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Prostate Cancer

Oncologic Outcomes of Incidental Versus Biopsy-diagnosed Grade Group 1 Prostate Cancer: A Multi-institutional Study

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Article info

Abstract

Background and objective: Patients diagnosed with grade group (GG) 1 prostate cancer (PCa) following treatment for benign disease ("incidental" PCa) are typically managed with active surveillance (AS). It is not known how their outcomes compare with those observed in patients diagnosed with GG1 on biopsy. We aimed at determining whether long-term oncologic outcomes of AS for patients with GG1 PCa differ according to the type of diagnosis: incidental versus biopsy detected.
Methods: A retrospective, multi-institutional analysis of PCa patients with GG1 on AS at eight institutions was conducted. Competing risk analyses estimated the incidence of metastases, PCa mortality, and conversion to treatment. As a secondary analysis, we estimated the risk of GG $\geq$2 on the first follow-up biopsy according to the type of initial diagnosis.
Key findings and limitations: A total of 213 versus 1900 patients with incidental versus biopsy-diagnosed GG1 were identified. Patients with incidental cancers were followed with repeated biopsies and multiparametric magnetic resonance imaging less frequently than those diagnosed on biopsy. The 10-yr incidence of treatment was 22%

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for incidental cancers versus 53% for biopsy (subdistribution hazard ratio [sHR] 0.34, 95% confidence interval [CI] 0.26–0.46, $p < 0.001$). Distant metastases developed in one patient with incidental cancer versus 17 diagnosed on biopsy and were diagnosed with molecular imaging in 13 (72%) patients. The 10-yr incidence of metastases was 0.8% for patients with incidental PCa and 2% for those diagnosed on biopsy (sHR 0.35, 95% CI 0.05–2.54, $p = 0.3$). The risk of GG $\geq$2 on the first follow-up biopsy was low if the initial diagnosis was incidental (7% vs 22%, $p < 0.001$).

Conclusions and clinical implications: Patients with GG1 incidental PCa should be evaluated further to exclude aggressive disease, preferably with a biopsy. If no cancer is found on biopsy, then they should receive the same follow-up of a patient with a negative biopsy. Further research should confirm whether imaging and biopsies can be avoided if postoperative prostate-specific antigen is low (<1–2 ng/ml).

Patient summary: We compared the outcomes of patients with low-grade prostate cancer on active surveillance according to the type of their initial diagnosis. Patients who have low-grade cancer diagnosed on a procedure to relieve urinary symptoms (incidental prostate cancer) are followed less intensively and undergo curative-intended treatment less frequently. We also found that patients with incidental prostate cancer are more likely to have no cancer on their first follow-up biopsy than patients who have low-grade cancer initially diagnosed on a biopsy. These patients have a more favorable prognosis than their biopsy-detected counterparts and should be managed the same way as patients with negative biopsies if they undergo a subsequent biopsy that shows no cancer.

1. Introduction

Approximately 10% of patients undergoing surgery to relieve lower urinary tract symptoms due to benign prostatic hyperplasia (BPH) are diagnosed with incidental prostate cancer (PCa) upon examination of pathologic specimens. Incidental PCa commonly presents as grade group 1 (GG1) disease [1]. International guidelines do not provide recommendations for the management of incidental cancers (stages T1a and T1b), leading to debate on whether it should be managed similarly to nonpalpable biopsy-diagnosed (T1c) favorable-risk disease [2–4]. Some authors argue that since usual predictors such as prostate-specific antigen (PSA) and Gleason score can guide decision-making the same way as T1c cases, incidental cancers should not be considered as different entities [4]. On the contrary, others argue that incidental PCa have a different natural history from T1c cases and should be considered separately in clinical guidelines [3].

Although incidental GG1 is not uncommon, data on long-term outcomes are limited [2,5]. Most men with incidental cancers are managed with active surveillance (AS) or observation, with typically a lower incidence of progression to higher-grade cancer or conversion to treatment, compared with patients diagnosed via biopsies and followed similarly [6–8]. Nonetheless, virtually all studies available on this topic are characterized by a short follow-up, and rarely evaluate metastases and disease-specific mortality [6–8]. A comprehensive assessment of the long-term outcomes of incidental PCa is crucial to assess whether a strict monitoring strategy such as AS is necessary for these patients.

Given this lack of comprehensive data, we conducted a large, multi-institutional study aimed at evaluating the long-term outcomes of patients with incidental PCa managed with AS compared with their counterparts diagnosed on biopsy.

