Challenges of quitting smoking and lung cancer screening

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Evidence on the effect of lung cancer screening on smoking cessation

In a recent publication, Brain and colleagues showed that participants to the UK Lung Cancer Screening (UKLS) pilot trial significantly increased smoking cessation in two years compared to non-participants. In fact, 15% of smokers in the screening arm and 10% in the control arm successfully quitted at two years from the first screening. The effect of the trial arm on quitting smoking was significant, with cessation rates of 15% and 10% at 2 years in intervention and control arms, respectively (1).

This result is in line with those of other randomized trials on screening for lung cancer with low-dose computed tomography (LDCT) that investigated the impact on smoking cessation.

The Danish Lung Cancer Screening Trial (DLCST) found a quit rate of 12% and a relapse rate of 11% in both arms at 1 year. The annual point prevalence quit rate increased to 24% after five screening rounds, whereas the relapse rate remained stable (2).

The NELSON trial on Dutch-Belgian males found a smoking abstinence at 2 years follow-up of about 14% in both arms (3).

In the US National Lung Screening Trial (NLST), which is the only study in which the control arm does chest radiography instead of usual care, after one year from the third screen 24% of smokers in both arms quitted, and higher quit rates were recorded in smokers with any screen-detected abnormality compared with those with normal screening results (4).

The effect of LDCT screening on smoking cessation was investigated also in three cohort studies carried out in US, namely the Early Lung Cancer Action Project (ELCAP), the Mayo study, and Pittsburgh Lung Screening Study (PLuSS) (5-8). The ELCAP study found a 35% cessation rate at 1 year and a prolonged abstinence of 29% (6). In the Mayo study the proportion of quitters after 1 and 3 years was 14% and 12%; moreover, 10% of former smokers relapsed after 1 and 3 years (7). The PLuSS study reported a quit rate of 16% after 1 year (8).

In all these studies, cohorts and trials, participants in both control and screening arms were offered a minimal smoking cessation intervention (smoking cessation brochure, information on smoking cessation centres, short counseling), and cessation rates were higher than those observed in the general population: 4% in the UK and Danish population (1,2), 3–7% in the Dutch population (3).

Moreover, in some studies (NLST, ELCAP, MAYO, PLuSS) a sort of dose-response relationship among the type or number of abnormalities in screen results and cessation was observed (4,5).

All these findings deny the hypothesis that undergoing LDCT screening may result in justification of continuing smoking and support instead the hypothesis that enrolment in screening may increase quitting (9).

Promoting smoking cessation in lung cancer screening programmes

Carrying out a LDCT test, as well as being involved

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in the control arm of a LDCT screening trial, increase quitting. However, in some trials (UKLS) cessation rates were significantly higher in experimental arm, whereas in others (DLCST, NELSON, NLST) no differences were observed by study arm. In the control arm of NLST a chest radiography examination was provided, and this could have determined similar cessation rates in both arms. On the contrary, in the UKLS trial, controls received usual care only, and this could explain their lower cessation rates. No conclusive results are available on the impact of LDCT test on smoking cessation rates in comparison to controls.

At least a part of the observed decline in smoking rates in both arms could be due to an overall effect of participation in trials, and to the voluntary nature of participating smokers who already have been contemplating quitting (1). There is evidence that heavy smokers, maybe less motivated to quit, are less likely to attend screening tests due to their pessimistic attitudes and fatalistic beliefs (10,11).

Therefore, screening could be an occasion to select smokers contemplating or ready to quit, that usually record higher cessation rates (12). Then, tailored smoking cessation programmes, that include both individual or group counseling and pharmacologic treatments, should be incorporated in the screening.

The impact of smoking cessation on mortality in lung cancer screening trials

There are few studies that estimated the impact of screening by smoking habits. In NLST current smokers at recruitment had a two-fold risk of dying from lung cancer compared to former smokers (13). Part of the reduction in mortality in current smokers could be due to quitting smoking in the study period. In fact, in the Italian cohorts selected from the Multicentric Italian Lung Detection (MILD) trial and its pilot, late quitters (those who stopped during follow-up) reported a 35% reduction in mortality, whereas early quitters (those who stopped before baseline) reported a 43% reduction in mortality compared to continuing smokers (14).

