



AUSL BA/4 – Ospedale “S. Paolo” – Bari
U.O. Complessa di Chirurgia Toracica



LA RADIOTERAPIA NEL TRATTAMENTO INTEGRATO DEL CANCRO DEL POLMONE NON MICROCITOMA

NSCLC I-II stadio

L'opinione del chirurgo



Francesco Carpagnano

Taranto, 20 gennaio 2006

Prognostic implications of stage grouping

Stage grouping combines subsets of patients classified according to TNM descriptors into stages, each having similar treatment options and survival expectations

Stage migration “Will Rogers phenomenon”

Mistakes in stage grouping

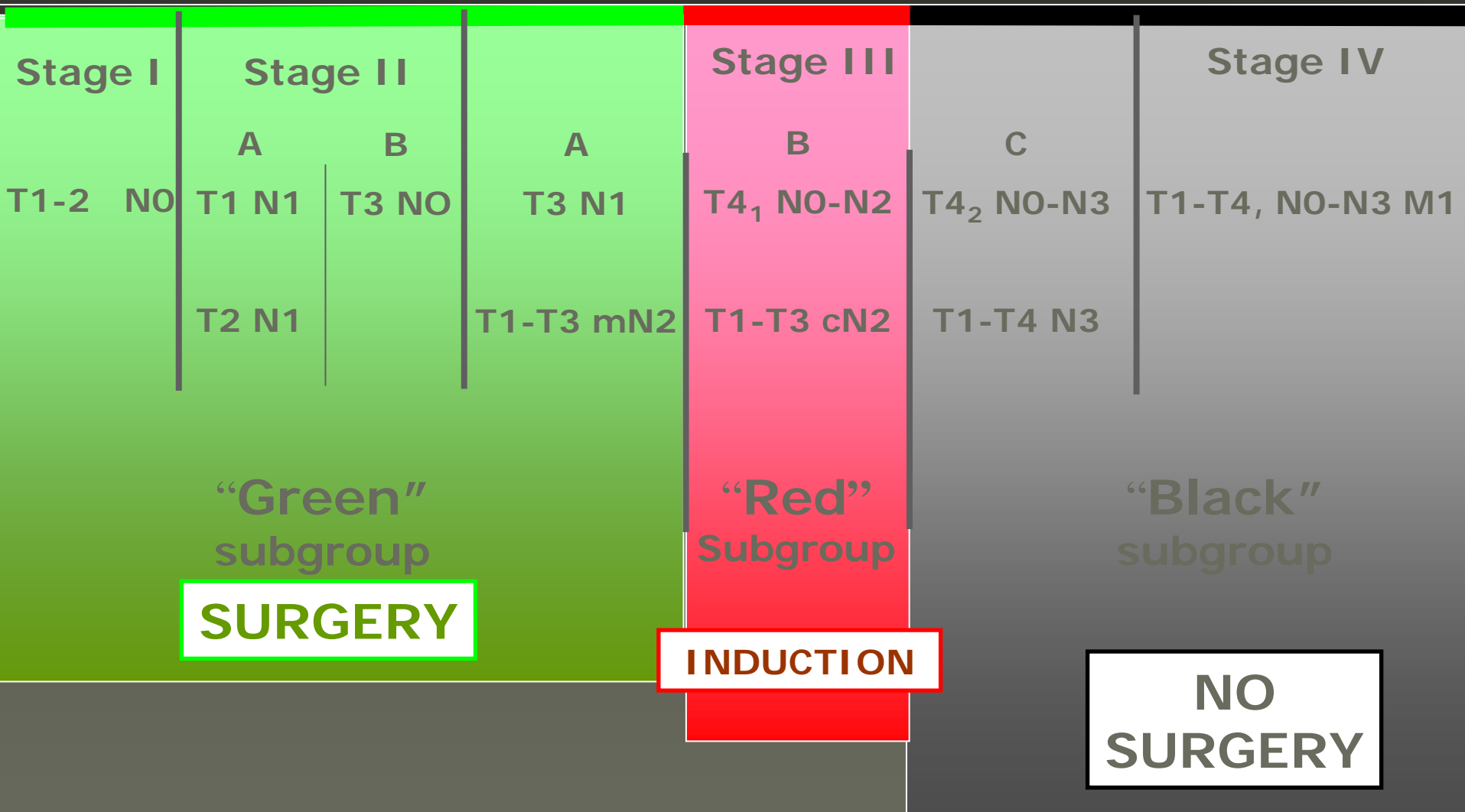
Mountain CF Revision in the International System for Staging for lung cancer. *Chest* 1997; 111:1710

Grunenwald' subgroups (green,red,black). *Seminars in Surgical Oncology* 2000; 18:137

TNM Stage Classification -1997-

TABLE 32-2 ■ The 5-Year Survival Rates in the Three Largest Series Reporting Stage-by-Stage Survival According to the 1997 Stage Classification*

	<i>Naruke</i>		<i>Mountain</i>		<i>Rami-Porta</i>	
	<i># Pts</i>	<i>% 5-Yr Survival</i>	<i># Pts</i>	<i>% 5-Yr Survival</i>	<i># Pts</i>	<i>% 5-Yr Survival</i>
STAGE I						
T1N0 (IA)	245	75	511	67	235	58
T2N0 (IB)	291	57	549	57	817	50
STAGE II						
T1N1 (IIA)	66	52	76	55	31	66
T2N1 (IIB)	153	38	288	39	290	42
T3N0 (IIB)	106	33	87	38		

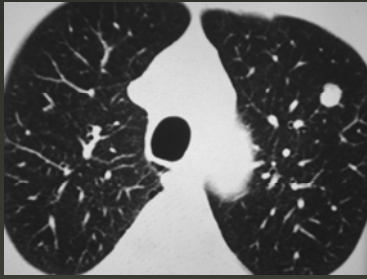


GREEN SUBGROUP

- T1-2 N0
- T1-2 N1
- T3 N0-1
- T1-3 mN2

SURGERY

Adjuvant Therapy ?



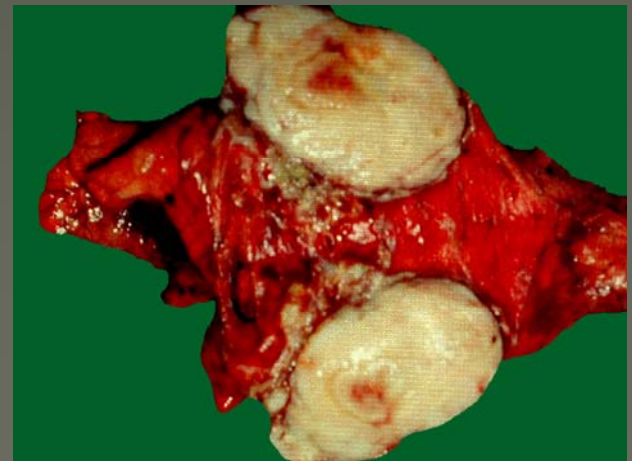
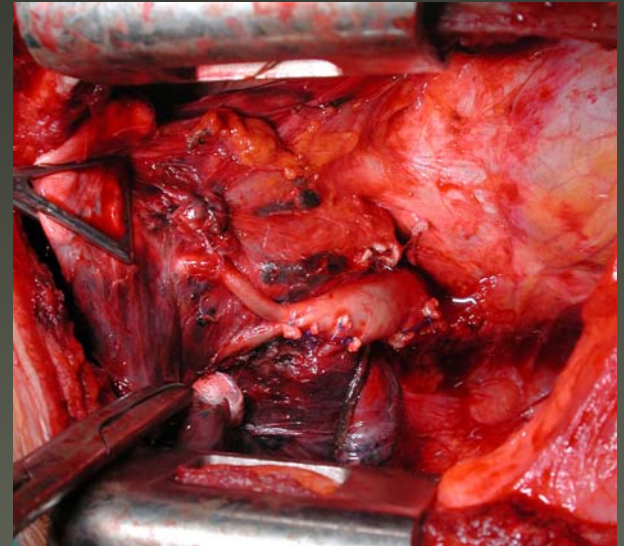
STAGE I DISEASE (T1N0-T2N0)

Surgical therapy is the recommended treatment of choice

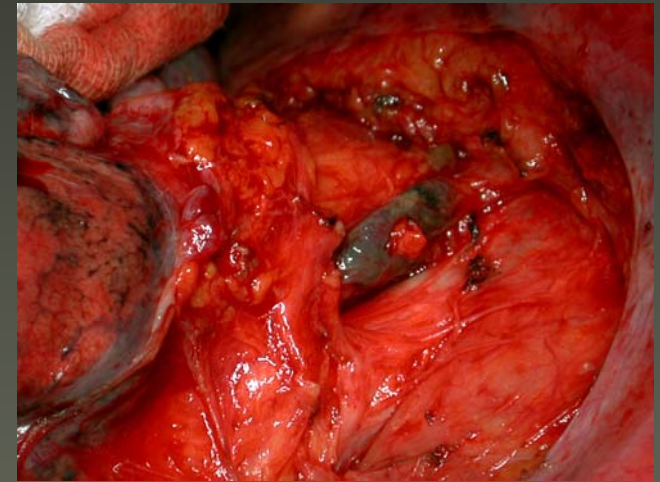
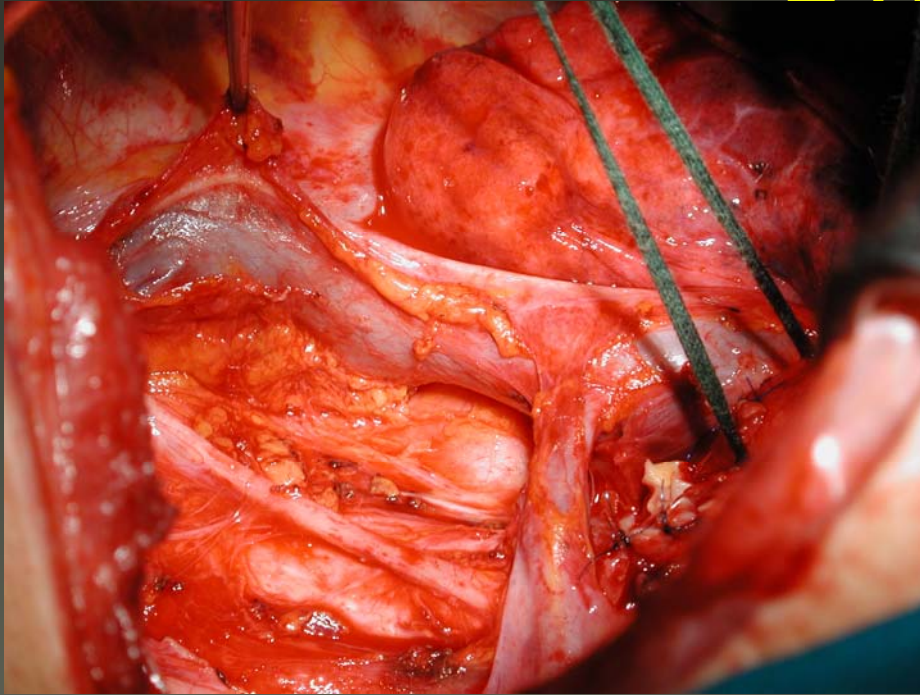
The LCSG completed a randomized clinical trial of lobectomy versus a lesser resection by wedge or segmentectomy in stage I carcinomas

This study suggests a 3-fold increased incidence of local recurrence in patients treated by lesser resection than lobectomy

Ginsberg ,1995

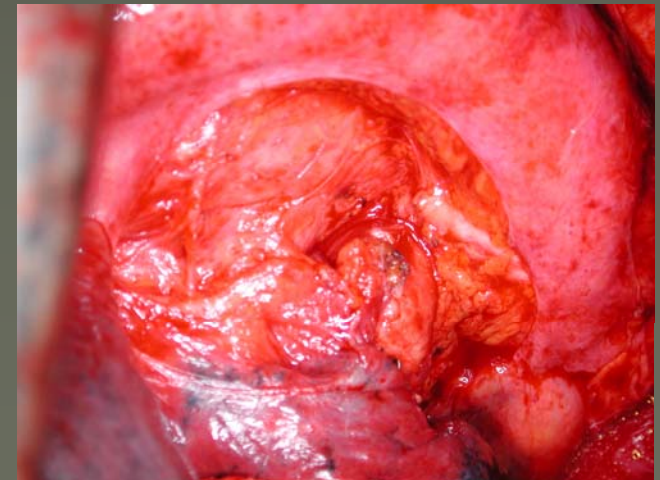


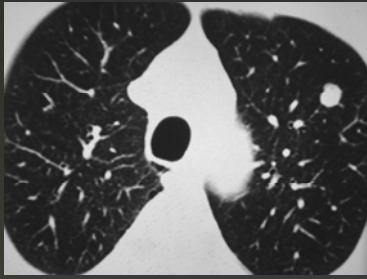
STAGE I DISEASE (T1N0-T2N0)



Systematic lymph node dissection or sampling is carried out to ensure that no hilar or mediastinal metastases is present

