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Prostate Cancer - An Overview

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Prostate Cancer - Epidemiology

- Most common non-cutaneous malignancy in US men since 1984
- 27% of all non-skin cancers in men
- 1 / 7 (15.3%) men will be diagnosed in their lifetime
- 1 / 38 men die from prostate cancer (2.6%)
- Incidence varies greatly by race with AA men experiencing 56% higher incidence than whites

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PSA introduced widely in 1989
- Incidence of PCa increased dramatically
- Precipitous fall in incidence in 1995
Mortality

- Second leading cause of cancer death in the US
- Estimated 10% of all cancer deaths
- Leading cause of death (35%) of those diagnosed with the disease (1973 - 2008)

Mortality - Declining since 1991

- 1. Early detection and stage migration
- 2. Increased utilization of curative options
- 3. Changes in reporting cause of death
- 4. Improvements in therapies for advanced disease
- 5. Increased risk of death from other / secondary causes

Racial Differences

- African-Americans and Jamaicans of African decent have the highest incidence of prostate cancer in the world.
- Although African-Americans experienced a greater decline in mortality than Caucasians since the early 1990s - death rates are still 2.4 x higher
- African-Americans at every stage get less aggressive treatment regardless of age, marital status, tumor risk, comorbidities compared to Caucasians
- Prostate cancer mortality among African-Americans and Caucasians is similar in equal access healthcare systems
Racial Differences

- American men of Asian descent have a lower incidence than white Americans but higher than men of similar ethnicity living in Asia.
- This implicates external factors - dietary, lifestyle, environmental - in the development of prostate cancer.

Global Incidence and Mortality

- Second most common cancer and 6th leading cause of death worldwide - estimated 899,000 cases and 258,000 deaths annually.
- Decreasing trends in prostate cancer mortality observed in high-income countries utilizing PSA screening.
**Age at Diagnosis**

- Rarely diagnosed in men < 50 (2%)
- Median age at diagnosis 67 (PSA era)
- 63% diagnosed after age 65
- Average age of death from prostate cancer - 77

**Stage at diagnosis**

- Stage migration (PSA era)
  - 81% of men have localized disease at diagnosis
  - 75% reduction in incidence of metastatic disease
  - Non-palpable cancers account for up to 75% of new diagnoses
Genetic Influences

- Strong familial component
- Risk increases according to number of affected family members, degree of relatedness, and age at diagnosis

Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer

Other Influences

- Smoking
  - Increased risk of disease recurrence after primary treatments
  - Increased risk of prostate cancer specific mortality
- Diet
  - Similar association but "Western" diet appears to play a role
- Obesity
  - Lower PSA at diagnosis
  - Increased risk of higher-grade PCs
  - Higher treatment failure rate
  - Higher disease-specific mortality
Chemoprevention

- Goal: decrease cancer incidence, mortality and treatment related toxicities
- Effective agents are nontoxic and inhibit specific oncogenic molecular carcinogenic pathways
- PCPT - finasteride reduced the prevalence of prostate cancer by 25% - observed increased incidence of high risk disease - use did not influence survival
- SELECT - neither selenium nor Vit E reduced the risk of prostate cancer. Use of Vit E was associated with an increased risk of prostate cancer

Sulforaphane

Diagnosis - Screening

- Prostate cancer rarely causes symptoms
  - symptoms suggest locally advanced / distant disease
  - urethral obstruction
  - hydronephrosis
  - impotence
  - bone pain
  - anemia
  - pathologic fracture
  - edema
Screening

- Testing for disease in healthy, asymptomatic individuals
- Goal - in the absence of successful prevention options, identifying disease as early as possible affords the opportunity for cure while minimizing morbidity

Screening - Randomized Trials

- PLCO - Prostate, Lung, Colon, Ovary - NIH (1993)
  - No reduction in 13 year mortality between screened and unscreened arms
  - Low power to detect difference between arms?
- ERSPC
  - European Randomized Trial of Prostate Cancer Screening
  - 21% reduction in mortality
  - Fewer men with advanced disease
  - Lower stage at presentation

Screening

- Trials identify risk of over-diagnosis of indolent disease
- Risk of overtreatment
Specialty Group Recommendations

- USPSTF
- PSA screening “D” rating
- American College of Preventative Medicine
- Recommends against screening with PSA/DRE
- American Cancer Society
- Men should have the opportunity to make an informed personal decision
- Earlier for high-risk populations
- AUA
- Shared decision making for men between 55-69

Diagnostic Modalities

- DRE - PPV 4 - 11% in men with PSA up to 2.9
- 33 - 84% PPV the PSA 3 - 9.9
- PSA and DRE do not always detect the same cancers and subsequently are considered complimentary

PSA Density (PSAD)

- Adjusting PSA total value to prostate volume
- PSA elevation due to benign adenoma vs malignancy
- PSAD > 0.15 in men with PSA between 4 and 10.
PSA Velocity

- PSA increase > 0.75 / year in men with PSA between 4 - 10

Gleason's Pattern

1. Small, uniform glands
2. More stroma between glands
3. Distinctly infiltrative margins
4. Irregular masses of neoplastic glands
5. Only occasional gland formation

<table>
<thead>
<tr>
<th>Grade Group</th>
<th>Gleason Score</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3+3=6</td>
<td>Only isolated, discrete, well-formed glands</td>
</tr>
<tr>
<td>2</td>
<td>3+4=7</td>
<td>Predominantly well-formed glands with loose component of poorly-differentiated transition glands</td>
</tr>
<tr>
<td>3</td>
<td>4+3=7</td>
<td>Predominantly poorly-differentiated transition glands with loose component of well-formed glands</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>Only poorly-differentiated transition glands, or predominantly poorly-differentiated transition glands, or predominantly lacking glands and loose component of well-formed glands</td>
</tr>
<tr>
<td>5</td>
<td>9-10</td>
<td>Lack gland formation (or with necrosis), with or without poorly-differentiated transition glands</td>
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</tbody>
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MRI - Prostate

- Assess presence of abnormal focus
- Treatment planning
- Focal Therapy
- Perineal Biopsy

Multiparametric MRI - prostate
Bone Scan

- Indications:
  - PSA > 10 - 20
  - High grade disease on biopsy
  - Symptoms

 MRI Prostate

- Abnormal Focus
MRI Prostate - Treatment Planning

- Locally advanced disease
- Bulky lymphadenopathy
- Bladder neck invasion

MRI Prostate - Focal Therapy
Diagnosis - TRUS Biopsy