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Main Article

Predictive indicators for thyroid cartilage involvement in carcinoma of the larynx seen on spiral computed tomography scans

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Abstract

Objectives: Recent studies have shown that the spiral computed tomography (CT) scan is a sensitive imaging modality for predicting neoplastic invasion of thyroid cartilage. The objectives of our study were: to assess the accuracy of pre-operative spiral CT in predicting thyroid cartilage involvement in patients with carcinoma of the larynx; and to elucidate the factors that would accurately indicate cartilage involvement.

Material and methods: Medical records, including spiral CT scans and pathological reports, were reviewed for 27 patients who had undergone laryngectomy in two major hospitals in south Wales. A consultant radiologist with special interest in cross-sectional imaging re-evaluated the scans to assess neoplastic involvement of the thyroid cartilage, based on definite, objective criteria. These criteria included: soft tissue asymmetry; loss of medullary space; spiky or irregular surface; distortion of cartilage framework; and abnormal soft tissue on both sides of the cartilage. The radiological findings were then correlated with the histopathological evidence of cartilage invasion by the tumour.

Results: Out of the 27 cases, 15 had evidence of histological invasion of thyroid cartilage. The most specific criterion to predict thyroid cartilage involvement was the presence of tumour on both sides of the cartilage (specificity of 91 per cent, sensitivity of 66 per cent). Combining two criteria increased both the sensitivity and the specificity to 86 and 91 per cent, respectively.

Key words: Laryngeal Neoplasms; Computed Tomography; Cartilage

Introduction

Carcinoma of the larynx accounts for two to five per cent of all cancers. Failure to identify neoplastic involvement of the thyroid cartilage may result in under-staging of the tumour, which may in turn affect the prognosis adversely. The most commonly employed staging system for laryngeal malignancies is based on the tumour–node–metastasis (TNM) classification. As per the TNM staging, involvement of the thyroid cartilage is designated as T_4 and the tumour would be staged as stage IV. In stage IV, even now, the most appropriate treatment option is total laryngectomy combined with post-operative radiotherapy. In less advanced cases (stage III or lower), organ preservation surgery and/or radiotherapy are viable options, with the aim to achieve cure with relatively reduced morbidity. Lately, developments in endoscopic laser surgery have allowed a reduction of the number of indications for total laryngectomy. However, endoscopic laser procedures are only suitable for cases with no direct extra-laryngeal spread. Primary radiotherapy in the presence of neoplastic cartilage invasion is invariably associated with a lower response rate and higher rates of tumour recurrence and radiation-induced chondronecrosis.[1,2] Nakayama and Brandenburg found that 50 per cent of tumours clinically and radiologically staged as T_3 displayed invasion of the thyroid cartilage, usually at the thyroid notch; 65 per cent of these potentially stage IV cancers had only microinvasion, without penetration of the thyroid cartilage.[3] Cartilaginous invasion is associated with a poorer response to radiation therapy, tumour recurrence and radiation-induced necrosis.[4,5]

The perichondrium covering the cartilage acts as a resistant barrier to invasion by tumour.[6] It has been shown that cartilage invasion mainly occurs where the attachment of the collagen bundles interrupts the perichondrial barrier. As the cancer cells multiply, they separate the collagen bundles, forming linear passageways through the perichondrium. Thus, the sites of attachment of the strongest membranes, such as the anterior commissure tendon, are also the most frequent sites of invasion. Invasion of

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the cartilage framework invariably takes place at the site of ossified or calcified cartilage.[7] Non-ossified cartilage is resistant to tumour infiltration due to its capacity to release proteins that inhibit tumour angiogenetic factor and collagenases.[8,9] However, Becker *et al*. noted that in 11 per cent of cases the cartilage invasion was limited to the non-ossified areas.[1]

Despite the increase in popularity of magnetic resonance imaging (MRI), computed tomography (CT) is still the imaging modality of choice for the assessment of laryngeal cancers. With the development of high resolution spiral CT scanners, the application of this imaging modality has increased significantly. Recent published reports have shown that CT may yield acceptable sensitivity for detecting neoplastic invasion of laryngeal cartilage if the diagnostic criteria are selected and combined appropriately.[10]

Material and methods

This was a retrospective study involving patients with carcinoma of the larynx who had undergone laryngectomy in two major hospitals in south Wales. A total of 27 patients were involved in the study. Nine of these patients underwent pre-operative radiotherapy but none received radiotherapy in the immediate two years prior to the surgery. The spiral CT scans of all these patients were viewed by a consultant radiologist with a special interest in cross-sectional imaging, who evaluated the scans and predicted the possibility of thyroid cartilage invasion based on the following defined criteria. The radiologist was unaware of the histological results at the time of reporting.

