Prostate Int xxx (2017) 1–4

Contents lists available at ScienceDirect

Prostate International

journal homepage: https://www.journals.elsevier.com/prostate-international

Research Article

Management and outcomes of Gleason six prostate cancer detected on needle biopsy: A single-surgeon experience over 6 years

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ARTICLE INFO

Article history:
Received 16 February 2017
Received in revised form
26 March 2017
Accepted 31 March 2017
Available online xxx

Keywords:
Prostate cancer
Gleason 6
Active surveillance

ABSTRACT

Objective: To assess the management and oncological outcomes in men diagnosed with Gleason score (GS) 6 prostate cancer on needle biopsy in a regional centre, as compared with published international data.

Patients and methods: A retrospective analysis was conducted of patients who were diagnosed with GS 6 prostate cancer via transrectal ultrasound-guided or transperineal biopsy between June 2009 and September 2015 under the care of a single surgeon. Data were obtained from a prospectively collected database.

Results: A total of 166 patients were diagnosed with GS 6 prostate cancer. The mean age was 61 (range 46–79) years, with mean prostate-specific antigen of 6.7 (0.91–26.8) ng/mL at diagnosis. Of 166 patients, 117 (70.5%) patients were enrolled into the active surveillance program with 82 (70%) meeting Prostate Cancer Research International Active Surveillance (PRIAS) criteria, 44 patients underwent immediate definitive treatment (88.6% radical prostatectomy and 9.1% radiotherapy) and five watchful waiting. With a median follow-up of 1.8 years, 37 (31.6%) patients on AS had definitive treatment [30 cases (81%) were attributable to disease progression, 4 cases (10.8%) to an abnormal magnetic resonance imaging result and 3 cases (8.1%) for patient preference]. In the 35 patients who underwent radical prostatectomy immediately after diagnosis, the GS was ≥7 in 29 cases (82.9%), and the final pathology was pT3a in 16 (51.6%) and pT3b in one (2.9%). In patients who underwent radical prostatectomy after being on AS, the proportion of GS ≥7 prostate cancer was 29/32 (90.6%), with pT3a in six (18.8%) and pT3b in three (9.4%) cases. Overall, 23.5% of patients had a multiparametric magnetic resonance imaging scan.

Conclusion: This single-surgeon cohort of GS 6 prostate cancer patients demonstrates a high proportion of cases managed with active surveillance, with comparable rates to international literature. The majority of cases who underwent immediate definitive treatment had significant disease, indicating that patients are being appropriately selected for active surveillance.

1. Introduction

Gleason score (GS) 6 prostate cancer is generally considered low risk of morbidity and mortality; autopsy studies and cystoprostatectomy case series suggest that a significant proportion of males harbour G6PCa for years without symptoms.[1–3] The challenge of balancing the potential harms arising from over diagnosis of a largely benign disease, and the need to be vigilant for higher grades of prostate cancer has given rise to the era of active surveillance (AS).

There is increasing long-term evidence for AS for managing GS 6 prostate cancer with deferred curative treatment until there is disease progression. Seven major AS trials now demonstrate carefully selected low-risk prostate cancers can be successfully managed without curative intent, with 99.7% cancer-specific survival rates, from a combined cohort of more than 4,000 patients.[4–10] Furthermore, the recently published randomised ProtecT study showed that mortality from prostate cancer was low, irrespective of treatment modality or AS.[11] However, the efficacy of AS is limited by the accuracy of the investigations used in the selection protocols. With the advent of multiparametric magnetic

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http://dx.doi.org/10.1016/j.prnil.2017.03.007

resonance imaging (mpMRI) and fusion biopsies, the risk of inadequate sampling of prostate biopsies is likely to be significantly reduced,[12] and incorporation of these emerging diagnostic tools into selection criteria will improve the accuracy of patient selection into AS.

We report on our experience of patients who were diagnosed with GS 6 prostate cancer from prostate needle biopsy between June 2009 and September 2015, at the time when multiparametric prostate MRI was being introduced. All patients were under the care of a single surgeon in a nonmetropolitan centre, and we compare outcomes of management with data from national and literature.

2. Patients and methods

A 6-year retrospective study from 1 June 2009 to 30 September 2015 was undertaken. It was approved by the Central Coast Human Research and Ethics Committee (Ref no: 0314-019C). Patients were selected from a prospectively maintained database of patients under the care of a single surgeon. All men diagnosed with G6PCa on transrectal ultrasound (TRUS) or transperineal biopsy were included. All biopsies performed were saturation protocol (16–30 cores depending on prostate volume). Data collected included demographics, diagnostic biopsy and prostate-specific antigen (PSA) results, subsequent biopsy results, MRI reports where available and the results of final pathology if progressing to definitive surgical therapy. Patients who were lost to follow-up or care transferred were excluded from subsequent analysis.

