

Pulmonary Metastasectomy

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Pulmonary Metastases

- Dramatic and emotional point for cancer patient
- Potential cure -> probable incurability
- Living without evidence of disease -> living with systemic disease
- Metastasectomy – QOL ↑, extend period of obvious disease

HISTORY

- First case: 1882, Weinlechner
 - 1930s, patients dying of pulmonary metastases failed to exhibit extrapulmonary disease at autopsy.
 - > reasonable to offer surgical resection of these lesions in the hope of prolonging patient survival with the development of systemic adjuvant chemotherapy.
 - The role of surgical resection of metastatic disease, however, is not universally accepted in the nonsurgical community.
- No randomized trial.

New pulmonary nodule

Primary lung cancer vs. metastasis

Original type of malignancy

	Metastasis	Primary lung cancer
Sarcoma	10	1
Melanoma	10	1
Genitourinary cancer	1	1
Colorectal cancer	1	1
Head and neck cancer	0.5	1

Criteria for metastasectomy

Primary tumor that has been definitely controlled.

Metastases limited to the lung that can be completely resected.

Ability of the patient to tolerate the planned operation.

Lack of a better alternative treatment.

The number of lung metastases.

The disease-free interval since treatment of the primary tumor.

The tumor doubling time, the presence of lymph node metastases.

The histology of the primary tumor.

Elevated serum markers such as carcinoembryonic antigen.

European Society of Thoracic Surgeons (ESTS)

Lung metastasectomy project



1. Optimal preoperative imaging
2. The role of mediastinal lymph node dissection
3. Surgical approach
4. The extent of surgical resection

GENERAL THORACIC SURGERY

LONG-TERM RESULTS OF LUNG METASTASECTOMY: PROGNOSTIC ANALYSES BASED ON 5206 CASES

The International Registry of Lung Metastases*

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Objectives: The International Registry of Lung Metastases was established in 1991 to assess the long-term results of pulmonary metastasectomy. **Methods:** The Registry has accrued 5206 cases of lung metastasectomy, from 18 departments of thoracic surgery in Europe ($n = 13$), the United States ($n = 4$) and Canada ($n = 1$). Of these patients, 4572 (88%) underwent complete surgical resection. The primary tumor was epithelial in 2260 cases, sarcoma in 2173, germ cell in 363, and melanoma in 328. The disease-free interval was 0 to 11 months in 2199 cases, 12 to 35 months in 1857, and more than 36 months in 1620. Single metastases accounted for 2383 cases and multiple lesions for 2726. Mean follow-up was 46 months. Analysis was performed by Kaplan-Meier estimates of survival, relative risks of death, and multivariate Cox model. **Results:** The actuarial survival after complete metastasectomy was 36%

	5yr survival	10yr survival
Complete metastasectomy	36%	26%
Imcompleure metastasectomy	13%	7%

... simple system of classification valid for different tumor types. (J Thorac Cardiovasc Surg 1997;113:37-49)

Radiologic Image

Imaging Requirements in the Practice of Pulmonary Metastasectomy

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Abstract: The primary imaging modality for the detection of pulmonary metastases is computed tomography (CT). Ideally, a helical CT scan with 3- to 5-mm reconstruction thickness or a volumetric thin section scanning should be performed within 4 weeks of pulmonary metastasectomy. A period of observation to see whether further metastases develop does not seem to allow better patient selection. If positron emission tomography is available, it may identify the extrathoracic metastatic sites in 10 to 15% of patients. Despite helical CT scan, palpation identifies the metastases not detected by imaging in 20 to 25% of patients and remains the standard. No data define the optimal interval for follow-up surveillance imaging.

Key Words: Imaging, Pulmonary metastasectomy, Lung metastases, Pulmonary nodule.

(J Thorac Oncol. 2010;5: S134–S139)

- What type and protocol of chest computed tomography scan (CT) should be performed in patients suspected to have pulmonary metastases?
- How should the images be reviewed?
- Are all nodules detected significant?
- How recently should a CT scan be done before metastasectomy?
- Is an observation period with serial CT scanning before metastasectomy beneficial?
- Should a positron emission tomography (PET) scan be performed before metastasectomy to diagnose extrathoracic or intrathoracic metastases?
- Is helical CT imaging adequate to avoid palpation of the lung?
- What interval of follow-up CT scans is necessary?

