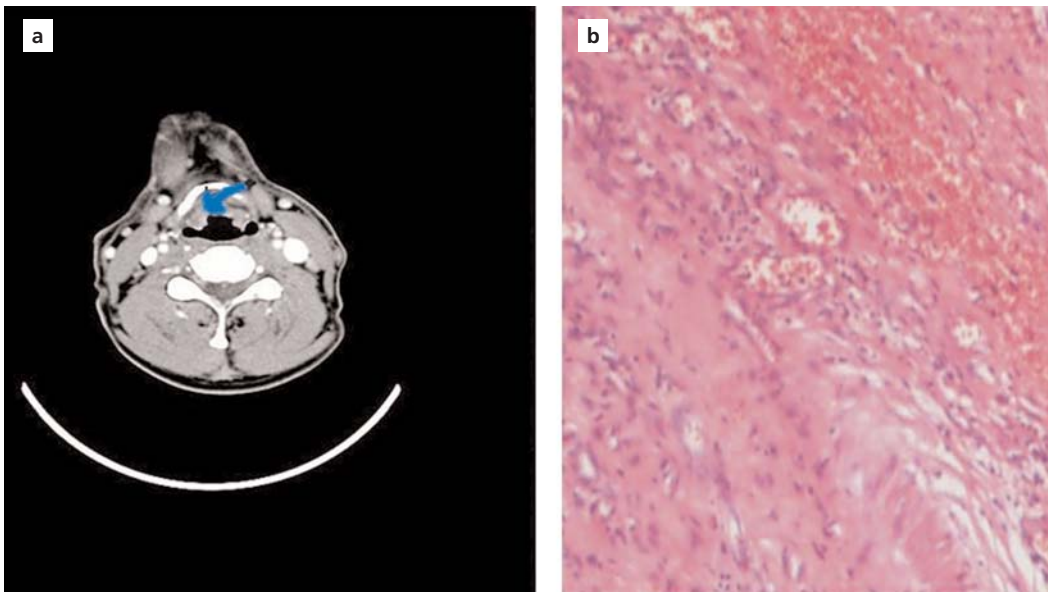

Fig. 1. (**a**) Contrasted axial CT imaging of epiglottis with infiltrative tumor, preepiglottic spread (arrow), and (**b**) its histopathological image (HE ×10).

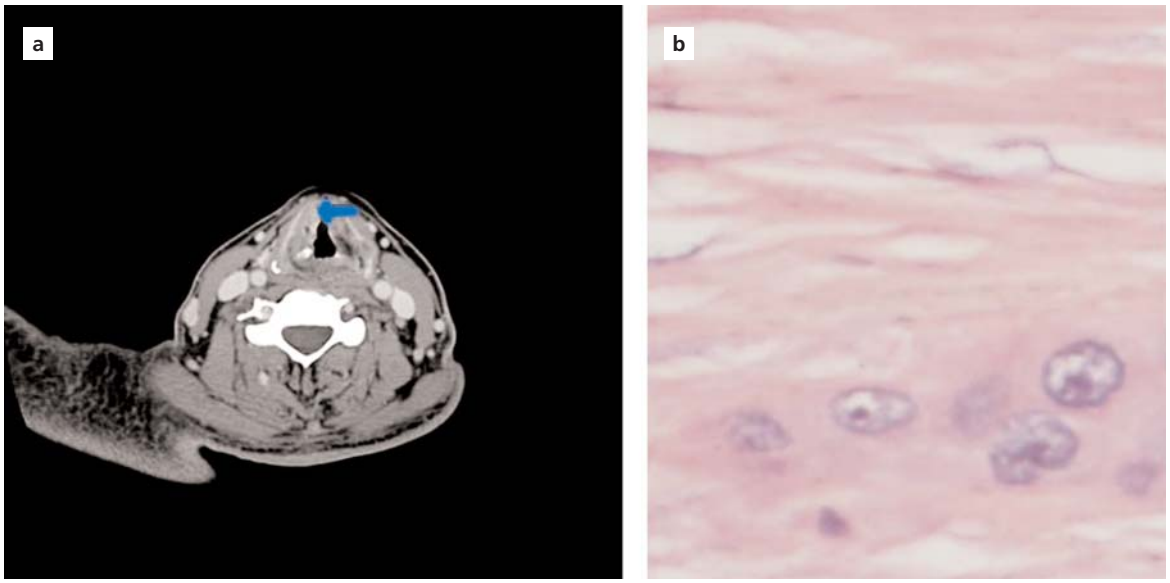

Fig. 2. (**a**) Contrasted axial CT imaging of a primary tumor located on right vocal cord and anterior commissure (arrow) and (**b**) its histopathological image (HE ×20).

