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Prostate Cancer

Variation in the Prescription of Androgen Deprivation Therapy in Intermediate- and High-risk Prostate Cancer Patients Treated with Radiotherapy in the Netherlands, and Adherence to European Association of Urology Guidelines: A Population-based Study

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Article info

Article history:
Accepted November 3, 2019

Associate Editor: Derya Tilki

Keywords:
Prostate cancer
Androgen deprivation therapy
Guidelines
Variation
Adherence

Abstract

Background: According to (inter-)national guidelines, (neo-)adjuvant and concurrent androgen deprivation therapy (ADT) in combination with external beam radiotherapy (EBRT) is optional for intermediate-risk prostate cancer (PCa) patients and is the recommended standard treatment for high-risk PCa patients.
Objective: The aim of this study is to provide insight into the prescription of ADT in intermediate- and high-risk PCa patients treated with EBRT in the Netherlands, and to evaluate adherence to European Association of Urology guidelines and factors affecting prescription.
Design, setting, and participants: All intermediate- and high-risk PCa patients between October 2015 and April 2016 were identified through the population-based Netherlands Cancer Registry. Variation in the prescription of ADT in patients with EBRT was evaluated. Multivariable multilevel logistic regression analyses were performed to determine the probability of ADT and to examine the role of patient-, tumour-, and hospital-related factors.
Results and limitations: Overall, 29% of patients with intermediate-risk PCa received ADT varying from 3% to 73% between institutions. From the multivariable regression analysis, higher Gleason grade, magnetic resonance imaging, and computed tomography

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https://doi.org/10.1016/j.euf.2019.11.005

(CT)-positron-emission tomography/CT prior to radiotherapy appeared to be associated with increased prescription of ADT. Among high-risk patients, 83% received ADT, varying from 57% to 100% between departments. A higher prostate-specific antigen level, more advanced tumour stage, and a higher Gleason grade were associated with increased prescription.

Conclusions: Less than one-third of intermediate-risk PCa patients treated with EBRT receive ADT. The variation in the prescription of ADT between different institutions is substantial. This suggests that the prescription is largely dependent on different institutional policies. The guideline adherence in high-risk PCa is fairly good, as the vast majority of patients received ADT as recommended. However, given the clear recommendations in the guidelines, adherence could be improved.

Patient summary: In this review, we looked at the variation of hormonal treatment in intermediate- and high-risk prostate cancer patients. We found substantial variation between institutions.

1. Introduction

(Neo-)adjuvant and concurrent ADT in combination with external beam radiotherapy (EBRT) is an established type of treatment in intermediate- and high-risk prostate cancer (PCa) patients. Many trials demonstrated a therapeutic benefit adding ADT to EBRT in high-risk PCa patients [1–3]. The role of ADT is less clear in the intermediate-risk group, but might have a positive treatment benefit as well [4–6]. Treatment recommendations concerning ADT prescription are incorporated in different international and national guidelines [7–9].

The European Association of Urology (EAU) guidelines for PCa state that high-dose radiotherapy and long-term ADT for at least 2 or 3 yr is recommended for high-risk PCa. Patients with intermediate-risk PCa and suitable for ADT can be given short-term ADT (4–6 mo) [9]. In the Dutch guidelines, the definition of high-risk disease slightly differs from the EAU guidelines, as patients with two intermediate-risk criteria are also considered at high risk. For patients with high-risk disease, the Dutch guidelines state that the optimal and standard treatment consists of high-dose radiotherapy with long-term ADT for at least 2 yr [8]. For patients with intermediate-risk disease, (short-term) ADT is not recommended.

ProZIB (acronym for: ProstaatkankerZorg In Beeld; meaning insight into PCa care) is a nationwide registration of PCa patients in the Netherlands implemented in the Netherlands Cancer Registry (NCR). Its main goal is to provide insight into clinical practice concerning PCa care in the Netherlands and to evaluate quality of care [10]. The current study aims to provide insight into the clinical practice concerning the prescription of ADT among intermediate- and high-risk PCa patients treated with EBRT, to evaluate guideline adherence and identify factors that might affect the initiation of ADT.

