Clinical Investigations

Respiration

Respiration 2000;67:630–637

Received: December 24, 1999
Accepted after revision: April 5, 2000

Predictors of Tracheobronchial Invasion of Suprabifurcal Oesophageal Cancer

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Key Words

Bronchoscopy · Oesophageal neoplasms · Oesophagectomy · Tumor staging · Trachea

Abstract

Background: Factors possibly predicting airway invasion of oesophageal cancer in the absence of frank oesophagotracheal fistulas have not been studied. ***Objectives:*** To identify possible predictors of airway invasion by oesophageal cancer that are readily accessible in the preoperative setting. ***Methods:*** We prospectively investigated 148 patients with newly diagnosed oesophageal cancer located at or above the level of the tracheal bifurcation and without any evidence of oesophago-respiratory fistulas or distant metastases. Demographic variables, respiratory parameters, results of bronchoscopy and other staging procedures (oesophagoscopy, swallow oesophagography, endosonography, CT and histology) and findings at surgery were compared between the patients with (n = 30) and without (n = 118) proven airway invasion and entered into a stepwise logistic regression model to evaluate their independent predictive roles. ***Results:*** Univariate analysis indicated that the incidence of airway invasion increased with the presence of suspect CT findings, the presence of respiratory symptoms, tumour length, T stage on endoscopic ultrasonography, and histopathologic grading of the primary cancer. A multivariate logistic regression model indicated that suspect CT findings (odds ratio, 4.4; 95% confidence interval 1.7–11.1, p = 0.002) and maximal tumour length >8 cm (odds ratio, 3.7; 95% confidence interval 1.4–9.6, p = 0.007) were associated independently with airway invasion. The accuracy of predicting airway invasion was 82.5% with both variables combined. ***Conclusions:*** The high incidence of airway involvement by oesophageal cancer and the difficulty to predict it accurately with clinical data or other staging procedures justifies the routine use of bronchoscopy in all patients with the tumour located at or above the level of the tracheal bifurcation. A particular effort to objectively prove or exclude airway invasion should be made in patients with tumours longer than 8 cm and/or with CT findings suggesting airway invasion.

Introduction

Due to the close anatomical relationship between the oesophagus and the tracheobronchial tree, oesophageal cancer located at or above the level of the tracheal bifurcation (so-called suprabifurcal oesophageal cancer) is associated with early airway invasion [1–5]. Patients with tu-

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mour invasion of the respiratory tract present a particulary challenging problem. Treatment options are limited and usually futile. Surgical resection is generally contraindicated. Radiotherapy, considered the therapy of choice, usually leads only to short-term palliation and may precipitate the occurrence of malignant oesophagotracheal fistulas.

Identifying the extent of the disease according to the TNM classification scheme [6] is the first and a critically important clinical step in the treatment of a patient with oesophageal cancer, because the results determine the appropriate type of therapy [7, 8]. To avoid futile attempts of surgical resection and to make adequate plans for the treatment, an accurate preoperative determination of cancer spread is extremely important. Bronchoscopy is currently the most accurate tool to assess possible tracheobronchial involvement [2, 4, 5, 9–13]. However, not all centres implement bronchoscopy routinely in the preoperative evaluation of patients with oesophageal cancer. In this report, we present our experience with bronchoscopy in the preoperative staging of suprabifurcal oesophageal cancer and attempt to correlate these findings and the findings at operation with the results of other staging procedures. The objectives of this study were to identify by a multivariate logistic regression model possible predictors of airway invasion by the oesophageal cancer that are readily accessible in the preoperative setting, and to determine how various factors could be combined to best predict airway invasion.

Patients and Methods

Subjects and Initial Evaluation

In a prospective protocol, all patients with untreated carcinoma of the cervical and thoracic oesophagus diagnosed between March 1, 1995, and August 31, 1998, underwent staging with swallow oesophagography, posteroanterior and lateral chest radiography, thoracoabdominal computed tomography (CT) scanning with intravenous and oral contrast enhancement, percutaneous sonography and oesophageal endoscopic ultrasound (EUS). Additional studies such as head CT, bone scintigraphy or magnetic resonance imaging were obtained as clinically indicated. The tumour was considered 'suprabifurcal' if its proximal end was located at or above the level of the tracheal bifurcation on radiographic studies [7]. Patients with infrabifurcal oesophageal cancer, with a frank oesophagotracheal fistula at presentation, with distant metastases (M1), those not operable due to poor general condition, and those with unresectable, locally advanced tumour were excluded from the present analysis.