2. Patients and methods

2.1. Study population

Data were retrieved from eight institutional AS databases under local ethics committee approval and were anonymized prior to the analyses. From an initial population of 2263 patients, we excluded ten with GG3 or GG4 on diagnosis, 13 with clinical stage T3, 48 with <1 yr of follow-up, and one diagnosed prior to 2005. Our study protocol allowed for the inclusion of patients with GG2. However, since those ($n = 78$) contributed for only 3.6% of the analytic cohort, we decided to include only patients with GG1 disease, resulting in a final study population of 2113 patients. Supplementary Table 1 displays the key patient selection criteria and follow-up characteristics for each institution. All but one institution mandated scheduled surveillance biopsies, mainly according to the Prostate Cancer Research Active Surveillance (PRIAS) protocol or every 2–3 yr. The main trigger for intervention was GG $\geq$2 on follow-up biopsies. Two institutions did not provide complete data regarding follow-up biopsies, multiparametric magnetic resonance imaging (mpMRI), and PSA assessments.

2.2. Outcome measurements

Metastases were defined as positive imaging outside the prostate, diagnosed on either conventional imaging (computed tomography [CT] or bone scan) or prostate-specific membrane antigen (PSMA) positron emission tomography

(PET)/CT. Imaging was performed at the time of biochemical recurrence or after a follow-up biopsy showed GG ≥2 disease, according to the treating physician's preference. Mortality was retrieved from death certificates or hospital charts. Deintensification was defined as when patients were moved to either only sequential PSA monitoring or watchful waiting, typically due to age, comorbidities, or patient preference.

2.3. Statistical analyses

We hypothesized that patients diagnosed with incidental PCa have better oncologic outcomes than those diagnosed on biopsy when followed on AS. We used competing risk analyses to estimate the incidence of metastases and disease-specific mortality according to the type of diagnosis (ie, incidental vs biopsy), considering death from other causes as a competing event, with Fine and Gray [9] competing risk regression to derive the subdistribution hazard ratio (sHR) for the difference between the two groups. Since the incidence of metastases and cancer-specific mortality depend on whether patients are treated, and the latter can depend on how intensively they are monitored on AS, we were concerned of an ascertainment bias had patients diagnosed on biopsy been followed more intensively [10,11]. We therefore calculated the number of mpMRI scans and biopsies in patients who were alive, not treated, and metastasis free at 2 and 5 yr after diagnosis, according to the type of their diagnosis. We then determined the incidence of

deintensification and any form of treatment, with deintensification as a competing event. We also hypothesized that the risk of high-grade cancer (GG ≥2) on the first follow-up biopsy might be lower if the initial diagnosis is on a BPH procedure rather than on a biopsy, and so we compared the risk of high-grade cancer on the first follow-up biopsy according to the type of diagnosis with a two-sample test for equality of proportions. For this exploratory analysis, we identified 1559 patients who underwent a first follow-up biopsy within 2 yr from the diagnosis. All analyses were performed with R version 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria), with the tidyverse (version 2.0.0), gtsummary (version 1.7.0), tidycmprsk (version 0.2.0), and R Markdown (version 2.21) packages.

3. Results

3.1. Cohort description

We analyzed 2113 patients with GG1 PCa managed with AS from June 2005 to December 2022. A total of 1900 patients were diagnosed on biopsy and 213 on a BPH procedure (Table 1). Clinical characteristics by institution are reported in Supplementary Table 2. Patients with incidental disease were slightly older than those diagnosed on biopsy (68 vs 66 yr, p = 0.001) and had lower PSA levels (3 vs 6 ng/ml, p < 0.001). Most of them had stage T1a (164, 77%) and were diagnosed on transurethral resection of the prostate (TURP;