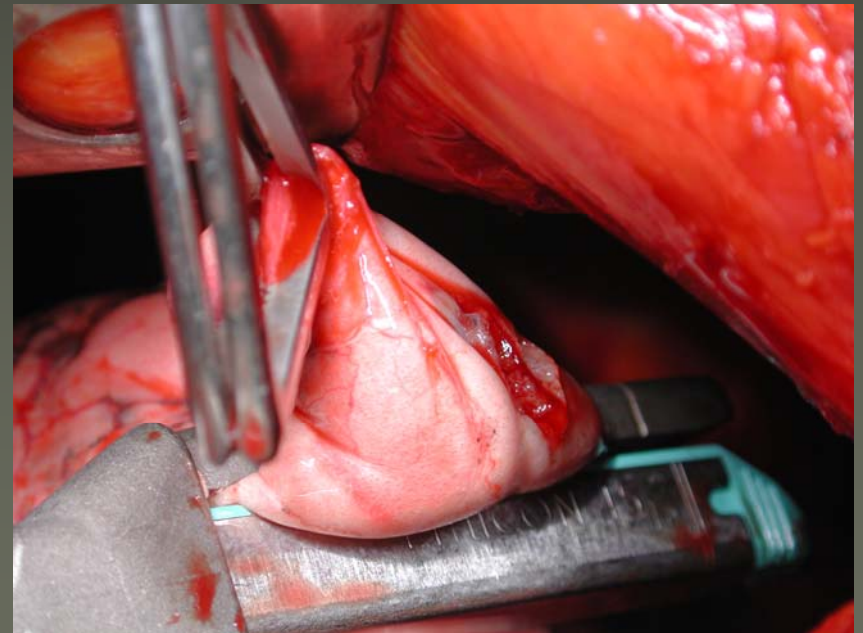
Mistakes in stage grouping



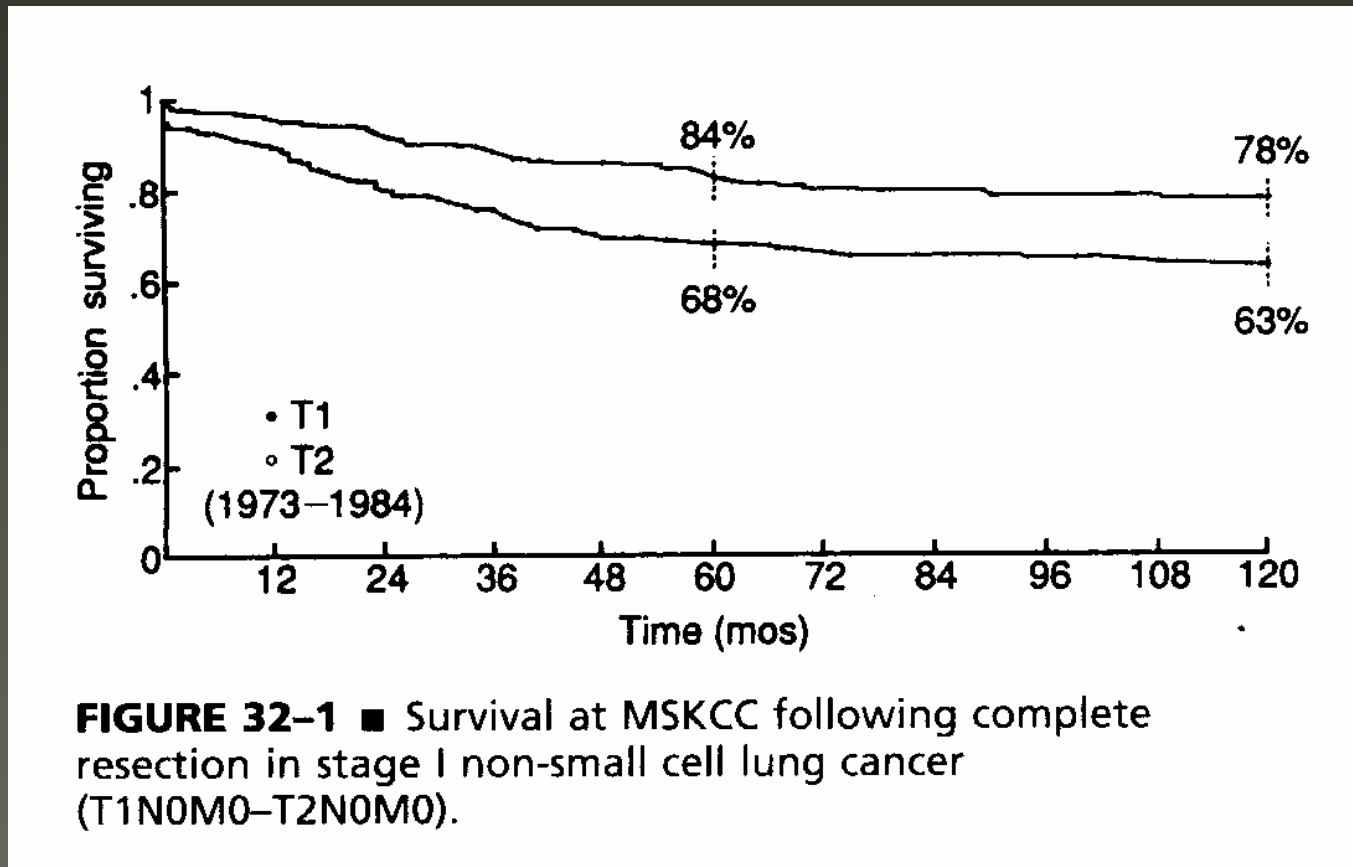


STAGE I DISEASE (T1N0-T2N0)

Limited resections in
patients with a limited
lung reserve



STAGE I DISEASE (T1N0-T2N0)



No adjuvant treatment is recommended for patients with stage I disease following resection, **although this continues to be investigated in clinical trials**

Patterns of recurrence at this stage of disease is a relapse at distant sites

STAGE II DISEASE (T1-2N1) i

Lobectomy is the procedure of choice in most patients

At this stage of disease, it is imperative a complete lymph node dissection because occult mediastinal metastases occur with increasing frequency

Role of sleeve lobectomy and vascular sleeve resection for N1 disease: the results appear identical to pneumonectomy

STAGE II DISEASE (T1-2N1) ii

The overall survival rate: 39% at 5 years

No difference in survival between T1 and T2 lesions

Histologic type: favored epidermoid over adenocarcinoma

The number of lymph nodes is significant

Local recurrence is higher in squamous cancer, distant metastases in adenocarcinoma

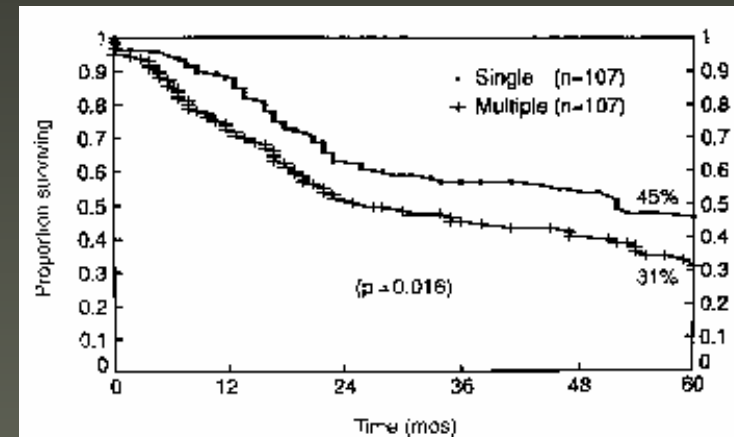


FIGURE 32-2 ■ Survival by number of N1 nodes involved following complete resection in stage II non small cell lung cancer (Martini et al, 1995).

Ginsberg RJ, 2002

STAGE IIB Disease T3N0

Tumors invading chest wall

T3N0 patients completely resected: 5-year survival rate
50%

Incomplete (macroscopic or microscopic
disease) resection: 5-year survival 0%

Postoperative radiation therapy does not have an impact
on survival

Tumors invading chest wall

T3N1

T1-3 mN2

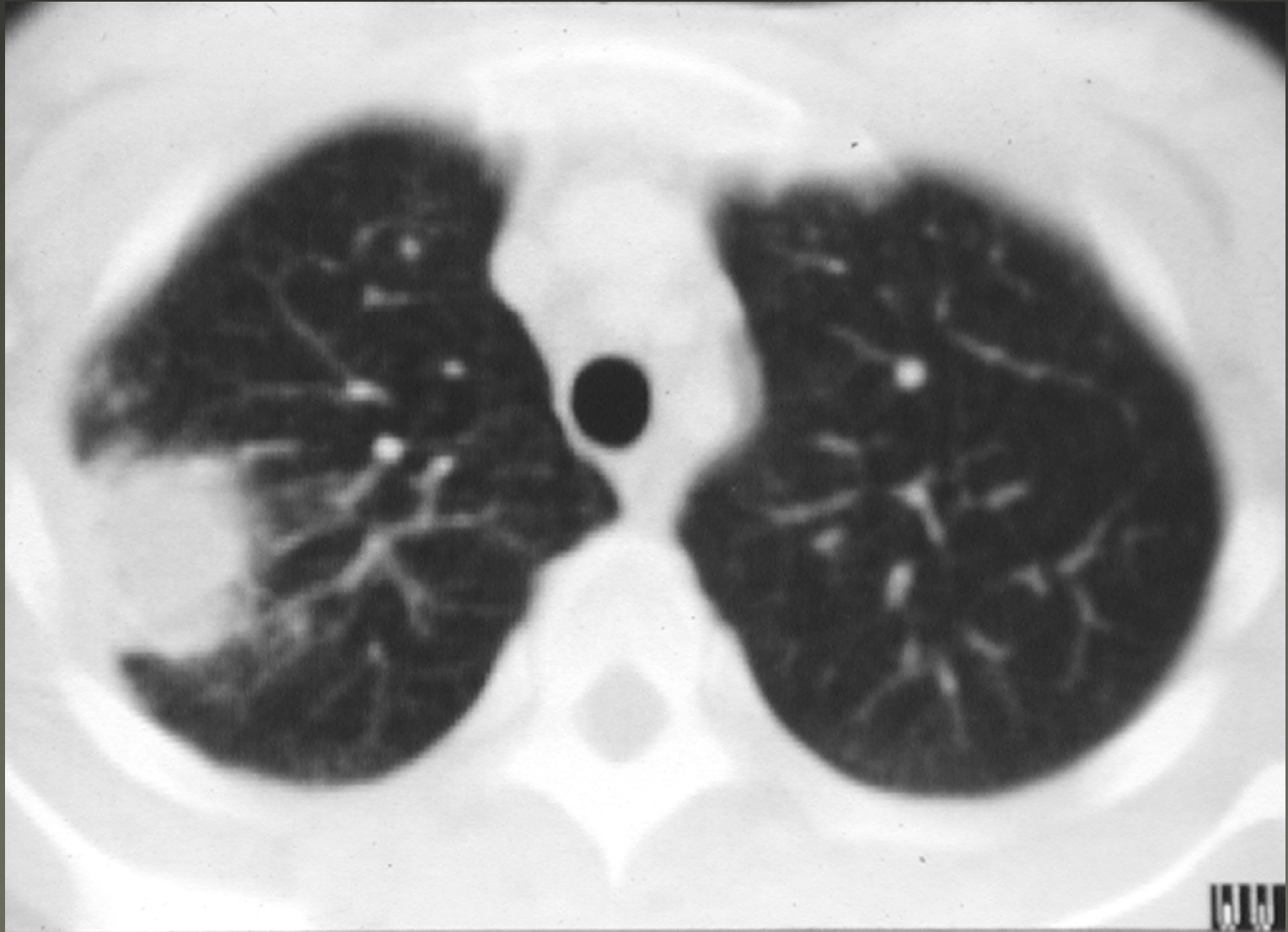
Factors that influence survival:

- completeness of resection of the tumor
- extent of invasion of the chest wall
- lymph node metastases

Whether or not en bloc resection of chest wall (versus parietal pleural only) is required in every instance remains a contentious issue

Chest wall reconstruction: this is rarely necessary with the resection of fewer than three contiguous rib segments

