

Negative chest X-rays in primary care patients with lung cancer

Sally Stapley, Deborah Sharp and William Hamilton

ABSTRACT

Background

The main investigation for suspected lung cancer in primary care is a chest X-ray. Reports from secondary care show that some patients with normal chest X-rays transpire to have lung cancer. The assumption is that this occurs rarely in primary care.

Aim

The aim of this study was to examine the frequency of misleading chest X-rays in primary care, and whether there were any particular symptoms associated with them.

Design of study

Retrospective cohort study of the primary care records of 247 lung cancer patients diagnosed between 1998–2002.

Setting

All general practices in Exeter Primary Care Trust, Devon, UK.

Method

All chest X-rays and all common symptoms of lung cancer reported to primary care were identified from the medical records. X-ray results were categorised into three groups by the radiologist's report: normal; abnormal but no malignancy suspected (together classified as negative X-rays); or abnormal with possible malignancy.

Results

Of the 247 patients, 164 (66%) had a chest X-ray taken in primary care during the year before diagnosis: 126 of these (77%) were abnormal with possible malignancy; 21 (13%) were abnormal but with no malignancy suspected; in 17 (10%) the X-ray was reported as normal. Thus, 38 of 164 patients (23%; 95% confidence interval = 16 to 32%) had a negative X-ray. Negative X-rays were less common in the 90 days before diagnosis. No particular symptoms were significantly associated with negative X-rays.

Conclusion

Nearly a quarter of chest X-rays requested from primary care in lung cancer patients are negative. Further investigation is warranted with continuing or changing symptoms, even if the X-ray is not suggestive of malignancy.

Keywords

diagnosis; lung cancer; primary health care; referral and consultation.

INTRODUCTION

Over 38 000 patients in the UK are diagnosed with lung cancer each year.¹ Most lung cancers are identified after symptoms have begun. These symptoms are usually first reported to primary care.² However, all the common symptoms of lung cancer occur in benign conditions as well as with cancer, so it is useful for the GP to be able to have a simple investigation to identify those with possible cancer.

The initial investigation for possible lung cancer in primary care is a chest X-ray. Recommendations for the use of these are given in the UK Referral Guidelines for Suspected Cancer.³ These were first published in 2000, and revised in 2005.⁴ They advise an urgent chest X-ray for any haemoptysis, or for persistent (defined as lasting longer than 3 weeks) chest pain, dyspnoea, weight loss, hoarseness, or cough. However, some chest X-rays in patients with lung cancer are normal. Additionally, many X-rays ordered in primary care report vague shadowing, usually ascribed to infection. If cancer is thought to be a possibility in such cases, repeat radiology is usually recommended. The Referral Guidelines suggest referral for specialist investigation despite a normal chest X-ray when there is a high suspicion of lung cancer, although this is not defined further. The proportion of lung cancers presenting to primary care with a normal chest X-ray is unknown.

Secondary care studies of patients with normal chest X-rays and lung cancer have studied patients

S Stapley, researcher, CAPER research practices, Exeter; D Sharp, PhD, FRCGP, professor, Academic Unit of Primary Health Care, University of Bristol; W Hamilton, FRCP, FRCGP, senior research fellow, Academic Unit of Primary Health Care, University of Bristol.

Address for correspondence

William Hamilton, Academic Unit of Primary Health Care, Department of Community Based Medicine, University of Bristol, The Grange, 1 Woodland Road, Bristol, BS8 1AU. E-mail: w.hamilton@bristol.ac.uk

Submitted: 22 September 2005; **Editor's response:** 12 January 2006; **final acceptance:** 25 January 2006.

©British Journal of General Practice 2006; 56: 570–573.

with either haemoptysis or with dyspnoea. Cancer is diagnosed in 6–21% of patients referred for further investigation with haemoptysis and a normal X-ray.^{5–9} For dyspnoea and normal X-rays, the yield of cancers is under 1%.^{10–12} These percentages depend on the particular criteria used for specialist referral, and do not answer the two questions most relevant to primary care. Firstly, what proportion of chest X-rays in patients with lung cancer presenting to primary care are normal or have vague abnormalities not considered worthy of further investigation (negative X-rays)? Secondly, are there particular symptoms that are associated with negative X-rays? We sought to answer these questions in an analysis of X-ray results from the largest reported primary care series of lung cancers.¹³

