

**Evoluzione
dell'approccio
al mesotelioma:
dalla multidisciplinarietà
alla interdisciplinarietà**

IL MESOTELIOMA PLEURICO MALIGNO: QUANDO E QUALE CHIRURGIA

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Brescia***

Quando?

La maggior parte delle linee guida pubblicate includono la chirurgia come componente essenziale nel trattamento del MMP

- diagnosi
- stadiazione
- palliazione
- trattamento
- recidiva

Quando?

- DIAGNOSI

Biopsia chirurgica con VATS o toracosopia medica

Ottenere tessuto per diagnosi istopatologica
e markers tumorali

Sensibilità 95%; Specificità 100%; valore predittivo negativo 94%

Materiale sufficiente per analisi multiple per med.
genomica

Quando?

- DIAGNOSI

Incisione per biopsia nella sede della probabile futura toracotomia
(principio disatteso da centri con poca esperienza)

Minuziosa descrizione dei reperti (anche con immagini e video) per documentare estensione e caratteristiche della malattia

Associare **talcaggio** per prevenire versamento e facilitare l'intervento chirurgico
(nota negativa: facile malinterpretazione delle Pet/Tc successive per falsi positivi)

U.O.C. Chirurgia Toracica - Brescia

Quando?

- DIAGNOSI

Chirurgia open:

con piccolo accesso in caso di
cavo pleurico inaccessibile per sinfisi

Quando?

- STAGING

Descrittivo: (T3/T4, aspetto delle placche pleuriche)

Biopsia chirurgica linfonodale se non accessibile con EBUS – EUS

Laparoscopia (sospetta estensione sottodiaframmatica)

Quando?

- PALLIAZIONE

Una pleurectomia parziale o un *debulking* possono essere considerati in pazienti sintomatici, non eligibili per chirurgia con intento radicale, con versamento recidivante/polmone incarcerato inespansibile

Intervento eseguibile anche in VATS

Intento:

- migliorare la funzione respiratoria
- migliorare QoL

Quando?

- TERAPIA

Chirurgia con intento macroscopicamente radicale
(MCR)

in pazienti con trattamento multimodale

Quando?

- TERAPIA

trattamento multimodale

- centrato su chirurgia ha una sopravvivenza globale del **15% a 5 anni** predittivo di una maggiore sopravvivenza⁽¹⁾

**non dissimile da altre patologie neoplastiche
localmente avanzate
(esofago, pancreas)⁽¹⁻²⁾**

¹ Taioli E., Wolf As, et al Determinants of survival in malignant pleural mesothelioma: a surveillance, epidemiology, and end results (SEER) study of 14.228 pts. *PLoS One* 2015; 10:e0145039

² Mayo SC, Nathan H., et al Conditional survival in pts with pancreatic ductal adenocarcinoma resected with curative intent. *Cancer* 2012;118:2674-81

Quando?

- TERAPIA

Chirurgia con intento radicale (MCR): **fattori prognostici per OS**

Intervento indicato per epiteliodi (ASCO) ⁽¹⁾
Possibile per bifasici a bassa percentuale sarc.
Sarcomatoidi N0 (chirurgia può essere l'unica
opzione data elevata chemioresistenza ⁽²⁻³⁻⁴⁾

1 Kindler HL, Ismaila N., et al: Treatment of malignant pleural mesothelioma: ASCO clinical practice guideline *J Clin Oncol* 2018;36(13):1343-73,

2 Sugarbaker DJ., Flores RM et al Resection margins, extrapleural nodal status and cell type determine postoperative long-term survival in trimodality Therapy of MMP: results in 183 patients. *J Thorac Cardiovasc Surg.* 1999;117(1):54-63

3 Musk AW., Olsen N., et al: Predicting survival in malignant mesothelioma. *Eur Respir J* 2011;38(6):1420-4

4 Saddoughi SA., Abdelsattar ZM., et al; National trends in the epidemiology of MMP: a national cancer data base study. *Ann Thorac Surg* 2018;105(2):432-7

Quando?

- TERAPIA

Chirurgia con intento radicale (MCR): **fattori prognostici⁽¹⁾ per OS**

- Istotipo epitelioide (differenze tra tubulopapillare, microcistico, trabecolare e solido)
- Sesso femminile
- No fumo tabacco
- No esposizione asbesto
- Lato sinistro
- Volume tumorale ($<500 \text{ cm}^3$)⁽²⁾
- Età
 - < 45 ⁽³⁾
 - > 70 anni ma minori di 80 ⁽³⁾

Il rischio di mortalità postop aumenta grandemente con l'aumentare dell'età dopo i 70 anni

1 Optiz I., Furrer K. Et al: *Thorac Surg Clin* 30 (2020) 435-449

2 Gill RR., Richards WG., et al. Epithelial malignant pleural mesothelioma after extrapleural pneumonectomy: stratification of survival with CT- derived tumor volume. *AJR Am J Roentgenol* 2012; 198(2):359-363

3 Yang CJ., Yan BV. Et al: Impact of age on long-term outcomes of surgery for MMP. *Clin Lung Cancer* 2016;17(5):419-26

Quando?

