Enhancing multi-disciplinary care for muscle invasive bladder cancer patients

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Associate Professor, Director of Urologic Oncology
Knight Cancer Network Symposium
3 March 2023
Disclosures

• OncLive: honoraria
Bladder cancer – in all its forms

- Represents ~ 6% of overall cancers
- Median age of onset is 73 years
- 3-4:1 ratio for M:F
- Smoking is main risk factor

- Comes in different forms:
  - Non – muscle invasive bladder cancer (NMIBC) = 75% of initial diagnoses
    - Recurs, but can often be treated with local therapy
  - Muscle invasive bladder cancer (MIBC) = 25% of initial diagnoses
    - Can metastasize, requires more aggressive treatment → ↑ morbidity and mortality

- The most expensive cancer to treat over the lifetime of the patient

Source: American Cancer Society
<table>
<thead>
<tr>
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**Staging**

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<td>M0</td>
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<td>M0</td>
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<td>M0</td>
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<td>T1 - 4a</td>
<td>N1</td>
<td>M0</td>
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<td>M0</td>
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<td>Stage group IVA:</td>
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<td>M0</td>
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<td>M1a</td>
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<tr>
<td>Stage group IVB:</td>
<td>any T</td>
<td>any N</td>
<td>M1b</td>
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</table>

- Transurethral resection of bladder tumor (TURBT) + exam + imaging = clinical staging

American Cancer Society

NMIBC

MIBC
NMIBC treatment

- **Low grade**: Endoscopic resection + perioperative intravesical chemotherapy instillation

- **High grade**: Endoscopic resection +
  - Adjuvant intravesical chemotherapy or immunotherapy (BCG)
  - Systemic immunotherapy
  - Surgical extirpation: radical cystectomy and urinary diversion

- Disciplines: urologic oncology, medical oncology
MIBC treatment

• Requires more radical approach
  • Neoadjuvant chemotherapy (NAC) + radical cystectomy (RC) and urinary diversion

• Trimodality therapy (TMT) = endoscopic resection, chemotherapy, radiotherapy
  • Response assessed post-treatment, if residual disease → salvage cystectomy

• Up to 25% of patients will have occult metastatic disease (LN)
What is the gold standard for MIBC?

- Has been radical cystectomy and urinary diversion
- Neoadjuvant chemotherapy if eligible
• Timing is critical
• Clinical trials may span multiple disciplines
• MIBC is aggressive → left untreated it is deadly *and* morbid
Surgery alone

Chemo+surgery

Surgery only

Chemo+radiation

Stein, JCO, 2001
Efstathiou, Eur Urol, 2012
Grossman, NEJM, 2003
Timing is everything

### Table: Timing and Lymph Node Metastases

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>Lymph node metastasis - Univariate</th>
<th>Lymph node metastasis - Multivariable*</th>
<th>Lymph node metastasis - Full Multivariable Model†</th>
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<tr>
<td>Age at RC</td>
<td>OR (95% CI)</td>
<td>P</td>
<td>OR (95% CI)</td>
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<tr>
<td>Number of chemotherapy cycles</td>
<td>0.99 (0.96–1.01)</td>
<td>0.325</td>
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<td>ASA score (&lt;3 vs ≥3)</td>
<td>1.11 (0.92–1.33)</td>
<td>0.288</td>
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<td>ECOG PS</td>
<td>0.75 (0.29–1.60)</td>
<td>0.462</td>
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<tr>
<td>Preoperative hydronephrosis (yes vs no)</td>
<td>1.32 (0.78–2.24)</td>
<td>0.299</td>
<td>1.39 (0.77–2.50)</td>
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<tr>
<td>Concomitant clinical CIS (yes vs no)</td>
<td>0.67 (0.36–1.23)</td>
<td>0.195</td>
<td>0.62 (0.30–1.29)</td>
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<tr>
<td>Clinical LVI (yes vs no)</td>
<td>1.52 (0.92–2.51)</td>
<td>0.100</td>
<td>1.71 (0.94–3.09)</td>
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<tr>
<td>Variant clinical histology (yes vs no)</td>
<td>1.35 (0.82–221)</td>
<td>0.241</td>
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<td>Clinical stage</td>
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<tr>
<td>CT1-T2, CT1 vs CT2</td>
<td>9.72 (1.28–74.01)</td>
<td>0.028</td>
<td>5.11 (0.65–40.25)</td>
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<tr>
<td>CT1, CT1 vs CT3–4</td>
<td>9.32 (1.23–70.76)</td>
<td>0.031</td>
<td>5.81 (0.74–45.70)</td>
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<td>Caspian-based NAC (yes vs no)</td>
<td>0.76 (0.41–1.43)</td>
<td>0.397</td>
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<td>Interval between NAC and RC, days (RW)</td>
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<tr>
<td>18–42 vs 0–64</td>
<td>1.24 (0.66–2.32)</td>
<td>0.510</td>
<td>1.13 (0.59–2.15)</td>
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<tr>
<td>18–42 vs 64–84</td>
<td>1.03 (0.42–2.51)</td>
<td>0.948</td>
<td>0.98 (0.39–2.44)</td>
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<td>18–42 vs ≥85</td>
<td>2.92 (1.20–7.10)</td>
<td>0.018</td>
<td>2.56 (1.03–6.38)</td>
</tr>
</tbody>
</table>