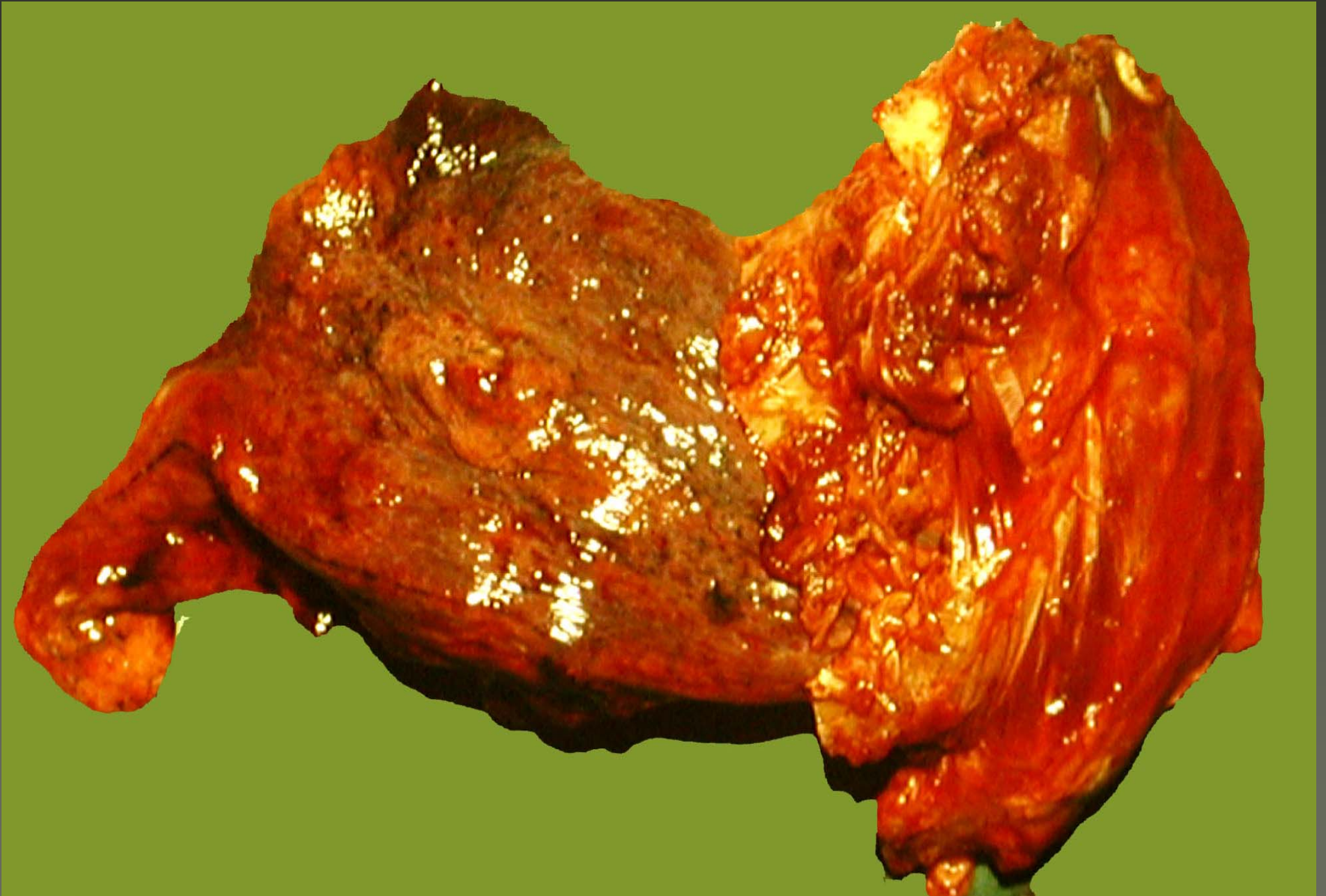
T3 CHEST WALL



T3 Chest wall



T3 CHEST WALL



Chest wall reconstruction (gore-tex)

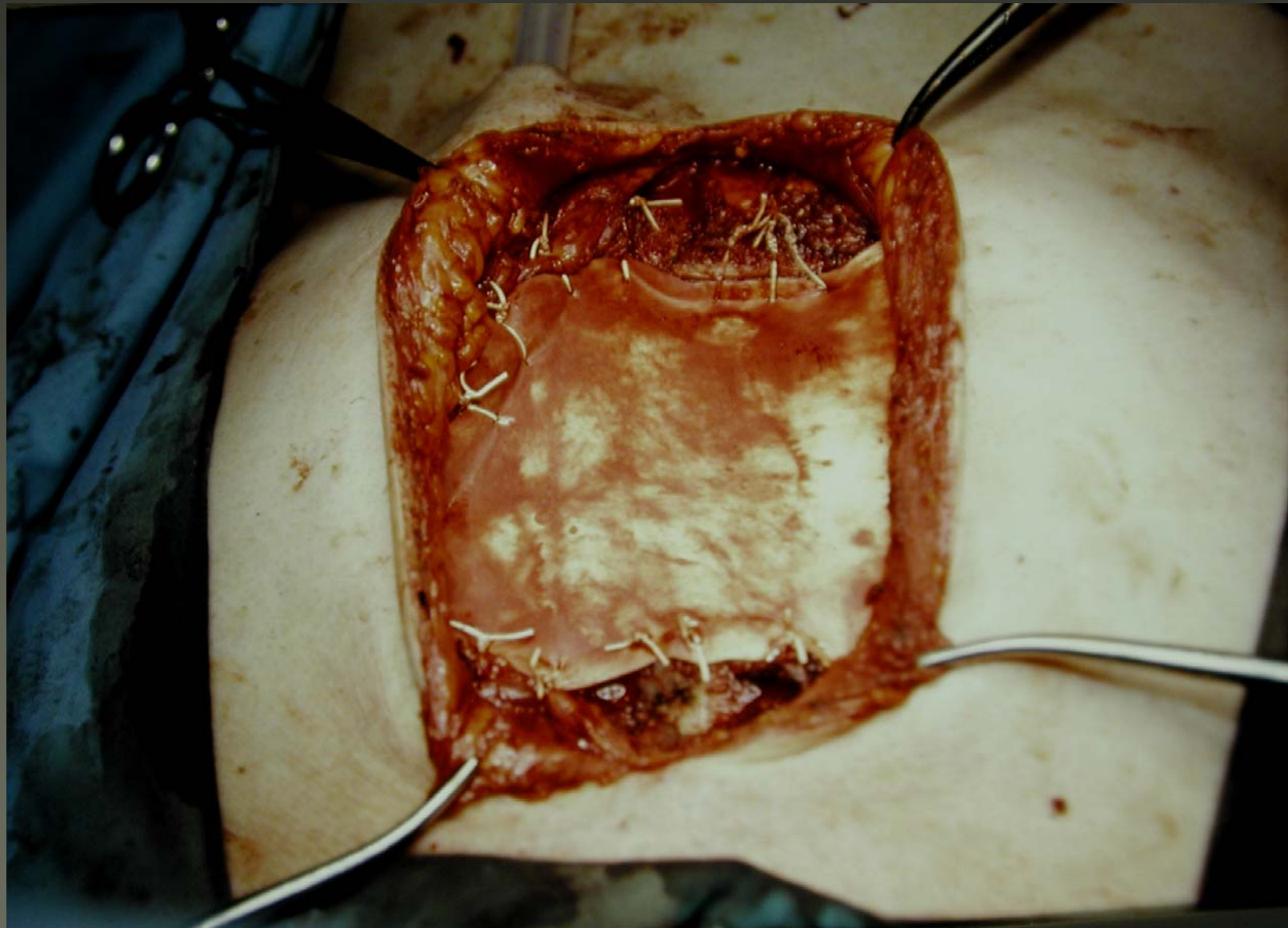


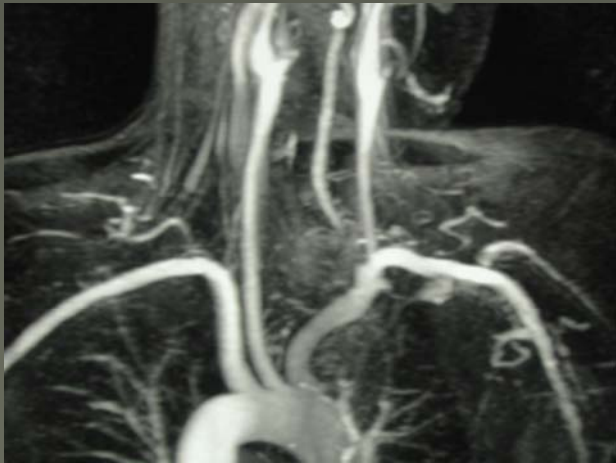
Table 2 Results of surgery for chest wall invasion (T3) in non-small cell lung cancer

Author (year)	No.	5-year SR(%)	Reference
Paone (1982)	32	35	Chest 81: 203
Patterson (1982)	35	38	Ann Thorac Surg 34:692
Piebler (1982)	93	33	Ann Thorac Surg 34:684
McCaughan (1985)	125	40	J Thorac Cardiovasc Surg 89:836
Allen (1991)	52	26	Ann Thorac Surg 51:948
Watanabe (1991)	42	43	Thorac Cardiovasc Surgeon 39:44
Albertucci (1992)	37(pl)	30	J Thorac Cardiovasc Surg 104:208
Pitz (1996)	125	29	Thorax 51:846
Downey (1999)	175	32	Ann Thorac Surg 68:188
Magdeleinat (2001)	201	24 !	Ann Thorac Surg 71:1094
Facciolo (2001)	105	61 !	J Thorac Cardiovasc Surg 121:649
Burkart (2002)	95	39	J Thorac Cardiovasc Surg 123:670

pl: pleura; SR: survival rate.

STAGE IIB Disease T3N0

SUPERIOR SULCUS
TUMOR



Superior Sulcus Tumors

By reason of their location in the pleural apex,
they invade adjoining structures early

Invasion of the lower brachial plexus,
especially the T1 nerve root

Shoulder and arm pain radiating to the inner
aspect of the upper arm (T1) and the ulnar
distribution in the fourth and fifth fingers of
the hand (C8)

Extension to the stellate ganglion with
consequent Horner's syndrome

Extension to the ribs or vertebrae

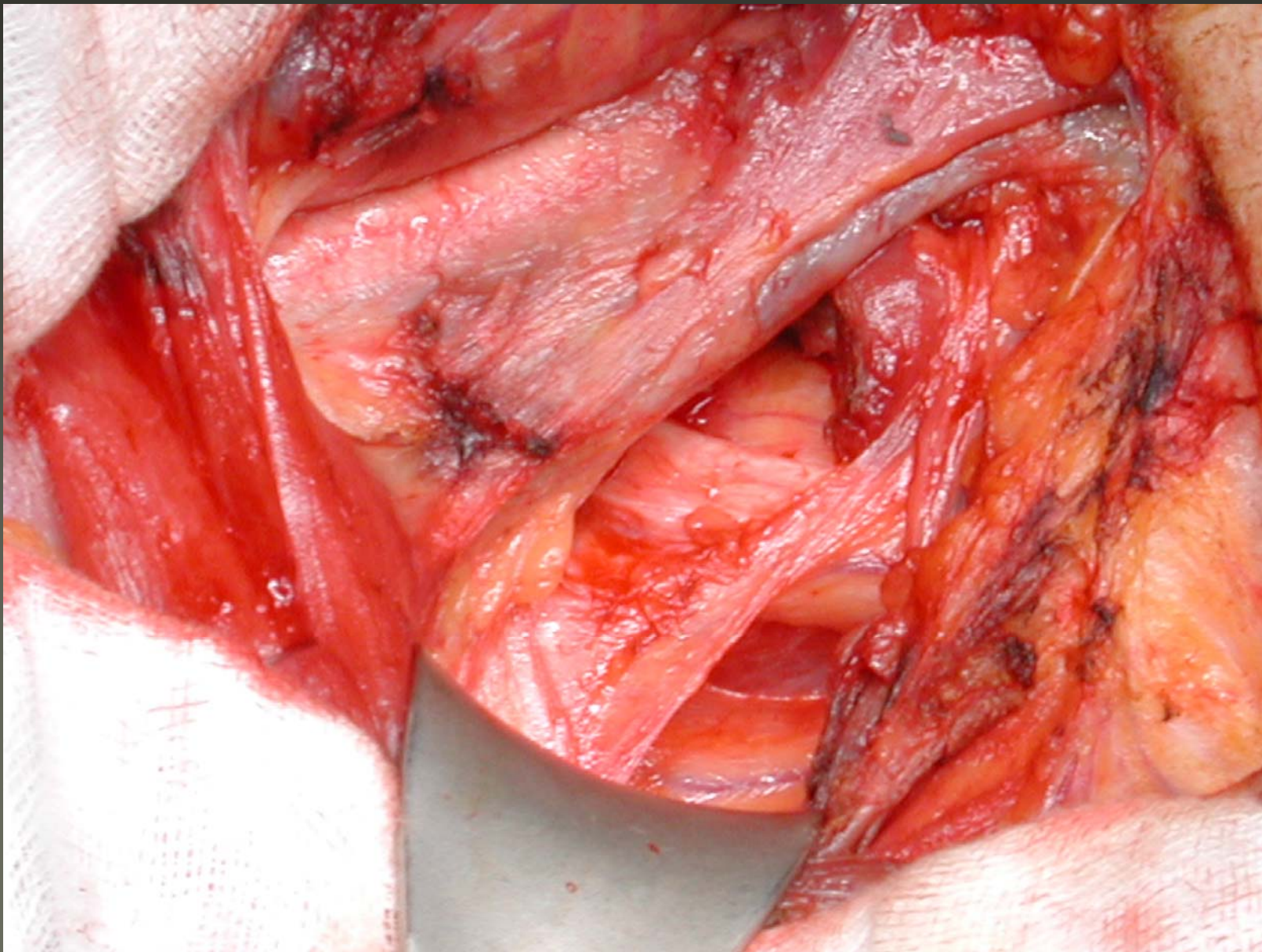
Superior Sulcus Tumors

The current standard therapy for this group of patients continues to be preoperative radiation followed by resection