- TERAPIA

Chirurgia con intento radicale (MCR): **fattori prognostici**

F-FDG Uptake
Valore falsato dal talcaggio

Quando?

- TERAPIA

Chirurgia con intento radicale (MCR): **fattori prognostici per OS**

Volume tumorale e **OS** ⁽¹⁾

91,2 cm³ 37,18 mesi

245,3 cm³ 18 mesi

511,3 cm³ 8 mesi

¹ Optiz I., Weder W., et al Pleural Mesothelioma: is the surgeon still there?. *Ann Oncol* 29:1710-1717,20186

Quando?

- TERAPIA

Chirurgia con intento radicale (MCR): **fattori prognostici per OS**

Riduzione volume della gabbia toracica > 5%



Alta probabilità di non resecabilità ⁽¹⁾

¹ Optiz I., Furer K., et al Preoperative identification of benefit from surgery for Malignant Pleural Mesothelioma: *Thorac Surg Clin* 30 (2020) 435-449

Quando?

- TERAPIA

Chirurgia con intento radicale (MCR): **fattori prognostici** ⁽¹⁾

Negativi per OS

- Bassa emoglobina
- Aumento piastrine
- Aumento LDH
- Aumento GB
- Aumento proteina C reattiva

Positivi per OS

- Neutofili/linfociti < 5
- Linfociti/monociti $> 2,74$ ⁽²⁾

ASCO non raccomanda questi
markers
(sens . e spec. non sufficiente per
predire outcome)

1 Optiz I., Furrer K. Et al: Preoperative identification of benefit from surgery for Malignant Pleural Mesothelioma. *Thorac Surg Clin* 30 (2020) 435-449

2 Yamagishi T., Fusjimoto N., et al: Prognostic significance of the lymphocyte to monocyte ratio in patients with MMP. *Lung Cancer* 2015;90(1):11-7

Quando?

- TERAPIA

Chirurgia con intento radicale (MCR): **fattori prognostici** ⁽¹⁾

Negativi per OS

- N + (IASLC : non differenza tra N1 e N2)
- Dolore toracico
- Performance status

Positivi per OS

- N 0

**Differente prognosi per
N+ con più linfonodi
positivi**

¹ ERS/ESTS/EACTS/ESTRO guidelines for the management of malignant pleural mesothelioma *Eur Respir J* 2020;55:1900953

Quando?

- TERAPIA

Chirurgia con intento radicale (MCR): **fattori prognostici**

N+ nel MMP deve essere interpretato
differentemente da N+ polmonare

ASCO: N+ controlaterale o sopraclaveare:
CHT neoadiuvante e riconsiderare
chirurgia⁽¹⁾

1 Kindler HL, Ismaila N., et al: Treatment of malignant pleural mesothelioma: ASCO clinical practice guideline J
Clin Oncol 2018;36(13):1343-73,

Quando?

- TERAPIA
- Chemioterapia di induzione

Risposta parziale o completa: migliore sopravvivenza
mediana ⁽¹⁾

Ospedalizzazione postoperatoria più lunga e mortalità
a 30 giorni aumentata; sopravvivenza identica ⁽²⁾

1 Rush VW., Gill R., et al., A multicenter study of volumetric computed tomography for staging malignant pleural mesothelioma. *Ann Thorac Surg* 2016;102(4):1059-66

2 Verma V., Ahern C., et al., Treatment of malignant pleural mesothelioma with chemotherapy preceding versus after surgical resection. *J Thorac Cardiovasc Surg* 157(2):758-766

Quando?

- TERAPIA
- Chemioterapia di induzione

Progressione di malattia cattivo indice prognostico ⁽¹⁾

Incremento del volume tumorale e riduzione del volume polmonare (anche indipendentemente) sono associati a prognosi povera

Progressione non controindica intervento (se MCR) ⁽¹⁾

¹ Optiz I., Furer K., et al Preoperative identification of benefit from surgery for Malignant Pleural Mesothelioma: *Thorac Surg Clin* 30 (2020) 435-449

Quando?

- TERAPIA
- RT di induzione

STUDIO SMART (Surgery for Mesothelioma After Radiation Therapy) ⁽¹⁾

25- 30 Gy in 3-5 frazioni giornaliere per 1 settimana.

Settimana successiva chirurgia (EPP)

120 paz. Mediana sopravv 27,3 mesi – 84% 3 anni (epitelioidi)-13% bifasico

- Mesotelioma + radiosensibile del NSCLC
- Risposta immune contro il tumore
- Minore perdita ematica durante intervento

CHT adiuvante solo se N+

¹ Donahoe L.L., De Perrot M., et al The role of Extrapleural Pneumonectomy in malignant pleural mesothelioma. *Thorac Surg Clin* 30(2020) 461-471

Quando?

- TERAPIA

Infiltrazione localizzata della parete
toracica può non controindicare
l'intervento, se possibile MCR

Quando?