**Note:** OR = Odds Ratio, CI = Confidence Interval

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Mmeje et al. *BJU Int.* 2018

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**Highlighted Text:**

- *Time from completion of chemotherapy to surgery >12 weeks*
- *Higher rate of LN metastases*
What normally happens

- Referral to urologic oncologist
- Urologist refers to medical and radiation oncologist
- Patient makes decision re treatment
- Patient starts chemotherapy
- Referred back to urologist for surgery or radiation oncologist for XRT
- Patient has surgery or XRT
- Pathology results → benefit to adjuvant therapy or if salvage treatment needed
- Referred back to appropriate specialty

Fragmented care, loss to follow up, failure to follow guidelines
How do you fix this?

• 51 studies (2005-2012)
• Various cancers
• Having a MDT →
  • Better clinical and process outcomes
  • Improved survival for colorectal, head and neck, breast, esophageal, lung cancers
  • Changed diagnostic or treatment decision making for prostate, pancreatic, upper GI, breast, melanoma, bladder, colorectal, head and neck and gynecological cancers

• MDTs recommended by
  
  Prades et al. *Health Policy*. 2015
Multi-disciplinary care for bladder cancer changes diagnosis and management

- 248 patients 2008 and 2012
- 79% needed additional studies
- 36% Δ in stage
- 33% Δ in treatment recommendation

Kulkarni et al. J Clin Oncol. 2017
Multi-disciplinary clinic (MDC) enhances adherence to clinical guidelines

- Neoadjuvant chemotherapy (NAC) is the standard of care in eligible patients prior to surgery
  - Rates of administration are low (~10-17%)*

- Assessed rate of NAC before/after establishing a MDC

- Rate increased from 7.7 to 26.4%

*during the time period that corresponded to this study
Multi-disciplinary approach expedites time to radical cystectomy

Efficient Delivery of Radical Cystectomy After Neoadjuvant Chemotherapy for Muscle-Invasive Bladder Cancer

A Multidisciplinary Approach

Ajja S. Alva, MD; Christopher T. Tallman, MS; Chang He, MS; Maha H. Hussain, MD; Khaled Hafez, MD; James E. Montie, MD; David C. Smith, MD; Alon Z. Weizer, MD; David Wood, MD; and Cheryl T. Lee, MD

- Median time of 6.9 weeks from end of chemotherapy to radical cystectomy by scheduling surgery at chemotherapy initiation

Academic center challenges

- OHSU has a broad catchment area
  - >50% pts come from outside metro area
- Travel is burdensome
- Delays in care?
- Coordination of care on the same day is convenient and less fragmented
  - Important when choosing between treatment options (e.g., surgery vs XRT)
Delays in care associated with receiving care in different centers

- Navigation can help ensure patients receiving chemotherapy in the community are not delayed due to handoffs.
- Pathological outcomes were similar regardless of chemotherapy location.

<table>
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<tr>
<th>Step</th>
<th>NAC in AMC</th>
<th>NAC in community</th>
<th>P value</th>
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<td>Initial visit to starting NAC</td>
<td>11</td>
<td>21</td>
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<td>Starting to ending NAC</td>
<td>64</td>
<td>68</td>
<td>0.33</td>
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<tr>
<td>Ending NAC to urology visit</td>
<td>24</td>
<td>30</td>
<td>0.48</td>
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<tr>
<td>Urology visit to cystectomy</td>
<td>32</td>
<td>37.5</td>
<td>0.18</td>
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<tr>
<td>Initial visit to cystectomy</td>
<td>128</td>
<td>162</td>
<td>0.006*</td>
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</tbody>
</table>

*P = 0.015 after adjusting for stage, comorbidity status, and distance to AMC.
Establishing a MDC for bladder cancer at OHSU

- OHSU Genitourinary Multidisciplinary (GU MDC) clinic

- Diagnoses: bladder, kidney, penile, testicular and all non-prostate GU cancers

- Established in October of 2020

- Biweekly half day of clinic
The Team

Jen-Jane Liu, MD
Sudhir Ishaqwal, MD
Marshall Strother, MD
Jacqueline Vuky, MD
Christopher Ryan, MD
Casey Williamson, MD
Crystal LeBoeuf, RN