METHOD

We identified all 260 patients aged 40 years or more with a primary lung cancer, living in Exeter Primary Care Trust, Devon, UK, diagnosed between January 1998 and September 2002. Cases were identified using two sources: the local cancer registry, and the computer systems of each primary care practice. Thirteen cases were not studied as their records were lost: eight after death of the patient and five where the patient had left Exeter after diagnosis. The main study was aimed at identifying and quantifying clinical features independently associated with lung cancer.¹³

The dates of reporting of any of the following symptoms to primary care were noted: haemoptysis, loss of weight, loss of appetite, dyspnoea, chest or rib pain, hoarseness, fatigue and cough, as were all records of chest X-ray requests. X-ray results were categorised into three groups with any disagreement resolved by consensus. The categories were:

- normal;
- abnormal but no malignancy suspected; and
- abnormal with possible malignancy.

Patients with indefinite abnormalities (such as ill-defined shadowing) were classified into group 2 or group 3 depending on the action suggested by the reporting radiologist. If any further investigation, such as a repeat chest X-ray or referral, was recommended (even if possible malignancy was not explicitly stated), or if malignancy was mentioned as a possibility, then the report was classified as group 3. For simplicity, groups 1 and 2 can be described as negative X-rays, and group 3 positive X-rays. The radiologists' reports were used as the only method of categorisation, as they would be all

How this fits in

The main investigation for suspected lung cancer is a chest X-ray, but in some cases these may not show the cancer. This study shows that up to a quarter of lung cancer patients have a primary care chest X-ray taken in the year before the diagnosis was made that does not reveal cancer. No particular symptom was associated with these chest X-rays. If a patient has continuing symptoms of possible lung cancer but a negative chest X-ray, further investigation may still be warranted.

that the GPs would have available to make their decisions about the need for further investigation.

RESULTS

We studied 247 cases, 170 (69%) in men and 77 (31%) in women, with mean ages of 72 and 68 years, respectively. Histology results were available for 237 of these: 80 (32%) had squamous carcinomas; 57 (23%) adenocarcinomas; 52 (21%) small cell; 21 (9%) large cell; and 27 (11%) unspecified carcinomas. The remaining 10 cases had been diagnosed clinically, all with strong radiological evidence, but were either too ill to have a biopsy or had declined one.

Of these 247, 164 (66%) patients had at least one chest X-ray requested from primary care in the year before diagnosis. A further four had an X-ray request made by the GP, but had been admitted to hospital before it was taken. The results of the first X-ray taken in the 164 patients were: 126 (77%) positive; 21 (13%) were abnormal but with no malignancy suspected (eight of these were reported as showing changes of chronic obstructive pulmonary disease, seven resolving infection, four cardiac failure, and two with pleural disease). In 17 (10%) the X-ray was reported as normal. Thus 38 of 164 patients (23%; 95% confidence interval = 16 to 32%) had a negative X-ray during the year before diagnosis. This equates to nearly one-sixth of all the cancer patients.

Table 1. First chest X-ray results in relation to the date of diagnosis.

Time before diagnosis (days)	Chest X-ray results		
	Positive X-rays	Negative X-rays	
		Normal	Abnormal, no cancer suspected
271–365	0	4	3
181–270	2	2	4
91–180	19	8	6
0–90	105	7	4
Total	126	21	17

Table 2. Chest X-ray results for particular lung cancer symptoms.

Symptom	Number of patients with this symptom	Chest X-ray results		
		Positive	Negative	
			Normal	Abnormal, no cancer suspected
Haemoptysis	41	20	2	6
Loss of weight	47	21	4	4
Loss of appetite	32	13	3	2
Shortness of breath	94	38	6	7
Chest or rib pain	68	23	5	2
Fatigue	50	17	2	1
Cough	120	60	6	11
Hoarseness	15	6	0	0

Chest X-ray results in relation to the time of diagnosis and subsequent X-rays

Table 1 shows the result of the first chest X-ray report, broken into four time periods before the diagnosis. The proportion of positive X-rays increased as the date of the X-ray approached the date of diagnosis: $\chi^2 = 58$, $P < 0.001$, 3 degrees of freedom. Six of the 17 patients with a normal X-ray had subsequent X-rays, all within 0–90 days of diagnosis: all were abnormal, with malignancy suspected in one, and possible malignancy in five. Nine of the 21 patients with an abnormal X-ray, but with no malignancy suspected, had later X-rays: one had the same result (taken at 91–190 days), and eight showed possible malignancy (one at 91–180 days, and seven at 0–90 days).