- TERAPIA

Al momento non ci sono criteri
generalmente accettati per
l'indicazione a chirurgia.

La corretta selezione rimane tuttavia il
parametro chiave per successo
chirurgico, bassa mortalità e morbidità

*BTS Guidelines: decisione su criteri
individuali del paziente*



U.O.C. Chirurgia Toracica - Brescia

Quale chirurgia?

- **nessuna chirurgia**
- **chirurgia limitata**
- **chirurgia MCR**
- **PD - ePD**
- **EPP**

Quale chirurgia?

Macroscopic Complete Resection (MCR)



EPP

PD
Extended PD (ePD)

Quale chirurgia?

**In passato la PD è stata spesso proposta
quando non indicata la EPP
(debulking)**

EPP eseguita su casi più evoluti

Quale chirurgia?

Rispetto a EPP,
PD non è stata codificata in passato

Rice D., Rush V., et al. Recommendations for uniform definition of surgical techniques for Malignant Pleural Mesothelioma: a consensus report of the international association for the study of lung cancer international study committee and the international mesothelioma interest group: *Thorac Oncol* 2011;6:1304-1312

Quale chirurgia?

Macroscopic Complete Resection (MCR)

Consensus 2011:

asportazione di tutto il tumore visibile e palpabile ⁽¹⁾

Ci sono però gruppi che definiscono MCR come:

“as complete as less than 1 cm of tumor left behind” ⁽²⁾

¹ Rice D., Rush V., et al Recommendations for uniform definition of surgical techniques for Malignant Pleural Mesothelioma: a consensus report of the international association for the study of lung cancer international study committee and the international mesothelioma interest group: *Thorac Oncol* 2011;6:1304-1312

² Sugarbaker DJ., Wolf AS., et al: Surgery for malignant pleural mesothelioma. *Expert Rev Respir Med* 2010;4:363-372

Quale chirurgia?

Macroscopic Complete Resection (MCR)

**Chirurgia radicale:
Sopravvivenza mediana > 3 anni**

PLEURECTOMIA PARZIALE

Periodo 1985-2012
34 studi
1916 pazienti

Rimozione parziale della pleura parietale e/o viscerale a scopo diagnostico o palliativo (residuo di malattia)

Lung Cancer 81 (2013) 319–327

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Lung Cancer

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Systematic review of pleurectomy in the treatment of malignant pleural mesothelioma

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ABSTRACT

Introduction: Pleurectomy/decortication (P/D) in the treatment of malignant pleural mesothelioma includes a number of procedures with different clinical indications and therapeutic intents. To unify the nomenclature, IMIG and IASLC recently defined P/D-related procedures according to surgical technique, including 'extended P/D', 'P/D' and 'partial pleurectomy'. The present systematic review aimed to assess the safety and efficacy of these techniques.

Methods: A systematic review of relevant studies was performed by electronic search of five online databases from 1985 to 2012 by two independent reviewers according to predefined selection criteria. **Results:** Thirty-four studies involving 1916 patients who underwent pleurectomy were included for quantitative analysis. These included 12 studies on 'extended P/D', 8 studies on 'P/D' and 14 studies on 'partial pleurectomy'. Perioperative mortality ranged from 0% to 11% and perioperative morbidity ranged from 13% to 43%. Median overall survival ranged from 7.1 to 31.7 months and disease-free survival ranged from 6 to 16 months. One study reported on quality-of-life outcomes using a standardized questionnaire suggesting superior outcomes for 'extended P/D' compared to extrapleural pneumonectomy.

Conclusions: Results of the present systematic review suggested similar perioperative mortality outcomes between different P/D techniques but a trend towards higher morbidity and length of hospitalization for patients who underwent 'extended P/D'. However, overall and disease-free survival appeared to favour 'extended P/D' compared to less aggressive techniques. Future studies on P/D should adhere to recent definitions to enable accurate analysis of similar procedures. Direct comparisons of pleurectomy to extrapleural pneumonectomy remain challenging, and should be restricted to 'extended P/D' procedures only.

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1. Introduction

Therapeutic surgical treatment of malignant pleural mesothelioma (MPM) includes extrapleural pneumonectomy (EPP) and pleurectomy/decortication (P/D), both of which can be incorporated into multimodality regimens involving neoadjuvant or adjuvant chemotherapy and adjuvant radiotherapy [1]. EPP is a form of cytoreductive surgery that aims to remove all visible tumour from patients who are deemed to have resectable disease, and involves en bloc resection of the pleurae, lung, ipsilateral hemidiaphragm, and ipsilateral pericardium, as originally described by Butchart in 1976 [2–4]. The definition of

pleurectomy, on the other hand, has been variable in regards to surgical technique, therapeutic intent and clinical indication.

