Prostate Cancer Early Detection & Management

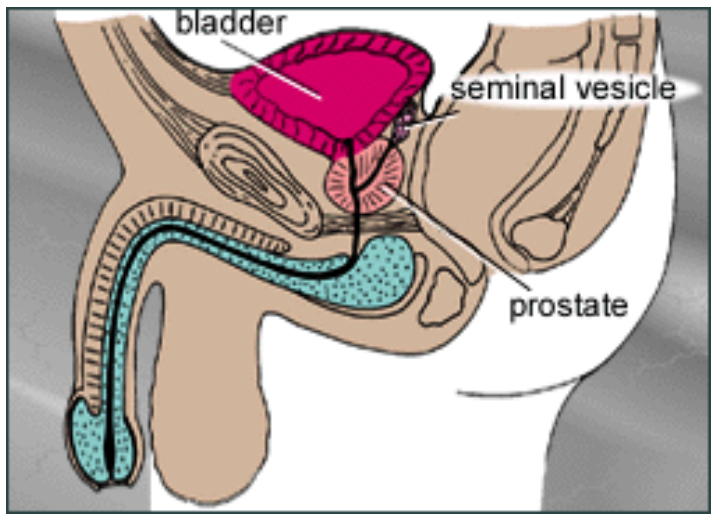
Dr M. Beheshti

M.D., F.R.C.S. (C)

William Osler Health Centre

What is the Prostate

- A Walnut Shape Gland Under the Neck of the Bladder, Around the Urethra;
- It Produces Semen;
- The Site of 3 Common Diseases in Men: Prostatitis, BPH and Prostate Cancer



SYMPTOMS OF PROSTATE DISEASE

- Frequency, Nocturia, Urgency, Incontinence;
- Difficult or Painful Urination; Hesitancy, Straining, Intermittency, Dribbling;
- Blood or Pus in the Urine;
- Pain in the Groin, Pelvic Area, Testicles, Back Area;
- Painful Ejaculation

CAP AND SYMPTOMS

"Early Stages May Have No Symptoms"