Nonspecific radiographic appearance

Critical importance

Chest CT : standard imaging modality

3 ~ 5mm slice thickness

Within 4 weeks of pulmonary metastasectomy

PET (role out occult distant metastases)

Follow-up

4~6 weeks after surgery

every 6 months for 2 years

every 1 years for at least 5 years

Lymph Node Status

TABLE 1. Incidence of Thoracic Lymph Nodes in Patients with Lung Metastases

Publication	Era	Primary	Patients	Nodal Spread	Percent
Loehe et al. ²	1996–1998	Mixed	63	9	14
Saito et al. ³	1990–2000	Colorectal	138	20	14
Ercan et al. ⁴	1985–1999	Mixed	70	20	29
Pfannschmidt ⁵	1996–2001	Mixed	245	80	33
Welter et al. ⁶	1993–2003	Colorectal	169	28	17
Menon et al. ⁹	2002–2005	Mixed	57	6	11
Weighted average					22

J Thorac Oncol 2010; 5: S166

Prognostic Significance of Lymph Node Metastasis Found During Pulmonary Metastasectomy for Extrapulmonary Carcinoma

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Background. The prognostic significance of lymph node metastasis in cancer patients is well documented. Pulmonary metastasectomy in selected patients is associated with improved survival. Little is known about the prognostic significance of lymph node metastases found during pulmonary metastasectomy for extrapulmonary carcinoma metastatic to the lung.

Methods. The records of all patients who underwent pulmonary metastasectomy and complete mediastinal lymph node dissection for extrapulmonary carcinomas at our institution from November 1985 through July 1999 were reviewed.

Results. Eight hundred eighty-three patients underwent pulmonary metastasectomy. Of these, 70 patients (7.9%) (44 men, 26 women) had concomitant complete lymphadenectomy. Median age was 64 years (range, 33 to 83 years). Median time interval between primary tumor resection and metastasectomy was 34 months (range, 0 to

188 months). Wedge excision was performed in 46 patients, lobectomy in 16, both in 7, and pneumonectomy in 1. Lymph node metastases were found in 20 patients (28.6%) and were classified as intrapulmonary or hilar (N1) in 9, mediastinal (N2) in 8, and both in 3. There were no operative deaths. Median follow-up was 6.6 years (range, 1.1 to 14.6 years). Three-year survival for patients with negative lymph nodes was 69% as compared with only 38% for those with positive lymph nodes ($p < 0.001$).

Conclusions. The presence of lymph node metastases at the time of pulmonary metastasectomy for extrapulmonary carcinoma has an adverse effect on prognosis. Complete mediastinal lymph node dissection should be considered at the time of pulmonary metastasectomy for carcinoma to improve staging and guide treatment.

(Ann Thorac Surg 2004;77:1786-91)
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3-year survival

Negative : 69%

Positive : 38%

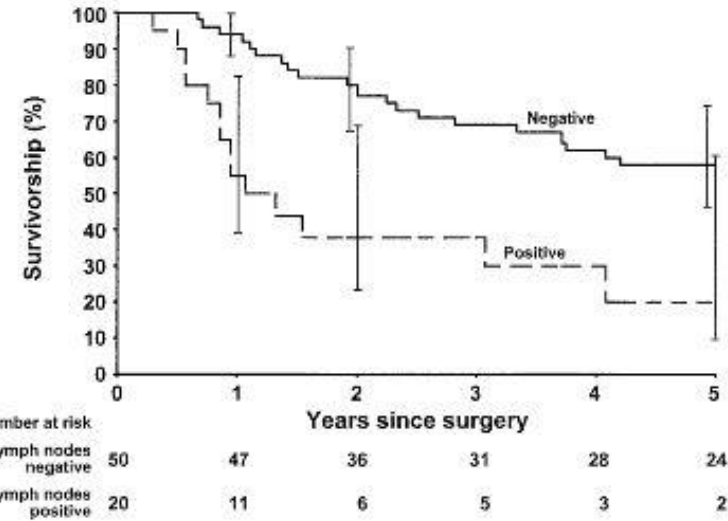


Fig 2. Estimated survival of 70 patients undergoing pulmonary metastasectomy and complete mediastinal lymphadenectomy without metastatic nodal involvement (negative) and with nodal involvement (positive). Zero time on the abscissa is date of first pulmonary metastasectomy and lymph node dissection. ($p < 0.001$).