Results

Pre-epiglottic space invasion was found on the preoperative CT images in 41 patients, 5 of whom had negative histopathological findings. The sensitivity, specificity, false-negative, false-positive, and accuracy rates of the CT findings for PES invasion were 83%, 87%, 16%, 12%, and 85%, respectively (Table 1). SR invasion was seen on CT in 49 patients, 9 of whom had negative histopathological findings; the sensitivity, specificity, false-negative, false-positive, and accuracy rates were 79%, 70%, 15%, 29%, and 79%, respec-

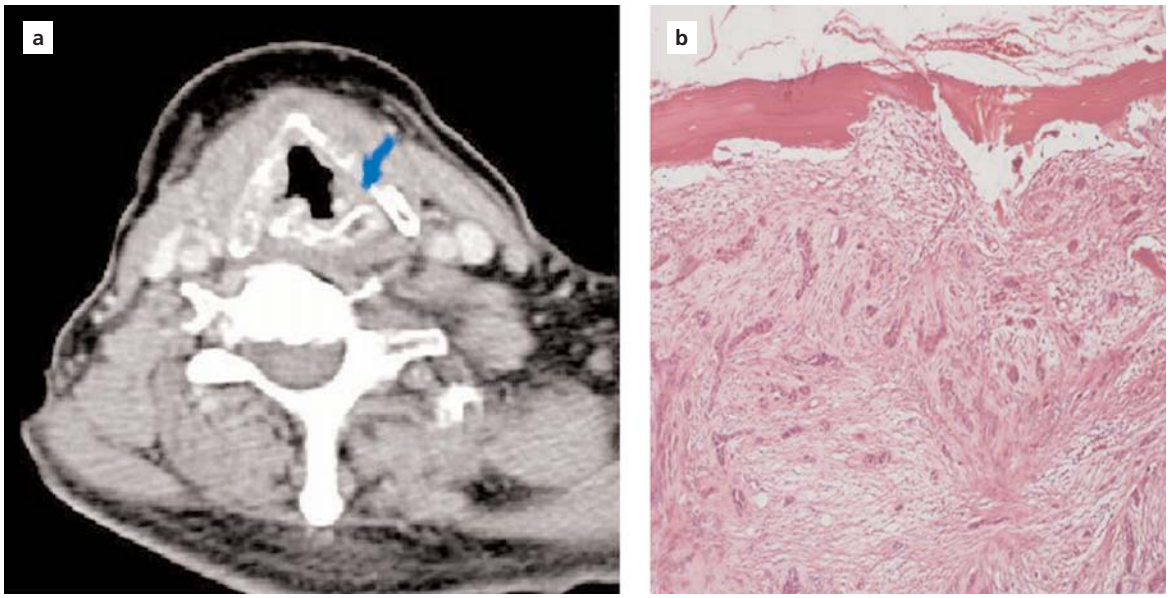

Fig. 3. (**a**) Contrasted axial CT imaging of thyroid cartilage with invasion especially on the right side and (**b**) its histopathological image (HE ×10).

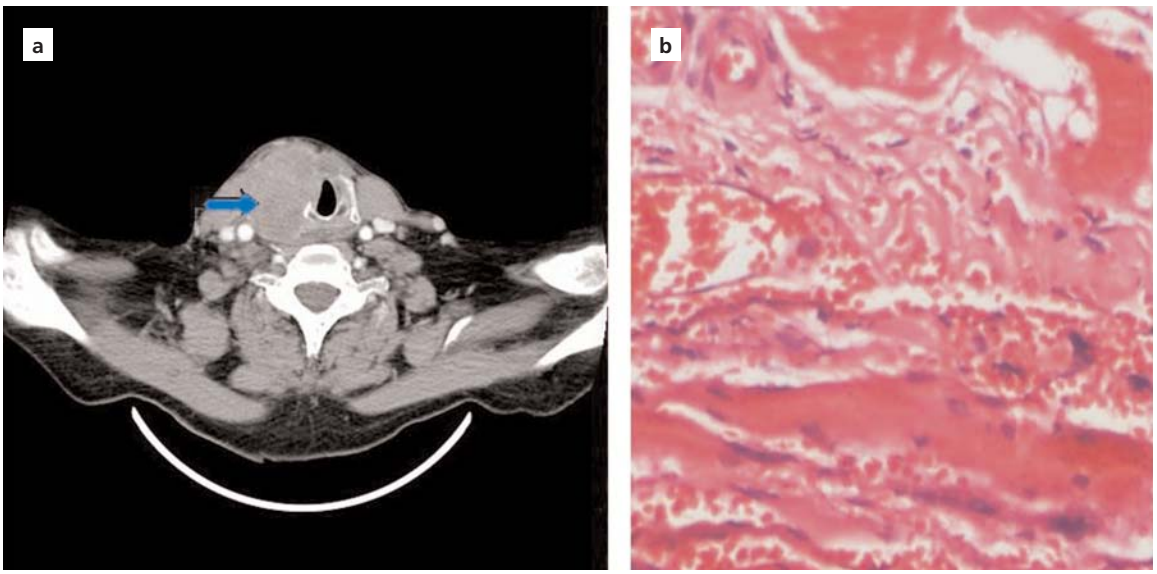

Fig. 4. (**a**) Contrasted axial CT imaging of extralaryngeal strep muscles with invasion and (**b**) its histopathological image (HE ×10).