With CT, contiguous 1-cm sections were obtained through the chest and abdomen. Tumour compression of the airways or any disappearance of the adjacent intervening tissue plane between the oesophageal lesion and the airways were regarded as possible signs of airway invasion. The assessment of tumour infiltration depth by EUS (uT stage) was based on the generally accepted five-layer structure of the gastrointestinal wall; lymph nodes which were regarded as metastatic (N1) were relatively hypoechoic with the same ultrasonographic pattern as the primary tumour and with clearly defined boundaries [14, 15]. The swallow contrast radiographs were carefully searched for any deformity of the oesophageal axis (angulation, deviation, tortuosity), as well as deep ulcerations and fistulas.

Bronchoscopy

Potential surgical candidates on the basis of the above examinations were referred to bronchoscopy. They were specifically asked about symptoms of haemoptysis, cough, dyspnoea, hoarseness and chest tightness. After obtaining written informed consent, fibreoptic bronchoscopy was performed as previously reported [2]. The complete tracheobronchial tree was examined; special attention was paid to the trachea and main bronchi. All direct tumour signs (exophytic intraluminal growth or infiltration of the tracheobronchial wall) and indirect signs (distortion or compression of normal structures, altered structure of the mucosa, teleangiectatic blood vessels, protrusion of the posterior wall of the trachea or a major bronchus, widened and immobile bifurcation, rigid and fixed tracheobronchial structures at breathing or coughing manoeuvres) were recorded, and three to five forceps biopsy specimens as well as brush cytology samples were taken from these areas. The same protocol was applied in cases of protrusion of the posterior airway wall with macroscopically normal appearance of the mucosa. If no abnormalities were noticed at bronchoscopy, brush cytology and three to four biopsies were routinely taken from the pars membranacea of the right main bronchus, left main bronchus, and the proximal, medial and distal third of the trachea.

Neoadjuvant Therapy, Surgical Resection, Histopathologic Assessment

After the initial staging, potentially operable patients either proceeded directly to oesophageal resection, or those with locoregionally advanced disease (defined as T3 or T4) received neoadjuvant therapy with 30 Gy radiation and 5-fluorouracil preoperatively [16, 17]. Those showing an incomplete response to neoadjuvant therapy underwent a second restaging bronchoscopy. Surgery was offered to all patients with possibly curable disease. In the study period, no patient was operated on without undergoing at least one preoperative bronchoscopy. The resectability criteria were established prior to the commencement of the study, and patients with distant metastases and airway invasion determined by bronchoscopy with cancer-positive microscopic examination were excluded. Subtotal transthoracic en bloc oesophagectomy with two-field lymphadenectomy was the procedure of choice [3, 18]. Tumour extent and tracheobronchial invasion were assessed intraoperatively and by histopathologic examination of the resected specimens. The pathologic stage was determined on the basis of the UICC TNM classification guidelines [6]. All patients were followed up until June 30, 1999; episodes suggestive of cancer invasion into the airways were specifically looked for.

Diagnostic Criteria

Absence of airway invasion at autopsy or an R0 resection [6] with regard to the airways and with long-term survival (>6 months) without any pulmonary problems was considered as the gold standard for the absence of tracheobronchial invasion. The gold standard for the presence of tracheobronchial invasion was a positive histology and/or cytology in samples taken at bronchoscopy with a tumour type

identical to the type of oesophageal cancer, or proof of airway invasion by histopathologic examination of the resected specimens.

Statistical Analysis

The variables evaluated regarding airway invasion by the oesophageal cancer included eight general characteristics (age, sex, smoking habits, duration of dysphagia, presence of respiratory symptoms, results of plain chest radiography, CT findings and lung function tests) and six tumour-specific characteristics: cancer cell type, histologic grade (G grade), proximal site of the tumour, tumour length (measured by contrast swallow oesophagoscopy and CT), tumour stage (uT) by EUS, and regional lymph node status (N, by EUS and CT).