Nodal Involvement at the Time of Pulmonary Metastasectomy: Experiences in 245 Patients

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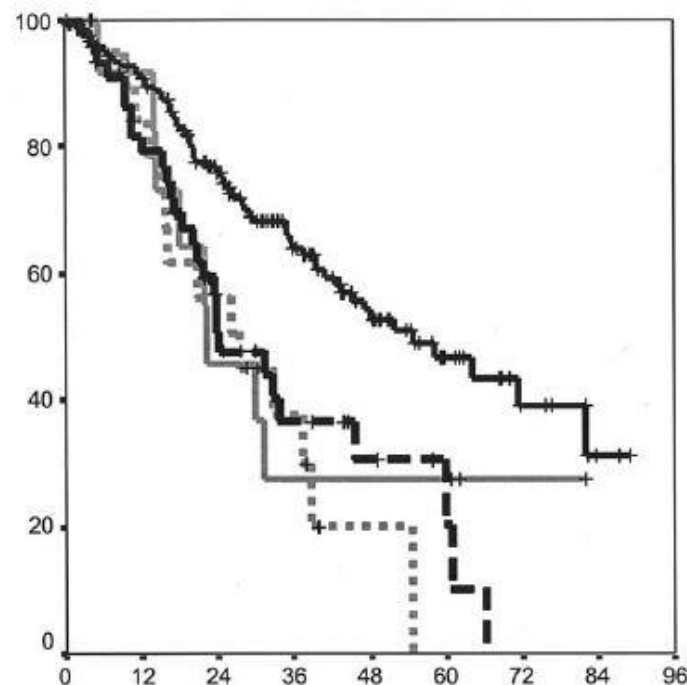
Background. Although routine systematic mediastinal and hilar lymph node dissection contemporary with pulmonary metastasectomy has not been uniformly performed in many thoracic surgical centers, the value of this procedure needs to be investigated.

Methods. Between 1996 and 2001, 245 patients (157 men, 88 women) underwent pulmonary resection of metastatic colorectal carcinoma, sarcoma, and renal cell carcinoma. Generally, systematic mediastinal and hilar lymph node dissection was performed concurrently with pulmonary metastasectomy. Patients were assessed for patterns of lymph node metastases. The frequency of lymph node involvement was determined. Patients and tumor characteristics were assessed to ascertain whether certain factors were likely to predict lymph node spread.

Results. Of the 245 patients (328 primary thoracic procedures), 165 had no lymph node involvement, 45 had pulmonary and hilar metastases, 22 had pulmonary, hilar, and mediastinal metastases, and 13 had only mediastinal involvement without pulmonary and hilar spread. Patients with more than one pulmonary metastasis or metachronous disease were more likely to have thoracic lymph node metastases. The risk for mediastinal lymph node involvement was even more likely for patients who had already pulmonary or hilar lymph node spread; the odds ratios (with 95% confidence intervals) were 1.30 (0.71 to 2.36), 1.32 (0.59 to 2.99), and 5.87 (2.73 to 12.6), respectively. Median survival for the group of patients after complete resection was 54.8 months (95% CI: 40.9 to 68.7); and for the patients with no lymph node involvement, it was 63.9 months (95% CI: 45.3 to 82.6); with N1 disease, 32.7 months (95% CI: 9.2 to 56.2); and with N1 + N2 disease, 20.6 months (95% CI: 5.1 to 36.1). The log-rank test revealed significance between N0 and N1 ($p = 0.018$) and N0 versus N1, 2 ($p = 0.001$).

Conclusions. We conclude that systematic mediastinal and hilar lymph node dissection contemporary with pulmonary metastasectomy offers a further understanding of metastatic disease and provides important information for complete surgical staging.

