Surgical Treatment of Non-Small-Cell Lung Cancer

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Table 109-1 Characteristics of Solitary Pulmonary Nodules Predicting Malignancy

Radiologic characteristics
Diameter >2 cm
Spiculation present
Upper lobe location
Clinical characteristics
Age >40 years
Positive smoking history
History of other cancer

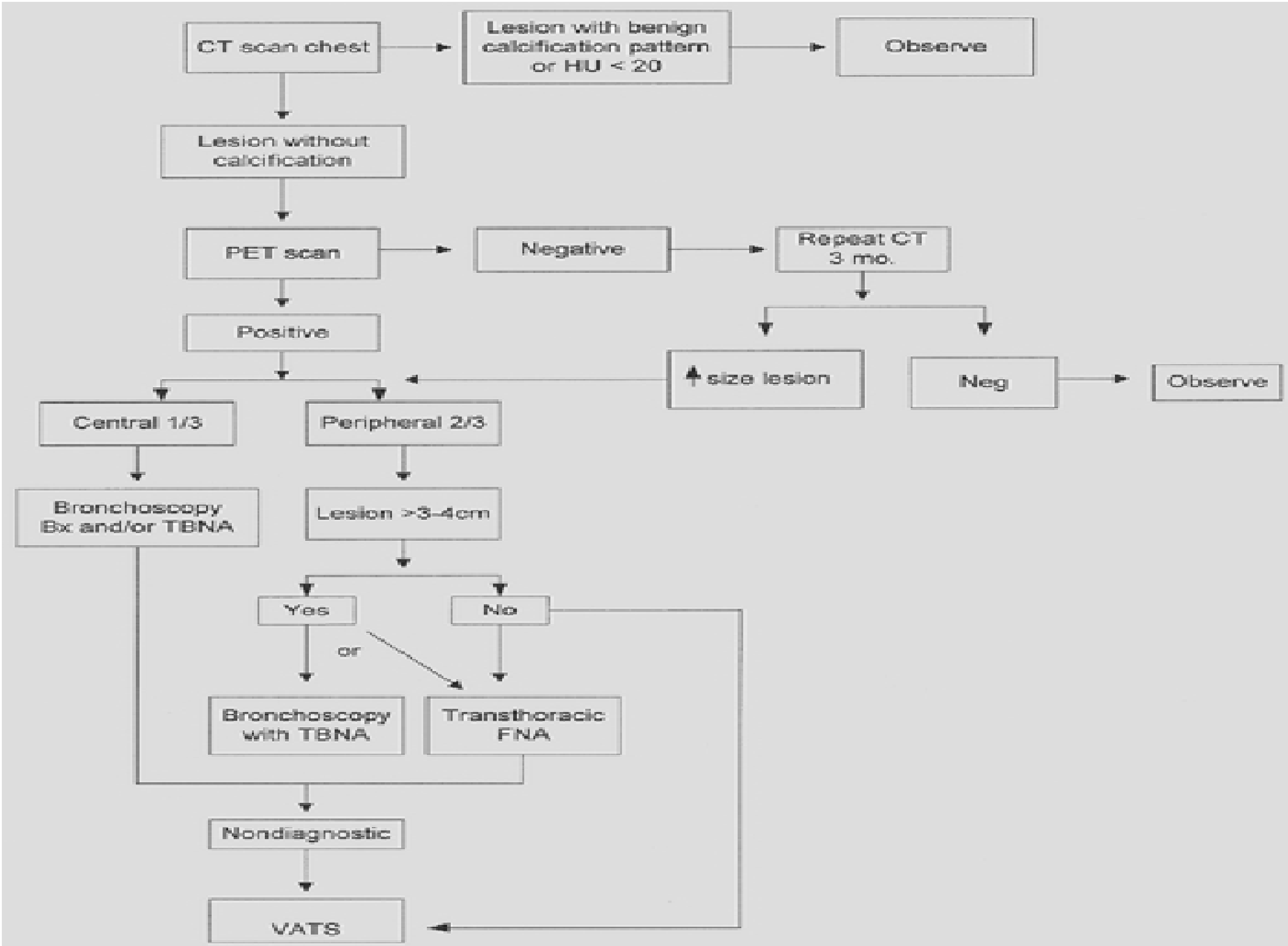

Figure 109-1. Algorithm for diagnosing lung cancer. (Adapted from Savage C, Morrison RJ, Zv
JB. Bronchoscopic diagnosis and staging of lung cancer. *Chest Surg Clin North Am* 2001;11:7C
permission.)

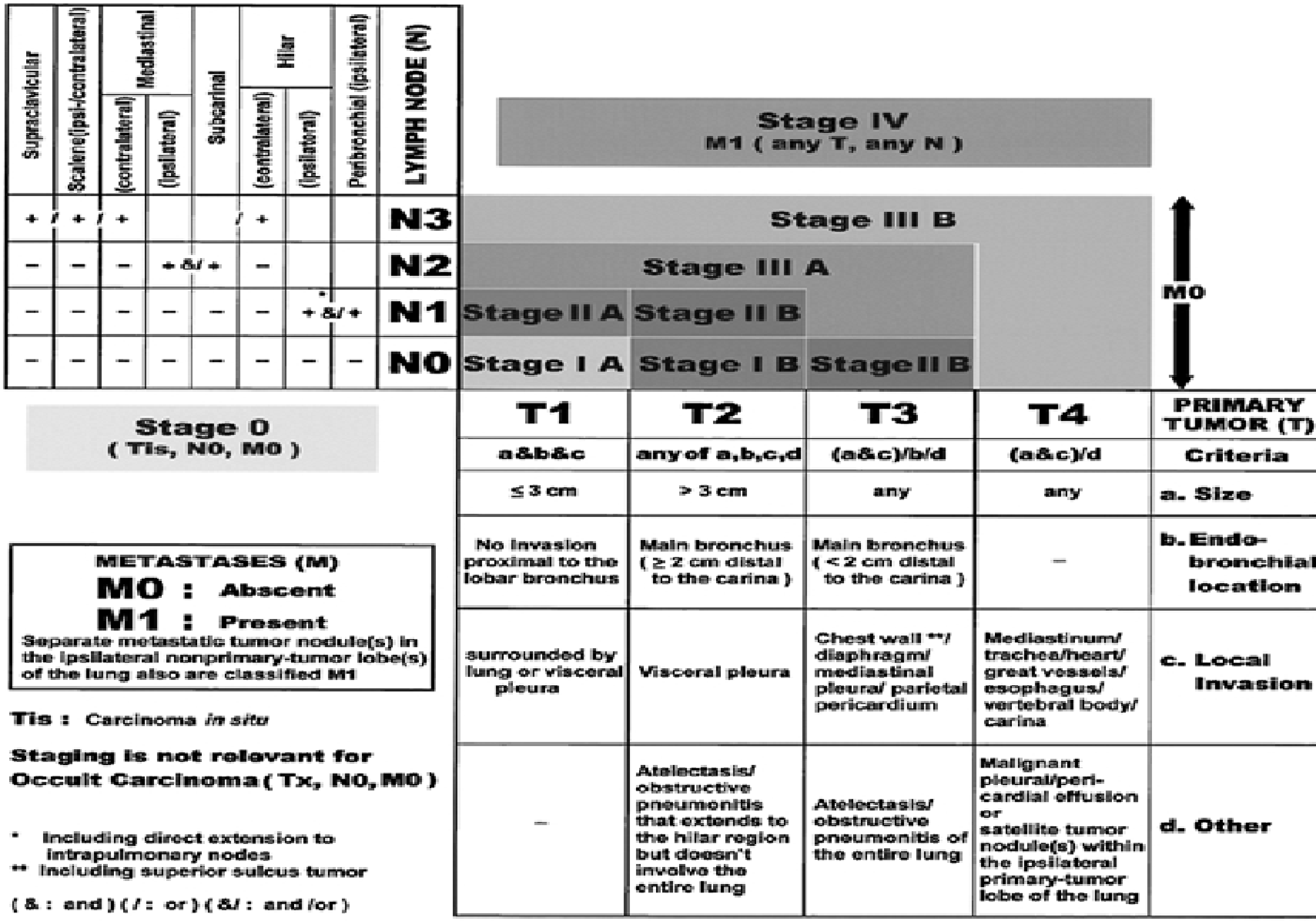

Figure 109-3. TNM staging of lung cancer. (See Color Fig. 109-3.) (From Lababede O, Meziane MA, Rice TW. TNM staging of lung cancer. *Chest* 1999;115:233. With permission.)

- 215,020 individuals (114,690 men and 100,330 women) will be diagnosed with cancer of the lung/bronchus and 161,will die of it in 2008.
- This incidence has risen markedly since 2003, when only 170,000 people were diagnosed with l cancer. From 2001 to 2005, the median age at diagnosis for cancer of the lung and bronchus was 71 years. None were diagnosed under age 20; approximately 0.2% between 20 and 34; 1.9% between 35 and 44; 8.8% between 45 and 54; 21.0% between 55 and 631.9% between 65 and 74; 28.9% between 75 and 84; and 7.3% at >85 years of age . The prevalence of non-small-cell lung cancer in the United States as of January 1, 2005, was chronicled in the same communication There were approximately 360,081 individuals alive who had a history of cancer of the lung and bronchus: 172,426 men and 187,65women. The probability of an American developing lung cancer increases with age: 0.020% at age 40, 0.185% at age 50, 0.487% at 60, 1.304% at age 70, and nearly 2% at age 80.

- Five-year survival, while still dismal for all patients with lung cancer.
- in 1976, the 5-year survival was 11.9%.
- in 2000, the survival rate is 16.2%.
- over 40% of patients regardless of smoking history present with metastatic disease at the time of diagnosis.
- For comparison, breast, prostate, and colon cancers present at a much earlier stage.

- ***Historical :Surgical resection for lung cancer , first successful pneumonectomy, Graham and Singer in 1933***.
- Subsequent advances have led to smaller resections and improved operative mortality rates.
- 1940:Bronchoplastic procedures.
- 1952:sleeve lobectomy for a bronchial carcinoma (Price-Thomas).
- 1940:lobectomy and segmentectomy.
- 1939: (Churchill and Bein) segmentectomy in a patient with bronchiectasis.

- Resection for Non-Small-Cell Lung Cancer Every patient with locoregional NSCLC should be approached as a potential candidate for resection clinical stage I and II NSCLC undergo resection as the definitive primary therapy.

- most papatients with stage Ib are offered adjuvant chemotherapy.

- clinical stage IIIA or IV primarily but rather considered for multimodality therapy.

- Only few patients with stage IV NSCLC be considered for resection.

Anatomic Considerations

- Complete resection is the goal of all operations for lung cancer.

progression of staging:

- from chest radiography to computed tomography (CT) of the chest and abdomen and other imaging.

- invasive assessment, most commonly surgical mediastinal evaluation and occasionally biopsy of extrathoracic sites, and, if indicated, to thoracic.

- In patients in whom the tumor is deem resectable, the appropriate procedure is carried out.

- If a tissue diagnosis is not made preoperatively, an operative biopsy is mandatory, particularly if more than a lobectomy is required.

- When the clinical and imaging data indicate that a complete resection cannot be achieved or that the clinical tumor stage is associated with a poor long-term outcome even with complete resection, operation is not indicated as initial therapy.

- Induction therapy before an attempted resection should be considered, or resection should be abandoned as an option.

- Tumors T4 lesions involvement of vital structures are mostly ***unresectable***.
- small numbers : ***superior vena cava***, ***aorta***, ***left atria***, ***pulmonary vein confluence*** appear to benefit from operation.
- **phrenic** or **recurrent laryngeal nerve** invasion, once considered an absolute contraindication to resection, are being included in multimodality protocols leading to operation.
- Patients with T3N0 (stage IIB)NSCLC due to chest wall invasion or carinal proximity are candidates for initial complete resection.
- operation for selected cases of “unresectable” T4 lung cancer, such as with tracheal involvement

- T4 tumors due to additional tumors or satellite nodules in the same lobe or malignant pleural effusion.
- Resection of tumors with satellite lesions in the same lobe is acceptable.
- Operation in cases of T4 cancer due to malignant pleural effusion contrast, offers no survival advantage over less invasive therapies.
- It is imperative to note that reports of successful surgery in advanced cancers constitute a truly minuscule fraction of lung cancers, are generally performed in high-volume centers, and cabe routinely extrapolated to the overall decision pathway for NSCLC .