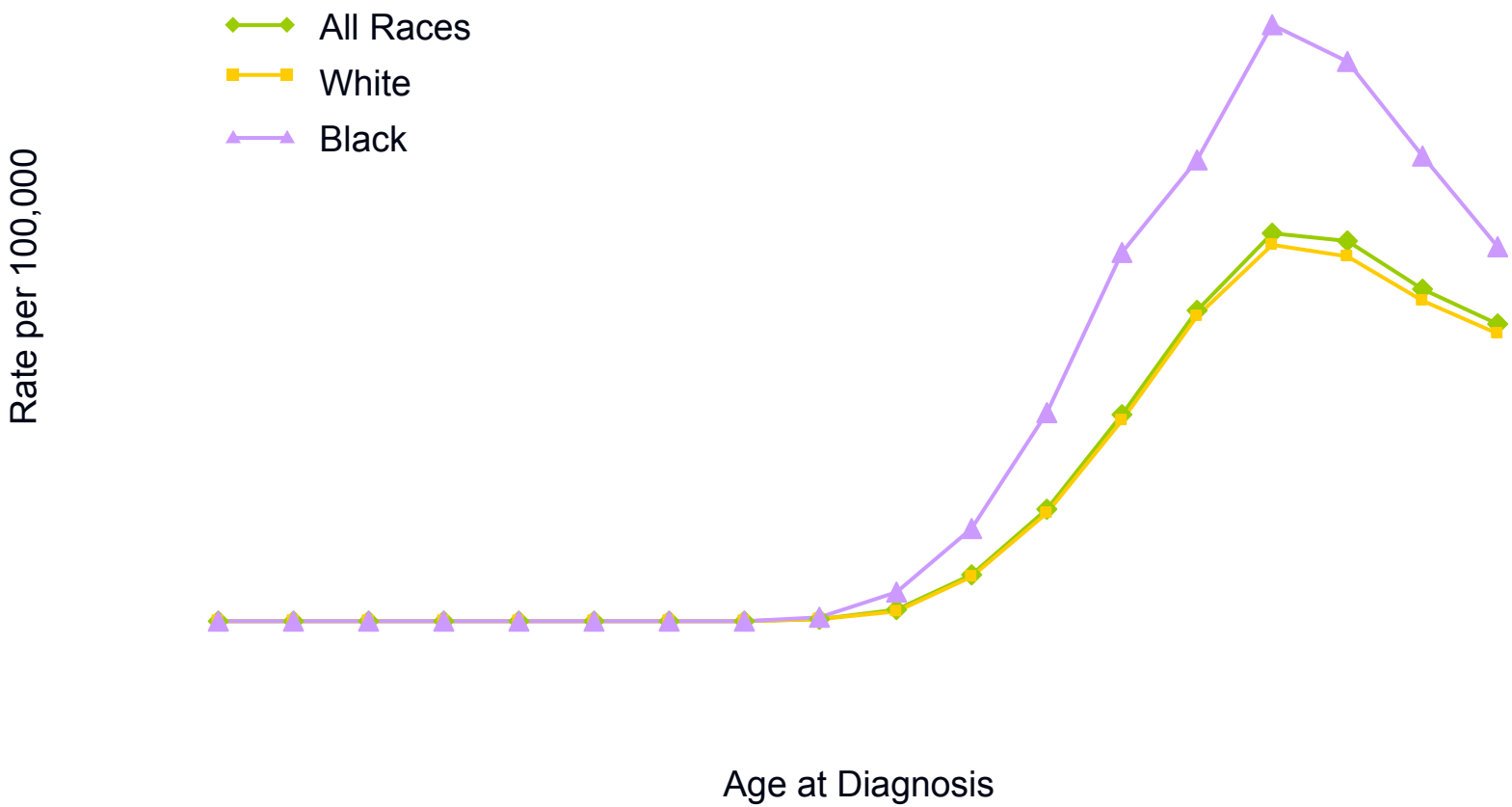
PROSTATE CANCER FACTS

- 1 in 7 men develop CAP in lifetime; 20,000 Men in Canada will develop CAP this year;
- 1 in 4 of these men die of CAP; 4,200 men with CAP will die from CAP each year;
- Most common CA in men;
- 2nd most deadly form of CA after lung CA

CAP Incidence

- Annually
  - 260,000 men diagnosed
  - 35,000 – 45,000 death from CAP
- Second most common cause of CA related deaths in men
- 1 in 6 men at age of 50 may get CAP

Crude Incidence Rate by Age



SEERs Database

CAP DIAGNOSIS

- DRE
- PSA
- TRUS BIOPSY

PSA NORMAL VALUE

- 0-4 ng/ml; Arbitrary Value
- In USA, PSA Value triggering Prostate Biopsy is Decreasing
- Normal Value Depends on Age

HOW TO DEAL WITH ABNORMAL PSA

- Age Adjusted PSA ;
- Free/Total PSA: >24% ;
- PSA Velocity, <0.75/ year ;
- PSA Density, <0.15 ;
- New Markers ;
- TRUS Biopsy of Prostate ;

PSA SCREENING AND DRE

- Men > age 50;
- Men with Life Expectancy > 10 years;
- Men with Family History of CAP or African American Should Begin Testing at Age 40;

PSA SCREENING

- Began in 1987
  - dramatic increase in diagnoses of CAP with arbitrary PSA of > 4
- Initial increase in CAP mortality
  - but since 1990 – 1992 mortality has dropped about 27%
- Despite PSA screening
  - lifetime risk of death remains stable at 3% for unknown reason

PSA AND EARLY CAP DETECTION

- Advanced stages of CAP(Stages T3, T4) decreased from 50% in 1988 to 20% in 1998
- No. of Early stages of CAP(T1) increased from 10% in 1988 to 30% in 1998
- Decreased Mortality of 25% now compared to 1990
- The picture is not clear however

Whitmore-Jewett Classification Stage D

Widespread (metastatic) cancer

D1 Cancer in pelvic lymph nodes

D2 Cancer in bone or other organs

RISKS OF PSA TESTING

- Anxiety ; PSA phobia
- CAP treatment side effects
- Over treatment of low risk CAP; 85-90% of these patients undergo curative treatment in Canada

ROLE OF PSA IN:

- Early CAP detection : controversial
- Monitoring CAP post treatment : Reliable

PROSTATE CANCER PREVENTION TRIAL:"PCPT"

