Active surveillance for men with low-risk prostate cancer

PAUL STURCH, ROGER KIRBY AND BEN CHALLACOMBE

Active surveillance is often advised as an initial management strategy for men with low-risk localised prostate cancer. In this review the authors examine popular strategies for patient selection, and question whether a more holistic approach could further enhance quality of life and life expectancy.

<table>
<thead>
<tr>
<th>BAUS</th>
<th>NICE (particularly suitable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical stage</td>
<td>T1c/2a</td>
</tr>
<tr>
<td>Gleason grade</td>
<td>≥3+4</td>
</tr>
<tr>
<td>PSA (ng/ml)</td>
<td>&lt;15</td>
</tr>
<tr>
<td>Biopsies positive</td>
<td>≥50%</td>
</tr>
<tr>
<td>Age (years)</td>
<td>50–80</td>
</tr>
<tr>
<td></td>
<td>T1–T2a</td>
</tr>
<tr>
<td></td>
<td>&lt;6</td>
</tr>
<tr>
<td></td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td>≤50% with &lt;10mm of any core</td>
</tr>
</tbody>
</table>

Table 1. BAUS1 and NICE criteria for entering active surveillance

As awareness of prostate disease increases, more men than ever before are being diagnosed with localised prostate cancer. Many of these with intermediate- and high-risk disease will go on to have radical treatment in the form of either surgery or radiotherapy. In those men with low-risk, low-volume disease, however, the risks associated with treatment may outweigh the risk of developing metastatic disease or dying of prostate cancer. A period of close monitoring with subsequent curative treatment if there is progression often seems a sensible way to proceed.

Urologists are therefore increasingly advising active surveillance (AS) as an initial management strategy. The question of how best to select, follow up and subsequently treat these men remains an open question. Unfortunately, there is no firm consensus on which patients are suitable for AS or how best to conduct the surveillance protocol. There are at least 16 different reported entry criteria for AS and therefore those who enter into an AS programme do so with some uncertainty.

In the UK, BAUS and NICE protocols are widely used (Table 1) and AS programmes based on these criteria have reported a rate of progression to radical treatment of up to 30 per cent over a median of three to five years. This raises the concern of whether the right patients are initially being selected for AS if one in three is destined to fail AS and proceed to surgical or radiotherapy intervention in so short a time (Boxes 1 and 2).

SURVEILLANCE VERSUS INTERVENTION
Recent findings from the Prostate Cancer Intervention versus Observation Trial (PIVOT) suggested that early radical surgical intervention did not significantly reduce mortality in men with low-risk localised prostate cancer compared with observation alone over a median follow-up of 10 years. This study supports the view that not all men require treatment for their prostate cancer and that radical surgery may not be beneficial to some men with low-risk disease. Although the study has significant limitations, what may be concluded is that, provided they are accurately staged and suitably followed up, patients with low-risk prostate cancer can be safely monitored and that radical treatment can be deferred until there is definite evidence of progression.
WHEN ARE TRUS BIOPSIES INSUFFICIENT?
Information from transrectal ultrasound (TRUS)-guided biopsy is currently used to risk stratify most patients entering AS. These biopsies can potentially understage prostate cancer, particularly if the prostate is large or if there is disease in the anterior or apical part of the gland.5

Transperineal biopsies may reduce uncertainty in selected cases by more detailed and comprehensive sampling. Unfortunately, transperineal biopsies are more expensive, time-consuming and would probably be impractical for widespread primary diagnostic use. However, transperineal biopsies should be considered as a primary biopsy in patients with a large prostate with areas inaccessible by TRUS biopsies, patients with a history of urinary sepsis, where PSA levels are out of keeping with TRUS biopsy results, or in the presence of a rapidly rising PSA following a negative TRUS biopsy. For patients managed by AS, instead of repeating TRUS biopsies, one could argue that transperineal biopsies should be recommended as the norm for follow-up biopsies.

THE ROLE OF MRI
The accuracy of multiparametric MRI in local staging of prostate cancer is improving and pre-biopsy prostate MRI has an increasing role in prostate cancer diagnostics and is also potentially useful in AS.7 The use of yearly surveillance MRI may provide a more accurate representation of disease progression than digital rectal examination (DRE), particularly for anteriorly located disease. If MRI is proven sensitive enough to pick up clinically significant disease, surveillance imaging could be used in place of repeat biopsies, reducing the risk of invasive and uncomfortable procedures to patients.

CELL CYCLE PROGRESSION MARKERS
Newer genetic markers, such as the Prolaris cell cycle progression (CCP) score developed by Myriad Genetics, may soon help clinicians to distinguish those patients in whom it is safe simply to monitor their disease from those who need intervention. A recent study reported that the measurement of the expression level of 31 genes involved with CCP from biopsy tissue provides the strongest independent predictor of cancer death outcome yet described (Figure 1).8

HOLISTIC MANAGEMENT
The first consultation with a man newly diagnosed with prostate cancer may be his first encounter with a clinician for a long time. As part of an holistic approach to patient care, while discussing AS, there is an opportunity to consider wider health issues.

Men are often fearful of a cancer diagnosis, but less concerned about the longer-term risks of cardiovascular disease. At this point the patient may well be more receptive to advice and motivated to sustained change. By following simple lifestyle modifications, including stopping smoking, improving diet, reducing alcohol intake, and sustained weight reduction through exercise, a valuable reduction in cardiovascular risk factors and diabetes can be achieved.9 Potentially, this will improve not only the outcomes of surgery, if required in the future, but also quality of life and sexual function, and will reduce the risk of mortality.

The accurate stratification of men with low-risk prostate cancer suitable for AS is vital to maintain the maxim ‘first do no harm’. Active surveillance protocols using MRI and transperineal biopsy techniques show promise in reducing uncertainty associated with TRUS biopsy and DRE alone. While we search for the safest way to diagnose and manage
these men, we must also do our best to empower them to take control of their own health and thereby improve their quality of life, whether or not they require surgical intervention in the future.

Declaration of interests: none declared.

REFERENCES