Carcinoma of the Prostate screening challenges

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Cancer of the prostate is now recognized as one of the principal medical problems facing the male population.

The estimated lifetime risk of disease in the United States is 17.6% for whites and 20.6% for African Americans, with a lifetime risk of death of 2.8% and 4.7%, respectively.
In Iraq the estimated number of patients with newly diagnosed carcinoma in 2013 was 18000, of whom 498 patients were diagnosed with carcinoma of the prostate which makes about 3% of all types of carcinoma.

In Alamal hospital during 2013, 102 patients were diagnosed with carcinoma of the prostate making about 2.9% of all types of cancer.

In cancer registry in Iraq, carcinoma of the prostate was number 13 among the most common tumors.
Based on GLOBOCAN estimates, about 14.1 million new cancer cases and 8.2 million deaths occurred in 2012 worldwide.
Prostate Cancer Incidence and Mortality Rates by World Area.
Prostate Cancer

- Risk Factors
  - Age-median age of diagnosis is 72 y
  - Smoking
  - High Fat/ Western diet
  - Family History-8-9% of all cancers due to inherited gene higher for younger men

- Incidence of prostate cancer increases with age so that up to 70-80% of men in their 80-90’s have autopsy evidence of prostate cancer
both genetics and environment play a role in the origin and evolution of this disease.

Familial and Genetic Influences

Sporadic cancers account for about 85% of all prostate cancers, and about 15% are familial or hereditary.
Inflammation, Infection, and Genetic Susceptibility

- Chronic inflammation leading to cellular hyperproliferation to replace damaged tissue contributes to the development of infection-associated cancers.
Androgens

- Androgens influence the development, maturation, and maintenance of the prostate, affecting both proliferation and differentiation of the luminal epithelium an important role in prostate carcinogenesis.
- One hypothesis is that the higher incidence of prostate cancer observed in African Americans may be related to elevated levels of circulating androgen.
- Long-term absence of androgen exposure to the prostate appears to protect against the development of cancer.
Other Influences

- Abnormal Sexual Activity.
- Vasectomy.
- Smoking.
- Insulin-like Growth Factor Axis.
- Diet.
- Decrease Vitamin D Level, Vitamin D Receptor, and Calcium.
- Dietary Fat.
- Obesity.
- Leptin.
- Alcohol Consumption.
• Premalignant Lesions
  • PIN-prostatic intraepithelial neoplasia
    – May be a precursor lesion to prostate cancer
      • Characterized by cytologically atypical cells with architecturally benign glands
      • Approximately 20% of patients with PIN will go on to have a subsequently positive biopsy
  
  • ASAP-atypical small acinar proliferation
    – Atypical glands and cells but can’t quite call it cancer
      • Up to 50% will have a future positive biopsy
Why we should raise awareness of prostate cancer?

- One of the most common cancers in men
- Not known how to prevent prostate cancer
- Earlier diagnosis can lead to more treatment options
- Evidence that many people still do not know a lot about the prostate and prostate cancer
Challenges in raising awareness

- Raising awareness of prostate cancer is controversial
- Complex disease
  - range of possible symptoms or no symptoms at all
  - no test to distinguish slow growing & aggressive forms of disease; can lead to over-treatment
- Problems with detection
• Raising awareness of prostate cancer is complex and controversial with disagreement over what should be done
• Within prostate cancer field is huge spectrum of views on whether awareness raising should be carried out. Some of medical community don’t think it’s wise, support groups and men with prostate cancer want us to be doing far more. Have to respond to those we represent and evidence based so take middle ground.
• Understanding of relationship between awareness raising and diagnosis of the disease is limited.
And that anyone with symptoms goes to GP quickly. Unfortunately with many cases of aggressive prostate cancer – no symptoms

However, by raising awareness could lead to increasing diagnoses of men who have slow growing form of cancer and in whom it would not have caused any problems in their lifetime. They may have treatments which have side effects that impact significantly on quality of life e.g. incontinence, impact on sexual function
• Difficult to agree simple key messages & calls to action – no clear prevention message

• Without clarity on testing, symptoms (many men don’t have them), call to action awareness messages become very complex when need to be simple. And cannot be specific about what we want men to do once they are aware. This forces our work to be general and less focussed.
Prostate Cancer

• Screening
  • Who should be screened?
    • AUA recommends all men 50 y and older with >10yr life expectancy be screened
    • African American men should be screened starting at age 45
    • Men with a paternal side family history should be screened at age
    • US Preventive Services Task Force: don’t even offer DRE or PSA
Arguments against screening

- Disease of mainly elderly men who are destined to die of competing causes
- Detection of clinically insignificant cancers
- Expensive—Initial estimates of screening men aged 50 to 70 years for prostate cancer $25 billion during first year alone
- Not effective in decreasing mortality from the disease
Differential Diagnosis