Table 1 – Baseline patient and disease characteristics

Characteristic	Biopsy (N = 1900)	BPH procedure (N = 213)	p– value
Age at diagnosis (yr), median (IQR)	66 (61, 70)	68 (63, 72)	0.001
Prior negative biopsy, n (%)	244 (18)	34 (16)	0.6
Unknown	540	5	
PSA (ng/ml), median (IQR)	6.0 (4.6, 7.9)	3.0 (1.8, 5.0)	<0.001
Unknown	–	11	
Prostate volume (cc), median (IQR)	50 (38, 69)	50 (36, 70)	0.4
Unknown	49	28	
PSA density (ng/ml/cc), median (IQR)	0.12 (0.08, 0.17)	0.07 (0.04, 0.11)	<0.001
Unknown	49	30	
Clinical stage, n (%)			
T1a	–	164 (77)	
T1b	–	49 (23)	
T1c	1707 (90)	–	
T2	193 (10)	–	
Type of initial histology, n (%)			
Systematic only	1406 (74)	–	
MRI targeted + systematic	479 (25)	–	
MRI targeted only	15 (0.8)	–	
TURP	–	145 (68)	
HoLEP	–	55 (26)	
Simple prostatectomy	–	13 (6.1)	
Total biopsy cores (n = 2096)	13 (12, 16)	–	
Total cores with cancer (n = 2092)	1 (1, 2)	–	
Timing of first MRI (n = 1734), n (%) [a]			<0.001
No MRI	167 (11)	101 (48)	
Before diagnosis	504 (33)	6 (3)	
After diagnosis, before first AS biopsy	658 (43)	54 (25)	
After first AS biopsy	193 (13)	51 (24)	
First MRI score (n = 1466), n (%)			0.02
PI-RADS/Likert 1–2	544 (40)	61 (55)	
PI-RADS/Likert 3	296 (22)	21 (19)	
PI-RADS/Likert 4	415 (31)	22 (20)	
PI-RADS/Likert 5	92 (7)	6 (6)	
Unknown	8	1	

AS = active surveillance; BPH = benign prostatic hyperplasia; HoLEP = holmium laser enucleation of the prostate; IQR = interquartile range; MRI = magnetic resonance imaging; PI-RADS = Prostate Imaging Reporting and Data System; PSA = prostate-specific antigen; TURP = transurethral resection of the prostate.
[a] In men for whom the timing of the first MRI could be determined either according to scan date or by use of MRI targeting on diagnosis.

145, 68%). There were significant missing data on history of prior negative biopsies, and there were some missing data on PSA and volume prior to diagnosis. After excluding 524 patients with missing data on timing of mpMRI and biopsies, we observed that patients with incidental cancers were monitored less intensively (Table 2). We evaluated the number of mpMRI scans and biopsies in 523 patients who remained on AS for at least 5 yr, and we found that 93% of those diagnosed on biopsy underwent at least one surveillance biopsy, versus 82% of men with incidental cancers ($p < 0.001$). Radiologic assessments within 5 yr were half as frequent in patients with incidental cancers (42% received one or more mpMRI scan) as those diagnosed on biopsy (84%, $p < 0.001$). The incidence of repeated biopsies at 2, 5, and 10 yr, for biopsy-diagnosed versus incidental cancer was as follows: 85% versus 71%, 94% versus 82%, and 96% versus 86%, respectively. On first magnetic resonance imaging (MRI), suspicious findings were approximately 10% more frequent in the biopsy group (Table 1).

3.2. Treatments and deintensification of follow-up

A total of 43 patients with incidental cancer and 775 diagnosed on biopsy were treated, mostly with radical prostatectomy, as shown in Table 3. The median follow-up for those not treated was 4.6 yr (interquartile range [IQR] 2.7–7.1 yr), and 109 patients were at risk of treatment at 10 yr. The 10-yr incidence of treatment was 22% for incidental cancers, compared with 53% for biopsy (sHR 0.34, 95% confidence interval [CI] 0.26–0.46, $p < 0.001$), as shown in Figure 1. Significantly more patients with incidental cancers had their follow-up deintensified than those undergoing biopsy: 29% versus 6.5% for biopsy (sHR 5.42, 95% CI 3.75–7.83, $p < 0.001$).

3.3. Metastases and disease-specific mortality

The median follow-up for those who did not die was 5.3 yr (IQR 3.2–7.9 yr). There were 213 patients at risk of metastases at 10 yr. Bone or visceral metastases developed in 17 patients diagnosed on biopsy and in one diagnosed on a BPH procedure, as summarized in Table 3. The 10-yr incidence of bone or visceral metastases for patients diagnosed on biopsy was 2% versus 0.8% for patients with incidental

Table 3 – Summary of treatments and metastases in the study cohort, by type of the initial diagnosis