The optimal initial management of NSCLC with clinically proven lymph node dissemination is also nonsurgical.

- ***N3*** disease remain of bounds for resection.
- even the anterior mediastinal nodes (station 3) have a dismal prognosis.
- ***N2 disease documented before thoracotomy:*** (clinical N2). Such patients are candidates for multimodality protocols .
- ***patients discovered N2 disease, particularly single-station, at thoracotomy:*** following an appropriate negative invasive evaluation (clinical N0–1, pathologic N2), should undergo resection at that time.
- ***N2 disease with obvious extracapsular involvement***: Careful consideration, before performing a pneumonectomy in the setting of.
- Resection is primary treatment in the patients without bulky lymphadenopathy found at operation carries a better prognosis than for patient with prethoracotomy N2 status.

Metastatic Disease

- multiple extra thoracic metastases is almost always an absolute contraindication to pulmonary resection.
- ***solitary metastasis (***cerebral metastasis + absence of other sites of disease) : resection of the primary lung cancer.
- . synchronous solitary adrenal metastases have been treated by combined resections.
- Except in unusual circumstances , primary lung resection is not indicated in the presence of other sites of dissemination, even if clinically thought to be isolated .
- In all cases of suspected single metastasis associated with limited intrathoracic disease, one must ensure that a distant lesion is solitary and that it is malignant before deciding against primary pulmonary resection.
- Brain metastases are usually diagnosed reliabby imaging and rarely require invasive confirmation

- solitary cerebral metastasis by CT scan ➔ (MRI) ➔ superior sensitivity .

- ***Additional imaging :*** abnormalities are detected (adrenalrenal, hepatic, or other mass is identified by CT).
- *plain radiographs*, *CT*, *MRI*, *ultrasound* , *PET*.

- solitary lesions ➔ equivocal ➔ percutaneous or open biopsy.

- ***In general and if reasonable, the metastasis is resected first, followed as soon as feasible by the lung resection***.

- Older Age age per se ➔ not a contraindication to resection.
- Long-term survival following resection ➔ not different for elderly patients.

- Cardiac Disease: (Despite with lung cancer are older and have a significant smoking history and other risk factors to coronary artery disease)➔
- ***cardiac morbidity is rare in patients undergoing a thoracotomy for carcinoma.***

- A myocardial infarction within 3 months before surgery carries some risk for reinfarction.
- If significant disease identified, many patients can still undergo pulmonary resection.
- Successful resection been performed***: after angioplasty***, ***concomitantly with coronary artery bypass surgery*** or ***sequentially within 2 weeks after*** b

- ***active coronary ischemia*** + ***lung cancer and require resection*** ➔ controversies over coronary stenting with a bare metal stent or a drug eluting stent
- require careful coordination between the team treating the lung can the cardiologists.

- ***latest recommendations***
- if the patient requires a stent in preparation for a lung resection metal stent be placed.
- The patient is at significant risk for the first 3 to 6 weeks after placement and should remain on aspi clopidogrel.
- At that point, clopidogrel may be stopped 5 days before the planned procedure. at day 3, the practic substituting a short-acting antiplatelet agent such as a small-molecule 2b3a inhibitor for clopidogrel should protect the coronary artery lesion and prevent excessive bleeding at the time of surgery.
- Dual antiplatelet therapy should begin on postoperative day 1

- Pulmonary Function Poor measured pulmonary function has traditionally been considered a formidable barrier to resection. Based on old unconfirmed data, elaborate schemas were established to filter only the best candidates for resection. We have learned from the experience with surgery to reduce lung volume that nearly all patients will tolerate some type of pulmonary resection. In general, individuals who function daily at a normal activity level, regardless of their measured parameters, will do well.
- patients who had upper lobectomies actually had better post operative function.
- pulmonary function testing (PFT) remains an important objective evaluation of a patient's ability to tolerate resection.
- no single parameter has proved to be reliably prognostic, and strict interpretation could deny resection to manphysiologically eligible patients.
- Of most importance is that the pronouncement that “patients require a postoperative residual FEof 800 mL,” Specifically, examples of cardiopulmonary fitness include the ability to climb one or more flights of stairs, the ability to walk more than a block without stopping, and the ability to perform house or yard work without difficulty.

- Office assessment of exercise capacity may include a modified 6-minute walk test.Standard PFTs should be performed and include the following: spirometry, including forced vital capacity (FVC), forced expiratoryvolume in one second (FEV1), and forced expiratory flow rate (FEF); and lung volumes, including total lung capacity (TLC), residualvolume (RV), functional residual capacity (FRC), and diffusing capacity of the lung for carbon monoxide (DL CO). The prime values arthe FVC, which is a surrogate for restrictive disease; the FEV1/FVC ratio, which is a dimensionless variable denoting the patient-specific obstructive disease; and the DLCO, which is a surrogate for oxygen diffusion defects.The predicted postoperative parameters (e.g., PPFEV1) can be estimated by multiplying the measured FEV1 by the expected numbeof segments remaining after resection, each of which is assigned a contribution to overall pulmonary function of 5%. A PPFEV1 of lesthan 30% of the patient's expected value may be cause for concern. Additional testing that may be helpful in equivocal situationsincludes quantitative ventilation/perfusion scanning and cardiopulmonary exercise testing.

- ***Principles of Surgery :***

- The goal ➔ complete resection ➔ negativity of the highest or most distant resected lymph node.

- Incomplete resection ➔ visible tumor behind (R2) ➔quality of life.

- Incomplete resection ➔ no therapeutic advantage.

- R2 resections ➔ unnecessary pain a suffering and temporally postpone any potential benefit of subsequent radiation therapy and/or chemotherapy.

- R1 resection ➔ leaving a microscopically positive resection margin

Every operation for lung cancer has three essential parts:

- establishment or confirmation of the diagnosis.
- the intrathoracic stage complete resection of the tumor.
- systematic sampling or complete dissection of all ipsilateral lymph node stations .

- ***diagnosis of cancer has not been secured before thoracotomy:***

- intentionally or inconclusive results ➔ establish a diagnosis intraoperatively before proceeding to resection.

- Stapled wedge resection - frozen section - fine-needle aspiration (FNA) - core needle biopsy.

- Incisional biopsy ➔ macroscopic violation of a potential neoplasm.

- rare instance of a tumor of uncertain ➔ lobectomy may be required complet resection ➔ 5-year survival rate of 9% .

Extensive parenchymal resections should not be done if the fluid is known to be malignant.

Resection generally should proceed when unsuspected lymphadenopathy is found at operation after appropriate invasive andnoninvasive staging evaluation.

Exceptions ➔unexpected extensive, fixed, or “bulky” adenopathy.

in a physiologically marginal patient, pneumonectomy should not be done in the presence of positive interlobar nodes or direct extension across major fissures.

In any case, there should be no hesitation to sample and assess by frozen section or cytologic aany nodal, pleural, or parenchymal tissue or pleural fluid that, if positive, would render resection inappropriate.The potential for incomplete resection is generally known preoperatively and should be discussed clearly with the patient

- Resection After a diagnosis of cancer has been made and resectability established, the appropriate pulmonary or extended resection, all with systematic lymph node sampling or lymphadenectomy, is carried out.
- For patients with adequate lung function, the curre standard cancer resections include lobectomy, bronchoplastic lobectomy, bilobectomy, and pneumonectomy, based on the ex disease. In some cases, an anatomic segmentectomy may be appropriate. At present, nonanatomic or “wedge” resection should considered as definitive therapy only in the minority of patients whose cardiac or pulmonary status mandates conservation of pulmonary parenchyma or in certain cases of synchronous or metachronous multiple tumors. There is increasing interest is asslimited operations for NSCLC that is considered low-grade by preoperative imaging such as “ground glass” opacity on CT scan .

- ***Lobectomy is the ideal operation for resection of a lung cancer***.
-
- Lobectomy ➔ well tolerance & sufficient lung volume to fill the pleural
- Lobectomy is associated with about half the operative mortality of pneumonectomy (abouversus 4%)
-

- bilobectomy →
- ***- resection of the right upper and middle lobes***
- (anterior segment of the right upper lobe or in the right middle lobe has spread across theminor fissure or approximates an incomplete fissure)

- ***- right lower and middle lobes***

  (the right lower lobe is central - interlobar vascular or nodal involvement)

operative mortality for bilobectois → ***higher than for lobectomy*** but ***lower than pneumonectomy.***

- Sleeve LobectomyA sleeve lobectomy consists of the resection of a lobe along with a circumferential segment of the adjacent mainstem broncgenerally an alternative to pneumonectomy. Bronchial P.1393continuity is restored and lung parenchyma preserved by anastomosis of the proximal and distal bronchial resection edges. operation is most often indicated for endobronchial tumors at the origins of the right- or left-upper-lobe bronchi.Occasionally, sleeve lobectomy is suitable for patients with limited nodal disease affixed to the bronchial wall at the orificelobes. Nodal disease of this type was the indication in 21% of the cases reported by Deslauriers and colleagues.57 Overall, thauthors achieved a complete resection in 87% of 142 sleeve lobectomies, with an operative mortality rate of only 2.5%. Thei10-year survival rates were 63% and 52%, respectively, for stage I tumors. Local recurrence was ultimately seen in 23% overa17% of completely resected cases.In 2007, Yildizeli of Dartevelle's group316 reported on 218 patients. They were able to perform a complete resection in 95.9series. Their operative mortality and the morbidity rates were 4.1% and 22.9%, respectively. Multivariate analysis showed thfactors for mortality and morbidity were compromised patients (p = 0.001), current smokers (p = 0.01), right-sided resectio0.003), bilobectomy (p = 0.03), squamous cell carcinoma (p = 0.03), and presence of N1 or N2 disease (p = 0.01). Their overand 10-year survival rates were 53% and 28.6%, respectively. After complete resection, recurrence was local in 10 patients,mediastinal in 20, and distant in 25. By multivariate analysis, two factors significantly and independently influenced survivastatus (N0–N1 versus N2; p = 0.01) and the stage of the lung cancer (stage I–II versus III, p = 0.02).Inferred from these series are the following criteria for optimum results of sleeve lobectomy. Patients should have adequatpulmonary function. The tumor should be limited to the lung so that a complete resection may be accomplished. Patients wnegative mediastinal nodes have the best survival. Patients with marginal pulmonary function, tumors invading structures othe lung, or positive nodes in the mediastinum technically may be resectable with a sleeve lobectomy but have higher comprates and shorter survivals than those without these findings.Sleeve resection of the pulmonary artery can be accomplished with or without a bronchial sleeve resection, but most cases degree of local invasion are inoperable or are treated by pneumonectomy. Ma and colleagues154 reported in 2007 on a metaof studies of pulmonary artery resection. Twelve studies met the defined criteria, including a total of 2,984 subjects havingresection, but only five studies including pulmonary artery resection. For pulmonary artery resection with sleeve lobectomyweighted mean operative mortality was 3.3%, and the complication rate 32.4%. The estimated combined hazard ratio for ovsurvival in 10 studies was 0.70 (95% CI: 0.62–0.79) in favor of sleeve lobectomy. The median overall survival was 26 months pneumonectomy, 60 months for the sleeve lobectomy alone, and 30 months for pulmonary artery resection and sleeve lobec