2. Patients and methods

Patients with PCa were identified through the population-based NCR. On a 2-weekly basis, the NCR receives notifications of histologically confirmed newly diagnosed cancers in the Netherlands by the national automated pathology archive PALGA between 1 October 2015 and 16 April 2016. For every malignancy, information on patient and tumour characteristics, disease stage, and treatment was extracted from the medical records by professional data managers. Owing to feasibility reasons (labour intensive and costly), we could do this only for approximately 6000 patients. For the current study, all patients from ProZIB with localised or locally advanced PCa without distant metastases (cT1–4, cN0–1/Nx, cM0) treated with EBRT with curative intent were included.

All patients were stratified into groups of intermediate-risk and high-risk PCa patients using the EAU and Dutch guidelines risk stratification [8,9]. Two treatment groups were defined: EBRT and EBRT with ADT. ADT was defined as an orchiectomy (very rarely used for long-term ADT), luteinising-hormone–releasing hormone (LHRH) agonist, LHRH antagonist, antiandrogen, or a combination of LHRH (anti)agonist and antiandrogens as first-line therapy. Intended duration of ADT was defined as short term if the duration was $\leq$6 mo, and as long term if the duration was $\geq$2 yr. Intended "life-long" ADT (n = 18), intermittent ADT (n = 2), and 12- and 18-mo ADT (n = 19) were regarded as long-term ADT. However, the duration of ADT was also not documented very well in the files. Therefore, we decided not to include the ADT duration in the analyses.

We evaluated the association of several patient- and tumour-related factors with the prescription of ADT. Comorbidity was scored according to the Charlson Comorbidity Index (CCI) score and categorised according to CCI score of 0, 1, or $\geq$2 [11]. Tumour stage was defined according to the International Union Against Cancer tumour-node-metastasis classification, edition 7.0 [12]. Tumour stages cT2 (n = 149) and cT3 (n = 109) were interpreted as cT2a and cT3a, respectively; cT2–3 (n = 32) was interpreted as cT2a, cT3–4 (n = 10) as cT3a, and cN0–1 (n = 4) as cN0. Clinical stage was determined based on the rectal examination, prostate-specific antigen (PSA), biopsies, and imaging performed before the start of treatment. In the Netherlands, most of the patients underwent magnetic resonance imaging (MRI) before treatment. PSA level in ng/ml at diagnosis and International Society of Urological Pathology (ISUP) Gleason grade group were evaluated as tumour-related factors [13]. The ISUP Gleason grade groups, compared with the Gleason score (GS), are as follows: group 1 = GS $\leq$ 6; group 2 = GS 3 + 4 = 7; group 3 = GS 4 + 3 = 7; group 4 = GS 4 + 4 = 8; and group 5 = GS 9 and 10.

The roles of several hospital-related factors were investigated. These include the use of an MRI scan and diagnostic computed tomography (CT) scan and/or positron-emission tomography (PET)/CT scan (regardless of the tracer type), and whether patients were discussed in at least one multidisciplinary team meeting. EBRT details were collected and categorised in prostate (fossa) or prostate and nodal. Finally, the prescriber of ADT was a urologist, a radiation oncologist, another physician, or unknown.

2.1. Statistical analyses

To evaluate practice variation in the prescription of ADT, crude and case-mix adjusted probabilities of ADT per radiotherapy institution were

assessed; age and the CCI score were used as case-mix factors. Radiotherapy institutions with <10 patients fulfilling the inclusion criteria were excluded from the analysis on institutional variation. Univariable and multivariable multilevel logistic regression models were used to evaluate the association between patient-, tumour-, and hospital-related factors and treatment with EBRT and ADT. All factors that were univariably associated with EBRT and ADT ($p < 0.10$) were included in the multivariable model. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

A total of 1275 patients fulfilled the inclusion criteria. The characteristics are shown in Table 1.

