Surgical therapy of mesothelioma, who should be operated

Walter Weder MD
Professor of Surgery
University Hospital Zurich
Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study

Tom Treasure, Loic Lang-Lazdunski, David Waller, Judith M Bliss, Carol Tan, James Entwisle, Michael Snee, Mary O’Brien, Gill Thomas, Suresh Senan, Ken O’Byrne, Lucy S Kilburn, James Spicer, David Landau, John Edwards, Gill Coombes, Liz Darlison, Julian Peto, for the MARS trialists

„These data, although limited, suggest that radical surgery in the form of EPP within trimodal therapy offers no benefit and possibly harms patients.“
The MARS feasibility trial: conclusions not supported by data

Walter Weder, Rolf A Stahel, Paul Baas, Urania Dafni, Marc de Perrot, Brian C McCaughan, Takashi Nakano, Harvey I Pass, Bruce WS Robinson, Valerie W Rusch, David J Sugarbaker, Nico van Zandwijk

THE LANCET Oncology

Lancet Oncol. 2011 Nov;12(12):1093-4
A systematic review of extrapleural pneumonectomy for malignant pleural mesothelioma.

Cao CQ, Yan TD, Bannon PG, McCaughan BC

*J Thorac Oncol* 2010; 1692-703

Median overall survival 9.4 to 27.5 months
Perioperative mortality 0 to 11.8%

The current evidence suggests that selected patients with malignant pleural mesothelioma may benefit from EPP, especially when combined with neoadjuvant or adjuvant chemotherapy and adjuvant radiotherapy.
Case 1

• 61 years old female
• chest pain, dyspnea
• Thoracoscopic biopsy: Epithelial Mesothelioma
• no asbestos exposure
Treatment + Follow-up

- Neoadjuvant Chemo with Cis/Pem (3 cycles)
- EPP → ypT2 ypN0 (0/17) cM0

Last CT-scan 09/11 (5.5 years later):
  No sign for recurrence or metastasis

Patient plays Tennis and Golf
Case 2

- 60 years old female
- cough, dyspnea
- thoracoscopic biopsy: Epithelial
- thoracoscopic biopsy: Mesothelioma
- no asbestos exposure
Neoadjuv. Chemo with Cis/Pem (3 cycles)

Pleurectomy, Wedge resection ML and LL

ypT2 ypN0 cM0

3 months later: recurrence thoracic wall

Treatment + Follow-up

3 months later: recurrence thoracic wall

resection and radiotherapy

17 months later: progression

Chemo with Paraplatin/Pem

27 months later: progression contralateral chest
SAKK 17/00: Overall survival

One-year survival: 69%
Median survival: 19.8 mo
[95% CI: 14.6-24.5]

Resected patients* (N=45, 74%)
One-year survival: 78%
Median survival: 23.0 mo
[95% CI: 16.6-32.9]

Weder and Stahel, Ann Oncol 2007
# EPP in multimodality therapy

<table>
<thead>
<tr>
<th>Investigator</th>
<th>CTX</th>
<th>EPP</th>
<th>RTX</th>
<th>MST (months)</th>
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<td>49</td>
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Overall survival by histology
ITT (n=185)

Median OAS
sarcomatoid (n=9) 6 months (95% CI: 6; 7)
epithelial (n=113) 21 months (95% CI: 18; 23)
biphasic (n=63) 14 months (95% CI: 8; 20)

log rank p=0.015
Overall survival by histology
EPP (n=124)

- sarcomatoid (n=2) 6 months (95% CI: -; -)
- epithelial (n=79) 22 months (95% CI: 18; 26)
- bi-phasic (n=43) 18 months (95% CI: 8; 27)

Log rank p=0.086
Influence of positive Lymphnode-stations after EPP

**Median OAS**
- ypN 0 (n=82) 23 months (95% CI: 20; 27)
- ypN >0 (n=42) 20 months (95% CI: 15; 25)

**Log rank p=0.027**
The Appearance of the Right Major Fissure After a Radical Pleurectomy

Azygos vein
Posterior segmental artery
Superior segmental artery
Basilar arterial trunk
Middle lobe arterial trunk

courtesy J. Friedberg
Mechanisms of PDT Effect

- Direct cell kill
  - Mitochondria
  - Cell membrane
  - Apoptosis
- Damage to neovasculature
- Immune response
  - Local
  - Systemic

courtesy J. Friedberg
28 patients (14/14) having modified EPP or RP and PDT (86% stage III/IV)
Completeness of P/D

S. Bölübkbas, Lung Cancer 2009
## Series with P/D in multimodality therapy

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Patients</th>
<th>CTX Setting</th>
<th>P/D</th>
<th>Other Modalities</th>
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</table>
Patients with malignant pleural mesothelioma

cT1-3 cN0-2 cM0

resectable tumor

- Age 18 - 70
- PS 0-1

- Age > 70, PS > 1
- co-morbidities / functional reserve

induction CTX
+ EPP
+ / - radiotherapy
SAKK 17/04

+ / - induction CTX
+ Pleurectomy / Decortication
+ / - adjuvant CTX

Phase I intracavitary CTX Cisplatin - Fibrin
Patients with malignant pleural mesothelioma

- fit for surgery
- not fit for debulking surgery

unresectable tumor

- partial pleurectomy
decortication

1. palliative CTX
2. talc pleurodesis

Phase I intracavitary CTX Cisplatin - Fibrin