Chest radiographs and the elusive lung cancer

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ABSTRACT

Background and Objectives: Lung cancer is the commonest cancer killer in the western world. Many patients have lung cancers first identified on chest radiograph (CXR). Potentially curable cancers are often missed on CXR. This study quantified the incidence of cases of lung cancer which were initially overlooked and studied the causes of delayed diagnosis. **Materials and Methods:** All consecutive patients discussed during a 3-month period at the local lung cancer multidisciplinary meeting (MDM) were identified. All imaging within two years prior to diagnosis of lung cancer were reviewed with its report. Any CXR examination which failed to raise the potential for lung cancer was blindly reviewed by four consultant chest radiologists. **Results:** 189 patients were identified from the MDM over three months. 38,049 CXRs were carried out in the trust over the same period. Of the 189 patients, 58 had previous CXRs within 2 years reported as normal. On review 27 (47%) showed an abnormality in the region of the lung subsequently shown to have cancer. 70% of lesions were central, obscured by the heart, diaphragm, clavicles or mediastinum. **Conclusions:** This study shows that 1 in 1,409 CXRs reported as normal harbours a visible lung cancer on retrospective review. In this group 14% of patients with lung cancer could potentially have been diagnosed earlier. Of those that had previous CXRs, 47% had abnormal CXRs reported as normal. This study qualifies the rate of missed lung cancer on CXR in clinical practice and highlights where on CXR cancers are missed.

Keywords: Chest radiograph, lung cancer, malignancy

INTRODUCTION

Lung cancer is the most common cause of cancer death in the UK accounting for 6% of overall national mortality and around 35,000 deaths a year. In 2008, lung cancer was estimated to account for 18% of cancer deaths worldwide. Both 1-year and 5-year survival are inversely proportional to disease stage.^[1,2]

International focus has moved to the development of lung cancer screening programs in high-risk patients (NLST in the USA,^[3] NELSON in Europe^[4]) with several studies in the UK and France nearing completion.^[5,6] The Fleischner

society provides guidance on the importance of following up incidental nodules identified on computed tomography (CT) scanning, highlighting the prevalence of lung cancer.^[7]

Nevertheless, the chest radiograph (CXR) remains the workhorse of chest imaging and the first-line investigation for the majority of symptomatic patients. Previous studies have shown CXR to have a poor sensitivity of 23% when compared to CT.^[8] Importantly, the performance of the CXR falls as the size of the lesions decrease, limiting the sensitivity for detecting the very lesions with greatest potential curability.^[3,8] When compiling the disease stage of patients at diagnosis, NICE found that almost 50% had Stage IV disease and only 14% had Stage I disease with more advanced disease stage at initial diagnosis negatively impacting treatment options and prognosis.^[9]

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How to cite this article: Walker AE, Murchison JT, Beek EV, Ritchie G, Sharkey J. Chest radiographs and the elusive lung cancer. Digit Med 2016;2:120-6.

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Access this article online

Quick Response Code

Website:

www.digitmedicine.com

DOI:

10.4103/2226-8561.194700

It has been shown that early cancers are only detected and interpreted correctly around 30% of the time, while in retrospect, 90% of peripheral cancers and 65%–70% of central lesions are evident on previous studies.^[10]

This study aimed to review patients with proven lung cancer and assess the potential for CXR to have detected the cancers in these patients earlier. We first sought to evaluate the prevalence of these missed cancers and relate the number of misses to the total number of CXRs taken. As a secondary measure, we assessed the location of these lesions on the CXR.

MATERIALS AND METHODS

After consent from the local Caldicott guardian, no further ethical approval was deemed required as this was considered an audit project that did not impact on patient outcomes. Patient information was collated over 3 months (January – March 2012) of all new lung cancer cases reviewed at the lung cancer multidisciplinary team (MDT) meeting in a large teaching hospital. This list was reviewed retrospectively to include only patients with a confirmed first presentation of lung cancer. Most patients included had pathological confirmation of disease but patients whose imaging and clinical course pointed to a diagnosis of malignancy, and in whom biopsy was not deemed in the patient’s interest, were also included in this study. Using the patient electronic database and picture archiving and communication system (PACS), further data on the remaining patients were accessed.

All patients with confirmed first presentation of lung cancer were searched on the Scottish national PACS system for previous imaging that included the chest. All imaging of patients performed within 2 years before their presentation at the lung cancer MDT, and the associated reports were assessed. Imaging and reports, which appropriately raised concern for malignancy or that prompted the MDT discussion and eventual diagnosis, were excluded from this study. This left a cohort of patients with imaging within the previous 2 years which had not raised the possibility of malignancy. Only CXRs were included in this study.