	Biopsy	BPH procedure
Treatments, n (%)		
Total patients treated	775	43
Radical prostatectomy	519 (67)	23 (53)
EBRT ± hormonal therapy	182 (23)	15 (35)
Brachytherapy	38 (4.9)	0 (0)
ADT monotherapy	10 (1.3)	3 (7.0)
Focal therapy	18 (2.3)	2 (4.7)
Chemotherapy	2 (0.3)	0 (0)
Other treatment	6 (0.8)	0 (0)
Metastases, n (%)		
Total patients with metastases	21	1
Lymph nodes + bone	11 (52)	0 (0)
Lymph nodes	4 (19)	0 (0)
Bone	4 (19)	1 (100)
Visceral	1 (4.8)	0 (0)
Lymph nodes + bone + visceral	1 (4.8)	0 (0)

ADT = androgen deprivation therapy; BPH = benign prostatic hyperplasia; EBRT = external beam radiation therapy.

PCa (sHR 0.35, 95% CI 0.05–2.54, $p = 0.3$; Table 4 and Supplementary Fig. 1). These apparently high rates may result from the increase in the use of molecular imaging in recent years, with 13 (72%) patients having metastases diagnosed by PSMA PET/CT; of the remainder, four had distant metastases diagnosed on bone scan and one had visceral metastases diagnosed on whole-body MRI. Supplementary Table 2 shows imaging characteristics for patients who developed metastases. No patient with incidental PCa died from the disease. A total of four patients diagnosed on biopsy died from PCa; the 10-yr incidence of disease-specific mortality for biopsy was 0.5% (95% CI 0.2–1%), as shown in Supplementary Figure 2.

### 3.4. Risk of higher-grade PCa on the first follow-up biopsy

In 1559 patients who underwent a biopsy within 2 yr from the diagnosis, 319 had higher-grade cancer, as shown in Supplementary Table 4. Among patients with incidental PCa who were reclassified, six (4%) had GG2, three (2%) GG3, and one (1%) GG4. The risk of higher-grade cancer was 22% for patients diagnosed on biopsy and 7% for those diagnosed on a BPH procedure, a difference of 15% (95% CI 10–20%, $p < 0.001$; Table 5). More patients diagnosed on a

Table 2 – Intensity of follow-up tests (biopsies and mpMRI scans) according to the type of the initial diagnosis, in 1589 patients with complete data on timing of biopsies and mpMRI scans, according to whether they reached 2 or 5 yr on active surveillance without receiving treatment or developing metastases, or being moved to a deintensified follow-up

Variable	Patients at risk at 2 yr			Patients at risk at 5 yr		
	Biopsy (N = 947)	BPH procedure (N = 190)	p value	Biopsy (N = 409)	BPH procedure (N = 114)	p value
Biopsies after diagnosis, n (%) [a]			<0.001			<0.001
0	169 (18)	58 (31)		30 (7.3)	20 (18)	
1	699 (74)	109 (57)		160 (39)	61 (54)	
2	76 (8.0)	21 (11)		173 (42)	22 (19)	
≥3	3 (0.3)	2 (1.1)		46 (11)	11 (9.6)	
Multiparametric magnetic resonance imaging assessments, n (%) [a]			<0.001			<0.001
0	263 (28)	135 (71)		67 (16)	66 (58)	
1	443 (47)	48 (25)		140 (34)	28 (25)	
2	188 (20)	7 (3.7)		122 (30)	13 (11)	
≥3	53 (5.6)	0 (0)		80 (20)	7 (6.1)	

