

Active surveillance and radical prostatectomy

C.H. Bangma

Erasmus MC, Rotterdam, The Netherlands

With the awareness on prostate cancer (PCa) and the ever-growing elderly population in Europe, the number of newly diagnosed cancers has increased steadily during the last decade. Early detection leads to a stage shift in which many of these cancers are claimed to be indolent. In early detection programmes the number of these cancers, that likely never become symptomatic during life, is estimated to be between 30–50%. These low-risk indolent cancers might be managed by active surveillance (AS) with deferred therapy in the case of reclassification to a higher risk. A number of AS programmes around the world are observing cohorts of men that have been included based on various criteria, and are managed with various schemes for monitoring. As these studies are maturing, surrogate markers are used to compare the intermediate outcome with studies on immediate invasive treatment, for example by radical prostatectomy. The pathological results of the immediate surgical series, as well as their long-term tumour-related clinical outcome, are per definition better than those on deferred therapy. The trade-off, however, lays in the comparison between side effects and quality of life.

In this presentation, the advantage of early detection will be discussed, and the methods for individual risk assessment in order to make a personalised decision to initiate a screening procedure. The inclusion for active surveillance or other minimally invasive therapies will be mentioned, and the results of randomised studies on radical surgery against watchful waiting are highlighted. Recommendations for further studies as well as for the multidisciplinary teams of radiologists and urologists with respect to current guidelines will be given.

The European randomised study of screening for prostate cancer (ERSPC) has proven that in the general population of men aged 55–70 years old PSA-based screening leads to a disease-specific mortality advantage of at least 30%, while also the number of men with metastases over a period of 11 years is decreased by 30% [1]. The Swedish partner of the ERSPC consortium showed that with a 12-year follow-up the mortality reduction reaches 44%, while

12 men with diagnosed cancer have to be treated in order to save one PCa death [2]. Quality-of-life studies within ERSPC show that the gain in this small proportion of men who submit themselves to screening and who will be diagnosed with cancer is seven more years to live, but that a large number of men have to live with the knowledge of having a cancer. The median duration of awareness of having a PCa can only be diminished by a reduction of over-diagnosis of men with indolent cancers [3]. There is currently no molecular marker that safely indicates upfront whether a man is at risk of having an aggressive disease that should be treated. Individual risk assessments on the risk of having a prostate carcinoma are best given by risk calculators based on data derived from the general population [4].

To select men for active surveillance, a number of parameters are used based on data from radical prostatectomy and of autopsy series by Epstein [5]. Cancer grade, PSA, the number of positive biopsies, and the prostate volume can be enriched with histology information showing the amount of tumour in the biopsies, in order to increase the accuracy of prediction of indolent disease. Once selected for active surveillance, monitoring of prostate histology by repeated biopsies and PSA has to be performed as the safest parameters known so far for a patient to remain classified as having a low-risk disease [6]. Studies on the value of ultrasound- and MRI-based imaging are ongoing. Approximately 20% of men shift towards invasive therapy after the first restaging biopsies, while over 4 years time 40% overall will obtain deferred therapy, whether based on risk upgrading, or due to anxiety. Of those, one third will be submitted to radical prostatectomy, and 20–30% will have a locally extended (pT3) tumour. As this is 3% of the original active surveillance population, it still is acceptable compared with upfront radical prostatectomy. However, the AS studies are immature, and long-term results have to be awaited. Methods to identify this relatively higher risk group by molecular tests are included in the ongoing studies. So far, AS is an attractive alternative to immediate treatment

for many patients, it delays side effects and costs in younger men, and it omits invasive therapy completely in elderly men. Guideline recommendations for AS are accepted and followed in over 80% of men and their physicians.

Radical prostatectomy is the traditional example of curative treatment for prostate cancer, at least for many urologists. Radiotherapy is the obvious alternative, and is offered in various forms like external beam radiotherapy and interstitial brachytherapy. In recent years a number of other therapies like HIFU (High Intensity Focal Ultrasound) and cryotherapy are being offered, both still in evaluation. Radical prostatectomy carries an overall 30% of side effects, ranging among all levels of urinary incontinence, erectile dysfunction and urethral strictures. The level of side effects is correlated with the patient's age and the surgical experience of the urologist. New techniques like laparoscopic prostatectomy have increased direct patient comfort and recovery, but there appears a limit to these improvements as robotic-assisted laparoscopic surgery has not fulfilled the high expectations of a reduction in side effects that were awaited based on the technical optical improvements of 3D imaging and visual enlargement.

Fundamental to the title of this presentation 'active surveillance and radical prostatectomy' therefore is the question how much to treat when treatment is needed because of the prognosis of the tumour at diagnosis. Few randomised studies exist that compare the expectant management with forms of invasive treatment, or the various forms of invasive treatment itself. The best randomised study between radical prostatectomy and watchful waiting is the Scandinavian prostate cancer group study 4 (SPCG 4) [7], that shows a tumour-specific benefit of 5.4% of surgery beyond waiting for men younger than 65 years old. With more than eight years' follow-up, survival curves appear to run parallel. In the ProtecT trial, which will be published in around 2015, surgery, radiotherapy and active surveillance are compared in a randomised fashion in men who underwent screening [8].

In the ESMO guidelines 2010 no treatment preference is given for low-risk disease, as 10-year disease-specific survival is 100% in non-randomised studies. For intermediate risk disease radical prostatectomy, external beam radiotherapy and brachytherapy are advised, while for high-risk and locally advanced disease external beam radiotherapy with endocrine therapy is the first option.

It is obvious that for the treatment decision of men with locally confined cancers that have been

detected early the quality of life issue is pivotal. With the improvement of imaging modalities, thoughts on the partial or focal therapy of cancers within the prostate have started, while minimising side effects. Repeated treatments of index lesions might render prostate cancer from a deadly into a chronic disease. Studies have to be designed that can rely on long-term biobanking and follow-up in order to validate these options.

For an individualised decision on treatment of this complex disease, a multidisciplinary approach is needed including urologists, radiotherapists and often oncologists. A discussion has started on the value of expert centres (Prostate Units) in Europe, which have been realised for breast cancer previously [9].

Conflict of interest statement

The author has no conflict of interest to disclose.

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