EDITORIAL

Changes in the Surgical Treatment of Lung Cancer

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The diagnosis and treatment of lung cancer has changed in many ways over the years, as we can attest after more than 20 years' experience. Survival rates, on the other hand, have hardly changed at all. Nonetheless, there has been progress and further developments are expected to improve our present ability to diagnose and treat the serious disease of lung cancer.

Although the focus of this editorial is treatment and not diagnosis, we would be remiss if we failed to mention important new techniques such as positron emission tomography and endoscopy, especially endoscopic surgery.[1-3] Nor should lung cancer staging be overlooked. The most recent revision of the TNM system was carried out by Mountain[4]; however, further revision is needed to include the subgroups present within each stage because prognosis depends on precise staging—even in stage I.[5]

In this article, we discuss the changes that have occurred over the past few years, especially in the treatment of stage I disease—the subject of an article by Padilla and colleagues in this month's journal.[6] Stage I offers the most favorable prognosis, yet it is precisely this stage which has been subject to the greatest amount of change and controversy.

The emergence of video-assisted thoracoscopy has had a significant impact on treatment, leading some groups to alter their surgical approaches to treating stage I lung cancer. Video-assisted thoracoscopic surgery was first described in 1994 by Giudicelli et al[7] and its utility was confirmed by later studies[8-10]—in Spain, particularly through the work of Loscertales et al.[10] According to recent studies, the survival rate for patients undergoing video-assisted lobectomy is similar to that of conventional surgery.[11,12] Patient enrollment in studies carried out thus far has been strictly limited to those with clinical features amenable to the technique: clinical stage I, neoplasms that are both peripheral and smaller than 5 cm, absence of significant pleural adhesions, nearly total interlobar fissure, and no pulmonary hilum involvement.[8] However, certain technical aspects of this procedure are still subject to debate. One study reported that video-assisted lobectomy can be performed without difficulty in patients with largely fused fissures.[13] Others have found that 2% to 3% of lymph nodes—an oncologically insignificant percentage—are missed in video-assisted mediastinal lymph node dissection.[14] The effectiveness of the technique for lung resection has been questioned and some authors report no significant differences between this technique and limited thoracotomy. Although Nomori et al[15] observed less pain in the early postoperative period with the new approach, they found no benefits—in terms of respiratory function—at 2 weeks postintervention. Nonetheless, lack of experience appears to be the main reason video-assisted lobectomy is not more widely used.

In the surgical treatment of stage I disease, the effectiveness of systematic lymph node dissection and its impact on survival is the object of a great deal of controversy. The article by Padilla and colleagues[6] is quite interesting because it provides a thorough discussion of this issue and the causes of death in patients undergoing surgery for stage IA lung cancer. It is clear that systematic lymph node dissection should permit better tumor staging, even though some authors—as the authors note—have reported finding no significant differences between systematic lymph node dissection and nodal sampling. Previous studies have reported that systematic dissection improves survival[16,17]; the findings of Padilla and colleagues, however, contradict those results. They conclude that more studies are clearly needed. It is important to note the numerous patients in the study with stage IA disease who died from causes unrelated to the surgically-resected tumor (39.7% of the deaths that occurred during the follow-up period). These results are similar to those reported by other recent studies.[18] Given this high rate of comorbidity, patients undergoing surgery for stage IA lung cancer should be intensively monitored afterwards.

Limited segmental resection has been described as a viable surgical option for stage I patients at high risk from surgery. In these cases, the tumor should be

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peripherally located, classified T1N0M0, and not be endoscopically visible. Even when these criteria were met, the classic trial carried out by the Lung Cancer Study Group found a high rate of locoregional recurrence.[19] Results of extended segmentectomy for patients at stage T1N0 with peripherally-located tumors smaller than 2 cm has been shown to be similar to those achieved by lobectomy.[20] A recent study suggested that candidate selection be based on imaging criteria of peripheral tumors likely to be less aggressive. In these cases, a segmentectomy would be justified.[21] The validity of segmental resection for stage IA lung cancer is still open to debate and more studies are needed to establish its equivalence—in terms of survival—to more extensive resections.

The use of induction chemotherapy to improve survival in early stages of lung cancer has also fueled a lively debate. The rationale behind this strategy is that many recurrences in patients treated for stage I and II lung cancers are due to micrometastatic tumors not detected during staging. However, this debate must remain unresolved until results from studies underway to test this hypothesis are reported. One such study—the Spanish NATCH trial—is currently in an advanced phase of case accrual.

Many authors argue that stage III lung cancers are inoperable due to their extremely poor prognosis. However, since Rosell et al[22] showed that induction chemotherapy improved survival in these patients, many studies—using a variety of chemotherapy agents—have attempted to confirm this therapeutic regimen. Findings published to date have not resolved the issues surrounding the use of neoadjuvant therapy: the side effects of chemotherapy; the use of computed tomography, positron emission tomography, or mediastinoscopy to assess results; surgical complications caused by neoadjuvant chemotherapy; the inclusion or not of stage IIIB cancers in this type of therapy; and, most importantly, the question of whether or not there is a significant increase in survival. Patients with stage III lung cancer are a heterogeneous group and the main problem in treating them with induction chemotherapy is the difficulty in distinguishing between those patients likely to respond to therapy and those unlikely to do so. The number of lymph node stations involved, proliferative activity, and tumor angiogenesis have all been described as factors involved in determining survival for stage III patients.[23-25] Indeed, tumor angiogenesis is a known prognostic factor in all stages of lung cancer.[26]

For now, tumor response to induction chemotherapy seems to be the key factor; patients with a positive (complete or partial) response have a better prognosis after lung resection. Cyjon et al,[27] in their study of patients with stage IIIA and IIIB neoplasms, observed a tumor response to induction chemotherapy and chemoradiation in 73% of the cases; 53% of patients underwent resection and survival at 3 years was 22%. Another study of patients with clinical stage IIIB cancer assessed the use of 5–fluorouracil and cisplatin neoadjuvant therapy combined with radiotherapy; the survival rate at 5 years was 22%.[28] The notable improvement in life expectancy reported after these studies seems to support the use of induction chemotherapy.

The question of whether postoperative adjuvant therapy is effective or not in pN2 cases is yet another unresolved issue in the treatment of patients with stage III lung cancer. A recent comparative study reported that, for completely resected stage IIIA (N2) lung cancers, the use of vindesine and cisplatin had no effect on survival.[29] Nevertheless, the use of adjuvant therapy in completely resected N2 lung cancers still has numerous supporters.

As the title of this editorial suggests, the surgical treatment of lung cancer has changed over time. Treatment for stage IA cancers has become less aggressive and neoadjuvant therapy is now used for stage III cancers. However, for stages II and IV, the traditional treatment protocol remains unchanged. Many issues are still unresolved and will require more experience, particularly the use of neoadjuvant chemotherapy in both early and advanced stages and the use of minimally-invasive surgical techniques in early stages.

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