To clarify and unify the definition of P/D, the International Mesothelioma Interest Group (IMIG), in collaboration with the International Association for the Study of Lung Cancer (IASLC), recently published a Consensus Report that classified pleurectomy-related procedures into three well-defined categories according to surgical technique, including 'extended P/D', 'P/D' and 'partial pleurectomy' [5]. This will enable future registries and studies to compare similar surgical procedures using a standardized nomenclature. The aim of the present systematic review was to apply the new IMIG and IASLC definitions to previous studies on P/D and to compare the safety and efficacy of these procedures in the treatment of MPM. Primary endpoints included perioperative mortality and long-term survival. Secondary endpoints included perioperative morbidity, disease-free survival and quality-of-life outcomes.

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Sopravvivenza media 9 – 13 mesi

U.O.C. Chirurgia Toracica - Brescia

Quale chirurgia?

Macroscopic Complete Resection (MCR): PD-ePD-EPP

BTS - ASCO - NCCN - ESMO

Analizzano pubblicazioni simili ma giungono a differenti conclusioni e hanno
prodotto differenti raccomandazioni

BTS: no chirurgia fuori da trials clinici (effetto dello studio MARS)

ASCO: massima citoriduzione per pazienti “early stage”

PD / EPP: sopravvivenza

Confronto difficile per:

- differenti indici di inclusione/esclusione
- protocolli differenti (induzione/adiuvante)
- trattamento chirurgico differente

		Mortalità	Mortalità 2 anni
1512	PD	1,7%	23,8%
1391	EPP	4,5%	25%

Sopravvivenza mediana:

- 53% degli studi meglio EPP
- 47% degli studi meglio PD

*Meta-Analysis of Survival After Pleurectomy Decortication
Versus Extrapleural Pneumonectomy in
Mesothelioma*

nuela Taioli, MD, PhD, Andrea S. Wolf, MD, Raja M. Flores,
TheAnnals of Thoracic Surgery

ma



Vol 99, Issue 2, Pages 472-480 (Feb 2015)

U.O.C. Chirurgia Toracica - Brescia

Quale chirurgia?

MARS TRIAL (2011)

12 ospedali UK, unico studio randomizzato su EPP vs No EPP (50 su 112)

Conclusioni: nessun vantaggio in OS e addirittura presenta un rischio per pazienti (*)

Conclusioni non supportate dai dati, casistica inadeguata e mortalità presentata nettamente superiore alle altre casistiche (11,8% a 30 gg vs ~ 4%)

* Treasure T., Lang-Lazdunski L., et al.: Extra-Pleural pneumonectomy vs no EPP for patients with MPP: clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study. *Lancet Oncol* 2011;12(8):763-772

PLEURECTOMIA e DECORTICAZIONE RADICALE

Asportazione della pleura viscerale e parietale MCR

Senza asportazione di diaframma e pericardio

Sopravvivenza media 12 – 18 mesi



Systematic review of pleurectomy in the treatment of malignant pleural mesothelioma

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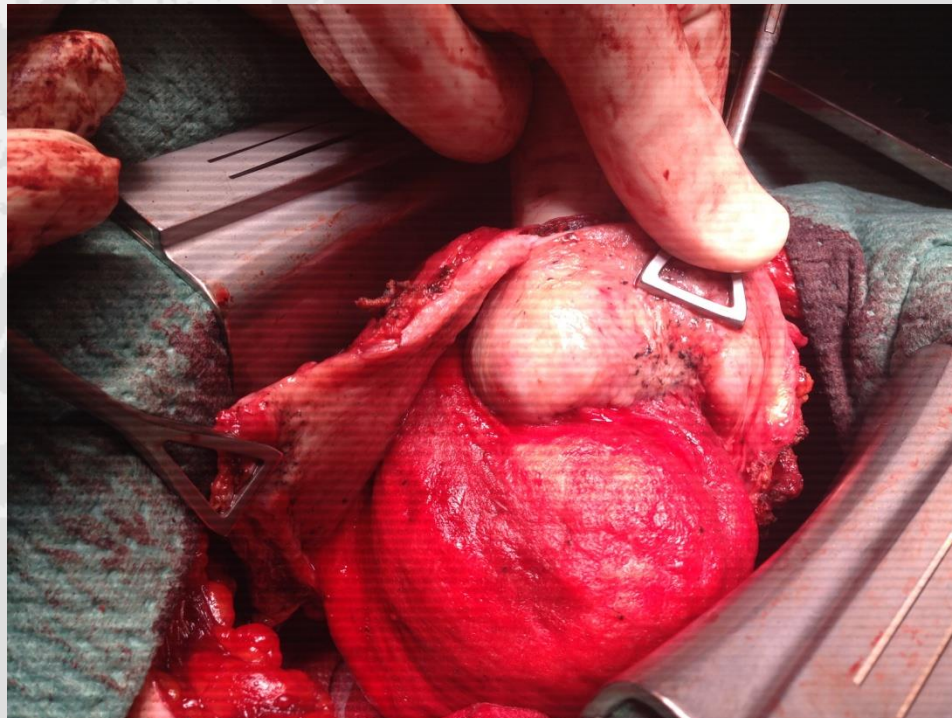
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PLEURECTOMIA e DECORTICAZIONE ESTESA (ePD)

Asportazione della pleura viscerale e parietale MCR con asportazione di diaframma e pericardio



