Abstract:
Lung cancer is the leading cause of cancer-related death worldwide among both men and women. Although advances in therapy have been made, the 5-year survival rates for lung cancer remain poor, ranging from 10% to 20%. One of the main reasons is late presentation, as only 25% of patients are amenable to cure at the time of presentation. Therefore, the emphasis on lung cancer screening (LCS) is growing with the current evidence that has shown benefits with low-dose computed tomography scan of the chest in high-risk populations. LCS remains a debated topic in Gulf Cooperation Council (GCC) countries, possibly due to a lack of local experience. In this article, we explore the rationale and give recommendations on the best approach for LCS in GCC.

Keywords: Low-dose computed tomography, Lung cancer, Lung cancer screening

Lung cancer is considered the most common cause of cancer-related death globally among both men and women representing 18.4% of all cancer deaths with more deaths than breast, colorectal, and cervical cancers combined.1 Despite advances in therapy the 5-year survival rates for lung cancer irrespective of stage and type is still poor, ranging from 10% to 20%.2 The major risk factor for lung cancer is smoking which is responsible for about 80%–90% of all lung cancer cases.3 Age is the other risk factor, the median age for diagnosis being around 70 years. There is a growing emphasis on lung cancer screening (LCS) with evidence showing benefits with low-dose computed tomography scan (LDCT) of chest in high-risk populations. Most of the evidence for LCS comes from developed countries where lung cancer incidence is high.

The age-standardized rate (ASR) of lung cancer in the Middle East and North African region is less than international rates with a range between 4.2 per 100,000 in Yemen and 23 per 100,000 in Lebanon.4 Lung cancer was found to be the seventh-most common cancer in the Gulf Cooperation Council (GCC) countries with a prevalence of 4.7% of all cancers. The average ASR ranged between 5.9 per 100,000 in Saudi Arabia and 29.0 per 100,000 in Bahrain in men and between 2.9 per 100 000 in the United Arab Emirates (UAE) and 11.0 per 100 000 in Bahrain in women.5 In Oman, the incidence rate is 5.4 per 100,000.6 The main reason for this low incidence in Oman is probably the low prevalence of tobacco use.7 However, a pooled analysis from all Gulf states showed that over 60% of lung cancer diagnosed in GCC countries were at an advanced stage with a 5-year survival rate as low as 10%–20%.8

Hence, regular screening or surveillance for those at high risk becomes important as early detection and more dynamic treatment can improve survival. Naturally, the most common cancers that can be detected early are of public health importance. In GCC

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countries, breast, colorectal, and cervical cancer may demand priority. However, based on the rise in lung cancer incidence in the region and the available evidence for mortality benefits, the rationale of implementing an LCS program is being discussed here.

Evidence

In the late 1990 and early 2000, various reports were published on LDCT for the early detection which was later confirmed by the two prospective randomized studies, The National Lung Screening Trial (NLST),[9] and the Nederlands-Leuven Longkanker Screenings Onderzoek (NELSON).[10]

The NLST, a randomized controlled trial (RCT) conducted in the USA, compared annual screening using LDCT with chest X-ray in high-risk population for 3 consecutive years.[11] The trial was terminated early after an interim analysis demonstrated statistically significant mortality benefits with a relative mortality reduction rate of 20% and an absolute mortality reduction rate of 6.7% in the LDCT arm of the study. Lung cancer was diagnosed in 1.1% of the LDCT group and 0.7% in the chest X-ray group. The detected lung cancers in the LDCT group were mostly (70%) early stages (I and II). The NELSON trial, an RCT conducted in the Netherlands and Belgium, compared screening in high-risk population using LDCT at baseline, 1 year, 3 years, and 5.5 years with no screening.[10] At 10 years of follow-up, the incidence of lung cancer was 5.8 and 4.91 cases per 1000 person-year in the screening and the control group, respectively. There was a significant reduction in lung cancer mortality as well, 24% and 33% lower in men and women, respectively, than the control group. There was a shift toward earlier-stage diagnosis (59% stage I and only 9% stage IV disease) in the LDCT arm. These results confirmed most of the major findings of the NLST.

Other large screening trials have also confirmed the potential mortality benefit of LCS. The Danish trial, an RCT of a high-risk group compared 5 years’ annual screening with LDCT with no screening.[12] At 5 years, there was no difference in lung cancer-related or overall mortality between the two groups. However, 53% of the detected cancers in the screening arm were stage I, and the false-positive rate at baseline was only 7.9%. The DANTE trial is another RCT that enrolled only male smokers or former smokers of at least 20 pack-years aged 60–74 years.[13] The study did not show mortality benefits between the screening and the control group initially. However, at 8.35 years from the baseline, 8.2% had lung cancer in the LDCT group and 6% in the control group with more stage I cancers in the screened group. The Multicentric Italian Lung Detection study also did not show any difference in lung cancer mortality initially but prolonged screening showed reduction in 10-year mortality rate.[14,15] Moreover, 63% of the detected cancers were stage I disease with 84% being surgically resectable. The German Lung Cancer Screening Intervention Study evaluated the annual LDCT for 4 years in high-risk group.[16] Despite the high false-positive rate in the first 3 years, the lung cancer detection rate was about 0.5% for each round. The UK Lung Cancer Screening demonstrated that a validated risk assessment model and population-based LCS approach using LDCT could detect lung cancer at early stages with about 85% at stage I or II.[17] The TALENT trial, a national LCS study conducted in Taiwan in 12,011 individuals.[18] The study recruited individuals aged 55–75 years with a negative chest X-ray and any of the following high-risk features: A family history of lung cancer that included first-, second-, or third-degree relatives; environmental smoking exposure; a history of chronic lung diseases, such as tuberculosis or chronic obstructive pulmonary disease; cooking without ventilation. Younger individuals could participate in the study if they had a family history of lung cancer. The study showed the benefits of LDCT in high-risk never smokers with significant lung cancer prevalence (2.6%) during the first round of screening. More recently, a meta-analysis of 8 trials found a significant reduction in lung cancer-specific mortality with LDCT screening (relative risk = 0.8, estimated absolute risk reduction = 0.4%, and number needed to screen = 250).[19] Although the reduction in all-cause mortality was not statistically significant the absolute reduction was consistent with that for lung cancer-specific mortality.

