Prostate Cancer

• Most common malignancy in men with an estimated 218,000 new cases expected in 2013

• Second most common cause of cancer related death in American men with over 32,000 deaths expected in 2013

• Potentially curable when caught in its early stages

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>1 in 2</td>
</tr>
<tr>
<td><strong>Prostate</strong></td>
<td>1 in 6</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>1 in 13</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>1 in 17</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>1 in 29</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 48</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1 in 55</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1 in 70</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>1 in 72</td>
</tr>
<tr>
<td>Kidney</td>
<td>1 in 69</td>
</tr>
<tr>
<td>Stomach</td>
<td>1 in 81</td>
</tr>
</tbody>
</table>

**Source:** DevCan: Probability of Developing or Dying of Cancer Software, Version 5.1

*Age-adjusted to the 2000 US standard population.

Celebrities with Prostate Cancer: Well After Surgery
Celebrities Diagnosed Too Late
Screening for Prostate Cancer

• PSA and DRE are not perfect markers for prostate cancer
• Most men die with rather than from prostate cancer
• Some men suffer side effects from prostate cancer treatment
• So the goal of screening should be to detect prostate cancer that is “risky” or threatening
USPSTF

• Gives prostate cancer screening a D grade
• The definite evidence of harm far outweighs the unproven benefit of PSA screening
• 8,000 comments received concerning the recommendation in the first 30 days (comment period)
• They stick with their recommendation against screening
Recent studies

Screening revisited:


Screening

PLCO:

• Randomization 50-74 yo men from 1993-2001
  • 38,350 men to intervention vs 38,355 to control
  • Screening: Annual PSA (6 yrs) and DRE (4 yrs)
  • Control: NO screening
  • Follow for ≥ 13 years

• Goal: whether or not screening reduces Prostate Cancer Mortality
Screening

PLCO:

• Findings after median 11.5 yrs
  • Prostate Ca diagnosis:
    • Screened-9% vs Control-7.8%
  • Prostate Ca Mortality:
    • Screened-0.24% vs Control-0.21%

Andriole et al, NEJM, 2009
PLCO Contamination

• Flaws:
  • Assumed that 10% with prev screening in control arm would continue
  • In actuality, Control Arm,
    • 44% of men in each arm had ≥1 PSA test before randomization
    • During trial, 52% had undergone PSA screening and 46% with DRE
  • Controls:
    • Only 15% decreased diagnosis
    • 93% of cancers were asymptomatic, organ-confined
  • Follow-up was 11.5 years from randomization, NOT treatment
European Screening Study

ERSPC:

• 162,243 men 55-69 yo randomized from 1991-2003

• Median follow-up - 9 years

• Screening:
  • Did NOT require annual PSA – only 2.1 tests averaged over course of study
  • DRE variable, but usually only if equivocal PSA
ERSPC:

- Prostate Cancer diagnosis: Screened-8.2% vs Control-4.8
- Death from prostate cancer: screened arm RR was 0.80 (95% CI 0.67–0.95; P=0.01)
  - Curves began to diverge at 7-8 years
- NNS to prevent 1 death=1410; NNT=48
Screening - Newer data

Mortality results from the Göteborg randomised population-based prostate-cancer screening trial

Jonas Hugosson, Sigrid Carlsson, Gunnar Aus, Svante Bergdahl, Ali Khatami, Pär Lodding, Carl-Gustaf Pihl, Johan Stranne, Erik Holmberg, Hans Lilja

- 20,000 men aged 50-64 yrs
- Screened every 2 years
- Followed median 14 years
- Screened:
  - Prostate cancer diagnosed: Screened-12.7% vs Control-8.2%
  - Prostate cancer death: Screened-0.5% vs Control-0.9%
    - RR Reduction = 0.56 (95%CI, 0.39-0.82, p=0.002)
    - Compared to ERSPC = 0.8
Screening - Newer data

Lower PSA threshold for biopsy (2.5-3 vs 4) and more frequent screening (2 vs 4 yrs)

- Lower contamination (3% vs 44%)

- **Longer follow-up with improved RR**

- NNS = 293 and NNT = 12 to prevent 1 Death
Screening

Bottom line:

• Educate and discuss with patients
• Screening saves lives
• Particularly for men who are younger and have a higher risk of prostate cancer
• Screening
  • Recommended by AUA
  • ACS has changed based on PLCO and ERSPS – “Talk to your doctor about pros/cons” starting at age 45-50
So how do we answer the screening concerns?

