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Detection of laryngeal carcinoma and epithelial hyperplastic laryngeal lesions via a rapid-access dysphonia clinic

P. L. A. Moore, F.R.C.S. (Ed.), F.R.C.S, D. Kim, M.Sc., M.R.C.S. (Ed.), G. Selby, M.B., Ch.B., D.W. Proops, B.D.S., F.R.C.S.

Abstract

Recent government initiatives in the UK have focused on streamlining oncology services by reducing waiting times between urgent referral, assessment and treatment of patients with possible cancer. The performance of the Quick Early Diagnosis Dysphonia Clinic of the Queen Elizabeth Hospital, Birmingham, between May 1997 and April 2001 was reviewed. Of 721 patients reviewed, 123 (17 per cent) had clinically suspicious laryngeal lesions. Thirteen cases of epithelial hyperplastic laryngeal lesions and 27 laryngeal malignancies were diagnosed. There was no statistical link between early cancer detection and assessment within two weeks of referral. However, rapid-access clinics for dysphonia serve an important role in the reassurance and multidisciplinary management of patients with persistent hoarseness. Greater financial commitments are necessary to achieve compliance with objectives for a maximum two-week wait for patients with suspected laryngeal malignancy.

Key words: Larynx; Laryngeal Neoplasms; Diagnostic Delay; Rapid Access Clinics

Introduction

Carcinoma of the larynx is the most common head and neck malignancy, with a yearly incidence of 4/100 000 in the UK.[1,2] There has been a steady rise worldwide in this yearly incidence; this has been attributed to increasing tobacco and alcohol consumption.[3–6] Progressive dysphonia is the most consistent symptom[1,2,7] and evaluation of this provides the best chance of early detection.[1]

The prognostic significance of early diagnosis of laryngeal cancer is well documented.[1] However, the diagnosis of laryngeal epithelial dysplasia confers a less certain prognosis. Although invasive cancers more frequently arise *de novo*, they can also originate from epithelial hyperplastic lesions; the risk of malignant transformation in simple epithelial hyperplasia and dysplastic lesions after 15 years is 0.3 per cent and 9.5 per cent, respectively.[8] Although there is uncertainty about the conditions under which epithelial hyperplastic lesions undergo malignant transformation, it is accepted that patients with these lesions require close long-term surveillance.[8]

Early cancer detection is being driven by British government initiatives to reduce waiting times between referral, diagnosis and treatment for all patients with suspected cancer.[9] One of the cornerstones of the government's cancer plan was implementation of a maximum two-week wait for an urgent outpatient appointment for suspected cancer patients. For the past 15 years, the Quick Early Diagnosis (QED) dysphonia clinic at the Queen Elizabeth Hospital, Birmingham, has satisfied this particular objective for patients with suspected laryngeal cancer. The performance of this particular clinic is the subject of the following longitudinal retrospective survey, which analyses diagnostic parameters between May 1997 and April 2001.

The objectives of this survey were:

(1) Assessment of the proportion of patients seen within two weeks of general practitioner (GP) referral
(2) Analysis of patients with diagnosis of laryngeal cancer
(3) Analysis of incidence of potentially precancerous lesions, i.e. epithelial hyperplastic laryngeal lesions (EHLL).

Methods and materials

All patients with dysphonia for longer than four weeks were sent by their GP directly to the QED unit of the Queen Elizabeth Hospital, Birmingham. This hospital provides general and specialist otolaryngology services for south Birmingham,

From the Department of Otolaryngology/Head and Neck Surgery, Queen Elizabeth Hospital, Birmingham, UK.
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serving a population of about 500 000. The QED unit arranges for patients to be seen within two weeks of urgent referral at a rapid-access dysphonia clinic headed by one of two consultant otolaryngologists. If a patient did not attend a scheduled outpatient appointment, their GP was contacted by letter to arrange a further appointment in the event of persisting symptoms. Each patient had detailed history and fibre optic laryngoscopy performed by an experienced ear, nose and throat surgeon. Diagnosis of nonsuspicious laryngeal conditions was made using clinical and endoscopic findings.

