Male Genitourinary Malignancies

Timothy Gilligan, MD
Cleveland Clinic Taussig Cancer Institute
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Diagnoses and Deaths

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<th>Cancer</th>
<th>Annual Cases</th>
<th>Annual Deaths</th>
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<td>Prostate</td>
<td>220,000</td>
<td>30,000</td>
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<tr>
<td>Bladder</td>
<td>70,000</td>
<td>15,000</td>
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<tr>
<td>Kidney</td>
<td>60,000</td>
<td>13,000</td>
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<tr>
<td>Testis</td>
<td>8,000</td>
<td>350</td>
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Data from American Cancer Society
Prostate Cancer

- Most common cancer in US men
  - 2nd leading cause of cancer death in US men
  - 218,000 estimated new cases in 2010
  - 32,000 estimated deaths for 2010
  - Usually asymptomatic at diagnosis

- Lifetime risk:
  - Diagnosis: 1 in 6 (16%)
  - Death: 1 in 36 (2.8%)
#1 Which of the following statements about prostate cancer screening is most accurate?

A. Screening for prostate cancer is generally recommended for men aged 50 and older.

B. Proper screening includes a digital rectal exam followed by PSA measurement

C. The only risk of prostate biopsy is discomfort

D. Screening for prostate cancer has been shown to reduce the risk of dying of prostate cancer in a randomized controlled trial.

E. It is rare for a man to have prostate cancer if his PSA is less than 4 ng/ml.

Prostate Cancer: Risk Factors

- **Age**
- **Race** - African American
- **Family history**
  - 2X risk with one 1st degree relative
  - 9X risk with two 1st degree relatives

- **Prior biopsy with high grade PIN**
  (prostatic intraepithelial neoplasia)
Prostate Cancer: Symptoms

■ PSA availability and Stage Migration
  – In the era of screening, most cancers asymptomatic and detected by PSA testing

■ Early stage disease rarely produces symptoms

Screening for Prostate Cancer

■ Goal
  – Detection of early disease in patient who would suffer from or die of disease and in whom treatment of early disease reduces that risk

■ High risk: start age 40-50
  – African-American
  – Family hx prostate cancer

■ Average risk: age 50
PCa Screening: Where is the data?

- Has dramatically increased the number of men diagnosed with prostate cancer.
- Different organizations have very different recommendations.
  - USPHSTF: Current recommendation is against screening for prostate cancer with PSA
  - American Cancer Society: recommends that men make an informed decision with their doctor about whether to be tested for prostate cancer
  - American Urological Association thinks USPHSTF recommendation sucks

PCA Screening: Where is the data?

- **US PLCO Trial** (JNCI 2012;104(2):125)
  - 76,000 men randomized to screening vs. no screening
  - By year 6, 52% of the control group had been screened
  - Mortality: 3.7 (scrn) vs 3.4 (control) per 10,000 person years.

- **European RCT of screening** (NEJM 2012;366(11):981)
  - 182,000 randomized (offered screening vs. not offered screening)
  - Rate of dx: 8.2% vs. 4.8% (PSA cutoff of 3.0 at most centers)
  - Rate Ratio for death from CaP: 0.79 (p=0.001)
  - There was no difference in overall mortality
  - To prevent one death from prostate cancer:
    - 1055 men would need to be screened
    - 37 men would need to be treated
Screening for Prostate Cancer

- **Who not to screen:** anyone with life expectancy < 10 years
- **How:** Serum PSA then Digital Rectal Exam
- **Draw PSA before DRE** (Answer B)
- **No role for imaging tests**
- **PSA velocity vs PSA Density vs % Free PSA**

(Δng/ml)/year  (ng/ml)/cc
False Positive PSA

- BPH
- Infection - prostatitis
- Inflammation/irritation - e.g. after DRE or bike ride (Answer B)

Infections after prostate bx

- 2.5% - 4.2% associated with infections
- 1%-2% associated with urosepsis
- Rare deaths have been reported
- Typically quinolone resistant *E. coli*

- Pre-bx rectal swab and culture may reduce risk
#2 Which of the following men should be referred for a prostate biopsy:

A) 47 y.o. with a PSA = 2.1, feels well, firm area on right lobe of prostate

B) 84 y.o. with PSA = 9.8, free/total PSA = 0.25, nocturia x ~15 years, diffusely enlarged prostate

C) 65 y.o. with PSA = 5.5, malaise, low grade fever, dysuria; prostate enlarged and tender

D) 61 y.o with yearly PSAs, of 2.2 - 2.6 - 2.9 - 3.9, feels well, prostate exam normal

E) (A) and (D)

Indications for Prostate Biopsy

• Abnormal DRE, regardless of PSA (patient A)

• PSA > 4

• PSA ‘velocity’ (rate of rise) > 0.75 ng/yr (patient D)

• Free/Total PSA < 0.15
PSA in PCA Screening

- Standard cut off for normal is 4 ng/ml
- Two thirds of men with a PSA between 4 and 10 will have normal biopsy results
- 15% of men with a normal DRE and PSA < 4 were found to have prostate cancer on random biopsies in the Prostate Cancer Prevention Trial (RCT of finasteride)

Prostate Cancer Risk Stratification

- PSA (<10 vs 10-20 vs >20)
- Gleason Sum
  - 2-6 = low risk
  - 7 = intermediate risk
  - 8-10 = high risk
- DRE
Treatment of localized prostate cancer

- Radical prostatectomy
- Radiation therapy
- Brachytherapy (interstitial implantation of radioactive seeds)
- Radiation + hormone therapy for locally advanced or high grade disease

How do you want it done?
How do you want it done?