The variables are expressed as means ± SD (continuous variables) or as a percentage of the group they were derived from (categorical variables). The binomial distribution was used to compute the 95% confidence intervals (CIs) for the frequency of findings. First, in a univariate analysis, the odds ratio (OR) was used to quantitate the degree of association between presumptive predictors and airway invasion, its 95% CIs were calculated and the association tested with Fisher's exact test or the χ^2 test. Differences in continuous variables between groups were tested by the two-sided Mann-Whitney U test. Rejection of the null hypothesis required a p value <0.05.

Multivariate logistic regression was then used to determine a set of variables with an independent predictive value [19]. Continuous variables which were significant in the univariate analysis were transformed using cutoffs defined as median values of the variable within the group of patients with airway invasion. With only 30 patients with airway invasion, the final model could include only up to three variables; they were selected by the forward stepwise selection method, with re-estimation of OR, CI, and p values at each step.

Results

Of the 316 patients presenting with newly diagnosed oesophageal cancer during the study period, 265 had the proximal cancer site at or above the level of the tracheal bifurcation. Of these, 117 patients could not be operated on due to reasons other than airway invasion (extensive local tumour mass in 28, distant metastases in 23, poor general condition in 47 and other reasons in 19 patients). In these 117 patients, the histologic and cytologic samples taken at bronchoscopy were all cancer negative, but a subsequent validation of these bronchoscopic results was not possible. In the remaining 148 patients, a definitive proof or exclusion of airway invasion could be obtained. They form the basis of this report. In none of these patients was airway invasion suspected before bronchoscopy; all were thought potentially operable before the bronchoscopy.

124 patients underwent surgery, on average 19.9 ± 27.9 (median 11) days after the first or the restaging bronchoscopy. All were operated with curative intent. Airway invasion by the oesophageal cancer was confirmed by examination of the resected specimens in 7 patients (6 of them died 0.5–13.5 months after surgery, 1 was alive 17 months after the operation). In the other 117, airway invasion was excluded both by the surgeon and the pathologist. Eight (6.8%) of the 117 patients died during hospitalization and 52 (44.4%) after discharge from hospital (on average 13.2 ± 10.5 months after the surgery, median 10.3), of causes unrelated to the bronchial tree. Fifty-seven patients (48.7%) were alive at the last follow-up on average 21.0 ± 12.0 (median 18) months after surgery, all without any pulmonary problems.

Table 1. Characteristics of patients with and without airway invasion

	Airway invasion	No airway invasion
Patients	30	118
Sex, males/females	26/4	90/28
Age, years	58.7 ± 6.9	56.0 ± 8.3
Smokers	24 (80%)	80 (68%)
Duration of dysphagia, weeks	19.7 ± 25.0	20.3 ± 39.2
Respiratory symptoms	10 (33.3%)	11 (9.3%)*
VC, % predicted	89.2 ± 14.9	96.5 ± 15.7**
FEV_1, % predicted	85.9 ± 19.1	93.1 ± 17.7
FEV_1/VC, %	73.8 ± 8.6	75.3 ± 6.6
PaO_2, mm Hg	75.6 ± 7.6	78.2 ± 7.1
$PaCO_2$, mm Hg	36.6 ± 3.9	37.0 ± 3.0

Values are means ± SD. * $p < 0.0008$, ** $p < 0.04$, vs. patients with airway invasion. VC = Vital capacity.

The patients were divided into two groups. The first group (n = 30) consisted of patients with unequivocal evidence of airway invasion by the oesophageal cancer. This was established by bronchoscopy with positive microscopic examination in 23 patients and at surgery in 7 patients. The other group (n = 118) consisted of patients in whom airway invasion was definitely ruled out. This was achieved at autopsy in 1 patient who died 46 days after bronchoscopy of sudden death, and in the other 117 perioperatively by the surgeon and following examination of the resected specimens by the pathologist. All the surgical patients without airway invasion discharged from hospital have survived >6 months without any pulmonary problems.

