Point/Counterpoint:

Quality of Life Considerations for Patients with Muscle Invasive Bladder Cancer

Pro Trimodality Therapy

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QOL Studies after Bladder-Sparing Trimodality Therapy (TMT)*

*Bladder tumor resection and chemoradiation
TMT Clinical Trials

- RTOG trials: 157 patients treated with TMT who survived 2-13 years (median follow-up 5.2 years)

<table>
<thead>
<tr>
<th>Late Pelvic Toxicity</th>
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<td>Grade 1</td>
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<td>Grade 5</td>
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- BC2001: 360 patients treated with radiation vs. TMT
  - Grade 3-4 late toxicity: GU 3.3%; GI 0.8%

Efstathiou JA, et al. JCO 2009
James ND, et al. NEJM 2012
MGH Urodynamics and QOL Study

221 patients treated with TMT on protocols 1986-2000, median follow-up 6.3 years

- 78% have compliant bladders with normal capacity and flow parameters
  - 85% have no or occasional urgency
- 25% have occasional to moderate bowel control symptoms
- 50% of men have normal erectile function

GETUG 97-015

Prospective Phase II study of 51 MIBC patients treated with TMT 1999-2001, without disease relapse, median follow-up 8 years

• Mean global QOL, physical, emotional, personal, cognitive, and social function scores >70%

• 100% satisfactory bladder function
  – 70% maintained bladder function scores 1 year after treatment

• 79% had sexual activity 18 months after treatment (vs. 56% pre-treatment)

Lagrange JL, et al. IJROBP 2011
Comparing Quality of Life after Surgery vs. Trimodality Therapy

- Little data comparing quality of life (QOL) after radical cystectomy (RC) vs. TMT\(^1\)
  - Randomized trial comparing RC to TMT (SPARE) closed early due to poor accrual\(^2\)
  - Both treatments have long-term effects on overall QOL, urinary, bowel, and sexual function, and self-image\(^3\)

Cystectomy vs. Radiation

Cross-sectional study from Karolinska Institute, Sweden

251 patients treated with cystectomy (incontinent and continent diversions)
58 patients treated with radiation
310 “control” individuals from general population

- Urinary function
  - After radiation: 74% had no or little urinary symptom distress

- Bowel function
  - After radiation: 32% had moderate or much bowel distress
  - After cystectomy: 24%
  - Control group: 9%

- Sexual function
  - After radiation: 38% had intercourse in last month
  - After cystectomy: 13%

Henningsohn L, et al. Radiother Oncol 2002
Review of TMT QOL Studies

Systematic review of 6 QOL studies after TMT
(2 prospective, 4 retrospective)

• TMT associated with:
  – Good general QOL compared to cystectomy
  – Satisfactory urinary function
  – Likely more bowel symptoms than cystectomy
  – Satisfactory sexual function

• Included studies were limited by sample size, variable follow-up, and non-validated instruments

Cross-sectional study of 173 patients diagnosed in 1990-2011, disease-free for ≥2 years
Treated at high-volume, academic medical centers with modern techniques

• Median follow-up: 5.6 years
  - 63% patients received cystectomy (n=109)
    - 82% ileal conduit and 18% neobladder diversions
  - 37% received TMT (n=64)
    - 9% required salvage cystectomy (n=6)

• Six validated QOL questionnaires, scored out of 100

Mak KS, Smith AS et al. ASCO GU 2015, ASTRO 2015, under review at IJROBP
MGH/UNC: Long-Term QOL

• Both cystectomy and TMT associated with good long-term QOL outcomes

• Compared to RC, TMT associated with:
  • Modestly higher general QOL (by 7-10 points)
  • Similar urinary scores
  • Modestly higher bowel function (by 3-7 points)
  • Markedly better sexual QOL (by 9-32 points)
  • Better informed decision-making (by 14 points)
  • Less concerns about appearance (by 14 points)
  • Less life interference from cancer or cancer treatment (by 9 points)
What about TMT patients who needed salvage cystectomy?

91 patients at MGH who underwent salvage cystectomy for persistent disease (n=50) or recurrent disease (n=41)*

<table>
<thead>
<tr>
<th>Clavien Scale Complication w/in 90 days of Surgery</th>
<th>Salvage Cystectomy</th>
<th>Radical Cystectomy (MSKCC series of 1142 patients)</th>
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</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>45%</td>
<td>26%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>38%</td>
<td>62%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>14%</td>
<td>11%</td>
</tr>
<tr>
<td>Grade 4</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Grade 5</td>
<td>2%</td>
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*No patients required cystectomy due to treatment toxicity* in MGH experience or on RTOG protocols

Does TMT offer better QOL than Cystectomy?

- Sexual function
- Adjustment to appearance and life interference
- Informed decision-making
- General QOL?

- Urinary function
- General QOL?
- Bowel function?
- Bowel function?
Conclusions

Both cystectomy and TMT can be used to treat bladder cancer.

More prospective studies are needed to evaluate outcomes (including QOL) after each treatment.
The best bladder you will ever have is the one you are born with

(even after bladder tumor resection and chemoradiation)

- Anthony Zietman, MD