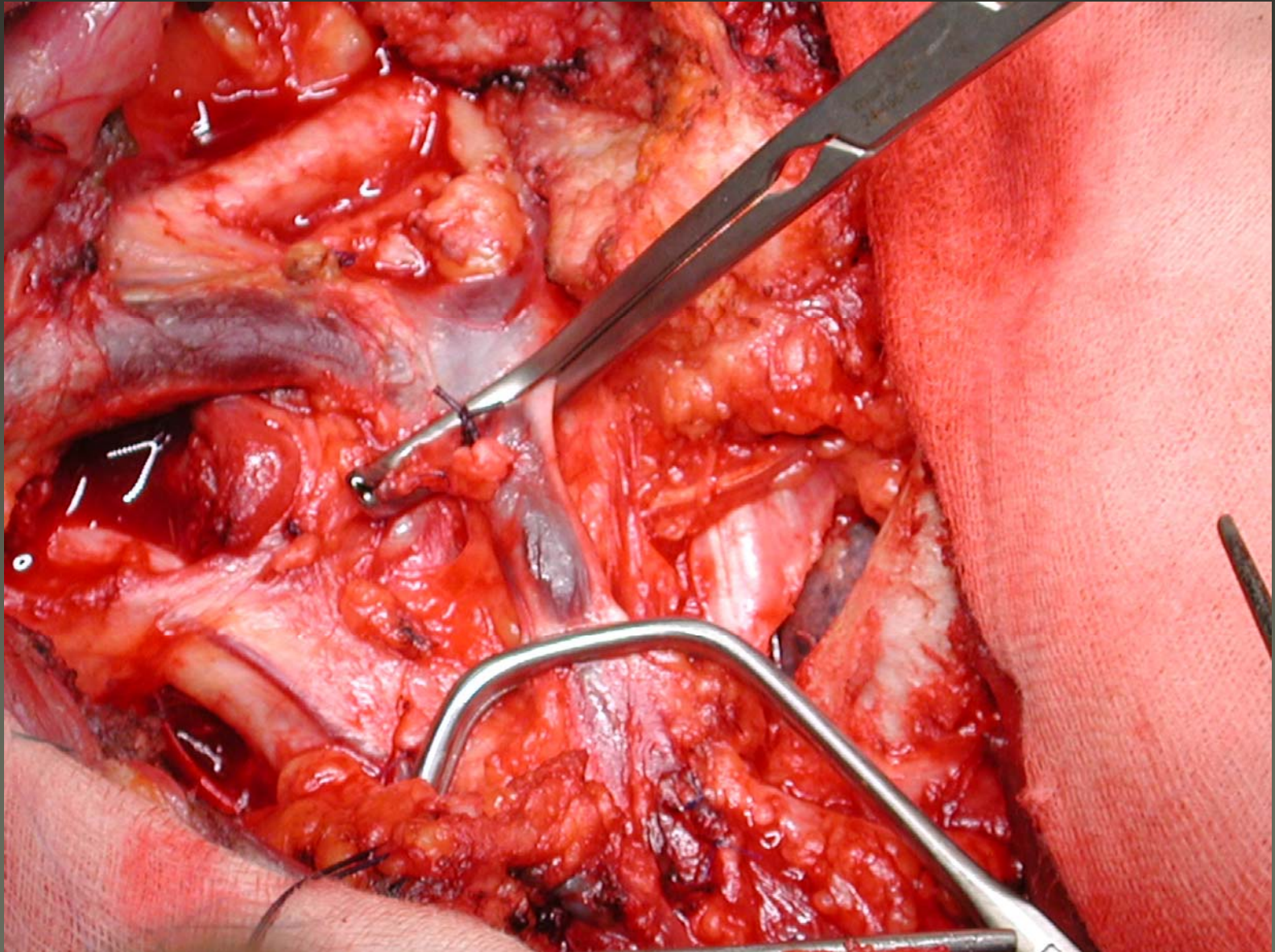
5-year survival 225 pts; R0 41%;
R1-2 9%

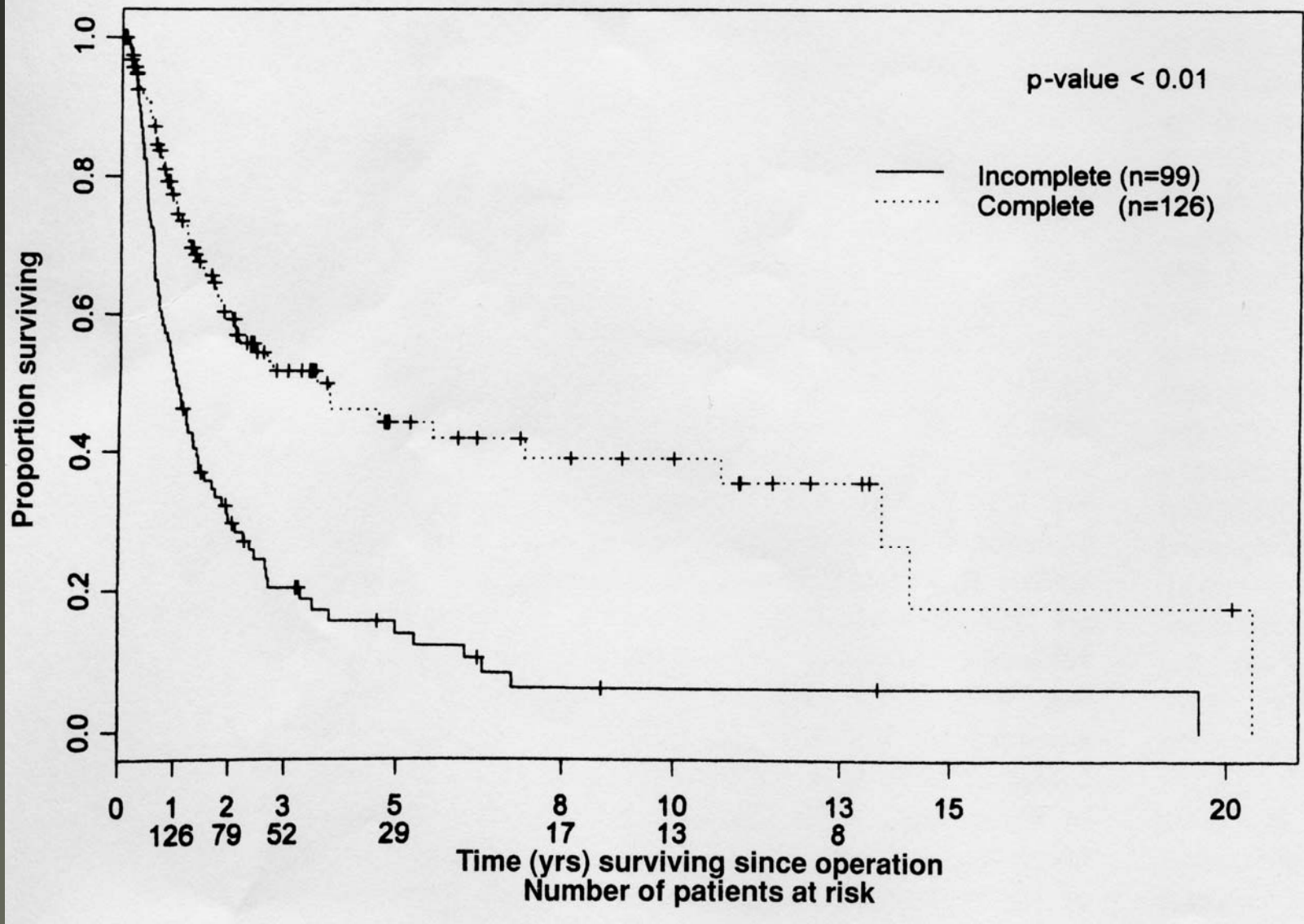
Rusch, 2000

TUMORE DEL SOLCO SUPERIORE

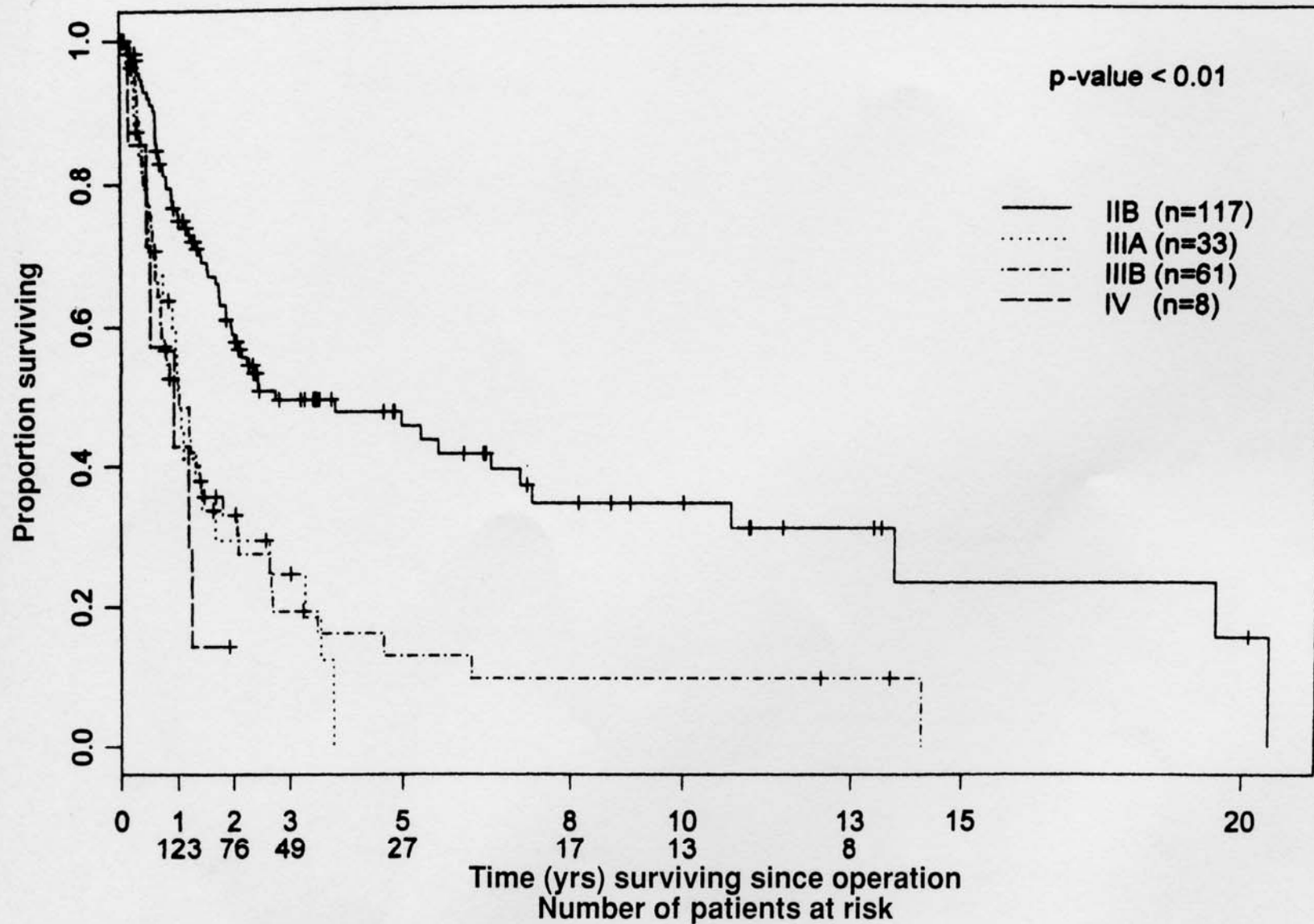


TUMORE DEL SOLCO SUPERIORE

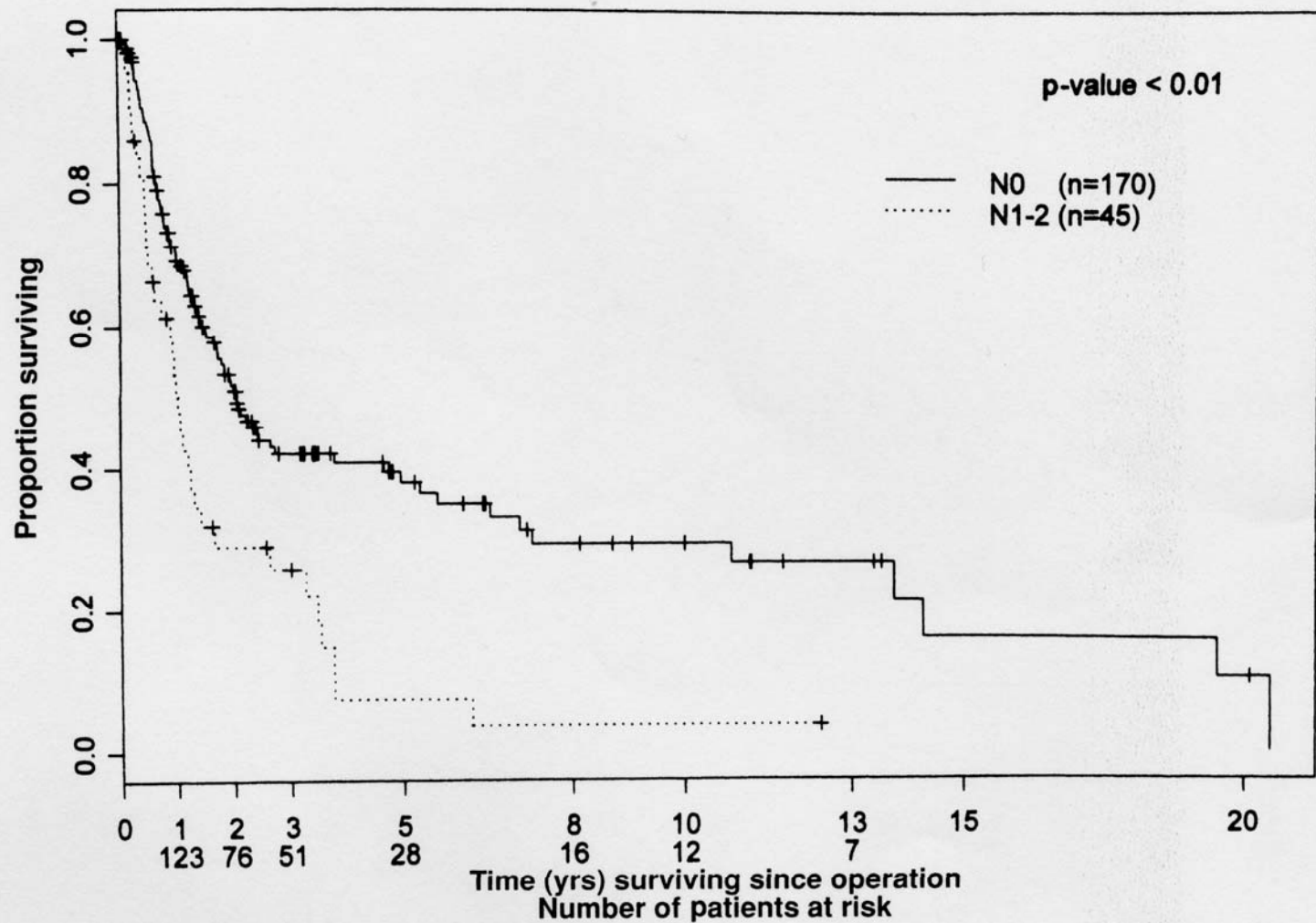




Survival curve of superior sulcus tumors stratified by complete resection



Survival curve of superior sulcus tumors stratified by stage



Survival curve of superior sulcus tumors stratified by nodal status

Superior sulcus tumor

It seems reasonable in view of the definite decrease in local recurrence and the possible survival benefit that postoperative radiotherapy be considered in patients with positive hilar and mediastinal nodes

