Are prostatic biopsies necessary in men aged ≥80 years?

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OBJECTIVE

To examine whether prostatic biopsies are necessary in all men aged ≥80 years, as men found to have prostate cancer are frequently treated with a ‘watch and wait’ policy or with hormonal withdrawal alone, and biopsies are associated with a small but significant complication rate.

PATIENTS AND METHODS

The findings on a digital rectal examination (DRE), the prostate-specific antigen (PSA) level, the biopsy and staging bone scan results for all men aged ≥80 years who had prostatic biopsies over a 3-year period were reviewed, together with those in a group of men aged <80 years for comparison. All biopsy samples had been examined in one of three histopathology units, and 33 consultant urological surgeons contributed.

RESULTS

In all, 210 biopsies from 205 men aged ≥80 years were identified, of whom 163 (79%) had biopsy-confirmed prostate cancer. All 29 men with a PSA level of ≥100 ng/mL, 98% of 47 with ≥50 ng/mL, 97% of 76 with ≥30 ng/mL and 92% of 101 with ≥20 ng/mL had biopsy cores containing cancer; 63% of men with a PSA level of <20 ng/mL had cancer on biopsy. In men with cancer and a PSA level of ≥30 ng/mL, 92% had Gleason grade ≥7 and 93% were treated with hormonal withdrawal alone. In all men with cancer the DRE was abnormal in 91%, the mean number of positive cores was 59% and the bone scan was positive in 18%. The DRE was abnormal in 77% of men with benign biopsies.

CONCLUSIONS

In men aged ≥80 years with a PSA level of ≥30 ng/mL, at least 97% had prostate cancer, >90% of whom had high-grade disease, and nearly all with cancer received active pharmacological treatment. In the vast majority of these men prostate biopsies did not alter their cancer management. The value of prostatic biopsy in this age group, with a PSA level of ≥30 ng/mL, is questionable.

KEYWORDS

prostate biopsy, cancer, octogenarians, PSA

INTRODUCTION

Prostate cancer is usually considered a tissue diagnosis commonly based on biopsy cores or chips obtained at TURP. Once prostate cancer has been confirmed, men with a life-expectancy of >10 years and localized disease might be offered radical treatment such as surgery, brachytherapy or radiotherapy, depending on the biopsy findings. In the UK, men aged 80 years have a median life-expectancy of 7.3 years [1] and octogenarians are not usually considered for radical treatment. Prostatic biopsies are taken in these men to obtain a tissue diagnosis, a Gleason score, a guide to the extent of cancer (assessed on the proportion of cores involved, percentage core involvement and bilaterally positive cores) and to direct management. However, prostatic biopsies have inherent complications, including discomfort, bleeding and sepsis [2], the latter being more common in older men [3]. TRUS-guided biopsies can miss a significant cancer in 10–30% of men [4–8] and there are cost implications to the patient and health service provider. The aim of the present study was to assess whether prostatic biopsies assist in the diagnosis and management of prostate cancer in men aged ≥80 years, and whether such a diagnosis could be inferred from other clinical findings and investigations in lieu of prostate biopsy results.

PATIENTS AND METHODS

The case notes of all men aged ≥80 years whose prostate biopsy pathology was submitted to the authors’ institutions over a 3-year period from January 2001 were reviewed. The data for a smaller group of men aged <80 years were extracted for comparison. Written advice about the biopsy procedure and possible complications was sent to all men undergoing biopsy, including instructions for antibiotic prophylaxis (ciprofloxacin 500 mg the night before, two doses on the day of the biopsy and two doses the day after biopsy). Patients receiving anticoagulation were asked to stop their treatment 5 days before biopsy; in men where short-term omission was relatively safe, clotting was checked before biopsy. Anticoagulation was re-started after any bleeding caused by the biopsy had stopped. Men requiring permanent anticoagulation were treated with i.v. heparin over the biopsy period. Local anaesthetic with 5 mL 0.5% marcaine mixed with 5 mL 1% lidocaine was administered in the periprostatic space before 1–12 cores were taken. The PSA level before biopsy, the DRE findings, the results of a radioisotope bone scan within 3 months of diagnosis and the treatment given were noted. The diagnosis was recorded from the biopsy report and where cancer was identified the Gleason sum score, the number of positive cores and the total number of cores were noted.

