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Commentary: Extended disease, but still not the end for patients

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CENTRAL MESSAGE

An original approach to selected cases in stage IV NSCLC is described suggesting superiority of lung resection over radiotherapy to control the primary tumor and increase survival in these patients.

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An interesting report from Mitchell and colleagues,[1] retrospectively compares the outcomes of 2 series of synchronous oligometastatic stage IV non–small cell lung cancer (NSCLC) patients considered for local consolidative therapy (LCT). Sixty-three patients were treated with radiotherapy and 25 with anatomical pulmonary resections. Three-year overall survival was 24.2% in the radiotherapy group and 58.2% after surgery. The authors conclude that pulmonary resection is associated with long-term survival and recommend that randomized clinical trials on stage IV NSCLC should include a surgical arm.

The prognosis and survival of patients with stage IV NSCLC is poor. Median survival rate in these patients is around 5 months.[2] Currently, the standard management is systemic therapy, including chemotherapy, targeted therapy, or immunotherapy after adequate genetic and molecular testing to allow for individual treatment decisions.[3,4]

Recently, LCT has been introduced into clinical practice as an option to treat a subset of patients with oligometastatic disease who did not experience disease progression after frontline systemic therapy. The term oligometastatic is applied in the literature to patients with up to 3 distant metastases[1,5] or up to 5 and includes malignant pleural effusion,[6] N2 disease,[1,5] and different metastatic locations.[7] It seems to be rather a subjective term meaning a burden of disease considered locally treatable (either by radiotherapy or surgery) after systemic therapy. Recently updated information on the multicenter randomized phase II trial by Gomez and colleagues[5] has demonstrated that LCT with radiotherapy or surgery prolongs progression-free and overall survival compared with maintenance therapy or observation. In their series, only 12% (3 out of 25) of patients in the LCT arm were treated by resection of the primary lung lesion, but neither the kind of resection nor the occurrence of postoperative complications are specified.

In the investigation by Mitchell and colleagues,[1] the term $LCT_{primary}$ is introduced. In their series, consolidative treatment was intended to control the primary pulmonary tumor, not the distant disease. Additionally, patients received LCT on metastatic sites either by surgery or radiotherapy. Surgery was more frequently indicated after lung resection compared with radiotherapy (60% vs 12.7%).

In the study by Mitchell and colleagues,[1] not every patient received systemic therapy before $LCT_{primary}$ (45% in the surgical and 63.8% in the radiotherapy subset) and surgery patients were younger and had smaller intrathoracic tumors. Although all limitations of the study are satisfactorily commented on by the authors in the Discussion section, surgical and radiotherapy patients seem to be quite different.

Some additional information on the series reported by Mitchell and colleagues[1] would be relevant. Besides the absence of postoperative mortality (meaning superb perioperative care in a series of cases such as this) the occurrence of postoperative adverse events is not mentioned and changes in patients' quality of life is not analyzed.

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Commentary: Surgery expanding to stage IV non–small cell lung cancer treatment?!

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CENTRAL MESSAGE

Durable overall survival rates can be achieved in surgically treated oligometastatic NSCLC.

There is an increasing body of evidence that the overall long-term survival of patients with oligometastatic non–small cell lung cancer (NSCLC) exceeds survival of patients with stage IV disease if all detectable disease is ablated.[1] Depending on the definition of oligometastatic disease (OMD) with numbers of metastases between 1 and 5, the real incidence is not clear and reports range from 16% to 26%.[2,3] The differentiation of this patient group from conventional stage IV patients might be based on a biologically different, more localized state of metastatic disease, but also the fact that advanced radiation techniques, including stereotactic radiotherapy (SABR) and minimal invasive surgery translate into improved disease control. Evidence comes from different randomized controlled trials: in the SABR-Stereotactic Ablative Radiotherapy versus Standard of Care Palliative Treatment in Patients with Oligometastatic Cancers Trial, 18 patients with NSCLC with up to 5 metastases were randomized to SABR or standard of care with a clear advantage for the former in terms of progression free survival.[4] Moreover, Gomez and colleagues conducted a phase 2 study in which 49 patients with up to 3 metastases were randomized to maintenance therapy or local consolidative therapy (LCT), including either radiation, SABR, consolidative chemotherapy, or surgery. The trial was closed early because of clear superiority in the treatment arm, with improved progression-free survival and overall survival.[5] Another phase 2 trial randomized 29 patients with up to 6 metastases to SABR plus maintenance chemotherapy or chemotherapy alone, yielding an increase in progression-free survival.[6] The role of surgery as a LCT modality in OMD for NSCLC is still unclear because only retrospective, albeit robust, data are available showing improved cancer-specific and overall survival.[7-10]

Mitchell and colleagues[11] report the retrospective analysis of NSCLC patients with OMD who underwent comprehensive LCT. The mortality rate of 0% for surgery was associated with a median survival time of 55.2 months

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