- Bronchoplastic Procedures. t is very hard to evaluate the use of bronchoplasty alone as an adjunct to complete resection, since any bronchus closed with s nstead of a stapler may be called technically a bronchoplasty. It permits the resection of a little extra bronchus without having esort to a sleeve lobectomy. A bronchoplastic resection is less often appropriate when bronchi other than those of the upper loare involved by NSCLC, but is occasionally undertaken in oncologically favorable situations or as an alternative to pneumonectopatients with limited lung function. The success of bronchoplastic resection in properly selected patients is also in the series reby Watanabe and colleagues,300 with late survival of 79% in stage I, 55% in stage II, 30% in stage III, and 45% overall.Although concern has been raised that the local recurrence rate is higher following bronchoplastic lobectomy than afterpneumonectomy, reports from centers with significant experience with this approach—including those of Vogt-Moykopf, 294 Tedand Deslauriers57 and their associates—show an acceptable operative mortality, a high rate of complete resection, and a late su

- PneumonectomyA pneumonectomy is required when a lobectomy or one of its modifications is not sufficient to remove all locoregional disease. Imust be kept in mind that a pneumonectomy is a radical procedure that can result in the loss of more than 50% of a patient's lunfunction and pulmonary vascular bed. The indications are central tumors that involve the main bronchus, large parenchymal canthat violate the fissures or invade the interlobar vessels, or hilar lymph node involvement. Pneumonectomy in the latter situatioshould be reserved for cases in which higher stations are benign and a complete resection is possible. The operative mortality fopneumonectomy is about twice that of lobectomy. Wada and associates295 noted a rate of 3% among 590 patients undergoingresection for lung cancer in Japan in 1994. Right pneumonectomy carries a higher risk than left pneumonectomy. An increasingnumber of patients with N2 disease or central, locally invasive cancers are now being treated by induction therapy. Because of textent of their disease, a high percentage require pneumonectomy (23% to as high as 53%). Despite the frequent technical difficposed by postinduction peribronchial and perivascular fibrosis, operative mortality in this group can be as low as 5%, but ranges 15%, as reported from several multicenter trials by Strauss269 and Weiden 305 and their associates. Albain and associates6 in 2005presented the data from the intergroup trial 0139, which randomized 429 patients with T1-3, N2, M0 NSCLC to chemoradiation aor followed by surgery. They reported a mortality rate of 26% for pneumonectomy, almost all on the right side. But subsequently2006, Daly and colleagues44 showed equal or better mortality for right pneumonectomy. They reported on 30 patients with localadvanced non-small-cell lung cancer who underwent pneumonectomy after 5,940 cGy of radiation and two cycles of etoposide acisplatin. To minimize post- pneumonectomy pulmonary edema, patients were treated with a protocol that included fluid restricand 48 hours of mechanical ventilation. Morbidity, mortality, and survival were examined. Of the 30 patients, 18 had right and 1pneumonectomies. Death occurred in four patients (13.3%) but in only one (5.6%) after right pneumonectomy.

- Extended Pneumonectomy.There are three types of extended pneumonectomy. The most commonly employed variation is an intrapericardial pneumonectnecessitated by encroachment of a central tumor at or near the entry of the P.1394pulmonary vessels (most often the artery central to its branches) into the pericardium. Division within the pericardium may proboth a greater margin of resection and a longer segment for safe transection of the vessel. Although this approach may be assowith a higher incidence of postoperative arrhythmias, the operative risk is not higher than for standard pneumonectomy.Another modification is a supra-aortic pneumonectomy and involves transecting the left mainstem bronchus more proximal thastandard left pneumonectomy closer to the trachea above and medial to the aortic arch. This approach is needed occasionally tumors originating high in the bronchus.The third variation is the carinal or sleeve pneumonectomy, consisting of resection of the lower trachea, the carina, and a maibronchus and its associated lung (usually the right) with a tracheobronchial anastomosis of the remaining lung. This procedure indicated for central lesions approximating or involving the carina that appear totally resectable by this approach. Although soearlier series reported operative mortality in as many as one-fourth to one-third of cases, reports by Dartevelle and associates5by Mitchell and colleagues179 have achieved mortality rates of 7% and 15%, respectively. The latter authors noted a decrease fr20% to 10% in operative mortality rates between the first and second halves of their series. Porhanov and colleagues215 reporteoperative mortality rate of 16% among 231 carinal resections. Some cases in these series were pure carinal resections or lobar carinal resections. The risk of the less often performed left carinal pneumonectomy is higher than that of the right lung.

Segmentectomy

- It is generally agreed that a segmentectomy is an acceptable operation for NSCLC when a patient has limited pulmonary resera small peripheral tumor confined to an anatomic segment. Whether segmental or wedge resection constitute adequate treatsmall peripheral cancers in general or for cancers in which the preoperative radiographic features suggest a low-grade tumor runder investigation. Although any segment can be removed by anatomic dissection, resections of the upper lobe segments or tsuperior segments of the lower lobes are performed most commonly. Lingulectomy, although encompassing two segments, is aform of segmentectomy and is often feasible for peripheral NSCLC.Jensik and colleagues123 reported the first large series of segmental resection for lung cancer. Among 123 patients, 5-year andyear survival rates were 56% and 27%, respectively. In an instructive analysis, Kodama and colleagues136 compared three groupatients with T1N0 NSCLC: (a) 46 patients undergoing segmentectomy as an intentional procedure, (b) 17 patients in whom seresection was viewed as a compromise because of limited lung function, and (c) 77 patients treated by lobectomy and lymph ndissection. There was no significant difference in late survival between the lobectomy group (88%) and the intentionalsegmentectomy patients (93%). However, the difference in survival between these two groups and patients undergoingsegmentectomy as a compromise procedure (48%) was significant. In a report by Warren and Faber297 comparing 68 patients wT1–2N0 tumors treated by segmental resection with 105 similar patients undergoing lobectomy, there was also an overall survidifference favoring the lobectomy group, but the differential was not significant for tumors =3 cm in size. However, for the toseries, the rate of locoregional recurrence was 23% following segmentectomy, as contrasted with 5% after lobectomy. The onlprospective experience, collected by the LCSG and reported by Ginsberg and Rubinstein, 87 indicates that local recurrence folllimited resection for T1N0 NSCLC (including both segmentectomy and wedge excision) is threefold higher than for lobectomy,although ultimate survival was not significantly different. Despite an increased risk for local recurrence, anatomic segmentalresection remains an appropriate option in patients with limited lung function and also in those with small peripheral tumors.

- Wedge ResectionIn contrast to segmentectomy, wedge resection is a nonanatomic operation that should be considered as definitive therapy onpoor-risk patients. Despite a higher risk of local recurrence when compared with anatomic resection, wedge excision may still preferable to alternative treatments. In an early nonrandomized series reported by Errett and associates, 69 wedge resection wperformed as a compromise operation in 97 patients with pulmonary impairment and compared with the outcomes in 100 patitreated by lobectomy. Despite higher predicted risk, the wedge resection group incurred only a 3% operative mortality rate, acompared with 2% in the lobectomy group; late survival was not statistically different. In patients with T1N0 NSCLC, Landrenecolleagues147 retrospectively compared 42 cases treated by open wedge resection, 60 by video-assisted wedge resection and 1standard lobectomy. Despite reduced pulmonary function and older age, there was no mortality in the combined wedge groupcompared with a 3% mortality rate in the lobectomy group. However, as in the LCSG experience, local recurrence rates were hin the open and VATS wedge patients (24% and 16%, respectively) than in the cases treated by lobectomy (9%). Although the 5-survival rate was significantly lower in the open wedge cohort than in the lobectomy patients (58% versus 70%), the 5-year surrate, at 65%, in the VATS patients was similar to that in the lobectomy group. The authors point out that the minimum requirefor an appropriate wedge resection for NSCLC include the following: a tumor <3 cm in diameter; a location in the outer third olung and technically amenable to adequate local excision, absence of endobronchial extension, clear margins by frozen sectiomediastinal and hilar lymph node sampling. When these criteria are met, wedge resection is an acceptable option in the few punable to tolerate an anatomic operation. The Cancer and Leukemia Group B (CALGB) has opened a trial of lobectomy versussublobar resection (segmentectomy or wedge resection) for cancers <2 cm. This trial was approved for accrual in 2007.With the use of radiation adjuncts, recent trials suggest that long-term results of wedge resection may be enhanced by applyinimplanted radiation seeds at the site of resection. The American College of Surgeons Oncology Group (ACOSOG) has establisherandomized trial comparing sublobar resection (wedge resection) to sublobar resection plus implanted radiation seeds. This triopened in 2006 and is expected to close in 2009.

- Minimally Invasive ResectionThoracoscopic techniques have been successfully employed for lobectomy, pneumonectomy, and local resection of NSCLC. Forsurgeons with experience and skill with this methodology, thoracoscopic approach is an acceptable alternative to open operationis essential that the same principles of lung cancer surgery that guide standard resection be maintained when minimally invasivetechniques are applied. This topic is addressed in detail in Chapters 33, 34, and 35.

- Evaluation of the Lymph NodesThe single most important prognostic surgical factor in NSCLC is the status of the mediastinal lymph nodes. Evaluation beginspreoperatively with a CT scan of the chest. Although there is controversy regarding the need for routine mediastinal evaluation, accessible nodes that are enlarged should undergo biopsy before thoracotomy. Nodes that are positive on PET scan, whether or nenlarged on CT, must undergo biopsy to rule out both metastasis and false-positive uptake. In addition, mediastinal node assessmshould be considered in all patients at high risk for metastasis, such as those with central tumors. In addition to mediastinoscopyextended mediastinoscopy, and anterior mediastinotomy (see Chapter 18), endobronchial ultrasound and esophageal ultrasound aoften useful (see Chapter 14). Thoracoscopy is no longer indicated as a method of primary mediastinal nodal staging except in eastage disease where the patient is a candidate for thoracoscopic lobectomy.At thoracic exploration, the surgeon should assess not only those nodes attached to the resected specimen but also any abnormalnodes and by systematic biopsy of each node station. The current minimum standard is a systematic sampling of each lymph nodestation draining a tumor. For right-sided resections, nodes should be taken from mediastinal levels 2, 3, 4, 7, 8, and 9 as well as the tracheobronchial angle and interlobar area (levels 10 and 11). On the left, the subaortic and anterior mediastinal nodes (leveand 6) should undergo biopsy as well as levels 7, 8, and 9. Systematic sampling is required because of the frequent finding ofpathologic N2 nodes involved in the presence of benign N1 levels (“skip” metastases), and even small, normal-appearing nodesharboring metastases, as demonstrated by Daly and colleagues. 42 The incidence of unsuspected N2 disease after various stagingpathways using modern imaging, including PET, and either routine or selective mediastinoscopy is at least 10%. Goldstraw andcolleagues, 88 for example, found pathologic N2 in 24% of clinical N0–1 cases. Further refinements of and experience with PET madecrease the gap between clinical and pathologic staging.Some surgeons believe that complete mediastinal lymph node dissection (MLD) is indicated for diagnostic and therapeutic reasonall resections for NSCLC. In the prospective randomized series reported by Sugi and associates272 and by Izbicki and colleagues,12however, MLD did not increase overall survival. Operations following induction therapy for known N2 NSCLC should include MLD invirtually all cases. Although improved survival with routine MLD has not been proven, this approach does minimize sampling erroridentifying N2 metastases that otherwise might have been missed, as shown by Graham and associates. 91 In a subsequent report the same group by Passlick and colleagues203 using immunohistochemical staining, no difference in survival was noted between t

- Selection of the Operative ProcedureThe appropriate operation depends on the clinical and surgical stage of the tumor and an accurate assessment of the structinvolved. Lung cancers may be classified as occult, peripheral, or central. Occult lesions are not seen radiographically, but tpresence is detected by sputum cytology or bronchoscopy. Central lesions are located radiographically within the central thhemithorax or bronchoscopically within or proximal to a segmental bronchus. Peripheral tumors are located beyond a segmebronchus and in the outer two-thirds of the lung.

