EDITORIAL

Screening for Lung Cancer: Balancing Hope With Doubt About Applicability

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Editorial to accompany the article: „Lung cancer screening using low dose CT scanning in Germany—extrapolation of results from the National Lung Screening Trial" by Andreas Stang et al. in this issue of *Deutsches Ärzteblatt International*

Smoking kills. The latest data could hardly be more alarming—in the year 2011, no fewer than 44 000 men and women in Germany died of lung cancer. The relative survival rate 5 years after the first diagnosis of bronchial carcinoma was only 21% for women and a mere 16% for men. Lung cancer causes more fatalities than any other malignancy in this country among men, and is the second most frequent cause of cancer death in women (1).

International studies

One of the reasons for the high mortality of lung cancer is late detection. In 2011 the US National Lung Screening Trial (NLST) was published. Its results showed for the first time that yearly screening by means of low-dose computed tomography (CT) lowers the rate of lung cancer death in very heavy smokers compared with conventional chest radiography (2). Previous, smaller studies had not revealed this effect so clearly (3).

Further studies, most of them in Europe, are ongoing (4). Results can be expected in 2 to 3 years at the earliest.

Extrapolation to Germany

The discussion is in full swing whether the findings of the NLST, with over 55 000 participants, justify endorsement of population-wide screening for lung cancer or even an active demand for its introduction (5, 6). With their extrapolation of the NLST data to Germany, published in this issue of *Deutsches Ärzteblatt International*, Stang et al. (7) attempt to estimate the effect of the same type of screening in this country. It is to their credit that they not only present the benefits but also turn the microscope on the harmful effects observed in the NLST. Moreover, sensitivity analyses reflect a range of effectiveness values that can be anticipated in the presence of various constraints on the basis of the US data.

Limitations

In general, Stang et al. (7) proceed on the assumption that the external validity of the NLST permits extrapolation of the results to the situation in Germany. Nevertheless, a few important limitations should be considered. Fulfillment of the "risk patient" criteria (dose not less than 30 pack-years and end of smoking, if applicable, no more than 15 years before recruitment) cannot be verified satisfactorily in screening of the general population: the vagueness and deliberate relaxation of these criteria ("eligibility creep") can lead to screening of a large number of persons at lower risk (5). The benefit of screening for these men and women would be substantially lower but the complications would remain largely unaltered, displacing the risk–benefit balance.

Furthermore, consensus would have to be reached on the procedures for screening. It would have to be decided, for example, whether the often irregularly shaped nodes should be assessed in terms of diameter (as in the NLST) or volume (as in the European studies [4]).

Quite rightly, Stang et al. draw attention to the very low postoperative mortality in the NLST. Unless the diagnosis of suspected tumors and the ensuing treatment in the German healthcare system universally match the very high standards of the NLST, extrapolation of the results will arouse unrealistic expectations. In addition, various aspects have yet to be properly clarified. For example, it remains open at what intervals screening should be offered in order to achieve the optimal benefit in relation to the radiation dose associated with every CT scan. It may well emerge that screening at longer intervals, with a lower cumulative radiation dose, is sufficient.

The limitations of low-dose CT screening in Germany might be less severe. Compared with the CT scanners used in the NLST, carried out between 2002 and 2007, modern multislice scanners use lower amounts of radiation. Moreover, the detection rates appear good and further diagnostic procedures seem to be required in only a small proportion of cases, while the number of interval cancers remains low (8).

Uncertainty remains—as for other modalities used for early detection of cancer (9)—with regard to the number of overdiagnosed bronchial carcinomas (indolent tumors). These are cancers that would not have led to clinically recognized disease during the person's lifetime, but are found on screening and therefore treated, with all the resulting complications. Overdiagnosis and overtreatment can never be observed directly; their magnitude can often only

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be estimated after the analysis of long-term randomized clinical trials or prospective studies. While Stang et al. deserve praise for taking account of this problem, the reported scale of overdiagnosis (calculated according to Patz et al. [10]) means that their figures represent at best a preliminary estimate.

The cost factor

Ultimately, every procedure used for screening is measured by the relationship between input and benefit, i.e., its cost effectiveness. As the authors themselves emphasize, it it usually difficult to apply calculations based on other countries' healthcare systems. The risk population and its baseline risk, the healthcare costs, and the effectiveness of screening would all have to be specifically analyzed for Germany. The published calculations from studies in the USA and Canada therefore provide only a rough indication of the potential cost effectiveness of lung cancer screening in this country.

European results needed

The NLST is by far the largest high-quality trial of the efficacy of lung cancer screening to show reduction of mortality in a high-risk group. Nevertheless, the European Lung Cancer CT Screening Trial (EUCT) investigators have decided—in view of the remaining open questions and the many uncertainties—not yet to recommend universal screening, even in a defined risk population. Rather, they prefer to await the results of ongoing European studies (4). This should all be borne in mind when considering how to interpret the extrapolations presented by Stang and colleagues.

Conflict of interest statement
The author declares that no conflict of interest exists.

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