Metastatic Epidural Spinal Cord Compression (MESCC)
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MESCC
Compression of the spinal cord from metastatic cancer located outside the spinal cord, subarachnoid space, and dura mater.

MESCC
- 5-14% of all cancer patients affected
- Over 20,000 new cases per year in the USA
- Major QOL/symptomatic issues
- About 1/3 of patients survive for 1 year in this condition

MESCC: Method of Spread
- 85% From vertebral body or pedicle
- 10% Through intervertebral foramina (from paravertebral nodes or mass)
- 4% Intramedullary spread
- 7% (Low) Direct spread to epidural space

MESCC: PRIMARY TUMORS
- Breast: 35%
- Lung: 20%
- Prostate: 9%
- Sarcoma: 7%
- Unknown primary: 7%
- Melanoma: 6%
- Other: 16%
100%
**MESCC: FIRST SYMPTOMS**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>95%</td>
</tr>
<tr>
<td>Weakness</td>
<td>5%</td>
</tr>
<tr>
<td>Ataxia</td>
<td>1%</td>
</tr>
<tr>
<td>Sensory loss</td>
<td>1%</td>
</tr>
</tbody>
</table>

**Symptoms and Signs at Dx**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>%</th>
<th>Signs</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>96</td>
<td>Weakness</td>
<td>86</td>
</tr>
<tr>
<td>Weakness</td>
<td>76</td>
<td>Sensory loss</td>
<td>78</td>
</tr>
<tr>
<td>Bladder/bowel</td>
<td>57</td>
<td>Abnl reflexes</td>
<td>56</td>
</tr>
<tr>
<td>Sensory loss</td>
<td>51</td>
<td>Ataxia</td>
<td>7</td>
</tr>
</tbody>
</table>

**MESCC: DURATION OF SYMPTOMS BEFORE DX**

2-5 months (median)

**MESCC: USEFUL STUDIES**

- MRI
- Plain Films
- (Bone Scan)

**MESCC: DDX**

- Metastatic cancer
- Herniated disk
- Benign bony lesions
- Abscess
- Primary tumor
- Other
Treatment Options

- Corticosteroids
- Radiotherapy
- Surgery
- ? SRS

MESCC: STEROIDS

- Work by decreasing edema
- Buy time
- Have side effects

MESCC: RADIOTHERAPY

- Dose usually 3,000 cGy
- Takes several days to take effect
- Does not stabilize spine
- At best, only arrests progression

Laminectomy

Not effective for anteriorly situated tumors (most)
- May not decompress
- No treatment of tumor
- No stabilization

Direct Decompressive Surgery

- Relieves compression
- Removes tumor
- Stabilizes spine

MESCC: RADICAL SURGERY RESULTS

- Uncontrolled and retrospective studies
  - 66-85% ambulatory overall
  - 20-60% of nonambulatory patients walked after surgery
A Randomized Trial of Direct Decompressive Surgical Resection in the Treatment of Spinal Cord Compression Caused by Metastasis


MESSC: Operational Definition
An epidural tumor causing actual displacement of the spinal cord on MRI

MESCC: SCHEMA

Dx Steroids Stratification
MRI 100 mg Decadron then 24 mg q 8°

Tumor Type
Ambulatory Status
Spinal Stability

Radiation-Alone Arm
• RT started within 24 hours after study entry.
• 30 Gy (3 Gy x 10 fractions.)
• Port 8 cm. wide (one VB above and below the visible lesion).

Surgery + RT Arm
• Surgery within 24 hours after study entry
• Aims of surgery
  – remove as much tumor as possible
  – provide immediate decompression
  – stabilize the spine (when needed)
• RT (30 Gy) within 14 days of surgery

Surgery Guidelines
• Anterior tumors
  – Cervical spine
    • anterior approach
  – Thoracic
    • transversectomy
    • anterior approach
Surgery Guidelines

• Lateral tumors  
  – lateral approach

• Posterior tumors  
  – laminectomy  
  – removal of any posterior tumor

Entry Criteria

1) Known cancer (Tissue Dx)
2) At least one sign or symptom
3) MRI demonstrated epidural lesion able to be approached surgically.
4) A single area of cord compression.
5) Not totally paraplegic (0/5 in both LE’s for) > 48 hours.
6) No prior RT to the area of spinal cord compression.
7) Expected survival at least 3 months
8) Age 18 or older
9) Tumor types excluded:  
  - lymphomas, leukemia, multiple myeloma, germ cell tumors, primary spinal tumors

Study Endpoints

• Primary  
  – Combined ambulatory rate  
  – Time ambulatory after treatment
• Secondary  
  – Rate and time continent after treatment  
  – Time ASIA and Frankel scores stayed up  
  – Narcotic and corticosteroid dose/changes  
  – Survival time

Ability to Walk

Ability to take 2 or more steps with each foot (4 steps total) alone (even if a cane or walker was required)
A.S.I.A. SCORE
Sum of the muscle strength ratings (0-5) for the following mm groups:
- Triceps
- Biceps
- Wrist extensors
- Wrist Flexors
- Hand Intrinsic
- Iliopsoas
- Quadriceps
- Ankle plant flexors
- Ankle dorsiflexors
- Great Toe Extensors

Frankel Score
- A: Complete; no motor or sensory
- B: Sensory only
- C: Nonambulatory; motor useless
- D: Ambulatory with neuro symptoms
- E: Normal neurological function

Study Endpoints
- Primary
  - Combined ambulatory rate
  - Time ambulatory after treatment
- Secondary
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Cross Over
1) If began Tx $\geqslant$ 3/5 LE strength, got surgery when dropped below 3/5.
2) If began with <3/5 (but >0/5), got surgery when dropped to 0/5.
3) If 0/5 at start, no surgery even if no improvement on RT.

