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Predicting the need for adjuvant radiation therapy according to EAU guidelines among patients with unfavorable intermediate-risk prostate after radical prostatectomy

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Keywords: D'amico risk groups, NCCN risk groups, nomogram, adjuvant radiation therapy, prostate cancer, radical prostatectomy.

Abstract

Objective:

To develop and internally validate a multivariable model for preoperatively predicting the indication for adjuvant radiation therapy after radical prostatectomy according to current guideline recommendations of the European Association of Urology (EAU) in National Comprehensive Cancer Network (NCCN) unfavorable intermediate-risk prostate cancer patients.

Methods:

Within a high-volume center database (01/2010-08/2024), we identified NCCN unfavorable intermediate-risk prostate cancer patients. Univariable logistic regression models addressed indication for adjuvant radiation therapy according to current guideline recommendations of the EAU (2026). Multivariable logistic regression models included the most informative, statistically significant preoperative predictors. Accuracy was quantified after 2000 bootstrap resamples for internal validation with Harrell's concordance index (c-index).

Results:

Of 9652 patients, 1154 (12%) had indication for adjuvant radiation therapy. Indication for adjuvant radiation therapy was associated with higher prostate volume (>45 and 25-45 cm^3), higher preoperative PSA value (continuous), suspicious clinical tumor stage (cT2), higher absolute number of positive biopsy cores and higher relative proportion of positive biopsy cores (both continuous), higher Gleason Grade Group on biopsy (GGG 3) and multiple intermediate-risk factors (3 and 2). Multivariable model c-index for the prediction of the indication for adjuvant radiation therapy was 0.709 (95% CI 0.689-0.722).

Conclusions:

In NCCN unfavorable intermediate-risk prostate cancer patients, preoperative patient and clinical tumor characteristics can be reliably used to predict the indication for adjuvant radiation therapy

after radical prostatectomy according to current EAU guideline recommendations (2026). Prior to clinical application, the present multivariable model should be externally validated.

1. Introduction

Prostate cancer is the most common malignancy among men worldwide [1]. When the disease is diagnosed at a localized stage, radical prostatectomy (RP), alongside radiation therapy, represents one of the established curative treatment options. Nonetheless, a subset of patients will require additional treatments. Adjuvant radiation therapy after RP is recommended for selected men with prostate cancer being at high risk of recurrence following RP [2–6]. Current guidelines from the European Association of Urology (EAU) recommend adjuvant radiation therapy for patients with pathological Gleason Grade Group (GGG) 4 or 5 and extraprostatic extension (pT3), with or without positive surgical margins as well as for patients with pathological lymph node invasion (pN1) [6].

Such adverse pathological features represent substantial risk factors for biochemical recurrence and disease progression [4,5]. However, the potential additional morbidity associated with adjuvant radiation therapy, such as increased genitourinary toxicities (e.g. urinary incontinence, urethral strictures, and erectile dysfunction), should be carefully weighed against its potential oncological benefits within a shared decision-making process [3]. Moreover, some patients may regret their initial decision to undergo RP if adjuvant radiation therapy is recommended postoperatively. Indeed, Shakespeare et al. reported a fourfold increase in decisional regret regarding initial treatment decision among such patients compared with those undergoing definitive radiation therapy [7].

Significant rates of tumor upstaging and GGG upgrading have been reported in patients with unfavorable intermediate-risk prostate cancer according to National Comprehensive Cancer Network (NCCN) criteria, placing this group at increased risk of requiring adjuvant radiation therapy [8,9]. Although these patients are informed preoperatively about the potential need for adjuvant therapies, accurately quantifying this risk remains challenging. Therefore, a predictive

model capable of reliably estimating the probability of adjuvant radiation therapy based solely on preoperatively known variables may be highly valuable in preoperative patient counselling.

In the present study, we quantified the risk of adjuvant radiation therapy according to current EAU guideline recommendations (2026) within a contemporary cohort of patients with unfavorable intermediate-risk prostate cancer treated with RP at a high-volume prostate-cancer center in Germany.

