

ORIGINAL ARTICLE

Primary care radiography in the early diagnosis of lung cancer

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Abstract

Finding an abnormality on a plain chest radiograph is usually the first definite evidence of a lung cancer, so this investigation is currently pivotal in the diagnosis of the disease. Although the National Institute for Clinical Excellence (NICE) has produced guidance on when a chest radiograph should be done for putative lung cancer presentations, cancer will usually be only one of a number of possible diagnoses, so this is somewhat artificial. Neither is there any evidence that obtaining a chest radiograph for these features leads to an improved outcome. Another major concern is the poor public awareness of the symptoms for which a chest radiograph is recommended. This article discusses the role of the chest radiograph in the early diagnosis of lung cancer with particular emphasis on the limited value of a single negative result and on the potential implications of interventions to increase the number of chest radiographs done in primary care.

Keywords: *Early diagnosis; lung cancer; plain chest radiograph; computed tomography; overdiagnosis.*

Introduction

In 2006 lung cancer killed over 34,000 people in the United Kingdom, accounting for 7% of all deaths^[1,2]. Despite intensive measures designed to improve the outcome of lung cancer in the United Kingdom, 5-year survival has remained at just over 5%. This compares poorly to the 13% reported in the United States and is also much higher in several other European Union countries^[3]. One explanation for the difference is that patients in the United Kingdom may have more advanced stage at presentation^[4].

Patients with lung cancer frequently present with non-specific respiratory symptoms for which a chest radiograph is a sensible early investigation, to narrow an initially broad differential diagnosis. Besides lung cancer, this includes respiratory tract infections, including tuberculosis, interstitial lung disease, exacerbation of chronic obstructive pulmonary disease (COPD), bronchiectasis and heart failure, to mention but a few. The plain chest radiograph is also the first investigation recommended by the National Institute for Clinical

Excellence (NICE) for the investigation of putative lung cancer presentations^[5]. Despite the importance of the plain film to the initial evaluation of lung cancer, its value in this context has received relatively little attention. This article discusses some of the complexities relating to this test in the context of lung cancer diagnosis.

The chest radiograph as a screening tool

We have learnt much about the value of the chest radiograph in the diagnosis of lung cancer from the mass screening studies of asymptomatic smokers, conducted in the 1980s^[6–12]. These studies have also provided important insights into the natural history of the disease. Muhm *et al.*^[13] reported on the ability of radiologists in the Mayo Lung Project mass screening study to identify lung cancers. Ninety percent of peripheral cancers identified and 65–70% of central cancers were believed retrospectively to have been present on previous films. Many of these tumours were small and indistinct and it is

doubtful whether many could prospectively have been identified, but these results do tell us about a lack of sensitivity of a single chest radiograph, especially in early disease. However, the failure of the chest radiograph mass screening studies to result in overall benefit does not appear to arise from a lack of sensitivity. More cases were identified at an early stage, and these did indeed have a good outcome. The problem was that substantially more cases than expected were identified, so, whilst disease-specific mortality fell, overall mortality was not improved^[6,8–10,14–17]. Although other explanations have been advanced, these data have led to the so-called overdiagnosis hypothesis: the concept that clinically indolent disease was revealed by screening, whilst the tumours with genuine lethal potential were not identified, presenting instead with symptoms in the interval between screening visits. Such a problem is not unique to lung cancer and appears to be inherent in screening for cancer of any type.

The implications of overdiagnosis

If the overdiagnosis hypothesis is accepted, it is possible that the apparently poor survival rate in the United Kingdom may merely reflect a lower detection rate of such biologically inconsequential tumours. This might arise if chest radiographs are obtained less frequently in primary care than in other developed countries. For example, the average patient with moderate or severe COPD, who carries as a consequence of this disease a very high risk for lung cancer, will suffer about one exacerbation per year, on average^[18]. Many of these exacerbations are likely to produce symptoms for which a chest radiograph is recommended by the NICE lung cancer guideline. If a lung cancer is identified on a chest radiograph performed for such an exacerbation, the tumour itself will have been coincidentally discovered and be asymptomatic. One might expect this scenario to arise frequently. In fact it appears to be infrequent in a UK population. In unpublished observations, I found that 65% of patients presenting with lung cancer in Doncaster in 2007 had not a single chest radiograph in the 6–10 years prior to the diagnosis (excluding the film following which the diagnosis was made). Thus, it is possible that the population of lung cancer patients identified in the United Kingdom is undiluted with cases of inconsequential tumours, resulting from a frugal chest radiograph ordering policy. It is possible that in the countries reporting superior survival figures, at-risk patients are more likely to receive a chest radiograph. In this case, the low survival rate seen in the United Kingdom would not be a cause of recrimination: actually quite the opposite, as the unnecessary woe and healthcare interventions would be prevented in the patients who have innocuous cancers.

There is some evidence in support of the hypothesis that apparent lung cancer outcomes in the United

Kingdom might be distorted by relatively fewer indolent cases identified coincidentally, as a result fewer radiographs being undertaken. Hart and Wall^[19] estimated that the annual per caput effective radiation dose in the United Kingdom in 2001/2002, from medical and dental procedures, was 0.38 mSv. Conventional radiographic and fluoroscopic examinations contributed about 34% of the dose. The per caput dose was low in comparison with other countries having similarly developed systems of health care. Scanff *et al.*^[20] estimated a per caput effective dose in 2002 of between 0.66 and 0.83 mSv in France and Borretzen *et al.*^[21] estimated the per caput effective dose at 1.09 mSv in Norway. Hart and Wall^[19] concluded that the lower radiation dose was partly due to a lower frequency of radiographs per head of population in the United Kingdom. The reasons for this difference are unknown, but anecdotally my primary care colleagues vividly recall publicity discouraging the use of chest radiographs in primary care in the 1970s and 1980s, and the notion that the ordering of a chest radiograph in primary care is frowned on remains current.

