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SCREENING

Finding the smoking gun in lung cancer

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Lung cancer has the highest mortality of all cancers, and although we have been able to pinpoint the risk factors of developing the disease with some accuracy, treatment efficacy has not improved at the rate we would have hoped. It is now relatively easy to identify a population that would be at high risk of developing lung cancer, with heavy smokers being at the front of the 'queue'. However, once we have identified these individuals, what screening and/or treatment program should we be offering them? Obviously, smoking cessation programs have to be part of any lung cancer mortality-reduction program, but effective screening of those individuals who have already been exposed to the carcinogens seems to be another obvious step in the right direction.

Now, we have the results at our fingertips that can help us to start to make some of the important policy decisions regarding screening for lung cancer. The first peer-reviewed data of a phase III randomized clinical trial have been released. This trial compared two lung cancer screening modalities in a population that consisted of 53,454 people with a history of smoking of at least 30 pack-years—who can be considered to be heavy smokers and, therefore, at high risk of cancer. As one of the leaders of this trial, Christine Berg, comments, "the randomized clinical trial is the gold standard for determining whether or not an intervention is effective." This trial randomized participants to either an annual low-dose helical CT scan or an annual chest radiography for 3 years, and then followed them up for a median of 6.5 years.

One impressive result of this trial, independent of the trial arm, was the high adherence rate. Across the three rounds of screening, 95% of those in the CT-scan group and 93% of participants in the radiography group were adherent to the screening. Unfortunately, the false-positive rate was also similarly high: 96.4% in the CT group and 94.5% in the radiography group. However, after any positive result was observed, this was followed up with further imaging and so invasive diagnostic procedures were rare.

Although there were many false positives, there were also more-favorable data from this trial. More lung cancers were identified in the CT group than in the radiography group (645 versus 572 cases per 100,000 person-years). However, in general, in the CT group these cancers were identified at an earlier stage. Berg explains the importance of this finding, "the ramifications are large as now non-small-cell lung cancer has been proven to be a collection of diseases that can be cured when detected at an early enough stage in their natural history."

Crucially, as Berg points out, "this is the first ever randomized clinical trial in lung cancer that has documented a reduction in lung cancer mortality from screening." There were 247 deaths per 100,000 person-years from lung cancer in the CT-scan group and 309 deaths per 100,000 person-years in the radiography group. This difference equates to a significant 20.0% relative reduction in lung cancer mortality in the CT-scan group.

This reduction in mortality that can be attributed to the screening is important for patients: "given the enormous public health problem of lung cancer the results will have implications for many current and former smokers at high risk of lung cancer who are older," says Berg.

Obviously, screening isn't free and will need to be shown to be viable in terms of healthcare spending in these times of more-limited health budgets. The data from this phase III trial will assist with these important decisions and should lead to improved treatment for patients.

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Original article The National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N. Engl. J. Med.* doi:10.1056/NEJMoa1102873