Lung Cancer in Saudi Arabia

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Introduction

Among the different cancer types, lung cancer is the most lethal type worldwide, claiming more than a million and a half lives annually. As the incidence increases, it is expected that around 150 million individuals will die in the 21st century. Therefore, international efforts to prevent lung cancer and improve the outcome of patients in whom lung cancer has been diagnosed should be a top health care priority. Sharing statistics and information on lung cancer burden and management approaches from different countries will help this cause. In this article, we describe the epidemiology, burden of disease, disease management, and challenges concerning lung cancer in the Kingdom of Saudi Arabia (KSA).

Epidemiology

Lung cancer was reported in 452 cases by the Saudi Cancer Registry in 2014, 1 which is a low incidence compared with the international rates (Fig. 1). These cases accounted for 3.9% of all cancer cases reported that year, ranking lung cancer as the fourth most common cancer in men and 17th most common in women. For males the median age at diagnosis was 66 years and for females it was 60 years, compared with 70 years in the United States according to the National Cancer Institute. The male-to-female ratio of 3.61:1 demonstrates the strong correlation with the prevalence of smoking in relation to sex differences. However, with the expected rapid growth of the population, specifically, the sevenfold predicted expansion of the elderly population, these statistics will rise drastically, closing the gap between local and international incidence rates. 2 In addition to an aging population, the growing popularity of smoking is another important factor.

Until the 1960s, smoking was banned in the KSA under religious law. Although it has become legal, it remains culturally unacceptable and considered reprehensible. A 2016 survey reported that the overall prevalence of current smoking was 28.9% in males versus 2% in females. 3 It is more common in younger Saudis, as the mean age of smoking initiation was 19 years, with 8.9% of ever-smokers starting before the age of 15 years. The same study showed that among non-smokers, around 23.3% of men and women were exposed to secondhand smoke for at least 1 day during the past 7 days.

The KSA adopted the WHO Framework Convention on Tobacco Control in May 2015, as a result of which, smoking has been banned in public places such as governmental, educational, and health care facilities. Two years later, in 2017, taxation on cigarettes was applied. Although there are no data measuring the effect of these laws, there is arguably a potential impact for these laws to lower the rates of smoking and its negative health outcomes, especially when combined with the efforts by Ministry of Health and community groups to control tobacco.

Screening

Screening for lung cancer among the high-risk population is proved to reduce mortality by 20%, as demonstrated in the National Lung Cancer Screening Trial. However, the trial was done among Western populations, in which lung cancer is more prevalent and kills more people than breast, prostate, and colon cancer combined. In addition to the lower prevalence in our population, such screening recommendations are less likely to be successful or cost-effective if adopted. The guidelines issued by the Saudi Lung Cancer Association (SLCA) and Saudi National Cancer Center 4 did not recommend mass screening for...
lung cancer as a national program with mandatory reim-
bursement, but they did provide guidance to health care
professionals who are considering providing lung cancer
screening to very high-risk patients at their own discretion.
This position was due to the small numbers of cases in the
KSA and lack of cost-effectiveness analysis on the feasibility
of doing computer tomography (CT) scans in the country.
Nonetheless, the recommendations emphasized the
importance of primary prevention through the smoking
cessation programs, as well as early identification of pa-

Figure 1. Comparison of the age-standardized rate for lung cancer among Saudis with the age-standardized rates in selected
countries. UK, United Kingdom; UAE, United Arab Emirates. Reprinted with permission from the Kingdom of Saudi Arabia
Saudi Health Council Saudi Cancer Registry.1

Diagnosis
Pathology
Physicians treating patients with lung cancer have ac-
cess to immunohistochemistry staining of the tumor to
identify lung cancer subtype. Molecular studies, including
testing for EGFR, ALK receptor tyrosine kinase (ALK), and
ROS1, can be conducted by all centers in the KSA, either by
sending out samples to laboratories in Western countries or
occasionally by in-house testing. Over the past year, one
major center has established the capacity to do next-
generation sequencing in-house for patients with lung
cancer in the KSA, and other centers may follow. Pro-
grammed death ligand 1 (PD-L1) testing is also available on
an in-house basis or by sending out samples.