The value of early diagnosis

It is possible to take a very nihilistic view that all the long-term non-small cell lung cancer survivors are those with biologically low-grade tumours, who would have survived almost whatever treatment they had, or had not, received. However, the division between tumours with and without lethal potential is likely to be an oversimplification. The variation in the rates of cancer progression between cases is clinically apparent and presumed to result from heterogeneity of tumour biology and host–tumour interactions. The existence of a group of patients with a relatively less aggressive lung cancer, that may be susceptible to cure if identified early, but not be curable if identified late, is as yet a matter of speculation. If it exists, earlier diagnosis should translate into higher rates of radical therapy and an overall improvement in mortality. Given the failure of mass screening to identify this group, we are at present in the position of trying to identify early symptomatic disease.

Long-term survival is not the only consideration in trying to improve lung cancer diagnosis: late diagnosis is usually bad for patients and their relatives. It is frustratingly common for patients to present for the first time with lung cancer only when they have become severely ill, yet after having suffered debilitating symptoms for a protracted period. Not only does the lateness of diagnosis obviate radical treatment options, it also prevents recruitment of appropriate medical and social inputs, including optimization of symptom control using palliative treatments, the planning of care and the time for the patient and family to adjust to the diagnosis.

The chest radiograph in symptomatic lung cancer

Contrary to previous dogma, it is not intrinsic to the disease that the interval between the onset of symptoms and the presence of a diagnosable cancer is short. Evidence is emerging confirming that patients suffer lung cancer symptoms for prolonged periods before diagnosis^[22,23]. It is also clear that most of the overall time to diagnosis is accounted for by delays in patients seeking attention or in primary care, with time following referral accounting for relatively much less time^[24]. These data support the introduction of measures to facilitate early presentation, including using social marketing techniques to educate patients and their primary care teams, for example on the symptoms recommended by NICE for an urgent chest radiograph.

The lack of specificity of a chest radiograph reported as suspicious of lung cancer means that it is usually necessary to perform more sophisticated diagnostic procedures, before a definitive diagnosis and certainly before treatment can be decided on. The chest radiograph is acting in this sense as a preliminary screening test to identify a population requiring further investigation. The problem with this approach is that a good screening test should produce few false-negatives (i.e. have a high sensitivity). The evidence for the sensitivity of the chest radiograph from the American mass screening data referred to above gives cause for concern, but there the population concerned was asymptomatic, American, and relied on older technology. Sensitivity in the reporting of radiographs from symptomatic patients will depend on the size and location of the tumour, which will vary according to the extent of the disease (likely to be more advanced in symptomatic cases), the presence or otherwise of intercurrent lung disease, the availability of prior radiographs for comparison and not least the skill of the reporting radiologist (each of whom will have varying thresholds for raising the possibility of lung cancer; i.e. having their own sensitivity and specificity). There is some evidence that a single chest radiograph may have a relatively poor negative predictive value (i.e. confidence that if it is reported to be normal, the disease is genuinely absent) in a UK population. In the study of Shapley *et al.*^[25], in the 12 months prior to the diagnosis, 38 of 164 lung cancer patients had previously had a negative radiograph. Negative radiographs were less common in the 90 days before diagnosis; films obtained earlier were quite frequently reported to be normal. These data indicate a 77% overall sensitivity for a single chest radiograph, if we accept that the disease was meaningfully present when all of the radiographs were obtained. The implication is that if a film has been normal, in the case of continuing suspicion of lung cancer, the appropriate strategy may be either to repeat the film, at say 2–3 months, or to refer

immediately to secondary care for consideration of bronchoscopy and/or computed tomography scanning.

An alternative strategy in the initial investigation of patients with lower respiratory symptoms for which lung cancer is a possible explanation, might be to go straight to low-dose chest computed tomography scanning. This would have much higher negative and positive predictive values than the plain radiograph, but the cost would be substantially greater. I believe that although this may be an option for the future, we first need to properly evaluate the humble, cheap and readily available plain radiograph.

Conclusions

The lack of sensitivity of the plain chest radiograph means that a single negative examination should not be relied on to exclude lung cancer. However, it is certainly possible for the chest radiograph to identify the disease at a radically treatable stage and the absence of any superior front-line test to evaluate lower respiratory symptoms that may portend lung cancer means that the plain chest radiograph will retain a central place in the diagnostic pathway for the foreseeable future.

With improved awareness of early lung cancer symptoms in patients and in their primary care practitioners, the diagnosis of symptomatic disease should be able to be made much earlier than at present. If more chest radiographs are ordered, coincidental discovery of biologically indolent cases would be expected to increase. Although this would improve disease-specific survival, this intervention would be harmful because those patients with inconsequential cancers will be unnecessarily exposed to the trauma, both physical and mental, that goes with the diagnosis (as seen in the mass screening studies). A more aggressive chest radiograph policy would only be of overall benefit if a significant number of tumours with lethal potential were also identified at a radically treatable stage. This important issue requires further study. At present the best hope of producing a meaningful improvement in lung cancer mortality appears to lie in the earlier diagnosis of genuinely symptomatic disease.

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