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EDITORIAL

Monitoring Subsolid Pulmonary Nodules in High-Risk Patients Is Even More Cost-Effective When Combined with a Stop-Smoking Program

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Lung-cancer screening with low-dose chest computed-tomography (CT) scans for smokers or ex-smokers was found to be effective according to two important randomized phase III studies. The National Lung Screening Trial (NLST)[1] enrolled 53,454 subjects at high risk for lung cancer and randomly assigned them to undergo three annual screenings with either low-dose CT or single-view chest X-ray. For subjects in the low-dose CT-screening arm, relative mortality rates declined 20.0% (95% confidence interval [CI]: 6.8–26.7; P=0.004) for lung cancer and 6.7% (95% CI: 1.2–13.6; P=0.02) for death from any cause. Low-dose CT yielded a positive screening-test rate of 24.2%, 96.4% of them false-positive results.

A European study[2] randomized a total of 13,195 men (primary analysis) and 2,594 women (subgroup analyses), 50–74 years old, to undergo CT screening at T0 (baseline), and years 1, 3 and 5.5, or no screening (controls). The CT-screening arm had significantly lower lung-cancer mortality (cumulative 10-year rate for death from lung cancer was 0.76 (95% CI: 0.61–0.94; P=0.01) compared to controls; for women, that 10-year rate was 0.67 (95% CI, 0.38–1.14). On average, 9.2% of the screened participants underwent at least one additional CT scan and the overall referral rate for suspicious nodules was 2.1%.

The results of those two trials led a certain number of countries to establish lung-cancer–screening programs, even though their findings are not readily adaptable to real-life practice, especially subject adhesion to the scheduled examinations, and the quality and interpretation of screening images obtained.[3] In every case, those programs generated a no negligible number of CT images showing anomalies[4] and the subsequent monitoring of those abnormalities (frequency of examinations, duration of follow-up) were responsible for important financial costs.[5] They also induced anxiety and distress.

The cost/efficacy ratio of those screening programs is a major concern of public health authorities. The outcomes of several medical–economic analyses showed that, in most cases, such screening programs were cost-effective, with incremental cost-effectiveness ratios (ICERS) of $40,000–$70,000/quality-adjusted life-year (QALY), which are acceptable for a willingness-to-pay threshold of $100,000/QALY.[6]

Pertinently, monitoring the anomalies identified on screening CT-scan images represents a large part of those costs. Several recommendations have been made for how to monitor those findings,[7] but ICERs for the different follow-up strategies have been examined more rarely.

Indeed, use of ICERs is the real contribution of Hammer et al.'s highly informative and complete analysis of all the existing recommendations in this domain, published in this issue.[8] Their modelization, based on reported data, primarily those from the NLST, took into account, among other, nodule characteristics (ground glass or solid), and its size. The monitoring intervals and the duration of follow-up were varied in that analysis. Compared to a no-monitoring strategy, at a willingness-to-pay threshold of $100,000/QALY for low-risk nodules, a 2-year follow-up interval and stopped follow-up after 2 years for ground-glass nodules and after 5 years part-solid nodules were cost-effectives effective stratégies, with an ICER of $99,970. In medical–economic terms, perpetual follow-up does not seem to be justified.

The model showed also that y, monitoring strategies with a CT scan every 2 years were more cost-effective than those based on imaging every 6 months, annually or every 3 years. Moreover, monitoring of nodules <6 mm or even <10 mm in diameter, was not pertinent in medical–economic terms, keeping in mind that the projections obtained with this model were the most mixed. Those findings are important for policy-makers, as well as clinicians, and provide a solid basis for reflection on the frequency and duration of follow-up for radiologic abnormalities discovered during a screening program.

Nonetheless, the study by Hammer et al. has several limitations. First, intrinsic to the model, is that it does not take each patient’s individual risk into consideration (more specifically, sex, older age, prior professional exposure(s), family history of lung cancer…) and all the potential CT-image findings (presence of emphysema, spiculation, site of the anomaly…). The use of a priori scores at inclusion of subjects in the screening programs should enable determination of the different risk of subsets and, thus, different follow-up strategies adapted to them.[9] It was shown, especially using the NLST data, that this approach improved the ICERs of these programs.[10] Finally, this modelization did not take into account the influence within these programs of the resources made available to stop smoking. The results of several studies showed that screening represents a privileged moment to encourage participants to stop smoking, with major impact on the risk of lung cancer.[11]

Having stopped smoking, the subjects included in the NLST screening program had a 38% lower risk of dying of lung cancer versus 20% for active smokers.[9] Studies showed that, at entry into screening programs, 65% of the participants expressed a strong desire to stop smoking, 20% were motivated to stop during the first month and 45% at 6 months.[12] The factors associated with the greatest incentive to do so were mainly older age, weak addiction to nicotine and awareness of the benefits of quitting.[12] The cessation rate during in screening program ranged from 6% to 42%, depending on the extent of initiatives made available. The rate was higher for patients with CT-identified anomalies: 17.7% versus 11.4% for those with normal imaging.[13] That observation was also reported in the NLST programm, with smoker rates declining for patients with a major anomaly on CT-screening images than without (respectively, OR: 0.811 [95% CI: 0.722–0.912]; P<0.001).[1] In contrast, higher rate of relapsed smokers among subjects with normal screening imaging was not found in that trial. Repeating advice and information about stopping smoking during different screening examinations also enhanced the cessation rate.[14]

The interventions evaluated were diverse: written information or leaflets given to participants during the screening, general or personalized digital information,[14] minor recommendations given by the oncologists, management of smoking cessation with cognitive–behavioral therapy and pharmacological aids, or personalized advice provided by a specialized nurse with telephone follow-up.

Qualitative studies also highlighted the importance of the interpretation of scan images on the emotional response of subjects and their motivation to stop smoking.

Such interventions added-on to lung-cancer–screening programs have a major impact on cost-effectiveness. The results of several analyses demonstrated 20%–40% ICER improvement for those programs that had implemented stop-smoking incitations.[15]

To conclude, monitoring of radiologic anomalies discovered during lung-cancer screening of active smokers or ex-smokers must be rigorously adapted to the risk factors of the subjects enrolled and always incorporate incentives cessation smoking actions.

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