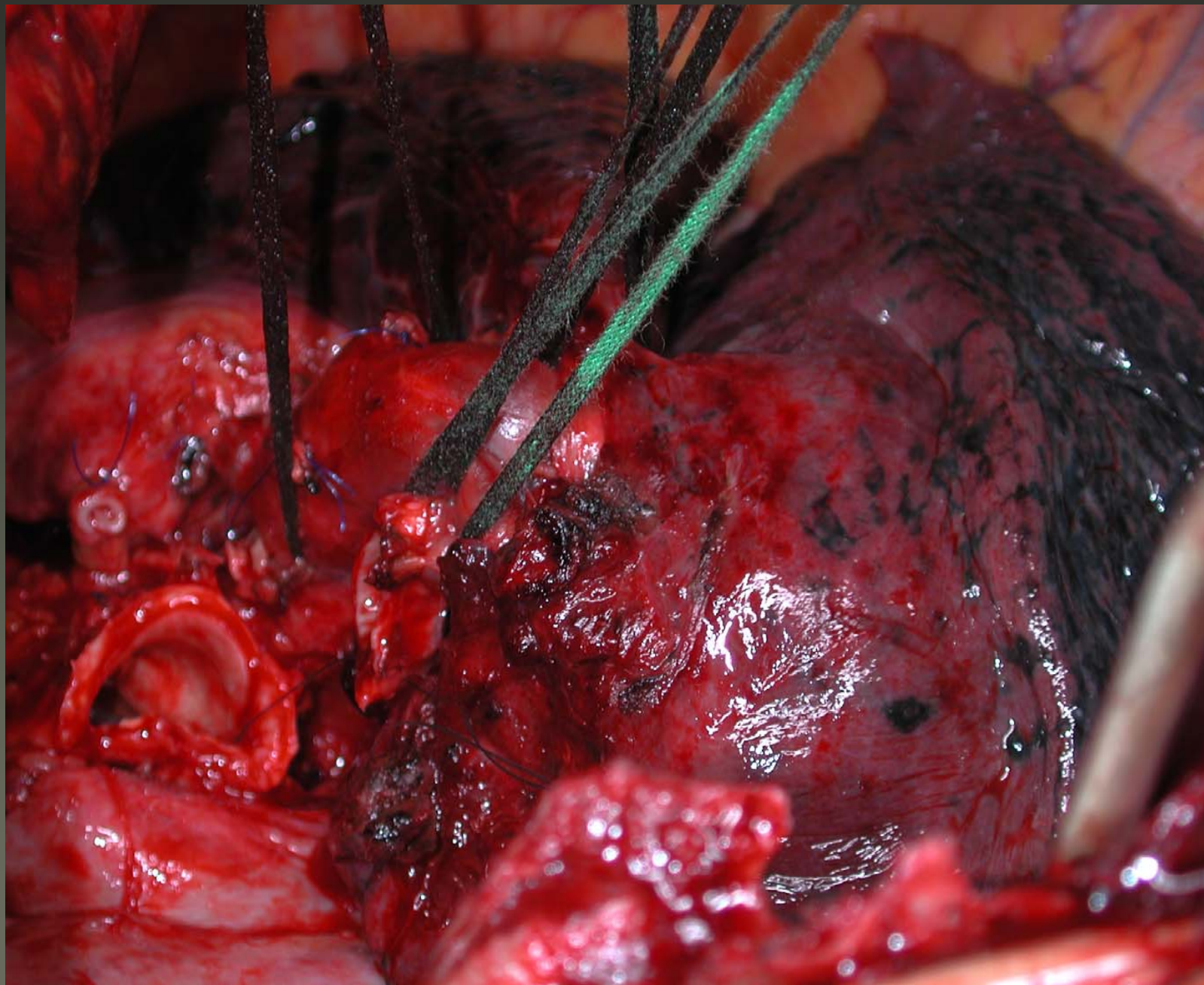
T3 - Tumors in proximity to carina

Central tumors that extend within 2 cm of the carina without carinal involvement

Nodal involvement severely affects prognosis

Sleeve lobectomy; pneumonectomy

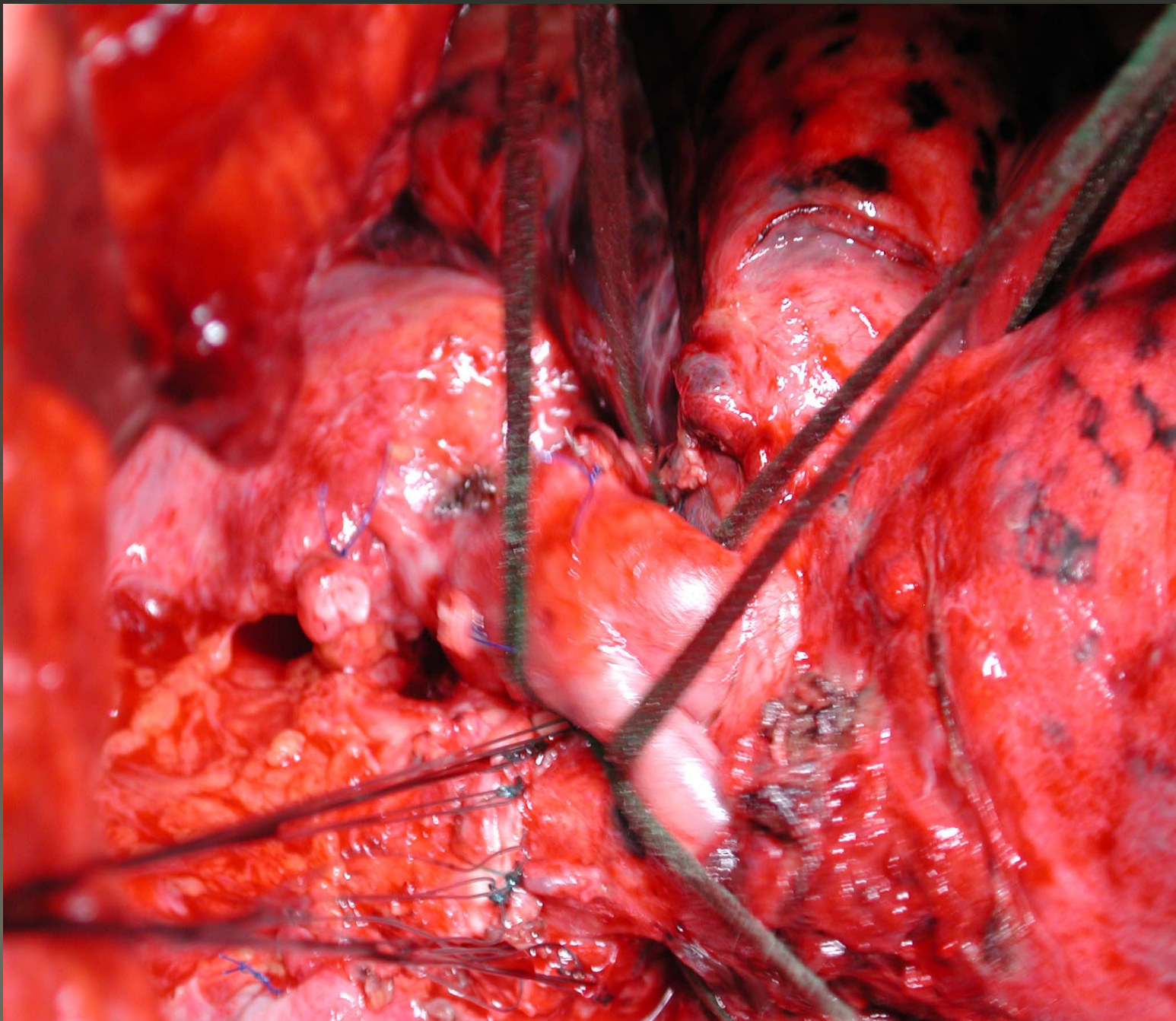
T3

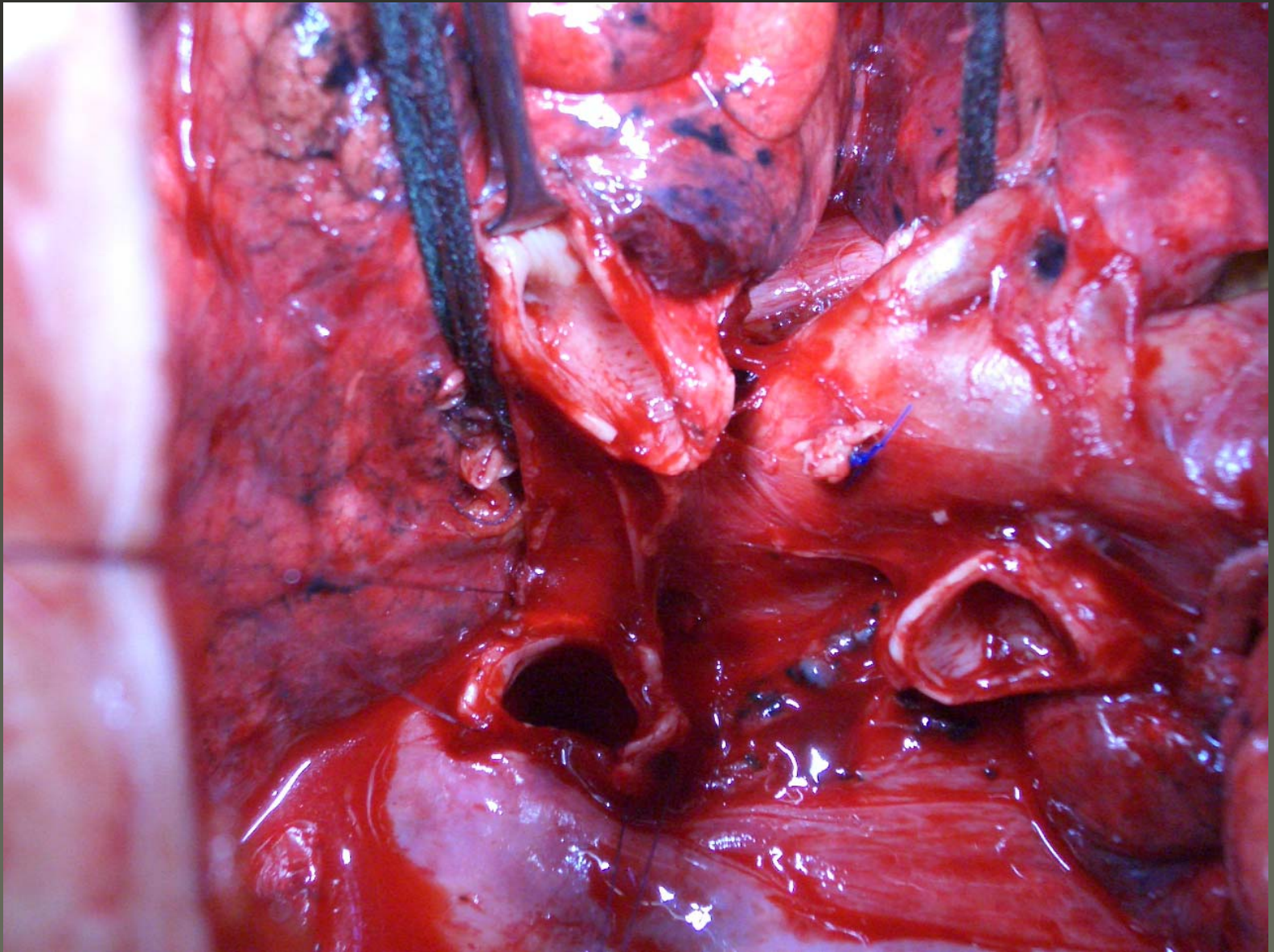


T3

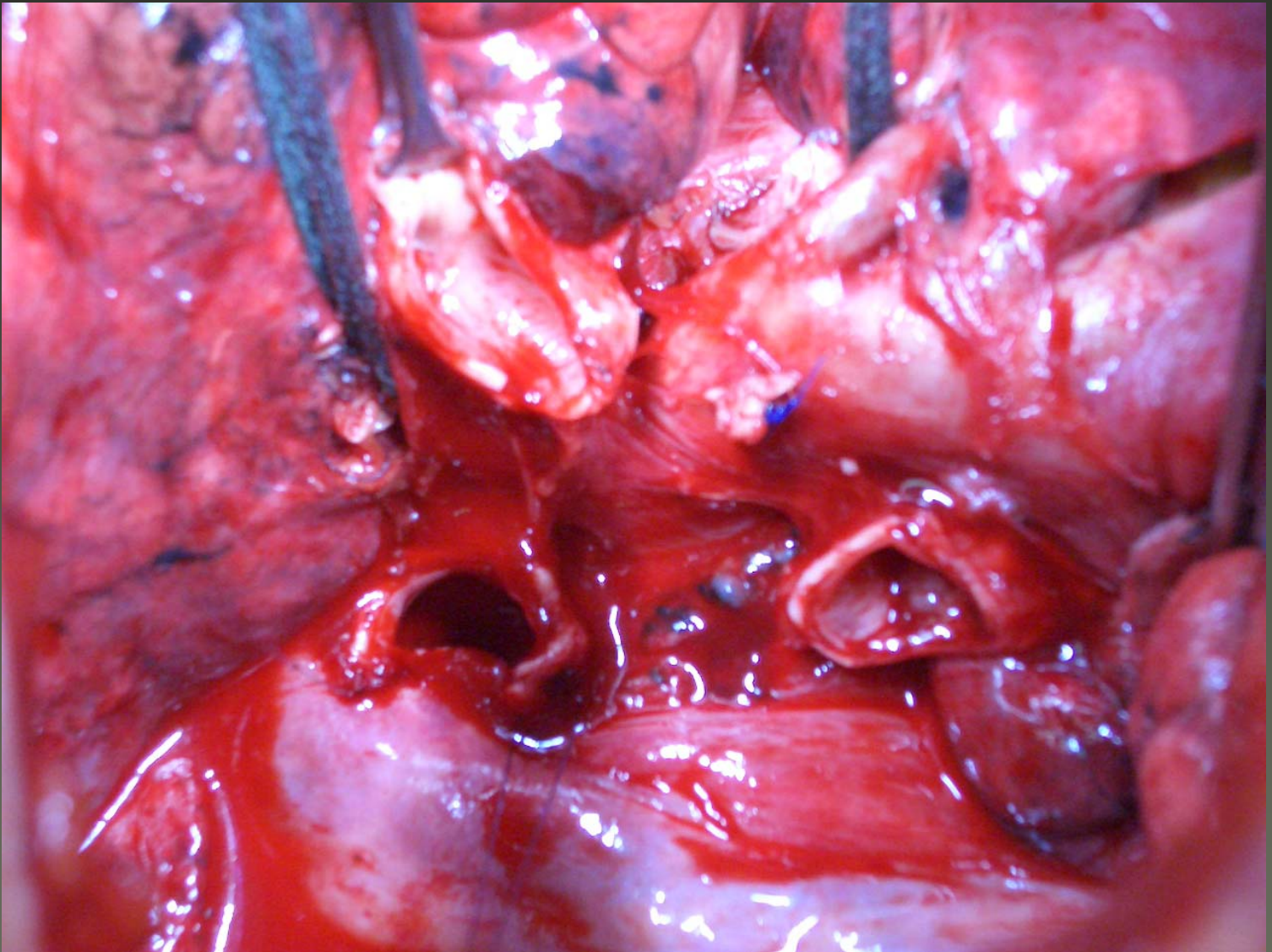


T3

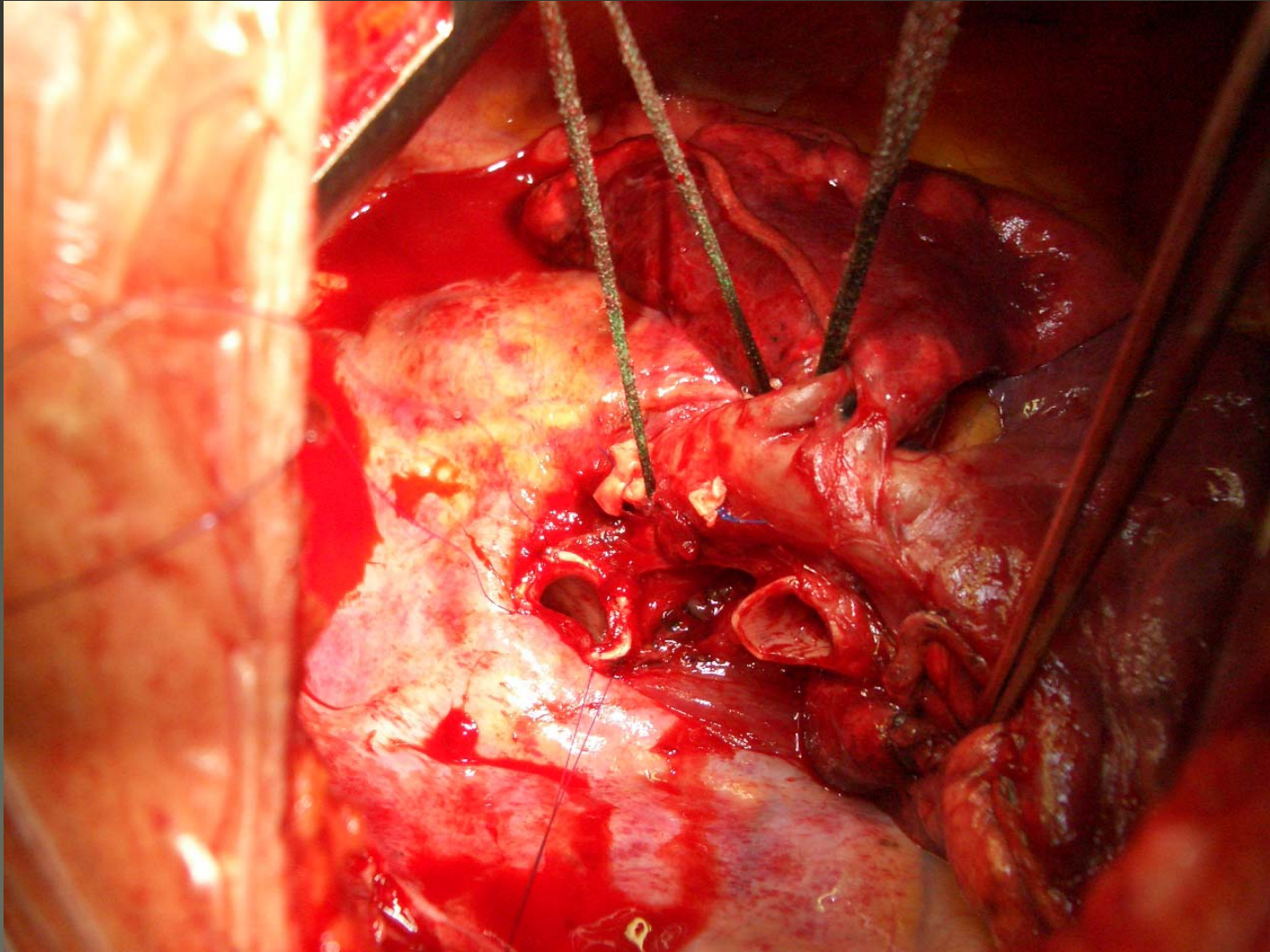




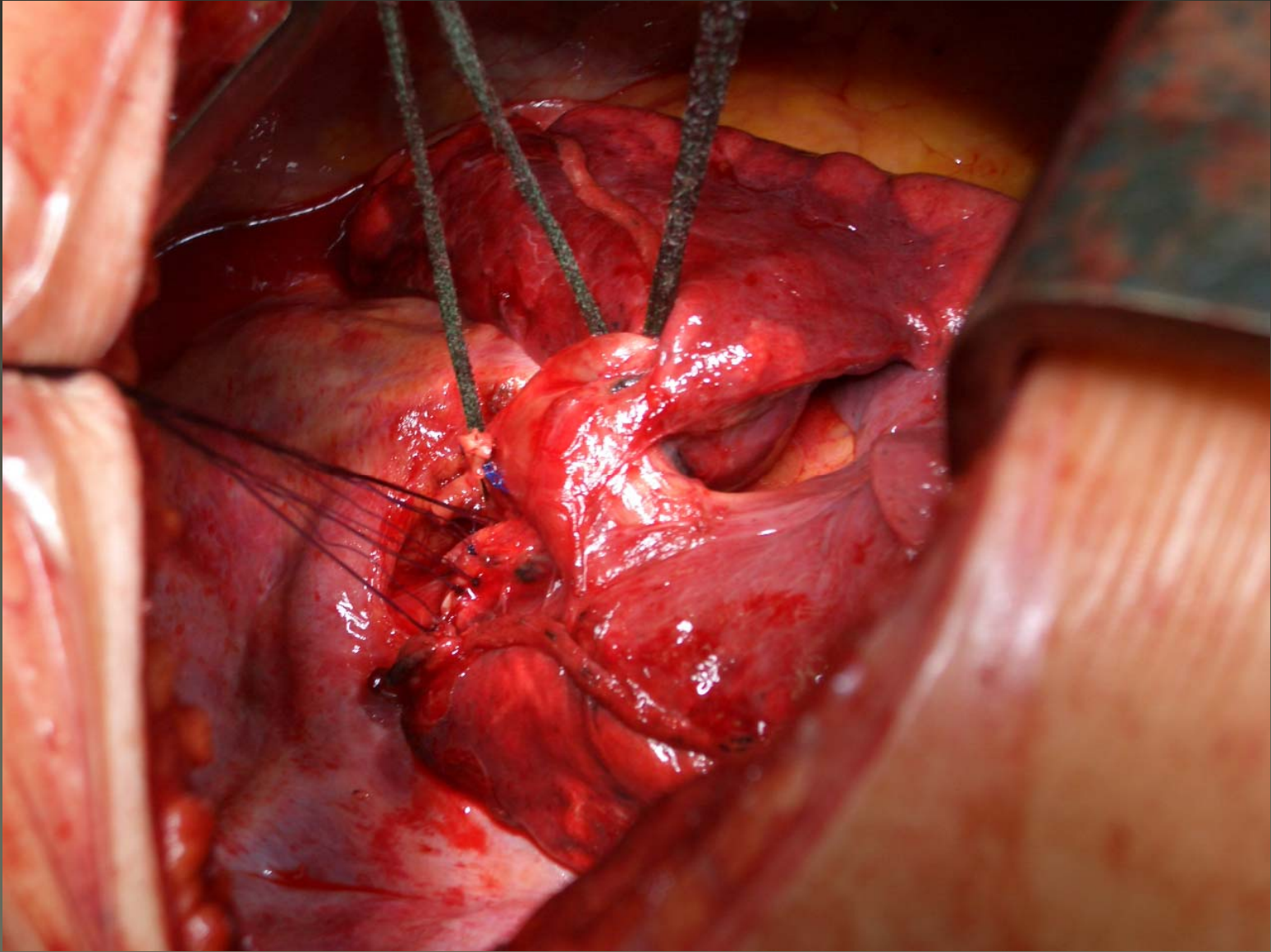
Upper right sleeve lobectomy



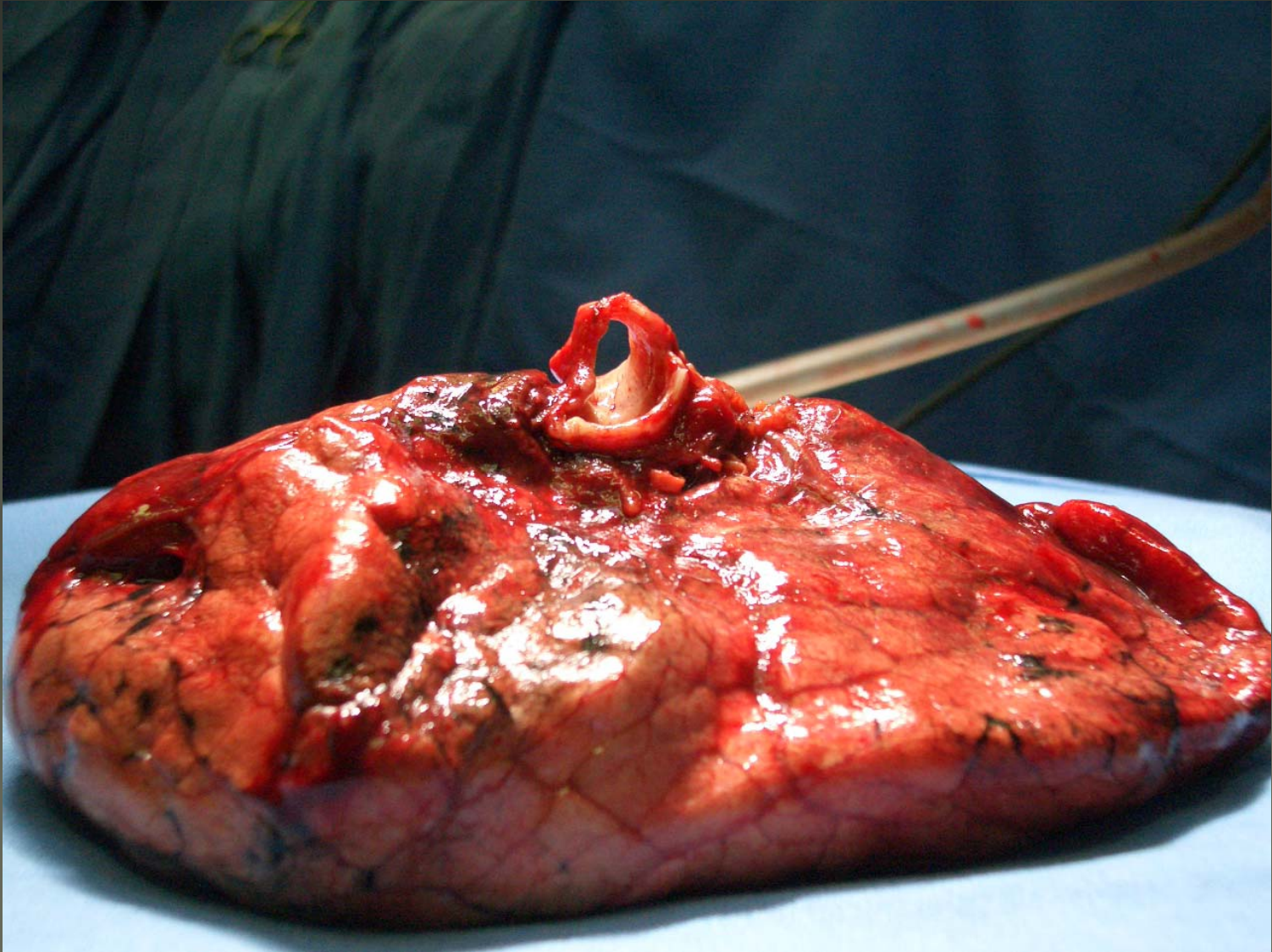
Upper right sleeve lobectomy



Upper right sleeve lobectomy



Upper right sleeve lobectomy



Upper right sleeve lobectomy

T1-2-3 N0

Postoperative radiotherapy in patients without evidence of lymphatic metastasis provides no significant survival benefit (*Van Houtte et al., 1980*) and may be detrimental to survival

T1-2-3 N1

Several studies reported that postoperative radiotherapy significantly increased the survival rate for patients with lymph node metastases for epidermoid carcinoma. The randomized prospective trial (LCSG 773) showed a decrease in local recurrence but without a significant increase in survival time (Weisenburger, 1986)

Several retrospective studies have shown increased survival rates in patients with adenocarcinoma with node-positive who have received postoperative radiotherapy (Choi et al 1980). There has not been a prospective randomized trial in patients with adenocarcinoma