(Ann Thorac Surg 2006;81:448-54)
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Number at risk	survival (months)									
	0	12	24	36	48	60	72	84	96	
N0	165	136	93	61	39	17	8	2	0	
N1	45	33	17	10	5	2	0	0	0	
N2	13	10	5	3	3	3	1	0	0	
N1+N2	22	15	10	5	1	0	0	0	0	

Mediastinal evaluation

EBUS, EUS, Mediastinoscopy

Thoracic Lymphatic Involvement in Patients Having Pulmonary Metastasectomy

Incidence and the Effect on Prognosis

Mariano García-Yuste, MD, PhD, Stephen Cassivi, MD, PhD,† and Cristian Paleru, MD‡*

Abstract: Mediastinal and hilar lymph node involvement are rarely reported in the literature concerning pulmonary metastasectomy. The first problem is to determine with accuracy the incidence and location of thoracic lymph node involvement in patients with lung metastases. Determination of the impact on survival of this type of lymphatic spread may contribute to assessing whether metastatic nodal disease identified preoperatively is an absolute contraindication to metastasectomy. Systematic mediastinal lymph node dissection has revealed a statistically significant difference in survival between patients with lymph node involvement and those without lymph node metastases. Videomediastinoscopy to identify involved mediastinal lymph nodes can be safely performed and may have a role in a more accurate staging of the metastatic disease. The authors conclude that attention should be paid to ensuring that we do not operate on patients in whom we will leave behind diseases that we cannot reach. The discovery of mediastinal lymph node involvement may also influence decisions with respect to postresection adjuvant therapy.

Key Words: Pulmonary metastasectomy, Lymphadenopathy, Lymphatic spread.

(J Thorac Oncol. 2010;5: S166–S169)

and gauge opinion in this respect, it is necessary to conduct the appropriate examination of clinical reports in which, apart from any other prognostic factors, the presence and significance of nodal involvement have been analyzed.

WHAT IS THE TRUE INCIDENCE OF THORACIC LYMPH NODE INVOLVEMENT?

The first problem is to determine the incidence of positive thoracic lymph nodes in patients with lung metastases. In the International Registry of Lung Metastases between 1991 and 1995 of 5206 patients, 4572 (88%) underwent a complete surgical resection of the metastases.¹ Data are available from this source on the incidence of lymph node involvement in a large number of patients. The primary tumor was epithelial in 2660 cases, sarcoma in 2173, germ cell in 363, and melanoma in 328. Metastases to hilar or mediastinal nodes were found in 5% of patients overall (239 cases), corresponding to 11% in germ-cell tumors, 8% of melanomas, 6% of epithelial metastases, and only 2% of sarcomas. This is the largest data set available nevertheless, there are some difficulties in interpreting these results:

1. The incidence of lymphatic spread from the pulmonary metastases to the usual lymphatic drainage of the lung is common.
2. LN involvement = worse survival
3. LN involvement → postresection adjuvant therapy ?

Surgical Approach

1. Need for palpation

2. Thoracotomy **vs** VATS

Excellent visualization of the pleural surface

vs

Bimanually palpate the entire lung

3. Bilateral exploration **vs** unilateral exploration

4. Simultaneous **vs** staged approach

(in patients with bilateral metastases)

Table 1

Results of the ESTS survey regarding the surgical approach for pulmonary metastasectomy

	No. of Patients	(%)
Which is your preferred approach for unilateral metastases		
Anterolateral thoracotomy	53	(36.3)
Video-assisted thoracic surgery (VATS)	42	(28.8)
Posterior muscle sparing thoracotomy	38	(26)
Posterolateral thoracotomy	33	(22.6)
Horizontal axillary thoracotomy	15	(10.3)
Vertical axillary thoracotomy	10	(6.9)
Sternotomy	2	(1.4)
Other	7	(4.8)
Which is your preferred approach for bilateral metastases		
Bilateral staged thoracotomy	96	(66.2)
Sternotomy (1-stage)	39	(26.9)
Bilateral sequential thoracotomy (1-stage)	28	(19.3)
Bilateral staged video-assisted thoracic surgery (VATS)	18	(12.4)
Bilateral video-assisted thoracic surgery (VATS) (1-stage)	11	(7.6)
Clamshell (1-stage)	11	(7.6)
Other	3	(2.1)

Role of Video-Assisted Thoracic Surgery in the Treatment of Pulmonary Metastases: Results of a Prospective Trial

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Background. A retrospective review revealed a 42% error rate between computed tomographic scan reports and thoracotomy findings; therefore, a prospective study was designed to compare the value of computed tomographic scans, video-assisted thoracoscopic exploration, and open thoracotomy in the management of pulmonary metastases.