2. Materials and Methods

2.1 Study population

Relying on our prospectively maintained institutional tertiary-care prostate cancer database, we retrospectively identified patients with NCCN unfavorable intermediate-risk prostate cancer patients treated with RP and lymph node dissection at the high-volume tertiary-care center, namely Martini-Klinik (Hamburg, Germany), between January 2010 and August 2024 (Figure 1). All patients with clinical suspicion of metastases at the time of surgery (cM1), neoadjuvant systemic therapy (chemotherapy and/or hormonal therapy), and previous radiation therapy of the prostate (salvage prostatectomy) were excluded. Only patients with complete data regarding clinical and pathological tumor stage, lymph node stage, GGG, body mass index (BMI), prostate volume, and proportion of positive biopsy cores were included in the study cohort (Figure 1). A total of 7,634 patients were excluded due to missing data. Of these, most had pNx disease or had unknown-risk prostate cancer (Figure 1).

Data assessment was approved by local scientific committee. Approval by the local ethics committee was obtained prior to data collection. All analyzed patients gave their written informed consent for data collection and analysis. Reporting follows the precepts established by the Declaration of Helsinki.

2.2 Study endpoints and covariates

The primary endpoint of the study consisted of predicting the indication for adjuvant radiation therapy after RP according to current EAU guideline recommendations (2026) [6]. For each patient, the following preoperative covariates were recorded: age at surgery (continuous, in years), BMI (continuous, in kg/m^2), prostate volume (>45 vs. 25-45 vs. <25 cm^3), prostate-specific antigen (PSA) value (10-20 vs. <10 ng/mL), clinical tumor stage according to digital rectal examination (cT

stage: cT2 vs. cT1), number of cores sampled on biopsy (>12 vs. ≤12), number of positive cores on biopsy (<5 vs 5-9 vs 10-14 vs ≥15), proportion of positive biopsy cores (continuous, in %), highest GGG on biopsy (GGG 3 vs. 2 vs. 1), number of intermediate-risk factors (≥2 vs. 1).

2.3 Statistical analyses

First, patient, clinical, and pathological tumor characteristics were tabulated according to the presence or absence of an indication for adjuvant radiation therapy. Descriptive statistics were presented using frequencies and proportions for categorical variables and median and interquartile range (IQR) for continuous variables. Differences between groups were assessed using the Chi-square or Fisher's exact test for categorical variables and the non-parametric Wilcoxon rank-sum test for continuous variables. Second, univariable logistic regression models were used to predict the indication for adjuvant radiation therapy. The accuracy of predicting the indication for adjuvant radiation therapy for all individual variables as well as their combination was quantified using Harrell's concordance index (c-index) [10]. A stepwise regression method with comparison of c-indices of each model was used to identify the most accurate multivariable model. The predictive accuracy of multivariable models was internally validated using 2,000 bootstrap resamples [10]. Additionally, the corresponding 95% confidence intervals (CI) were estimated. Finally, to illustrate the effect of each included risk factor within the multivariable model and to estimate the individual risk of a single patient prior to RP, a nomogram was plotted.

R software environment was used for statistical computing and graphics (R version 4.3.2; R Foundation for Statistical Computing, Vienna, Austria) [11]. The statistical significance level was set at $p<0.05$.

3. Results

3.1 Patient and clinical characteristics

Overall, 9652 patients with NCCN unfavorable intermediate-risk prostate cancer were identified and deemed eligible for study inclusion (Figure 1). Median age at surgery was 65 years (IQR 59-69 years), median BMI was 26.3 kg/m^2 (IQR 24.5-28.7 kg/m^2), median prostate volume was 28 cm^3 (IQR 21-38 cm^3), and median preoperative PSA value was 7.6 ng/ml (IQR 5.4-11.0 ng/ml; Table 1). Regarding clinical tumor characteristics, most patients exhibited cT2 stage (64%) and harbored GGG 2 on biopsy (53%). Median number of positive biopsy cores was 5 (IQR 3-7) and median proportion of positive biopsy cores was 50% (IQR 33-67%). Forty-nine percent of included patients had one intermediate-risk factor, 51% two or more intermediate-risk factors.