3.1. Intermediate-risk PCa

Of intermediate-risk patients, 29% were treated with ADT (Table 2). This proportion ranged largely between radiotherapy departments, varying from 3% to 73% (Fig. 1A). After case-mix adjustment, the variation was 5–67%. In three of 11 (27%) radiotherapy institutions, >40% of patients received ADT, whereas in four of 11 (36%) <20% received ADT.

The results of the uni- and multivariable analyses of factors associated with ADT in intermediate-risk PCa are displayed in Table 3. It appeared that a higher ISUP Gleason grade was positively associated with increased prescription of ADT (ISUP Gleason grade group 3 vs 1: odds ratio [OR] 8.3, 95% confidence interval [CI] 2.3–29.9, and 2 vs 1: OR 3.7, 95% CI 1.2–11.6). Patients with MRI (OR 2.9, 95% CI 1.1–7.7) and patients with diagnostic CT-PET/CT (OR 3.3, 95% CI 1.3–8.5) also had an increased probability of ADT. The intended duration of the ADT was short term in 51% of patients, long term in 31.7%, and unknown in 18%. In 86.1%, ADT was prescribed by the urologist, in 10.1% by the radiation oncologist, and in 3.8% by another/unknown physician. These results were not included in the analyses because only patients undergoing ADT have a prescribing physician and are therefore not an influencing factor for ADT variation.

3.2. High-risk PCa

Of all 930 patients with high-risk PCa, 83% received ADT (Table 2). The variation in ADT prescription over institutions is displayed in Fig. 1B. The proportion of patients with ADT varied from 57% to 100% between institutes (Table 2 and Fig. 1B). After case-mix adjustment, the variation was 60–96%. In eight of the 20 (40%) radiotherapy departments, <80% of patients received ADT.

In Table 3, the results of the uni- and multivariable multilevel analyses of factors associated with ADT are presented. It appeared that higher PSA, higher clinical tumour stage, and higher ISUP Gleason grade were all positively associated with increased prescription of ADT (PSA [per 1 unit increase]: OR 1.04, 95% CI: 1.02–1.06, and cT3–4 vs cT1-cT2b: OR 4.6, 95% CI: 2.6–8.1, and ISUP Gleason grade group 5 vs 1: OR 40.2, 95% CI: 11.9–135.6; 4 vs 1: OR 6.5, 95% CI 3.1–13.4; 3 vs 1: OR 3.3, 95% CI 1.5–7.3). Of 930 high-risk patients, long-term ADT was planned in 63%, the intended duration was short term in 14.9%, and the intended duration was unknown in 22.8%. ADT was prescribed by a urologist in 83.8%, by a radiation oncologist in 10.8%, and by another/unknown physician in 5.5%. A positive association between ADT prescription and nodal radiation (high risk; OR 5.95, 95% CI 2.16–19.39, $p = 0.0024$) was found.

Table 1 – Patient and tumour characteristics of all patients diagnosed with prostate cancer in the ProZIB period and treated with external beam radiation therapy (*N* = 1275)