Diagnostic Imaging
Whereas patients predominantly present at late
stages, early-stage lung cancer can possibly be managed
with curative intent. Consequently, accurate radiological
staging and early diagnosis cannot be overstressed. Im-
aging modalities such as magnetic resonance imaging
(MRI) and CT are available in all regions of the country
(Fig. 2). In contrast, positron emission tomography CT is
available in only six centers, of which four are in Riyadh
and two are in the Eastern Region. Riyadh also has two
centers with MRI CyberKnife technology and MRI
spectroscopy.

Other Modalities
Use of more invasive diagnostic tools such as video-
assisted thoracic surgery and endobronchial ultrasound
for tissue diagnosis and staging are available in tertiary
centers. Tissue diagnosis is usually obtained by pulmo-

ary physicians, interventional radiologists, or thoracic
surgeons. Who performs the initial biopsy depends on the availability of expertise and the tumor location.

**Surgical Approaches**

Surgery remains the main treatment modality for early NSCLC. It should be performed with curative intention even after exploration and intraoperative stage confirmation. There are about 30 trained consultant thoracic surgeons who are managing lung cancer in tertiary hospitals. The main focus of their work is dealing with early-stage lung cancer with curative-intent surgery. However, they are also involved in obtaining diagnostic specimens and performing mediastinal staging and metastasectomy.

**Radiation Approaches**

Radiotherapy field has elicited a huge interest in the KSA, with major efforts made to cope with the rapidly growing advance in technical aspects of radiotherapy. There are approximately 50 consultant radiation oncologists and 28 external beam radiotherapy machines capable of treating lung cancer that are distributed over 13 radiotherapy centers in six cities across the KSA. Available modalities to treat lung cancer range from intensity-modulated radiotherapy for conventional radical lung cancer treatment of stage 2 or 3 to stereotactic body radiotherapy (SBRT) for high-risk operable cancer, inoperable early-stage lung cancer, and oligometastases. Because of the importance of management of oligometastatic disease (OMD), an OMD clinic was established in one tertiary center, and national OMD guidelines are being developed. Intensity-modulated radiotherapy technique has been broadly adopted in all radiotherapy centers for lung cancer treatment. Linear accelerator–based SBRT is available in four centers. The CyberKnife system (Accuray, Sunnyvale, CA) with synchrony respiratory technology is a unique innovative system capable of tracking moving tumors. These technical innovations are being utilized mainly for a lung SBRT technique to deliver a precise and accurate ablative radiation dose to the tumor while sparing healthy lung tissue and nearby critical organs. This innovative technique is available in three centers in the KSA. Advanced respiratory solutions such as four-dimensional CT are available, and fiducial tracking for a CyberKnife machine is functionally operating in the two most distinguished tertiary centers, which is sufficient for a technique with this novelty and sophistication (Table 1).

**Systemic Therapy**

Although many international guidelines are readily available, countries should adapt or develop their own guidelines that are customized (or harmonized) to their population and local setting. The SLCA, in collaboration with the Saudi National Cancer Center, has created a set of guidelines that is relevant to our patient population, including patients’ characteristics, disease biology, and practice setting. For example, one-third of Saudi patients have mutations, which is a much higher proportion than in the Western

**Table 1. Distribution of Radiotherapy Centers with Available Technique Modalities for Lung Cancer in Saudi Arabia as of December 20, 2018**

<table>
<thead>
<tr>
<th>Region</th>
<th>Radiotherapy Centers</th>
<th>Linear Accelerators</th>
<th>Lung IMRT VMAT</th>
<th>Respiratory Gating Lung SBRT</th>
<th>Tumor Tracking Lung SBRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riyadh</td>
<td>5</td>
<td>13</td>
<td>5</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Makkah</td>
<td>5</td>
<td>8</td>
<td>5</td>
<td>No Data</td>
<td>0</td>
</tr>
<tr>
<td>Eastern</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Tabuk</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>No Data</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>27</td>
<td>13</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Percentage—</td>
<td>—</td>
<td>100%</td>
<td>31%</td>
<td>23%</td>
<td></td>
</tr>
</tbody>
</table>