Chest X-ray results in relation to the presenting symptom

The X-ray results for particular symptoms are shown in Table 2. Only symptoms occurring in the 30 days before the X-ray were counted, on the assumption that they prompted the X-ray request. For patients with multiple symptoms, the X-ray result is shown under each symptom. The proportion of positive X-rays was not significantly different across the eight symptoms: $\chi^2 = 3.7$, $P = 0.81$, 7 degrees of freedom.

DISCUSSION

Summary of main findings

A chest X-ray was taken in primary care in two-thirds of patients presenting with symptoms of lung cancer. In those who had an X-ray taken, the report was not suggestive of cancer in almost a quarter: indeed, over 10% of X-rays were reported as entirely normal. Although X-rays suggestive of malignancy became more common in the 3 months before diagnosis, even then, over 10% of X-rays were still negative.

Negative X-rays occurred with all the common symptoms of cancer other than hoarseness.

Strengths and limitations of the study

This is the first study to examine this issue from a primary care perspective. The number of cancers was large, and X-rays had been taken in the majority. The study was based in all practices in one area, and identified almost all cancers. A small number may have missed registration by the local cancer registry. These would have been patients diagnosed out of the locality and who did not return for treatment, probably because they had died. Although it is possible some of these had had a primary care chest X-ray, no diagnosis of lung cancer had been entered on the practice computer: if so, our practice searches should have identified them. It is very unlikely that these few missing patients would alter our findings greatly. We were also able to date the reporting of the symptoms to primary care and the X-rays accurately. However, we only studied symptoms that had been recorded in the primary care records, so some symptoms may be missing.

Comparison with existing literature and implications for clinical practice

There are two main explanations for the findings. Firstly, a chest X-ray reported as normal could be truly normal, with the lesion too small to be identified, or hidden behind intra-thoracic structures or the skeleton.¹⁴ Lung cancers vary in their growth rate, with doubling times as low as 7.5 days,¹⁵ although the mean doubling time is approximately 125 days.¹⁶ Faster growing tumours may be too small for the radiologist to detect, yet become visible soon afterwards.

This study did not investigate any possible errors in radiological reporting. Some of the negative X-rays may have been misreported. This has been shown before, with 'miss' rates of 19% and 24% from two secondary care studies.^{17,18} The first of these studies examined only nodular lesions, so is difficult to compare with the study reported here.¹⁷ The second paper studied 58 patients with lung cancer (out of an approximate 300 seen in the hospital over the period of study): 28 had had an X-ray before the one in which the cancer was identified.¹⁸ On review, 14 of these 28 X-rays were abnormal, with hilar or nodular lesions being the commonest missed abnormality.

Not all patients in this study had an X-ray requested by primary care. This can partly be explained by the 26 patients without any of the common symptoms of lung cancer. Others may have been diagnosed while attending secondary

care, perhaps as an outpatient, or identified during routine pre-operative investigation, or when admitted as an emergency. Even so, it is clear that some patients with symptoms warranting an X-ray are not having one.

This study aimed to answer two questions. The first answer — of approximately a quarter of X-rays being normal or misleading — means that GPs who suspect lung cancer cannot rely on a negative X-ray to dispel the possibility. If clinical suspicion remains, usually as a result of continuing symptoms or the development of new ones, then further investigation is warranted. This could be a repeat X-ray, or referral for CT scanning or bronchoscopy (although the former also has a 'miss' rate).¹⁹ The second answer is that all common symptoms of lung cancer may be associated with negative X-rays. The only exception to this was the small number of patients with hoarseness who all had positive X-rays. This may simply reflect the small numbers in this group. Alternatively, hoarseness may be a late symptom with an extensive tumour invading the trachea, or disrupting the recurrent laryngeal nerve. A third guide to primary care investigation can be derived from our results. Few X-rays were positive more than 6 months before diagnosis. Therefore, if a patient has a symptom suggestive of possible cancer, little reassurance can be taken from a negative X-ray result more than 6 months old.

Earlier symptomatic diagnosis of lung cancer may not provide a mortality benefit — indeed the survival of patients with missed lesions on X-rays matched the survival of those with no diagnostic delay in one hospital series.¹⁸ However, earlier diagnosis may reduce morbidity, both in terms of earlier amelioration of symptoms and possibly less extensive surgery. Furthermore, there are psychological disadvantages from delays in diagnosis. This may be compounded by a negative X-ray result, which can only serve to raise hopes in the short-term.