The basic characteristics of the patients are given in table 1. Most patients were men. There was no significant difference between the two groups regarding sex, age, smoking history, and the time lapse from the onset of symptoms of oesophageal cancer (mainly dysphagia or

Table 2. Tumour-related differences between the groups (univariate analysis)

	Airway invasion n = 30	No airway invasion n = 118	p value	OR	95% CI
Cancer cell type					
Squamous cell cancer	25	110			
Adenocarcinoma	3	4			
Small cell cancer	1	1			
Carcinosarcoma	0	2			
Undifferentiated carcinoma	1	1			
Squamous cell cancer, % of all	83	93	NS		
Proximal end of tumour, cm from incisors	24.2 ± 3.4	24.7 ± 4.3	NS		
Tumour stage (EUS)					
uT1	0	8			
uT2	0	15			
uT3	14	72			
uT4	4	1			
EUS not possible	12	22			
Tumour stage (EUS), % of all					
uT3 + uT4	100	76	0.022	5.6	1.3–24.1
uT3 + uT4 + EUS not possible	100	81	0.009	7.3	1.7–31.8
Tumour length, cm					
Swallow contrast	6.7 ± 2.7 (n = 17)	5.4 ± 2.2 (n = 73)	0.036		
CT	7.3 ± 2.0 (n = 20)	6.0 ± 2.3 (n = 73)	0.029		
Esophagoscopy	8.0 ± 2.4 (n = 23)	5.6 ± 2.3 (n = 83)	<0.0001		
Maximum of the above examinations	8.3 ± 2.2 (n = 29)	6.4 ± 2.4 (n = 111)	<0.0001		
Mean of the above examinations	7.2 ± 2.1 (n = 29)	5.7 ± 2.1 (n = 111)	0.0008		
Tumour > 5 cm, % of all					
Swallow contrast	59	45	NS	1.7	0.8–5.0
CT	85	57	0.024	4.2	1.2–14.5
Esophagoscopy	83	45	0.0012	5.9	2.0–17.3
Tumour > 6.5 cm, mean of examinations, % of all	52	32	0.043	2.3	1.0–5.3
Tumour > 8 cm, maximal value, % of all	52	18	<0.001	4.6	2.7–10.5
Tumour grade G3 + G4, % of all	79	55	0.018	3.1	1.2–8.0
N stage N1, % of all	76	72	NS		

odynophagia) to bronchoscopy. One third of the patients with airway invasion had respiratory symptoms (mainly dyspnoea and hoarseness), as opposed to only one tenth in those without airway invasion (p = 0.0008, OR 4.2, 95% CI 2.0–9.1). All patients had a normal plain chest radiograph. Patients with airway invasion had a slightly but significantly lower vital capacity than those without airway invasion; there was no significant difference in the mean values of other lung function tests between the two groups.

The data related to the oesophageal tumour are presented in table 2. There was no difference in the frequency of any histological tumour type between the two groups; in both groups the majority of the patients had squamous cell cancer. The mean location of the proximal site of the tumour was similar in both groups.

Endosonography showed possible invasion outside the oesophagus (uT4 category) in 4 patients with and 1 patient without airway invasion. In none of them direct airway infiltration was suspected. In all patients with airway invasion, the primary tumour extent was uT3 or uT4, or it was not possible to pass the ultrasonic probe alongside the tumour. On the contrary, one fifth of the patients without airway invasion had a uT1–2 category. The OR for having an airway invasion was 7.3 (95% CI 1.7–31.8) in patients with category uT3–4 and those where EUS was not possible, as opposed to patients with a uT1–2 category.

The incidence of airway invasion increased with tumour length, as measured by swallow oesophagography, CT, and oesophagoscopy. The OR for tumours longer than 5 cm being associated with airway invasion was 1.7 (tumour length measured by swallow oesophagography),

Table 3. Combination of findings predictive of airway invasion

Positive findings	Airway invasion (n = 30)		No airway invasion (n = 118)	
	n	%	n	%
0–1	5	17	50	42
2–3	15	50	61	52
4–5	10	33	7	6

4.2 (CT), and 5.9 (oesophagoscopy), as opposed to shorter tumours. However, airway invasion occurred also in patients with short tumours (<4 cm). The association between tumour length and airway invasion was best evidenced by comparing the mean or the maximal value of the three different examinations. 52% of the patients with, but only 18% of those without a tumour length >8 cm in any examination, had airway invasion (OR 4.6).

