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Screening for lung cancer

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Abstract

The lethality of lung cancer is related to the advanced stage at diagnosis. Initial studies have demonstrated that screening computed tomography (CT) is effective in diagnosing lung cancer at an earlier stage when compared with current clinical practice, however the best clinical approach for screening detected nodules has to be defined. The population to be identified as high risk should be over 50 years of age and should have smoked at least one pack/day for 20 years. CT protocols should use multidetector CT, low dose and a 2.5 reconstruction interval. Diagnostic work-up on detected nodules should be designed according to size and consider CT at 3 or 12 months to evaluate doubling time, CT enhancement, PET/CT and/or FNAB or VATS. The prevalence of lung cancer in the screened population is 1.1%–2.7%, and the incidence is 0.2%–1.1%. Eighty-one percent of cancers are diagnosed in stage I. The percentage of surgery performed for benign lesions ranges from 21% to 55%. In our series, the overall mortality rate was 3.2% in 5 years. The results of randomized clinical studies, when available, will assess the real efficacy of CT in reducing lung cancer related mortality.

Keywords: *Radiography of lung neoplasms; epidemiology of lung neoplasms; X-ray computed tomography; mass screening methods.*

Introduction

Lung cancer is one of the absolute priorities in oncology because of its mortality, incidence, social and economic impact. Prevention strategies aimed at reducing cigarette smoking had poor results[1]. The lack of clinical signs at the early stages and therapeutic inefficiency for advanced stages, lead to the evidence that early diagnosis should reduce lung cancer related mortality, as in early stages 70% of cases can be treated successfully with surgery[2]. This justifies the need to study the impact on survival of a lung cancer screening program with stronger motivation than those used for assessing and spreading the standard protocols for breast, prostate and colonic cancer screening[3]. Opportunities for screening for lung cancer have been debated for years, but several studies have shown that conventional chest X-ray and sputum examination did not satisfy the primary criteria of a screening test[4,5], until the value of low-dose spiral CT

in detecting small parenchymal lesions was demonstrated by some reports[6,7].

The diagnostic imaging technique to be applied was stated in the first ELCAP report[6], which describes the CT tumour detection rate as four times higher than chest X-ray, and by studies demonstrating similar accuracy of low-dose spiral CT and conventional CT in detecting pulmonary nodules[8].

While awaiting the new promising techniques of molecular biology, multidetector computed tomography[9–11], with the use of low dose protocols, is nowadays widely recognized as the best technique for lung tumour screening.

The high accuracy, together with the low biological and economical costs, justify the success of the protocols for the early detection of lung cancer by low-dose spiral CT. This is confirmed by the growing number of ongoing studies all over the world.
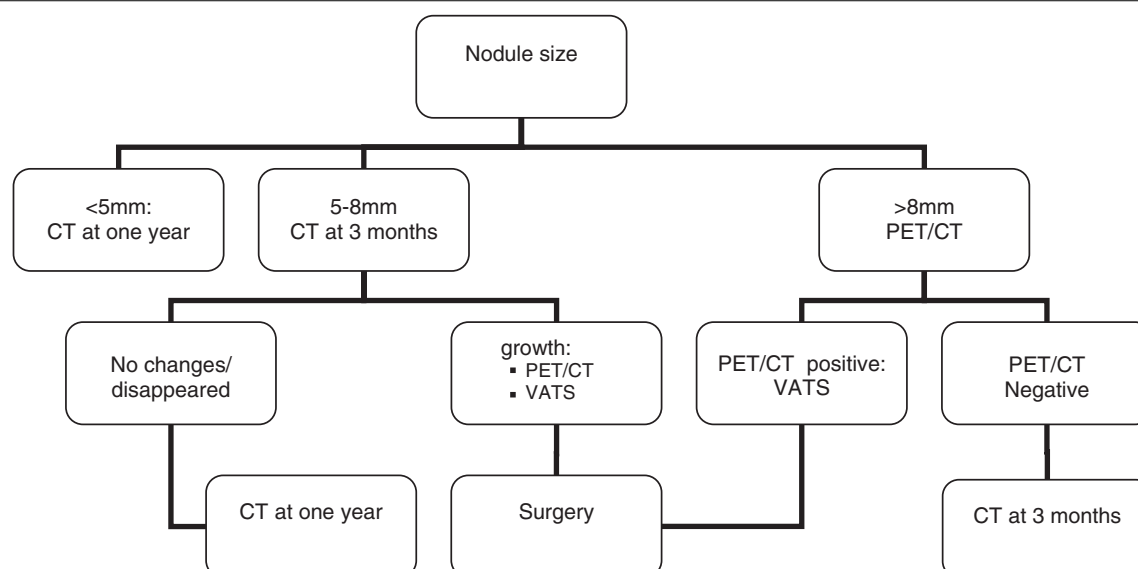
Figure 1   **Protocol for the management of lung nodules.**