Data of history and examination findings were recorded prospectively on a pro forma sheet which was kept with the patient's clinical records. This study analyses attendance and performance data of patients seen in this clinic between 1997 and 2001 – a total of eight consultant years. Outcome measures under scrutiny included attendance rates, success in providing early appointments, symptom duration, detection rates (for both EHLL and laryngeal carcinoma) and outcomes. Attendance and referral rates were obtained from the QED database, while other parameters were obtained by perusing available casenotes.

Further analysis for significant trends was performed using EpiInfo® (version 6) free software (produced and distributed by the World Health Organization) to analyse 2×2 contingency tables.

Results

Database analysis

A total of 1149 patients were referred to the QED dysphonia clinic between May 1997 and April 2001. Of these, 930 (81 per cent) attended their scheduled appointments. As seen from Table I, the proportion of patients seen within two weeks of urgent referral decreased over the four years of the study. Overall, 652 patients (70 per cent) were seen within two weeks of referral by their GPs.

Casenote analysis

i. *Patient characteristics.* A retrospective casenote survey was performed for patients listed in the QED database for the period in question. All casenotes were requested from the Trust's medical records department; 721 (78 per cent) were obtained. Of these, 460 (64 per cent) were female, and 261 (36 per cent) were male; 510 (71 per cent) were seen within two weeks of referral; 368 (51 per cent) had never smoked, 149 (21 per cent) were ex-smokers, and 204 (28 per cent) were current smokers.

For 613 patients (85 per cent) the duration of dysphonia was documented in the clinical records; of these, 204 (33 per cent) had symptoms for less than two months, 186 (30 per cent) for two to four months and 223 (37 per cent) had hoarseness lasting longer than four months.

TABLE I

PATIENTS SEEN WITHIN TWO WEEKS OF REFERRAL

Year	n	Seen within 2 weeks n (%)
1997	219	191 (87%)
1998	258	206 (80%)
1999	275	153 (56%)
2000	178	102 (57%)

TABLE II

FREQUENCY OF CLINICALLY BENIGN DIAGNOSES

Diagnosis	n	Frequency (%)
Functional dysphonia	228	32
Reflux	154	22
Voice abuse	64	9
Laryngitis	54	7
Normal	52	7
Candidiasis (endoscopic diagnosis)	21	3
Other	25	3
Total	598	83

ii. *Diagnosis.* All patients were subject to flexible nasopharyngolaryngoscopy; of these, 598 (83 per cent) had normal or clinically benign findings. The frequencies of specific diagnoses are summarized in Table II. This shows that cases of functional dysphonia, reflux pharyngitis, voice abuse and nonspecific laryngitis accounted for 70 per cent of all cases seen during the period under study.

In contrast, 123 patients (17 per cent) were seen with clinically suspicious laryngeal lesions requiring microlaryngoscopy and histological assessment (Table III). Of these cases, 56 (45 per cent) were histologically benign, 27 (22 per cent) had normal microlaryngoscopies, 13 (11 per cent) were epithelial hyperplastic lesions and 27 (22 per cent) had histologically confirmed carcinoma. Of the latter, eight (30 per cent) had advanced lesions.

The overall prevalence of laryngeal cancer in our sample was 3.8 per cent (95 per cent confidence interval = 2.3–5.1 per cent). The positive and negative predictive values for flexible nasendoscopy are 22 per cent and 100 per cent respectively; in other words, nasendoscopy alone had a 22 per cent success rate in diagnosing laryngeal cancer in this patient cohort. As shown in Table IV, eliciting a smoking history improves the diagnostic accuracy of nasendoscopy for laryngeal carcinoma; all patients with laryngeal cancer were current or former smokers. Similarly, 13 cases of EHLL – 1.4% of patients – were diagnosed. There were no non-smokers with such lesions, compared with two ex-smokers (1.3 per cent) and 11 smokers (5.4 per cent).