BPH = benign prostatic hyperplasia; mpMRI = multiparametric magnetic resonance imaging.
[a] Two institutions (St. Antonius Utrecht and Medical University of Innsbruck) provided partial data on dates of mpMRI and biopsy assessments. Therefore, patients for whom we could not derive the timing of assessments were excluded.
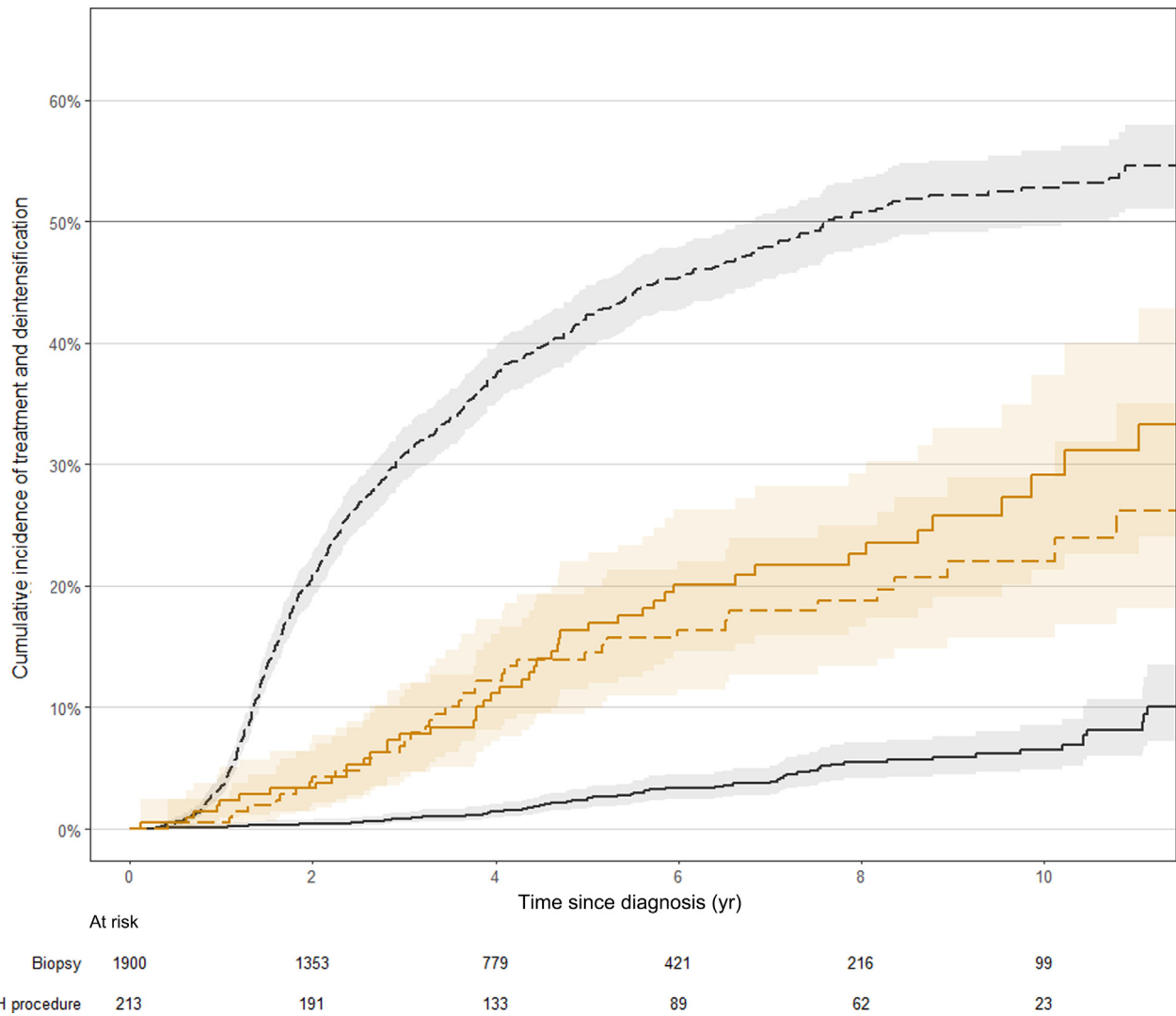
Fig. 1 – Cumulative incidence of treatment (dashed lines) and deintensification of monitoring (solid lines) in patients diagnosed on biopsy (black lines) or on a procedure for urinary obstruction (orange lines). The shaded areas represent the 95% confidence intervals. Note that the y axis is truncated at 60%. BPH = benign prostatic hyperplasia.

Table 4 – Ten-year cumulative incidence and subdistribution hazard ratios, with 95% confidence intervals, of key outcomes in the study cohort

Outcome	Biopsy		BPH procedure		Subdistribution hazard ratio (95% CI) [a]	p value
	Events	Incidence (95% CI)	Events	Incidence (95% CI)		
Metastases, including lymph nodes	21	3 (1–4)	1	0.8 (0.1–4)	0.28 (0.04–2.01)	0.2
Metastases, bone or visceral	17	2 (1–3)	1	0.8 (0.1–4)	0.35 (0.05–2.54)	0.3
Other-cause mortality	89	10 (8–12)	19	14 (8–21)	1.17 (0.71–1.93)	0.5
Prostate cancer mortality	4	0.5 (0.2–1)	0	–	–	–
Treatment (any form)	775	53 (50–56)	43	22 (16–29)	0.34 (0.26–0.46)	<0.001
Treatment (RP, EBRT)	701	49 (46–52)	38	20 (14–26)	0.33 (0.24–0.46)	<0.001
Deintensification	70	6.5 (4.9–8.5)	49	29 (21–37)	5.42 (3.75–7.83)	<0.001

BPH = benign prostatic hyperplasia; CI = confidence interval; EBRT = external beam radiation therapy; RP = radical prostatectomy.
[a] Estimate from univariable Fine and Gray competing risk regression model.