Does Local Treatment Affect Outcomes

- Increased survival with prostatectomy vs surveillance in **non-screening-detected disease**
Does Local Treatment Affect Outcomes

- Increased survival with prostatectomy vs surveillance in non-screening-detected disease
- Increased survival with radiation therapy plus androgen deprivation compared to AD alone
- No randomized controlled trials comparing surgery vs external beam radiation vs radioactive implants

Hormone Therapy

- Object: Block testosterone production or action
- Methods:
  - Orchiectomy
  - LHRH Agonists (Goserelin, Leuprolide, others)
  - Antiandrogens (Bicalutamide, Flutamide)
  - Block adrenal androgen production
Which of the following are side effects of hormone therapy for advanced prostate cancer?

A) Anemia  
B) Osteoporosis  
C) Impotence  
D) Features of Metabolic Syndrome (DM, CAD)  
D) All of the above  
E) (B) and (C)
Testicular Cancer

Testis Cancer
Introduction

- Most common solid tumor among men 15-35
  - New cases: 8400
  - Deaths: 380
  - Even metastatic disease is curable

- Serum markers uniquely helpful: **AFP, HCG, LDH**
  - Elevated AFP = NSGCT (i.e., predicts histology)
  - Degree of elevation highly prognostic
  - Marker half life during chemo predicts prognosis
  - Rise in markers the most common sign of relapse
Testis Cancer: Risk factors

- **Cryptorchidism**
  - Risk in both testes: undescended and contralateral

- **Family History**
  - Brother more than father

- **Prior contralateral cancer**
  - Median interval 5 yrs;
  - ~2% will develop contralateral tumor

- **Dysgenetic gonads**
  - E.g., Klinefelter’s syndrome (47,XXY) associated with extragonadal (mediastinal) GCT

Testis Cancer Presentation and Diagnosis

- **Painless/Painful** testicular enlargement/mass

- **Testicular US** (solid heterogeneous mass vs. hydrocele, hernia)

- **Inguinal orchiectomy** for any solid lesion
  (Testis biopsy CONTRAINDIANTED)

- May present with signs/sx of metastatic disease
  - RP nodes, lungs, mediastinum most common
  - Bone, liver, brain portend poor prognosis

- Isochromosome 12p in an undifferentiated cancer
  (e.g., bx of mediastinal mass or RP mass) is diagnostic of germ cell tumor
Testis Cancer
Presentation and Diagnosis

- **Keep in mind:**
  - GYNECOMASTIA can be the presenting sign even without a palpable testicular mass
  - Retroperitoneal masses in men aged 15 to 50 are often germ cell tumors (either metastatic or primary)

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Testis Cancer: Classification

- **Germ Cell Tumors**
  - Seminoma*
  - Non-Seminoma

  * Needs to be 100%

- Embryonal Carcinoma
- Teratoma
- Yolk Sac Tumor
- Choriocarcinoma
#6. A 28 yo baseball star presents with a painless left testicular mass. PE otherwise normal. The most appropriate next step should be:

A) Testicular Ultrasound  
B) Ultrasound-guided trans-scrotal testicular biopsy  
C) Radical inguinal orchiectomy  
D) Trial of antibiotics  
E) Whole body PET scan

Stage I Testis Cancer: No clinical evidence of cancer outside the testis

- **Radical Orchiectomy – All Pts**
- **Post-surgery:**
  - **Seminoma**
    - Surveillance (18% relapse)
    - Radiation Therapy
    - Chemotherapy
    - Long-term survival = 99% with any of these
  - **Non-Seminoma**
    - Surveillance (30% relapse)
    - RPLND
    - Cisplatin-based chemotherapy
    - Long-term survival = 99% with any of these
Staging Germ Cell Tumors

- Lymphatic drainage from the testicles is to the retroperitoneum.
- Spread of testis cancer is very predictable:
  - Testis → Retroperitoneal lymph nodes → lungs, liver, etc
    - Stage I = testes only
    - Stage II = retroperitoneum
    - Stage III = distant metastases or highly elevated tumor markers
- All stages have a high cure rate
- Curative chemotherapy for metastatic testis cancer was one of the major breakthroughs in medical oncology

Stage IIc or Greater Testis Cancer

- Cisplatinum-based chemotherapy
- Cure rate
  - Good risk ~ 90%
  - Intermediate risk ~ 80%
  - Poor risk ~ 50%
#8. A 21 y.o. man with stage III NSGCT requires chemotherapy. Which of the following might you not expect as a late toxicity?

A. Biliary cirrhosis  
B. Infertility  
C. Acute leukemia  
D. Raynaud’s phenomenon  
E. Peripheral neuropathy  
F. Hearing loss  
G. Cardiovascular disease
Bladder Cancer: Key facts

- Male:Female ratio= 2.5:1
- Major risk factor is smoking and occupational exposure
- Most often presents with hematuria
- Low grade cancers very rarely life-threatening
  - High grade cancers very dangerous and often multifocal
  - Superficial tumors removed via cystoscopy tend to recur
- Muscle-invasive tumors treated with cystectomy or chemo-radiation
- Metastatic Bladder Cancer
  - Systemic chemotherapy – MVAC or GC

Renal Cancer
Renal Cell Cancer: Key facts

- Male:Female ratio= 2:1
- Major risk factor is smoking
- Von Hippel Lindau disease (hemangioblastomas, RCC)
- Most often presents with hematuria
- Biopsy rarely indicated unless metastatic
- Limited disease: Surgery
- Advanced disease
  - Cytoreductive Nephrectomy an option
  - Targeted therapy (Anti-VEGF therapy/ mTOR inhibitors)
  - Biologics (Interferon alpha, interleukin 2)

Thank You and Good Luck!