- Occult TumorsMost cases of occult NSCLC are brought to attention in screening programs for high-risk people or those who present with hecough, or wheezing. Because the lesion cannot be localized precisely anatomically, Cortese and colleagues39 had to performlobectomy 70% of the time and larger resections in the remaining patients. In a report of 94 cases by Saito and associates,24resections included 58 lobectomies, 12 bilobectomies, 11 sleeve lobectomies, and 12 pneumonectomies.In some patients, when occult NSCLC is confined to the bronchial mucosa or is an in situ carcinoma covering <3 cm of the msurface, or in medically inoperable cases, photodynamic therapy (PDT) has been used successfully as primary treatment, as by Lam146 as well as by Kato,129 Cortese,40 and Weigel307 and their associates. Alternatively, brachytherapy can be deliverethrough bronchoscopically placed catheters, as reported by Taulelle and colleagues.279 Weigel and Martini306 reviewed thesother endobronchial approaches, such as laser, electrocautery, and cryoablation (see also Chapter 112). In most cases, howdepth of invasion cannot be determined with certainty, and some have associated lymph node involvement.

- Peripheral TumorsThe major considerations in the surgical evaluation of a peripheral tumor are its location within the lobe and its relation to otherstructures. Lesions that are clearly surrounded by parenchyma and confined to a single lobe are treated by lobectomy andoccasionally by lesser resections. When a P.1396peripheral tumor invades other structures, en bloc resection is often necessary. If a tumor abuts the chest wall on CT, the possibof pleural invasion should be entertained, especially if the patient has associated pain. If the tumor approximates an interlobarfissure, the possibility of extension into an adjacent lobe should be considered. In all such cases, the operation should be plannediscussed with the patient by including the possibility of chest wall resection, bilobectomy, or pneumonectomy, as appropriate.

- Chest WallTumors invading the chest wall are often resectable. The involved ribs should be transected several centimeters beyond the of gross involvement. In most cases, one rib and intercostal tissue above and below the tumor should also be included in theresection. Chest wall reconstruction is carried out as needed to prevent physiologic impairment due to paradoxical chest wallfunction or for cosmetic reasons (see Chapter 49). For posterior defects, support by the remaining chest wall muscles and scausually sufficient, whereas anterior and lateral defects more often require reconstruction.Although full-thickness resection is mandatory for tumors invading the osseous and muscular structures of the chest wall, thercontroversy regarding the necessity of chest wall resection when invasion is confined to the parietal pleura. McCaughan anassociates173 reported good results in such cases treated by the development of an extrapleural dissection plane when posstripping away the lung and parietal pleura from the endothoracic fascia, and proceeding to a full-thickness resection onlymargin was positive on frozen section. However, the experience of Trastek and colleagues283 suggests that chest wall resepreferable even when invasion is confined to the parietal pleura. Ratto and associates221 stated that no attempt should bestrip parietal pleura away and that an en bloc resection should be carried out when a tumor is firmly affixed to the parietasupport of this approach, Albertucci and associates7 found in 1992 that a histologic complete resection was achieved in onlof their patients treated by extrapleural dissection as compared with all of those undergoing a standard chest wall resectioFor isolated chest wall invasion with N0 or N1 positive nodes, there is no known role for neoadjuvant therapy. Trials for staIIIA are under way, but whether this question can be answered from these trials is unclear, since the studies are not stratiftype of tumor. Studies by Rusch 242 and Kunitoh 143 and their colleagues suggest that neoadjuvant chemoradiotherapy is besuperior sulcus tumors but not specifically for isolated chest wall tumors. Superior sulcus tumors are dealt with separately chapter. Ginsberg and colleagues86 found no benefit for the use of brachytherapy in patients who had a complete resectiochest wall tumors. They also found only a 9% five-year survival for the use of brachytherapy with or without preoperative opostoperative external beam radiation in patients who had an incomplete resection of their chest wall tumor. Similarly, adtherapy after complete resection of a chest wall tumor is not indicated. Gould and colleagues90 from the Mayo Clinic repor1999 on their experience with 92 T3N0 patients. They found that patients with completely resected T3 N0 M0 NSCLC have local control and overall survival irrespective of primary location, type of surgery performed, or use of adjuvant radiation

- DiaphragmAs noted by Rocco and associates236 and by Riquet and colleagues,233 the diaphragm is rarely involved by direct extension despite the large area of contact between this structure and the base of the lung. When invasion occurs, that portion of thdiaphragm should be resected with a wide margin of normal tissue without regard to the extent of the defect. Although unhelpful for NSCLC, it is feasible to resect and replace an entire hemidiaphragm. Unless the defect is small and can be closewithout tension, it should be replaced with a prosthetic material. Alternatively, a variety of muscle flaps can be used. Whearea of diaphragm has been resected or when the phrenic nerve has been resected, it is important that the diaphragm bereconstructed near the position of full inspiration to avoid paradoxical motion. When the defect is peripheral, it may be poreinsert the remaining cut edge at a higher level on the chest wall and thereby obviate the need for prosthetic material, aby Daly. 43

- PericardiumTotal resection of the pericardium on the left can be performed without reconstruction. Partial defects should be closed to prherniation and strangulation of the left ventricle. On the right side, all pericardial defects, regardless of size, require repair. potential problem if the pericardium remains open following right pneumonectomy is torsion of the heart into the hemithorax the axis of the venae cavae, with consequent near total occlusion of venous inflow. Large defects can be closed with the pericfat pad, a pleural flap, or nonautologous material such as bovine pericardium or polytetrafluoroethylene (PTFE). Many surgeonsuggest that a small opening be left in the repair or that the prosthetic material be fenestrated to prevent intrapericardial fluaccumulation and potential subsequent cardiac tamponade.

- Vertebrae umors invading the vertebral bodies are rarely cured. Under most circumstances vertebral body invasion is considered T4 disease nd thus unresectable. DeMeester and colleagues53 described a technique of partial vertebral resection for tumors fixed to theparavertebral fascia. They use a tangential osteotomy through the transverse process, costotransverse foramen, and superficialvertebral body (Fig. 110-1). The authors emphasize that this approach is not suitable for patients with radiographic evidence of destruction. Grunenwald and associates,94 however, reported on a small group of patients with radiographic evidence of osseouinvasion treated by en bloc pulmonary resection and complete vertebrectomy with reconstruction by a combined anterior andposterior approach. In a subsequent report,95 this group had a 14% late survival in 19 patients treated by partial or totalvertebrectomy. This technique should be limited to rare cases in which the tumor extent is completely delineated, node-negativtotally resectable, and, after careful evaluation with MRI, does not involve the spinal canal.

- Superior Sulcus TumorsResection of peripheral tumors involving the apex of the chest and the lower portion of the brachial plexus (superior sulcus orPancoast tumors) is discussed in Chapter 38. Although they P.1397invade the chest wall, these challenging lesions are viewed as a distinct entity because of their unique clinical, anatomic, andsurgical features. Since these tumors invade the first and/or second rib, the traditional margin easily obtained on lower chest wlesions is impossible. Therefore, when a superior sulcus tumor is deemed potentially resectable at presentation, operation ispreceded by induction therapy with chemotherapy and radiation therapy. Two trials recently completed show that there is a beresponse rate, resection rate, and an extended survival. Rusch and associates245 reported in 2007 on the ECOG 9416 (Intergrou0160) and Kunitoh and colleagues143 reported in 2008 on the Japan Clinical Oncology Group Trial 9806. The ECOG trial had a 76complete resection rate with a 44% 5-year survival. The Japanese trial had a 68% complete resection rate and a 56% 5-year survResection involves removal of the involved portions of the apical chest wall—typically including the first, second, and third ribs andthe T1 nerve root—along with lobectomy. A lesser pulmonary resection is now considered inadequate by most surgeons. Invasion ofthe vertebral body or of the subclavian vessels and clinical N2 disease generally contraindicate primary operation and a moreaggressive approach, especially after induction therapy, should remain the subject of clinical investigation. These tumors may beresected through either a high posterolateral thoracotomy or an anterior approach using a cervical incision with extension down tothe second intercostal space and resection of the first and second costal cartilages. Darte- velle and colleagues50 have used theanterior approach alone to perform extensive vascular resection along with lobectomy in this setting. It is important to bear in minthat these tumors are in an advanced stage; thus many patients do not reach the surgical option. Kappers and colleagues127 reviewtheir experience in the Netherlands in 2008. They found that 38% of their patients did not complete therapy for a variety of reasonincluding progression to stage IV disease, comorbidity, unresectability (extensive tumor growth and/or persisting N2–3 status) orinsufficient response to induction treatment.

- Central TumorsCentral tumors are more likely to be associated with malignant lymphadenopathy and to involve mediastinal structures. Accor-dingly, careful imaging and invasive evaluation are mandatory before consideration of thoracotomy. By definition, complete resrequires at least a lobectomy and often requires a pneumonectomy or more extended procedure. Central bronchial T3 lesions ansome T4 cancers involving the carina can be treated successfully by primary operation, in the latter situation usually by a carinapneumonectomy. The selection, techniques, and results of resection in this setting are discussed in Chapters 29 and 31. Thedecreasing mortality rate associated with these extensive procedures has been noted previously.Infrequently, for a small lesion in the left mainstem bronchus, a localized bronchial sleeve resection with pulmonary conservatiobe carried out, as reported by Cerfolio and Bryant36 in 2007. Localized tumors involving the pulmonary veins (even with extensiointo the pericardium and left atrium) may be amenable to resection by excision of a contiguous cuff of the atrium, using vasculaclamps and sutured closure or vascular staplers.Central NSCLC with local invasion limited to the mediastinal pleura and adipose tissue but not involving deeper structures is alsooften suitable for total resection. With exceedingly rare exceptions, in contrast, tumors invading the superior vena cava or the aor its branches should not be addressed by primary operation but rather considered for resection in a few cases only afterpostinduction reassessment. It cannot be overemphasized that in all cases of locally invasive NSCLC considered for resection, thabsence of N2 lymphadenopathy should be confirmed by rigorous preoperative staging.

- Simultaneous Cardiac Operation and Pulmonary ResectionWhen a patient requires myocardial revascularization or any other cardiac procedure and also has a resectable lung cancer, question of simultaneous versus staged procedures arises. This clinical situation can arise during the physiologic assessment cancer patient being considered for resection or in the preoperative radiographic evaluation of a cardiac patient. When the cancer can be resected through a median sternotomy, the timing of the procedures is largely a matter of the surgeon's prefeand patient-specific factors. P.1398The experiences reported by Terzi 281 and Danton 47 and their colleagues support the safety and efficacy of simultaneous opeThe cardiac procedure should be performed first, without complications. Pulmonary resection is carried out after reversal ofanticoagulation and confirmation of hemodynamic and hemostatic stability. Generally a lobectomy is carried out, althoughpneumonectomy has been reported by Piehler210 and Danton 47 and their associates. Because cardiac retraction required duringtranssternal left lower lobectomy may cause hemodynamic problems, most left-lower-lobe tumors should be resected at a separatsession. Limited resections should be used only with the appropriate indications. In all cases except emergent cardiac surgery, a fustaging evaluation of the lung tumor should be carried out before operation.Combined procedures have the advantage of a single operation and recovery as well as absence of delay in cancer treatment.However, concerns have been raised about the adverse oncologic effect of immunosuppression and the possibility of tumordissemination associated with cardiopulmonary bypass if the cardiac operation is performed before or concurrently with thepulmonary resection. This might be answered by comparing on-pump and off-pump procedures combined with lung resection.Schoenmakers and associates257 in 2007 made this comparison in 43 patients: 28 had lung resection followed by coronary arteryrevascularization on-pump and 14 had off-pump coronary artery bypass first followed by lung resection. No difference in survivalbetween groups was found. Subsequently however, in 2008, Dyszkiewicz et al.64 reported their experience with 25 patients havingoff-pump coronary bypass procedures and an associated resection for lesions ranging equally between IA and IIIA disease. Althoughthey report in the abstract that 68% survived during the observation period, the Kaplan–Meier curve tells a different story. Themedian survival was 30 months, with zero probability to survive as long as 5 years. All of their patients died of recurrent disease.