	N (%)/mean (SD)/ median (Q1–Q3)
Age (yr)	71.0 (6.0)
Charlson Comorbidity Index score	
0	652 (51.1)
1	346 (27.1)
≥2	277 (21.7)
PSA (ng/ml)[a]	12.2 (8.0–23.9)
Clinical tumour stage of disease	
cT1a-cT1b	7 (0.6)
cT1c-cT2b	572 (44.9)
cT2c	127 (10.0)
cT3a-cT3b	540 (42.4)
cT4	29 (2.3)
Clinical nodal stage of disease	
cN0	914 (71.7)
cN1	129 (10.1)
cNx	232 (18.2)
ISUP Gleason grade group	
1	227 (17.8)
2	388 (30.4)
3	193 (15.1)
4	252 (19.8)
5	210 (16.5)
Unknown	5 (0.4)
Risk group according to EAU guidelines	
Intermediate risk: cT2b or GS = 7 or PSA 10–20	276 (21.7)
High risk: cT2c-4 or GS >7 or PSA >20 and/or N+	930 (72.9)
Unknown	10 (0.8)
Risk group according to Dutch guidelines	
Intermediate risk: cT2b-c or GS = 7 or PSA 10–20	178 (14.0)
High risk: cT3–4 and/or GS >7 and/or PSA >20 and/or cN+ or 2 intermediate-risk risk factors	1029 (80.7)
Unknown	9 (0.7)
MRI prior to start EBRT	
No	319 (25.0)
Yes	956 (75.0)
CT scan and/or PET/CT scan prior to start of EBRT	
No	848 (66.5)
Yes	427 (33.5)
Patients discussed in MDT meeting prior to start of EBRT	
No	115 (9.0)
Yes	1160 (91.0)
EBRT details	
Prostate (fossa)	1136 (89.1)
Prostate and nodal	111 (8.7)
Unknown	28 (2.2)

CT = computed tomography; EAU = European Association of Urology; EBRT = external beam radiation therapy; GS = Gleason score; ISUP = International Society of Urological Pathology; MDT = multidisciplinary team; MRI = magnetic-resonance imaging; PET = positron-emission tomography; PSA = prostate-specific antigen; SD = standard deviation.

[a] Median (Q1–Q3).

Table 2 – Proportion of patients treated with adjuvant ADT and variation in proportion of patients treated with adjuvant ADT between radiotherapy departments, according to EAU risk group and Dutch guidelines risk group

	Total	Adjuvant ADT	*N* used for variation[a]	Variation in min.-max. proportion of patients with ADT (%)
	N	*N* (%)		
EAU risk group				
Intermediate risk: cT2b or GS = 7 or PSA 10–20	276	79 (28.6)	225	2.9–73.3
High risk: cT2c-4 or GS >7 or PSA >20 and/or N+	930	771 (82.9)	930	56.8–100.0
Dutch guidelines risk group				
Intermediate risk: cT2b-c or GS = 7 or PSA 10–20	178	44 (24.7)	118	0.0–61.5
High risk: cT3–4 and/or GS >7 and/or PSA >20 and/or cN+ or 2 intermediate-risk risk factors	1029	806 (78.3)	1029	57.3–100.0

ADT = androgen deprivation therapy; EAU = European Association of Urology; EBRT = external beam radiation therapy; GS = Gleason score; max. = maximum; min. = minimum; PSA = prostate-specific antigen.
[a] All patients treated with EBRT in a radiotherapy institution with at least 10 patients within this risk group.

3.3. *Adherence to the Dutch guidelines*

In case variation in the prescription of ADT is evaluated by the Dutch classification of intermediate- and high-risk PCa, results are fairly the same. Overall, 25% of intermediate-risk PCa patients received ADT, varying from 0% to 62% between departments. Of all high-risk patients, 78% received ADT; the proportion of patients with ADT varied from 57% to 100% between departments (Table 2).

4. Discussion

In this study, we provided insight into the clinical practice concerning the prescription of ADT among intermediate- and high-risk PCa patients treated with EBRT in the Netherlands. Variation was found in the prescription of ADT between individual institutions. This variation was most pronounced in intermediate-risk PCa patients. Although for high-risk patients adherence to the guidelines was generally good, as the majority of patients received ADT, here a few institutions deviated considerably.

