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Lung cancer screening—the surgeon's perspective

Caecilia Ng · Herbert Maier · Florian Augustin

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Summary Results from lung cancer screening trials are promising and show improved survival of lung cancer patients, mainly due to a shift in tumor stages at the time of detection. More lung nodules for histopathologic workup and earlier tumor stages translate into more patients and work load for thoracic surgical units. This article provides a view on lung cancer screening from a thoracic surgeon's perspective.

Keywords Lung cancer · Screening · Patient pathway · Surgical treatment · Limited resection

Introduction

In 2015, 2956 men and 1904 women were diagnosed with lung cancer in Austria, making it the second most common cancer for both men and women [1]. Also in 2015, 2396 men and 1493 women died because of lung cancer, which accounts for 19% of all cancer-related deaths. Fifty-eight out of 100,000 Austrians are diagnosed with lung cancer per year and 47 die from lung cancer in Austria (age-adjusted data), making it the number one reason for cancer-related death [1]. While incidence and mortality rates have declined slightly for men in recent years, they are still on the rise for women (Fig. 1). Disseminated disease including nodal and distant metastasis account for more than three times the number of localized diseases. As tumor stage at diagnosis is of prognostic relevance, a high number of advanced tumor stages at diagnosis cause the high mortality of lung cancer [1, 2].

C. Ng · H. Maier · F. Augustin, MD (✉)
Department of Visceral, Transplant and Thoracic Surgery, Center of Operative Medicine, Medical University of Innsbruck, Anichstraße 35, 6020 Innsbruck, Austria
florian.augustin@i-med.ac.at

These facts about incidence and distribution of lung cancer cases in Austria clearly highlight the burden of this disease. Recent advancements in treatment, like checkpoint inhibitors, are able to improve survival [4, 5]. And yet, they rarely cure patients and long-term survivors of metastatic disease are uncommon. Tumor stage has still the biggest influence on overall and cancer-specific survival [6]. To really improve survival, patients need to be diagnosed at an early stage of disease. Two randomized controlled trials on screening for asymptomatic lung cancer among high-risk patients have proven that mortality in lung cancer declines due to a stage shift to more favorable lung cancer stages [7, 8]. Therefore, a recently published European position statement strongly suggests implementing lung cancer screening programs across Europe [9].

Lung cancer screening

Two randomized controlled trials showing reduction of mortality from lung cancer serve as basis for a current discussion to establish lung cancer screening programs: The National Lung Screening Trial (NLST) conducted in the US; and the NELSON Trial conducted in the Netherlands and Belgium [7, 8].

The NLST was published in 2011 and enrolled more than 50,000 persons at high risk for lung cancer (age 55 to 74 years and a history of cigarette smoking of at least 30 pack–years) to either low-dose CT or single-view posterior–anterior chest radiography, both performed on an annual basis. In short, results showed a relative reduction of 20% in mortality from lung cancer in this high-risk study group [7].

The NELSON Trial randomized more than 15,000 patients at high risk to develop lung cancer (age 50 to 75 years, and a history of cigarette smoking of ≥15 cigarettes daily for ≥25 years or ≥10 cigarettes