- ***Synchronous Lung Cancer:***

- second primary lung cancer in patients previously treated for NSCLC ➔ **10%.**

- ***Multiple sites adenocarcinoma > multiple sites of SCC in airways.***

- Both synchronous lesions OR metastases ➔ challenges.

- synchronous lesions primaries: 1. ***histology must be differen***t or***, if similar, the neoplasms must have an origin from carcinoma in situ or be loin different pulmonary segments and have no carcinoma in the lymphatic vessels and nodes common to both lesions and noextrapulmonary metastasis.***
- the criteria for tumors of similar histology, regarding the separate primaries if two or more of the following five conditions were met: (a) anatomically distinct, (b) presence of associat premalignant lesions, (c) absence of systemic metastasis, (d) no mediastinal disease, and (e) different DNA ploidy.

- primary lung and metastatic disease→
- three IHC markers:
- ***thyroid transcription factor-1 (TTF-1)***
- ***cytokeratin 7 (CK7)***
- ***cytokeratin 20 (CK20)***

- TTf-1 → lung primaries 73% of the time.
- CK7 → adeno of pulmonary and breast >> (GI)
- CK20 → more prevalent in GI adenocarcinoma

- ***Incomplete resection of NSCLC:***

- ***1. macroscopic disease left behind***
- 2. ***microscopic positive margins***
- ***3. involvement of the highest resected mediastinal lymph node***
- ***4. presence of remaining intrapulmonary or distant metastasis***

- Grossly incomplete resection ➔ not result in long-term survival.

- With current staging methods, grossly complete resection should be achieved in 99% or more of operated patients.

- ***Except*** under very unusual circumstances (infection,bleeding, pain that cannot be palliated by other means) ➔ ***intentional incomplete resection should not be considered***.

- ***patients who undergo incomplete resection may have a poorer quality of remaining life than those treated by multimodalities or by supportive care.***

- ***Residual tumor at the bronchial resection margin also has prognostic value.***

- three categories : (a) gross disease, (b) microscopic tumor in the peribronchial tissue (c) microscopic residual cancer at the mucosal or submucosal margin.

- first two findings portend a poor prognosis, late survival without adjuvant therapy occurred in about one-fourth of patients in the third group.
- importance of lymphatic invasion as a negative factor regardless of the bronchial or extrabronchial location of positivity.
- Because of these findings, ***intraoperative frozen section assessment of the airway margin should be employed frequen***tly

- When an involved margin is detected only on final pathologic review (especially when lymphatic invasion and lymph node disease are absent), reoperation to achieve more proximal airway resection should be consider

- external radiation therapy has not been shown to prolong survival in the overall spectrum of incompletely resected NSCLC, adjuvant radiation therapy should be considered because local control may be enhanced
- The role of brachytherapy is also unclear.
- Complete resection requires all of the following: free resection margins proved microscopically; systematic nodal dissection or lobe-specific systematic nodal dissection; no extracapsular nodal extension of the tumor; and the highest mediastinal node removed must be negative. Whenever there is involvement of resection margins, extracapsular nodal extension, residual positive lymph nodes, or positive pleural or pericardial effusions, the resection is defined as incomplete. When the resection margins are free and no residual tumor is left but the resection does not fulfill the criteria for complete resection, there is carcinoma in situ at the bronchial margin or positive pleural lavage cytol- ogy, the term uncertain resection is proposed.

- Results of Surgical TreatmentSurgical results are judged by the same standards as other modalities in terms of long-term survival and disease-free interval.Chemotherapy and radiation therapy take place over relatively prolonged time periods with symptoms and toxicities developing ohours to days and resolving over days to weeks. In contradistinction, surgical results begin at the operating room door and can bedefined in the number of minutes in the operating room. The consequences of operation are immediate and are dependent on theacute stress response to the operation, immediate and intermediate perioperative complications, postoperative length of stay, daand weeks of recovery and rehabilitation, and short- and long-term incisional pain syndromes. The acute risk is dependent mainly patient-specific factors, such as age, gender, race, comorbidities and prior (neoadjuvant) therapy. Tumor-related factors areimportant insofar as they dictate the extent of resection.Long-term survival is determined by multiple factors. At present, the most valuable predictors are the tumor stage and
P.1400the tumor node metastasis (TNM) subsets within each stage. As emphasized, the ability to accomplish a complete resection is also

- paramount and largely depends on the tumor stage. In assessing surgical results, the concept of clinical stage versus pathomust be clearly appreciated (see Chapter 109). The clinical stage is based on a synthesis of all invasive and noninvasive stuof resection. The pathologic stage is determined from the resected tissue and may or may not coincide with the clinical stSurgical decisions are made based on the clinical stage, but most surgical reporting is based on the pathologic stage. In 20colleagues79 authored for the College of American Pathologists an update on their reporting checklist, which includes cell tumor dimensions; tumor grade; invasion into visceral pleura, large veins, lymphatics; surgical margins; number of positivetotal number by station; and other tumors. In the age of routine CT and PET scanning, fewer cases have disparate clinical pathologic staging. In a study on the additive value of mediastinoscopy to CT and PET, Meyers and associates176 noted thatpatients had an upstaging by mediastinoscopy. More importantly, in patients with stage IA lung cancer, the total differenceclinical staging and postresection pathologic staging was 5.6%. Lee and colleagues148 in 2007 noted that central tumors >2 high potential for radiologically occult N2 metastasis. They also noted that if the primary tumor had an SUV >4, 10% had raoccult metastasis. However, most were discovered with mediastinoscopy. Thus there should be very close correlation betwPET, and mediastinoscopy preresection clinical staging and final postresection pathologic staging.The vast literature on the surgical treatment of NSCLC is confusing. A few general principles for assessing individual reportfacilitate comparison. Of obvious importance is the time period encompassed, not only because of variations in imaging bubecause of evolution of surgical techniques and philosophy and clinical staging methods. Of utmost importance is recognitisubset of patients on which the conclusions are based (whether the entire group, all operated patients, or only those who complete resection). Many authors use the diminishing denominator to present more optimistic results. Perspective may beby noting the actual number of long-term survivors with respect to the initial number of cases, in addition to the actuarial of survival. Although the latter is a valid figure for statistical reporting, the methodology is such that a numerically small scohort may yield a surprisingly favorable actuarial probability of survival.Another variable requiring attention is the use of preoperative and postoperative adjuvant treatments that, in many surgicare not factored into the conclusions. Similarly, it is very rare for surgical reports to include all patients who present with stage, especially when advanced, but rather only those selected for operation. Before sweeping conclusions can be drawn,must view the presented experience in the overall spectrum of lung cancer.This discussion focuses on surgical results based on TNM staging and simple anatomic factors. Late results are presented asactuarial survival unless otherwise specified. Although the current staging system by Mountain182 will be replaced in the fuseventh edition, the material is presented according to the currently used system. Table 110-3 presents survival by stage asubsets from the reports of Mountain,182 van Rens and colleagues,289 Naruke and associates,190 and Asamura et al.14 Thesseries were selected as representative because of their large numbers of patients, their span of nearly three decades and continents, and their presentation of the material in a similar format.Many other valuable reports are noted in the text and tables of this chapter. Reports that are unclear or present the maternonstandard fashion, without a cogent alternative point, are not included. For now, the recommendations for changing thesystem are under consideration. Because the recommendations radically change some stages and make it impossible to cogroups, no attempt is made to include the proposed changes in a discussion of results by stage.

- Incidentally Discovered Non-Small-Cell Lung CancerAlthough incidental NSCLC does not constitute a specific stage, many of the least advanced tumors are detected in this manner, the results of resection in this group are excellent. These tumors may present in two ways. The tumor may not be apparent onradiographic studies and present with symptoms such as persistent cough or hemoptysis. Alternatively, the lesion may be discoveon radiographic screening studies.Most radiographically occult cancers are squamous cell lesions, and many involve the large airways. Saito and colleagues249 repor94 patients with occult squamous lung cancer who were treated by resection. Although all were clinical stage I, pathologic staginshowed 16 TisN0 (stage 0), 72 T1N0 (stage IA), and 6 stage IIA and B (4 T1N1 and 2 T2N1). The 5-year actuarial survival rate overawas 80%. Watanabe and coworkers303 treated 20 patients with occult central cancers, mainly by bronchoplastic resections, and na 10-year survival of 92%. Among 98 cases of centrally located occult cancers reported by Koike and associates,137 most underwelobectomy or bilobectomy, pathologic stages included 5 TxN0, 19TisN0, 63 T1N0, and 11 T2N0, and the late survival rate was 81%overall and 89% for in situ lesions. Sagawa and colleagues248 performed segmentectomy for suitable, more peripheralradiographically occult cancers in 58 patients. The 5-year survival rate in this series was 83% overall. Most reports, however, notedisturbing incidence of synchronous and metachronous multiple aerodigestive squamous cancers in this patient population. Saito associates249 noted an incidence of 9.6% synchronous and 7.4% metachronous lesions.Screening of large populations of at-risk patients has generated a new conundrum. Many lesions discovered at screening are smallperipheral ground-glass lesions that turn out to be noninvasive bronchioloalveolar cancers. A number of these patients have morethan two similar lesions in disparate parts of the lungs. Raz and associates222 noted in 2007 that 36% of their patients over 5 yearhad incidental cancers detected on screening. These lesions were mostly noninvasive bronchioloalveolar cancers. The patients hacurative resections, but the study was not powered to determine whether there was a difference in survival compared with patiewho had symptomatic tumors. Earlier, in 2005, Ashton and Jett13 made the observation that “Although there are promising data the sensitivity of these newer screening methods, especially low-dose CT, for detecting early lung cancer, none of the publishedtrials are controlled, and they have not yet proven a decrease in mortality.” They issued a strong caution that any patient desirinscreening should be part of a controlled trial to attempt to answer the role of screening and early ablation or resection of low-gramalignancies.

- Stage I: Localized Node-Negative Non-Small-Cell Lung CancerTumors of relatively small size that are contained within a single lobe without lymph node metastasis defines the stage of noncell cancer that should have the best prognosis. When the cancer is <3 cm, it fits the definition of a T1N0M0 stage IA tumor. Fsurgical standpoint, simple lobectomy with lymph node sampling or lymphadenectomy is the operation that produces an R0 reIt is akin to removing a diseased bush from a hedge. It completely removes the disease along with the roots, so as to prevent ispread to other bushes within the hedge. Lesions >3 cm but that otherwise fit the definition above are classified as T2 tumorsLesions of this size often extend out of the zone of one lobe. Other descriptors have been added to this T stage—such as viscerpleural involvement, location in a main bronchus >2 cm from the carina, or causing bronchial obstruction—simply because tumthis size often have these characteristics. Theoretically, they have a greater chance for local spread and for metastasis. SurgiT2 tumors may require more than a single lobectomy to obtain a complete resection. These lesions are classified as T2N0M0 stcancers. Yet complete resection should lead to a good long-term result. The 1997 staging system recognized these facts and

- Influence of Size on SurvivalEven in cases of limited stage I node-negative NSCLC, additional factors may influence survival, including tumor size, cell type, ancentral versus peripheral location. Among these variables, the size of the primary lesion most consistently has been found toinfluence prognosis. Read and associates224,225 noted significantly better survival for T1N0 tumors =2 cm than for T1 lesions betw2 and 3 cm. Similarly, Ishida and coworkers117 found a more favorable prognosis for tumors <1 cm compared with those 2 to 3 cmno difference between T1N0 cancers =1 cm and tumors 1.1 to 2 cm. Padilla and colleagues199 reported markedly better late survifor smaller-diameter pT1N0 tumors (87% at 5 years and 74% at 10 years for =2 cm versus 65% at 5 years and 49% at 10 years forcancers 2.1–3 cm). In the P.1402provocative report of the IASLC group studying T stage for possible revision, Rami-Porta et al. 219 noted that there was a breakpoisurvival using log-rank analysis between T1N0 tumors <2 cm and tumors 2 to 3 cm in size (Fig. 110-3). They also found a break in tT2 tumors 3 to 5 cm and 5 to 7 cm in size independent of other qualifiers for T2, such as bronchial obstruction and visceral pleurainvolvement. The 5-year survival among the 7,116 node-negative T1 and T2 patients divided into these groups was 77%, 71%, 58%,49%, respectively.