TABLE III

CLINICALLY SUSPICIOUS LESIONS

Diagnosis	n	%
Benign lesions	56	45
Normal	27	22
Hyperplasia / dysplasia	13	11
Carcinoma (total)	27	22
Early carcinoma	19	16
Advanced carcinoma	8	6

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TABLE IV
DIAGNOSTIC ACCURACY VS. SMOKING HISTORY

Smoking history	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence (CI) (%)
Never	0	95	0	100	0
Ex-smoker	100	91	7	100	0.7 (0–1.4)
Current smoker	100	67	30	100	12 (7.8–16.6)
Total	100	86	22	100	3.8 (2.4–5.2)

CI = confidence interval

iii. *Analysis of laryngeal cancer incidence.* As mentioned previously, a total of 27 patients received histologically confirmed diagnoses of laryngeal cancer. This represents 22 per cent of all patients with clinically suspicious endoscopic findings. When patients seen within two weeks of referral were compared with those seen after this interval, 20 cancers (incidence of 3.9 per cent) were detected in the former group – 40 per cent of these advanced – while seven cases (2.8 per cent) of squamous cell carconoma (all early) were detected in patients seen more than two weeks after referral. There was no significant difference in detection rates between these two groups (odds ratio 0.84; chi-square = 0.15; $p = 0.69$). This lack of significance of detection ratios persisted for similar analyses of subgroups with long symptom duration ($p = 0.39$) and short symptom duration ($p = 0.41$). Although almost twice as many females as males were seen in this study, the respective detection rates of both EHLL and carcinoma – as expected – were higher for males (4.2 per cent and 9 per cent) than for females (0.4 per cent and 1.3 per cent); these differences were statistically significant ($p = 0.0003$ and 0.00005, respectively).

iv. *Symptom duration.* Information on length of presentation was collected for 631 patients. Table V shows the relative incidence of laryngeal cancer and EHLL in groups of long (more than two months) and short (less than two months) symptom duration. For both laryngeal hyperplasia and carcinoma, the difference between patients with long and short duration was not significant, although the difference approached statistical significance for laryngeal carcinoma ($p = 0.09$). Power analysis revealed that at least 990 subjects would have to be analysed for the latter difference to become significant.

Discussion

Diagnosis of laryngeal cancer at an early stage impacts positively on patient prognosis.[1,2] As hoarseness is almost universal in laryngeal cancer,[2,7] the persistence of this symptom is an important risk factor in early detection. The incidence of laryngeal cancer is steadily increasing in the UK.[10] This increase has been attributed to increasing consumption of tobacco and alcohol.[6,10]

Government commitments to the reduction of waiting times for diagnosis and treatment of cancer have resulted in oncology units being required to see all suspected cancer patients within two weeks of urgent GP referral.[9] Our study revealed a decrease in the number of referrals seen within this time over the duration of the study. This may be due to overall increase in the workload of the department, but was also contributed to by the high rate of non-attendance (20 per cent) for patients with scheduled appointments. However, increase in our consultant staff has facilitated mobilization of an extra consultant to be assigned to our rapid-access dysphonia clinic. This should achieve better compliance with government targets, but another audit spiral would be needed to confirm this.

Although many laryngeal cancers arise without progression through precursor clinical stages,[4] identification and follow-up of patients with EHLL is important for early detection of subsequent malignant transformation. In our study, 1.4 per cent of all patients had either hyperplastic or dysplastic lesions. To our knowledge, no similar studies on rapid-access dysphonia clinics have assessed detection rates of EHLL.

The detection rate for laryngeal cancer in our study was 3.8 per cent. This rate is similar to data previously reported in the first loop of this audit spiral by Hoare *et al.*,[1] and correlates with known incidences of laryngeal cancer. Similarly, the ratios between early and advanced cancers were similar to those in Hoare's study[1] and to figures reported by the Birmingham/West Midlands Regional Cancer Registry.[11]

There was no statistical evidence for the supposition that rapid referral would lead to increased detection of early stage laryngeal tumours. Although any reduction of the proportion of advanced laryngeal cancer would be of great clinical and financial importance, power analysis revealed that a sample of 3200 patients would be needed in order to have an 80 per cent probability of proving a 3 per cent reduction of the incidence of advanced tumours. Such large numbers may be achieved by a coordinated multicentre trial. Similarly, analysis for symptom duration showed differences in detection rates which – although interesting – did not reach

