EDITORIAL

Active monitoring vs treatment for localised prostate cancer

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NO SIGNIFICANT DIFFERENCE IN PROSTATE CANCER MORTALITY WAS SEEN IN MEN WITH localised prostate cancer who underwent active monitoring compared with surgery or radiotherapy, at ten years' follow-up, in a large UK trial. However, both treatment approaches were associated with lower rates of metastasis and disease progression.[1]

The ProtecT study commenced in 1999 and recruited men until 2009. Over this period, 82,429 men in a number of UK centres had a PSA test. Of these, 2,664 were diagnosed with localised prostate cancer and 1,643 agreed to undergo randomisation as part of the trial.

There were 545 men randomised to active monitoring, 553 to radical prostatectomy and 545 to radiotherapy. The men had a median age of 62 and PSA of 4.6 ng/ml at initial prostate check. Three-quarters (77%) had a Gleason score of 6, and 76% had a T1c tumour i.e. most had low-grade, low-risk localised disease.

There were only 17 deaths from prostate cancer during the study, eight in the active monitoring, five in the surgery and four in the radiotherapy arms. Not surprisingly given the low event rate of prostate cancer deaths, no statistical difference was seen between the groups.

With respect to secondary outcomes, no difference was seen in all-cause mortality between the groups, but higher rates of metastasis and disease progression were seen in the active monitoring group. The rate of development of metastases was 6.3 events per 1,000 person-years (95% CI: 4.5-8.8) in the active monitoring group, compared with 2.4 (95% CI: 1.4-4.2) and 3.0 (95% CI: 1.9-4.9) in the surgery and radiotherapy arms respectively. Higher rates of disease progression were also observed in the active monitoring group 22.9 events per 1,000 person-years (95% CI: 19.0-27.5) compared with 8.9 per 1,000 person-years (95% CI: 6.7-11.9) in the surgery group and 9.0 per 1,000 person-years (95% CI: 6.7-12.0) in the radiotherapy group.

In an accompanying paper in the *NEJM*, the authors also present the first analysis of patient reported outcomes at six years' follow-up in the ProtecT trial.[2] Prostatectomy had the greatest negative impact on sexual function and urinary continence, and while there was some recovery with time, it had the greatest negative impact throughout the study. Radiotherapy had little impact on urinary continence, but a negative impact on sexual and bowel function.

The study authors caution: 'Men with newly diagnosed, localised prostate cancer need to consider the critical trade-off between the short-term and long-term effects of radical treatments on urinary, bowel and sexual function and the higher risks of disease progression with active monitoring.'

The study does support the trend away from active treatment of low-risk localised disease – indeed, it is important to remember that the men in the study who did not receive active treatment went on to an active monitoring programme, less rigorous than a modern active surveillance protocol, and so outcomes may be adversely affected by this compared with current standard practice. Likewise, surgical treatment for localised prostate cancer has moved on. Most men in ProtecT had an open radical prostatectomy and 24% had positive surgical margins compared with accepted rates now of 15%, using laparoscopic or robotic prostatectomy.

'The findings must not be used to push men with more aggressive disease away from active treatment'

An accompanying editorial in the *NEJM*,[3] by a cancer specialist in Boston, USA, concludes: 'that PSA monitoring, as compared with treatment of early prostate cancer, leads to increased metastasis. Therefore, if a man wishes to avoid metastatic prostate cancer and the side effects of its treatment, monitoring should be considered only if he has life-shortening coexisting disease such that his life expectancy is less than the 10-year median follow-up of the current study'.

This seems to me to be an overreaction to an increased rate of metastasis of 3-4 events per 1,000 patient-years, weighed against the side effects of treatment that can be avoided by men who choose active surveillance/monitoring over radical therapy.

ProtecT seems to support the use of active monitoring/surveillance in low-risk patients, but this does not mean that it is a sensible option for all men newly diagnosed with prostate cancer. Most men in ProtecT had low Gleason grade, low-risk disease and the findings must not be used to push men with more aggressive disease away from active treatment.

REFERENCES
1 Hamdy FC, Donovan JL, Lane JA et al. 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. *N Engl J Med* 2016;375:1415-24
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