Background

Rwanda is a landlocked country in East Africa with an estimated population of approximately 12.5 million in 2018, making it the second most densely populated country in Africa.1,2 Rwanda is counted among low-income countries, with a little more than 80% of Rwandans living in rural areas. Women represent approximately a half of the population.3 Figure 1 is the map of Rwanda in relation to its neighboring countries.

Rwanda’s health system is made up of both public and private facilities, with the Ministry of Health in responsibility of policy making and the Rwanda Biomedical Center in charge of coordinating health program implementation at the national level.4 To provide fair access to care, the country uses a comprehensive, integrated, and multitier methodology to deliver health prevention and services. The system’s organization and national facility layout prioritize geographic equity, with most of the population living within 5 km of the nearest health center. The journey of a patient begins in the community, either through community health workers who connect the patient to care or through an individual’s decision to seek care at a local health post or health center.4 Patients are treated according to the services provided by each level of health facility, and patients who require advanced management are referred to the next level of care. Approved services are covered by public and private health insurances, with the patient co-paying between 0% and 15% of the cost of services depending on the type of insurance and their socioeconomic status, whereas the remaining amount is covered by insurances.4

Cancer treatment is currently accessible in the country in tertiary and teaching hospitals. Components of lung cancer care consisting of imaging, pathology, surgery, chemotherapy, and radiation treatment are available in selected hospitals.5

The Rwandan National Cancer Registry, which is a population-based registry, has been established recently, although accurate numbers are yet to be reported in the GLOBOCAN reports.6 For many years, cancer incidence and mortality figures have been drawn as estimates from registries in neighboring countries. According to a report by the Global Cancer Observatory of the International Agency for Research on Cancer, lung cancer ranked seventh in Rwanda in 2020, with 346 new cases accounting for 3.9% of all cancer cases. The total number of deaths was 313, accounting for 5.2% of all cancer deaths in Rwanda.6

Despite advancements, the health care system still faces a considerable number of setbacks, including understaffed oncology services and poor access of cancer care especially at low levels leading to presentation of disease at advanced stages.7

Screening, Smoking Prevalence, and Smoking Laws

In Rwanda, there are no official lung cancer screening programs. Basic imaging platforms such as radiographs,
ultrasounds, computed tomography (CT) scans, and magnetic resonance imaging are available.\textsuperscript{5,7} Little is known regarding accurate numbers and the nature of tobacco use. For example, in 2013, 12.8\% of Rwandans aged 15 to 64 years were reported to be smokers, and more recently, a count of 2000 deaths was estimated to be secondary to tobacco use.\textsuperscript{8}

The Rwandan government passed the Act Relating to Tobacco Control in April 2013. The law included provisions such as banning smoking in all indoor public spaces, public awareness and education campaigns, protection against secondhand smoke exposure, Tobacco Advertising Promotion and Sponsorship regulation, a commitment to ending illicit trade, and administrative sanctions and penalties for noncompliance with the required measures. This Act aligns with the WHO Tobacco Policy Recommendation issued in 2003 aimed at minimizing the public demand for tobacco. The policy clearly insists on the need to consider both price- and non-price-based interventions as a way toward limiting tobacco demand and consumption.\textsuperscript{9}

In addition, the Government of Rwanda is currently implementing and enforcing the WHO Framework Convention on Tobacco Control in partnership with a number of multisector stakeholders. This includes a variety of tobacco laws and orders aimed at raising tobacco taxes, encouraging business owners to comply with tobacco control laws and regulations, coupled with reducing and possibly eliminating secondhand smoke exposure.\textsuperscript{10} With all these measures met, tobacco-induced lung cancer cases are expected to decrease.

Management of Lung Cancer in Rwanda

Diagnosis, Staging, and Pathology

Figure 2 illustrated that Rwanda tertiary hospitals and cancer services provided. Imaging for diagnosis and staging of lung cancer in Rwanda is still limited to a few referral and tertiary hospitals that have CT, and most of these are based in the capital Kigali. In 2022, a total of nine CT scan machines were operational in the country both in public and private health care facilities. Among these facilities, only two have the expertise to perform image-guided lung biopsies for suspicious lung lesions identified on CT scan. Image-guided biopsy is still at its infancy and only very low-risk large peripheral lesions are included. Once image-guided biopsies are done, tissue is taken to pathology for analysis, and later, the cases are prepared for a multidisciplinary team discussion once the tissue diagnosis and staging are available. There are no positron emission tomography scan and mediastinoscopy available in the country.

In Rwanda, the pathologic diagnosis of lung cancer is generally made on resection specimens, small biopsy and cytologic specimens. These include cytologic and histologic preparations and immunohistochemical stains. Small biopsy specimens are obtained through bronchoscopy, needle, or core biopsies. There are no modalities for molecular testing within the country. On most of the cases, the diagnosis is based on light microscopy. Now that lung cancer
therapy is becoming personalized for individual patients on the basis of the histologic cell type and subtypes of lung cancer (adenocarcinoma versus squamous) and molecular status, on small biopsies, efforts are always made to further classify NSCLC into a more specific histologic type, such as adenocarcinoma or squamous cell carcinoma, whenever possible. For the few cases where the diagnosis is not straightforward on light microscopy, the final diagnosis is made in conjunction with immunohistochemistry. The most often used and available panel of immunostaining diagnostic biomarkers are chromogranin A, cytokeratin 7 (CK7), CK20, pancytokeratin, p63, synaptophysin, and thyroid transcription factor 1.

Surgery

Different cancer treatment modalities are provided in approximately five hospitals in Rwanda, as illustrated in Figure 1. Cancer surgery is available in all the five hospitals, but surgery for lung cancer is performed at only 1 center nationwide. Surgery is generally divided into the following 2 categories: surgery for diagnosis and surgery for cure.