• Improve the specificity of PSA
• Stop screening men who are unlikely to benefit
• Diminish overtreatment by offering active surveillance more than currently
Risk Stratification

- PSA
- Clinical Stage
- Gleason Grade
- Number and extent of positive biopsies
- PSA velocity/ PSA kinetics
- Imaging (Bone scan, CT, MRI)
<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>Points</th>
<th>N</th>
<th>% of cohort</th>
<th>% fail</th>
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<td>721</td>
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<tr>
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<td>6.1-10</td>
<td>1</td>
<td>453</td>
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<td>14</td>
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<td>10.1-20</td>
<td>2</td>
<td>209</td>
<td>15</td>
<td>28</td>
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<tr>
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<td>20.1-30</td>
<td>3</td>
<td>36</td>
<td>3</td>
<td>33</td>
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<tr>
<td></td>
<td>&gt;30</td>
<td>4</td>
<td>20</td>
<td>1</td>
<td>55</td>
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<tr>
<td>Gleason</td>
<td>1-3/1-3</td>
<td>0</td>
<td>1068</td>
<td>74</td>
<td>12</td>
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<td>1</td>
<td>239</td>
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<td>20</td>
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<tr>
<td></td>
<td>4-5/1-5</td>
<td>3</td>
<td>132</td>
<td>9</td>
<td>28</td>
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<tr>
<td>T-stage</td>
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<td>0</td>
<td>1410</td>
<td>98</td>
<td>14</td>
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<td>T3a</td>
<td>1</td>
<td>29</td>
<td>2</td>
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<tr>
<td>% pos bx</td>
<td>&lt;34%</td>
<td>0</td>
<td>911</td>
<td>63</td>
<td>10</td>
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<tr>
<td></td>
<td>&gt;34%</td>
<td>1</td>
<td>528</td>
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<td>0</td>
<td>51</td>
<td>4</td>
<td>6</td>
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<tr>
<td></td>
<td>&gt;50</td>
<td>1</td>
<td>1388</td>
<td>96</td>
<td>15</td>
</tr>
</tbody>
</table>
Do Nothing?!

- 331 patients with a median follow-up period of 84 months (range 24–132 months)
- 101 patients (31%) came off active surveillance because criteria for intervention were fulfilled,
- 32 patients (10%) received radical treatment although they did not fulfill the criteria for intervention
- The overall survival was 85% and the disease-specific survival was 99%
- Three patients died of prostate cancer
Survival Benefit to Surgery

May 12, 2005 with f/u May 2, 2011

The NEW ENGLAND JOURNAL of MEDICINE

Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer

Anna Bill-Axelson, M.D., Lars Holmberg, M.D., Ph.D., Mirja Ruutu, M.D., Ph.D., Michael Häggman, M.D., Ph.D., Swen-Olof Andersson, M.D., Ph.D., Stefan Bratell, M.D., Ph.D., Anders Spångberg, M.D., Ph.D., Christer Busch, M.D., Ph.D., Stig Nordling, M.D., Ph.D., Hans Garmo, Ph.D., Juni Palmgren, Ph.D., Hans-Olov Adami, M.D., Ph.D., Bo Johan Norlén, M.D., Ph.D., and Jan-Erik Johansson, M.D., Ph.D., for the Scandinavian Prostate Cancer Group Study No. 4*
Survival Benefit to Surgery

Bill-Axelson, A et al NEJM 2005
DaVinci Robotic System
Advantages to the RALP

- Data suggesting:
  - Lower blood loss
  - Earlier discharge
  - Quicker return to regular routine
  - Lower rate of bladder neck contraction
  - Earlier return of continence