Systematic review of pleurectomy in the treatment of malignant pleural mesothelioma

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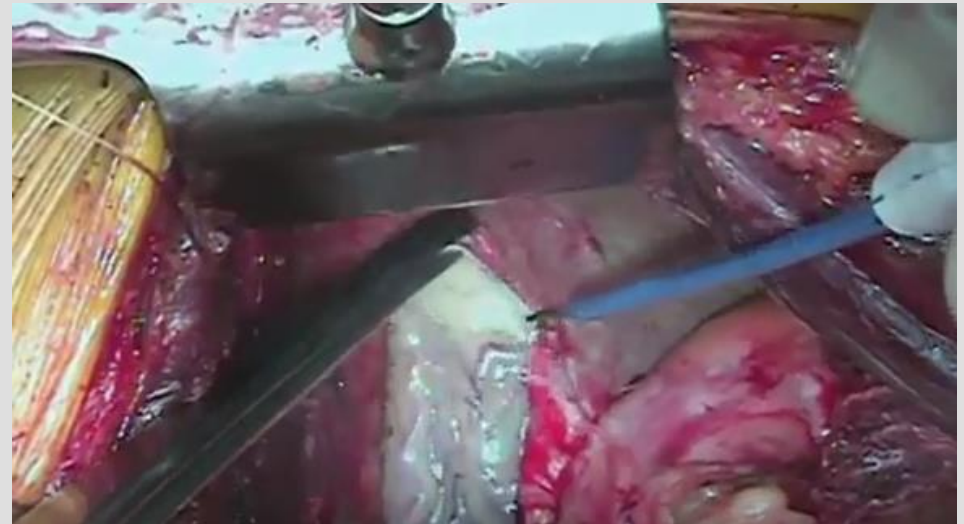
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Sopravvivenza media 15 – 25 mesi