Table 5 – Outcomes on the first follow-up biopsy, in 1559 patients who underwent a biopsy within 2 yr from diagnosis

Initial diagnosis	n	No cancer	GG1	GG ≥2	Risk (%) of GG ≥2 (95% CI) [a]
Biopsy	1408	477	622	309	22% (20–24%)
BPH procedure	151	87	54	10	7% (3–12%)

BPH = benign prostatic hyperplasia; CI = confidence interval; GG = grade group.
[a] Difference of 15% by two-sample test for equality of proportions (p < 0.001).

BPH procedure had no cancer at all in their confirmatory biopsy (n = 87, 58%), compared with patients diagnosed on biopsy (n = 477, 34%).

4. Discussion

The long-term outcomes of incidental GG1 PCa have poorly been characterized, leading to a persistent lack of practice guideline recommendations, even in the most recent updates [3,4,12]. Our study shows that men with incidental PCa are assessed less frequently with mpMRI and biopsies, and therefore had a lower 10-yr incidence of treatment than those diagnosed on biopsy. The incidence of distant metastases was also lower for incidental PCa.

Few groups have reported the outcomes of patients with incidental disease managed with observation (AS or watchful waiting), but, in general, a low risk of progression to treatment and disease-specific mortality has been reported [5–8,13]. For example, Descazeaud et al [13] evaluated a consecutive series of patients with Gleason ≤6 T1a disease who underwent further treatment only upon signs of progression, demonstrating an incidence of progression of 15% at 5 yr, similar to our 5-yr estimate, without any patient developing distant metastases. When patients with incidental cancers are monitored with contemporary AS criteria, results are similar [6–8]. Luzzago et al [6] observed a 3-yr rate of discontinuation of 20% for incidental cancers versus 35% for those diagnosed on biopsy. However, there were similar rates of biopsy progression, plausibly explained by a difference in the surveillance intensity of incidental cancers, similar to our findings. A significant proportion of patients in their cohort had GG2, explaining the higher incidence of treatment than what we observed in our multi-institutional cohort.

Metastases in men with incidental PCa who are on AS are as rare as those reported for patients diagnosed on biopsy [14,15]. In line with our findings, Herden et al [7] evaluated a cohort of 68 patients with incidental PCa and reported that only one individual with stage T1a GG1 cancer developed metastases during AS. The incidence of metastases in our study was high compared with that of historic cohorts of patients with predominantly very–low-risk disease, which is typically below 1% [14,15]. We believe that this is due to the increasing adoption of PSMA PET/CT to assess biochemical failure. This imaging modality has higher detection rates for distant metastases than conventional imaging in the primary setting [16]. There is also evidence from recent studies on AS that the use of PSMA PET/CT is associated with a significant risk of stage migration of cancers otherwise considered localized by conventional imaging [17,18]. Another explanation is the inclusion of patients with higher-risk features, for which AS is discouraged by the PRIAS criteria [19]. We did not use any PSA density or number of positive core selection criteria; we recognize this as a further plausible reason for the higher than expected incidence of metastases [14].

