Quality of Life after Treatment of Localised Prostate Cancer

Dr Jeremy Grummet
Clinical Uro-Oncology Fellow
May 28, 2008
Why?

- This is important
  - May be viewed as soft science
  - Until we know which treatment is best (may never happen), arguably most important issue
  - Publications by Dr Joyce Davison et al
- 10th anniversary of 1st validated CaP-specific QOL instrument
- Recent study in NEJM

Outline

- Definition
- Importance
- Measurement
- Literature
Definition

• What is HRQOL?
• Based on 1948 WHO definition of health:
  – Not merely the absence of disease, but a state of complete physical, emotional and social well-being
• Physical, psychological and social domains of health, influenced by a person’s experiences, beliefs, expectations and perceptions
• Re disease or treatment: symptoms, degree of bother, impact on functional status
• Patient’s perspective, not doctor’s

Importance of HRQOL

• Why is HRQOL so important in the setting of localised CaP?

• In most cancers, when diagnosed at a curable stage:
  – survival (quantity of life) is of primary importance
  – HRQOL, although important, is secondary
Importance of HRQOL

• Example:
  • 55yo man with early stage cancer in ascending colon
  • Treatment leads to cure, HRQOL unchanged post-op, dies of MI at 80
  • No treatment leads to metastatic disease and death at 60

Importance of HRQOL

• Survival advantage of 20 yrs, therefore decision to treat is obvious
• HRQOL secondary
  – In treatment, small risk of temporary stoma only
Importance of HRQOL

• When diagnosed at a curable stage, CaP can be totally different, especially when low risk disease

• HRQOL may assume equal, or possibly even greater, importance than survival

• 4 reasons

Importance of HRQOL

• 1) Being slow-growing tumour, active treatment may not confer a survival advantage

• 70 yo man, PSA 6.5, Gleason 3+3
  – Treatment: ED, dies at 85 of CCF
  – WW: active sex life for 5 years, dies at 85 of CCF, had asymptomatic non-metastatic CaP
  – Survival not affected by treatment but HRQOL certainly is
    • PRIMUM NON NOCERE
Importance of HRQOL

2) Patients typically live for well over a decade post-treatment whether cancer cured or not
   – Accentuated by earlier detection due to PSA

Patients have to live with effects of treatment for a *long time*

3) Standard treatment modalities have similar survival rates but different side effect profiles
   – RP vs XRT vs BT
Importance of HRQOL

• 4) All treatment modalities may cause varying degrees of impairment to *intimate* bodily functions

• Delicate anatomical location of prostate
  – Local treatments can cause dysfunction
    • Sexual
    • Urinary
    • Rectal
  – Major impact on HRQOL

Points on HRQOL

• Severity of symptom does not necessarily correlate with degree of bother *(Penson J Urol 2003)*

• Specific symptom deterioration post-treatment can even be associated with general improvement in HRQOL *(Talcott Eur J Cancer 2005)*
  – Presumably due to mental shift whereby consequences of treatment accepted as long as cancer cure attempted
Measuring HRQOL

- Various instruments (questionnaires) have become available in recent years
- Generic
  - SF-36: Medical Outcomes Study 36-Item Short Form considered gold standard for general HRQOL (Ware Med Care 1992)
    - 8 domains, incl. social function, emotional well-being, role limitation
Measuring HRQOL

• Cancer-specific
  – QLQ-C30: EORTC Quality of Life Core Questionnaire (Aaronson JNCI 1993)
  – Domains significant to all cancer patients, incl. nausea, fatigue, pain

• Prostate cancer-specific
  – UCLA-PCI: Prostate Cancer Index (Litwin Med Care 1998)
    • First validated instrument for HRQOL in CaP
    • 20 questions
    • 6 domains assessing urinary, sexual and bowel function and bother
Measuring HRQOL

- EPIC: Expanded Prostate Cancer Index Composite (Wei Urology 2000)
  - Modification of UCLA-PCI, still assessing function and bother in all domains
  - 50 questions
  - Includes irritative symptoms in urinary domain
    - More sensitive for impact of EBRT and brachytherapy
  - Additional domain assessing effects of hormone therapy