- Designed in 1992 to see if Proscar would reduce CAP
- Men with normal DRE & PSA ≤ 3.0
- Incidence of CAP decreased by 25% in Proscar group
- Most striking: 25% of men in placebo group developed CAP despite normal PSA and DRE
  - 15% of those had PSA of < 4

PCPT further analysis

- A man with PSA of 3-4:
  - Risk of CAP – 30%
  - Risk of high grade CAP – 9.4%
- A man with PSA of 1 -2:
  - Risk of CAP – 20%
  - Risk of high grade CAP – 2.6%
- 1/3 of 211 men with Gleason ≤ 6 died of CAP

IS PSA RELIABLE?
PCPT Revealed :

- Even normal PSA may be associated with CAP
- 10% of men with PSA of 0.5-1.0 had CAP
- High Grade CAP was seen in 1-2% in men with PSA <2.0 and in 10% if PSA was 2-4.0

Treatment Options for CAP

- Therapies of curative intent (definitive therapy)
  - Radical prostatectomy
    - Retropubic
    - Perineal
    - Laparoscopic
  - Radiotherapy (RT)
    - External beam radiation
      - 3-D conformal RT
      - Intensity Modulated Radiation Therapy (IMRT)
    - Brachytherapy
  - Cryotherapy
  - Combination of therapies
- Hormonal therapy
  - Bilateral orchiectomy
  - LHRH-A
  - Anti-androgen
  - Combined Androgen Blockade (CAB)
- Watchful Waiting

To Decrease Prostate CA Mortality

- PSA should be lowered than 4

- To allow PSA get to higher level, based on PCPT data, places patient at risk of a larger, higher-grade and less curable CAP

LOWERING PSA TO DETECT CAP

- Leads to diagnosis of an enormous number of harmless form of CAP

Over Diagnosis & Over Treatment of CAP

- A major concern

CHALLENGES IN CAP TREATMENT

- Word “cancer” evokes a response that we may over treat some patients with low risk disease

- To find the biologically significant disease but not automatically treat those who are not at risk

The challenge for urologists is:

- To find biologically significant CAP in those group of patients who are on active surveillance and to intervene to decrease mortality and morbidity (even if they are years down the road)

What is "Clinically Insignificant" cancer?

- Without treatment will not lead to death or morbidity

- Majority of good risk patients

PROBLEM WITH WATCHFUL WAITING

- Biopsy may under-stage and under-grade tumor
- PSA doubling time may not reflect disease progression

The Active Surveillance Hypothesis

- Delayed curative therapy offered effectively to the subset of patients with rapid progression, while the majority of favorable risk patients can be managed with observation, resulting in improved QOL

HOW TO FOLLOW PATIENTS ON ACTIVE SURVEILLANCE

- PSA doubling time if increases rapidly

- Repeat biopsy at 3 – 6 months
  - More important than PSA
    - IF negative: good progress
    - IF shows significant disease: treat

FACTORS TO DECIDE ON ACTIVE SURVEILLANCE

- PSA doubling time
- Age
- Presence of co-morbidity
- Tumor Grade:
  - Most powerful predictor of survival
  - 10 times greater mortality rates with higher Gleason Scores compared to those with lower Gleason scores
- Tumor Volume

CAP RISK CATEGORIES

- Low Risk : all of
  - PSA<10
  - Gleason < 6
  - Stage T2a Or Less
- Intermediate Risk : all of
  - PSA<20,
  - Gleason < 8
  - Stage T1/2
- High Risk : any of
  - PSA >20
  - Gleason >8
  - Stage T3a

Criteria Defining Significant Progression

- PSA doubling time < 3 years, based on at least 3 separate measurements over a minimum of 6 months
- Clinical progression:
  - Double the size of lesion on DRE
  - Patient requiring TURP
  - Distant metastasis
- Increasing Gleason score on re-biopsy

Watchful Waiting

=

Active Surveillance

- Can be utilized in low grade CAP
- "Capsure" : 95% progression free rate at one year and 65% at 5 years.
- At 5 years 2/3 of patient on watchful waiting and 1/3 gone to other treatment

Active Surveillance with Selective delayed Intervention

- Is the way to manage good risk prostate cancer

What We Know

- ≥ 30% of men harbor CAP
- Systematic prostate biopsy results in CAP detection in 25% (PCPT)
- Screening increases the incidence to mortality rate from 2.5:1 to 15:1
- Radical prostatectomy reduces CAP mortality by 50% in an intermediate high risk population; but number needed to treat = 17:1 (one life saved in 17 patients treated