3.2 Pathological characteristics

Among 9652 patients with NCCN unfavorable intermediate-risk prostate cancer treated with RP, 1154 (12%) had an indication for adjuvant radiation therapy (Table 2, Figure 2). Of these, 1028 patients (89%) exhibited pathological lymph node invasion (pN1), 1023 (89%) had a non-organ confined tumor stage (pT3/pT4), 262 (23%) harbored GGG 4 or 5, and 464 (40%) had positive surgical margins (R1) in the RP specimen.

3.3 Univariable and multivariable logistic regression models addressing the indication for adjuvant radiation therapy

In univariable logistic regression models predicting the indication for adjuvant radiation therapy, eight of the nine covariates were statistically significant (Table 3). These risk factors were age (odds ratio [OR] 1.02, 95% CI 1.01-1.03), higher prostate volume (>45 cm^3: OR 1.70, 95% CI 1.4-2.05; and 25-45 cm^3: OR 1.41, 95% CI 1.22-1.63), higher preoperative PSA value (OR 1.08, 95%

CI 1.06-1.09), higher clinical tumor stage (cT2: OR 2.26, 95% CI 1.96-2.63), higher number of positive biopsy cores (≥15: OR 2.37, 95% CI 1.23-4.23; 10-14: OR 2.26, 95% CI 1.84-2.76; 5-9: 1.52, 95% CI 1.32-1.74), higher proportion of positive cores on biopsy (OR 1.01, 95% CI 1.01-1.02), higher GGG on biopsy (ISUP 3: OR 2.43, 95% CI 1.72-3.54), and higher number of intermediate-risk factors (≥2: OR 1.92, 95% CI 1.69-2.18). Corresponding c-index values were 0.543, 0.549, 0.592, 0.584, 0.569, 0.581, 0.591 and 0.579, respectively (Table 3).

In multivariable logistic regression models, all included covariates were independent predictors, namely higher prostate volume (>45 cm^3: OR 1.60, 95% CI 1.31-1.96; and 25-45 cm^3: OR 1.33, 95% CI 1.15-1.54), higher preoperative PSA value (OR 1.08, 95% CI 1.06-1.10), higher clinical tumor stage (cT2: OR 1.91, 95% CI 1.63-2.24), higher number of positive biopsy cores (≥15: OR 1.63, 95% CI 0.82-3.04; 10-14: OR 1.34, 95% CI 1.03-1.72; 5-9: 1.27, 95% CI 1.08-1.484), higher proportion of positive biopsy cores (OR 1.014, 95% 1.011-1.017), higher GGG on biopsy (ISUP 3: OR 3.53, 95% CI 2.46-5.22), and higher number of intermediate-risk factors (≥2: OR 1.21, 95% CI 1.03-1.43). The c-index of predicting the indication for adjuvant radiation therapy based on preoperative patient and clinical tumor characteristics was 0.709 (95% CI 0.689-0.722) after 2000 bootstrap resamples for internal validation. The multivariable model was graphically displayed using a nomogram format in which the preoperative PSA value represented the most influential risk factor for the indication for adjuvant radiation therapy after RP (Figure 3).

4. Discussion

The estimated risk of requiring adjuvant radiation therapy following RP may influence the choice of the initial therapeutic strategy and contribute to treatment-related decisional regret among prostate cancer patients [7]. A tool capable of quantifying this risk could therefore facilitate shared decision-making and support counseling provided by urologists and radiation oncologists regarding curative treatment. In this context, our working group recently developed and externally validated the Martini-Klinik nomogram designed to predict the need for adjuvant radiation therapy after RP in accordance with current EAU guideline recommendations for high-risk prostate cancer patients and relying exclusively on clinical and patient-dependent variables available preoperatively [12,13]. In the present study, we hypothesized that patient and clinical tumor characteristics may predict the indication for adjuvant radiation therapy in NCCN unfavorable intermediate-risk prostate cancer patients. Data from 9652 NCCN unfavorable intermediate-risk prostate cancer patients treated with RP and lymph node dissection between January 2010 and August 2024 at a high-volume center were included in the present analyses. We tested this hypothesis according to standard testing criteria and made several noteworthy observations.