Measuring HRQOL

- EPIC-26
  - Reduction of EPIC
  - Excludes overlapping items
  - High correlation with original (Miller JCO 2005)
  - Likert scale response converted to scale of 0-100, higher = better QOL

- Go to http://roadrunner.cancer.med.umich.edu/epic/
**EPIC Scoring**

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Study Types

• Cross-sectional and Longitudinal
  • Cross-sectional
    – Snapshot of post-treatment HRQOL
    – Easier to conduct than longitudinal
    – Limitations
      • Does not assess what happens over time
      • Unable to control for baseline (pre-treatment) differences

Study Types

• Longitudinal
  – Advantages over cross-sectional
    • Assesses HRQOL over time (especially important when long period involved and changes known to occur)
    • Potential to account for baseline (pre-treatment) differences between patients
Results of Studies

• Cross-sectional (Penson J Urol 2003)
  – General HRQOL
    • Not affected by treatment
  – Prostate cancer-specific HRQOL
    • Treatment appears to have profound effect on sexual, urinary and rectal function
    • Incontinence worse with RP, rectal problems worse with radiation modalities
    • Despite age-matched controls, unable to conclude that results are true treatment effects (no baseline)

Results of Studies

• Longitudinal
  – NEJM March 2008
  – JCO April 2005
Current Data

- Multi-institutional
- Prospective
- Current modality methods: RP, XRT, BT
  - RP
    - Open/lap/robotic
    - +/- Nerve-sparing
  - XRT conformal/IMRT
  - +/- ADT in XRT and BT groups
Study Features

- Longitudinal
  - 0, 2, 6, 12, 24 months
  - Enrolled 2003-6
- 1201 patients, 625 partners
- Parameters assessed
  - Changes in HRQOL in patient
  - Associated distress in partner
  - Satisfaction with treatment outcome

Instruments

- EPIC-26
  - Sexual
  - Urinary
    - Incontinence
    - LUTS
  - Rectal
  - Hormonal
- Service Satisfaction Scale for Cancer Care
Follow-up

- 9.3% did not complete follow-up

### Patient Interview Completion Rates

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<th>Follow-up (mo)</th>
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<td>No. of patients</td>
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<tr>
<td>No. of patients who completed the interview</td>
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<td>1133</td>
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### Numbers by Treatment Modality

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<th>BT</th>
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<td>Total</td>
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<td>Total</td>
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<td>+ADT</td>
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<td>292</td>
<td>306</td>
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<td>NS</td>
<td>93%</td>
<td>7%</td>
<td>69%</td>
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<tr>
<td>NNS</td>
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<td>31%</td>
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<tr>
<td>Alone</td>
<td>89%</td>
<td>11%</td>
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<tr>
<td>+ADT</td>
<td>89%</td>
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**Sexual Domain**

- * Indicates clinically signif (>1/2 SD) and stat signif difference from baseline
- NS led to better sexual QOL
  - Neuropraxia may explain nadir to recovery
  - Needs to be addressed: traction-free dissection? (Masterson BJU 2008)

**Sexual Domain**

- Adding ADT to XRT worsened sexual QOL
  - 94% had <1 yr ADT
- Cannot discern ADT effect on BT as is mixed group
Urinary Incontinence Domain

- Worst at first post-surgical assessment, most improvement by 6 months
  - Needs to be addressed: PRDMP? (Nguyen BJU 2008)
- Significant incontinence at 2 yrs with BT

LUTS Domain

- LUTS *improved* after RP
- Also above baseline at 2 yrs for XRT
- Although improved after initial nadir, remained below baseline at 2 yrs for BT
Rectal Domain

- Reduced QOL for XRT and BT remained for 2 yrs

Hormonal Domain

- ADT reduced QOL in XRT and BT patients
- Symptoms persisted up to 2 yrs with XRT
### Degree of Bother over Time

#### Other Outcomes

- For each domain, changes in HRQOL were significantly distressful for partner

- Outcome satisfaction at 1 yr
  - For patient
    - Significantly associated with changes in sexual, hormonal, LUTS domains
  - For partner
    - Significantly associated with changes in sexual domain

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### Table 2: Percent of Patients Reporting Specific Levels of Distress or Disturbance for Each Quality of Life Domain, as Questioned in the EPIC-24 Survey

