Extrapleural Pneumonectomy for Malignant Mesothelioma: Pro

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Malignant Pleural Mesothelioma (Epidemiology)

- Incidence: 7/mil (Japan) to 40/mil (Australia)


- Latency 40 years for mesothelioma & asbestos

- Median survival 9-17 months (6-9 mos. w/o tx)
Malignant Pleural Mesothelioma (Diagnosis)

- Presentation: Variable (Cough/Chest Pain in 60%)
- Avg length to diagnostic imaging is usually 2-3 months
- Plain film radiographs
Malignant Pleural Mesothelioma (Diagnosis)

- CT Scan – chest
- FNA/Cytology:
  - Inadequate for dx
- Tissue for definitive diagnosis:
  - Thoracotomy, pleural bx
  - Thoracoscopic bx
  - CT-guided pleural bx
Malignant Pleural Mesothelioma (Staging)

• AJCC adopted staging guidelines set forth by International Mesothelioma Interest Group (IMIG) of 1995
Resectable Staging

- **T1** - Tumor involves ipsilateral parietal pleura, with or without focal involvement of the visceral pleura.
- **T1a** - Tumor involves ipsilateral parietal (mediastinal, diaphragmatic) pleura. No involvement of the visceral pleura.
- **T1b** - Tumor involves ipsilateral parietal (mediastinal, diaphragmatic) pleura, with focal involvement of the visceral pleura.
- **T2** - Tumor involves any of the ipsilateral pleural surfaces with at least 1 of the following:
  - confluent visceral pleural tumor (including fissure)
  - invasion of diaphragmatic muscle
  - invasion of lung parenchyma
- **T3** - Tumor involves any of the ipsilateral pleural surfaces with at least 1 of the following:
  - invasion of the endothoracic fascia
  - invasion into mediastinal fat
  - solitary focus of tumor invading the soft tissues of the wall
  - non-transmural involvement of the pericardium
Not surgically resectable

- T4 - Involvement all of the ipsilateral pleural surfaces with at least one of the following:
  - Extension to the internal surface of the pericardium w/wo effusion, peritoneum, mediastinal structures, contralateral pleura, spine
  - Diffuse extension or multifocal mass in chest wall with or without rib destruction
• N0 - No lymph node involvement
• N1 - Involvement of ipsilateral bronchopulmonary, hilar lymph node
• N2 - Involvement of ipsilateral mediastinal and/or internal mammary and/or peri-diaphragmatic lymph node
• N3 - Involvement of any contralateral mediastinal and/or internal mammary and/or supraclavicular lymph node
• M0 - No extrathoracic metastasis
• M1 - Extrathoracic metastasis, hematogenous or in non-regional lymph nodes
# Malignant Pleural Mesothelioma (Staging)

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Malignant Pleural Mesothelioma (Staging)

- AJCC adopted staging guidelines set forth by International Mesothelioma Interest Group (IMIG) of 1995

- Alternative staging established by Sugarbaker and colleagues
Brigham and Women’s Hospital Staging System

I - Within the capsule of the parietal pleura: ipsilateral pleura, lung, pericardium, diaphragm

II - Invading chest wall or mediastinum: esophagus, heart, opposite pleura
- Positive lymph nodes within the chest

III - Through diaphragm to peritoneum; opposite pleura
- Positive lymph nodes outside the chest

IV - Distant blood-borne metastases
Histologic Grading/Type

- **Epithelioid type:** Best prognosis overall, most frequent type (60%)

- Biphasic (Mixed, 30%)

- Sarcomatoid type (10%)
Tri-modality Therapy

1. Adjuvant or neoadjuvant chemotherapy (Platinum-based, includes pemetrexed)

2. Adjuvant or neoadjuvant radiotherapy

3. Surgery (?)
Extrapleural Pneumonectomy (EPP)

• Originally described for treatment of tuberculous emphysema (1949)
• *En bloc* resection of affected lung, pericardium and hemi-diaphragm
• As described by Sugarbaker DJ:
  – Involves sampling of nodes: hilar, paraesophageal, inferior pulm lig, peridiaphragmatic & subcarinal
  – Left…includes…aortopulmonary
Sugarbaker et al.

- Retrospective review n=183
- All patients received adjuvant chemoradiotherapy
- 3.8% perioperative mortality:
  - 3 due to PE
  - 2 due MI
  - 1 cardiac herniation into pericardial defect
  - 1 respiratory distress
- 50% perioperative morbidity (All)
  - 24.5% major
  - 41% minor
Sugarbaker et al.

- Median survival: 19 months
- 2-year survival rates: 38%
- 5-year survival rates: 15%

- Positive prognostic variables:
  - Epithelioid subtype
  - Negative margins at time of surgery
  - Absence of extrapleural LN involvement
Sugarbaker et al.

1. 19 months median survival versus historical controls of 5-12 months
2. 3.8% perioperative mortality versus 1976 published mortality of 31% (Butchart and colleagues)
3. Identified significance of histology in outcomes (epithelioid better vs. those with sarcomatoid histology)
4. Identified extrapleural lymph node involvement as significant negative prognostic factor (revised staging)
Batirel et al.

• Single institution prospective feasibility trial (Turkey)

• N=20, all within stage III (IMIG) diagnosis

• All intent to treat with EPP, 54 Gy XBR, platinum-based therapy (initially with gemzaar, then to pemetrexed)
Batirel et al.

- Median survival = 17.2 months (n=20)
- 4 patients unable to perform EPP (2 with diffuse disease, 1 with micromets to intercostals and 1 did not tolerate SLV)
- 19.6 mos for those capable of EPP
- 23.9 mos if tolerated tri-modal therapy
Pagan et al.

- Prospective feasibility trial of trimodal therapy (Italy)
- N=54
- 4.5% 30-day mortality, overall complication rate 50% with major morbidity 36%
- Total median survival 20%
Treasure et al.

- Published in 2011
- 12 centers cooperating in United Kingdom
- Prospective feasibility trial: initial enrollment period: 1 year (Actual 3 years)
- 112 registered, 50 enrolled successfully, n=24 to EPP, 26 to no EPP
- Of 24 who enrolled successfully, 16 successfully received EPP
Treasure et al.

- Median survival 14.4 mos. with surgery versus 19.5 mos. without
- Corrected hazard ratio: 1.90 favoring no surgery
Treasure et al.

- Criticisms abound – recruitment period extended to 3 years
- 16 patients received EPP and chemoradiotherapy in 12 centers
- 5 patients in “surgical arm” did not undergo surgery (3 voluntarily refused and 2 with medical advice) and 3 in the “non-surgical arm” ultimately received EPP
- Operative mortality was 18%
Conclusions

• Extrapleural pneumonectomy is safe in the right hands
• Extrapleural pneumonectomy is the standard of care for management of malignant pleural mesothelioma
• Additional studies are needed to evaluate efficacy of EPP versus non-historical controls
References