First, we observed that a considerable proportion of patients harbored adverse pathological features after RP. Specifically, 44% of patients exhibited extraprostatic extension (pT3-pT4), 3.2% showed an upgrading to GGG ≥4, 19% of the overall cohort had positive surgical margins and 11% had pathological positive lymph nodes. These observations highlight the pathological heterogeneity within the NCCN unfavorable intermediate-risk group and the necessity of thorough preoperative patient counseling regarding the potential need for adjuvant therapy.

The distributions of upgrading and positive surgical margin findings corroborate with previous large population-based analyses [8,9,14]. Conversely, rates of extraprostatic extension and rates of pathological lymph nodes reported within the present study are higher than those previously reported. Analyses of the National Cancer Database (NCDB) demonstrated upstaging rates

ranging from 20-33% among intermediate-risk patients treated with RP across the studied time period from 2006 to 2020 [9]. Similarly, within the Surveillance, Epidemiology, and End Results (SEER) database, Sorce et al. recorded upstaging rates to non-organ-confined disease of 33% and upgrading rates to GGG ≥4 as low as 6.6% in 7269 NCCN unfavorable intermediate-risk patients [14]. Reported rates of positive lymph nodes in the unfavorable intermediate-risk category ranged from 2.8 to 4.7% [8,14]. These differences between the currently and previously reported proportions may be attributed to differences in clinical characteristics between the study cohorts with a higher proportion of patients exhibiting cT2 disease and higher median preoperative PSA value in the present single prostate cancer center study cohort relative to the population-based cohort of Sorce et al. The differences in the rates of positive lymph nodes may be explained by the extent of pelvic lymph node dissection, and therefore, higher number of sampled lymph nodes at our institution. In addition, specialized uropathologists at our institution who perform comprehensive pathological preparation of the specimens, may contribute to the higher lymph node count observed relative to other institutions.

In consequence, 12% of patients in our cohort met the criteria for adjuvant radiation therapy according to current EAU guideline recommendations (2026). Lymph node invasion represented the most frequent pathological feature contributing to the indication for adjuvant radiation therapy in the present study cohort (89%). It is therefore not surprising that our model relies on similar parameters as the highly established predictive tools, such as the Briganti 2019 and Memorial Sloan Kettering Cancer Center (MSKCC) nomograms, which estimate the probability of pelvic lymph node invasion, seminal vesical invasion, or organ-confined disease [15–17]. This overlap supports the clinical relevance of our model inputs and facilitates comparison with existing predictive tools. However, differences in endpoints and patient cohorts warrant further validation in independent patient cohorts.

Second, we identified several preoperative patient and tumor characteristics that were associated with the indication for adjuvant radiation therapy. Specifically, in patients with the indication for adjuvant radiation therapy, median prostate size was larger (30 vs. 28 cm^3), median preoperative PSA values were higher (8.9 vs. 7.4 ng/mL), and a suspicious clinical tumor stage (cT2: 78 vs. 62%) was more common. Moreover, median number of positive biopsy cores (6 vs. 5), median proportion of positive biopsy cores (58 vs. 50%) was higher, and GGG 3 (16 vs. 9%) was more frequent in patients with indication for adjuvant radiation therapy. These differences validate the rationale of our hypotheses that patient and clinical tumor characteristics may predict the indication for adjuvant radiation therapy among unfavorable intermediate-risk prostate cancer patients.

Third, stepwise regression method with comparison of c-indices of each multivariable model was used to identify the most accurate multivariable model predicting the presence of adverse pathological features warranting adjuvant radiation therapy according to current EAU guideline recommendations (2026). The most accurate multivariable model included the following seven risk factors: prostate volume, preoperative PSA value, clinical tumor stage, number of positive biopsy cores, proportion of positive biopsy cores GGG on biopsy, and number of intermediate-risk factors. The c-index for predicting the indication for adjuvant radiation therapy of the most accurate multivariable model was 0.709 within the present study cohort of NCCN unfavorable intermediate-risk patients after 2000 bootstrap resamples for internal validation. In the present cohort that was used for multivariable model development, preoperative PSA value represents the most influential variable within the prediction model. This observation is consistent with prior evidence demonstrating that PSA correlates strongly with upstaging, upgrading and consequently a higher likelihood of indication for adjuvant radiation therapy [14]. Age at surgery was not included in the final multivariable model despite achieving statistical significance in the univariable analyses, as it only marginally improved the model's discrimination and was therefore omitted to avoid unnecessary model complexity [10]. To the best of our knowledge, we are the first to report such