Negative or misleading chest X-rays in lung cancer are quite common in primary care. This is a genuine problem for GPs, as the predictive values for individual symptoms are relatively low.¹³ Therefore, most negative X-rays will be true negatives. However, in the presence of continuing or changing symptoms, doctors cannot be reassured by a negative result. Whether this negative result is due to the lesion being genuinely invisible or as a result of radiologist error is immaterial: further investigation is appropriate.

Funding body

Project funding from the UK Department of Health

(reference 121/7523). The funding source had no role in the study other than financial support. The views expressed in the publication are those of the authors and not necessarily those of the Department of Health. All authors had full access to all data, and take final responsibility for publication. William Hamilton is funded through his research practice (Barnfield Hill, Exeter) and RCGP/BUPA and NHS Fellowships

Ethics committee

The study was approved by the North and East Devon research ethics committee (LREC reference 2001/8/121)

Competing interests

The authors have stated that there are none

Acknowledgements

We wish to thank all 21 general practices in Exeter, the Dendrite cancer registry, and the Patients and Practitioners Service Agency, without which this project would not have been successful.

REFERENCES

1. Cancer Research UK. *CancerStats monograph 2004*. London: Cancer Research UK, 2004.
2. Hamilton W, Sharp D. Diagnosis of lung cancer in primary care: a structured review. *Fam Pract* 2004; **21**: 605–611.
3. Department of Health. *Referral guidelines for suspected cancer*. London: Department of Health, 2000.
4. National Institute for Health and Clinical Excellence. *Referral guidelines for suspected cancer* (NICE revision 2004–2005). London: NICE, 2004.
5. Lederle FA, Nichol KL, Parenti CM. Bronchoscopy to evaluate hemoptysis in older men with nonsuspicious chest roentgenograms. *Chest* 1989; **95**: 1043–1047.
6. O'Neil KM, Lazarus AA. Hemoptysis. Indications for bronchoscopy. *Arch Intern Med* 1991; **151**: 171–174.
7. Kaminski J. Frequency and causes of hemoptysis and role of bronchoscopy in patients with normal chest roentgenogram hospitalized in the Department of Physiopneumology Silesian Medical University in the years 1961–1996. *Pneumonol Alergol Pol* 2001; **69**: 663–668.
8. Hirshberg B, Biran I, Glazer M, Kramer MR. Hemoptysis: etiology, evaluation, and outcome in a tertiary referral hospital. *Chest* 1997; **112**: 440–444.
9. Colice GL. Detecting lung cancer as a cause of hemoptysis in patients with a normal chest radiograph: bronchoscopy vs CT. *Chest* 1997; **111**: 877–884.
10. Nielsen LS, Svanegaard J, Wiggers P, Egeblad H. The yield of a diagnostic hospital dyspnoea clinic for the primary health care section. *J Intern Med* 2001; **250**: 422–428.
11. Pratter MR, Curley FJ, Dubois J, Irwin RS. Cause and evaluation of chronic dyspnea in a pulmonary disease clinic. *Arch Intern Med* 1989; **149**: 2277–2282.
12. DePaso WJ, Winterbauer RH, Lusk JA, *et al*. Chronic dyspnea unexplained by history, physical examination, chest roentgenogram, and spirometry. Analysis of a seven-year experience. *Chest* 1991; **100**: 1293–1299.
13. Hamilton W, Peters TJ, Round A, Sharp D. What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. *Thorax* 2005; **60**: 1059–1065.
14. Shah PK, Austin JHM, White CS, *et al*. Missed non-small cell lung cancer: radiographic findings of potentially resectable lesions evident only in retrospect. *Radiology* 2003; **226**: 235–241.
15. Shyu CL, Lee YC, Perng RP. Fast-growing squamous cell lung cancer. *Lung Cancer* 2002; **36**: 199–202.
16. Chapman BE, Yankelevitz DF, Henschke CI, Gur D. Lung cancer screening: simulations of effects of imperfect detection on temporal dynamics. *Radiology* 2005; **234**: 582–590.
17. Quekel L, Kessels A, Goei R, van Engelshoven J. Miss rate of lung cancer on the chest radiograph in clinical practice. *Chest* 1999; **115**: 720–724.
18. Turkington P, Kennan N, Greenstone M. Misinterpretation of the chest x ray as a factor in the delayed diagnosis of lung cancer. *Postgrad Med J* 2002; **78**: 158–160.
19. Gurney JW. Missed lung cancer at CT: imaging findings in nine patients. *Radiology* 1996; **199**: 117–122.