

**Society of Surgical Oncology
Annotated Bibliography**

**Thoracic Non-Small Cell Lung Cancer
2nd Edition
June, 2001**

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General Review

1. Silvestri GA, et al: Specialists Achieve Better Outcomes than Generalists for Lung Cancer Surgery. Chest 1998; 114: 675-680.

The first study in Thoracic Surgery studying the Impact of Additional Training and Specialization on the Results of Lung Cancer Surgery.

2. Bach PB, et al: The Influence of Hospital Volume on Survival after Resection for Lung Cancer. N Engl J Med 2001; 345: 181-8.

Retrospective review from the SEER database. Not only is the perioperative morbidity and mortality lower in the high volume hospitals but the long-term survival of the lung cancer patients is also improved.

3. Ginsberg RJ, et al.: (The Lung Cancer Study Group): Modern Thirty-Day Operative Mortality for Surgical Resections in Lung Cancer. J Thorac Cardiovasc Surg 1983;86: 654-658.

Multi-institutional prospective data collected by the LCSG over a period of 12 years (2200 resections) reflecting modern day surgical mortality rates in the treatment of lung cancer.

4. Harpole DH Jr, et al.: (The National VA Surgical Quality Improvement Project): Prognostic models of 30-day morbidity and mortality after major pulmonary resections, J Thorac Cardiovasc Surg 1999; 117: 969-79.

This is the largest prospective dataset of major pulmonary resections, including a detailed risk-adjustment model from the National VA QI program.

Screening

5. Henschke CI, et al.: Early Lung Cancer Action Project: Overall Design and Findings from Baseline Screening. Lancet 1999; 354: 99-10.

Initial report from the North American ELCAP, which corroborates the Japanese suggestions of a potential role for LD Spiral CT in screening for Lung Cancer in populations at risk.

6. Patz EF Jr, Goodman PC, Bepler G.: Screening for Lung Cancer N Eng J Med 2000; 343:1627-33.

Superb, up-to-date, review on the topic.

Staging and Prognostic Factors

7. Mountain CF: Revisions in the international system for staging lung cancer. Chest 1997; 111: 1710-1717.
8. Mountain CF, Dresler CM: Regional Lymph Node Classification for Lung Cancer Staging. Chest 1997; 111: 1718-23.

Revisions of the 1986 Staging System and of the AJCC Nodal Map describing NSCLC staging as it remains.

9. Dales RE, Stark RM, Raman S.: Computed Tomography to Stage Lung Cancer-Approaching a Controversy Using Meta-Analysis. Am Rev Respir Dis 1990; 141: 1096-1101.

A metaanalytic review of the data addressing the accuracy, sensitivity and specificity of CT as a mediastinal staging tool.

10. Luke WP, et al: Prospective Evaluation of Mediastinoscopy for Assessment of Carcinoma of the Lung. J Thorac Cardiovasc Surg 1986; 91: 53-56.

One of the largest series addressing the role of routine mediastinoscopy in the evaluation of lung cancers.

11. Pieterman RM, et al.: Preoperative Staging of Non-Small-Cell Lung Cancer with Positron Emission Tomography. N Eng J Med 2000; 343(17): 254-61.

12. Dwamena BA, et al.: Metastases from Non-Small-Cell Lung Cancer: Mediastinal Staging in the 1990s-- Meta- analytic Comparison of PET and CT. Radiology 1999; 213(2): 530-536.

Part of the most recent and up to-date published documentation on the value of FDG PET in staging potentially resectable NSCLC (meta-analysis).

Surgical Treatment of Stages 1A-1B-1IA-1IB- 1IIA (T3N1)

13. Ginsberg RJ, Rubenstein L and the Lung Cancer Study Group (LCSG 821): Randomized Trial of Lobectomy Versus Limited Resection for T1N0 Non Small Cell Lung Cancer, Ann Thor Surg 1995; 60: 615-623.

A Phase III prospective randomized cooperative group trial comparing lobectomy to segmentectomy and wedge resections in the management of T1N0 tumors. (Prospective) Updated data in Ann Thorac Surg 1996; 62:1249-50).