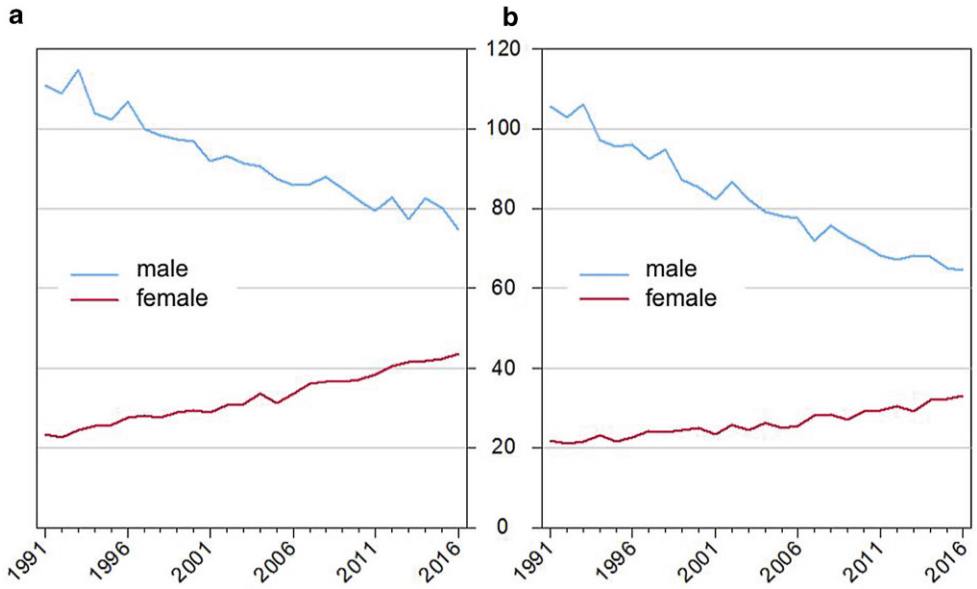

Fig. 1 Age-adjusted **a** incidence and **b** mortality for men and women with lung cancer in Austria. © STATISTICS AUSTRIA. Republished with permission of Statistik Austria, adapted and translated from [3]

daily for ≥30 years) to either low-dose CT or no screening [8, 10]. After 10 years with variant screening intervals ranging from 1 to 2.5 years, the risk to die from lung cancer was reduced by 26% in the screening group. This reduction of mortality was explained due to a higher rate of tumors diagnosed at early stages (stage IA, 50%; stage I and II, 70%) in the low-dose CT group, while the rate of stage III and IV tumors was around 70% in the control group compared to a little over 10% in the screening group [11]. A stringent diagnostic workup of newly diagnosed lung nodules focusing on tumor volume and volume doubling time improved the positive predictive value to 41% compared to 3.8% for low-dose CT in the NLST [11].

Surgeon's perspective

As seen in the two randomized controlled trials, lung cancer screening will have two main effects. First, it will generate a large number of patients diagnosed with lung nodules that need to be followed, histologically proven, and eventually resected. In the NELSON Trial, screening resulted in 2.2% positive results and finally in lung cancer in about 0.9% of all screens performed [11]. Many of these interventions will involve surgeons, or at least a surgical unit that organizes further diagnostic steps, schedules and admits patients who await tissue confirmation via bronchoscopy, transbronchial biopsy or CT-guided biopsy, and discusses results with patients and family members as many of these patients are considered "surgical patients". However, it has to be mentioned that a positive result in a CT screening should not directly lead to a surgical resection without tissue confirmation, as surgery by itself poses some risks.

Second, as seen in both the NLST and the NELSON Trial, screening will cause a considerable stage shift of newly diagnosed lung cancers [7, 11]. Surgical resection in the screening arm was three-times as likely as in the control arm [11]. Due to this predictable shift in tumor stages with more early stage lung cancers, there will be more cases suitable for a primary surgical approach [12].

The capacity challenge

Using the data from the NELSON Trial, there will be about one lung cancer for every 100 low-dose CT scans performed in the population at risk [11]. Clearly, the impact of a screening program on a surgeon's daily practice strongly depends on the number of people that actually undergo screening. The question now is, how many new lung cancer cases can be managed by the current thoracic surgery services? As known from any service industry, if the influx to the system is higher than its output, queueing will become a serious problem. If more patients are diagnosed with lung cancer than thoracic surgery units can handle due to their limited operating room capacities, waiting times for surgery will increase.

Is there an influence of the delay to surgery on oncologic outcome? There are some data that delay between diagnosis and initiation of treatment leads to dismal outcome in lung cancer patients [13]. The authors suggest a timely planning of resection and minimization of any delay beyond that needed to perform a complete preoperative evaluation to improve survival.

