

technique and the traditional quadrantectomy is that the nipple-areolar dermis is excised instead of normal skin.

Our results are similar to previously published data and show that the most important predictor of nipple-areola complex involvement, other than clinical finding of such involvement, is the central location.

The requirement for conservative surgery in centrally located small size tumours has induced others to conceive incisions which allow removal of sufficient parenchyma to ensure radicality yet conserve the areola and nipple. However, the literature and our study indicate that central lesions correlate with a high incidence of involvement of the areola and nipple suggesting their removal. It is no problem to sacrifice these when a good cosmetic result can be achieved by plastic remodelling.

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# The Value of Twice Yearly Bronchoscopy in the Work-up and Follow-up of Patients with Laryngeal Cancer

Luci Rachmat, Gerard C. Vreeburg, Nico de Vries, Gert-Jan Hordijk, Herman Lubsen, Johannes J. Manni and Gordon B. Snow

The aim of this retrospective study was to investigate the usefulness and feasibility of twice-yearly bronchoscopy and sputum cytology in patients with laryngeal cancer. In 170 selected patients, 500 (both initial and during follow-up) bronchoscopies were performed. There was a maximum follow-up of 34 months. 5 (2.8%) male patients developed lung cancer. In only 2 of them was the diagnosis based on bronchoscopy alone. After treatment with curative intent, both patients developed a recurrent lung carcinoma. According to most patients' experience, regular bronchoscopy is unpleasant. It is concluded that twice-yearly bronchoscopy and sputum cytology in patients with laryngeal cancer is not useful as a routine procedure. At present, chemoprevention of second primary tumours seems the most promising adjunctive treatment modality.

*Eur J Cancer*, Vol. 29A, No. 8, pp. 1096-1099, 1993.

## INTRODUCTION

SECOND PRIMARY TUMOURS develop in 10-20% of patients with laryngeal cancer [1-8]. The majority (up to 12.5% of the total) of those second primary tumours occur in the lungs. This phenomenon is explained by the concept of "field-cancerisation"

which assumes that the whole mucosa of the respiratory tract is exposed to the same carcinogens, in particularly those in cigarette smoke and alcohol [9]. Second primary tumours and intercurrent diseases are the most important causes of death in patients with cured, early stage laryngeal cancer [10, 11]. As an adjunct to

cessation of smoking, two theoretical options are available to combat this serious problem: screening and chemoprevention [12–15].

In many centres panendoscopy is performed during initial work-up in order to rule out a second primary tumour [16–23]. The majority of the second primary tumours occur, however, metachronously, that is more than 6 months after the diagnosis of the index-tumour. The usual screening in the follow-up period for second primary tumours in the lungs is a once-or twice-yearly chest X-ray. This kind of follow-up does not increase the life expectancy and its value is being questioned [24–29]. Twice-yearly bronchoscopy combined with sputum cytology could possibly be more effective in detection of lung cancer at an early stage. Early stage lung cancer is often not detectable on chest X-ray, but since the majority are localised centrally in the lung, they seem to be amenable to detection by bronchoscopy [30]. The costs and the burden for the patient are, however, considerable.

We report the results of a multicentric pilot study on the value of twice-yearly bronchoscopy combined with sputum cytology in patients with a high probability of being cured of laryngeal cancer. The following three questions were addressed: (1) is twice-yearly bronchoscopy combined with sputum cytology in patients with a cured laryngeal cancer as an adjunct to the normal follow-up more effective in detection of second primary tumours in the lung than the routine follow-up alone; (2) is this kind of follow-up feasible; (3) which fraction of the total number of patients with laryngeal cancer is eligible for such a screening procedure?

#### PATIENTS AND METHODS

Between January 1985 and August 1987, 453 new patients with squamous cell carcinoma of the larynx were diagnosed at the Departments of Otolaryngology/Head and Neck Surgery of the Free University Hospital Amsterdam (AZVU), the Academic Hospital Nijmegen (AZN) and the Academic Hospital Utrecht (AZU) in the Netherlands. 170 of those 453 patients were eligible for periodic bronchoscopy and sputum cytology. Patients in a poor physical condition (Karnofsky scale < 80), with other serious (malignant or not malignant) disease, undergoing non-curative treatment, older than 70 years or with serious obstruction of the upper airway were considered ineligible. Informed consent was obtained from all patients. A questionnaire was mailed to 95 patients of the AZVU and AZN in order to ascertain the implications of this sort of follow-up. This questionnaire was not used at the AZU. In cases of tumour in the lung, the diagnosis of second primary tumour or lung metastases was based on a combination of the clinical picture, chest X-ray and histopathology (for criteria for differential diagnosis between lung metastasis or primary lung cancer, see [15]).