- Influence of Location on SurvivalThe location of the primary lesion may influence the results of resection. Peripheral T1N0 tumors have a better prognosis thacentral lesions. Although Read and colleagues226 found that nonsquamous T1N0 patients fared worse overall after resection tsquamous cases, the difference was largely confined to central cancers. When the tumor did not communicate with a segmesubsegmental bronchus, the effect of cell type was negated. The presence of airway communication for both cell types confsignificantly poorer outlook, dramatically so for nonsquamous histology (Fig. 110-4). Likewise, the influence of peripheral vecentral location negated the effect of tumor size in the experience reported by Sagawa and colleagues247. Assessing only NSCarising in or peripheral to a subsegmental bronchus, they recorded similar 5-year survival rates for smaller or larger T1N0 lesfor tumors 2 to 3 cm in diameter and 83% for smaller cancers). The favorable influence of parenchymal location is also emphthe report of Kodama and associates,136 who achieved a 5-year survival rate of 93% in 77 patients with peripheral pT1N0 NSCtreated by lobectomy and 88% in 46 cases following intentional lesser resection.

Influence of Cell Type on Survival

- Certain less common cell types negatively influence postresection prognosis. Although variously subclassified, large-cellneuroendocrine carcinoma (LCNEC) and similar types of NSCLC are associated with a worse prognosis than other histologies, as notedby Iyoda120 and Takei275 and their colleagues. In the former series, the 5-year survival rate was 67% for resected stage I cases versus88% for stage I NSCLC of other histologies. Garcia-Yuste and coworkers81 noted 5-year survival in only 33% of resected stage I LCNECpatients. Hiroshima and associates105 found a lowered survival rate in resected stage I adenocarcinoma patients when 10% or more othe cells showed neuroendocrine differentiation. The LCSG, however, as reported by Linnoila and associates,151 did not find asignificant influence of such differentiation. Also, Zacharias and colleagues320 noted a survival comparable with that involving othercell types (88%) in stage I LCNEC. Similarly, some authors, such as Riquet and colleagues234 and Ruffini and associates,242 report thatadenosquamous cancers are associated with a poorer prognosis than other types of NSCLC following resection of stage I cases,whereas other series, such as those of Ishida119 and Hsia108 and their associates, found no difference. The surgical prognosis forpatients with node-negative mixed small-cell and non-small-cell lesions is considerably worse than for pure NSCLC. Hage andcolleagues96 reported 5-year survival rates of 50% and 26% for mixed tumors of pathologic stage IA and IB, respectively, many ofwhich were also treated with preoperative or postoperative chemotherapy.In addition to cell type, other routinely reported histologic features of NSCLC likely correlate broadly with postresection prognosis instage I cases. Increasing degrees of vascular invasion and perineural involvement appear to portend a less favorable prognosis. Highelevels of cellular differentiation or grade, lymphocytic response, and scar formation have been found to be associated with longersurvival following operation. As for basic histology, however, none of these factors appear to be determinative in low-stage cancers,and they are not currently used to determine stage or therapy. Brundage and associates26 reviewed this issue.For the majority histologies of squamous cell and adenocarcinoma, there has been difficulty comparing older reports to present serieowing to an evolution in the histologic appearance and behavior of the spectrum of adenocarcinomas. Some older series note adifference in late survival based on cell type, with T1N0 squamous histology usually conferring an improved prognosis overadenocarcinomas, large-cell lesions, and mixed cancers of comparable extent. Gail and associates, 78 reporting for the LCSG, showedsignificantly lower recurrence and death rates per patient per year for squamous versus nonsquamous or mixed histologies, notingthat at 3 years, 90% of resected patients with T1N0 squamous cancer were free of recurrence, as opposed to only 62% of those withnonsquamous histology. Similarly, Read and colleagues224 concluded that 5-year postresection survival is more often realized forT1N0 squamous tumors than for comparable adenocarcinomas. Macchiarini155 and Kodama136 and their associates, in contrast, didnot detect a significant difference in outcome for T1N0 disease based on the subsets of non-small-cell histology. Many otherseries—including those reported by Shields,261 Ichinose, 110 Harpole,99,100 and Fang73 and their associates—have also not establisheda statistically significant difference in survival based on squamous versus nonsquamous histology, although absolute long-term survivis often slightly higher in squamous cases. Occasional reports, such as that of Rena and colleagues, 228 note better survival for stage Iadenocarcinomas than for squamous cancers.Part of the evolution of adenocarcinomas is the rise in unifocal bronchioloalveolar cell carcinoma (BAC), which generally
  P.1404has a favorable prognosis. Although the 2004 World Health Organization definition of BAC, as published by Travis et al., 284 has beennarrowed to include only noninvasive lesions composed entirely of BAC, thoracic surgeons have long noted that patients with early-stage pure BAC, mixed BAC and adenocarcinoma, or adenocarcinoma with BAC features fare well with resection. Higashiyama andcolleagues104 classified 206 resected peripheral adenocarcinomas <2 cm into four groups based on the extent of any BAC componentand found a correlation between increased percentage of BAC and survival, with a 100% 5-year survival rate in stage I pure BACpatients. Carretta and coworkers33 also found a favorable effect of increasing BAC histology in mixed lesions, with 5-year survival

- Stage IBIn the databases of Mountain183 as well as those of van Rens289 and Naruke 190 and their colleagues, postresection survival forpathologic T2N0 lung cancer is 57%, 46%, and 60%, respectively. Survival rates fall to 38% and 42% in the latter two reports for clinicastage IB NSCLC. It is striking that the most optimistic upper limit of late survival for stage IB disease in the series listed in Table 110-generally falls below the lower figures for stage IA lesions.Specific variables within stage IB that influence prognosis have not been assessed as extensively as have those for IA disease becausethe subsets are new and most reports have focused on T1N0 cases. It seems reasonable to assume that the basic factors noted earliefor T1N0 NSCLC generally apply in higher stages and substages but that their influence diminishes with advancing tumor extent.Larger tumor diameter and nonsquamous histology may correlate with a poorer prognosis, but the data are sparse. Harpole andcolleagues99 found that larger tumors were associated with a more limited survival than smaller ones, but the groupings were 2 to 4cm versus tumors larger than 4 cm; hence some cases were likely stage IA. Carbone and associates32 noted a statistically significantdifference in 5-year survival rates for resected T2N0 cancers between 3 and 5 cm versus those >5 cm: 62% and 51%, respectively.These authors suggested that NSCLC tumors >5 cm be upgraded to T3. This is in line with the analysis published by Rami-Porta andassociates219 for the IASLC staging reanalysis project. Even this project has skirted the issue of factors other than size.Involvement of a main bronchus further than 2 cm from the carina or a lesion causing lobar atelectasis, both defining features ofsome T2 primaries, are not clearly negative prognostic indicators. In fact, central T2 cancers limited to the bronchial wall (oftenoccult), as noted by Naruke 189 and Watanabe 301 and their colleagues, have an excellent postresection survival. In contrast, directinvasion of the visceral pleura (another defining feature of some T2 lesions) clearly correlates with a poorer prognosis thancomparable T2 cancers without pleural involvement, as noted early by Brewer25 and also by Merlier and colleagues.175 Harpole andcolleagues99 found that visceral pleural invasion
P.1405was a significant predictor of poor outcome, with 5-year survival rates of 44% for invasive lesions versus 67% for those without pleuratransgression and respective 10-year survival rates of 62% and 37%. Ichinose and colleagues110 reported similar findings. Manac'h andassociates161 noted 5-year postresection survival in 61% of stage I patients without pleural involvement versus 46% of those withpleural invasion. The LCSG, reported by Gail and associates,78 noted a 1.66-fold increase in recurrence rates in stage I patients whethe visceral pleura was involved by cancer.

- Stage II: Non-Small-Cell Lung Cancer with N1 Adenopathy or Resectable LocalInvasionThe 1997 system divides stage II lung cancer into two subsets. Stage IIA is limited to T1N1M0 lesions, whereas IIB includes both positive (T2N1M0) and node-negative (T3N0M0) cases. Stage IIA and T3N0 stage IIB include small numbers of patients. Stage IIArepresents a very small proportion of patients based on clinical staging. Pathologic T1N1 is more common but remains a small gThe 5-year survival rate for patients with cT1N1 cancer is only 34% in the databases of both Naruke and associates190 and ofMountain 182; for pT1N1 cases, the rates are 53% and 55%, respectively. Survival for pT1N1 patients in the series of van Rens anassociates289 is 52%. The Ludwig Lung Cancer Study Group152 reported their results as median survival time (4.8 years for resecT1N1 patients, significantly longer than the median of 2.3 years for T2N1). As noted in Table 110-5, about a half or more of patoperated on for pT1N1 NSCLC do not survive 5 years.As in stage I, variables that may affect prognosis include tumor size, histology, and location. In addition, in stage II and higher,node metastases come into play in most cases. The impact of any single nonnodal factor is less clear than in stage I. Holmes,10reporting the LCSG experience, confirmed a significant difference favoring squamous T1N1 cancers at 5 years (75% versus 52% fnonsquamous histology). In a mixed group of T1–2N1 cases, Ichinose and colleagues111 also found better results with squamous cancers. In contrast, Martini167 and Yano315 and their coworkers did not find a significant histologic variance, although squamotumors had an 8% to 10% numerical survival advantage over other cell types. The data with respect to tumor size are also limiteconflicting, and not focused by stage II subset. Within stage II, however, Martini and associates167 found that tumors <3 cm hadhigher survival rate than those >5 cm, but other series have not found an impact of size. The influence of central versus periphtumor location has not been studied sufficiently to allow meaningful conclusions.

- T3N0 TumorsStage IIB also includes node-negative tumors that invade potentially resectable structures (T3N0M0). Naruke and colleagues190reported a 22% 5-year survival for clinical T3N0 and 32% for pathologic T3N0. The corresponding rates calculated by Mountain182 w22% and 38%, and van Rens and associates289 noted a survival rate of 33% for resected pT3N0 NSCLC. By far the largest surgicalexperience involves tumors invading the parietal pleura or chest wall. It must be stressed that a high proportion of patients in mansurgical reports were treated with preoperative or postoperative radiation therapy or both. With the exception of the Intergroupstudy of superior sulcus tumors, a statistically significant effect of this adjuvant approach has not generally been demonstrated. Din T3 categories other than chest wall invasion are limited. Detterbeck and Socinski 58 have provided a valuable comprehensive revof this subject.The results of resection for chest wall T3 cancers are summarized in Table 110-6. The major correlates of long-term survival are nonegativity and complete resection. When both criteria are met, late survival is realized in 29% to 56% of surgical cases, averaging42%. Efficacy of resection is markedly limited when malignant lymphadenopathy accompanies chest wall invasion or stage IIIA. Theexperience of Downey and colleagues62 for complete resection is typical. They noted a 5-year survival rate of 49% for completelyresected T3N0. Complete resection yielded an overall survival rate of 32%, versus only 4% for either grossly or microscopicallyincomplete resections (Fig. 110-7).The extent of invasion is divided pathologically into parietal pleural involvement versus extension into muscle and bone. This is oftdifficult to determine at the time of operation. While some tumors may dissect easily off of the chest wall by extrapleural dissectiincomplete resection leads to a markedly reduced survival rate. In patients with T3N0 disease, McCaughan and associates173 achiea 5-year survival rate of 62% for parietal pleural T3 as opposed to 35% for muscle and bone invasion, but the difference was notstatistically significant. Likewise, Casillas,35 Elia, 68 and Akay3 and their colleagues noted no significant difference between patientreated by extrapleural dissection versus full-thickness chest wall resection. In contrast, Albertucci and associates7 stressed theimportance of en bloc chest wall resection for all peripheral tumors densely adherent to the chest wall. These authors found asignificant incidence of incomplete resection and lower survival (33% versus 50%) for extrapleural dissection. Facciolo andassociates72 also advocate en bloc chest wall resection and report a 67% late survival for T3N0 cases amenable to complete resectiDoddoli and associates61 reiterated this admonition. They found, in patients with parietal pleura involvement alone, that chest waresection resulted in a 63% 5-year survival, while extrapleural dissection resulted in only a 39% 5-year survival. NSCLC involving alimited area of the parietal pleura and only superficial invasion may be treated adequately by pulmonary resection combined with