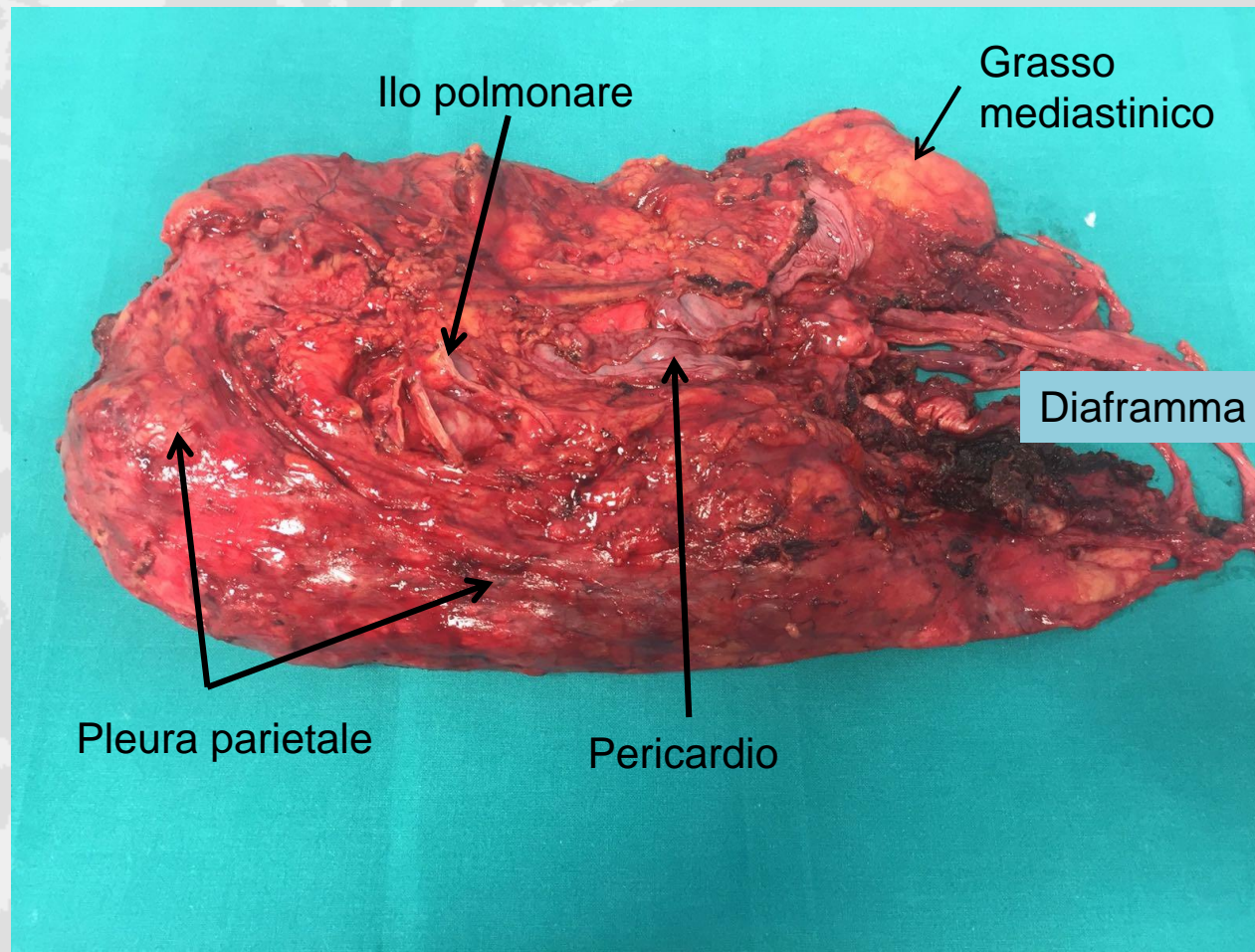


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EPP (EXTRAPLEURAL PNEUMONECTOMY)

Asportazione di tutto il sacco pleurico insieme al polmone con asportazione di diaframma e pericardio



PD / ePD complicanze

Author, Year	Number of Cases P/D; EPP	Complications P/D Total (%); Specific (n)	Complications EPP Total (%); Specific (n)
Allen, 1994 ⁴³	56; 40	26.8%; AR (5), PAL (6)	30%; AR (3), BPF (2), CHT (1)
Pass, Kranda, 1997 ⁴⁴ ; Pass, Temeck, 1997 ⁴⁵	39; 39	AR (2), PF (1)	AR (14), BPF (7)
Aziz, 2002 ⁴⁶	47; 64		21%; ARDS (6)
de Vries, 2003 ⁴⁷	29; 17	PAL (3)	
Okada, 2008 ⁴⁸	34; 31	15%; AR (3)	48%; AR (8), BPF (2), CHT (2), PF (2)
Schipper, 2008 ⁴⁹	44; 73	9%	50.7%; ARDS (4), BPF (5), PE (3), PF (6)
Borasio, 2008 ⁵⁰	12; 15	33%; AR (1)	60%; AR (4)
Mineo, 2010 ⁵¹	44; 27	13.6%; DVT (2)	33%; AR (4), BPF (2), DVT (2)
Luckraz, 2010 ⁵²	90; 49	AR (8)	AR (2), BPF (7)
Friedberg, 2011 ²⁸	14; 14	AR (3), CHT (2), DVT (4), PAL (1)	AR (3), CHT (1), DVT (6), PE (1)
Rena, 2012 ⁵³	37; 40	24%; AR (2)	62%; AR (17), ARDS (1), BPF (1), PE (1), PF (1)
Nakas, 2012a ³¹ ; Nakas, 2012b ⁵⁴	85; 127	PAL (20)	
Lang-Lazdunski, 2012 ⁵⁵	61; 25	27.7%; AR (2), ARDS (1), CHT (4), PAL (10)	68%; AR (7), ARDS (1), BPF (2), PE (1)
Bovolato, 2014 ⁵⁶	202; 301	10.4%; AR (9), PAL (5)	21.6%; AR (32), ARDS (1), BPF (3), DVT (2), PE (3), PF (3)
Kostron 2017 ²⁹	26; 141	58%; AR (4), ARDS (1), CHT (2), DVT (1), PAL (15)	38%; AR (50), ARDS (2), BPF (17), CHT (10), DVT (1), PE (4), PF (7)

Mortalità media 1,7%

Morbilità 13 – 48%

Grande variabilità per differenza nelle coorti dei pazienti e nella definizione di morbidità

- Perdita aerea prolungata (2-3 sett)
- Sequele da drenaggio prolungato
- Perdita ematica (2-3 Litri)
- Coagulopatia
- Simili a EPP (FA, DVT, IMA, empiema)

Meta-Analysis of Survival After Pleurectomy Decortication Versus Extrapleural Pneumonectomy in mesothelioma

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anuela Taioli, MD, PhD, Andrea S. Wolf, MD, Raja M. Flores, TheAnnals of Thoracic Surgery Vol 99, Issue 2, Pages 472-480 (Feb 2015)



RESEARCH ARTICLE

Determinants of Survival in Malignant Pleural Mesothelioma: A Surveillance, Epidemiology, and End Results (SEER) Study of 14,228 Patients

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1/8

Abstract

Introduction

Left untreated, malignant pleural mesothelioma (MPM) is associated with uniformly poor prognosis. Better survival has been reported with surgery-based multimodality therapy, but to date, no trial has demonstrated survival benefit of surgery over other therapies. We evaluated whether cancer-directed surgery influenced survival independently from other predictors in a large population-based dataset.