Methods. Eligibility included any patient with only one or two ipsilateral pulmonary metastases identified on computed tomographic scan who was being considered for surgical resection. Initially video-assisted thoracic surgery was performed and all lesions identified were resected. A thoracotomy adequate for complete lung palpation was then carried out and any additional lesions found were removed.

Results. Eighteen patients of a planned 50 were treated before closure of the study. Four patients (22%) had no additional lesions found at thoracotomy. The primary

sites of tumor were colon (10), breast (3), and one patient each skin (squamous), cervix, kidney, melanoma, and sarcoma. Four patients (22%) did have additional lesions at thoracotomy, which were benign. In the remaining 10 patients (56%) additional malignant lesions were found at thoracotomy after video-assisted thoracoscopic exploration. After 18 patients were entered, analysis of the early results disclosed a 56% failure rate of a computed tomographic scan and video-assisted thoracic surgery to detect all lesions. Being within the 95% confidence interval (32% to 78%), the study was abandoned.

Conclusions. We conclude that video-assisted thoracic surgery should be used only as a diagnostic tool in managing lung metastasis. A thoracotomy is required to achieve complete resection, which is the major survival prognosticator for satisfactory long-term results.

(Ann Thorac Surg 1996;62:213-7)

Comparison of pulmonary nodule detection rates between preoperative CT imaging and intraoperative lung palpation

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KEYWORDS:

Pulmonary metastasectomy;
Thoracoscopy;
CT imaging

Abstract

BACKGROUND: Recent advances in computed tomographic (CT) imaging have improved the detection rate of pulmonary metastasis. The aim of this study was to test the hypothesis that the pulmonary nodule detection rate for preoperative CT imaging and intraoperative palpation are now equivalent.

METHODS: A retrospective review of 108 pulmonary metastasectomies in 84 patients was performed. The number of nodules detected on preoperative CT imaging by radiologist report was compared with the number of malignant nodules identified on pathology. Secondary outcome measures were operative approach and primary malignancy.

RESULTS: Sarcoma metastases were the most common indication for resection ($n = 54$ [50%]). Thirty-three percent of metastasectomies were performed using a thoracoscopic approach. When thoracotomy was used, significantly more nodules were palpated and resected than were identified on preoperative CT imaging (3.24 vs 2.12, $P < .001$). Significantly more of these nodules were confirmed malignant on final pathology (2.40 vs 1.60, $P = .01$). This difference was not seen for thoracoscopic resections.

CONCLUSIONS: Although the sensitivity of CT imaging has improved, a significant number of malignant pulmonary nodules are detected intraoperatively that are not identified on preoperative imaging. Patients undergoing pulmonary metastasectomy require careful intraoperative palpation of lung parenchyma, and therefore open thoracotomy remains the standard of care.

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What Are the Considerations in the Surgical Approach in Pulmonary Metastasectomy?

Tamas F. Molnar, Cengiz Gebitekin,† and Akif Turna‡*

1. Thoracotomy seems to be the preferred approach
even with bilateral metastatic disease.
2. Sequential thoracotomy with an interval 3~6 weeks, interval CT.
(Bilateral metastatic disease)
3. With regard to VATS, the evidence for its superiority is a matter of debate.
4. VATS seems appropriate for diagnostic procedures,
but it is not the standard for therapeutic pulmonary metastasectomy.
5. No alternative to palpation currently exists.

Correlation between preoperative CT scan and lung metastases according to surgical approach in patients with colorectal cancer

Introduction: The number of lung metastases (M1) of colorectal carcinoma (CRC) in relation to the findings of computed tomography (CT) is the object of study.

Methods: Prospective and multicenter study of the Spanish Group for Surgery of CRC lung metastases (GECMP-CCR). The role of CT in the detection of pulmonary M1 is evaluated in 522 patients who underwent a pulmonary metastasectomy for CRC. We define M1/CT as the ratio

Results: 93 patients were performed by video-assisted surgery (VATS) and 429 by thoracotomy. In 90%, the M1/CT ratio was ≤ 1 , with no differences between VATS and thoracotomy (94.1% vs 89.7%, $p=0.874$). In the remaining 10% there were more M1s than those predicted by CT ($M1/CT > 1$), with no differences between approaches (8.6% vs 10%, $p=0.874$). 51 patients with $M1/CT > 1$, showed a lower median DSS (35.4 months vs 55.8; $p=0.002$) and DFS (14.2 months vs 29.3; $p=0.025$) compared to 470 with $M1/CT \leq 1$. No differences were observed in DSS and DFS according to VATS or thoracotomy.