- Superior Sulcus TumorsSuperior sulcus (including Pancoast) tumors have been the focus of much surgical attention and debate. Superior sulcus tumors arthose that occupy part or the entire apex of the chest, thus making the superior extent of resection inadequate due to limitation the neurovascular bundle to the upper extremity. Patients with classic Pancoast tumors have some or all of P.1408the symptoms of Horner's syndrome indicating invasion of the stellate ganglion and potentially the nerve root of T1. While superiosulcus tumors may be classified as a T3 lesion, all Pancoast tumors are, by nature, T4 tumors. Chapter 38 reviews the techniques results of resection of these challenging lesions. Vallieres and colleagues288 provided an extended review of superior sulcus tumors in 2001. Apical lung cancer invading the tinlet was considered unresectable and uniformly fatal until Shaw and associates258 demonstrated in 1961 that radiation folloradical resection could yield long-term survival. The extensive early experience of Paulson206 highlights the P.1409limitations of surgery, because only 60% of patients presenting with Pancoast tumors were deemed suitable for treatment paincluding resection. Of interest, Anderson and associates10 noted in 1986 that durable pain relief following resection indicatfavorable outlook. They observed a 73% 5-year survival rate among those with durable pain relief, in contrast to no long-tersurvivors among those with persistent discomfort. Sartori and associates252 made similar observations.

- T3 Tumors Invading Structures Other Than Chest WallData are limited regarding the results of resection in other types of T3 tumors. Mediastinal invasion limited to the pleura is classifieas T3 (Table 110-8). Data in this condition is difficult to dissect out of the literature because many patients had vital organinvolvement and/or mediastinal nodal disease. Martini and associates168 reviewed 102 surgical patients with mediastinal invasion.Excluding N2 disease, superior vena cava obstruction, superior sulcus cancers, and malignant pleural effusion and applying currentcriteria for T3 and T4, they studied 58 patients. Of these limited T3 lesions, complete resection was possible in only 38 cases (66%), and the 5-year survival rate was 36%. Pitz and colleagues212 noted a 25% postoperative 5-year survival rate in patients with T3cancers invading the mediastinum who had a complete resection. Riquet and coworkers235 reported 5-year survival in 35% ofmediastinal T3 NSCLC patients. Watanabe and associates295 reported 43% late survival in a small group of patients following coresection in the presence of limited pericardial invasion.Survival rates for main bronchial cancers classified as T3 because of tracheal carinal proximity vary widely (Table 110-9). Firmconclusions regarding the incidence and outcome of proximal bronchial T3 NSCLC are hampered by problems of definition, largbecause lesions at the right-upper-lobe origin may variably be classified as T2, T3, or T4 based on subjective assessment of theradiographic and bronchoscopic features and interpretation of the staging criteria. Pitz and associates212 reported a 40% survivfor proximal bronchial T3 lesions. Mitchell and colleagues179 at the Massachusetts General Hospital reported the largest series i2001, with 60 patients. In that experience, a 51% 5-year survival rate was achieved in 34 patients with T3N0 disease, with a 32survival for N1 and only 12% for N2 disease. By extrapolation from the considerable literature on bronchoplastic and carinal res(see Chapters 29, 30 and 31), however, it appears that complete resection of node-negative main bronchial T3 cancers yieldsreasonable late survival. N1 and N2 disease is a strong negative factor.

- Despite the fact that the hemidiaphragms abut a large surface of lung parenchyma and that direct invasion in this area is potenresectable, there is a paucity of reported surgical experience (Table 110-10). Weksler and associates308 found only eight cases ireview spanning two decades at Memorial-Sloan Kettering. All four patients with N2 disease died of their lung cancers, with a msurvival of only 92 weeks. Only a single N0 patient was alive at 70 weeks at the time of the report. The diaphragmatic lesions aldiffered from the usual current spectrum of peripheral T3 NSCLC in that seven were squamous cancers and one had adenosquamhistology. Inoue and associates115 reported no 3-year survival in five operated patients with diaphragmatic invasion, despite coresection and N0–1 status. For unclear reasons, more recent reports suggest an improved outcome. Rocco and associates236 andRiquet and colleagues233 achieved long-term survival in completely resected T3N0 cases of 39% and 27%, respectively. Yokoi ancoworkers317 performed combined lung and diaphragmatic resections in 26 cases of T3N0 and 29 cases of T3N1–2 lung cancer.Complete resection of N0 and of N1–2 cases yielded 5-year survival rates of 28% and 18%, respectively. In all these series, there no late survival following incomplete resection.In contrast to lower-stage lesions, tumor size and histology are less predictive for T3 cancers. In general, invasive squamous canmore favorable than adenocarcinoma. Although most reports indicate no statistically significant difference, Mountain 181 found trend in favor of squamous cell histology, and Ratto and associates221 reported that patients with squamous cell cancer invadinchest wall fared better with both complete and incomplete resection than did those with adenocarcinoma. In T3 disease with emediastinal invasion or carinal proximity, Pitz and coworkers212 also achieved better results in squamous cell cases. The experi

- tage IIIA: Non-Small-Cell Lung Cancer with Mediastinal Lymph Node Involvement T1–3N2) or T3N1 Disease he T3N1 subset of stage IIIA represents a minority of cases. The results of resection for chest wall T3N1 cancers along with thef the T3 tumors are summarized in Table 110-5. When malignant lymphadenopathy accompanies chest wall invasion, the efficesection is markedly limited. Five-year survival rates in the presence of N1 metastasis range from 8% to 35%, with an average ith lymphadenopathy and incomplete resection, operation alone is associated with minimal late survival. Downey and colleag oted a 5-year survival rate of 27% for completely resected T3N1 compared to 49% for T3N0 and 15% for T3N2 but close to zeroncomplete resection. 2 disease comprises the bulk of stage IIIA. Investigations, deliberations and debate concerning the best therapy for this stage umbled for the last three decades. The next three decades will produce a variety of studies on the molecular staging of tumor hich may change our staging system entirely. But during the recent past, changes in attitude and approach to N2 identificatio anagement were marked by major milestones in diagnosis including the ubiquitous availability of noninvasive tools such as CT ET and the wide acceptance of the invasive procedure of mediastinoscopy. The near future will further our pretherapy diagnoccuracy through the less invasive procedures of esophageal ultrasound and endobronchial ultrasound. he seminal study of the past era was that of Pearson and associates, 207 who found that resection in mediastinoscopy-positive long with adjuvant radiation in most instances, was associated with a 5-year survival rate of only 9%. In contrast, survival in ediastinoscopy-negative, pathologically positive cases (cN0–1, pN2) was almost threefold higher at 24%. The operated cN2 patepresented only one fifth of all such cases evaluated during the study and were deemed to have surgically favorable N2. onetheless, only 64% had a complete resection. It is noteworthy that complete resection in this setting increased the 5-year sate to only 15%. There were no late survivors in the 36% who had incomplete resections. These authors also noted that there wurvival with surgery alone in five prior reports of mediastinoscopy-positive patients. On analysis, no subsequent series has neghese conclusions. Table 110-11 lists a number of comparable studies including those of Pearson and colleagues.207 For the moshe authors identified groups that had a complete resection. They show the patients that they operated on with unsuspected N isease and those with known preresection N2 disease. The overall survival average was 29.2% for unsuspected N2 and 14.4% fonown N2 disease. ecause of our growing diagnostic accuracy, we should encounter only very rare cases of pathologic N2 positivity where surgicaesection was the first modality. Virtually all patients with localized lung cancer, regardless of T size, should undergo invasive ediastinal staging by ultrasound and/or mediastinoscopy to obtain tissue for pathologic confirmation. Therapy should be plaround pathologic, not clinical stage. Even in stage I cancers, studies by Asamura14 and associates demonstrated surprise N2 din a significant number of patients with tumors <2 cm. FDG-PET negativity in T1 disease also is no substitute for invasive media valuation. In 2006, Kim and colleagues130 found combined CT–PET scanning in T1 tumors to provide a high specificity and posit redictive value of mediastinal nodal staging, although the sensitivity was only 87%. With time, the accuracy of staging is improllowing the patients with N2 lymph nodes to be siphoned away for multimodality trials. Reports in the literature where surgicaesection is the intentional first modality will be rare and dated. Multimodality therapy treatment and results for this stage areovered in detail in Chapter 117.

- Stage IIIB: Non-Small-Cell Lung Cancer with Unresectable Local Invasion or N3LymphadenopathyCurrently, stage IIIB includes all T4 lesions regardless of N stage and all N3 with any T stage. One of the factors complicating sconsideration of stage IIIB is that it represents a very inhomogeneous group. In the 1997 staging system, already a diverse cohopatients with more than one parenchymal site of cancer within a single lobe have been added to T4. Although these cases overhave survival following clinical staging similar to that of T4 and N3 patients, the place of operation in this setting is presently nall as clear as in other stage IIIB cases.Proposals made by Goldstraw and colleagues89 for the IASLC for the next staging revisions include changes in the T4 designatioThese are related to downstaging cancers with satellite nodules in the same lobe from T4 to T3 and synchronous lesions in theipsilateral lung but a different lobe from M1 to T4. In addition, pleural effusions, now considered to be T4 are proposed to beupstaged to M1a. These subsets will be discussed in this section, since there is little data currently and the staging schema haschanged yet.Although stage IIIB is defined as unresectable disease, an exceptional T4 case may be suitable for operation. In the overwhelmmajority, however, primary operation is of no oncologic value, and operative mortality is high. Any benefit with respect to loccontrol is offset by the discovery of distant metastasis proximate to the time of resection. In the series of Mountain,182 the 5-ysurvival rate was 6% for clinical T4 and 3% for N3 disease. In the database of Naruke and associates, 190 the late survival rate wfor all operated stage IIIB patients and 3% for N3 patients. The surgical series of van Rens and colleagues289 does not include Nbeyond stage IIIA. The role of multimodality therapy in stage IIIB NSCLC is discussed in Chapter 117. There is a degree of subjein defining some cases of T4 versus T3 mediastinal invasion and carinal involvement.T4 Secondary to Proximity to Main CarinaThe largest surgical experience with T4 NSCLC encompasses tumors involving the carina (see Chapter 31). In properly selected treated at centers with experience, late survival can be realized in up to 40%, as reported by Watanabe,300 Deslauriers,57 Roviand Mitchell 179 and their colleagues. However, operative mortality may remain high. Porhanov and colleagues215 reported anoperative mortality rate of 16% among 231 carinal resections.T4 by Direct Extension Into Vital StructuresSimply put, T4 lesions invade structures without which the body cannot survive. Under certain circumstances, resection is possEach type of lesion has its own problems and survival rate. These lesions include those involving the superior vena cava, heart the atria), pulmonary artery, aorta, esophagus, and vertebral body.Superior Vena Cava.Tangential resection and primary closure or patching of the superior vena cava (SVC), as well as circumferential resection requgraft reconstruction, has been reported by Dartevelle, 49 Nakahara,186 and Tsuchiya285 and their colleagues. Late survival, howis limited to a few cases (one reported by Inoue and associates114 and 2 of 30 cases in the series of Tsuchiya and associates285)the experience of Burt and associates,29 there was no late survival among 18 cases of NSCLC invading the SVC and treated bypulmonary resection, brachytherapy, or both. The rarity of lung cancers suitable for caval resection is underscored by the repoDartevelle and colleagues.48,49 In their earlier paper, 5 of 13 SVC resections (31%) were performed for lung cancer. In the subs4 years encompassed in the updated series, only two cases of NSCLC were added. All six patients had malignant adenopathy, a