Data from the Saudi Health Council Cancer Registry. IMRT, intensive modulated radiotherapy; VMAT, volumetric modulated arc therapy; SBRT, stereotactic body radiotherapy.
Therefore, if all efforts have failed to profile tumors, including circulating tumor DNA, the guidelines allow use of tyrosine kinase inhibitors (TKIs) for second- or third-line therapy in our own population if the patient’s EGFR status is unknown (Fig. 3).

Figure 3. Schematic of systemic therapy of approach for NSCLC in the Kingdom of Saudi Arabia. *If EGFR status unknown, a tyrosine kinase inhibitor can be used as second- or third-line therapy. PDL1, programmed death ligand 1; ALK, ALK receptor tyrosine kinase; RET, ret proto-oncogene; HER2, erb-b2 receptor tyrosine kinase 2; MET, mesenchymal epithelial transition; TPS, tumor proportion score.

Table 2. Cancer Therapeutic Agents Use for Lung Cancer Management in Saudi Arabia

<table>
<thead>
<tr>
<th>Medication</th>
<th>Use in the KSA</th>
<th>Registered in the SFDA*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard chemotherapy agents:</strong> platinum drugs, taxan, pemetrexed, topotecan, etoposide, vinorelbine, cyclophosphamide, vincristine, doxorubicin, etc.</td>
<td>Used routinely</td>
<td>Yes</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>Used occasionally in EGFR-mutated disease</td>
<td>Yes</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>Most-used EGFR TKI</td>
<td>Yes</td>
</tr>
<tr>
<td>Afatinib</td>
<td>Rarely used in EGFR-mutated disease</td>
<td>Yes</td>
</tr>
<tr>
<td>Osimeritinib</td>
<td>Used for a few patients as second-line therapy in T790-mutated disease; not used routinely</td>
<td>Yes</td>
</tr>
<tr>
<td>Crizotinib</td>
<td>Most-used ALK TKI, and used in a few ROS1-positive patients</td>
<td>Yes</td>
</tr>
<tr>
<td>Alectinib</td>
<td>Used for a few patients as second-line therapy; used less as first-line therapy</td>
<td>Yes</td>
</tr>
<tr>
<td>Ceritinib</td>
<td>Used in few patients</td>
<td>Yes</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>Commonly used as second-line therapy</td>
<td>Yes</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>Commonly used as first-line therapy with PD-L1 expression &gt;50%; rarely used as first-line combination therapy with chemotherapy</td>
<td>Yes</td>
</tr>
<tr>
<td>Atezolizumab</td>
<td>Increased use in second-line therapy</td>
<td>Yes</td>
</tr>
<tr>
<td>Cabozantinib</td>
<td>Rarely used in RET-positive disease</td>
<td>No</td>
</tr>
<tr>
<td>Vandetanib, adotrastuzumab, dabrafenib, trametinib, dacotininib, brigatinib, lotlatinib</td>
<td>No data on use</td>
<td>No</td>
</tr>
</tbody>
</table>

Data from the Saudi Food and Drug Administration.6
*As of December 30, 2018.
ALK, ALK receptor tyrosine kinase; KSA, Kingdom of Saudi Arabia; PD-L1, programmed death ligand 1; RET, ret proto-oncogene; SFDA, Saudi Food and Drug Administration; TKI, tyrosine kinase inhibitor.
All patients with lung cancer have access to standard chemotherapy agents, including pemetrexed, taxanes, platinum drugs, gemcitabine, and others. However, initially the tumor is profiled. Patients with a driver mutation such as EGFR, ALK, and ROS1 are treated by targeted therapy, whereas patients who have wild-type tumors will be treated by either immunotherapy (if the level of PD-L1 expression is at least 50%) or by systemic chemotherapy (for patients with a PD-L1 tumor proportion score of 50%) (see Fig. 3). All tertiary centers have access to at least one EGFR TKI; the main such medication used in the KSA is erlotinib. There are a few patients who have used osimertinib, especially in the second-line setting, and it is being proposed for first-line therapy in the updated version of the guidelines. Access to ALK TKIs (crizotinib and alectinib) is available in the KSA for patients with ALK mutation. Immunotherapy with three checkpoint inhibitors (nivolumab, pembrolizumab, and atezolizumab) is approved in metastatic lung cancer; all three are available in the country, but availability varies from one institution to another (Table 2).