Criteria

Soft tissue asymmetry. This is seen when tumour is present adjacent to the thyroid cartilage, leading to asymmetry of the laryngeal sections.

Medullary space sclerosis. This includes thickening of the outer or inner aspect of the cartilage as well as increased ossification of the medullary cavity, either partial or total.

Spiky surface. This includes undulation, wave-like shaping or indention of the cartilage. This can be due to localized lysis, punched-out defects in the cartilage or erosion.

Distorted framework. This sign is present when the alignment of the cartilage framework is distorted.

Abnormal tissue on both sides of the cartilage. This is present when radiologically detectable tumour on both sides of the cartilage is seen, with or without an identifiable breach of the cartilage.

Results

The results are shown in Table I. All patients had soft tissue asymmetry on spiral CT, as expected. However, only 12 of them had cartilage invasion. Soft tissue asymmetry alone was a poor indicator of cartilage invasion. Obliteration of the medullary space or sclerosis was seen in six patients. A spiky surface was noted in five and the cartilage framework

TABLE I

POSITIVE DIAGNOSTIC CRITERIA*

Case	Soft tissue asymmetry	Medullary space sclerosis	Spiky surface	Distorted framework	Abnormal soft tissue on both sides	Histology
1	+			+	+	+ve
2	+				+	+ve
3	+	+			+	+ve
4	+				+	+ve
5	+			+	+	+ve
6	+			+	+	+ve
7	+		+		+	+ve
8	+					−ve
9	+					+ve
10	+					−ve
11	+					−ve
12	+				+	+ve
13	+					−ve
14	+					−ve
15	+	+				+ve
16	+		+		+	+ve
17	+					−ve
18	+					−ve
19	+					−ve
20	+					+ve
21	+	+				+ve
22	+	+	+		+	+ve
23	+					−ve
24	+					−ve
25	+	+	+	+	+	−ve
26	+	+	+			+ve
27	+					−ve

*In the 27 cases studied. + = sign present; +ve = positive; −ve = negative

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TABLE II

SENSITIVITY, SPECIFICITY, POSITIVE PREDICTIVE VALUE AND NEGATIVE PREDICTIVE VALUE OF DIAGNOSTIC CRITERIA USED

Criteria	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Medullary space sclerosis	33	91	83	52
Spiky surface	26	91	80	50
Distorted framework	20	91	75	47
Abnormal tissue on both sides	66	91	90	68
Two criteria combined	86	91	93	85

was distorted in four. Eleven scans showed evidence of abnormal soft tissue on both sides of the cartilage.

The presence of any of these features, along with soft tissue asymmetry, has been found to be a strong indicator of cartilage invasion. However, one patient who had all five radiological criteria did not have any pathological evidence of cartilage invasion. The histological examination in this case revealed the presence of extensive cartilage necrosis.

The sensitivity, specificity, positive predictive value and negative predictive value are shown in Table II.

TABLE III

SENSITIVITY AND SPECIFICITY OF CT SCANNING IN IDENTIFYING CARTILAGE INVASION, VARIOUS REPORTS

Author	Year	Sensitivity (%)	Specificity (%)
Castelijns *et al.*[17]	1988	46	91
Sulfaro *et al.*[18]	1989	47	88
Becker *et al.*[11]	1995	66	94
Zbaren *et al.*[12]	1996	67	87
Becker *et al.*[1]	1997	61	92
Amilibia *et al.*[19]	2001	54	91
Current series	2006	86	91

