



Letter to the Editor

The National Lung Screening Trial. A Before and After in Lung Cancer Screening With Low-Dose Computed Tomography[☆]

El National Lung Screening Trial. Un antes y un después en el cribado de cáncer de pulmón con tomografía computarizada de baja dosis

As a radiologist, I would like to congratulate the authors of the article “Lung Cancer Screening with Low-Dose Computed Tomography after the National Lung Screening Trial. The Debate is Still Open” for their comprehensive review of this topical controversial issue, and to express my agreement with most of their arguments, particularly with regard to the idea that an early lung cancer detection program with low-dose computed tomography (LDCT) should be studied as part of a structured and multidisciplinary process.¹

There are, however, some inconsistencies between the title of the article, which appears to recognize the landmark represented by the National Lung Screening Trial (NLST) and the recommendations made by the authors based on the heterogeneous characteristics and varying results of the different lung cancer screening programs carried out to date. Some of the data reported by the authors (referring to radiation exposure or the LDCT slice thickness, for example) which they appear to use as the basis of some of their recommendations are questionable, or at least, more typical of the earliest screening studies and unacceptable according to the standards established by the NLST.^{2–5} With regard to the economic impact, there are preliminary data suggesting that an early lung cancer detection program with LDCT would not only cost less than other widely accepted cancer screening programs (cervical, breast), but that in comparison with these other cancers, the cost per life-year saved would also be more favorable.^{6,7}

As the first randomized clinical trial to show a reduction in lung cancer-specific mortality of 20.3% in a high-risk population, the design and results of the NLST represent a turning point. Although there are still questions to be answered and areas for improvement, the principal conclusion of the NLST is that LDCT screening in a certain risk group reduces lung cancer mortality. Most previous clinical trials (with suboptimal designs and smaller study populations) have shown that LDCT is a useful diagnostic tool for the early detection of lung tumors in subjects at risk, but these studies lack the consistency and quality of the NLST. Accordingly, I believe that the real point of departure for making updated recommendations for a hypothetical lung cancer screening program must be the NLST.

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The authors’ comment saying “. . .we do not recommend lung cancer screening with CT for smokers or ex-smokers outside of the context of individual counseling” is not consistent with the primary conclusion of the NLST (the reduction of lung cancer-specific mortality with LDCT screening in a specific risk group), particularly when the title of the article appears to recognize the importance of this trial. Indeed, what the NLST has come to show (and its results have been quickly translated into the clinical practice guidelines of several American scientific societies) is that LDCT screening of a specific risk group reduces lung cancer mortality, and so could be implemented within a structured, multidisciplinary program guaranteeing comparable results.⁴ The professionals involved (and the selected participants) must be aware of the potential risks and benefits of a screening program of these characteristics, but in the end it will be the participant who decides to use the program or not.

The recommendation of the authors to “unite our efforts to make sure that healthcare professionals are alerted to lung cancer symptoms, while improving their training and making smokers aware of the risk they have for developing lung cancer” is insufficient if the aim is to achieve early detection of this disease and reduce mortality. In some countries there are already more ex-smokers than active smokers who meet NLST criteria, so excluding the growing population who have quit smoking but who still have an increased risk of developing lung cancer does not seem to be a very advisable measure.

The debate is not only still open, but must remain open and receptive to the scientific evidence and opinions that will ultimately determine whether LDCT has a significant role in the early detection of lung cancer.

Conflicts of Interest

I declare that I have no conflict of interest nor have I received funding from any sources.

References

1. Ruano-Ravina A, Pérez-Ríos M, Fernández-Villar A. Cribado de cáncer de pulmón con tomografía computarizada de baja dosis después del National Lung Screening Trial. El debate continúa abierto. Arch Bronconeumol. 2013, January, pii: S0300-2896(12)00287-6.
2. The National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365:395–409.
3. National Lung Screening Trial Research Team. The National Lung Screening Trial: overview and study design. Radiology. 2011;258:243–53.
4. Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, et al. Benefits and harms of CT screening for lung cancer. A systematic review. JAMA. 2012;307:2418–29.
5. Henschke CI, McCauley DI, Yankelevitz DF, Naidich DP, McGuinness G, Miettinen OS, et al. Early lung cancer action project: overall design and findings from baseline screening. Lancet. 1999;354:99–105.

6. Pyenson BS, Sander MS, Jiang Y, Kahn H, Mulshine JL. An actuarial analysis shows that offering lung cancer screening as an insurance benefit would save lives at relatively low cost. *Health Aff (Millwood)*. 2012;31:770–9.
7. Wisnivesky JP, Mushlin AI, Sicherman N, Henschke C. The cost-effectiveness of low-dose CT screening for lung cancer: preliminary results of baseline screening. *Chest*. 2003;124:614–21.