Adjuvant chemotherapy studies from ASCO 2003-2004

	IALT (ASCO 2003)	JBR. 10 (ASCO 2004)	CALGB 9633 (ASCO 2004)
N	1867	482	344
Stage	I, II and III	IB and II	IB
Adjuvant therapy	Cisplatin-based/ some RT	Cisplatin Vinorelbine/ no RT	Carboplatin Paclitaxel/no RT
5Y relapse-free survival	39.4% vs 34.3%	61% vs 48%	61% vs 50%
5Y survival	44.5% vs 40.4%	69% vs 54%	71% vs 59%

ANITA

A prospective randomized study of Adjuvant Chemotherapy with Navelbine + Cisplatin in completely resected Non Small Cell Lung Cancer

On Behalf of the Adjuvant Navelbine International Trialist Association

J.Y. Douillard¹, R. Rosell², M. De Lena³, A. Le Groumelec⁴, A. Torres⁵, F. Carpagnano⁶

¹ Centre René Gauducheau, Nantes, France; ² Hospital Universitari Germans Trias i Pujol, Badalona, Spain; ³ IRCCS Oncologico, Bari, Italy; ⁴ CH. Chubert, Vannes, France; ⁵ Hospital Clinico San Carlos, Madrid, Spain; ⁶ Ospedale San Paolo, Bari, Italy

ANITA

Primary end-point

- **Survival**

Secondary end-points

- **Relapse-free survival**
- **Chemotherapy-related toxicity**

Exploratory analyses

- **Chemotherapy compliance**
- **Survival according to N status**
- **Pattern of relapse**
- **Influence of radiotherapy**

Inclusion criteria

- Histologically proven NSCLC**
- TNM (*Mountain 1986*) stage: I (except T1N0), II and IIIA**