What we know

- CAP progresses slowly in most of low risk patients, with a long window of curability
- Mortality rates have fallen in both screened and unscreened populations by 20% (life style change?)
- 97% of men with well differentiated CAP received radical therapy in 2002

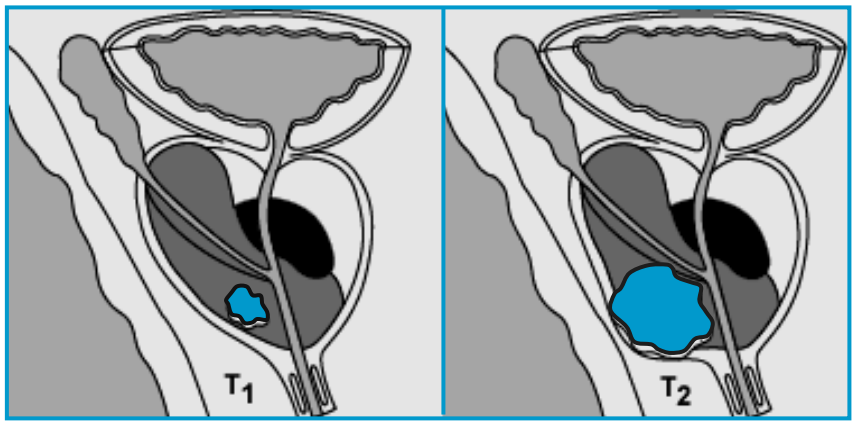
What we don't know

- How to pick the patients with curable aggressive cancer for radical treatment

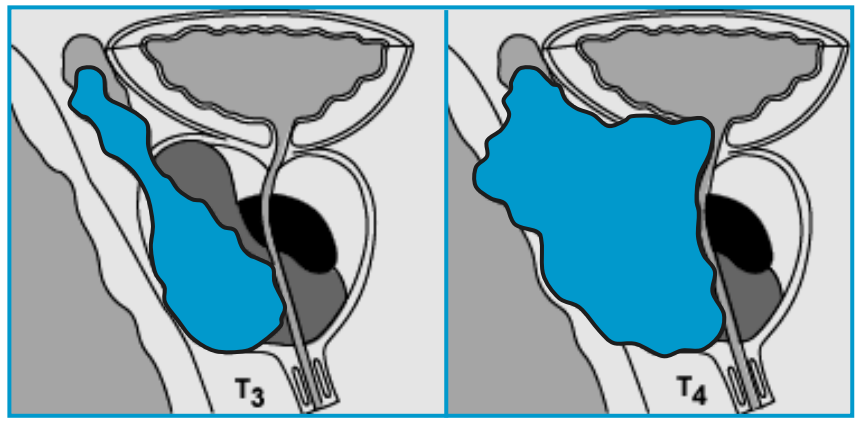
We need to recognize T1C a prostate cancer

- T1A
  - Incidental post TURP
  - ≤ 5% of chips
  - No Gleason pattern 4 or 5
- T1C – a
  - Based on systematic biopsy (≥ 12 cores)
  - < 1/3 of cores involved
  - ≤ 10% of Total surface area
  - No Gleason pattern 4 or 5
  - PSA ≤ 10

The 4 Stages of Local Prostate Tumor Growth



Localized disease



Locally advanced disease

65 Year old male, PSA 4.5, Gleason 6, TIC, 2/10 cores involved

- Median life expectancy in Canada 16 years
- This is 2 – 3 times the median PSA DT for good risk patients
- 50% chance PSA will be < 10 (4.5 x 2.3) at end of his life
- 20% chance of rapid PSA DT (< 3 years); 85% chance of cure if treated when PSA = 10
- Increased chance of failure due to surveillance : 1.4%
- Chance of avoiding therapeutic intervention is 60 – 80%

Conclusion

- Most good risk patients (PSA < 10, Gleason ≤ 6, ≤ 33% of cores positive) may not need treatment
- Long window of curability for those who choose active surveillance
- Median PSA doubling time in good risk patients is 7 years
- Patients with a PSA DT > 3 years are at a low risk of CAP death
- PSA doubling time is cheap & readily available

Thank you