Table 1   Prevalence, incidence and percentage of stage I tumours detected by low-dose CT in published lung cancer survey studies

	Prevalence			Incidence		
	Subjects	Tumours (%)	Stage I (%)	Subjects	Tumours (%)	Stage I (%)
ELCAP	1000	2.7	81	1184	0.59	85
Mayo Clinic	1520	1.4	59	1464	0.2	0
EIO	1000	1.1	54	996	1.1	100

Methods

Although the various screening campaigns sometimes apply different inclusion criteria, the epidemiologic data identify the high risk population in asymptomatic subjects of both genders, over 50 years of age, smokers or ex-smokers (within the previous 10–15 years) of at least 20 cigarettes a day for at least 20 years.

In order to reduce the cost/benefit ratio of the test, lung cancer screening is based on the application of low-dose protocols to avoid exposure to excessive amounts of radiation. The low-dose technique ensures good spatial resolution and high contrast resolution, and guarantees high sensitivity for the detection of lung nodules up to 2 mm in diameter[12,13]. CT protocols differ according to different scanners: we report an example applied to LightSpeed CT 16-rows (General Electric, Milwaukee, Wl, USA): thickness of acquisition 2.5 mm; standard reconstruction filter; 40 mA; 140 kV; rotation time 0.8 s; speed 35 mm/rotation; collimation 10 mm.

Results

The introduction of multidetector CT, with the use of thin sections, resulted in an increase in the number of lung nodules detected[10,11], thus making the definition of

diagnostic algorithms very relevant. The most important parameter to define the diagnostic work-up is the nodule diameter[14] and its changes over time[15]. Although there is no clinical evidence, it is widely accepted that lung nodules less than 5 mm in size can be safely checked at 1 year intervals: this follow-up schedule allows identification of early stage malignancies, while avoiding unnecessary anxiety and useless radiation in the majority of those being screened[14,16].

The evaluation of the nodule characteristics (solid, partially solid, non-solid), depending on the ability to obscure the lung parenchyma[17], and its morphologic appearance[18–20] are important to determine the grade of suspicion.

Apart from follow-up to evaluate volume doubling time, diagnosis can be reached by PET or PET/CT[21], CT enhancement with contrast media via i.v. injection[22,23], FNAB/FNAC[24] or surgical biopsy. Several authors have suggested different protocols for the management of lung nodules[25–27]: we suggest the algorithm shown in Fig. 1. The preliminary results of observational studies show high sensitivity of the technique in detecting lung nodules.

In the ELCAP report, 23% of patients had one or more non-calcified nodules; the European Institute of Oncology study detected 284 nodules in 199/1035 subjects (19%). A large number of these nodules were

benign and the prevalence of lung cancer was 2.7% and 1.1% in the two series.

At the second year CT, the incidence of lung cancer was 0.59% and 1.1%[16,28,29] (Table 1).

The results from the observation of the stage at diagnosis are encouraging: 81% of patients had a stage I tumour[28], with a good prognosis (survival rate at 5 years of 63% for stage IA and 46% for stage IB)[30]. Epidemiologic data in the US show that the diagnosis at stage I is made in only 20% of cases not resulting from screening projects[31].

The percentage of invasive procedures performed for benign lesions ranges from 21% to 55%[32].

Discussion

The high prevalence of benign nodules detected by CT and reported as false positive results is the major criticism against programs for early detection of lung cancer. The use of a dimensional cut-off should reduce the number of false positives and the recall rate[29] with no major impact on the cancer detection rate.

Some authors state that the screening results are affected by an overdiagnosis bias, as CT reveals a significant percentage of non-aggressive tumours that would never cause the death of the patient, because of slow growth and other risk factors related to age and smoking habits. This could explain the increase of survival in cancer patients enrolled in screening campaigns, without a corresponding reduction of mortality.

Early diagnosis does not necessarily result in a reduction of mortality; there are no definitive data on the outcome of the subjects enrolled in screening programs.

At the end of their screening project at the Mayo Clinic, Swenson and colleagues[33] did not demonstrate any significant difference in mortality when comparing their results with those from a study performed in the 1970s by conventional chest X-ray.

Our data on 1035 volunteers, enrolled in a screening project in 2000–2001, with only 30 subjects lost to follow-up at 5 years, show 42 lung cancers detected, 9 deaths from lung cancer, 11 for other cancers, 7 for cardiovascular diseases and 6 for other causes, resulting in a mortality rate of 3.2% in 5 years.

The analysis of costs of a screening program is still an open issue. The costs are extremely variable from one study to another, and data reported range from 2500 to 2,300,000$ per year of saved life[34–36].

To assess the real efficacy of CT in reducing lung cancer related mortality and to introduce this test into clinical practice, we are all waiting for the results of the randomized clinical studies recently started all over the world.

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