Clinical Trials 2 – key papers

Case 1

This British study on haematuria clinic diagnostic yield was published in the *British Journal of Urology International* in 2006. The results are often asked in examinations!

Edwards TJ, et al. A prospective analysis of the diagnostic yield resulting from the attendance of 4020 patients at a protocol-driven haematuria clinic. *BJUI* 2006;**97(2)**:301-5.

1. According to the 'Joint consensus on the initial assessment of haematuria' by the Renal Association and BAUS in 2008, how should we classify haematuria?
2. On urine dipstick testing, what is classified as abnormal?
3. What is the overall prevalence of malignant disease for patients presenting with haematuria in the Edwards et al. paper?
4. How reliable is an ultrasound of the renal tract in detecting an upper tract tumour?

Case 2

This paper was published in *The Lancet* in 2005. It was a randomised clinical trial examining the role of postoperative radiotherapy after radical prostatectomy. Definitely one to know!

Bolla M, et al. Postoperative radiotherapy after radical prostatectomy: a randomized controlled trial (EORTC trial 22911). *The Lancet* 2005;**366(9485)**:572-8.

1. Which patients were included in this study?
2. What were they randomised to receive and what was the primary endpoint?
3. Summarise the results?

Case 3

These two landmark articles, examining the effects of prostate cancer screening on reduced prostate cancer related death rates were published in 2009 in the *New England Journal of Medicine.*

Andriole GL, et al. Mortality results from a randomized prostate cancer screening trial. *NEJM* 2009;**360(13)**:1310-19.

Schröder FH, et al. Screening and prostate-cancer mortality in a randomized European study. *NEJM* 2009;**360(13)**:1320-8.

1. What were the basics of trial design in the North American Prostate, Lung, Colorectal Ovarian (PLCO) trial?
2. What were the results of the trial?
3. Why have these results been criticised?
4. What were the basics of trial design in the European Randomised Screening for Prostate Cancer Trial?
5. What were the results of this trial?

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Answers

Case 1

1. Visible haematuria (VH): urine is coloured pink or red. Non-visible haematuria (NVH): otherwise referred to as 'microscopic haematuria' or 'dipstick positive haematuria'. This is further sub-divided as follows: Symptomatic non-visible haematuria (s-NVH) – symptoms include lower urinary tract symptoms (LUTS): hesitancy, frequency, urgency, dysuria; asymptomatic non-visible haematuria (a-NVH).
2. One + or greater is classified as significant. Trace haematuria should be considered negative. There is no distinction in significance between non-haemolysed and haemolysed dipstick-positive haematuria.
3. Overall prevalence was 12.1%, with visible haematuria being 18.9% and non-visible haematuria being 4.8%.
4. In this study there were 73 upper tract tumours, of which three cases were identified on IVU after a normal ultrasound.

Case 2

1. Patients were recruited post radical retropubic prostatectomy who had NOMO tumours and one or more pathological risk factors: capsule perforation, positive surgical margins, invasion of seminal vesicles.
2. Patients were randomly assigned to a wait-and-see policy or to immediate postoperative radiotherapy (60Gy conventional irradiation delivered over six weeks). The primary endpoint was biochemical progression-free survival.
3. After a median follow-up of five years, biochemical progression-free survival was significantly improved in the irradiated group (74·0%, 98% CI 68·7-79·3 vs. 52·6%, 46·6-58·5; p<0·0001). Clinical progression-free survival was also significantly improved (p=0·0009). The cumulative rate of locoregional failure was significantly lower in the irradiated group (p<0·0001). Therefore, immediate external irradiation after radical prostatectomy improves biochemical progression-free survival and local control in patients with positive surgical margins or pT3 prostate cancer who are at high risk of progression.

Answers - continued

Case 3

1. 76,693 men, between the ages 55-74, were randomised to either annual prostate specific antigen (PSA) screening tests for six years and rectal exam or usual care as the control. Published follow-up was at 7-10 years' post randomisation. Primary outcome measure was prostate cancer specific mortality.
2. There were 2820 cancers in the screened group and 2322 in the control group (rate ratio 1.22, 95% CI 1.16 to 1.29). Incidence of prostate cancer death was 50 in the screened group and 44 in the control group (rate ratio 1.13, 95% CI 0.75-1.70). In conclusion at 7-10 years' follow-up there was no significant difference between the study groups.
3. High level of contamination in the control group due to 'PSA contamination'. Follow-up was only 7-10 years, whereas prostate cancer related deaths may occur much later.
4. 182,000 men, between the ages 50-74, were randomised to PSA screening once every four years or a no screening group. The primary outcome measure was prostate cancer specific mortality.
5. Median follow-up of nine years, prostate cancer incidence was 8.2% in the screened group and 4.8% in the control group. The rate ratio for death in the screened group was 0.80, 95% CI 0.65-0.98. This meant that 1410 men would need to be screened and 48 additional cases of prostate cancer would need to be treated to prevent one death. Therefore, PSA based screening reduced the rate of prostate cancer related death by 20%.