TABLE V
INCIDENCE OF LARYNGEAL CANCER: RELATION TO SYMPTOM DURATION

Symptom duration	Patients (n)	Laryngeal cancer n (%)	Advanced cancer n (%)	EHLL n (%)
<2 months	204	3(1.5%)	0(0%)	4(2%)
>2 months	426	17(9%)	7(1.6%)	9(4.5%)

EHLL = epithelial hyperplastic laryngeal lesion

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statistical significance. A reasonable sample size (990) would be necessary to impart adequate power to this analysis, lending credence to the intuitive suggestion that long symptom duration may be a high risk factor in this cohort. This premise, however, remains unproven. These findings lend further evidence to the fact that the preclinical behaviour and characteristics of individual laryngeal cancers are the main determinants of its stage at eventual detection.[4,7,8]

- **Early referral and attendance at hospital is imperative for detection of malignancy**
- **This is a retrospective study of 930 patients seen over four years in an early diagnostic dysphonia clinic**
- **There was no statistical link between early detection of neoplasia and assessment within two weeks of referral, but details of smoking history and symptom duration were important in predicting likely malignancy; the authors suggest that these details be included in the referral letter**
- **Although in this study 70 per cent of patients were seen within two weeks of referral, a greater financial commitment will be needed to satisfy the objective of a maximum two-week wait**

Conclusion

Early assessment and treatment of dysphonia alleviates patient anxiety. Even when examination yields clinically benign lesions, targeted treatment – in the form of reassurance, speech therapy or minor surgery – can be initiated on a multidisciplinary basis. This occurs in our unit, but requires greater financial and staffing commitments than a dedicated cancer detection programme currently provided. This study shows that inclusion of smoking history and symptom duration in the referral criteria can improve the detection accuracy of a rapid-access programme. This can provide a cost-effective way of streamlining attendance at a rapid-access dysphonia clinic.

References

1 Hoare TJ, Thompson AC, Proops DW. Detection of laryngeal cancer – the case for early specialist assessment. *J R Soc Med* 1993;**86**:390–2
2 Watkinson JC, Gaze MN, Wilson JA. Tumours of the larynx. In: *Stell and Maran's Head and Neck Surgery*. 4th edn. Oxford: Butterworth-Heinemann, 2000
3 Teppo H, Koivunen P, Sipita S, Jokinen K, Hyrynkangas K, Laara E, *et al*. Decreasing incidence and improved survival of laryngeal cancer in Finland. *Acta Oncol* 2001;**40**:791–5
4 Ferlito A. The natural history of early vocal cord cancer. *Acta Otolaryngol (Stock)* 1995;**115**:345–7
5 Cann CI, Fried MP, Rothman KJ. Epidemiology of squamous cell cancer of the head and neck. *Otolaryngol Clin North Am* 1985; **18**:367–86
6 Rafferty MA, Fenton JE, Jones AS. The history, aetiology, and epidemiology of laryngeal carcinoma. *Clin Otolaryngol Appl Sci* 2001;**26**:442–6
7 Miziara ID, Cahali MB, Murakami MS, Figueiredo LAP, Guimaraes JRR. Cancer of the larynx: correlation of clinical characteristics, site of origin, stage, histology and diagnostic delay. *Rev Laryngol Otol Rhinol (Bord)* 1998; **119**: 101–4
8 Kambic V. Epithelial hyperplastic lesions – a challenging topic in laryngology. *Acta Otolaryngol (Stock)* 1997; Supplement **527**:7–11
9 Department of Health. *The NHS Cancer Plan: A Plan for Investment, A Plan for Reform*. 2001. www.doh.gov.uk/cancer
10 Robin PE, Reid A, Powell DJ, McConkey CC. The incidence of cancer of the larynx. *Clin Otolaryngol* 1991; **16**:198–201
11 Robin PE, Powell J, Holme GM, Waterhouse JAH, McConkey CC, Robertson JE. *Clinical cancer monographs Vol. 2: Cancer of the larynx.* London: Macmillan Press, 1989

Address for correspondence:

Mr Phillip Moore,
25 Waterside Close,
Bordesley Green,
Birmingham B9 4QJ, UK.

E-mail: plamoore@rcsed.ac.uk

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