tively (Table 2). AC invasion was seen on CT in 38 patients, 15 of whom had negative histopathological findings; the sensitivity, specificity, false-negative, false-positive, and accuracy rates were 69%, 55%, 30%, 44%, and 64%, respectively (Table 3). TC invasion was seen on CT in 28 patients, 16 of whom had negative histopathological findings; the sensitivity, specificity, false-negative, false-positive, and accuracy rates were 84%, 71%, 15%, 28%, and 76%, respectively (Table 4). Finally, ELS was seen on CT in 25 patients, 7 of whom had negative histopathological findings; the sensitivity, specificity, false-negative, false-positive, and accuracy rates were 75%, 87%, 24%, 12%, and 83%, respectively (Table 5).

According to the McNemar test, the difference between the CT findings and histopathological findings was significant only for TC invasion ($p<0.05$). Given the small sample size, the Z test was used as a second test. This showed that the differences between the CT findings and histopathological findings were significant for ELS and PES, AC, TC, and SR invasion ($p< 0.05$).

Discussion

More than 90% of laryngeal cancers are SCC. Most cases occur in male smokers 51 to 60 years of age. SCC is classified into three types: infiltrative, bulky, and mixed. SCC may be restricted to the mucosal or submucosal regions, or deep invasion can occur.[6] As endoscopic examination has a limited ability to detect submucosal or deep invasion, radiological imaging is often performed. Sometimes, however, radiologi-

Fig. 5. Contrasted axial CT imaging of an early stage primary tumor on the right subglottic region, invasion to this site is observed by the pathologist macroscopically.

Table 1. Comparison of preoperative CT and postoperative histopathology in preepiglottic space invasion.

Preoperative	Preepiglottic space invasion (histopathologically)						
CT	+	%	-	%	Total	%	p
+	41	46.06	5	5.61	46	51.68	0.774
-	8	8.98	35	39.32	43	48.31	
Total	49	55.04	40	44.93	89	100	
Sensitivity							83%
Specificity							87%
False (+) value							12%
False (-) value							16%
Accuracy							85%

Table 2. Comparison of preoperative CT and postoperative histopathology in subglottic region invasion.

Preoperative	Subglottic region invasion (histopathologically)						
CT	+	%	-	%	Total	%	p
+	49	55.05	9	10.11	58	65.16	1.000
-	9	10.11	22	24.71	31	34.83	
Total	58	65.16	31	34.82	89	100	
Sensitivity							84%
Specificity							70%
False (+) value							29%
False (-) value							15%
Accuracy							79%

Table 3. Comparison of preoperative CT and postoperative histopathology in anterior commissure invasion.

Preoperative	Anterior commissure invasion (histopathologically)						
CT	+	%	-	%	Total	%	p
+	38	42.69	15	16.85	53	59.55	0.860
-	17	19.10	19	21.34	36	40.44	
Total	55	59.79	34	38.19	89	100	
Sensitivity							69%
Specificity							55%
False (+) value							44%
False (-) value							30%
Accuracy							64%

cal imaging also fails to reveal the depth of invasion because of the tumor location, radiologist's interpretation, or imaging device used.[7]

The most common site of invasion is the TC (37% of cases), and such invasion most frequently involves the midline.[8] Once cartilage invasion occurs, the tumor is stage T3 or T4, and the success rate of RT decreases while the risk of recurrence, chondronecrosis, and a nonfunctional larynx after RT increase. In the past, conservative laryngeal surgery was used to manage laryngeal cancer with minimal cartilage invasion. More recently, however, more invasive surgery has been preferred.[9] The reported sensitivity and specificity of CT for detecting cartilage invasion range from 46% to 91% and 68% to 94%, respectively.[10] Because the TC consists of unmineralized hyaline cartilage, signs of invasion are difficult to detect.[11] In this study, the sensitivity, specificity, false-negative, false-positive, and accuracy rates of the preoperative CT findings of cartilage invasion were 83%, 87%, 16%, 12%, and 85%, respectively. These results concur with the literature; nevertheless, there was a significant difference in the CT and postoperative histopathological findings of TC invasion.