14. Martini N, et al: Management of NSCLC with Direct Mediastinal Involvement. Ann Thorac Surg 1994; 58: 1447-51.

One of the rare series addressing T3 mediastinal disease as a separate group from other T3 tumors. (Retrospective data).

15. Downey RJ, et al: Extent of Chest Wall Invasion and Survival in Patients with Lung Cancer, Ann Thorac Surg 1999; 68: 188-93.

The largest series on the topic. Survival depends on the completeness of resection and on the nodal status. (Retrospective data)

16. Keller SM, et al.: (ECOG): Mediastinal lymph node dissection improves survival in patients with stages II and IIIA non-small cell lung cancer. Ann Thorac Surg 2000; 70(2): 358-65.

Concluded in a survival benefit for radical nodal dissection over systematic sampling for right sided tumors only... Non randomized data pulled out of the ECOG 3590 trial which was comparing adjuvant radiotherapy alone to adjuvant chemoradiotherapy after complete resection of stages II and IIIA NSCLC. (See reference below).

The only published randomized study to date addressing the therapeutic role of radical nodal dissection concluded differently. (Izbicki JR, et al. Effectiveness of radical systematic mediastinal lymphadenectomy in patients with resectable non-small cell lung cancer: results of a prospective randomized trial. Ann Surg 1998; 227(1): 138-44). Such results emphasize the importance of the ACOSOG Z30 trial, which is designed to help answer this question. (See below)

Surgical Treatment of Stage IIIA (N2)

17. Pearson FG, et al.: Significance of positive superior mediastinal nodes identified at mediastinoscopy in patients with resectable cancer of the lung. J Thorac Cardiovasc Surg 1982; 83:1-11.

A classic from The Toronto Thoracic Group demonstrating the value of routine mediastinoscopy in identifying a subset of N2 patients who are unlikely to benefit from resection alone. (Retrospective data, pre-induction chemotherapy era).

18. Martini N, Flehinger BJ, Zaman MB, and Beattie EJ: Results of Resection in Non-Oat Cell Carcinoma of the Lung with Mediastinal Lymph Node Metastases. *Ann Surg* 1983; 198(3): 386-397.

The experience of The Memorial Sloan Kettering Cancer Center when mediastinoscopy was not done routinely. When carefully dissected, this paper actually describes the same subset of N2 patients as in the Toronto paper who may benefit from upfront surgery, however many more patients required “open & close” thoracotomies. (Retrospective data, pre-induction chemotherapy era)

Adjuvant Therapy for Resectable NSCLC

19. Weisenburger TH, Gail M, and The LCSG: Effects of postoperative mediastinal radiation on completely resected stage II and stage III epidermoid cancer of the lung. (LCSG 771) *N Eng J Med* 315: 1377-81, 1986.

A cooperative group phase III randomized trial showing that adjuvant radiotherapy, despite reducing the incidence of loco-regional recurrences after complete resection of squamous cell cancers, has no effect whatsoever on the survival of the patients. (Prospective)

20. Stevens, RJ, et al. The MRC Lung Cancer Working Party: The role of postoperative radiotherapy in non-small cell lung cancer: A multi center randomized trial in patients with pathologically staged T1-2, N1-2, M-0 disease. *British Journal of Cancer* 74: 632-639, 1996.

Twenty years after the LCSG 771 study, the question is revisited: open to all NSCLC histologies, still no survival benefit...(prospective)

21. Stewart LA, and the PORT Metaanalysis Trialists Group: Postoperative radiotherapy in NSCLC: Systematic review and metaanalysis of individual patient data from nine randomized controlled trials. *Lancet* 352: 257-63, 1998.

A meta-analytic review of the question, which suggests a detrimental effect of adjuvant radiotherapy after the complete resection of stage, I and II NSCLC. No detriment or survival advantage in stage III. (Meta-analysis)

22. Feld R, et al.: (LCSG 801): Adjuvant chemotherapy with cyclophosphamide, doxorubicin, and cisplatin in patients with completely resected stage I NSCLC. *J Natl Cancer Inst* 1993; 85:299.