Extent of Surgical Resection

Resection with **free** margins

Preservation as **much normal** lung parenchyma as possible.

ESTS survey

Wedge resection >>> Precision excision >> Segmentectomy > Lobectomy

Pneumonectomy (64%-relative contraindication, 23%-absolute contraindication)

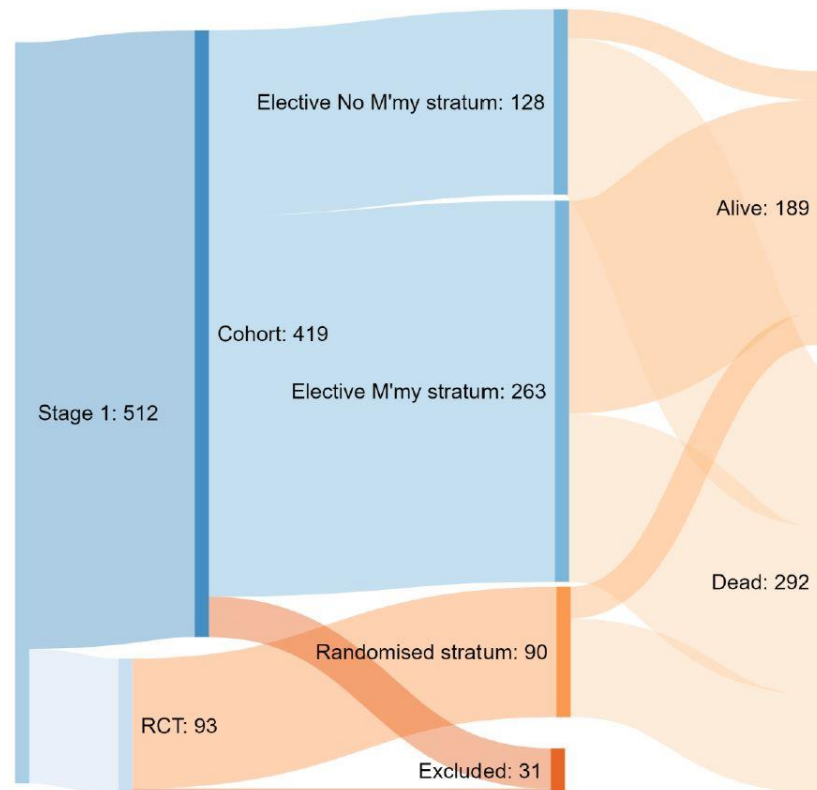
ESTS survey

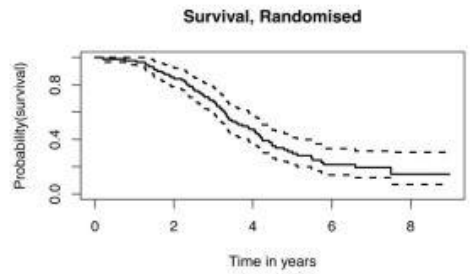
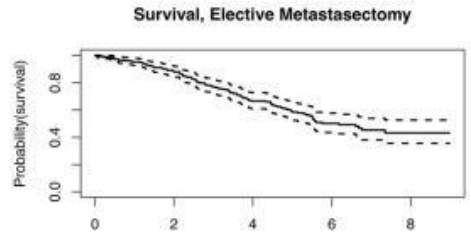
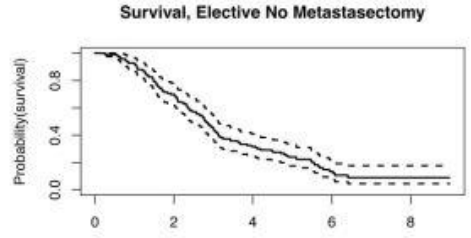
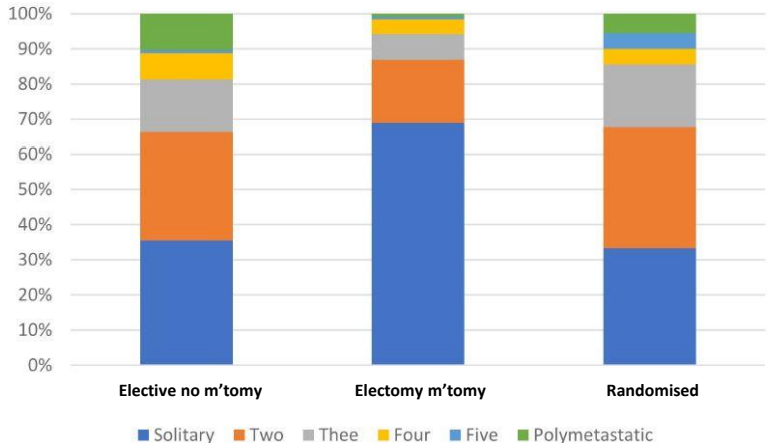
Surgical staplers >> Electrocautery > Direct suture