The Wilcoxon two-sample, Fisher’s exact and chi-square test were used where appropriate, with the least-squares fitting analysis used for regression analysis.
RESULTS

In all, 205 men aged ≥80 years who had had 210 prostate biopsy sessions were identified from the three centres, with 33 consultant urologists contributing patients. The racial mix was not recorded; the median (range) age was 83 (80–93) years and the median PSA level was 19 (0.8–3832) ng/mL (Table 1). Of all 1578 biopsies taken at these centres, 13% were in men aged ≥80 years; overall 162 (79%) of these men had cancer identified at prostatic biopsy. The characteristics of the elderly men who had positive biopsies were compared to those with negative biopsies. Patients with cancer at biopsy were significantly more likely to have an abnormal DRE (P = 0.023) and a higher PSA level (P < 0.001). The predictive value of various PSA thresholds were further analysed. All 26 men who had a PSA level of ≥100 ng/mL had prostate cancer, as did 98% of men with a PSA level of ≥50 ng/mL, 90% with ≥30 ng/mL, 91% with ≥20 ng/mL and 62% with <20 ng/mL (Table 2). There was no correlation between age in men ≥80 years and the incidence of cancer (least-squares regression analysis, r = 0.160, P = 0.58). The highest PSA level in a patient with a benign biopsy was 61.6 ng/mL. At all PSA ranges most cancers were Gleason ≥7 (Table 2). The extent of cancer within each patient’s prostate in terms of the number and proportion of positive cores did not strongly correlate with PSA levels (Table 2). Five men had two biopsies at intervals of 1–2 years; in all cases the first biopsy was benign, with cancer being diagnosed at second biopsy in three patients with PSA levels persistently at 8–22 ng/mL and Gleason scores of 7, 7 and 9.

The predictive value of other investigations in this population of elderly men was also studied. A radioisotope bone scan to identify metastatic cancer spread was performed in 103 of the 210 men; 98 had positive biopsies and five had negative biopsies. Of those with cancer, 18 men (18%) had unequivocal bony metastases identified, a further 24 (24%) had equivocal scans and 56 (57%) had negative scans. None of the five patients with no cancer diagnosis had a positive bone scan. The lowest PSA level with a positive bone scan was 3.4 ng/mL. The sensitivity of bone scanning for diagnosing prostate cancer in these men was low, at 18%, although it was 100% specific. Those patients who had a bone scan were a selected group with a higher median PSA level (30.3 ng/mL) than the entire study population, so the test might have performed differently had it been applied across all 210 patients. A bone scan was more sensitive for patients with higher PSA levels, reaching a maximum sensitivity of 48% for those with a PSA level of >100 ng/mL.

The DRE was sensitive as a predictor of positive biopsies, but much less specific; 126 of 139 (91%) patients with cancer had an abnormal DRE, but so did 29 of 38 (76%) patients with benign biopsies, equating to a sensitivity of 91% and a specificity of 24%.

Most patients (80%) diagnosed with cancer went on to receive active treatment, either in the form of hormonal withdrawal using antiandrogens or GnRH analogues, external beam radiotherapy, or a combination of both (Table 3). It was not possible to determine whether radiotherapy was palliative or with curative intent, and no distinction was made between GnRH agonists, antiandrogens or bilateral orchidectomy. Two patients, both aged 81 years, with Gleason 9 disease, PSA levels of 18 and 22 ng/mL but negative bone scans, received neoadjuvant hormonal therapy followed by radiotherapy. All patients with a PSA of ≥40 ng/mL received hormonal withdrawal therapy.

### Table 1: Comparison of the characteristics of men aged ≥80 years over with positive or negative prostate biopsies

<table>
<thead>
<tr>
<th>Variable</th>
<th>All biopsies</th>
<th>Cancer biopsies</th>
<th>Benign biopsies</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>210</td>
<td>162</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Median (range):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>83 (80–93)</td>
<td>83 (80–93)</td>
<td>83 (80–91)</td>
<td>0.99*</td>
</tr>
<tr>
<td>PSA level, ng/mL</td>
<td>19.0 (1–3832)</td>
<td>26.6 (3–3832)</td>
<td>10.4 (1–62)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Positive bone scan, % (n/N)</td>
<td>17 (18/103)</td>
<td>18 (18/98)</td>
<td>0 (0/5)</td>
<td>0.38*</td>
</tr>
<tr>
<td>Abnormal DRE, % (n/N)</td>
<td>88 (155/177)</td>
<td>91 (126/139)</td>
<td>76 (29/38)</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

*Wilcoxon two-sample test; †Fisher’s exact test.