One of the many negative phase III randomized LCSG studies evaluating adjuvant CAP chemotherapy. (Prospective)

23. Niiranen A, et al: Adjuvant chemotherapy after radical surgery for NSCLC: A randomized study. J Clin Oncol 1992; 10: 1927-1932.

The only positive phase III randomized adjuvant CAP chemotherapy trial. Restricted to N0 patients, only 50 patients in each arm...(Prospective)

24. Stewart LA, Pignon JP, and the NSCLC Collaborative Group: Chemotherapy in non-small cell lung cancer: a meta-analysis using updated data on individual patients from 52 randomized clinical trials. Brit Med Jour 1995; 311:899.

A meta-analytic analysis of the potential role of adjuvant chemotherapy in NSCLC suggesting a non-statistically significant 13% reduction of the risk of death and a possible 5% absolute benefit in survival at 5 years with the use of a adjuvant platinum based chemotherapy. (p 0.08) (Meta-analysis)

25. Wada H, et al.: Adjuvant chemotherapy after complete resection in non-small cell lung cancer. J Clin Oncol 1996; 14:1048.

A positive 3 arm randomized study showing a significant improvement in 5-year survival for patients receiving adjuvant oral UFT chemotherapy for 1 year after surgery. (Prospective)

26. Richardson GE, et al.: Smoking Cessation after Successful Treatment of Small- Cell Lung Cancer is Associated with Fewer Smoking-related Second Primary Cancers. Ann Intern Med 1993; 119: 383-390.

Small Cell related but clearly demonstrating the benefits of smoking discontinuance after the successful treatment of a first lung cancer.

27. Keller SM, et al.: (SWOG 3590) A Randomized Trial of Postoperative Adjuvant Therapy in Patients with Completely Resected Stage II or IIIA NSCLC. N Eng J Med 2000; 343 (17): 1217-22.

The latest North American randomized Phase III intergroup trial failing to show an advantage of adjuvant combined cisplatin/ etoposide given concurrently with radiotherapy versus adjuvant radiotherapy alone. (Randomized, prospective)

Induction Therapy for resectable NSCLC

28. Rosell R, et al.: A randomized trial comparing preoperative chemotherapy plus surgery with surgery alone in patients with NSCLC. N Eng J Med 1994; 330: 153-8.

29. Roth JA, et al: Randomized trial comparing perioperative chemotherapy and surgery and surgery alone in resectable stage IIIA NSCLC. J Natl Cancer Inst 1994; 86: 673-680.

Both the Rosell and the Roth series are the first randomized phase III trials to have shown a significant advantage of induction chemotherapy over that of surgery alone in the management of “higher” stage, potentially resectable NSCLC. Small numbers but statistically significant.

Addendum: Both have updated their early follow-up since.

30. Rosell R, et al.: Pre-resectional Chemotherapy in Stage IIIA NSCLC: a 7 year assessment of a Randomized Controlled Trial. Lung Cancer 1997; 47:7-14.
31. Roth JA, et al.: Long-Term Follow-up of Patients Enrolled in a Randomized Trial Comparing Perioperative Chemotherapy and Surgery with Surgery Alone in Resectable Stage IIIA NSCLC Lung Cancer 1998; 21: 1-6.
32. Pisters KMW, Ginsberg RJ, Giroux DJ, et al: Induction Chemotherapy before Surgery for Early-Stage Lung Cancer: a Novel Approach. J Thorac Cardiovasc Surg 2000; 119: 429-39.

The BLOT study, a phase II prospective multicentered study showing the feasibility and safety of induction carboplatin and paclitaxel chemotherapy followed by resection for early clinical stages NSCLC. This study has led to the ongoing phase III SWOG 9900 study. (See below)

Treatment of Stage IIIA and IIIB

33. Dillman RD, et al.: A Randomized Trial of Induction Chemotherapy plus High-Dose Radiation versus Radiation Alone in Stage III NSCLC. N Engl J Med 1990; 323: 940-5.