Reply[☆]

Réplica

To the Editor,

Thank you for the letter¹ regarding our article.² We agree that the NSLT³ was a landmark in lung cancer screening, but we cannot agree with the contents of the letter.

There is a great degree of heterogeneity regarding slice thickness. The NLST does not specify the thickness used and, as might be expected, a strong correlation can be observed between thinner slices and the greater detection of positive nodes.²

It is suggested that the dose of radiation received with CT is questionable. The data we used were obtained from the US Food and Drug Administration website (<http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm095505.htm>) and the NLST authors themselves have stated that “the effective dose from conventional chest CT varies considerably in clinical practice but is on the order of 8 mSv”.⁴ These data support the arguments we put forward in the section of the article discussing the risk of cancer due to radiation.

To say that the screening program would cost less than cervical, breast or colon cancer screening programs and that the cost per life-year saved would be more favorable in lung cancer screening is not supported by the scientific evidence. An article is cited in which the cost modeling uses (a) a screening age range of 50–64 years (the NLST includes subjects between 55 and 74 years of age) and (b) a proportion of subjects who are negative in the first screening of 79% (in the NLST this percentage is 72.7%).⁵ These data clearly favor the cost-effectiveness of CT in lung cancer screening. The number of positive nodes increases significantly with age. Another recent cost-effectiveness study states that the cost of CT screening is over \$100 000 per quality-adjusted life-year (QALY),⁶ a cost which cannot be covered by the healthcare system. Also to be taken into account are the intangible costs of anxiety for the 25% of patients with a positive node detected on screening and the lack of resources for managing the thousands of false positives, in whom the imaging studies, and, in a large percentage, invasive procedures for determining the nature of the nodes will have to be repeated, which would lead to the saturation of hospital Respiratory Medicine departments. The CT in itself is substantially more expensive than a mammogram, occult blood test or cervical smear test.

It is surprising that no reflection is made regarding something so fundamental in a screening program as the downstaging in

Luis Gorospe

Departamento de Radiodiagnóstico, Hospital Universitario Ramón y Cajal, Madrid, Spain

E-mail address: luisgorospe@yahoo.com

successive screening rounds which should be required of any screening program. It is difficult to explain how in the NLST, the percentage of subjects with stage IIIA, IIIB or IV disease is 37.8% in the first round, 31.2% in the second and 30.4% in the third round of screening.³ At least 30% of the cancers detected are at a stage in which surgery is not the first treatment of choice.

Even assuming that the NLST should be a point of departure for the discussion on CT lung cancer screening, too many questions remain unanswered. While they remain so, we cannot talk of an efficient, cost-effective, safe and fair screening modality, despite the NLST results.

Conflict of Interests

The authors declare that they do not have any conflict of interests.

References

1. Gorospe L. El *National Lung Screening Trial*. Un antes y un después en el cribado de cáncer de pulmón con tomografía computarizada de baja dosis. *Arch Bronconeumol*. 2013.
2. Ruano-Ravina A, Pérez Ríos M, Fernández-Villar A. Cribado de cáncer de pulmón con tomografía computarizada de baja dosis después del *National Lung Screening Trial*. El debate continúa abierto. *Arch Bronconeumol*. 2013. <http://dx.doi.org/10.1016/j.arbres.2012.10.003>, pii:S0300-2896(12)00287-6.
3. The National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Eng J Med*. 2011;365:395–409.
4. National Lung Screening Trial Research Team. The National Lung Screening Trial: overview and study design. *Radiology*. 2011;258:243–53.
5. Pyenson BS, Sander MS, Jiang Y, Kahn H, Mulshine JL. An actuarial analysis shows that offering lung cancer screening as an insurance benefit would save lives at relatively low cost. *Health Aff (Millwood)*. 2012;31:770–9.
6. McMahon PM, Kong CY, Bouzan C, Weinstein MC, Cipriano LE, Tramontano AC, et al. Cost-effectiveness of computed tomography screening for lung cancer in the United States. *J Thorac Oncol*. 2011;6:1841–8.

Alberto Ruano-Ravina,^{a,b} Mónica Pérez Ríos,^{a,b}
Alberto Fernández-Villar^{c,*}

^a Departamento de Medicina Preventiva y Salud Pública, Universidad de Santiago de Compostela, Santiago de Compostela, La Coruña, Spain

^b CIBER de Epidemiología y Salud Pública, CIBERESP, Spain

^c Departamento de Neumología, Complejo Hospitalario Universitario de Vigo, Vigo, Pontevedra, Spain

* Corresponding author.

E-mail address: alberto.ruano@usc.es (A. Fernández-Villar).

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