The histopathologic grading of the oesophageal cancer was higher in patients with airway invasion than in those without airway invasion. 79% of the patients with and 55% of those without airway invasion belonged to the G3–4 category (poorly differentiated or undifferentiated; OR 3.1, 95% CI 1.2–8.0). The regional lymph node status on EUS and CT did not differ between the patients with or without airway invasion. 76% of the patients with and 72% of those without airway invasion had suspicious regional lymph nodes on EUS or CT.

The CT findings were predictive of airway invasion. The disappearance of the intervening tissue plane between the tumour and the airway wall, sometimes with compression of the airway, was found in 57% of the patients with but in only 20% of those without airway invasion ($p < 0.0001$, OR 5.12, 95% CI 2.8–9.4).

A combination of the five aforementioned factors (suspect CT findings, tumour length >8 cm or >6.5 cm as mean of the investigations, respiratory symptoms, uT stage 3–4, G grade 3–4) showed that the smaller the number of positive factors demonstrated by the patients, the lower the incidence of airway invasion by oesophageal cancer ($\chi^2 = 19.9$, $p < 0.0001$, table 3). With less than two positive findings, the presence of airway invasion was unlikely (5/55), with more than three positive factors it was very likely (10/17).

In the multivariate logistic regression of all covariates from the univariate analysis, suspicious CT findings of airway invasion emerged as the most important variable, followed by the maximal tumour length >8 cm as an additional and independent predictor. With both variables in the model, the OR for the presence of airway invasion was 4.4 (95% CI 1.7–11.1, p = 0.002) in the presence of a suspect CT finding and 3.7 (95% CI 1.4–9.6, p = 0.007) with maximal tumour length >8 cm, as opposed to the absence of these characteristics. With both variables combined, the accuracy of predicting airway invasion was 82.5%. Our final model eliminated all non-significant effects from the previous models. It shows variables that are both significant and independently predictive of airway invasion by oesophageal cancer. The inclusion of a third parameter into the model did not significantly improve the prediction.

The correlations of bronchoscopic findings with tumour length and the uT and G category are presented in table 4. The incidence of macroscopic abnormalities (predominantly protrusion of the pars membranacea) increased with tumour length (mean of swallow oesophagography, oesophagoscopy, and CT) and uT stage, but not with the tumour grade. However, macroscopic abnormalities in the central airway were also found in patients with short tumours and low uT categories. Microscopic proof of malignancy in samples from these macroscopic abnormalities was achieved only in patients with tumours longer than 4 cm and in patients in the uT3–4 stage.

Discussion

Diagnostic methods to detect distant metastasis of oesophageal cancer have recently improved. However, it remains difficult to accurately predict the extent of invasion into neighbouring organs, such as the aorta, pericardium and airways. The incidence of airway invasion found at oesophageal resection is 3.7–7% in patients undergoing preoperative bronchoscopy, and could be as high as 12.5–23.8% if bronchoscopy was omitted in the preoperative staging [2]. In patients with airway invasion, surgery does not confer any survival benefit and should be withheld. Preoperative exclusion of airway invasion is therefore of paramount importance. Although bronchoscopy has a low complication rate in experienced hands, it is costly, invasive and not always agreeable to the patient. We therefore analyzed factors possibly enabling the prediction of airway invasion by oesophageal cancer, aiming also at identifying factor(s) indicating that preoperative bronchoscopy could be omitted.