The first randomized trial showing an advantage of combining chemo and radiotherapy in treating stage III disease. Updated follow-up in 1996 Dillman RO, et al.: Improved Survival in Stage III NSCLC: Seven Year Follow-up of CALGB 8433 Trial. J Natl Cancer Inst 1996; 88: 1210-5.

34. Albain KS, et al: Concurrent cisplatin/etoposide plus chest radiotherapy followed by surgery for stages IIIA (N2) and IIIB NSCLC: Mature results of Southwest Oncology Group Phase II study 8805. Journal Clinical Oncology 13: 1880-1892, 1995.

The largest phase II multicentered trial evaluating the safety and feasibility of induction chemoradiotherapy and surgery in pathologically proven stages IIIA and IIIB diseases. This study has led to the ongoing Intergroup 0139 phase III trial. (See below)

35. Rusch VW, et al.: Induction Chemoradiotherapy and Surgical for NSCLC of the Superior Sulcus: Initial Results of Southwest Oncology Group Trial 9416 (Intergroup Trial 0160) J Thorac Cardiovasc Surg 2001; 121: 472-83.

The largest prospective series evaluating the safety and feasibility of combined modality therapy in the treatment of Pancoast Tumors. Early results, but considered by many the new standard of care for resectable Pancoast Tumors.

36. Furuse K, et al.: Phase III Study of Concurrent versus Sequential Thoracic Radiotherapy in Combination with Mitomycin, Vindesine, and Cisplatin in Unresectable Stage III NSCLC J Clin Oncol 1999; 17:2692-2699.

Phase III study suggesting the superiority of concurrent chemoradiotherapy over that of the sequential delivery in good performance status patients with stage III disease.

Treatment of Stage IV

37. Rapp E, et al.: Chemotherapy can Prolong Survival in Patients with Advanced NSCLC- Report of a Canadian Multicenter randomized Trial. J Clin Oncol 1988; 6: 633-41.

A phase III randomized study showing the survival and quality of life assessment superiorities of chemotherapy over that of supportive care alone in treating good performance status patients with stage IV disease.

38. Shepherd FA, et al.: Prospective randomized trial of docetaxel versus best supportive care in patients with non-small-cell lung cancer previously treated with platinum-based chemotherapy. J Clin Oncol. 2001 Apr 1; 19(7): 2108-9.

One of the growing numbers of experiences demonstrating benefits of second line chemotherapy in good performance status patients. (Randomized, prospective)

39. Wronski M, Arbit E, Burt M, Galicich JH.: Survival after surgical treatment of brain metastases from lung cancer: a follow-up study of 231 patients treated between 1976 and 1991. J Neurosurg 1995 Oct; 83(4): 605-16.

The largest series of patients who have had resection of brain metastases as part of a curative attempt for NSCLC.

MEDIASTINAL TUMORS

Thymoma

40. Venuta F, et al.: “*Multi-modality Treatment of Thymoma: A Prospective Study* “ Ann Thorac Surg 64: 1585-92, 1997.
41. Shin DM, et al.: A multidisciplinary approach to therapy for unresectable malignant thymoma. Ann Intern Med. 1998 Jul 15; 129(2): 100-4.

Interesting early experiences with the combined modality therapy of thymomas.

Germ Cell Tumors

42. Ganjoo KN, et al.: Results of modern therapy for patients with mediastinal nonseminomatous germ cell tumors. Cancer. 2000 Mar 1; 88(5): 1051-6.

The Indiana University 14 year experience with primary NS-GCT of the mediastinum.

Mesothelioma

43. Sugarbaker DJ, et al.: “Resection margins, extrapleural nodal status, and cell type determine postoperative long term survival in trimodality therapy of malignant pleural mesothelioma: Results in 183 patients. J Thorac Cardiovasc Surg 1999; 117: 54-65.

The largest reported series of extrapleural pneumonectomies and adjuvant chemo and radiotherapy for mesothelioma.