The access to timely treatment and expertise does affect patients’ outcomes, and the data from one tertiary center revealed favorable 5-year survival of our patients compared with the Surveillance, Epidemiology, and End Results data (Fig. 4).

Challenges

There are multiple challenges that should be addressed to attain optimal lung cancer management in the KSA. The first challenge is the lack of a systematic approach to prevent lung cancer in the primary care setting. Most lung cancer cases are discovered in advanced, difficult to manage stages. Globally, only 15% of cases are diagnosed at an early stage. The KSA falls within the international range, with only 14% of cases diagnosed early with localized tumors. To achieve higher numbers, education for the public and primary health care providers about smoking, screening, and early detection is required. Although there are national efforts invested in smoking cessation initiatives, smoking continues to be widespread—noticeably, the use of hookah or shisha (water pipe) in recent years. Data show that only 53.2% of ever-smokers have reported receiving advice on quitting smoking from health care professionals during the past 12 months. Despite this, we still find high levels of smokers among youth and exposure to secondhand smoke. There is also a need for active public awareness campaigns, in which Saudi medical students are active participants and which are a major part of medical schools’ extracurricular activity.

Another challenge that some patients in remote regions face is inconvenient access to a cancer care facility, as all tertiary cancer facilities are clustered in the major cities. Many patients have to travel long distances to seek cancer care, which is a great physical, mental, and financial burden to patients and their families. The Ministry of Health is working in multiple parallel projects to systematically establish cancer facilities in smaller cities.

As for access to pharmacological treatment, the Saudi Food and Drug Administration approves up-to-date medications and supports their availability, particularly...
in the era of targeted therapy and immunotherapy (see Table 2). Yet, access to these medications may vary among health care facilities and tertiary cancer centers, as it is dictated by local pharmacy and therapeutics committees in institutions with their own budgets and priorities. There are plans to have a unified purchasing entity for the whole KSA, which may alleviate the restricted access to some of these medications. Unfortunately, access to palliative care and home health is scarce owing to lack of community and home health services for patients with lung cancer and other cancers. This has resulted in patients being hospitalized for a long period of time for end-of-life care. Initiatives to address this obstacle are currently in the early stages of development.

On the other hand, patients are relieved of health care’s great financial burden, as the law guarantees that all Saudi patients with cancer receive care free of charge. Charitable nongovernmental organizations assist with other costs that may not be covered by the government. These nonprofit organizations and societies should receive recognition, as they are an integral part of increasing the quality of life of patients with lung cancer.

Most tertiary centers have tumor boards, although lung cancer–specific tumor boards exist in only a couple of institutions. The SLCA promotes a multidisciplinary approach by having monthly tumor boards at which teams from different hospitals are present and hold discussion in multidisciplinary team fashion, and they are broadcast online for other remote centers to join. National guidelines for lung cancer management have been published for many years by multidisciplinary experts, and recently, lung cancer prevention and screening guidelines were published. SLCA facilitates the dissemination of knowledge and new practices in the KSA and the region.

In conclusion, lung cancer is not as common in the KSA as in other parts of the world. Nevertheless, if the risk factors and the challenges that we have mentioned are not addressed, the numbers of cases will increase drastically. Although significant advances in the management of this disease have been realized, there are many plans under way to enlist more resources to be better prepared to control this fatal disease through prevention and effective treatment.

References