### Table 2: Prostate cancer characteristics in men aged ≥80 years at different PSA thresholds

<table>
<thead>
<tr>
<th>PSA level, ng/mL</th>
<th>% (n/N) of Gleason ≥7</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥100</td>
<td>100 (29/29)</td>
<td>8 (7–10)</td>
</tr>
<tr>
<td>≥50</td>
<td>98 (45/46)</td>
<td>8 (7–10)</td>
</tr>
<tr>
<td>≥30</td>
<td>92 (68/74)</td>
<td>7 (5–10)</td>
</tr>
<tr>
<td>≥20</td>
<td>91 (85/93)</td>
<td>7 (5–10)</td>
</tr>
<tr>
<td>&lt;20</td>
<td>71 (49/69)</td>
<td>7 (5–10)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PSA level, ng/mL</th>
<th>No. of positives</th>
<th>No. of negative</th>
<th>% positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥100</td>
<td>102 (60)</td>
<td>42 (40)</td>
<td>63 (62)</td>
</tr>
<tr>
<td>≥50</td>
<td>102 (80)</td>
<td>22 (22)</td>
<td>80 (79)</td>
</tr>
<tr>
<td>≥30</td>
<td>102 (93)</td>
<td>22 (22)</td>
<td>80 (79)</td>
</tr>
<tr>
<td>≥20</td>
<td>102 (93)</td>
<td>22 (22)</td>
<td>80 (79)</td>
</tr>
<tr>
<td>&lt;20</td>
<td>102 (93)</td>
<td>22 (22)</td>
<td>80 (79)</td>
</tr>
</tbody>
</table>

### Table 3: The treatment received by patients with positive prostate biopsies, as n (%)

<table>
<thead>
<tr>
<th>Patients with cancer on biopsy</th>
<th>Active surveillance</th>
<th>All</th>
<th>Hormonal withdrawal</th>
<th>EBRT and hormonal withdrawal</th>
<th>Neoadjuvant hormonal withdrawal + EBRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>All PSA levels</td>
<td>127 (25 (20)</td>
<td>102 (80)</td>
<td>92 (73)</td>
<td>8 (6)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>PSA ≥30 ng/mL</td>
<td>60 (4 (7)</td>
<td>56 (93)</td>
<td>54 (92)</td>
<td>2 (2)</td>
<td>0</td>
</tr>
<tr>
<td>PSA &lt;30 ng/mL</td>
<td>67 (21 (31)</td>
<td>46 (69)</td>
<td>38 (57)</td>
<td>6 (9)</td>
<td>2 (3)</td>
</tr>
</tbody>
</table>

**EBRT**, external beam radiotherapy.
Over a third of the patients in the study had a PSA level of ≥30 ng/mL before biopsy; 96% of these patients (74/76) had positive biopsies, giving a specificity of 96% and a positive predictive value of 97% for this PSA threshold. Many patients with a PSA lower than this were also found to have prostate cancer (88/134), such that the sensitivity was 46%, and the negative predictive value 34%. The cancer found at biopsy in men with a PSA level of ≥30 ng/mL had a Gleason score of ≥7 in 92%; 16% had Gleason 3 + 4, 22% Gleason 4 + 3, 20% Gleason 8, 28% Gleason 9 and 5% Gleason 10. In men with a PSA level of ≥30 ng/mL, 22% had a positive bone scan and 89% an abnormal DRE. Of those men aged ≥80 years who presented with a PSA level of ≥30 ng/mL, 92% proceeded to received hormonal withdrawal, 3% hormonal withdrawal, and only 7% had expectant management.

Patients with a PSA level of ≥30 ng/mL had fewer biopsy cores taken and a greater percentage of positive cores than patients with a PSA level of <30 ng/mL (chi-square P = 0.004 and 0.02, respectively), suggesting that clinicians are already limiting the number of biopsy cores with reference to the individual's PSA level.

Eighty-seven consecutive men aged ≤79 years and with a PSA level of ≥30 ng/mL who had prostate biopsies taken over the same period at two of the institutions were examined for comparison. The results were similar; all men with PSA level of ≥100 ng/mL, 96% with ≥50 ng/mL and 92% with ≥30 ng/mL had cancer. In all, 89% of men had Gleason ≥7 disease. A third of men were treated with radiotherapy with or without long-term androgen withdrawal, and the remaining two-thirds with hormonal therapy alone.