Suspicious CT findings were identified as the most powerful independent predictor of airway invasion by oesophageal cancer. CT proved particularly helpful in

Table 4. Frequency of bronchoscopic findings (in %) in relation to tumour length, uT stage, and G grade

Bronchoscopy	Mean tumour length, cm			Tumour stage, EUS		Tumour grade, histology	
	<4	4–8	>8	uT 1 + 2	uT 3 + 4	G 1 + 2	G 3 + 4
Normal macroscopy and microscopy (n = 90)	18	70	12	25	75	45	55
Macroscopic abnormality, negative microscopy (n = 35)	6	76	18	18	82	46	54
Proven tumour invasion (positive macroscopy and microscopy, n = 23)	0	50	50	0	100	17	83
Statistical significance		p = 0.0004		p = 0.0001		NS	

revealing a relationship between the tumour and the tracheobronchial tree. In our opinion, the bronchoscopist should have a CT scan available for review before the procedure in order to be able to take the biopsies from the areas most suspicious of tumour invasion. However, with rare exceptions of extensive tumour spread into the trachea or the presence of a fistula, CT cannot definitely prove the presence of airway wall infiltration by the tumour. CT cannot differentiate the individual layers of the oesophageal wall; it is also difficult to differentiate the tracheal wall from the closely abutting tumour by CT [4, 20]. In our previous study on 100 patients with suprabifurcal oesophageal cancer, the results of bronchoscopy and CT were discordant in 40% of the cases; although both methods showed comparable sensitivity and negative predictive value in the diagnosis of airway involvement, the specificity, positive predictive value, and the overall accuracy were substantially higher for bronchoscopy than CT [2]. Therefore, patients with normal bronchoscopic results should not be excluded from potentially curative therapy solely because of CT signs of tumour spread to the airways.

The incidence of airway invasion increased with tumour length. A tumour length >8 cm was identified as the second independent predictor of airway invasion in the logistic regression model. Previous reports [4, 5, 10–12, 21, 22] also described a correlation between tumour length and airway invasion, or between tumour length and invasion into other neighbouring organs [8]. The length of the lesion, especially as depicted by the swallow contrast, is however not an accurate reflection of the true size of the tumour [5, 12]. The length of the tumour also provides little information on its thickness and volume. Moreover, in patients with suprabifurcal oesophageal cancer, by definition only the proximal part of a long tumour may be in contact with the central airways, with the distal parts being far away from the central airways. Further, in our analysis, airway invasion was also observed in a significant number of patients with shorter tumours. It is therefore somewhat surprising that the length of the tumour emerged as the second most important predictor of airway invasion in this study.

Although respiratory symptoms occurred significantly more often than in patients without airway invasion, only one third of the patients with airway invasion had some respiratory symptoms (dyspnoea, hoarseness, cough or haemoptysis). In a 9-year retrospective review, Argyros and Torrington [23] observed macroscopic endobronchial abnormalities in all 3 symptomatic and in 8 of 17 asymptomatic patients with a newly diagnosed oesophageal cancer; however, specimens for microscopic examination were not systematically obtained. The authors concluded that bronchoscopy is a low-yield procedure in the evaluation of patients with oesophageal carcinoma unless pulmonary symptoms of cough and/or haemoptysis or chest radiographic abnormalities are present. Watanabe et al. [24] evaluated 14 patients and found that the likelihood of endobronchial tumour involvement increased when respiratory symptoms were present (4 of 5 had positive bronchoscopic findings); the yield of a positive bronchoscopy in the absence of pulmonary symptoms was low (2 of 9 positive bronchoscopic findings). Although significant in univariate analysis in our study, the presence of respiratory symptoms was not identified as an independent predictor by multivariate analysis.

The uT stage and the invasivity of the cancer, as reflected by the histopathological G grade, had also a direct bearing on the frequency of airway invasion. This association has not been described before. EUS is currently the most accurate means to assess the depth of wall penetration by oesophageal cancer [14, 15]. Intuitively, we had expected the uT 3–4 stage to be most closely associat-

ed with the airway invasion. This was not the case, probably because the T4 tumours might break through the circumferential boundaries of the oesophagus at other sites than the airways, and because, due to the limitations of the current ultrasonic probes, EUS is not able to reliably assess tumour invasion into the airways [7, 14].

The finding of a slightly but significantly lower vital capacity in patients with airway invasion, in the presence of no significant difference in the values of FEV_1, FEV_1/vital capacity and the blood gas values, is difficult to explain. At bronchoscopy, the tumour encroachment on the airways was never considered great enough to cause a ventilatory limitation. The lung fields were clear on chest X-ray in all patients, and CT did not indicate loss of volume or an interstitial process. We currently have no explanation for this finding.