Those who stopped smoking have a reduced risk of dying from lung cancer and from other causes, and, above all, from cardiovascular diseases, compared to smokers. Results from the MILD cohorts showed that the effect of stopping smoking in participants undergoing repeated LDCT screening was to significantly reduce the overall mortality: stopping smoking showed a positive effect on overall mortality three-fold to five-fold greater than that achieved by early detection in the NLST (14).

Moreover, stopping smoking is more effective than screening even on lung cancer mortality. In fact, whereas the relative risk of death from lung cancer for current smokers compared to former smokers is around 3 (15), the relative risk of death from lung cancer in NLST control arm compared to screening arm is about 1.25 (16).

Cost-effectiveness of lung cancer screening programmes

Although the sensitivity of LDCT screening is quite high, e.g., over 90% across the three screening rounds in NLST, the specificity is still low, ranging from 73% to 84% (16). This determines a large number of false positives, which often require additional follow-up examinations, enhancing costs.

Screening was proved to prevent the greatest number of deaths from lung cancer among NLST participants who were at highest risk (17), therefore a strictly targeted programme could be more effective (18). This was done in the UKLS pilot trial where participants were selected using a prediction model which includes age, sex, family history of lung cancer, smoking duration, personal history of other cancers and non-malignant respiratory diseases, and asbestos exposure (1). In most trials, the selection of participants was only based on age (e.g., between 55 and 74 years) and smoking history (e.g., a minimum of 30 pack-years of smoking and no more than 15 years since quitting).

In terms of cost-effectiveness, the NLST LDCT screening was reported to be cost-effective by US standards, yielding estimated incremental cost-effectiveness ratios (ICERs) of US$52,000 per life-year gained and US$81,000 per quality-adjusted life-year (QALY) gained (19). If stringent eligibility criteria are applied, LDCT screening could be cost-effective also at a population level: annual screening between ages 60–75 for persons who smoked ≥40 pack-years and who currently smoke or quit ≤10 years ago (about 10% of the US population) yielded an ICER of US$41,114 per life-year gained (20). By further selecting the highest-risk screened sample, an ICER of CAD$20,724/QALY was found (21).

Combination of smoking cessation interventions and lung cancer screening

Interventions for smoking cessation are more cost-effective than LDCT screening, given the lower costs and the higher

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effectiveness in preventing overall mortality. As an example, an annual smoking cessation therapy (e.g., repeated each year if continuing smoking) that costs about US$300 and achieves a 16% 1-year abstinence rate, recorded an ICER of about US$15,800/QALY (22).

However, delivering smoking cessation interventions only would not allow to prevent lung cancer deaths in hardcore and former smokers.

Combining lung cancer screening with an intensified smoking cessation programme would yield a 9% reduction in cumulative lung cancer mortality 25 years after their introduction in a US region with a relatively high smoking prevalence and lung cancer incidence (23). In Italy, combining a smoking cessation intervention (funding treatment, setting up an active quitline, promoting counseling among health professionals, enhancing cigarettes' taxes) with a three-round annual LDCT screen for current and former heavy smokers aged 55 to 74 years, could reduce overall and lung cancer mortality by respectively 33% and 26% compared to no intervention after 25 years. Screening could bring an early decrease in lung cancer and respiratory diseases, followed by a more substantial drop in all-cause deaths in subsequent decades due to tobacco control policies (24).

The integration of cessation interventions could enhance the cost-effectiveness of LDCT screening. Annual combined screening ad cessation therapy programmes recorded an ICER around US$152,000/QALY (22). An organized screening programme with a cessation intervention have an ICER of CAD$33,420 and CAD$29,820 for 15% and 25% levels of smoking cessation (25).

Conclusions

Given that participation to screening increases smoking cessation, which could be further increased by integrating smoking cessation programmes into the screening pathway, combining smoking cessation intervention with LDLC screening could be the best strategy. Further studies are needed in order to find the best options to integrate both interventions.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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