Diagnostic and therapeutic pathways of those patients diagnosed with positive results in the screening programs therefore need close attention. With conventional patient pathways, patients spend weeks

waiting for appointments with specialists, slots for PET-CT scans, CT-guided biopsies and multidisciplinary tumor boards until a surgical procedure is scheduled. With re-organization of theses pathways from a department-centered to a patient-centered approach, there is huge potential to shorten these waiting times. One way to optimize patients' pathways is to dedicate slots for PET and CT-guided biopsies specifically for patients with positive screening results. During the same hospital admission, patients should see a pulmonologist to evaluate lung function and rule out any contraindication to surgical treatment. Ideally, results of these diagnostic tests will be presented during the next multidisciplinary tumor board without delay and a final treatment plan can be determined. Theoretically, in a patient-centered approach this workup could be achieved in less than one week. Using such an approach of process optimization, the Toronto East General Hospital was able to reduce the time from suspicion to final diagnosis from a median of 128 days to 20 days [14]. Not only PET scans, CT-guided biopsies and pulmonary function testing, but also surgical units should establish these dedicated slots to assure a timely treatment of these patients. If the operating room capacity of the surgical unit is already at its limits with current patient numbers, a screening program is likely to result in progressive delay to surgical treatment. To avoid this delay, some surgical units might simply increase operating room capacity by improving patient turnover times between surgical procedures or by training surgeons to reduce procedure times. Other hospitals with already optimized turnover times and competitive procedure times but still short in operating room capacity will need to assign more capacity to thoracic surgical departments. A dedicated multidisciplinary team should analyze patient pathways to improve overall efficiency of the unit.

Screening programs therefore should not only determine a protocol on how to manage nodules detected during different screening rounds, but they should also encourage a discussion of possible optimization of patient pathways by setting ambitious time goals. One *realistic* goal could be a time limit of 4 weeks from a positive screening result to definitive surgical treatment; an *ambitious* goal would set the limit to 2 weeks. Moreover, this improved pathway not only impacts overall survival but also reduces patients' distress of a positive screening result, as those with a true positive result feel that everything is being done to help them without unnecessary delay; those with a false positive result get the final diagnosis within a short amount of time and reduce the time they live in anxiety [14]. Clearly, this process optimization is impossible without a dedicated and concerted effort of all specialties involved.

The technical challenge

The prospected shift in tumor stages poses another important question for thoracic surgeons. What is the optimal surgical strategy to treat patients with early stage lung cancer? Minimally invasive access to early stage tumors has not only shown equal oncologic outcomes but also reduced postoperative pain and a better quality of life [15, 16]. However, there is still an ongoing debate whether conventional video-assisted thoracic surgery (VATS) or a robotic approach is superior, whether uniportal access is better than two or three ports, and if awake surgery without double lumen intubation is suitable for major lung surgery at all [17–19]. Many of these questions need to be solved to avoid insecurity of health care professionals and patients alike. To date, no major survival benefit or difference in postoperative pain and recovery between the various minimally invasive surgical approaches has been demonstrated in a high-quality randomized controlled trial. Many thoracic surgeons feel that the technique a surgeon feels most comfortable with to achieve optimal outcome for the patient is the single best one.

And yet, there is one technical aspect that will change surgical practice within the next few years. Since the study from Ginsberg and Rubinstein in 1997, the gold standard for lung cancer resections was lobectomy [20]. However, more and more data indicate that a limited resection might be a valid alternative for tumors with 2 cm in diameter or less [21, 22]. Results of two major randomized controlled trials comparing lobectomy to segmental resections for small tumors in the US (CALGB 140503) and Japan (JCOG0802/WJOG4607L) are greatly awaited to solve this question, as many of the diagnosed tumors in screening programs will fall into this group.

Limited resections, if oncologically suitable, do provide a lung-functional advantage compared to lobectomies and also improve patients' reintegration to life with a faster return to daily activities and work [23]. Moreover, if patients survive early stage lung cancer, they face an up to 10% risk of acquiring a second lung primary [24]. Limited resections with preserved lung tissue would increase the likelihood of a patient to still be fit for repeat curative treatment.

In summary, lung cancer screening will definitely impact a surgeon's daily practice. A higher case load due to the expected stage shift will challenge traditional patient pathways and limited operating room capacities. Smaller tumors will change the type of surgical resection if results of ongoing trials prove the oncologic equality of limited resections.

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Conflict of interest C. Ng, H. Maier and F. Augustin declare that they have no competing interests.

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