- received adjuvant radiation. Neither of the two cases with N2 disease survived beyond 8 months, whereas two of four N1 patientsdied at 1 month and 38 months, and two were alive at 16 and 52 months. A higher late survival rate of 25% was noted in the eightpatients reported by Bernard and coworkers.19 Spaggiari and colleagues266 presented their experience with 28 patients whounderwent SVC resection and graft replacement for lung cancer. The overall 5-year survival rate was 15%. Misthos and colleagues18reported in 2007 that only one out of nine patients survived 5 years, while they achieved a 30.7% 5-year survival among 16 patientsundergoing aortic tangential resection during the same period.Aorta.Operation for tumors invading the aorta has been performed in even fewer instances. Klepetko and associates134 reported five casof combined left lung and aortic resection; three patients with N2 disease died between 17 and 27 months, and two with pathologiT4N1 disease were alive at 14 and 50 months. Nakahara,186 Horita,107 and Tsuchiya, 285 along with their colleagues, also reportedaortic resection for T4 lung cancer, but the long-term results of this aggressive approach, usually requiring cardiopulmonary bypasare not specified. In the report of Burt and colleagues, 29 there were no late survivors among 19 patients with aortic involvement.Similarly, there were no 3-year survivors in the eight cases of Bernard and colleagues. 19 Misthos and colleagues180 achieved a 30.75-year survival. Endografting has now been reported by Marulli and coworkers170 as an adjunct to resection, thus avoiding the neefor cross-clamping or bypass.Heart.Cardiac resection is difficult to evaluate because resection of the intrapericardial veins and a portion of atrium or the intrapericarportion of the pulmonary artery is not infrequent for central tumors. Little to no data exist for this subset of patients. Only casereports exist of resection of other parts of the heart.Hasegawa and associates102 reviewed the use of cardiopulmonary bypass in 2003 finding the results to be dismal. They applied it fvariety of vascular resections. Of the eleven patients in their series one patient died in the hospital due to MRSA (multiply resistanStaphylococcus aureus) mediastinitis and local recurrence. Eight patients died due to recurrence with a median postoperative survless than a year. Two patients developed recurrent disease 37 and 41 months postsurgery. One patient who had no evidence ofrecurrence died of aspiration pneumonia 10 months after surgery.

- Pulmonary Artery.T4 cancers involving the pulmonary artery trunk are rarely resected. There were no late survivors among seven patients whounderwent main pulmonary trunk resection in a series by Tsuchiya and colleagues.285 In contrast, Rendina, 227 Shrager,262 andBernard19 and their associates have clearly demonstrated that tangential or circumferential resection of the right or left proxipulmonary artery is beneficial in appropriate cases. Overall late survival rates in these reports were 38%, 48%, and 20%, respecThe lower figure in the last instance is likely due to the inclusion of only patients with intrapericardial pulmonary artery invasiEsophagus.Combined resection of lung cancer and esophagus is rare. Results have been poor. However, occasional cases of resection ofaerodigestive fistulas have been reported. In general today, stenting would be used to accomplish palliation. This is reviewed Chapters 113 and 144.

- Vertebral Body.Although technically feasible in a few instances, as discussed earlier, the utility of total vertebrectomy is unknown. Grunenwacolleagues95 reported 19 cases of total vertebrectomy or hemivertebrectomy; their 2- and 5-year survival rates were 53% and respectively.T4 with Nodal DiseaseIn general, only patients with T4 tumors who, after rigorous imaging and invasive assessment, appear to be node-negative andand safely resectable should be considered for operation. Such patients are few in number. The extensive disappointing experT3N1–2 disease is compounded in the far lesser experience with T4 primaries associated with nodal metastasis. Bernard andcoworkers19 reported a mixed cohort of resected T4 cases that they grouped into low-, intermediate-, and high-risk categorieon survival. Patients with N0–1, upper lobe or main bronchial T4 cancers had a 3-year survival rate of 36% and were deemedfavorable. In the intermediate and high-risk groups, defined by various permutations of N disease and tumor location, 3-year srates were 4% and 0%, respectively.Stamatis and associates267 in 1999 reported limited success for T4 with nodal involvement using an aggressive inductionchemoradiation protocol. Patients received induction cisplatin and etoposide followed by combined chemotherapy and 45 Gy tumor and mediastinum and 30-Gy prophylactic cranial radiation. They do not state the number of patients who began this strtherapy, but they had 10 patients with T4N0-1 and 14 patients with T4N2 who had operation. The median and 5-year survival T4N0-1 was 26.5 months and 37.5%; for T4N2, it was 20 months and 33%.

- T4 by Malignant Pleural EffusionTumors associated with a pleural effusion containing malignant cells or diffuse pleural carcinomatosis, are not resectable. AlthougOhta and associates193 reported a 5-year survival rate of 13% following lung resection and parietal pleurectomy, the number ofsurvivors is very small, and adjuvant
  P.1416chemotherapy achieved borderline statistical significance in this experience. The authors recommend against pleuropneumonectopreferring partial lung resection and pleurectomy. Yokoi and colleagues,318 in contrast, performed pleuropneumonectomy, includicomplete diaphragm resection on 11 patients. Although the actuarial 5-year survival rate was 54%, the five cases of T4N2 NSCLCremained disease-free for only 4 to 14 months, and one of the two T4N1 patients was disease-free for only 6 months. Becauseeffective palliation of effusive symptoms can be achieved by a variety of minimally invasive means (see Chapter 68), local control not a valid argument for operation in cases of malignant effusion.However, if the effusion is not malignant, but is caused by atelectasis secondary to an obstructing cancer or other etiology, the utof operation is dependent on other clinical staging factors. Earlier, Decker52 noted that resectable cases in this setting were few inumber (only 5% of operated patients with cytologically negative effusions had limited disease and were late survivors). Ruffini anassociates238 presented a series of small pleural effusions discovered intraoperatively. Cytology was positive in 53% of 45 cases, annegative in 47%. The median survival in the setting of a cytologically malignant effusion was only 6 to 9 months, whereas the negacytology group had 3- and 5-year survival rates of 68% and 56%, respectively. Benign effusions associated with pulmonary malignanremain confusing despite the clear statement in the current (and future) staging schema. It is worth quoting the staging manual

- Most pleural (and pericardial) effusions with lung cancer are due to tumor. In a few patients, however,multiple cytopathologic examinations of pleural (pericardial) fluid are negative for tumor, and the fluid isnon-bloody and is not an exudate. Where these elements and clinical judgment dictate that the effusion is notrelated to the tumor, the effusion should be excluded as a staging element and the patient should beclassified as T1, T2, T3, or T4.

- N3 Disease esection of N3 disease has been carried out through sternotomy, bilateral thoracotomy, or cervical dissection combined with horacotomy and in a few instances has achieved complete removal of all known neoplasm. However, this approach has not been hown to result in long-term survival. A Southwest Oncology Group trial (8805) included a few patients with N3 disease. This studwas not powered to evaluate N3 disease, and the data does not break out this group for independent analysis. Albain and associa eported in 1995 that following induction chemoradiotherapy, three year survival was poor. Sakao and associates250 looked at th

- age IV: Non-Small-Cell Lung Cancer with Distant Metastases tastasis of non-small-cell lung cancer does not discriminate. It occurs in virtually any organ. Surgeons become involved whenCLC metastasizes to the brain, bone, liver, and adrenal glands. For nearly all instances, there is no long-term benefit for a surgproach to the primary site in the presence of other areas of nonpulmonary M1 disease. Although the 5-year survival rate for surtients with M1 disease in the series of Naruke and associates190 was 5% overall, they included multiple parenchymal cancers. In untain's database,182 the cumulative survival for patients with M1 disease was 1%.rain Metastasisveral series have shown apparent improved survival of about 10% to 20% with removal of a synchronous or metachronous solitarain metastasis (SBM) and pulmonary resection for otherwise limited NSCLC. As many as one-third of patients with brain metasta presentation have a solitary lesion, but most also have extracerebral distant foci or advanced locoregional disease. Althoughsection of the cranial lesion may offer optimal neurologic palliation, pulmonary resection should be undertaken only in cases th uld have been suitable for curative primary resection in the absence of M1 disease and only after a thorough evaluation to dether sites of metastatic disease. e first large experience was reported by Magilligan and colleagues, 160 who found a 5-year survival rate of 21% and a 10-yearrvival rate of 15% in 41 synchronous and metachronous cases of SBM. In a series of synchronous and metachronous cases, Read asociates225 reported a 21% 5-year survival rate following complete resection of both the SBM and the primary site in 27 cases asmpared with a median survival rate of only 6.4 months in patients who underwent noncurative resection of either or both sites.rt and associates30 reported 185 consecutive patients who underwent craniotomy for NSCLC (65 synchronous and 120etachronous). Strikingly, in this series reported by a very aggressive surgical group, 37% of the 65 synchronous cases were notnsidered for pulmonary resection and among the 41 thoracotomies, incomplete or no resection occurred in 22%. The overall latrvival rate was 13% at 5 years and 7% at 10 years. Granone and associates93 reported a 17% 3-year survival rate in 30 cases ofnchronous and metachronous brain M1. In a series of 28 patients with synchronous metastasis, Billing and colleagues21 noted a ar survival rate of 21%, whereas Bonnette and colleagues22 reported a lower figure of 11% in 103 cases. Solitary metachronousain lesions seem to have a better long-term benefit from resection. Although Mussi and colleagues184 note only a 6.6% 5-yearrvival rate for combined resection in synchronous SBM, their reported survival for metachronous lesions was 19%.vorable factors in the setting of synchronous SBM include N0 disease, lower T factor, and adenocarcinoma. Favorable factors intting of metachronous SBM include N0 status, lobectomy, and disease free interval. In the case of Mussi and colleagues,184 the erval between lung and brain operation was =14.5 months. a randomized trial, Patchell and associates204 found that the addition of adjunct whole-brain radiation therapy (WBRT) followimplete resection of SBM significantly decreased brain recurrences and death from neurologic causes. Experience has been gainth precision techniques such as the gamma knife with success in inaccessible lesions such as brainstem as reported by Kased anlleagues128 in 2008. Fuentes and associates74 tried to review the world experience in 2006 but found the terminology and thefinition of solitary to be so poor across studies that no conclusion could be made. This
P.1417 nd in reporting has continued as recently as 2008 in a report by Yang and colleagues. 314

- Adrenal MetastasisThe importance of documenting the nature of a solitary adrenal mass in patients with otherwise resectable lung cancer has beennoted. Experience with resection of both synchronous and metachronous adrenal metastases from NSCLC is limited. Luketich andBurt153 reported on 14 patients with synchronous NSCLC and solitary adrenal metastases, all treated initially with cisplatin-basedchemotherapy. Eight patients ultimately underwent resection and had a median survival of 31 months, as compared with 8 month or those treated with chemotherapy alone. Porte and colleagues216 identified 11 cases of solitary adrenal metastases in 598consecutive patients with otherwise operable or resected NSCLC at their institution. Among eight patients with synchronous disea reated by resection, the median survival time was only 10 months, although one patient remained cancer free at 66 months. Of t hree cases of metachronous lesions, two died at 6 and 14 months, and one was alive at 6 months. Porte and colleagues217 later eported 43 patients from eight centers. The median survival time was about 16 months for both synchronous and metachronousdisease; 2-, 3-, and 4-year survival rates were 29%, 14%, and 11%, respectively. Tanvetyanon et al. 277 in 2008 reviewed 10publications contributing 114 patients. They noted that 42% of patients had synchronous metastases and 58% had metachronousmetastases. The median disease-free interval for metachronous adrenal metastases was 12 months. Complications fromadrenalectomy were infrequent. Although the median survival was shorter for patients with synchronous metastasis than those witmetachronous metastasis (12 months versus 31 months), the 5-year survival estimates were equivalent, around 25%. These reports uggest that a small subset of patients who qualify for adrenal resection may demonstrate late survival after resection.