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 deaths worldwide. Both one year and 5 years survival are inversely proportional to disease stage [1]. Current statistics in Scotland, which has a population of approximately 5.2 million, show an incidence of approximately 1 in 1000 with 8 in 10,000 people dying due to lung cancer [2]. Similar incidence rates exist in larger countries, and in the USA approximately 160,000 die due to lung cancer each year [3].

Smoking is the primary reason for developing lung cancer. Therefore, smoking cessation is the best prevention for this fatal illness. However, as the lung cancer epidemic has been developing, ways of detecting the disease earlier have been explored. This is based on the fact that early, Stage 1, screening
detected lung cancer has a 5-year survival rate in excess of 85%, whereas more advanced lung cancer invariably leads to death in less than 2 years [4].

**Chest radiograph**

In the early 1980s, a lung screening programme using 4-monthly chest radiographs in high risk patients was developed at the Mayo Clinic [5]. Subjects selected were over 45 year old male heavy smokers defined as one pack/day. They were randomly assigned to a control group (4,593 patients) or repeated chest radiograph follow up at 4 month interval (4,618 patients) after they had undergone an initial chest radiograph and sputum cytology examination that were both normal. The follow up success was 75% at 4 months, and 92 lung cancers were detected by chest radiograph (of which 7 also had sputum cytology positive findings), while 15 patients had normal chest radiograph with abnormal sputum cytology for an overall incidence of 109 (2.4%). A significant number of these lung cancers were visible in retrospect. Furthermore, 52 of the lung cancer were early stage, while the 35 were already advanced stage disease at the time of detection.

Another study in New York randomised a similar population of 10,040 subjects to annual chest radiograph only vs additional 4-monthly sputum cytology [6]. This study showed similar outcome between the two groups, with 288 detected lung cancers equally distributed between the two groups.

It was concluded from this study that the 4-monthly screening for lung cancer using chest radiography and sputum cytology, although capable of detecting up to 20% of lung cancers, was unable to improve mortality advantage over patients who were offered annual testing [7].

A more recent attempt at using chest radiograph screening was carried out in the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial [8]. This study randomised 154,901 men and women aged 55-74 years to either standard care (77,456) or annual screening (77,445) for four years during the period 1993-2001. The number of lung cancer deaths was equal in both groups (1213 vs 1230) with similar stage and histology outcomes. The (Nederlands-Leuvens Longkanker Screenings Onderzoek) NELSON study is a Dutch/Belgian project, which recruited 20,000 high-risk subjects and randomised half of them for low-dose CT and the other half for chest radiograph screening [13]. It is the largest European study and has sufficient power to enable a statement whether low-dose CT screening has benefit over chest radiography screening.

Another study from Canada has just reported the first screening round results and is focused on inclusion of cytology using autofluorescence bronchoscopy as well as modelling approaches towards optimisation of predictive value for lung nodules [18].

A potential risk associated with screening is the false positive results that can lead to further investigations and additional costs. A randomized, controlled trial of low-dose CT versus chest radiography (n = 3318 in both arms) as part of the National Lung Screening Trial (NLST) demonstrated a false-positive rate of 21% and 9% for single low-dose CT and chest radiography screening, respectively [19]. A total of 7% of participants with a false-positive low-dose CT examination and 4% with a false-positive chest radiography subsequently underwent an invasive procedure.

Another potential risk associated with lung cancer screening is the potential increased risk of lifetime cancers as a result of ionising radiation. The estimated risk of cancer from exposure to CT ionising radiation is reported to be more when the screening is started earlier in life, or on annual basis, and in females. A study reported an estimated 5.5% increase in lung cancer risk attributable to annual CT-related radiation exposure and concluded that a mortality benefit of considerably more than 5% may be necessary to outweigh the potential radiation risks [20].

Screening programs are associated with additional costs, both from the screening procedure and the follow up interventions. Previous studies reported that screening for lung cancer appeared to be cost-effective in high risk, more elderly populations [21,22]. Other studies questioned the potential cost

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effectiveness of lung cancer screening. However, their results were based on lower estimated effectiveness of screening than what was demonstrated by the NLST [23,24].

A more recent cost-utility analysis of lung cancer screening by low dose CT reported that repeat annual lung cancer screening in high risk adults aged 50-64 was highly cost-effective [25]. The study also indicated that offering smoking cessation interventions with the screening program improved the cost-effectiveness of lung cancer screening between 20-45%.

A contrary report was published as part of a health technology assessment, which suggested that lung cancer screening would not be cost-effective [26]. However, it should be considered that this report was issued prior to the results of most of the recent large lung cancer screening trials.

DISCUSSION

Clearly, based on the above studies, CT is superior to chest radiographs for screening in lung cancer. Although the NLST appears to have answered the question conclusively, there are still ongoing studies that may influence the manner in which screening will be approached in the future. Significant debate is still ongoing as to how often we should be screening, the optimal population that could benefit, interpretation of nodules, avoidance of false positive results and approaches including PET-CT, MRI and autofluorescence bronchoscopy for instance [27-33]. Many of these points are still undergoing evaluation, and future study results are eagerly awaited.

There are some additional points to be taken into consideration, which may still give chest radiographs a potential role for screening of lung cancer.

First, chest radiographs have matured from a technical perspective, and the wide introduction of digital chest radiographs offers a new approach to application of Computer Assisted Diagnosis (CAD). Thus, several studies have shown greater sensitivity for lung nodule detection using CAD methodologies, and this may be of benefit when using the test as a screening test [34,35]. However, a conclusive study showing the benefit of screening with chest radiography and added CAD has not been performed and could be important in this respect.

Second, chest radiographs are by far the cheaper of the two imaging modalities and more commonly available. This is an important issue, particularly in countries that are less well developed and where smoking continues to be on the increase and the lung cancer epidemic is on the rise. It may not be feasible to arrange for large-scale screening using CT and in these circumstances, one could consider reaching for chest radiographs.

Overall, it is highly likely that low-dose CT screening for patients at high risk for developing lung cancer is a cost-effective approach which will lead to improved outcome due to earlier detection and treatment of this highly lethal malignancy. In countries that have the resources available, it makes sense therefore to use low-dose CT as a screening methodology. For countries where finances or logistics render low-dose CT screening impossible to deliver, chest radiographs on an annual basis should be considered and additional use of CAD may improve sensitivity for earlier lesions.

REFERENCES

1. Lung cancer mortality statistics.