multivariable model addressing the indication for adjuvant radiation therapy within a contemporary large-scale cohort of NCCN unfavorable intermediate-risk patients. Therefore, direct comparison of the present multivariable model to any other is not possible. However, taken the recently published Martini-Klinik nomogram for the prediction of the indication of adjuvant radiation therapy into account that was developed and externally validated in patients with NCCN high-risk prostate cancer, the c-index of 0.709 reported within the present study is slightly lower than the c-index of 0.761 previously reported in the NCCN high-risk cohort [12]. This difference may reflect greater heterogeneity within the cohort of unfavorable intermediate-risk prostate cancer patients. Nevertheless, the c-index of 0.709 observed in the present study surpasses the commonly accepted threshold of 0.700, which should be exceeded by a model to warrant consideration for prediction in individual patients.

Taken together, within the cohort of 9652 NCCN unfavorable intermediate-risk prostate cancer patients only a minority of 1154 patients (12%) had the indication for adjuvant radiation therapy after RP based on current EAU guideline recommendations (2026). The indication for adjuvant radiation therapy was associated with higher prostate volume, higher preoperative PSA value, suspicious clinical tumor stage in digital rectal examination, higher absolute number and higher relative proportion of positive biopsy cores, higher GGG on biopsy, and multiple intermediate-risk factors. The multivariable model developed within the current study exhibited a robust c-index value of 0.709 for predicting the indication for adjuvant radiation therapy. The current analyses demonstrate that RP alone is generally sufficient as a treatment option for patients with NCCN unfavorable intermediate-risk prostate cancer. However, a minority of patients has an indication for adjuvant therapy after RP. The newly developed multivariable model may therefore serve as a valuable tool in preoperative patient counseling and shared decision-making in NCCN unfavorable intermediate-risk prostate cancer patients, enabling the identification of patients at increased risk of adverse pathological outcome on RP specimen. Moreover, the present multivariable model may

facilitate appropriate preoperative counseling regarding this risk of multimodal treatment, including postoperative adjuvant radiation therapy. Preoperative estimation of the likelihood of adjuvant radiation therapy may improve patients' and clinicians' expectation setting and reduce decisional regret. Patients with a high predicted probability of requiring adjuvant radiation therapy after RP may consider alternative treatment strategies, whereas those with a low predicted risk may be more inclined to pursue surgical management. Together, these findings emphasize the role of preoperative risk stratification to support individualized, more informed, and patient-centered treatment decision-making.

Despite its novelty and strengths, limitations of the study should be acknowledged. First, although relying on a prospectively maintained database, the study design was retrospective. Therefore, it shares the same limitations as previous retrospective single-center studies such [18–21]. Second, a large number of patients (n=7634) were excluded due to missing data, most commonly unavailable pathological lymph node status (pNx). This observation primarily reflected the absence of pelvic lymph node dissection (PLND) that was not routinely performed in all patients. Patients without PLND were excluded, lymph node invasion represented the most frequent pathological feature contributing to the indication for adjuvant radiation therapy (89%). One has to keep in mind, that the nomogram therefore is only capable for patients undergoing PLND, which might reflect a more aggressive subgroups of NCCN unfavorable intermediate-risk prostate cancer patients. Third, multiparametric magnetic resonance imaging (mpMRI) associated variables such as number, location and degree of PIRADS lesions were not available. This limitation is shared with the recently published Martini-Klinik nomogram for the prediction of the indication for adjuvant radiation therapy in high-risk prostate cancer patients [12]. As mpMRI is currently not reimbursed for early detection of prostate cancer by German public health insurance and it was therefore available only for a minority of patients. Previous studies have demonstrated that the inclusion of mpMRI-associated variables may improve the clinical utility of predictive tools