Our findings compare well with two other investigations from the USA and Australia, on treatment variation in ADT of patients treated with EBRT [14,15]. In the large US National Cancer Database study, 95 941 PCa patients were included. The retrospective cohort analysis of intermediate-risk patients has shown a decreasing trend in the prescription of ADT with EBRT from 50% in 2004 to 38% in 2012 [16]. By contrast, the ADT prescription in high-risk PCa increased slightly from 75% to 80% in 2012. In addition, patients treated in the northeast of the USA are more likely to receive ADT and patients in the west are less likely to receive ADT [15]. Despite the fact that these data are older, it can be concluded that large regional variation in the prescription of ADT existed in the USA in 2012. In Australia, 1809 were evaluated; 32% of the patients with favourable intermediate-risk PCa, 46% with unfavourable intermediate-risk PCa, and 84% with high-risk PCa received ADT [7,14]. They also described practice variation between public versus private institutes (66% vs 47% patients received ADT) and regional centres versus metropolitan areas (78% vs 59% patients received ADT). The authors suggested that differences in patient preferences might have played a role. The US Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) database included 1337 men with localised PCa. They observed substantial variability in the use of ADT in academic versus community hospital clinical practice (OR 2.0, 95% CI 1.0–4.0) [17]. In addition, they suggest that clinical practice is more dependent on institutional practice and information provision patterns than on personalised treatment decisions [18]. The Italian dataset Choosing Treatment for Prostate Cancer (CHOICE) evaluated the patterns of the prescription of ADT and adherence to the EAU in 1075 PCa patients. The EAU adherence is low in Italy, with a rate of 26.5% guideline-discordant ADT use. Geographical areas varied the most; in Central and South Italy, patients were more likely to receive ADT [19].

4.1. *Factors affecting prescription of ADT*

A higher ISUP grade group and diagnostic imaging before treatment (MRI and/or CT-PET/CT) were positively associated with an increased use of ADT in intermediate-risk PCa patients. Other factors such as tumour stage and PSA were not associated with ADT prescription.

For high-risk PCa patients, PSA level and ISUP grade were positively associated with an increased ADT prescription; however, diagnostic imaging before treatment was not. In general, men receiving ADT have higher-risk characteristics than those receiving EBRT alone, as a recent analysis of the US CaPSURE database showed [17]. Our findings are generally well in line with this.

The fact that, in our analysis, diagnostic imaging is associated with increased ADT use for intermediate-risk PCa only is intriguing. A higher rate of upgrading instead of downgrading tumour stage through imaging might be an explanation for the higher prescription rate of ADT for intermediate-risk PCa patients. Change in clinical stage after imaging could not be included in our study because this information was not documented in the medical files of patients. Perhaps for high-risk patients, ADT is already considered a necessity.