Cons and Pros of Lung Cancer Screening

Besides the mortality benefits and the high percentage of early-stage lung cancer detection, other benefits of LCS include the positive effects on smoking cessation and the detection of coronary vascular disease on the CT chest among those enrolled.[20,21] The number needed to screen with LDCT to prevent one lung cancer death was 320 in the NLST which is much less than the 780–2000 and 1250 mammography and colonoscopy screenings for breast and colon cancer, respectively.[11,22,23] On the other hand, overdiagnosis bias leads to exposing the patients to unnecessary risk of further interventions. The estimated overdiagnosis risk was 18.5% and 19.7% in NLST and NELSON trials, respectively.[11,10,24] Nevertheless, the overdiagnosis rate was reduced to 8.9% in the NELSON trial with the extension of follow-up to 11 years.[10] The false-positive results that lead to unnecessary further workup put the patients under stress, anxiety, and increased cost.[25,26]

Recommendations

LCS should be considered in a high-risk population to save lives, and it must be carried out in dedicated
centers. Implementing screening program must guarantee that the patient has access to all services from screening to diagnosis to treatment and should consist of a multidisciplinary team including medical specialists, diagnostic and interventional radiologists, pathologists, pulmonologists, medical oncologists, radiation oncologists, thoracic surgeons, specialist nurses, and social workers.\(^{[27]}\)

LCS remains a debated topic in GCC countries, possibly due to a lack of local experience. There are no national programs in the region offering mass screening, though some organizations or societies may screen high-risk patients on an individual basis. Reassuringly, integrated screening programmers are being developed in a few of these countries. Although there are established screening guidelines by the Saudi Lung Cancer Association and the resources for screening are available in the country, these remain clearly underutilized.\(^{[28]}\) Recently, national-level screening program and referral pathway have been proposed in UAE.\(^{[29]}\)

Although nonorganized screening or screening by individual institutions may complement the aim, it will not lead to the desired outcome. The suggested patient selection criteria for LDCT screening based on the currently available evidence includes age 50–80 years, current or former smokers who have quit within the preceding 15 years with 20 pack-year smoking and without a prior history of lung cancer. The candidate must be fit for surgery and the screening should be annual until 15 years have passed from the date of smoking cessation, or they turn 80 years or become unfit for surgical intervention.\(^{[30,31]}\) There are a lot of practical barriers for accessing target groups and identifying patients that fit screening inclusion criteria.\(^{[32]}\) Since we have a well-established primary health care system in the GCC states, we can introduce an electronic patient record-based clinical reminder system for the general practitioners. Early screening imaging referrals and easy access to screening multidisciplinary team specialists can easily be provided. Outreach campaigns, online surveys, mass education programs, and partnership with other screening programs are the other ways to recruit the vulnerable. Maybe we have to go beyond the traditional ways and involve the social media and the press.

However, given the lower prevalence of lung cancer in some GCC population, it cannot be taken for granted that the mass screening will be successful or cost-effective. Establishing a successful program would require adequate resources for diagnosis and treatment as well as commitment from the target populations. Low participation in breast cancer screenings was reported from Qatar, Saudi Arabia, Bahrain, and Oman.\(^{[33]}\) The resources of the health authorities and the government should at this stage be utilized for mass education programs aimed to create awareness and promoting tobacco cessation. However, running a pilot screening program taking into consideration the cultural, demographic, ethnic, and geographical factors could give more insight into the usefulness of LCS in GCC. A major advantage is the existence of a well-organized healthcare infrastructure and the close collaboration between the health ministries in the GCC states. As clinicians, we must keep advocating for measures such as smoking cessation and early diagnosis of lung cancer.

**Conclusions**

The basis of screening is detecting disease at an early, asymptomatic stage when it is likely to be more responsive to treatment. However, neither advancing the time of diagnosis nor the improved survival does always justify screening because of several sources of bias. We have come a long way with respect to diagnosis and treatment in the last one decade after the NLST. Most of the studies were done in populations where lung cancer is very prevalent and maybe these screening interventions will not be successful or cost-effective in the Gulf region at this point in time. Resources should be unitized for mass education programs and promotion of tobacco cessation with the plan for a shared LCS module in the near future.

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**Conflicts of interest**

There are no conflicts of interest.

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