- Equal cancer cure rates
  - Continence and potency data related to surgeon
  - Safety higher in high volume hospitals
Robotic Volume by Year
2012 429,1740 cases overall
Radiation Therapy
Types of Radiation Therapy

- External beam radiation therapy (EBRT)
  - X-rays (aka photons)
    - Conventional
    - 3D-CRT
    - IMRT (Intensity Modulated Radiation Therapy)
  - Electrons (superficial penetration)
  - Particle therapy (e.g. protons, carbon ions)

- Brachytherapy (“short-therapy”)
  - Interstitial
  - Low dose rate (e.g. I-125, Pd-103) - permanent
  - High dose rate (HDR) (e.g. Ir-192) - temporary
IMRT

- 25 Gy
- 45 Gy
- 65 Gy
- 70 Gy
- 76 Gy
- 78 Gy
- 80 Gy
Radiation Therapy

• Advantages
  • Saves lives
  • Avoids surgery
  • Low risk of side effects

• Disadvantages
  • Irritative voiding symptoms (urinary and stools)
  • Bleeding
  • Cancer risk
  • Difficult to salvage
  • Cost
What is new in screening and treatment?

- MRI “fusion biopsies”
- For men with rising PSA and prior negative prostate biopsies
- Allows identification of lesions and directed biopsies for enhanced diagnosis

- Molecular risk stratification

- New therapies for men with advanced and high risk prostate cancer (Sipuleucel T, Abiraterone acetate, Enzalutamide)
Prolaris and AUA Risk

Univariate p-values: AUA<10^{-3}, AUA+Prolaris<10^{-5}

AUA RISK

- HIGH
- INTERMEDIATE
- LOW

AUA RISK %

AUA + PROLARIS RISK %

Data on file Myriad Genetic Laboratories, Inc
Genome Dx

• GenomeDx platform employs high-resolution, whole-genome analysis approach to profile RNA expression signatures.

• Very powerful technique to explore over a million individual RNA molecules from genes and non-coding regions of the human genome.

• Prostate Cancer test near commercialization
Genomic Health

- Maker of Oncotype Dx for breast cancer and for colon cancer.
- They have an mrna expression array test that is undergoing evaluation and validation currently
- Identification of Prostate Cancer-Expressed MicroRNAs Associated with Clinical Recurrence (cR) and Prostate Cancer Specific Survival (PCSS) Following Radical Prostatectomy (RP) presented at GU ASCO
UCSD Genitourinary Malignancies Program

• **Urology**
  – Christopher Kane, MD
  – J. Kellogg Parsons, MD, MHS
  – Ithaar Derweesh, MD
  – A. Karim Kader, MD, PhD
  – Christina Jamieson, PhD

• **Medical Oncology**
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  – James Mike Randall, MD

• **Radiation Oncology**
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  – Arno Mundt, MD
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Urologic Oncology
Prostate & Kidney Cancer

Christina Jamieson, PhD
Cancer, Cell Biology, Endocrinology, Genomics, Immunology, Molecular Biology, Translational Research

Karim Kader MD, PhD
Robotic Surgery
Urologic Oncology
Bladder Cancer
Urologic Oncology Clinical Excellence

- Great access and communication
- Multidisciplinary care - well integrated
  - Neoadjuvant chemo/ADT for high risk prostate cancer
  - Neoadjuvant TKI for high risk kidney cancer
  - Primary and adjuvant/salvage radiation therapy with fiducial markers and dose escalation
- High quality minimally invasive surgery
- Robotic radical prostatectomy
  - Low complication, high quality outlier UHC
- Robotic radical cystectomy for bladder cancer patients
  - Low blood loss and enhanced safety for elderly patients
- Robotic and Open Partial nephrectomy
  - Very high proportion of nephron sparing surgery vs. radical nephrectomy
- Extensive retroperitoneal lymph node dissection for testes cancer

- High risk advanced kidney cancer surgery (IVC thrombus)
- Innovative clinical trials