CXRs were placed on a work list and reviewed by four consultant radiologists with a respiratory interest. A further twelve control CXRs without lung cancer, from the same period, were added to the work list to reduce reporter bias. The consultants were aware of the normal control CXRs included but were unaware of the number of normal controls added. Even in retrospect, many of

the CXRs reviewed would not have cancers visible, either because of the location of cancer or because of tumor growth in the time span between the film and the time of diagnosis. These cases also acted as normal controls. The consultants were blinded to clinical information and subsequent imaging. Previous imaging of each patient and associated reports were made available to reviewing consultants to simulate the original reporting scenario.

Images were scored on a template with the consultants asked to determine if there was an area on the radiograph suspicious for malignancy, and if present, in which of six zones of the lungs, this abnormality was detected, namely, right or left and upper, middle, and lower zones.

The completed results from all four consultants were collated, and the results compared. The region of lung in which the malignancy was subsequently diagnosed on CT was compared with the work list results. Where all four consultants or three of the four agreed on an abnormality in the same region of lung, which correlated with the subsequent cancer region, this was considered a true abnormality. If two or fewer consultants considered an abnormality, this was considered as cancer not visible on the CXR.

RESULTS

The MDT discussed 369 cases over the 3-month period. After exclusion of benign disease, recurrent disease, and duplicate patient discussions, 189 patients with a new diagnosis of malignancy remained. Of these patients, 63 had previous imaging within 2 years that did not prompt concern for malignancy or lead to further investigation. The majority of these images were CXRs (*n* = 58). The remaining images comprised musculoskeletal (MSK) radiographs (*n* = 2) and CT of the chest investigations (*n* = 3). These other studies will be considered further in the discussion. These 58 CXRs compared with a background rate of 38,049 CXRs being carried out in the trust over the same 3-month period. This amounts to missing one lung cancer in 1409 reported CXR (0.07%).

Table 1: Distribution of reviewer responses

	4 reviewers correct	3 reviewers correct	2 reviewers correct	1 reviewer correct	0 reviewers correct
Abnormal films	15	12	4	16	11
Control films	9	2			1

After blinded review, including control radiographs, 27 CXRs (47%) were found to show a true abnormality while the remaining 31 (53%) were deemed negative with cancer not clearly evident. Table 1 demonstrates a division of the number of reviewers who identified the appropriate abnormality within each CXR. Furthermore, demonstrated is the number of reviewers who correctly identified control CXRs as normal. One control radiograph was identified as abnormal by all reviewers though the area of abnormality identified varied between the four reviewers. Using the same qualification for identifying abnormal radiographs, requiring at least three reviewers to agree, this meant that no false positives were recorded.

Four radiographs included in the study had not been formally reported by the radiology department as is the protocol for some specialty referred and inpatient radiographs in one center in accordance with local and IR(ME)R legislation. All four of these were found to show a true abnormality in our study.

The size of the lesions on radiograph measured retrospectively ranged from 7 to 70 mm. Within the true abnormality group, this ranged from 9 to 70 mm with a median of 25 mm. Within the unappreciable cancer group, where a lesion could be inferred the following review of subsequent CT, the size on radiograph ranged from 7 to 60 mm with a median of 25 mm.

Time between radiograph and subsequent CT ranged from 1 to 495 days. Within the true abnormality group, this range was 1 day to 428 days with a median of 22 days. Within the unappreciable cancer group, time to

CT ranged from 1 to 495 days with a median of 123 days. This time, delay is important to appreciate, as the longer the interval, the more likely it is that the CXR would not have shown cancer as it increased in size during the subsequent period.

Of the true abnormalities, 63% were right-sided lesions with distribution in the upper, middle, and lower zones of 37%, 34%, and 29%, respectively [Figure 1]. The unappreciable cancers were subsequently showed on CT to be 55% on the right, with 45% in the upper, 26% in the middle, and 29% in the lower lung zones.

These results equate to one radiograph harboring a visible, but not identified, malignancy in every 1409 CXRs reported. In our cohort, 14.3% (27/189) of all our lung cancer patients could potentially have been diagnosed at an earlier stage by CXR. Furthermore, 46.5% (27/58) of those patients with previous chest imaging could have been diagnosed earlier.