Other instrument (Harmonic scapel, Ligasure) – rarely used.

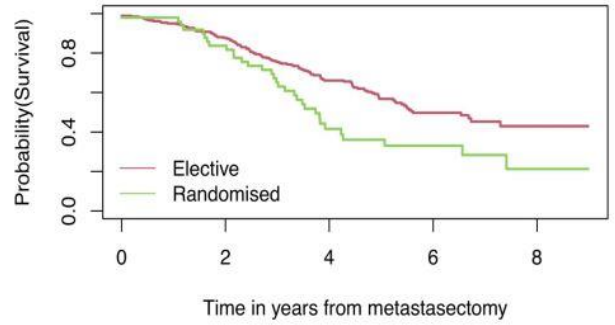
Since the establishment of the International Registry of Lung Metastases in the 1990s, pulmonary metastasectomy has been an area of debate between surgeons and oncologists. However, the lack of controlled trials and studies limited by short follow-up and small cohorts did not allow to overcome some skepticism; moreover, the heterogeneity of these patients in terms of demographic, biologic and histologic characteristics represents a clear limit even in the largest series.

Pulmonary Metastasectomy in Colorectal Cancer (PulMiCC) Cohort Study: analysis of case selection, risk factors and survival in a prospective observational study of 512 patients.





Survival, All Metastectomy Patients



	0	2	4	6	8
Solitary	263	224	140	53	10
Multiple	49	41	16	10	1

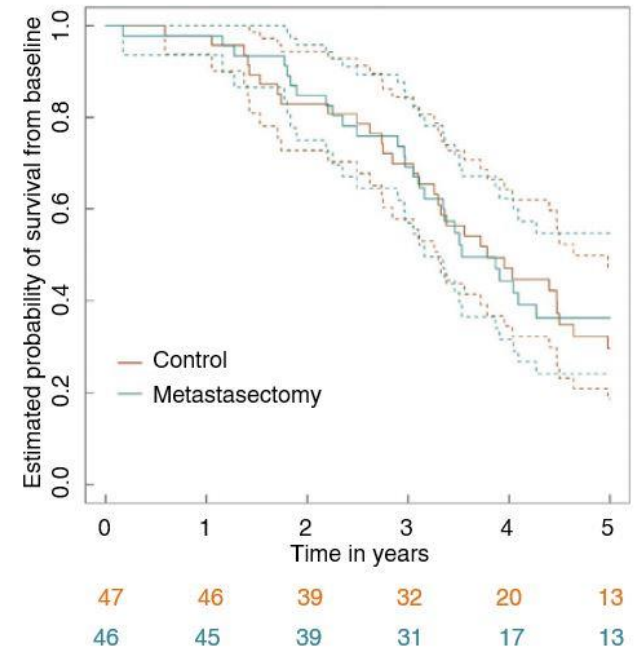
5a	128	88	38	10	2
5b	263	227	147	56	12
5c	90	77	41	12	2

Pulmonary Metastasectomy in Colorectal Cancer: updated analysis of 93 randomized patients – control survival is much better than previously assumed

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Figure 2 Sankey flow diagram of trial outcomes. y, years.



Summary

Prognostic factors

The number of lung metastases.

The disease-free interval since treatment of the primary tumor.

The tumor doubling time

The presence of lymph node metastases.

The histology of the primary tumor.

No randomized controlled study

Thank you !