Chapter

Introductory Chapter: Recent Progress in Lung Cancer Treatment - The Value of Multiple Perspectives

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1. Introduction

The remarkable advances in lung cancer management that we have witnessed in the past two decades did not arise in a vacuum. Surgeons, radiation oncologists, medical oncologists, pulmonologists, palliative care specialists, radiologists, pathologists, laboratory scientists, and patients have long collaborated to make the vision of improved cure rates, survival, and quality-of-life a reality.

2. Surgery

Minimally invasive surgery (MIS) has altered the landscape of thoracic surgery. Thoracotomies had been standard-of-care for lung cancer resections until the advent of video-assisted thoracoscopic surgery in the mid-1990s. While initially utilized primarily for patients with favorable anatomy and good pulmonary function, this has been increasingly adopted for use in more frail patients with more technically challenging anatomy [1]. Robotic-assisted thoracoscopic surgery was approved in the early-2000s with the help of even more sophisticated technology that imitated the manual dexterity of an open procedure.

With both approaches, there were initial concerns that there would be higher rates of complications as well as margin-positive resections that could translate into more intensive adjuvant regimens or poorer survival outcomes. Both techniques have substantial learning curves, but surgeons and centers gradually accumulated experience and increased the proportion of patients who underwent surgeries with a minimally invasive approach. Over a relatively short period of time, adoption of MIS has led to improved perioperative outcomes like pain, complications, length of hospital stay, and in-hospital costs without compromising oncologic outcomes [2, 3]. Not only has MIS allowed surgical patients to regain independence sooner than they would have otherwise, but also patients who may have not previously considered surgery due to the risk of morbidity might now be candidates for this potentially curative modality.

3. Radiotherapy and other ablative therapies

Nonsurgical local approaches have also expanded in scope due to developments in technology. Radiotherapy can now be administered with exceptional accuracy

and precision despite physiologic lung motion. This is largely due to improvements in image-guidance, 4-dimensional motion management, and beam modulation approaches that allow for higher biologically effective doses to the target, less scatter doses to normal organs, and more convenient treatment schedules.

Due to these advances, more ablative doses were made possible in the form of stereotactic body radiotherapy (SBRT), also known as stereotactic ablative body radiotherapy. Since its development in the mid-2000s, SBRT has been proven to be a valid alternative to surgical resection in early-stage disease, showing local control in the 90–98% range at 3–5 years with acceptable toxicity [4, 5]. SBRT has also been increasingly utilized in oligometastatic and oligoprogressive disease, with survival benefits demonstrated when used as consolidative therapy after systemic therapy [6, 7].

For inoperable locoregionally advanced non-small cell lung cancer, fractionated radiotherapy has been traditionally combined with chemotherapy with curative intent. With improved knowledge on appropriate radiotherapy dosing and the advent of consolidative immunotherapy, we can achieve better outcomes than we have ever seen before [8, 9]. Furthermore, image-guided ablative therapies like radiofrequency ablation, microwave ablation, and cryoablation have a wide range of potential indications. They can be particularly effective in situations that are not amenable to surgical or radiotherapeutic interventions due to safety concerns.

4. Systemic therapy

For more advanced disease, precision medicine has greatly expanded in its ability to address specific mutations and biomarkers with customized combinations of chemotherapy, targeted therapy, and immunotherapy. Drugs can now specifically target mutations like EGFR and ALK, effectively controlling even the most widespread metastases. Outcomes have continued to improve with refinements in successive generations of these agents [10, 11]. In addition, immunotherapy has been successfully used as monotherapy for patients with PD-L1 expressing tumors [12], or added to chemotherapy for patients with high, low, and no PD-L1 expression [13]. This has led to standard treatment regimens for most patients with stage IV non-small cell lung cancer. These combinations have also extended to extensive-stage small cell lung cancer, with the addition of concurrent and maintenance immunotherapy representing the first major pharmacologic advance in the upfront treatment of this disease in several decades [14, 15].

Even for tumors that develop resistance to initial therapies, novel blood-based and tissue-based diagnostic testing can help clinicians formulate a truly personalized approach to oncologic management, leading to the possibility of long-term survival that was unimaginable even a decade ago. Combining these systemic therapies with local therapies in the oligometastatic and oligoprogressive setting has led to unique regimens that have dramatically altered disease trajectories.

5. Palliative care

Palliative management of bone metastases has improved due to enhanced patient selection algorithms and surgical stabilization techniques by orthopedic surgeons and neurosurgeons, in addition to the judicious use of radiotherapy. Brain metastasis management has also evolved through increased utilization of upfront stereotactic radiosurgery [16] rather than whole-brain radiotherapy, mitigating potential cognitive effects without a survival detriment [17]. Furthermore,

integration of early palliative care for patients with advanced lung cancers has also contributed not only to improved quality-of-life, but also to survival [18].

6. Future directions and conclusions

Moving forward, utilization of cutting-edge technologies like circulating tumor biomarkers, machine learning, gas plasma, and nanotechnology may offer exciting new opportunities in screening, diagnosis, and therapy. While these may be in earlier stages of development than more standard modalities, they represent promising avenues for research and clinical application.

If the inspirational innovations discussed in this chapter are any indication, the future of personalized care for patients with lung cancer is exciting.

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