such as the Briganti 2019 nomogram to predict lymph node involvement in prostate cancer patients [15]. Future iterations of the Martini-Klinik model should examine whether mpMRI-associated variables improve its accuracy in estimating the indication for adjuvant radiation therapy according to current EAU guideline recommendations. Additionally, emerging prediction tools incorporating prostate-specific membrane antigen positron emission tomography (PSMA-PET/CT) findings, such as the Amsterdam-Sydney-Brisbane nomogram, demonstrated predictive accuracy comparable to the Briganti 2019 nomogram, indicating that PSMA-PET/CT-derived variables may enhance future iterations of the Martini-Klinik nomogram [22,23]. Last but not least, although the present multivariable model demonstrates reliable predictive performance within our cohort, its generalizability to other patient populations and clinical settings remains uncertain. Therefore, external validation in independent cohorts is required to confirm its discrimination, calibration, and clinical utility before it can be recommended for broader use in clinical practice. Despite these limitations, the present study establishes the feasibility of a multivariable model to predict and quantify the likelihood of the indication for adjuvant radiation therapy based on preoperative patient and tumor characteristics, supporting individualized counseling and patient-centered decision making.

5. Conclusions

In patients with NCCN unfavorable intermediate-risk prostate cancer undergoing PLND, preoperative patient and clinical tumor characteristics can be reliably used to predict the indication the need for adjuvant radiation therapy after RP according to current EAU guideline recommendations (2026). The novel multivariable model demonstrates robust predictive accuracy and the enclosed nomogram enables individualized risk estimation, supporting clinicians in preoperative patient counseling. However, the present multivariable model, developed at a single institution, should be externally validated in an independent cohort to ensure its generalizability prior to broader clinical application.

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7. Tables

Table 1 Descriptive characteristics of 9652 unfavorable intermediate-risk prostate cancer patients according to the National Comprehensive Cancer Network (NCCN) treated with radical prostatectomy (RP) between 01/2010 and 08/2024.

Characteristic		Overall, n=9652	No indication for adjuvant treatment, n = 8498 (88%)[1]	Indication for adjuvant treatment, n = 1154 (12%)[1]	p-value[2]
Age at surgery (in years)		65 (59, 69)	64 (59, 69)	66 (60, 70)	**<0.001**
BMI (in kg/m^2)		26.3 (24.5, 28.7)	26.3 (24.5, 28.6)	26.3 (24.5, 28.7)	0.8
Prostate volume (in cm^3)		28 (21, 38)	28 (21, 37)	30 (23, 40)	**<0.001**
	<25	3,343 (35%)	3,027 (36%)	316 (27%)	**<0.001**
	25-45	4,972 (52%)	4,335 (51%)	637 (55%)	
	>45	1,337 (14%)	1,136 (13%)	201 (17%)	
PSA (in ng/ml)		7.6 (5.4, 11.0)	7.4 (5.3, 10.9)	8.9 (6.2, 12.8)	**<0.001**
	<10	6,434 (67%)	5,765 (68%)	669 (58%)	**<0.001**
	10-20	3,218 (33%)	2,733 (32%)	485 (42%)	
cTstage	cT1	3,521 (36%)	3,271 (38%)	250 (22%)	**<0.001**
	cT2	6,131 (64%)	5,227 (62%)	904 (78%)	
Number of positive biopsy cores		5 (3, 7)	5 (3, 7)	6 (4, 8)	**<0.001**
Proportion of positive biopsy cores (in %)		50 (33, 67)	50 (33, 67)	58 (40, 75)	**<0.001**
Gleason Grade Group on biopsy	1	456 (5%)	422 (5%)	34 (3%)	**<0.001**
	2	5,106 (53%)	4,656 (55%)	450 (39%)	
	3	4,090 (42%)	3,420 (40%)	670 (58%)	
Number of intermediate-risk factors	1	4,733 (49%)	4,328 (51%)	405 (35%)	**<0.001**
	≥2	4919 (51%)	4170 (49%)	749 (65%)	
Robotic-assisted radical prostatectomy		4,900 (51%)	4,433 (52%)	467 (40%)	**<0.001**
Nervesparing		9,091 (96%)	8,086 (97%)	1,005 (89%)	**<0.001**
Adjuvant radiation therapy		200 (2%)	96 (1%)	104 (9%)	**<0.001**

[1]Median (interquartile range); n (%); [2]Wilcoxon rank sum test; Pearson's Chi-square test; Fisher's exact test

Table 2 Pathologic characteristics of 9652 NCCN unfavorable intermediate-risk prostate cancer patients treated with radical prostatectomy (RP) between 01/2010 and 08/2024.

