Treatment of muscle invasive bladder cancer

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<table>
<thead>
<tr>
<th>Treatment</th>
<th>AGE &lt;70</th>
<th>AGE &gt;70</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYSTECTOMY</td>
<td>234</td>
<td>143</td>
</tr>
<tr>
<td>RADIOTHERAPY</td>
<td>166</td>
<td>495</td>
</tr>
</tbody>
</table>
Survival data

- Population based
- Reported results of large series
Survival is better after surgery?

- Variations in the use of total cystectomy and in the use of pelvic RT among the regions of Ontario were not associated with variations in survival.
- Survival was correlated with tumour related parameters

Survival is better after surgery?

- Stein et al: 1054 cystectomy patients 5- and 10-YS 60% and 43%
- Rödel et al: 415 RT patients 5- and 10-YS 51% and 31%

However, cystectomy series:
- included 213 T0, Ta, Tis patients
- excluded 112 inoperable patients

If comparison is restricted to operable muscle-invasive disease, 5-YS:
- radical cystectomy 47%
- Conservative therapy 45%

Stein JP et al JCO Feb 1 2001: 666-675
Conclusions Surgery vs RT

- No good evidence to favour one over the other in cure rates
- Morbidities do differ
  - Functional bladder vs artificial bladder
  - Long term surveillance following RT
  - Psychology for patient of surgical cures easy to understand vs retaining a diseased organ
  - Potency much better after RT
Bladder RT
Bladder Preservation Strategies

- Primary radiotherapy with salvage cystectomy (UK approach)
- Radiotherapy with interim cystoscopy and radiotherapy for good responders (the Boston approach)
- Chemoradiotherapy
  - Neoadjuvant therapy
  - Synchronous therapy
  - Adjuvant therapy
Salvage cystectomy data

- No of cystectomies = 38/159 (24%)
- Median time to cystectomy = 12 months
  (Range = 56 days - 10 years)
- Unknown number of inoperable radiotherapy failures
- No difference in cystectomy rate, time to cystectomy

Percentage of Surviving Patients without a bladder

8
14
18
23
25
22
27
24
18
14

Primary Radiotherapy

- The overall cystectomy rate after radiotherapy is 24%.
- The risk of cystectomy persists for 10 years.
- The proportion of patients living without their bladders remains between 20-30% up to 8 years after treatment.

But of course the use of RT gives you a small poorly functioning bladder
Functional outcomes – RT vs Surgery

- 71 patients RT, 325 patients surgery, 460 controls
- Postal questionnaire, self completed
- Examined
  - Bowel function
  - Urinary function
  - Sexual functioning
  - Lymphoedema
  - Well being

Results

- 74% RT patients had “little” or “no distress” in urinary tract functioning
- 38% of RT patients reported intercourse in previous month vs 13% cystectomy pts
- 32% RT pts had GI symptoms vs 24% cystectomy pts

Further reading

Can we select good responders?

- Biological markers
- Select patients for radiotherapy on basis of initial response to therapy
  - Rationale for Boston approach
Pharmacogenomic Study in Bladder Cancer

- Neoadjuvant chemotherapy
- Check cystoscopy
  - TURBT
  - Tissue
  - DNA array analysis
  - Serum marker analysis
  - Correlation with paraffin archive
  - Correlation with clinical outcomes
- RT +/- chemotherapy
  - Chemosensitive
  - Chemoresistant/
    Clinical preference
- Cystectomy
  - Tissue
  - Correlation with clinical outcomes
- Check cystoscopy
Can we select good responders?

- Biological markers
- Select patients for radiotherapy on basis of initial response to therapy
  - Rationale for Boston approach
Boston approach

- Initial radiotherapy to 40Gy
- Check cystoscopy
- pCR or unfit for cystectomy receive boost to 64.8Gy
- <pCR and medically fit undergo immediate cystectomy

Kaufman et al. Proc ASCO 2001 Abstract 683
Results – Boston approach

190 patients

41 (22%) Immediate cystectomy

25 (13%) delayed cystectomy

124 (65%) retained bladder

Kaufman et al. Proc ASCO 2001 Abstract 683
Can we improve local control rates?

- Neoadjuvant therapy
- Synchronous therapy
- Adjuvant therapy
MRC Trial - Loco-regional Control

Lancet 1999; 354: 533-40
## Neoadjuvant studies - bladder

<table>
<thead>
<tr>
<th>Group</th>
<th>Trial arm</th>
<th>Control</th>
<th>Pts</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>EORTC/MRC</td>
<td>CMV/RT or cyst</td>
<td>RT or Cyst</td>
<td>875</td>
<td>5% improvement</td>
</tr>
<tr>
<td>USA Intergroup</td>
<td>MVAC + Cyst</td>
<td>Cyst</td>
<td>200</td>
<td>HR 0.74, p=0.027</td>
</tr>
<tr>
<td>Nordic</td>
<td>Pt/Adri/RT/Cyst</td>
<td>RT or Cyst</td>
<td>311</td>
<td>Trend</td>
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<tr>
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<td>Pt/RT</td>
<td>RT</td>
<td>255</td>
<td>NS</td>
</tr>
<tr>
<td>Cueto</td>
<td>Pt/Cyst</td>
<td>Cyst</td>
<td>121</td>
<td>NS</td>
</tr>
</tbody>
</table>
Cisplatinum and RT +/- surgery

![Diagram of trial design. Choice of preoperative or radical radiotherapy is made before randomization to concurrent cisplatin or to no chemotherapy control arms.](Diagram)

- Coppin et al, J. Clin Onc. 14:2901-2907
Cisplatinum and RT +/- surgery

Coppin et al, J. Clin Onc. 14:2901-2907
Conclusions

- The best bladder you’ll get is the one you’re born with
- and
- Bladder sparing techniques should be considered in all patients before cystectomy
Acknowledgements

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For further information please contact:
Erica Denholm (RMH) or Rachel Mount (Birmingham) via trial website
www.bc2001.org.uk