PSA – A SIMPLE BLOOD TEST?

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WHAT IS PSA?

- PSA is a glycoprotein produced by the prostate cells and secreted in high concentrations and stored in the seminal vesicles; it is important in sperm motility.
- It is specific to the prostate NOT prostate cancer.

WHAT IS THE NORMAL VALUE?

PSA has age specific cut off values:

40 – 49 ≤ 2.5 ng/ml

50 – 59 ≤ 3.0 ng/ml

60 – 69 ≤ 4.0 ng/ml

70 + ≤ 5.0 ng/ml

(NICE, 2005).

FACTORS AFFECTING PSA

- BPH/Size
- UTI - treat repeat 6/52
- Catheterisation - monitor
- Acute urinary retention – treat, monitor
- Prostatitis – treat, repeat 3/12
- TURP – wait 3/12
- 5 α-reductase inhibitors e.g. Finasteride

NICE

According to NICE a DRE and PSA test are recommended for patients with:

- Inflammatory or obstructive LUTS
- ED
- Haematuria
- Lower Back Pain
- Bone pain

REFER VIA CANCER REFERRAL OFFICE

BENEFITS OF PSA TEST

- May provide reassurance if the test is normal
- May find cancer before the symptoms develop
- May detect cancer treatment is most effective in early stages
- DRE must be carried out by expert practitioner at the time of requesting PSA

DISADVANTAGES OF PSA

- It can miss cancer, and provide false reassurance
- It may lead to unnecessary anxiety and medical tests
- It might detect slow growing cancer that may never cause any symptoms or shortened life span
- The main treatments of prostate cancer have significant side-effects, and there is no certainty that the treatment will be successful

WHAT ARE PATIENTS TOLD?

- Ensure informed consent before PSA requested
- The complexities of the PSA test
- What happens if the PSA test is raised
- Treatments & Risks of early prostate Cancer

DOES SCREENING SAVE LIVES?

Results from 3 major randomized controlled trials recently reported

- European Randomized Study of Prostate Cancer (ERSPC)
- Goteborg (Swedish) Trial
- Prostate, Lung, Colon and Ovarian Trial (PLCO)

EUROPEAN RANDOMIZED STUDY OF PROSTATE CANCER (ERSPC)

- Began in 1991 in 7 European countries
- 162,000 men randomized to screening versus usual care
- Men aged 55 – 69
- Median follow-up 9 years

EUROPEAN RANDOMIZED STUDY OF PROSTATE CANCER (ERSPC)

Findings

- More cancers detected with screening
  - 5990 cancers in screening group
  - 4307 cancers in control arm

- Fewer prostate cancer deaths in screening group
  - 261 deaths in screening group
  - 363 deaths in control arm

Conclusion

20% lower risk of prostate cancer death in the group invited to screening

EUROPEAN RANDOMIZED STUDY OF PROSTATE CANCER (ERSPC)

Concerns with study

- To prevent one prostate cancer death
  - 1410 men screened
  - 48 men treated
- Variation in screening and follow-up protocols
- Minimal to no participation of men of African origin

GOTEBORG (SWEDISH) TRIAL

- Began in 1995 in city of Goteborg
- 20,000 men randomized to screening (PSA every 2 years) versus usual care
- Men aged 50 – 64
- Median follow-up 14 years

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GOTEBORG (SWEDISH) TRIAL

Findings

- More cancers detected with screening
  - 1138 cancers in screening group
  - 718 cancers in control arm
- Fewer prostate cancer deaths in screening group
  - 44 deaths in screening group
  - 78 deaths in control arm

Conclusion

40% lower risk of prostate cancer death in the group invited to screening

GOTEBORG (SWEDISH) TRIAL

Other findings

- No difference in overall mortality
  - 1981 in screening group
  - 1982 in control arm
- To prevent one prostate cancer death
  - 293 men screened
  - 12 men treated
- Prostate cancer mortality benefit not seen until 7-8 years after randomization
- 40% of men with screen detected cancer chose active surveillance over curative treatment

GOTEBORG (SWEDISH) TRIAL

Concerns with study

- Low PSA threshold for biopsy
  - 2.5ng/ml
  - 1 in 3 men who were not screened underwent biopsy at some point during the study
- No information on quality of life issues and side effects of treatment
- No participation of men of African origin

PLCO

- Began in 1993 in 10 centers throughout USA
- 73,000 men randomized to annual screening versus usual care
- Men aged 55 – 74
- Median follow-up 10 years

PLCO

Findings

- More cancers detected with screening
  - 2820 cancers in screening group
  - 2332 cancers in control arm

- More prostate cancer deaths in screening group
  - 7 years
    - 50 deaths in screening group
    - 44 deaths in control arm
  - 10 years
    - 92 deaths in screening group
    - 82 deaths in control arm

Conclusion

No mortality benefit among those invited to screening

PLCO

Concerns with study

- 44% of men had at least one PSA test prior to the study
  - May have excluded more aggressive prevalent cancers
  - Selectively included men with prostate cancers not detected by PSA screening (bias against showing a screening effect)

- Many men in the usual care group were screened during the course of the study
  - 40% year 1
  - 52% year 6

- Less than half of those with a positive screen result had a biopsy

DOES SCREENING SAVE LIVES?

- There is a higher rate of early stage detection and prostate cancer death rates have fallen during the PSA era – but it is not clear that this is primarily due to screening

- Other possible reasons for this decline

  - Disease is found earlier because of increased awareness and use of diagnostic PSA testing

  - There has been substantial improvements in treatment over the past 2 decades

SUMMARY: PROSTATE CANCER SCREENING

Potential Benefits

- PSA screening detects cancers earlier
- Treating PSA detected cancers may be more effective, but this is uncertain
- PSA screening may contribute to the declining death rate, but the extent is unclear

Potential Harms

- False negatives and false positives are common
- Overdiagnosis and overtreatment are problems, but the magnitude is uncertain
- Treatment related complications and side effects can be significant

BOTTOM LINE

Uncertainty about degree of benefits and magnitude of harm

Clinicians should

- Educate men regarding uncertainties, risks and potential benefits of screening and treatment
- Provide risk assessment tools to estimate a man's overall risk of prostate cancer
- Recognize and inform those men who are at increased risk of prostate cancer
  - African origin
  - Family history
  - Abnormal digital rectal exam
  - Prior negative prostate biopsy lowers risk
- Recognize men who are not likely to benefit from prostate cancer early detection and who should therefore not be screened

THE ROLE OF PSA AFTER DIAGNOSIS

- To ensure a response to primary treatment
- To monitor state of remission
- To monitor for recurrence
- To monitor need for second line treatment

CONCLUSIONS

- PSA is a valuable test when used appropriately.
- Should always be done *after* informed consent gained.
- If raised for not obvious reason e.g. UTI urgent cancer referral to urology.