DISCUSSION

The advent of PSA testing since the late 1980s, and improvements in TRUS and biopsy techniques, have meant that more men have been diagnosed with prostate cancer. Prostate biopsy is useful in the diagnosis and treatment of prostate cancer, giving a tissue diagnosis, prognostic information such as Gleason grade and an estimate of tumour bulk. In early stages of the disease treatment is aimed at cure, but radical treatment is rarely offered to patients with a life-expectancy of <10 years, as the risk of metastatic disease and prostate cancer death is not substantially reduced, while the morbidity associated with treatment can cause harm. Indeed, active surveillance for localized prostate cancer is often associated with prolonged, morbidity-free survival [9]. In more elderly men, with limited life-expectancies, a prostate biopsy might do no more than confirm a strong clinical suspicion and have little impact on the choice of treatment.

Prostate biopsy alone can cause complications and costs; side-effects are reported in 64–78% of men having prostate biopsies and up to 4.3% of men have side-effects sufficiently severe to require hospital admission [10–12]. Furthermore, the incidence of side-effects increases with age [3]. Prostate biopsies are reported to miss 10–30% of significant prostate cancers [13–15] and the incidence of ‘missed’ tumours increases with prostate size [4–8]. In men with persistently elevated PSA or an abnormal DRE several sets of biopsies can be required to make the diagnosis, increasing the likelihood of a patient having unwanted effects. Currently, clinicians treat various conditions, including recurrent prostate cancer, based on a blood test, so is a tissue diagnosis essential. Several recent studies suggest that those who have had a radical prostatectomy, with or without adjuvant hormone therapy, are 11–25% more likely to be disease-free at 5 years compared with those who are followed up [16–18]. For the time being, however, the results of this study are likely to be of greater clinical relevance than the results of the above-mentioned studies.

The aim of the present study was to establish whether elderly men who are unlikely to be offered radical treatment could be spared the morbidity of prostate biopsy and treated on the strength of other clinical variables. Given that 13% of all prostate biopsies in the study were taken in patients aged ≥80 years, more selective biopsy in this group could help to reduce the workload and expenditure. Cancer is very common in this age group, with 79% of men having positive biopsies, an incidence that would increase if more second biopsies had been taken.

The optimum test for predicting which patient aged ≥80 years has prostate cancer without resorting to biopsies would have a high specificity at the expense of a lower sensitivity. This would allow prostate cancer to be presumed with confidence in those testing positively, while other patients not meeting the criteria could proceed to biopsy. In the present study the PSA level before biopsy emerged as the most useful variable, while the bone scan results and DRE findings were less useful. A PSA threshold of 30 ng/mL offered a high specificity of 96% and a sensitivity of 46%. Such a threshold also encompassed 36% of all men in the study. The cancers identified within these patients had a Gleason score of ≥7 in 92% of men.

Most patients received active treatment despite their age, most frequently in the form of hormonal withdrawal. The Medical Research Council study and other studies suggest that those with locally advanced or metastatic disease benefit from early hormonal withdrawal. However, men in the younger group were spared the morbidity associated with treatment can be presumed with confidence in those testing positively, while other patients not meeting the criteria could proceed to biopsy. In the present study the PSA level before biopsy emerged as the most useful variable, while the bone scan results and DRE findings were less useful. A PSA threshold of 30 ng/mL offered a high specificity of 96% and a sensitivity of 46%. Such a threshold also encompassed 36% of all men in the study. The cancers identified within these patients had a Gleason score of ≥7 in 92% of men.
not proposed for biopsies, and it is likely that urologists are already exercising discretion in this age group.

In conclusion, the present study showed that a significant proportion of prostate biopsies taken are in men aged ≥80 years, and cancer detection rates are high. In octogenarians with a PSA level of >30 ng/mL, 96% had prostate cancer, and prostate cancer of a high Gleason grade was found in 92% of men. Furthermore, 92% received medical therapy with hormonal withdrawal alone. It might be possible to manage men aged ≥80 years without taking prostate biopsies and not altering their overall treatment. In reality, a pragmatic course must be steered between altering their overall treatment. In octogenarians life-expectancy to the morbidity of prostate cancer, and prostate cancer of a high Gleason grade was found in 92% of men.

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CONFLICT OF INTEREST

None declared.

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