CHAPTER 10

SUMMARY

This thesis comprises two parts, in which the evolving role of surgery in the multimodality treatment of locally-advanced non-small cell lung cancer treatment is studied. In the first part, the role of surgery as part of planned trimodality treatment is explored. In the second part, its role in the treatment of persistent or recurrent disease is analyzed.

PART I  Surgery as part of trimodality treatment for locally advanced NSCLC

There are several national and international guidelines recommending radical intent chemoradiotherapy or treatment approaches that include surgery for patients with clinical stage IIIA NSCLC. However, thus far it has been unclear how these guidelines are applied in daily practice in the Netherlands. Chapter 2 describes the current use of several treatment strategies for patients with clinical stage IIIA NSCLC in the Netherlands, using data from the Netherlands Cancer Registry (NCR) during the period 2010 until 2013. In this national cohort, including nearly 5000 patients, chemoradiotherapy was used in 45% of patients, and 15% were treated with surgery was part of the treatment. The 4-year survival was 51% in patients treated with induction therapy and surgery, compared with 39% for patients receiving chemoradiotherapy. Patients treated with surgery were younger (median 60 vs 66 yrs), and those with induction treatment prior to surgery did best when aged under 69, had squamous histology and underwent lobectomy instead of a bilobectomy or pneumonectomy. An unexpected finding was the poor agreement of only 51% between clinical and pathological TNM stage in those patients treated with upfront surgical resection ± adjuvant therapy, with a majority of the patients being clinically over-staged. For clinical stage IIIB NSCLC, we explored national patterns of care between 2010 and 2014, a period in which the TNM 7th edition was used nationally. Results are described in Chapter 3, which has a secondary focus on the use of surgery for these patients. In this period, 4401 patients were diagnosed with clinical stage IIIB, of which clinical N2 (37%) or N3 nodal disease (63%) was pathologically confirmed in only 50.8%. Radical intent treatment consisted of chemoradiotherapy in 48% of patients and surgery in 2.2% of patients, with a decrease of the use of chemoradiotherapy from 65% for patients aged <60 years to 13% for patients aged 80 years or older. Overall survival for surgery was 28 months, followed by chemoradiotherapy (19 months), chemotherapy (9 months), radiotherapy (8 months) and best supportive care (3 months). In Chapter 4, our institutional outcome of chemoradiotherapy and trimodality treatment for locally advanced NSCLC is described and discussed. Patients treated with trimodality therapy were younger and were more likely to have T4 tumors rather than N2-disease determining their clinical stage IIIA. With a median follow-up of 30 months, median survival was not reached for the trimodality group. Patients with N0-1, and larger volume tumors (represented by a radiotherapy planning target volume >500cm3) had superior survival when treated with trimodality therapy compared with chemoradiotherapy. In Chapter 5, we showed
surgery after induction chemoradiotherapy can be performed safely, with a 90-day mortality of 5.5%, and has promising long term overall and event-free survival of 75.9 and 58.7 months, respectively (median follow-up 80.4 months).

PART II New roles for surgery after chemoradiotherapy: recurrent or persistent disease and complications

For patients with recurrent or persistent tumor after radical chemoradiotherapy, therapeutic options with curative intent are limited. For selected patients, surgery or re-irradiation (Chapter 8) can be considered. Results from the surgical approach, are outlined and discussed in Chapter 6. All patients had high dose chemoradiotherapy (>60Gy), as their initial treatment for locally advanced NSCLC (10 patients stage IIA, 5 stage IIB). The median time of surgery was 21 months after the last day of radiotherapy. Although surgery in an area long after completion of high dose radiotherapy is believed to be hazardous, we report that selected patients with locoregional recurrence or persistent tumor after high dose chemoradiotherapy, can undergo salvage surgery with acceptable morbidity and mortality, even when a pneumonectomy is required. For patients who do not have recurrent or persistent disease after high dose chemoradiotherapy, but suffer from severe complications after such therapy, such as bronchial stenosis, hemorrhage and esophageal-respiratory fistula, we show that surgical procedures are high risk interventions, as described in Chapter 7. For the majority of patients, operated on for structural complications after chemoradiotherapy, all formerly treated with 60 Gy or more, pulmonary cavitation was the indication for surgical intervention. Other complications for which surgery was performed were esophago-respiratory fistulae, hemorrhage, bronchial stenosis, esophageal stenosis and bronchiectasis. The 30- and 90-day mortality was 20% and 27%, respectively, reflecting that this is a high risk patient group. Therefore, surgery is only justified in those patients with highly debilitating or life threatening complications.