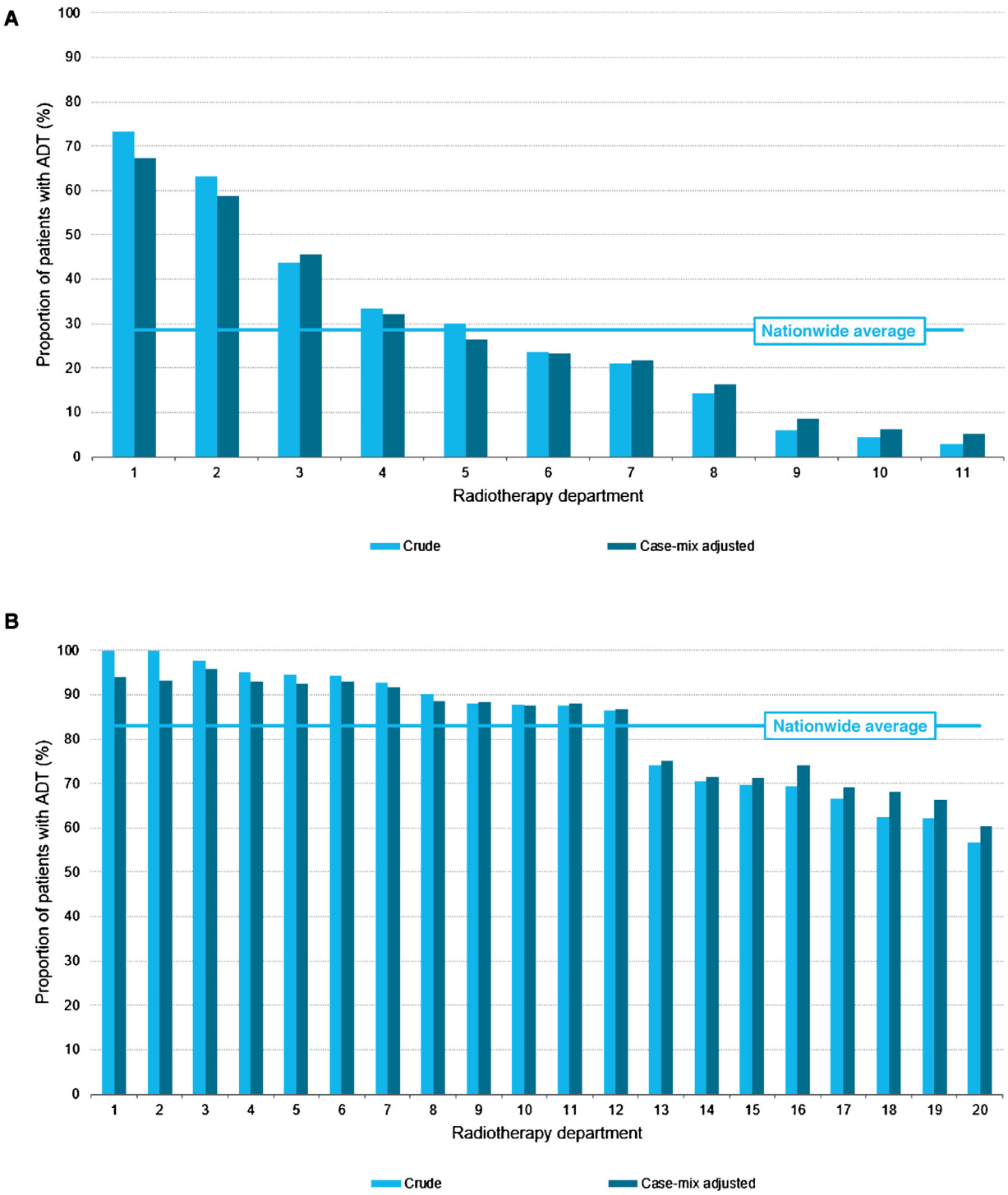

Fig. 1 – (A) Crude and case-mix adjusted (adjusted for age and Charlson comorbidity score) proportion of patients within EAU intermediate-risk group treated with adjuvant ADT and nationwide average, according to radiotherapy department. (B) Crude and case-mix adjusted (adjusted for age and Charlson comorbidity score) proportion of patients within EAU high-risk group treated with adjuvant ADT and nationwide average, according to radiotherapy department. ADT = androgen deprivation therapy; EAU = European Association of Urology.

4.2. Observed treatment variation and adherence to guidelines

In high-risk PCa, guideline adherence is fairly good, and the observed variation in the prescription of ADT is limited. For intermediate-risk PCa, large variation between institutions is observed possibly due to the fact that the EAU guidelines do not provide firm recommendations concerning ADT in these patients. The impact is expected to be lower in the intermediate-risk group, due to the fact that the evidence for ADT use is less clear and therefore guidelines differ in advice regarding EBRT with ADT. Many physicians in the Netherlands prefer to use the EAU guidelines, as these are

Table 3 – Patient characteristics and odds ratios (ORs) with 95% confidence intervals (CIs) of patient-, tumour-, and hospital-related factors associated with ADT in patients within EAU intermediate-risk group, based on a univariable multilevel logistic regression analysis (n = 276), and in patients within EAU high-risk group, based on a multilevel logistic regression analysis (n = 930)