- Totally resected (R0) within 42 days**
- WHO PS: 0, 1 or 2**
- 18 > Age ≤ 75 years**
- Fit to receive chemotherapy**
- Written informed consent**

Study Design

- ❑ Open, multicentric, randomized study (1:1).
- ❑ Stratified after surgery by centre, stage and histology.
- ❑ **→ 800 patients to be included.**
- ❑ Alpha= 5%, Beta= 10%, Power= 90 %
- ❑ One sided test
- ❑ Delta expected in the 2-year survival rate: 10%
- ❑ Expected deaths: 466 events



* Radiation therapy was upon center choice

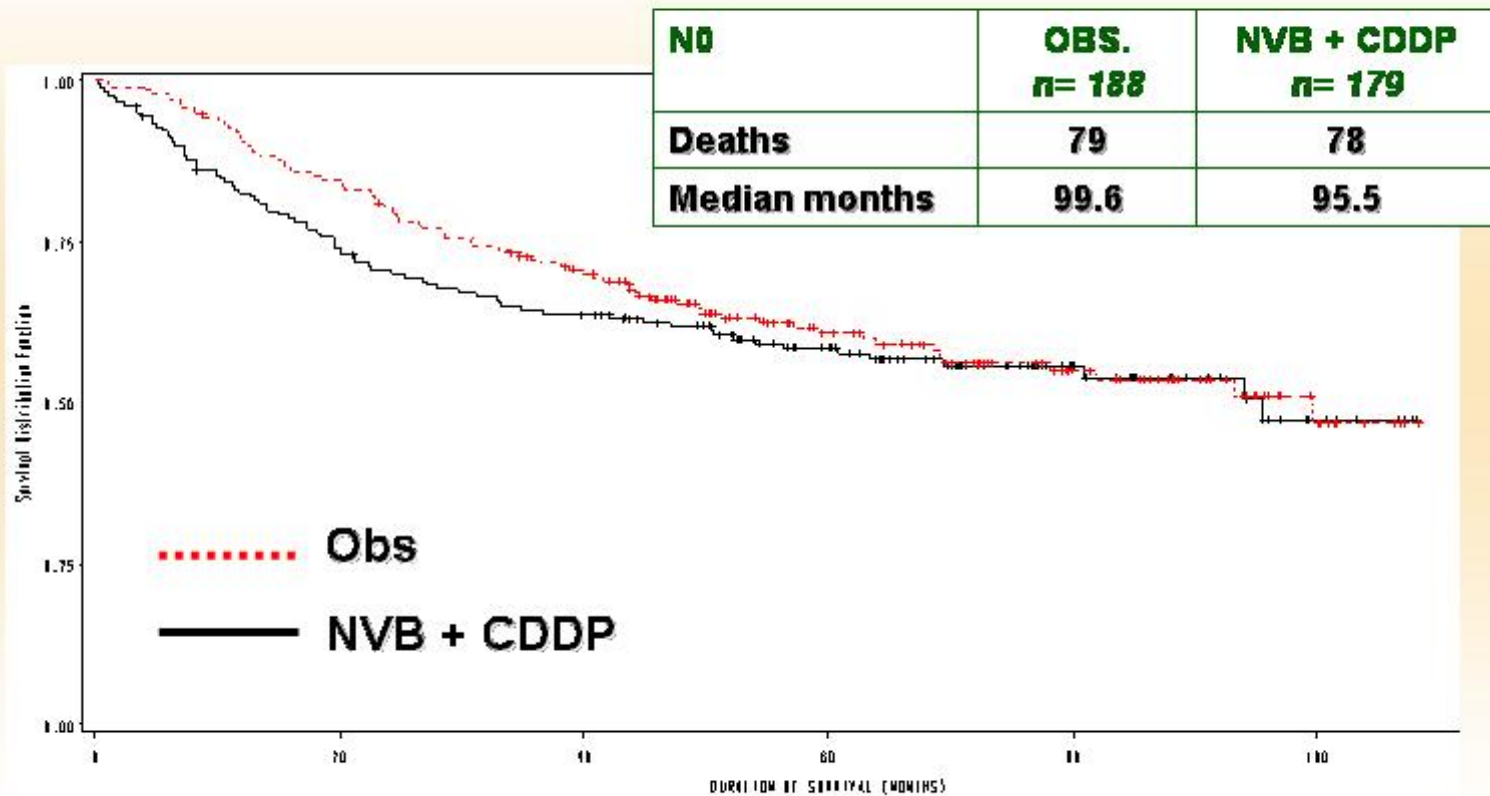
Type of Surgery, pTNM, Histology

	OBS	NVB+CDDP
Type of surgery	n= 433	n= 407
Pneumonectomy	35.8%	38.1%
Lobectomy	58.4%	57.2%
Stage	n= 433	n= 407
I (pT2 N0)	34.2%	35.4%
II	30.5%	29.2%
IIIA	35.3%	35.4%
Histology	n= 433	n= 407
Squamous	58.9%	60.0%
Non Squamous	41.1%	40.0%
PORT	33.3%	21.6%
Chemotherapy at relapse	48%	39.2%

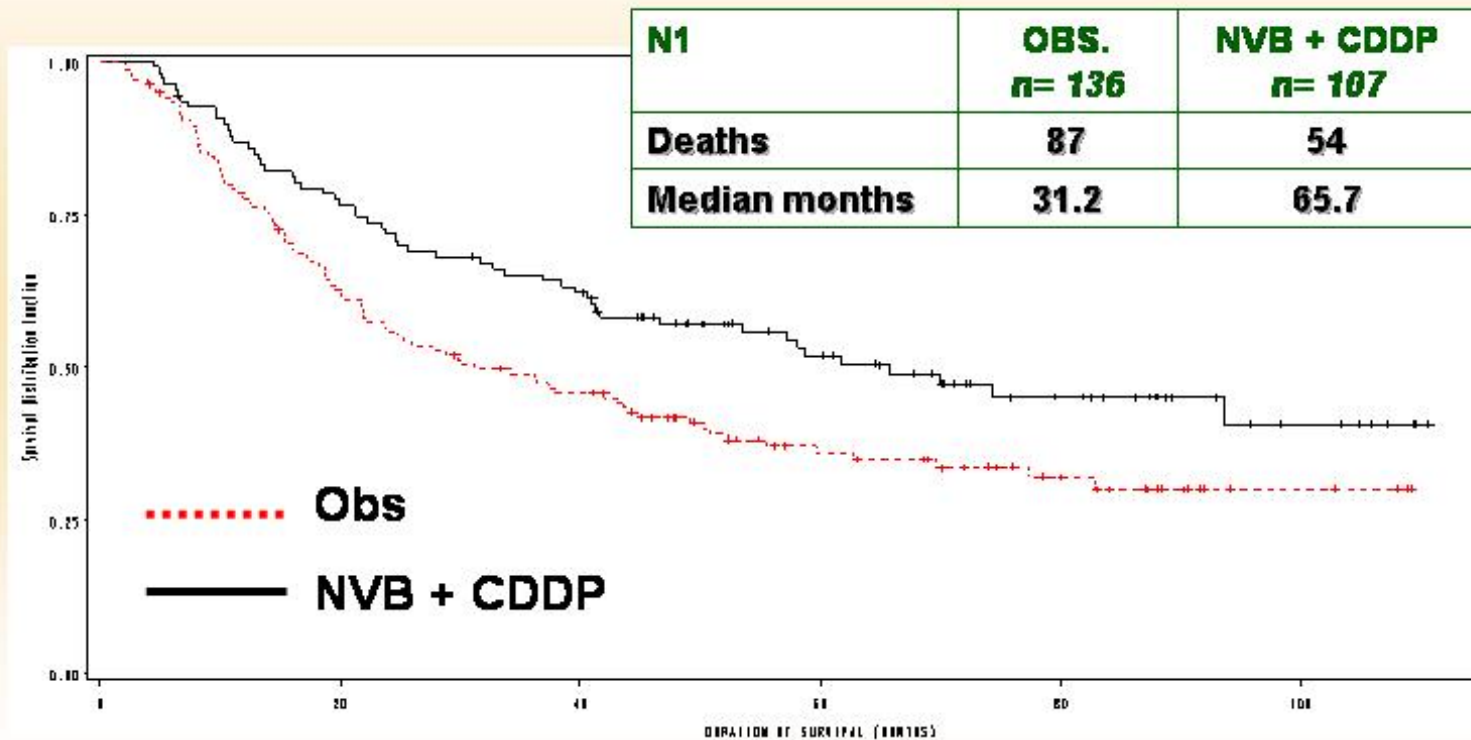
Survival: COX Univariate Analysis

COVARIATES	UNIVARIATE	
	P value	Hazard ratio [95% CI]
Age: \geq 55 years < 55 years	0.04	1 0.81 [0.67 - 0.99]
WHO Performance Status: 0 1-2	0.012	1 1.27 [1.05 - 1.52]
Type of surgery: Pneumonectomy Other type	0.001	1 0.73 [0.60 - 0.88]
Radiotherapy: No Yes	0.003	1 1.34 [1.10 - 1.63]
Stage: IIIA IB-II	< 0.001	1 0.54 [0.45 - 0.65]
Lymph Nodes N: N+ N0	< 0.001	1 0.53 [0.44 - 0.65]
Histological type: Adenocarcinoma Other type	0.733	1 0.97 [0.80 - 1.17]