DISCUSSION

The results of this single teaching hospital cohort show that 27 potentially reportable abnormalities on CXR were present on a total background of 38,049 CXR being carried out over the same period. This amounts to missing one lung cancer in 1409 reported CXR (0.07%).

There are particular areas on the CXR where detection of lung lesions is notoriously more difficult: lesions superimposed on the hilum, clavicles, heart, or diaphragm; and lesions within the upper lobes.^[8,11] These constitute classical radiological teaching as review areas.

In this study, the area on the CXR where lesions were correctly identified retrospectively was spread evenly over the lung zones. Figure 1 demonstrates the approximate size, based on review of the radiographs with hindsight, and location of the abnormalities deemed true abnormalities. Seventy percent of our missed lesions

Figure 1: The circled areas demonstrate the position and approximate size of the missed true abnormalities on chest radiograph highlighting the classical chest radiograph review areas

Figure 2: This left upper zone ill-defined opacity was missed on initial radiograph (a). Computed tomography subsequently showed a spiculated lung cancer in the left upper lobe (b)

were obscured by the heart, mediastinum, clavicles, or diaphragms reiterating the classical radiological review areas. Figures 2-4 depict examples of these lesions from our study. Chest lesions can also be masked by less common prosthesis and medical adjuncts. Figure 5 demonstrates a right lower lobe lesion that was overlooked, presumably due to the overlying breast implant. Figure 6 shows an electrocardiogram lead covering a right upper zone mass.

This study describes the incidence of missed lung cancers in patients with previous imaging and highlights the

importance of practice audit. We have visually demonstrated the common areas of missed malignant lung lesions.

Of the non-CXR examinations identified by the sample, these included an unreported lung nodule (3 mm parenchymal nodule in the right lower lobe) on a CT of the chest subsequently developing into cancer. While the low yield of follow-up for small lung nodules is well appreciated throughout radiology, our CT case documents the importance of follow-up of nodules detected on cross-sectional imaging.

Two MSK radiographs also harbored lung tumors which were both felt to be present on review. These comprised

Figure 3: Solid mass behind the left heart border was missed on this occasion (a). Computed tomography shows a left hilar mass (b)

Figure 5: The right lower zone lesion, partially obscured by breast implant, was missed on this (a) and a previous radiograph before diagnosis was subsequently made on computed tomography (b)

Figure 4: A lesion below the right hemidiaphragm was missed (a), subsequently shown on computed tomography (b)

Figure 6: A spiculated lesion in the right upper zone was missed because it was obscured by the right cardiac monitoring lead (a). Later the mass was demonstrated on computed tomography (b)

Figure 7: Highlighting the importance of reviewing the whole radiograph. This shoulder radiograph was reported as normal (a) before computed tomography revealed and underlying lung cancer (b)

Figure 8: A further musculoskeletal radiograph was reported normal (a). A right hilar tumour was subsequently diagnosed on computed tomography (b)

Figure 9: The circled areas demonstrate the location and size of the lung lesions in the unappreciable group subsequently diagnosed on computed tomography

shoulder radiograph [Figure 7] and an anteroposterior thoracic spine radiograph [Figure 8]. This highlights the importance of reviewing the whole film. It also highlights a potential downside of focused, nonspecialist reporting where the potential for not recognizing significant abnormalities outwith the field of expertise is raised. Figure 9 demonstrates the size and location of the unappreciable lung lesions that were subsequently diagnosed on CT.

Missing lung cancer on CXRs is well recognized with the miss rate ranging from 10% to 50%.^[12] Our results fall within this reported range. We have shown an incidence of missed lung cancer on CXR of approximately 0.07%. This may seem low, but given the sheer volume of CXRs carried out in our region with a population of around 800,000, one lung cancer is overlooked approximately every 3 days. This highlights the importance of practice audit, and how such risk could be addressed through continuous training and expert interpretation of all performed radiological examinations. It is easy to identify overlooked pathology in retrospect, but the number of cases being overlooked is sobering. Other areas in radiology suffer a similar limitation. Mammography false-negative rates are quoted at 20% by the government while the SIGGAR study showed even cross-sectional imaging to be limited with a 7% false-negative rate of CT colon.^[13,14] This paper adds to evidence that we should be wary in assessing blame when looking back and should recognize missing lung cancer on CXR is a common occurrence. This should be appreciated in the setting of modern medicolegal practice. However, given that it is relatively common, by raising awareness and by

addressing possible causes, it may be possible to reduce the number of overlooked cases and to detect some cancers earlier.