In the category of diagnostics, the most performed procedures are open lung mass biopsy with wedge or incisional biopsy and video-assisted lung biopsies. The patients are evaluated and discussed with radiology for possibility of image-guided biopsy. Those declined for image-guided biopsy are further evaluated for endobronchial bronchoscopic biopsy or surgical biopsy.

Patients with confirmed malignancy on tissue diagnosis are further discussed at tumor board meeting consisted of oncologists, radiologists, surgeons, and physicians. Those deemed for upfront surgery or multimodality therapy are evaluated by thoracic surgeons for resectability, performance evaluation, respiratory reserve, baseline blood workup, nutritional parameters, frailty assessment, an arterial blood gas, and six-minute shuttle walk test.

Our standard protocol of resection is anatomical lobectomy with mediastinal lymph node sampling. On occasional circumstances, a pneumonectomy would be warranted for patients with very central tumors if radiation is not anticipated as adjuvant therapy. Segmental or wedge resections have been reserved for small nodules or isolated metastatic disease. We do not perform video-assisted lung resections owing to lack of expertise locally.

On the basis of final pathology and lymph node samples, the patient may only need surgery or referred for adjuvant therapy.

Medical Oncology

Chemotherapeutic treatment for lung cancers is provided at two of the three cancer centers in the country. All generic cytotoxic chemotherapies for SCLC and NSCLC are available, and targeted therapy on the basis of biomarkers testing has been introduced since 2019, and data have been published. All patients with metastatic lung cancers receive the guideline-recommended therapy, starting typically with carboplatin and paclitaxel (NSCLC) or platinum-based therapy (usually with etoposide) for SCLC. The most often requested biomarkers are EGFR, ALK, ROS-1 and programmed death-ligand 1, and the available first-line treatment medications, as provided in the national guidelines, are detailed in Table 1.

Table 1. Available Systemic Therapies as Provided by National Guidelines

<table>
<thead>
<tr>
<th>Neoadjuvant</th>
<th>Adjuvant</th>
<th>Metastatic (Cytotoxic Targeted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line: Platinum-based chemotherapy (carboplatin cisplatin) + taxane—concurrent with radiation therapy (definitive treatment)</td>
<td>NSCLC: Platinum-based chemotherapy</td>
<td>Platinum-based chemotherapy EGFR—first line: erlotinib; Second line: afatinib ALK—first line: alectinib PD-L1 (high &gt;50%)—pembrolizumab + pemetrexed + cisplatin PD-L1 (1%–50%)—pembrolizumab + carboplatin + paclitaxel</td>
</tr>
<tr>
<td>SCLC (limited stage): First line: Platinum-based doublet (carboplatin cisplatin) + etoposide</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PD-L1, programmed death-ligand 1.
Given the fact that there is no facility conducting biomarker testing in the country, and the subsequent delay in receiving results, most patients with metastatic disease are started on cytotoxic treatment before switching to targeted therapy suitable to their profiling.

Biomarker testing and most chemotherapeutic and targeted therapy medications are only available on private insurance scheme, but public health efforts are being made to provide essential chemotherapy on the larger public community based health insurance. Private insurance funders reimbursing testing and treatment only cover approximately 10% of the general population and only reimburse between 85% and 90% of the total cost of the treatment, making the management of lung cancer one of the most expensive for the common Rwandan patient.11

Radiation Oncology

Radiotherapy has an important role in the treatment of lung cancer. Currently, there is one center offering radiotherapy services in the country, with only eight clinical oncologists and three medical physicists in the country.

The radiotherapy facility was launched in 2020 at the Rwanda cancer center, located in one of the referral hospitals in the city of Kigali, at the Rwanda Military Hospital. The facility has two machines using the volumetric modulated arc therapy technique and serves all patients with cancer from the country and in the region. From 2019 to 2021, the center had treated only 12 patients with lung cancer, and most were patients with NSCLC.

Table 2 provides a picture of the current oncology workforce in the country, relevant to lung cancer care, as per the numbers in the national medical council registry.

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Number</th>
</tr>
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<tbody>
<tr>
<td>Clinical oncologists</td>
<td>8</td>
</tr>
<tr>
<td>Medical oncologists</td>
<td>2</td>
</tr>
<tr>
<td>Cardiothoracic surgeon</td>
<td>1</td>
</tr>
<tr>
<td>Internists who do bronchoscopies</td>
<td>2</td>
</tr>
<tr>
<td>Pathologists</td>
<td>21</td>
</tr>
</tbody>
</table>

Conclusion

Lung cancer management in Rwanda is at its nascent phase, and efforts have been made to provide most of the elements needed for its diagnosis and treatment at most tertiary, teaching hospitals. As patients present at advanced stages similarly to other resource-limited countries, concerns exist regarding potential underdiagnosis of the disease. Areas needing more focus in the future are availing newer staging modalities (mediastinoscopy, positron emission tomography-CT scan), molecular testing for patients locally, while keeping the access to surgery, and cytotoxic chemotherapeutic agents as a priority.

CRediT Authorship Contribution Statement

Brandon A. Niyibizi, Eulade Muhizi: Conceptualization, Data curation, Investigation, Writing – original draft preparation.

Diana A. Ndoli, Ivan Rukundo, Thierry Z. Muvunyi, Maurice Musoni, Damas Dukundane: Data curation, Investigation.

Emmanuel Rudakemwa, Fidel Rubagumya: Writing - review & editing.

Achille V. C Manirakiza: Conceptualization, Data Curation, Investigation, Writing – original draft preparation, Writing - review & editing.

References