Methods

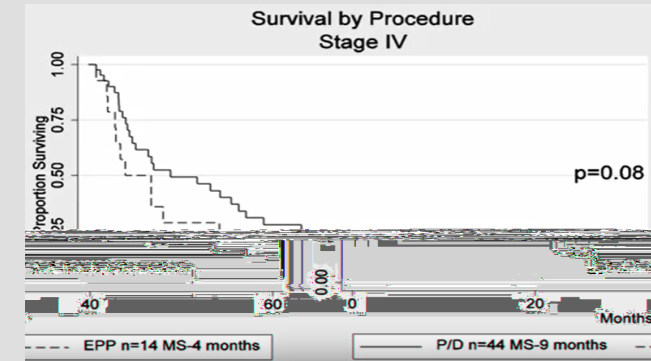
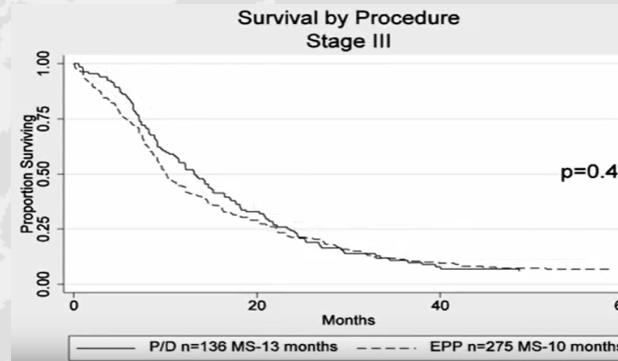
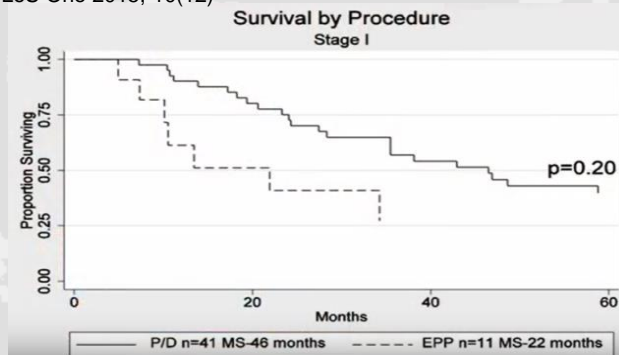
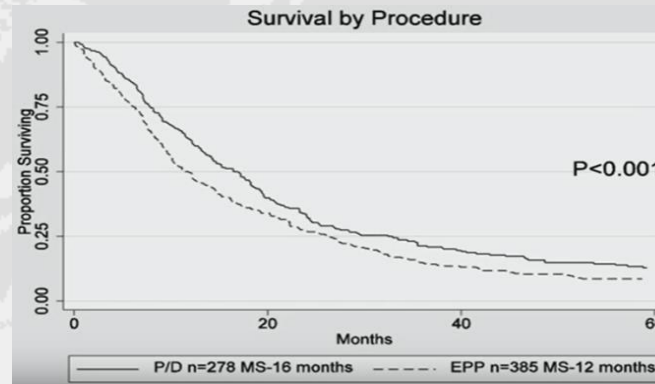
The SEER database was explored from 1973 to 2009 to identify all cases of pathologically proven MPM. Age, sex, race, year of diagnosis, histology stage, cancer-directed surgery, radiation, and vital status were analyzed. The association between prognostic factors and survival was estimated using Cox regression and propensity matched analysis.

Results

There were 14,228 patients with pathologic diagnosis of MPM. On multivariable analysis, female gender, younger age, early stage, and treatment with surgery were independent predictors of longer survival. In comparison to no treatment, surgery alone was associated with significant improvement in survival [adjusted hazard ratio (adj HR) 0.64 (0.61–0.67)], but not radiation [adj HR 1.15 (1.08–1.23)]. Surgery and radiation combined had similar survival as surgery alone [adj HR 0.69 (0.64–0.76)]. Results were similar when cases diagnosed between 1973 and 1999 were compared to cases diagnosed between 2000 and 2009.

PD / EPP sopravvivenza SEER Database (NCI) (Surveillance Epidemiology & End Results)

Taioli E., et al. Determinants of Survival in Malignant Pleural Mesothelioma: a Surveillance, Epidemiology, end End Results (SEER) Study of 14228 patients
PLoS One 2015; 10(12)



(PD stadi iniziali - EPP stadi più avanzati ?)

U.O.C. Chirurgia Toracica - Brescia

PD / ePD

Attualmente la procedura chirurgica più utilizzata per:

- Meglio tollerata
- Minore mortalità (1,7% vs 4,5% EPP)
- Funzione polmonare postoperatoria meno alterata
- Possibilità di offrire l'opzione chirurgica anche a paz con funzione respiratoria meno favorevole o più anziani
- Pazienti meglio disposti a tollerare terapia adiuvante e trattamenti della recidiva
- QoL migliore dopo 6-12 mesi (ma dolore e tosse uguali a EPP)

Chirurgia ad elevato impegno

U.O.C. Chirurgia Toracica - Brescia

PD / ePD

Ma....