Reviewing our local practice has highlighted the classical radiological review areas on the CXR as areas of cancer misses. We have also seen the importance of the classical teaching of “edge of film” review with MSK radiographs highlighted by missed cancers. These missed lesions provide a useful educational resource for all radiologists, with our misses highlighting the classical review areas and also the limitations of radiographs in detecting lung lesions. The importance of reviewing previous imaging where available cannot be overstated in this setting. The ability to assess chronicity and rate of growth of lesions is invaluable in forming an appropriate report.

Several methods have been utilized in research to try and improve the poor sensitivity of radiographs. Computer-aided detection (CAD) has been used by several studies and has shown some improvement in detection of lung lesions, particularly in less experienced readers; however, this comes with an increased false-positive rate.^[15] One such study compared a control group against radiographs with missed lung lesions. CAD was shown to detect cancer in almost half of the abnormal radiographs. This came at a cost of 4 false-positive lesions detected per abnormal radiograph and 2.4 false-positive lesions per control radiograph.^[16] Screening has also been considered in a variety of forms to detect more cancers. Low-dose CT has been used in a variety of small and large trials, with doses at 20%–25% of diagnostic chest CT.^[17] A Mayo Clinic trial following 1520 smokers over 3 years with low-dose CT detected 41 lung cancers; importantly, more than half of these cancers were Stage IA and were potentially resectable. As with CAD, the downside of this increased pickup rate was a large number of false positives generating extra workload and invasive procedures; 2800 nodules were followed up in this patient cohort.^[18] The National Lung Screening Trial in the United States from 2002 to 2004 recruited 53,456 smokers and ex-smokers and randomized them into low-dose CT and CXR follow-up. Results published in 2011 showed a 20% reduction in lung cancer mortality in the CT group and a 6.7% reduction in overall mortality.^[3] This has prompted a recommendation from the US Preventative Services Task Force in support of low-dose CT screening.^[19] This, together with other ongoing trials, has reinforced the call for low-dose CT

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lung cancer screening in high-risk patients.^[4-6] It should be realized that many more patients undergo CXRs than those considered at high risk for lung cancer, and we detect lung lesions in nonsmokers in significant numbers due to influences of passive smoking or due to underlying cancer elsewhere. In addition, radiologists are uniquely able to pick up lung lesions early by realizing the importance of peripheral viewing in MSK radiographs or the realization that overlying leads and implants can mask lesions as seen in our cohort.

The importance of follow-up films after consolidation should also be stressed. Consolidation can occur surrounding a mass or as a result of a central obstructing lesion with peripheral atelectasis. Case series have shown that up to 50% of lobar collapse can be due to an obstructing central tumor.^[20] In all cases, a follow-up CXR following initial treatment is highly recommended to ensure the CXR returns to normal. An American retrospective study showed a large number of delayed lung cancer diagnosis was due to follow-up advice from the radiology report not being followed.^[21] Our study included three cases with consolidation which did not suggest follow-up imaging which led to delay in diagnosis. All three of these were deemed true abnormalities on review. Furthermore, there were eight patients in whom consolidation was reported, and follow-up advised but not acted upon. These were excluded from our study as the CXR report had raised appropriate concern.

The main limitation of this study is a lower reviewer threshold to report abnormalities on these radiographs, knowing this was a lung cancer review. The addition of control radiographs was intended to reduce this bias. However, providing further control radiographs to simulate a reporting session would have required considerable reporting time by the reviewing consultants.

CONCLUSION

We have shown that patients who present with lung cancer have frequently undergone previous chest imaging where in retrospect there were clues to the underlying diagnosis. We have quantified how commonly lung cancer is missed on CXR and have shown roughly how many CXRs are performed for every lung cancer missed. This study reinforces the importance of the classical radiological review areas on the CXR as areas of cancer misses in real practice. The teaching of “edge of film” review with MSK radiographs is also highlighted by cases of missed cancers. This work reiterates the need