- Not all patients with an elevated PSA concentration have CaP. Other factors that elevate serum PSA include BPH, urethral instrumentation, infection, prostatic infarction, or vigorous prostate massage.
- Induration of the prostate is associated not only with CaP, but also with chronic granulomatous prostatitis, previous TURP or needle biopsy, or prostatic calculi.
- Sclerotic lesions on plain x-ray films and elevated levels of alkaline phosphatase can be seen in Paget’s disease and can often be difficult to distinguish from metastatic CaP.
The main diagnostic tools used to look for evidence of CaP include: DRE, serum concentration of PSA and transrectal ultrasonography (TRUS) with biopsy.

Diagnosis depends on the presence of adenocarcinoma in operative specimens, prostate biopsy cores or aspiration needle cytology.

Histopathological examination also allows grading of the tumour.
A-Digital rectal examination (DRE)

- The majority of CaPs are located in the peripheral zone of the prostate and may be detected by DRE when the volume is about 20 mL or larger.
- The risk of a positive DRE turning out to be cancer is heavily dependent on the PSA value.
• **Digital Rectal Examination**
  • Picks up 25% of the cancers that we find
  • Overall abnormal 6-15% of men diagnosed with prostate cancer
  • Gives other important information such as screening for occult blood and for rectal cancer
Of the biggest challenges that we face in performing DRE for patients with suspected prostate cancer, is feeling of shame of such a procedure due to the cultural and social background of our society.
PROSTATE-SPECIFIC ANTIGEN

- Enzyme responsible for liquefaction of the semen
- Sensitive but not very specific
  - 25% positive predictive value to detect disease
  - Affected by many other things such as enlarged prostates, prostatitis/infection, biopsy/trauma
  - NOT affected by digital rectal exam or sexual activity
- Predictive of tumor stage
- Most predictive factor for biochemical recurrence
- Excellent tumor marker for detecting recurrent disease
Numerous strategies to refine PSA for cancer detection have been explored.

Their common goal is to decrease the number of false-positive test results.

This would increase the specificity and positive predictive value of the test and lead to fewer unnecessary biopsies, lower costs, and reduced morbidity of cancer detection.
Attempts at refining PSA have included **PSA velocity** (change of PSA over time), **PSA density** (standardizing levels in relation to the size of the prostate), **age-adjusted PSA reference ranges** (accounting for age-dependent prostate growth and occult prostatic disease), and **PSA forms** (free versus protein-bound molecular forms of PSA).
One of the challenges for PSA testing is the unavailability of this test in all primary health care centers and even in some hospitals, besides many patients find it costly to do it in the private labs.
Different CaPs appear differently on TRUS. The classic picture of a hypoechoic area in the peripheral zone of the prostate will not always be seen.

TRUS has two potential roles in the diagnosis of CaP:

1. To identify lesions suspected of malignancy.
2. To improve the accuracy of prostate biopsy.
Prostate biopsy should be considered in men with an elevated serum PSA, a DRE, or a combination of the two.

Ultrasound-guided transrectal 18G core biopsy has become the standard way to obtain material for histopathological examination. Multiple cores can be taken with a low risk of complications if antibiotic prophylaxis is used.
• Predictive Models
  • Preoperative Nomograms
    • Available at Nomograms.org
    • Available for pre treatment, post RRP, and radiation
    • PSA continues to be a driving variable
  • Partin tables
    • Recently updated, also useful for prediction of outcomes

Partin et al. *Urology* 2001
How to Increase the Benefits and Reduce the Risks of Screening for Prostate Cancer

• Risk-adjust screening by age and PSA (reduce false positives)
• Reduce false positive PSA results by repeating (verifying) positives and by adding additional markers (4 kallikrein panel or -2(pro)PSA) (reduce indications for biopsy)
• Active surveillance for low-risk cancers (reduce harms of unnecessary therapy)
• Refer patients who need treatment to high-volume physicians or centers (reduce harm of necessary therapy)

• Begin PSA testing at age 45

• For men age 45 - 59
  • PSA $\geq 3$ ng/ml: consider biopsy
  • PSA $> 1$ but $< 3$ ng/ml: return for PSA every 2-4 years
  • PSA $< 1$ ng/ml: return for PSA in 5 years or at age 50 or 60, whichever comes first

• For men age 60 – 70
  • PSA $\geq 3$ ng/ml: consider biopsy
  • PSA $> 1$ but $< 3$ ng/ml: return for PSA every two years
  • PSA $< 1$ ng/ml: no further screening

• For men age 71 or higher
  • No further screening
THANK YOU