The PES or Boyer's space is a triangular region that contains a large amount of fat and small amounts of elastic fibers, collagen fibers, and lymphatic vessels. This space is bordered by the hyoepiglottic ligament superiorly, thyrohyoid membrane and thyroid cartilage anteriorly, and epiglottis and thyroepiglottic ligaments posteriorly.[12] Because the epiglottis is a weak barrier, laryngeal cancer can spread to the PES. Once PES invasion occurs, the tumor is stage T3, the prognosis after RT is poorer, and the local metastasis rate increases.[13] The reported sensitivity and specificity of CT findings for PES invasion are 86% and 73%, respectively.[14] In this study, the sensitivity, specificity, false-negative, false-positive, and accuracy rates of the preoperative CT findings were 84%, 71%, 15%, 28%, and 76%, respectively, which concurs with the literature.

Table 4. Comparison of preoperative CT and postoperative histopathology in thyroid cartilage invasion.

Preoperative	Thyroid cartilage invasion (histopathologically)						
CT	+	%	-	%	Total	%	p
+	28	31.46	16	17.97	44	49.43	0.027
-	5	5.61	40	44.94	45	50.56	
Total	33	37.07	56	62.91	89	100	
Sensitivity							84%
Specificity							71%
False (+) value							28%
False (-) value							15%
Accuracy							76%

Table 5. Comparison of preoperative CT and postoperative histopathology in extralarengeal invasion.

Preoperative	Extralaryngeal invasion (histopathologically)						
CT	+	%	-	%	Total	%	p
+	25	28.08	7	7.86	53	59.55	0.791
-	8	8.98	49	55.05	36	40.44	
Total	33	37.06	56	62.91	89	100	
Sensitivity							75%
Specificity							87%
False (+) value							12%
False (-) value							24%
Accuracy							83%

The SR is a transition zone between the larynx and trachea, where stratified squamous epithelium changes to respiratory epithelium. Primary cancer of the SR is rare, and most SR cancer occurs as a result of invasion from other parts of the larynx. In the past, a laryngeal tumor at the level of the cricoid cartilage was called SR cancer. The conus elasticus is found between the free border of the vocal cord and upper part of the cricoid cartilage; it serves as a relative barrier, and a tumor may spread laterally and anteriorly to the SR along the conus elasticus. When a tumor invades this membrane, cricoid invasion follows, and the tumor is stage T4.[15] Souza et al. reported that the accuracy, sensitivity, and specificity of CT findings for SR invasion were 95.0%, 100.0%, and 93.5%, respectively, while we obtained sensitivity, specificity, false-negative, false-positive, and accuracy rates of preoperative CT findings of 79%, 70%, 15%, 29%, and 79%, respectively.[16] Our results are lower than those previously reported, possibly because SR region invasion can be confused with bulging of a tumor.

According to Olofsson, the AC is a small region limited by the anterior angle of the ventricles and is located 2 to 3 mm inferior to the anterior parts of the vocal cords. Tumors in the midline of the laryngeal surface of the epiglottis invade the AC. This results in TC invasion along Broyles' ligament.[17] When a tumor is closer than 2 to 3 mm from the AC, conservative surgery to protect the voice is no longer appropriate. With gross tumor invasion of the AC, the reported accuracy of CT was 96.5%.[18] In our study, the sensitivity, specificity, false-negative, false-positive, and accuracy rates of the preoperative CT findings were 69%, 55%, 30%, 44%, and 64%, respectively. Our results are lower than reported, possibly because of the poor quality of imaging, high tumor grade, and bulging of the vocal cord tumors.

Extralaryngeal spread can occur in many ways. The tumor can penetrate the cartilage and spread to the strap muscles and anterior and lateral soft tissues. Spread to the anterior soft tissues can follow invasion of the thyrohyoid membrane, pre-epiglottic space, paraglottic space, and constrictive muscles. Spread to the piriform sinus laterally and to the interarytenoid, postcricoid, hypopharynx, and proximal esophagus posteriorly can be seen, as can spread to the cricothyroid membrane and cervical trachea inferiorly. Once such spread occurs, the tumor is deemed stage T4. In one study, the sensitivity and positive predictive value of preoperative CT findings of ELS were 82% and 49%, respectively.[19] In our study, the sensitivity, specificity, false-negative, false-positive, and accuracy rates of preoperative CT were 75%, 87%, 15%, 12%, and 76%, respectively, concurring with previously reported values.

Conclusion

Our study is first reported in the literature that evaluated all of the critical regions for the total or partial laryngectomy on computed tomography in advanced laryngeal cancer. Statistical analysis showed that preoperative CT imaging does not provide dependable information about ELS or invasion of the PES, AC, TC, or SR. Consequently, these regions are potential preoperative traps. Tumor invasion to these regions affects patient management and should thus be assessed during surgery using frozen section analysis.

Conflict of Interest: No conflicts declared.

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