Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial:
"Seeing through the smoke"
ITS Journal club article review

Article Summary

Clinical question
In patients aged between 50-74 years old that are regarded as high risk for developing lung cancer, does CT screening reduce lung-cancer mortality compared to no screening over ten years?

Methods
This population-based, randomised, controlled trial consisted of 13,195 men and 2594 women, who were current smokers or ex-smokers with a significant pack year history. A total of 18 persons were lost to follow-up.
Data was collected through national registries in Belgium and the Netherlands.

Results
The incidence of lung cancer was 5.58 and 4.91 cases per 1000 person-years in the screening group and control group, respectively.
The cumulative rate ratio for death from lung cancer at 10 years for men was 0.76 (95% confidence interval [CI], 0.61 to 0.94; P=0.01) in the screening group as compared to control.
The rate ratio for death from lung cancer for women was 0.67 (95% CI, 0.38 to 1.14) in the screening group as compared to control.
No difference was found in all-cause mortality (rate ratio 1.01; CI 0.92-1.11).
No adverse events were reported.

Conclusions
The authors concluded that lung-cancer mortality was significantly lower among those who underwent volume CT screening than among those in the control group.

Critical appraisal

This is a large, well-designed trial with an intervention that is widely available and acceptable to the targeted population. The high adherence rate to screening (90%) suggests lung malignancy is an imperative issue to the public. These factors are essential when introducing an intervention for screening.(2)

The use of an independent cause-of-death committee decreases the risk of bias the data analysis.(3) The external validity of the trial is strengthened by the inclusion criteria including a population that are high risk for developing lung cancer.(4)

The authors report no adverse events occurred. This outcome is likely to be incorrect considering a prior systematic review on lung cancer screening found a 0.5% incidence of major complications for patients, who underwent invasive follow-up procedures.(5) Could the risks of screening match the benefits, given the failure to show a reduction in all-cause mortality?

The reduction in lung-cancer mortality for women was seen in the NLST and German Lung Cancer Screening Intervention Trial.(6, 7) The smaller cohort of women in this trial may contribute to an over-estimation of this benefit.

There is a possibility of over-diagnosis due to lead-time bias within this trial considering the high incidence of early stage lung cancer in the screening group in comparison to control (58% versus 13.5%, respectively) with no change in all-cause mortality.(8)

Reflection

The current emerging evidence suggests the CT screening can be effective at reducing lung-cancer mortality. However, there is not sufficient evidence at present for a defined screening regime with either a proven time interval for screening, duration of screening, or differences incorporated due to sex.

The above trials are striving to reduce the poor outcomes related to lung malignancy in this high-risk cohort.(9) However, an alternative approach would be to incorporate precision medicine into lung-cancer screening.(10) The identification of specific molecular biomarkers in high-risk patients would radically change practices as over-diagnosis and interval cancers would likely be reduced. Unfortunately, this integration is unlikely to occur in the near future.(11)

A cost effectiveness analysis of this trial should be undertaken to elucidate if CT screening is a financially viable choice.

References

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