Early Stopping Required
- Targeted accrual 200 patients, with planned interim analysis at 50% accrual
- Observed p-value = 0.001

Patient Accrual
- 123 Patients Evaluated
- 114 Eligible Patients
- 101 Entered in the Trial
Table 1: Patient Characteristics (N = 101)

<table>
<thead>
<tr>
<th></th>
<th>RT-alone</th>
<th>Surgery+RT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Gender</td>
<td>73%</td>
<td>60%</td>
<td>0.48</td>
</tr>
<tr>
<td>Age (median)</td>
<td>60 yrs</td>
<td>60 yrs</td>
<td>0.92</td>
</tr>
<tr>
<td>Walking at Dx</td>
<td>69%</td>
<td>60%</td>
<td>0.80</td>
</tr>
<tr>
<td>Primary Tumor</td>
<td>Lung: 26%</td>
<td>Lung: 26%</td>
<td>0.54</td>
</tr>
<tr>
<td></td>
<td>Breast: 12%</td>
<td>Breast: 14%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other: 62%</td>
<td>Other: 60%</td>
<td></td>
</tr>
<tr>
<td>Continent</td>
<td>63%</td>
<td>60%</td>
<td>0.78</td>
</tr>
<tr>
<td>Frankel Score</td>
<td>0</td>
<td>D</td>
<td>0.44</td>
</tr>
<tr>
<td>ASIA Score</td>
<td>90</td>
<td>89</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Table 2: Follow-up Times

- **RT-Alone Group**: 93 days median (range 0 - 1,117 d)
- **Surgery + RT Group**: 102 days median (range 0 - 1,940 d)

P = 0.10

Table 3: Combined Ambulatory Rates

<table>
<thead>
<tr>
<th></th>
<th>Surgery + RT</th>
<th>RT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continued to walk or regained ability to walk</td>
<td>42/50 pts (84%)</td>
<td>29/51 pts (57%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Graph: Ambulatory Time After Tx (All)
- Surgery + RT: median 122 days
- RT-alone: median 13 days

HR=6.5 (95%CI, 2.9-9.8)
P = 0.003, log rank
Multivariate Analysis

Covariates Examined
- Treatment
- Age
- Gender
- Primary tumor
- Level and position of tumor
- Stability of spine
- Frankel and ASIA scores at entry
- Time between motor symptoms and MESCC
- Time between Dx of 1° tumor and MESCC

Suggestions:
- Surgical treatment P = 0.0017
- Frankel score at entry P = 0.0008
- Breast primary P = 0.029

Non-Ambulatory Patients (N=32)

<table>
<thead>
<tr>
<th></th>
<th>Surgery+RT</th>
<th>RT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regained Ability to Walk after Tx</td>
<td>10/16 pts 62%</td>
<td>3/16 pts 19%</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Combined Urinary Continence Rates

<table>
<thead>
<tr>
<th></th>
<th>Surgery+RT</th>
<th>RT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continued to be continent or regained continence</td>
<td>37/50 pts 74%</td>
<td>29/51 pts 57%</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Survival Factors

Multivariate Analysis

- Surgical treatment  $P = 0.04$
- Breast cancer  $P = 0.003$

Corticosteroid Use

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery + RT</td>
<td>1.6</td>
<td>0.1 - 44</td>
</tr>
<tr>
<td>RT-Alone</td>
<td>4.2</td>
<td>0 - 50</td>
</tr>
</tbody>
</table>

P = 0.0093
### Narcotic Use

- **Surgery + RT**
  - Median: 0.4
  - Range: 0 - 60

- **RT-Alone**
  - Median: 4.8
  - Range: 0 - 200

\[ \text{P} = 0.002 \]

Mean daily morphine equivalent dose (mgs)

### 30 Day Mortality and Morbidity

<table>
<thead>
<tr>
<th></th>
<th>Surgery</th>
<th>RT</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>6 %</td>
<td>14 %</td>
<td>0.32</td>
</tr>
<tr>
<td>ASIA ↓</td>
<td>14 %</td>
<td>40 %</td>
<td>0.0064</td>
</tr>
<tr>
<td>Frankel ↓</td>
<td>9 %</td>
<td>39 %</td>
<td>0.0008</td>
</tr>
</tbody>
</table>

### Post-Op Complications

- 6/50 (12%) of Pts in the Surgery + RT arm
  - 3/6 failure of fixation or graft
  - 3/6 wound infection or skin breakdown

### Time in Hospital

- **RT- alone**
  - Median: 10 days
  - Range: 0 - 41 days

- **Surgery + RT**
  - Median: 10 days
  - Range: 2 - 51 days

\[ \text{P} = 0.86 \]

### Salvage Surgery

- 10 Patients in the RT-Alone arm (20%) crossed over to receive surgery when they deteriorated and lost ability to walk on RT.
  - 3/10 (30%) improved and regained the ability to walk
  - 4/10 (40%) had surgical complications

### Day Entered Study

- P = 0.11
Conclusion

Surgery + RT is superior to RT-Alone in the treatment of spinal cord compression caused by metastasis

Conclusion

Surgery works best when given as initial treatment for MESCC

– Better overall result
– Better result in ambulatory patients
– Poor response as salvage therapy (30% vs 62% regain ability to walk)
– High complication rate after salvage therapy (40% vs 12%)

Indications for Surgery

• Unknown primary tumor
• Relapse after RT
• Progression while on RT
• Intractable pain
• Patients with a single area of cord compression who have not been totally paraplegic for longer than 48 hours.