Correspondence to N. de Vries.

L. Rachmat and J.J. Manni are at the Department of Otolaryngology/Head and Neck Surgery, Academic Hospital Nijmegen, P.O. Box 9101, 6500 HB Nijmegen; G. C. Vreeburg is at the Department of Otolaryngology/Head and Neck Surgery, Academic Hospital Maastricht, P.O. Box 5800, 6202 AZ Maastricht; N. de Vries and G. B. Snow are at the Department of Otolaryngology/Head and Neck Surgery, Free University Hospital Amsterdam, P.O. Box 7057, 1007 MB Amsterdam; and G.-J. Hordijk and H. Lubsen are at the Department of Otolaryngology/Head and Neck Surgery, Academic Hospital Utrecht, Postbus 85500, 3508 GA Utrecht, the Netherlands.

Revised 23 Oct. 1992; accepted 20 Nov. 1992.

*Table 1. Total (initial and subsequent) number of bronchoscopies. All 170 patients who had bronchoscopy during initial laryngoscopy, or within 6 months of it, were offered twice yearly repeated bronchoscopy*

Bronchoscopy (n)	Patients (n)
1x	170
2x	118
3x	90
4x	65
5x	33
6x	16
7x	5
8x	3
Total	500

#### RESULTS

Of the total 453 new patients, 170 underwent bronchoscopy during follow-up and 283 did not. Bronchoscopy was not performed in 235 of these 283 patients because of poor physical or mental condition, poor prognosis based on the laryngeal cancer or too short a life-expectancy, or because of contraindications such as serious airway obstruction due to a bulky laryngeal cancer and/or oedema, poor pulmonary condition or practical reasons such as lack of time and capacity problems. Informed consent was not obtained in 9 patients and follow-up was performed elsewhere in 39 patients. Of the 170 patients who underwent bronchoscopy, 63 (42%) were AZVU patients, 75 (38%) were AZN patients and 32 (32%) were treated at the AZU. Table 1 shows the number of bronchoscopies performed in these 170 patients. In 109 bronchoscopy was combined with initial laryngoscopy. In the other 61 patients, laryngoscopy was already performed elsewhere and not repeated after referral, or laryngoscopy and bronchoscopy could not be combined due to a bulky, obstructing laryngeal tumour. In those patients, the bronchoscopy was performed later, but in all cases within 6 months. In total, 500 bronchoscopies were done. The mean age was 58 years (range 39–70). The maximal follow-up in the AZVU, AZN and AZU was 70, 54 and 18 months, respectively.

In the 170 screened patients, 5 (2.8%) second tumours and 6 (3%) metastases in the lung were found. Table 2 shows whether the diagnosis was based on bronchoscopy, chest X-ray or complaints [15]. In all 5 patients, the diagnosis was confirmed histopathologically.

*Table 2. Primary lung cancers and metastases, detected by bronchoscopy, chest X-ray or based on diagnostic tests performed because of complaints*

	AZVU	AZN	AZU
Bronchoscopy		1P	1P
Chest X-ray	2M	2P	1M
Complaints	1P	2M	1M

P = primary lung cancer, M = lung metastasis.

In supraglottic carcinomas more lung cancers were found than in glottic cancers (3/34 = 8.8% vs. 1/69 = 1.5%). There was 1 patient with a transglottic cancer. The patients with lung cancers will briefly be discussed (Table 3).

In a 42-year-old male the diagnostic work-up was based on complaints, almost 2 years after the laryngeal cancer—the patient received radiotherapy. In a 69-year-old patient a lung tumour was detected on the chest X-ray. Curative treatment was not possible. Although during the last cytological investigation atypical epithelium had been noted, unfortunately no further analysis had taken place. In a 43-year-old patient a lung tumour was detected on doing routine chest X-ray—after resection of the right upper lobe he is free of disease at 22 months. In a 60-year-old man a lung tumour was found by bronchoscopy during follow-up—he underwent lobectomy. 27 months postoperatively, a recurrence was found by bronchoscopy for which he received palliative radiotherapy. In addition, a 63-year-old male underwent pneumectomy after a lung cancer was found during initial bronchoscopy. This patient died 9 months later due to recurrent lung and laryngeal cancer.

6 patients developed multiple lung metastases. In 3 cases the diagnosis was made on chest X-ray. In the other three, diagnostic investigations were started as a result of complaints. In 3 patients the metastases were confirmed histologically and in 1 cytologically; the other 2 patients were in too poor a condition to obtain material for histological or cytological examination.