44. Rusch VW, et al.: A phase II trial of surgical resection and adjuvant high-dose hemithoracic radiation for malignant pleural mesothelioma. J Thorac Cardiovasc Surg. 2001 Oct; 122(4): 788-95.

The first report showing the feasibility of high-dose hemithoracic adjuvant therapy after extrapleural pneumonectomy for mesothelioma. Phase II but the best local control reported to date.

Recent Abstracts

1. Depierre A, Milleron B, Moro D, and the French Thoracic Cancer Group: Phase III trial of neo-adjuvant chemotherapy in resectable stage Ib, II, IIIa NSCLC: the French Experience. Proc Am Soc Clin Oncol 1999; 18: 465a. Abstract 1792.

The first randomized phase III trial addressing induction chemotherapy in early clinical NSCLC.

2. Ohmatsu H, Kakinuma R, Nishiwaki Y, et al.: Lung Cancer Screening with Low Dose Spiral CT. Proc Am Soc Clin Oncol 1999; Abstract 1787.

Data from the Japanese Anti-Lung Cancer Association that has triggered all the excitement about the possible screening role of Low dose Spiral CT in populations at risk.

3. Gandara DR, Lovato LC, Albain KS, et al.: Prolonged Survival in Pathological Stage IIIB NSCLC with Concurrent Chemoradiotherapy followed by Consolidation Docetaxel: A Phase II Study (SWOG 9504) Proc Am Soc Clin Oncol 2000; 19: 490a. Abstract 1916.

Historically, the best results for IIIB disease. Consolidation Docetaxel appears encouraging. Results updated at ASCO 2001 Gaspar L, et al. : Consolidation Docetaxel Following Concurrent Chemoradiotherapy in Pathologic Stage IIIB Non-Small Cell Lung Cancer (NSCLC) (SWOG 9504): Patterns of Failure and Updated Survival. Proc Am Soc Clin Oncol 2001; 20: abstract 1255

4. Sauvaget J, Rebischung J, Vannetzel J, and the GEARC: Study of Neo-Adjuvant MVP versus MVP plus chemo-radiotherapy in Stage III NSCLC. Proc Am Soc Clin Oncol 2000; 19: 495a. Abstract 1935.

Single institution phase III study comparing the strategy of induction chemotherapy alone versus that of induction chemotherapy and radiotherapy given sequentially.(n= 92) Despite higher response rates and resectability rates in the latter group, the patterns of failure were equivalent as were the 3 year survival rates and median survival for both IIIa and IIIb diseases.

5. Harubumi Kato, et al.: A Randomized Phase III Study Comparing Ubenimex (Bestatin) Versus Placebo as Postoperative Adjuvant Treatment in Patients with Stage I Squamous Cell Lung Cancer. Proc Am Soc Clin Oncol 2001; 20: abstract 1225.

A positive phase III trial of adjuvant immunomodulator therapy for 2 years after R0 resection of stages I NSCLC.

Ongoing Phase III Surgical Trials

SWOG 9900: Surgery with or without induction carboplatin/ paclitaxel chemotherapy for clinical Stage IB, IIA, IIB and T3N1 diseases. (Paul A. Bunn, Chair)

RTOG 9309 (INT 0139): Induction concurrent chemoradiation therapy (cddp/etoposide) with or without resection for IIIA N2 disease. (David S. Ettinger, Chair)

CALGB 9633: Adjuvant carboplatin/ paclitaxel or not after complete resection of IB disease. (Gary M. Strauss, Chair)

ACOSOG Z0030: Mediastinal lymph node sampling versus complete lymphadenectomy in patients with N0 and N1 (less than hilar) NSCLC. (Mark S. Allen, Chair)

ACOSOG Z0040: Prognostic significance of occult metastases with resectable NSCLC. (RG Cohen, Chair)

ACOSOG Z0050: The Utility of PET in Staging of Patients with Potentially Operable NSCLC. (CE Reed, Chair)

EORTC 08941: Surgery versus radiotherapy for IIIA N2 disease after induction cisplatin or carboplatin containing chemotherapy. (TAW Splinter, Chair)