CT = computed tomography

Discussion

Magnetic resonance image scanning has become increasingly involved as a sensitive imaging modality for detecting neoplastic involvement of the thyroid cartilage, primarily because of its high negative predictive value. However, recent reports have shown its positive predictive value to be only 68–71 per cent.[10–12] This low positive predictive value is due to the failure of MRI to distinguish oedema and inflammation surrounding the tumour from true cartilage invasion. In addition, MR imaging can be a lengthy, expensive procedure. Patient motion as simple as swallowing during the scanning may generate significant artefacts. Magnetic resonance imaging also overestimates cartilage invasion.[13] Computed tomography scanning provides a clearer illustration of bony structures and calcification than does MRI. It is less expensive, faster and less susceptible to motion artefacts. For all practical purposes, the CT scan continues to be widely used for diagnosing neoplastic involvement of the cartilage. Although MRI is significantly more sensitive, it is less specific than CT in detecting neoplastic cartilage invasion.[14,15]

With the introduction of spiral CT in the late 1990s, the quality of the reconstructed image improved significantly. Spiral CT is entirely dependent on the emergence of 'slip ring' technology, which allows electrical energy to be transmitted to the gantry as it passes along the patient, allowing acquisition of CT data in a helical (corkscrew) fashion. This enables the technologist to acquire anatomical data from a patient as a volume rather than as a series of slices. Spiral CT is also a faster process, with less discomfort to the patient, and is dynamic, with high resolution giving slices in continuity.[16]

The predictability of CT scans in the determination of laryngeal cartilage invasion varies considerably among published reports (Table III). Until recently, the presence of tumour on both sides of a laryngeal cartilage was the only accepted CT criterion for the confirmation of neoplastic tumour invasion. However, since then, a number of other diagnostic signs have been described to aid the diagnosis of cartilage invasion.[1]

Soft tissue asymmetry was present in all the cases, as expected. In essence, this just denotes the presence of tumour in the larynx. In our series, tumour was present on both sides of the cartilage in 11 cases, of which 10 had histological evidence of cartilage involvement. The sensitivity, specificity and positive predictive value of this sign were 66, 91 and 90 per cent, respectively. The sensitivity of this sign was relatively low as it was present only in the most advanced cases.

Sclerosis of the cartilage was described by many authors as a useful, sensitive and specific radiological sign for the detection of cartilage involvement. Becker *et al*. found that cartilage sclerosis had a sensitivity of 82 per cent and a specificity of 79 per cent.[1] Nix and Salvage pointed out that cartilage sclerosis could occur due to reactive inflammation of the cartilage and therefore was not a useful early radiological sign of neoplastic cartilage invasion when taken in isolation.[20] According to the same authors, sclerosis of the cartilage had a sensitivity of only 62 per cent and a specificity of 42 per cent in detecting tumour invasion. We observed that the sensitivity of cartilage sclerosis was rather low, at 33 per cent, but that this sign had an acceptable specificity of 91 per cent. In a study assessing the significance of sclerosis in identifying tumour invasion of cricoid and arytenoid cartilage, the authors concluded that this was not a reliable sign, with a positive predictive value of only 46 per cent.[21] However, the specificity of this sign varies from one cartilage to another, being lowest in the thyroid cartilage.[1]

Soft tissue asymmetry was the only sign present in all the cases. We observed that the presence of at

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least two criteria considerably increased the usefulness of CT in predicting cartilage invasion. As shown in Table III, if any two criteria were present, the sensitivity, specificity and positive predictive value were 86, 91 and 93 per cent, respectively. These findings agree with those of other published reports.[1]

- **This study assessed the accuracy of pre-operative spiral CT in predicting thyroid cartilage involvement in patients with laryngeal carcinoma**
- **The spiral CT scans and pathological reports of 27 patients undergoing laryngectomy for carcinoma were studied**
- **The presence of tumour on both sides of the larynx was the most reliable method of predicting cartilage invasion**

The CT appearance of laryngeal chondroradionecrosis is non-specific, but the diagnosis can be suggested in the presence of fragmentation and collapse of the thyroid cartilage and/or in the presence of gas bubbles around the cartilage.[22] However, the presence of post-radiation chondronecrosis makes it difficult to radiologically differentiate between persistent or recurrent tumour and severe radiation effects. Of the nine patients in our series who received pre-operative radiotherapy, only three had histological evidence suggestive of cartilage invasion. One patient with negative histology had extensive necrosis of the laryngeal cartilage, probably as a result of radiotherapy. None of our patients received radiotherapy during the two years prior to surgery.

Conclusion

The advent of the spiral CT scan has improved the usefulness of CT in predicting cartilage invasion. Combining more than one diagnostic criteria enhances the sensitivity and specificity of this imaging modality.

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