81 (85%) of the 95 questionnaires were returned. The majority of the responders found periodic bronchoscopy of use. The bronchoscopy was, however, experienced as a heavier burden than the usual ENT investigation and chest X-ray. Bronchoscopy (and the local anaesthesia) was reported as very unpleasant, an emotional burden and time-consuming by many responders.

## DISCUSSION

We report the results of a multicentric study on the value of twice-yearly bronchoscopy combined with sputum cytology in patients with laryngeal cancer. The aim of the study was to investigate whether twice-yearly bronchoscopy combined with sputum cytology as a adjunct to standard follow-up is more effective than routine follow-up alone, whether this kind of follow-up is feasible and what percentage of the total group of laryngeal cancer patients is eligible for such a screening procedure.

The results are disappointing. The extra screening was only performed in less than half of the total group of patients (38%) and had no advantage above standard follow-up alone. Although

second cancers in the lung were found in 3% of patients in a relatively short time interval, no lives were saved in those patients.

These data are in contrast with those of Rodriquez, *et al.* [7], (Table 4) who performed twice-yearly bronchoscopy with laryngectomy for laryngeal cancer in 286 patients. In 36 (12.6%) a lung cancer was found with a follow-up of 3 years. In 6 of those 36 patients, no clinical symptoms of lung cancer were present while the chest X-ray was clear. The diagnosis of lung cancer was based on the findings during bronchoscopy. Surgical therapy proved to be possible in 7 of 36 patients. In 4 of those, the chest X-ray was normal and the lung cancer was detected by bronchoscopy.

In 62% of the total number of patients no periodic bronchoscopy was performed for various reasons. Unfortunately, since this was not a randomised study, a comparison for mean survival between the screened and not-screened groups is not possible, since the two groups were not comparable with regards to age, tumour stage and general condition. The screened patients were already selected and were in general younger. Differences in tumour stage distribution also accounted for not performing bronchoscopy. In general, the not-screened patients died earlier of the laryngeal cancer itself and of intercurrent diseases, were less motivated for follow-up or diagnostic procedures in case of suspicion of malignancy, and were in some cases followed-up elsewhere.

The questionnaire showed that many patients reported bronchoscopy as very unpleasant. The majority of the responders found the procedure acceptable however, since it provided a feeling of safety. In many patients in which bronchoscopy was performed (Table 1), the motivation for bronchoscopy every 6 months decreased with time. Both the mental and the physical burden were regarded by many as considerable. In those cases who felt so, the attending physicians were often reluctant to motivate and convince patients to carry on with the procedure. It should be emphasised that one of the aims of the study was to investigate whether the burden for patients was within reasonable limits.

We conclude that twice-yearly bronchoscopy as a routine procedure in patients with cured laryngeal cancer should not be regarded as feasible. The procedure is at best feasible in a very small minority of highly selected and highly motivated patients. Given the reported extra burden for patients and personnel and the cost-effectiveness, routine bronchoscopy cannot be regarded to be a useful and justified procedure. At present, chemopreven-

Table 3. Clinical characteristics of second primaries in the lung

n	Age	Location (laryngeal)	Stage	Therapy	Bronchoscopies	Follow-up time (months)*
1	42	S/G	T2N0Mx	Rt	2	22
2	63	S	T1N0M0	Pneu	1	3
3	69	S	T3N2M0	Rt	3	34
4	43	G	T1N0M0	Lobect	3	21
5	60	S	T1N1M0	Lobect	1	6

\*Time interval between first and second tumour.

S = supraglottic, G = glottic, Rt = radiotherapy, Pneu = pneumectomy, Lobect = lobectomy.

Table 4. Incidence of lung cancer in patients with laryngeal cancer as reported in the literature

	Larynx n	Lung n (%)	Maximum follow-up (years)
Christensen <i>et al.</i> , 1987	415	32 (7.7)	18
Rodriquez <i>et al.</i> , 1984	286	36 (12.6)	3
Hordijk <i>et al.</i> , 1983	691	81 (11.7)	22
Gluckman <i>et al.</i> , 1983	2135	69 (3.2)	30
de Vries <i>et al.</i> , 1986	748	64 (8.6)	19
Shikhani <i>et al.</i> , 1986	420	22 (5.2)	10
Wagenfeld <i>et al.</i> , a,b	903	38 (4.2)	10
Present study, 1991	170	5 (2.9)	4.5

tion seems a more realistic procedure to the threat of second primary tumours [12, 13].

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