Medical Staff
- 3 urologic oncologists
- 2 medical oncologists
- 1 radiation oncologist
- 1 RN navigator

Not pictured:
Monica Griffin, PAS
Solen Sanchez, PAS
Molly Thomas, BA
GU MDC structure

• Referral received: goal is for ‘first touch’ within 24-48h by RN navigator

• Pre-clinic review:
  • Pathology slide review
  • RN navigator referral review
    • Determine if any labs or imaging need to be completed prior and schedule

• Care team meeting just prior to review:
  • History, imaging, eligibility for clinical trials
Metrics

- 10/2020 to 2/2023
- Lead time of 17d between patient contact and appointment
  - 27d for urology clinic
- 31 patients enrolled on clinical trials

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<th>Year</th>
<th>All NPV</th>
<th>NPV MIBC</th>
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<tr>
<td>2020 (9 mo)</td>
<td>123</td>
<td>52</td>
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<tr>
<td>2021 (12 mo)</td>
<td>108</td>
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<td>2022 (9 mo to date)</td>
<td>235</td>
<td>64</td>
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<td>TOTAL</td>
<td>466</td>
<td>168</td>
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Diagnosis breakdown:
- Renal cell carcinoma: 37%
- Bladder cancer: 36%
- Urothelial carcinoma: 13%
- Testis cancer: 14%
- Not bladder cancer: 13%
Taking a closer look at the MIBC population

• **Goal:** Compare treatment times and type in patients seen in the GU MDC to a historical cohort seen in urology clinic (URO) prior to establishment of MDC

• **Time frame**
  • URO 12/2018 – 8/2020
  • MDC 10/2020 – 8/2021

• **Metrics**
  • Referral to first visit
  • Referral to initial consultation
  • Referral to initiation of treatment(s)

• **Assess treatment patterns**
  • Surgery, radiation
Do multidisciplinary clinics expedite care for muscle invasive bladder cancer?

Colin Boehnlein BS1, Rebecca Agnor MS2, Crystal LeBeouf RN3, Sudhir Isharwal MD1, Christopher W Ryan MD3, Jenna Kahn MD4, Jacqueline Vuky MD3, and Jen-Jane Liu MD1

Departments of Urology1, Knight Biostatistics2, Medical Oncology3, and Radiation Oncology4, Oregon Health & Science University, Portland OR

Presented at Western section of American Urological Association Meeting October 2022

- Referral to initial consultation quicker with MDC
  - MDC 22d vs URO 27d, p<0.05

- No significant difference for days between consultation and initiation of treatment
  - ~47 days for both
• High rate of utilization for NAC in both clinics (>70%)

• MDC increased:
  • Utilization of chemotherapy + radiation
    • MDC 32% vs URO 10%
  • Receiving NAC at OHSU
    • 37% vs 23%

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<th>Demographics</th>
<th>MDC N=63</th>
<th>UC N=93</th>
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<tr>
<td>Male</td>
<td>48 (76.2%)</td>
<td>74 (79.6%)</td>
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<tr>
<td>Female</td>
<td>15 (23.8%)</td>
<td>19 (20.4%)</td>
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<tr>
<td>Mean Age</td>
<td>71.8</td>
<td>69.2</td>
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<td>Median Age</td>
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<td>Surgery</td>
<td>21 (33.3%)</td>
<td>64 (68.8%)</td>
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<td>Neoadjuvant Chemotherapy</td>
<td>15 (71.4%)</td>
<td>48 (75.0%)</td>
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<tr>
<td>NAC Prior to Initial Consult</td>
<td>1 (6.7%)</td>
<td>22 (45.8%)</td>
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<td>Chemotherapy only</td>
<td>14 (22.2%)</td>
<td>6 (6.5%)</td>
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<td>Chemotherapy + Radiation</td>
<td>20 (31.7%)</td>
<td>9 (9.7%)</td>
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<td>Radiation</td>
<td>1 (1.6%)</td>
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<td>Other treatment</td>
<td>2 (3.2%)</td>
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<td>No treatment</td>
<td>5 (7.9%)</td>
<td>12 (12.9%)</td>
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<table>
<thead>
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<th>Chemotherapy Location</th>
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<tr>
<td>OHSU</td>
<td>23 (46.9%)</td>
<td>21 (33.3%)</td>
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</table>
Final thoughts

• Bladder cancer care is complicated and requires a team-based approach

• Multi-disciplinary clinics can facilitate better care for bladder cancer patients
  • Seen faster
  • More treatment options presented
  • High rate of guidelines based treatment
  • Does not delay care
References

Thank you!

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Crystal LeBoeuf RN

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Sudhir Isharwal MD
Jenna Kahn MD
Marshall Strother MD
Casey Williamson MD
Austin Peterson
Monica Griffin
Kayla Martin
Molly Thomas