Population-based studies showed high disease-specific mortality for patients with untreated incidental GG1 [5]. Scheipner et al [5] analyzed the Surveillance, Epidemiology, and End Results (SEER) database and observed that PCa mortality for patients with GG1 incidental cancer who are not initially treated is 2% at 6 yr. This finding is in contrast with the established evidence of the very low disease-specific mortality rates in patients with GG1 on biopsy who are monitored with AS, which is typically around zero [14,15]. In our dataset, none of the patients with incidental cancer died from the disease itself, and PCa-specific mortality for patients diagnosed on biopsy was 0.5% at 10 yr, in line with the available evidence from historic AS cohorts [14,15]. The best explanation of this discrepancy is that we analyzed a highly selected cohort of men with GG1 diagnosed incidentally. All patients were selected for AS at referral centers and received diagnostic assessments to rule out aggressive PCa before surgery, as reflected by the number of patients who had a negative biopsy prior to diagnosis (16%), and to a lesser extent, mpMRI (3%). This resulted in more favorable disease features and better oncologic outcomes than those reported in previous population-based studies [5]. Since patients in this cohort were selected, our risk estimates underestimate the risk for a patient yet to undertake any pre- or post-TURP workup; hence, our results are not generalizable to the whole incidental GG1 population. Evidence from population-based studies indicates that the risk of high-grade cancer on post-TURP biopsies is approximately 20%, supporting that further evaluation is required if GG1 is found incidentally [20]. On the contrary, this figure was as low as 7% in our cohort and reflects patient selection. We should also highlight that, due to the small number of events, our risk estimate was imprecise, with an upper 95% CI bound of 12%. Literature on biopsy outcomes after incidental PCa is scarce. Lee et al [21] observed an incidence of higher-grade cancer of 18% in 17 patients with Gleason 6 on TURP who underwent a subsequent biopsy, further highlighting that the prevalence of Gleason ≥7 is higher in unselected populations. Moreover, when patients with incidental GG1 undergo immediate radical prostatectomy, rates of adverse pathology are similar to that of patients with biopsy GG1, as observed by Tsaur et al [22], although their study population was selected for surgery, overestimating the risk of adverse pathology of unselected populations [23]. Considering an incidence of GG ≥2 of around 20% in patients who underwent a biopsy due to a suspicion of higher-grade cancer and the incidence of our study (7%), we speculate that the true risk of GG ≥2 in an unselected population lies in between [20]. This indicates that it is unlikely that a biopsy is required in all men with incidental GG1; however, additional research is required to establish whether noninvasive tools such as mpMRI and PSA density can be used for biopsy decision-making [24]. Capitanio et al [25] proposed a postoperative PSA threshold below 1 ng/ml to identify patients with incidental PCa at a very high probability of harboring no cancer at all if submitted to radical prostatectomy. Such thresholds could therefore be used as an initial screening after BPH surgery; however, whether biopsies can safely be avoided if PSA is <1 ng/ml should still be assessed.

Another relevant finding is that men with incidental PCa were followed less intensively, reflecting the possible belief in the urologic community of an inevitably indolent course of this disease [4]. The difference in the incidence of treat-

ment at 10 yr was >50%, but the difference in the number of biopsies at 5 yr was 10%; therefore, the overall lower risk of treatment is only partially explained by the less intense follow-up. Moreover, the incidence of further assessments, namely, mpMRI and biopsies, has been confirmed to be low also in a population-based study of patients with incidental PCa not necessarily selected for AS [20]. By contrast, the probability of having no cancer at all on the first follow-up biopsy supports the conclusion that patients with incidental GG1, once further evaluated without evidence of aggressive cancer, will unlikely benefit from stringent AS monitoring and should therefore be followed the same way as a man with a negative biopsy, a conclusion similar to that of a recent population-based analysis of patients with incidental PCa in Denmark [20].

The main limitations of our analyses include the lack of a central pathology review, standardized protocols, and different follow-up schedules adopted at institutions. While most centers performed a rebiopsy 1 yr after diagnosis and every 2–3 yr thereafter, others performed biopsies with longer intervals, and some did not mandate for scheduled biopsies, resulting in effects on conversion to treatment given by different timing of assessments [11]. The two groups had >50% difference in the 10-yr incidence of treatment, with a 10% difference in biopsy intensity. If both groups were followed similarly (eg, with biopsies every 2 yr), we would observe an equally higher incidence of treatment in both groups, due to an expected higher detection rate of GG ≥ 2 disease [26].

5. Conclusions

Patients with incidental GG1 PCa receive less intense follow-up and undergo treatment less frequently than those diagnosed on biopsy. Clinicians already appear to follow such a less intensive follow-up, which might be justified since the risk of higher-grade cancer on the first follow-up biopsy was below 10% in our selected population. Patients with incidental GG1 PCa should receive an adequate risk assessment with a postoperative PSA evaluation, mpMRI, and preferably peripheral zone biopsies to exclude the presence of aggressive disease, and only if GG1, or favorable GG2, is confirmed, then AS should be the management of choice. If the biopsy shows no cancer, the management should be that of a patient with a negative biopsy. Further research should clarify the role of postoperative PSA and mpMRI in the decision regarding whether to perform a biopsy.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2024.08.004.

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