to ensure that consolidation clears and is not masking a more central cancer, particularly in high-risk patients. The importance of formally reporting all CXRs by an experienced radiologist is also stressed. Early cancer detection improves outcomes. There are major national and international initiatives to detect cancer early. The CXR is the initial imaging performed in the most new cases of lung cancer. By highlighting causes of lung cancer miss on the CXR, we have provided a learning tool which we hope will improve detection of lung cancer at an earlier stage and contribute toward improved lung cancer outcomes.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Available from: <http://www.cancerresearchuk.org/cancer-info/cancerstats/types/lung/mortality/uk-lung-cancer-mortality-statistics>. [Last cited on 2013 May 05].
2. ISD Scotland. Information and Statistics. Lung Cancer and Mesothelioma. Available from: <http://www.isdscotland.org/Health-Topics/Cancer/Cancer-Statistics/Lung-Cancer-and-Mesothelioma/>. [Last cited on 2016 Aug 28].
3. National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, *et al.* Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011;365:395-409.
4. Oudkerk M, Heuvelmans MA. Screening for lung cancer by imaging: The Nelson study. *JBR-BTR* 2013;96:163-6.
5. The UK Clinical Network Study Portfolio. Available from: <http://www.public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=10297>. [Last cited on 2013 Oct 06].
6. Blanchon T, Bréchet JM, Grenier PA, Ferretti GR, Lemarié E, Milleron B, *et al.* Baseline results of the Depiscan study: A French randomized pilot trial of lung cancer screening comparing low dose CT scan (LDCT) and chest X-ray (CXR). *Lung Cancer* 2007;58:50-8.
7. MacMahon H, Austin JH, Gamsu G, Herold CJ, Jett JR, Naidich DP, *et al.* Guidelines for management of small pulmonary nodules detected on CT scans: A statement from the Fleischner Society. *Radiology* 2005;237:395-400.
8. Sone S, Li F, Yang ZG, Takashima S, Maruyama Y, Hasegawa M, *et al.* Characteristics of small lung cancers invisible on conventional chest radiography and detected by population based screening using spiral CT. *Br J Radiol* 2000;73:137-45.
9. National Institute for health and care excellence. Lung cancer: Diagnosis and management. London: NICE; 2011.
10. Muhm JR, Miller WE, Fontana RS, Sanderson DR, Uhlenhopp MA. Lung cancer detected during a screening program using four-month chest radiographs. *Radiology* 1983;148:609-15.
11. Shah PK, Austin JH, White CS, Patel P, Haramati LB, Pearson GD, *et al.* Missed non-small cell lung cancer: Radiographic findings of potentially resectable lesions evident only in retrospect. *Radiology* 2003;226:235-41.

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12. Royal College of Radiologists. Available from: <http://www.rcr.ac.uk/docs/radiology/pdf/LungCancerReportNewsletterv14.pdf>. [Last cited on 2013 May 23].
13. NIH National Cancer Institute. Breast Cancer. Available from: <http://www.cancer.gov/types/breast/mammograms-fact-sheet#q4>. [Last cited on 2016 Jul 19].
14. Halligan S, Wooldrage K, Dadswell E, Kralj-Hans I, von Wagner C, Edwards R, *et al.* Computed tomographic colonography versus barium enema for diagnosis of colorectal cancer or large polyps in symptomatic patients (SIGGAR): A multicentre randomised trial. *Lancet* 2013;381:1185-93.
15. van Beek EJ, Mullan B, Thompson B. Evaluation of a real-time interactive pulmonary nodule analysis system on chest digital radiographic images: A prospective study. *Acad Radiol* 2008;15:571-5.
16. White CS, Flukinger T, Jeudy J, Chen JJ. Use of a computer-aided detection system to detect missed lung cancer at chest radiography. *Radiology* 2009;252:273-81.
17. ACRIN/NLST CT Technique Comparison Chart. American College of Radiology Imaging Network. Available from: http://www.acrin.org/Portals/0/Protocols/6654/forms/qcforms/CT_Technique_Chart.pdf. [Last cited on 2013 July 05].
18. Swensen SJ. CT screening for lung cancer. *AJR Am J Roentgenol* 2002;179:833-6.
19. Humphrey LL, Deffebach M, Pappas M, Baumann C, Artis K, Mitchell JP, *et al.* Screening for Lung Cancer with Low-dose Computed Tomography: A Systematic Review to Update the U.S. Preventive Services Task Force Recommendation. Available from: <http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/lung-cancer-screening>. [Last cited on 2015 Jan 04].
20. Woodring JH. Determining the cause of pulmonary atelectasis: A comparison of plain radiography and CT. *AJR Am J Roentgenol* 1988;150:757-63.
21. Singh H, Hirani K, Kadiyala H, Rudomiotov O, Davis T, Khan MM, *et al.* Characteristics and predictors of missed opportunities in lung cancer diagnosis: An electronic health record-based study. *J Clin Oncol* 2010;28:3307-15.