2.1. Definitions

Disease progression reclassification on repeat needle biopsy was defined as significant increasing volume of disease or upstaging of GS on serial prostate biopsy. Insignificant disease at prostatectomy was defined as stage T2 or less, GS 6 or less, and less than 0.5 mL of tumour volume.

2.2. Data analysis

Data were analysed using GraphPad Prism 6.0 (GraphPad Software Inc., La Jolla, CA, USA). Continuous variables were analysed using the Student unpaired *t* test and categorical variables with Fisher's exact test, with a significance level set at 5% for all calculations.

3. Results

3.1. Patient demographics

A total of 166 patients were diagnosed with GS 6 prostate cancer via needle biopsy during the study period. The mean age at diagnosis was 61.2 (range 46.2–78.7) years, with mean PSA 6.7 (range 0.91–26.8) ng/mL, PSA density 0.2 (range 0.02–0.7) and TRUS prostate volume 48.5 (range 15–125) mL at diagnosis. Baseline characteristics of the AS and immediate therapy cohort are outlined in Table 1.

Of this cohort of patients, 117 (70.5%) patients were enrolled into the AS program ($n = 82$, 70% meeting Prostate Cancer Research International Active Surveillance (PRIAS) criteria), and 44 (27%) underwent immediate definitive treatment ($n = 4$, 9.1% meeting PRIAS criteria); 35 patients underwent radical prostatectomy (RP), four patients received radiotherapy, one patient was commenced on androgen deprivation therapy and five cases were suitable for watchful waiting.

3.2. Active surveillance

After enrolment in AS, the mean time until the first repeat biopsy was 103 days (standard deviation 30.2 days), and time between subsequent biopsies was 1.43 years (standard deviation 0.52 years).

Excluding nine patients who were lost to follow-up or whose care was transferred, 66 (61%) patients remain on AS with a median follow-up of 1.9 years (maximum 5.59 years). Thirty-seven (31.6%) patients progressed to definitive treatment after a median of 1.07 years (range 0.34–3.53) on surveillance. Of these, 30 cases (81%) treatment was precipitated by disease reclassification at repeat biopsy, four cases (10.8%) were attributable to an abnormal MRI and three patients (8.1%) elected treatment owing to anxiety (see Table 2). Five cases have crossed to watchful waiting (4.27%).

Excluding the nine cases lost or transferred, 44 (40.7%) patients on AS had disease reclassification on a subsequent biopsy; nine (20.5%) were reclassified on the basis of GS being upgraded, 17 (38.6%)% on the basis of increasing number of biopsy cores or maximum core involvement with cancer, and 18 (40.9%) met both of these criteria. Of patients who received an immediate confirmatory repeat biopsy at approximately 3 months, 18 cases (27.7%) were reclassified. The median time from diagnosis to reclassification was 1.28 years. Patients enrolled in AS who fell outside the PRIAS criteria were more likely to be reclassified on the basis of biopsy (57.6% vs. 30.6%) and in less time (median 1.11 years vs. 1.53 years) than PRIAS patients. In these 44 patients, 30 (68.2%) have undergone definitive treatment, and 14 patients (31.1%) remain on AS and are being further investigated with mpMRI.

3.3. Outcomes of treatment with RP

There were 35 patients who underwent RP immediately after diagnosis. The final GS was ≥ 7 in 29 cases (82.9%), and extracapsular disease was present in 16 (51.6%) cases as pT3a, and one case (2.9%) as pT3b; eight cases with extracapsular extension also had a positive surgical margin. Two patients had insignificant disease on final pathology; one of these patients met the PRIAS criteria for enrolment into AS, but elected to have a laparoscopic RP performed.

There were 32 patients who underwent RP after being on AS, four patients met the PRIAS criteria for continued AS on repeat biopsy but instead progressed to RP; two of these elected definitive

Table 1
Patient characteristics at baseline (diagnosis)

	Total ($n = 116$)	Active surveillance ($n = 117$)	Definitive therapy ($n = 49$)	*P*
	Mean ± SD	Mean ± SD	Mean ± SD	
Age (yr)	61.2 ± 6.4	61.2 ± 6.4	61.8 ± 6.9	0.55
PSA (ng/mL)	6.8 ± 4.1	6.2 ± 3.0	8.1 ± 5.7	<0.01
Prostate volume (mL)	48.4 ± 21.9	50.8 ± 23.1	43.1 ± 17.7	0.03
PSA density (ng/mL/mL)	0.16 ± 0.10	0.13 ± 0.06	0.21 ± 0.15	<0.01

PSA, prostate-specific antigen; SD, standard deviation.

Please cite this article in press as: March B, et al., Management and outcomes of Gleason six prostate cancer detected on needle biopsy: A single-surgeon experience over 6 years, Prostate Int (2017), http://dx.doi.org/10.1016/j.prnil.2017.03.007