	N (%)/mean (SD)/ median (Q1–Q3)	% ADT	Univariable model			Multivariable model		
			OR	95% CI	p value	OR	95% CI	p value
Factors associated with patients within EAU intermediate-risk group								
Age (yr)	71.41 (5.46)		1.044	0.98–1.10	0.24	–	–	–
Charlson Comorbidity Index score								
0	139 (50.4)	22.3	–	–	0.14	–	–	–
1	81 (29.4)	34.6	1.99	0.93–4.26				
≥2	56 (20.3)	35.7	1.92	0.81–4.57				
PSA (ng/ml)	9.90 (7.15–13.0)		1.04	0.96–1.12	0.30	–	–	–
ISUP Gleason grade								
1	52 (18.8)	13.5	–		0.0085	–	–	0.0078
2	164 (59.4)	28.1	3.41	1.12–10.35		3.71	1.19–11.61	
3	60 (21.7)	43.3	7.50	2.18–25.78		8.32	2.31–29.90	
MRI prior to start EBRT								
No	88 (31.9)	13.6	–	–	0.0719	–	–	0.0360
Yes	188 (68.1)	35.6	2.26	0.92–5.53		2.89	1.08–7.73	
CT and/or PET/CT prior to start of EBRT								
No	229 (83.0)	27.5	–	–	0.0525	–	–	0.0184
Yes	47 (17.0)	34.0	2.42	0.99–5.94)		3.28	1.26–8.54	
Patients discussed in MDT meeting prior to start of EBRT								
No	32 (11.6)	6.3	–	–	0.0699	–	–	0.1252
Yes	244 (88.4)	31.6	5.25	0.85–32.55		4.08	0.62–26.75	
Factors associated with patients within EAU high-risk group								
Age (yr)	71.13 (6.12)		0.97	0.94–1.00	0.06	0.96	0.92–1.00	0.06
Charlson Comorbidity Index score								
0	488 (52.5)	83.8	–	–	0.19	–	–	–
1	240 (25.8)	84.2	1.05	0.66–1.65				
≥2	202 (21.7)	79.2	0.68	0.43–1.08				
fPSA (ng/ml)	16.0 (9.0–30.5)		1.03	1.02–1.05	<0.0001	1.04	1.02–1.06	0.0001
Clinical tumour stage of disease (cT)								
cT1-cT2b	234 (25.2)	76.5	–		<0.0001	–		<0.0001
cT2c	127 (13.7)	63.0	0.44	0.26–0.78		1.69	0.62–4.67	
cT3-cT4	569 (61.2)	90.0	2.54	1.63–3.96		4.59	2.58–8.14	
Clinical nodal stage of disease (cN)								
cNx	119 (12.8)	67.2	0.53	0.32–0.88	0.0002	1.06	0.55–2.07	0.0620
cN0	682 (73.3)	82.8	–	–		–	–	
cN1	129 (13.9)	97.7	9.61	2.83–32.70		4.80	1.29–17.78	
ISUP Gleason grade								
1	113 (12.2)	56.6	–	–	<0.0001	–	–	<0.0001
2	221 (23.8)	75.1	2.20	1.29–3.74		1.91	1.00–3.65	
3	133 (14.3)	82.7	4.11	2.18–7.73		3.29	1.49–7.26	
4	252 (27.1)	89.3	6.17	3.41–11.16		6.45	3.10–13.42	
5	210 (22.6)	97.6	28.31	10.39–77.12		40.23	11.94–135.56	
Unknown	1 (0.1)	100	–	–		–	–	
MRI prior to start of EBRT								
No	200 (21.5)	83.5	–	–	0.0381	–	–	0.5149
Yes	730 (78.5)	82.7	0.57	0.34–0.97		0.80	0.40–1.62	
CT and/or PET/CT prior to start of EBRT								
No	557 (59.9)	81.9	–	–	0.0294	–	–	0.7818
Yes	373 (40.1)	84.5	1.60	1.05–2.43		0.93	0.52–1.65	
Patients discussed in MDT meeting prior to start of EBRT								
No	69 (7.4)	68.1	–	–	0.0780	–	–	0.5407
Yes	861 (92.6)	84.1	1.77	0.93–3.36		1.27	0.56–2.91	