<table>
<thead>
<tr>
<th>Quality of Life Domain and EPIC Questionnaire Item</th>
<th>Prostatectomy 3-Mo.</th>
<th>6-Mo.</th>
<th>12-Mo.</th>
<th>24-Mo.</th>
<th>External Beam Radiation Therapy 3-Mo.</th>
<th>6-Mo.</th>
<th>12-Mo.</th>
<th>24-Mo.</th>
<th>Brachytherapy 3-Mo.</th>
<th>6-Mo.</th>
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Summary

• Evidence supporting what we see in clinic
• Some surprises
  – Significant incontinence problems at 2 yrs for BT
  – Ongoing LUTS, rectal problems for BT
  – Ongoing hormonal problems after cessation of ADT
  – Suggestion of LUTS reducing QOL more than incontinence
    • Corroborated in AUA 2008 abstract 305
• Much room for improvement in short-term period post-RP
  – Avoidance of NVB traction
  – Sphincter stabilization

Limitations

• Not randomised
  – Stat sig difference between treatment groups across all characteristics, except mean BMI
  – Selection bias may have influenced outcomes
  – Results guide post-treatment expectations, but cannot be used to compare between modalities

• NS RP not stratified into unilateral vs bilateral
• No WW or AS arm
• Short follow-up
Long-Term Data

• Report in JCO (Miller et al 2005)

• New assessment of cohort previously studied as cross-section

• Comparison made with earlier results

• Patients had received RP, 3D-CRT, or BT and were compared to control group
Long-Term Data

• 1014 patients in initial study
• Median post-treatment assessment time of 2.6 years
• Selection:
  – Consecutive recipients of RP, 3D-CRT or BT in single institution from 1995-9
  – Control group
    • Age-matched local volunteers
    • No history CaP

• Of 964 eligible men in current study:
  665 RP   147 3D-CRT   84 BT   112 controls
• 709 consented (response rate 73%, similar in each treatment group)
• Median post-treatment time 6.2 yrs (4-8 yrs)
• Significant group differences:
  – 3D-CRT group significantly older than other groups (median 76 vs 67-70 years)
  – 2/3 BT patients also received hormone therapy cf. 1/3 of each of RP and 3D-CRT patients
• HRQOL instruments
  – SF-12
  – EPIC-26
Long-Term Data

• Results
  – General HRQOL similar between treatment groups and controls, as per original study
  – Treatment does not seem to interfere with general HRQOL up to 8 years afterwards

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<tr>
<td>Urinary - irritative</td>
<td>89</td>
<td>92</td>
<td>84</td>
<td>81*↑</td>
</tr>
<tr>
<td>Urinary - incont.</td>
<td>92</td>
<td>80*</td>
<td>86↓</td>
<td>78*↓</td>
</tr>
<tr>
<td>Rectal</td>
<td>96</td>
<td>94</td>
<td>84*</td>
<td>87*↑</td>
</tr>
<tr>
<td>Sexual</td>
<td>63↓</td>
<td>39*</td>
<td>35*↓</td>
<td>28*</td>
</tr>
</tbody>
</table>
Long-Term Data

• Limitations
  – No baseline, controls as surrogate
  – Selection bias
    • Should not compare across treatment modalities
  – Non-response bias
    • E.g. older age and poorer HRQOL among non-responders may have favoured RP group outcomes
  – Single institution
  – Not stratified for adjuvant ADT
  – Clinically significant change not defined

• Summary:
  – For RP patients, HRQOL stabilises within first 2 years
  – For radiation patients, for both modalities, HRQOL continues to evolve long-term in different ways for different domains
Conclusions

• HRQOL is crucial in patients with localised CaP
  – Treatment may not lead to longer survival
  – Patients likely to live a long time after diagnosis
  – Different treatments have comparable efficacy but different side effect profiles
  – Treatments interfere with intimate bodily functions

Conclusions

• Instruments are available to measure HRQOL
  – For research
  – In clinic to determine baseline, help optimise patient choice of treatment
Conclusions

• Patients should be informed of latest and best HRQOL data, based on current treatment methods
• Likely to guide individual patient to most appropriate treatment for him

• As always, as urologic surgeons, we can improve

Future

• Surgical techniques to minimise reduction in HRQOL need to be tested across institutions
• Outcomes must be measured using validated HRQOL instruments