- 95% ripresa di malattia locale⁽¹⁾ per rischio R1
- 39% recidiva sul polmone per linfangite ⁽²⁾
- Rischio di insemminazione della toracotomia
- Infezione del cavo residuo per perdita aerea persistente sottostimato ⁽³⁾
- Rt dopo PD elevato rischio di polmonite da raggi

1 Flores RM., Pass HL., et al: Extrapleural pneumonectomy versus pleurectomy/decortication in the surgical management of MPP: results in 633 patients. *J Thorac Cardiovasc Surg* 2008;135:620-6

2 Donahoe L.L., De Perrot M., et al The role of Extrapleural Pneumonectomy in malignant pleural mesothelioma. *Thorac Surg Clin* 30(2020) 461-471

3 Optiz I., Weder W.: Pleural mesothelioma: is the surgeon still there? *Ann Oncol* 29:1710-17,2018

EPP

- IASLC: migliore sopravvivenza per stadi iniziali con EPP ⁽¹⁾
- Differenza di risultati di PD e EPP dipende da esperienza dei centri (enorme variabilità in morbidità, mortalità, OS, DFS, QoL) ⁽²⁾
- STS database: volume di attività condiziona risultati (centri con meno di 5 EPP/anno hanno incidenza significativamente più alta di ARDS) ⁽³⁾
- EPP se MCR ottenibile solo con asportazione del polmone ⁽⁴⁾
(molti pazienti sono già funzionalmente pneumonectomizzati)

1 Rush VW., Giroux D., et al., Initial analysis of the international association for the study of lung cancer mesothelioma database. *J Thorac Oncol* 2012;7(11):1631-9

2 Optiz I., Weder W.: Pleural mesothelioma: is the surgeon still there? *Ann Oncol* 29:1710-17, 2018

3 Burt BM., Cameron RB., et al: Malignant Pleural Mesothelioma and the Society of Thoracic Surgeons database: an analysis of surgical morbidity and mortality. *J Thorac Cardiovasc Surg* 2014;148(1):30-35

4 Optiz I., Weder W.: et al A nuanced view of Extrapleural Pneumonectomy for malignant pleural mesothelioma. *Ann Transl Med* 2017;5(11):237

CHEMIOTERAPIA IPERTERMICA INTRAOPERATORIA (IHC)

IPERTERMIA e CHEMIOTERAPIA

- Da tempo note le alterazioni del tessuto tumorale dopo ipertermia (40-42°)
(edema, emorragia, alterazioni dell'attività replicativa)
- L'associazione con chemioterapici aumenta l'attività antiblastica
- Nota e largamente utilizzata la perfusione ipertermica localizzata (arti, fegato ecc.)
- CHT con platino aumenta radiosensibilità del tessuto neoplastico

U.O.C. Chirurgia Toracica - Brescia

CHEMIOTERAPIA IPERtermica INTRAOPERATORIA (IHC)

RAZIONALE

NEUTRALIZZAZIONE FOCI TUMORALI MICROSCOPICI RESIDUI

NEUTRALIZZAZIONE CELLULE ESFOLIATE DURANTE L'INTERVENTO

U.O.C. Chirurgia Toracica - Brescia

IHC NOSTRO PROTOCOLLO

dosaggi tissutali platino:

sulla superficie di contatto con il lavaggio ipertermico e in profondità nella parete si ottengono in media concentrazioni rispettivamente oltre **100** volte superiori e anche **5** e **10** volte superiori rispetto ad una chemioterapia sistemica considerata terapeutica

RISULTATI CHIRURGIA TORACICA DI BRESCIA

	N° PZ	MORTALITA'	%
PLEURECTOMIA DECORTICAZIONE (12 PT + IHC)	94	1 DISSEZIONE AORTICA	0.9
PNEUMONECTOMIA EXTRAPLEURICA PERICARDIECTOMIA EMIDIAFRAGMECTOMIA (44 PT + IHC)	133	5*	3.7
TOTALE	227	6	2.6

- Polmonite ab ingestis in pz con fistola tracheoesofagea post intubazione
- Ipertensione polmonare
- 2 ARDS
- 1 perforazione aortica

U.O.C. Chirurgia Toracica - Brescia

RISULTATI CHIRURGIA TORACICA DI BRESCIA

Mediana sopravvivenza:

- PD: 9,7 mesi
- EPP 12.2 mesi

PD o e/PD MCR: follow-up 13-55 mesi
media 32 mesi
mediana 30 mesi

EPP + IHC + IMRT:

1 anno:	69,4%
2 anni:	56.4%
3 anni:	48.3%
4 anni:	41 %
5 anni:	23.5%

U.O.C. Chirurgia Toracica - Brescia

CONCLUSIONI

La chirurgia mantiene un ruolo fondamentale nello studio e nel trattamento di pazienti attentamente selezionati

PD o ePD dovrebbero essere preferite quando MCR
EPP presenta mortalità a breve termine 2,5x superiore alla PD o ePD

Se intraoperatoriamente con PD o ePD non è perseguibile MCR per
infiltrazione del parenchima polmonare o ilare:
valutare EPP
(pazienti che allo studio preop. risultino candidabili)

CONCLUSIONI

Se la chirurgia è eseguita in centri ad alto volume:

non vi sono in letteratura apparenti differenze in sopravvivenza, mortalità postoperatoria o riospedalizzazione tra le differenti tecniche chirurgiche

Ciò conferma la validità di entrambe le opzioni per il trattamento del MMP