ADT = androgen deprivation therapy; CT = computed tomography; EAU = European Association of Urology; EBRT = external beam radiation therapy; fPSA = free PSA; ISUP = International Society of Urological Pathology; MDT = multidisciplinary team; MRI = magnetic-resonance imaging; PET = positron-emission tomography; PSA = prostate-specific antigen; SD = standard deviation.

considered more up to date. However, the Dutch national guidelines are also used. The guidelines differ in risk stratification and treatment advice. The first difference is the definition of high- and intermediate-risk PCa; patients who have two risk factors defining intermediate-risk PCa (following Dutch guidelines) are considered to have a high risk. On the contrary, the EAU classification considers patients with cT2c disease as high-risk patients. In addition to differences in risk stratification, the recommendation regarding ADT differs. The EAU guidelines state that patients with intermediate-risk PCa suitable for ADT can be given short-term ADT (4–6 mo), whereas the Dutch guidelines do not recommend EBRT with ADT for these patients [8,9]. This leaves room for personal interpretations

and hence practice variation. One might argue that this is not necessarily a bad thing, and that physicians can discuss the benefits and doubts of adding ADT to EBRT with patients to make a shared decision. Unfortunately, patient preference concerning ADT could not be evaluated in this study. However, it is not to be expected that patient preference differs largely between institutions, and therefore our results suggest that clinical practice is largely dependent on institutional practice and information provision patterns instead of personalised treatment decisions, and therefore, the observed variation is unwanted. Given the firm and clear advice in both guidelines concerning the prescription of ADT in high-risk PCa, the observed variation, although limited, is unacceptable. A step, in order to reduce this variation in the Netherlands, could be the adaptation of one guideline, instead of having two guidelines.

One of the limitations in our study is that the number of patients with intermediate-risk PCa is relatively small. However, the numbers appear to be sufficient to illustrate large variation in the use of ADT. Collection of data on outcome and late toxicity following radiotherapy was out of reach of the ProZIB project because of limited funds. In our observational study, individual patients' preferences and reasons for not prescribing ADT could not be included because the institutional registration was insufficient. The variation has been discussed within the Dutch Society of Radiotherapy and the Dutch Society of Urology. Reasons given for nonadherence were expected nonacceptable side effects of ADT, an increased risk of cardiovascular events with ADT, and doubts on the effectivity of the combination of EBRT and ADT.

5. Conclusions

The variation in the prescription of ADT in patients with intermediate-risk PCa between institutions is substantial. This suggests that the prescription of ADT in these patients is largely dependent on different departmental policies. One of the explanations might be differences in recommendations between the Dutch and European guidelines. Nevertheless, given the firm and clear recommendations in the guidelines, adherence could be improved.

Author contributions: Barbara Lily Thérèse Rijksen had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.*Study concept and design:* Aben, Pos, Hulshof.
Acquisition of data: Vernooij, Jansen.
Analysis and interpretation of data: None.
Drafting of the manuscript: None.
Critical revision of the manuscript for important intellectual content: None.
Statistical analysis: None.
Obtaining funding: None.
Administrative, technical, or material support: None.
Supervision: van Andel, Wijsman, D.M. Somford, M.B. Busstra, R.J.A. van Moorselaar, C.A. Hulsbergen-van de Kaa, G.J.L.H. van Leenders, P. Hamberg, F. van den Berkmortel, J.J. Fütterer, L.A. Kiemeney, I.M. van Oort.
Other: None.

Financial disclosures: Barbara Lily Thérèse Rijksen certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

Acknowledgements: ProZIB is funded by the Dutch Cancer Society (KWF2013-5942). The authors thank the registration team of the Netherlands Comprehensive Cancer Organisation (IKNL) for the collection of data for the Netherlands Cancer Registry.

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