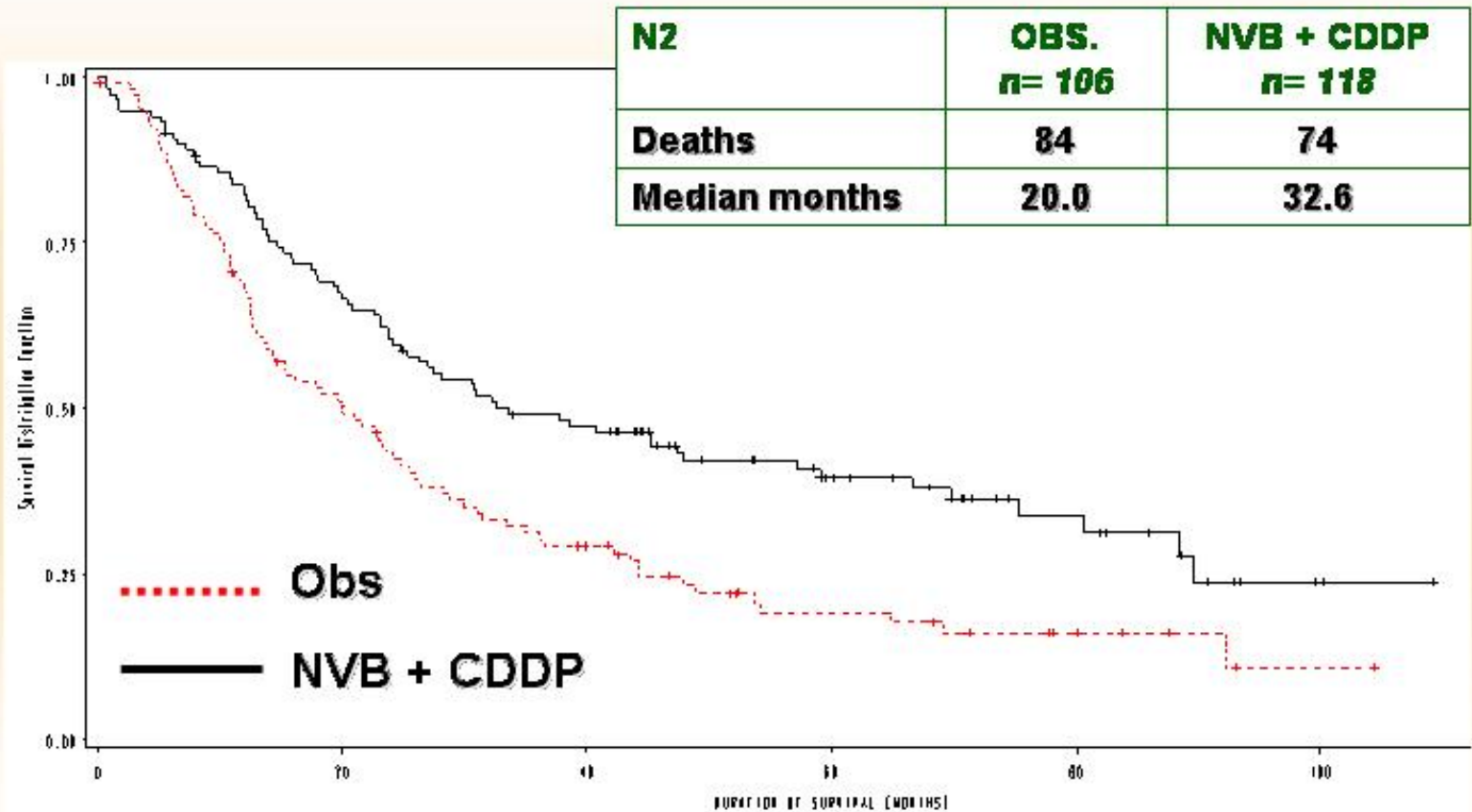
Overall Survival – N0



Overall Survival – N1



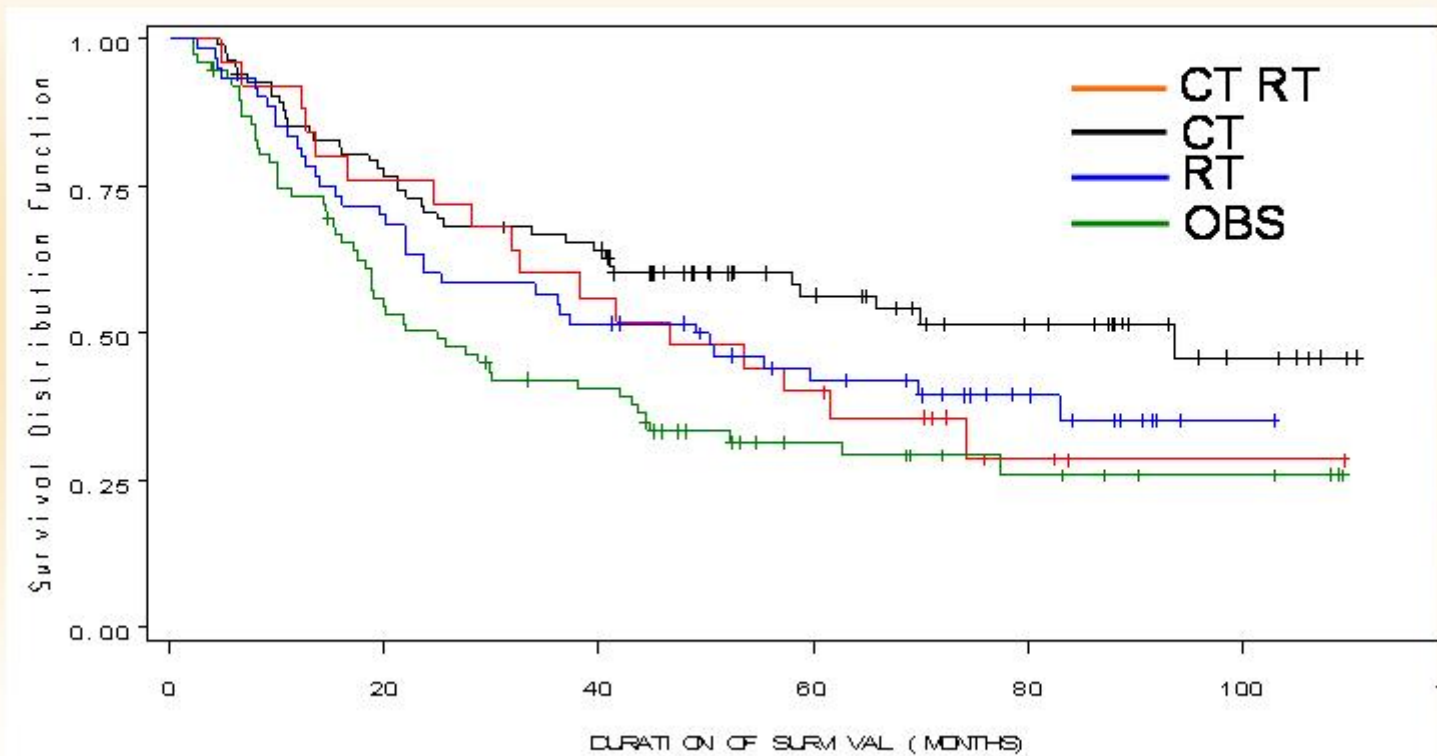
Overall Survival – N2



PORT in N1 Patients

N1	RADIOTHERAPY		NO RADIOTHERAPY	
	No CT	IV VRL+CDDP	No CT	IV VRL+CDDP
N=243				
Number of patients	60	25	76	82
Median survival, mos	50.2	46.6	25.9	93.6
1 year - survival	83.1%	92.0%	73.4%	85.3%
2 year - survival	61.1%	76.0%	51.7%	70.4%
5 year - survival	42.6%	40.0%	31.4%	56.3%
% deaths	35 (58%)	17 (68%)	52 (68%)	37 (45%)

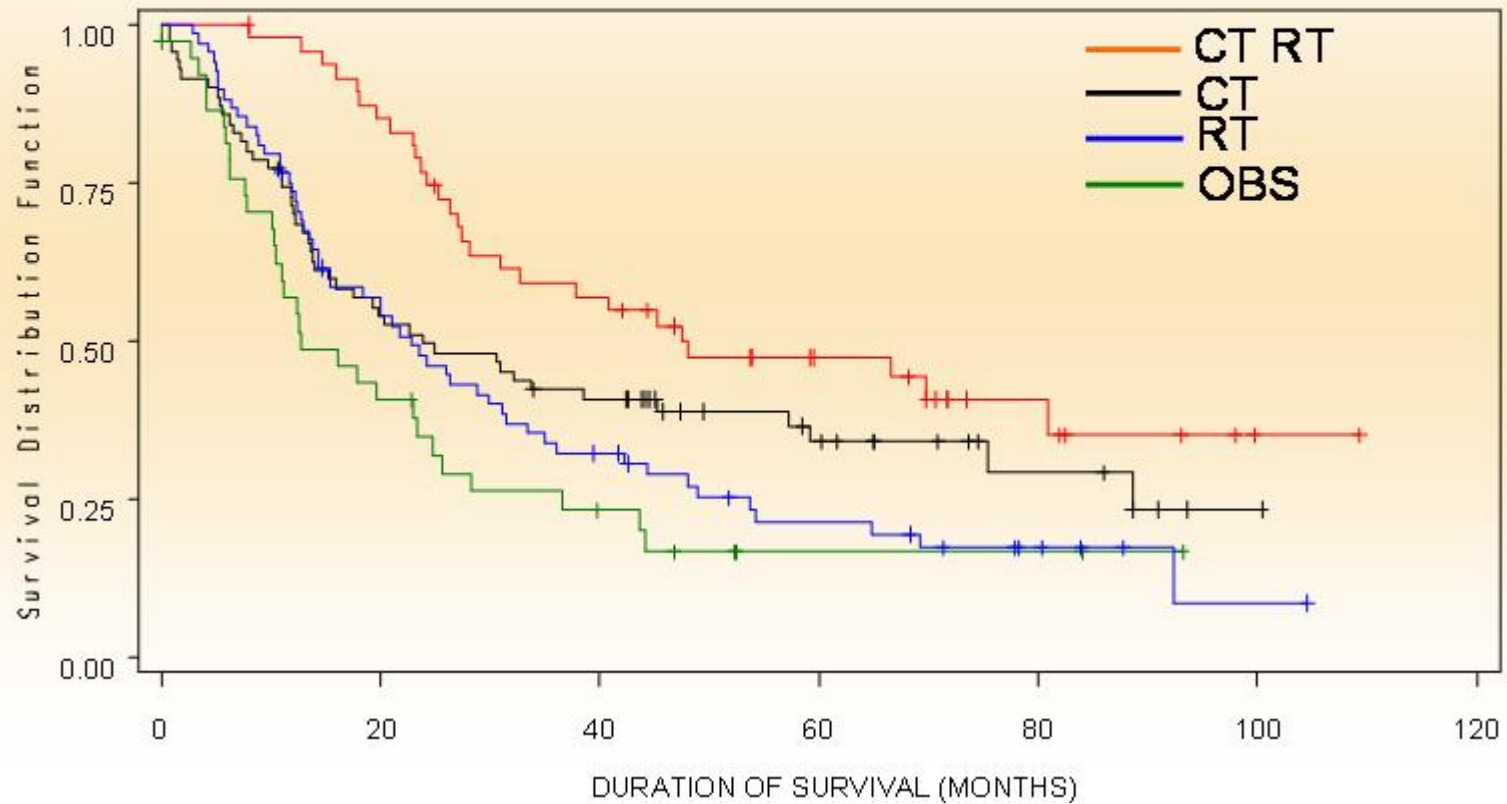
PORT in N1 Patients



PORT in N2 Patients

N2	RADIOTHERAPY		NO RADIOTHERAPY	
	No CT	IV VRL+CDDP	No CT	IV VRL+CDDP
N=224				
Number of patients	68	48	38	70
MS, mos	22.7	47.4	12.7	23.8
1 year survival	73.5 %	97.9 %	56.8 %	71.2 %
2 year survival	47.6%	76.6%	34.8%	49.4 %
5 year survival	21.3%	47.4%	16.6%	34.0 %
% deaths	54 (79%)	28 (58 %)	30 (79%)	46 (66%)

PORT in N2 Patients



Conclusions

- **Significant improvement in survival with adjuvant navelbine/cisplatin**
- **The effect of navelbine/cisplatin in stage IB not demonstrated**
- **The effect of post-operative radiotherapy should be investigated in randomized studies in stage IIIA**
- **7- and 10-year survival should be assessed**



OSPEDALE S. PAOLO - BARI
ALTELLI, BARI 4



OSPEDALE S. PAOLO - BARI
U.O. COMPLESSA DI CHIRURGIA TORACICA

Oncologia toracica

Lo stato dell'arte
alla fine del 2006

Presidente Francesco Carpagnano

BARI

30 novembre - 2 dicembre 2006

Palace Hotel