None of the above indices had sufficient discriminating power. We feel that bronchoscopy to prove or exclude an airway invasion should be performed in all potentially operable patients, independent of the results of other staging procedures. Even short tumours with low G grade may be associated with airway invasion, in contrast to large locally advanced tumours, which could be resected curatively.

Considering the combination of the five aforementioned factors (suspicious CT findings, tumour length, respiratory symptoms, uT stage and G grade), the smaller the number of positive factors demonstrated by the patients, the lower the incidence of airway invasion by the oesophageal cancer (table 3). Therefore, a careful evaluation of a combination of these five factors might be useful in predicting lesions that have not invaded the airways (and have a good chance for a complete resection), as well as those lesions where airway invasion is very likely and multiple biopsies at bronchoscopy are therefore necessary to reliably exclude it.

The longer the tumour and the higher the T stage, the more frequent was the incidence of suspect macroscopic abnormalities and positive biopsy findings at bronchoscopy (table 4). However, many of the patients in whom airway invasion was eventually excluded at surgery had suspect macroscopic abnormalities at bronchoscopy. A significant number of positive macroscopic findings were found without actual mucosal invasion, mostly in the shorter tumours. The tumour mass does not correlate directly with infiltrative growth. Some carcinomas of the oesophagus can grow to bulky masses without invasion of the surrounding structures. They have a better prognosis than infiltrative carcinomas which may erode into blood vessels and the trachea at early stages [11]. This highlights the importance of extensive sampling of all bronchoscopically found abnormalities for microscopic examination, in order to reduce the rate of falsely positive bronchoscopic findings.

Seven cases of airway invasion were found at surgery; consequently, the rate of falsely negative bronchoscopic examinations was 4.7%. One reason for the false-negative findings may be the infiltrative nature of the tumour. Large stretches of submucosal and surrounding tissues may be infiltrated with little mucosal deformity. Also, large tumour masses may be concealed by macroscopically normal mucosa or only small mucosal lesions.

Limitations of the Study

To develop and validate a predictive model of airway invasion, ideally a part of the patients in the database should have been randomly selected to constitute the developmental sample and the other part the validation sample. This was not possible due to the low number of patients with airway invasion (n = 30). The low number of patients with airway invasion also did not allow to test more than three of the most important parameters in the multiple regression analysis. Further, the absence of tumour length measurement on some of the swallow contrast, CT and endoscopic examinations made it necessary, in order to achieve sufficient numbers for the multivariate analysis, to combine these examinations and use the mean and the maximal values from them. The length of the lesion, above all as depicted by swallow contrast, is not an accurate reflection of the true size of the tumour [12].

Intuitively, the main discriminative factor for airway invasion would be the location of the oesophageal cancer with regard to the airways. The incidence of airway invasion of infrabifurcal cancer is much lower than that of the suprabifurcal cancer [2]. Because not all patients with infrabifurcal oesophageal cancer undergo bronchoscopy at our institution, the inclusion of such patients would have introduced a bias in the analysis. Although not formally proved, we still consider the location of the tumour with regard to the airways to be the most important factor regarding possible tracheobronchial invasion by the oesophageal cancer.

In conclusion, we found that prediction of airway invasion by suprabifurcal oesophageal cancer can be made by taking into account the CT signs of possible airway invasion, the maximal length of the tumour, the presence of respiratory symptoms, and the uT and G stages of the tumour. On multivariate analysis, only CT signs of possible airway invasion and the maximal length of the tumour were found to be independently and significantly predic-

tive of airway invasion. None of these parameters, however, had sufficient predictive power to definitely exclude or prove airway invasion. Because of the important therapeutic consequences, bronchoscopy with extensive biopsies, particularly in patients with suspicious CT findings and/or a tumour length >8 cm, remains the obligatory method and the standard for detecting airway invasion by oesophageal cancer. Our analysis, by refining the association of these factors with airway invasion, might constitute a useful tool for the assessment of patients with oesophageal cancer and the potential impact of therapeutic decisions.

Acknowledgment

The authors thank Dr. R.W. Hauck and R. Lembeck for performing some of the bronchoscopies in this study.

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