Characteristic	Overall, n = 9,652[1]	No indication for adjuvant treatment, n = 8498 (88%)[1]	Indication for adjuvant treatment, n = 1154 (12%)[1]	p-value[2]
pTstage				
pT2a	309 (3.2%)	304 (3.6%)	5 (0.4%)	
pT2b	13 (0.1%)	13 (0.2%)	0 (0%)	
pT2c	5,075 (53%)	4,949 (58%)	126 (11%)	
pT3a	2,849 (30%)	2,453 (29%)	396 (34%)	
pT3b	1,395 (14%)	775 (9.1%)	620 (54%)	
pT4	11 (0.1%)	4 (<0.1%)	7 (0.6%)	
pTstagegrouped				**<0.001**
pT2	5,397 (56%)	5,266 (62%)	131 (11%)	
pT3/pT4	4,255 (44%)	3,232 (38%)	1,023 (89%)	
pNstage				**<0.001**
pN0	8,624 (89%)	8,498 (100%)	126 (11%)	
pN1	1,028 (11%)	0 (0%)	1,028 (89%)	
GGGRP				
1	151 (1.6%)	151 (1.8%)	0 (0%)	
2	6,732 (70%)	6,392 (75%)	340 (29%)	
3	2,466 (26%)	1,914 (23%)	552 (48%)	
4	34 (0.4%)	13 (0.2%)	21 (1.8%)	
5	269 (2.8%)	28 (0.3%)	241 (21%)	
Rstatus				**<0.001**
R0	7,782 (81%)	7,103 (84%)	679 (59%)	
R1	1,790 (19%)	1,326 (16%)	464 (40%)	
Rx	80 (0.8%)	69 (0.8%)	11 (1.0%)	

[1] Median (IQR); n (%); [2] Wilcoxon rank sum test; Pearson's Chi-square test; Fisher's exact test.

Table 3 Univariable and multivariable logistic regression models addressing the indication of adjuvant radiation therapy after radical prostatectomy in 9652 unfavorable intermediate-risk prostate cancer patients according to the National Comprehensive Cancer Network (NCCN). For each variable, c-indices evaluate the concordance between predicted and observed indication of adjuvant radiation therapy after radical prostatectomy.

	Univariable				Multivariable*			
	OR	**95% CI**	**p-value**	**c-index**	**OR**	**95% CI**	**p-value**	**c-index**
Age at surgery (continuous)	**1.02**	1.01, 1.03	**<0.001**	0.5425	—	—		
BMI (continuous)	1.004	0.986, 1.022	0.7	0.5016	—	—		
Prostate volume (Ref. <25 cm^3)	—	—		**0.5487**	—	—		
25-45 cm^3	**1.41**	1.22, 1.63	**<0.001**		**1.33**	1.15, 1.54	**<0.001**	
>45 cm^3	**1.70**	1.40, 2.05	**<0.001**		**1.60**	1.31, 1.96	**<0.001**	
PSA (continuous)	**1.08**	1.06, 1.09	**<0.001**	**0.5917**	**1.08**	1.06, 1.10	**<0.001**	
cTstage 2 (Ref. cT1)	**2.26**	1.96, 2.63	**<0.001**	**0.5841**	**1.91**	1.63, 2.24	**<0.001**	
Number of positive biopsy cores (Ref. <5)	—	—	—		—	—	—	
5-9	**1.52**	1.32, 1.74	**<0.001**	**0.5690**	**1.27**	1.08, 1.48	**0.004**	**0.7043** **0.7087****
10-14	**2.26**	1.84, 2.76	**<0.001**		**1.34**	1.03, 1.72	**0.027**	
≥15	**2.37**	1.23,4.24	**0.006**		**1.63**	0.82, 3.04	0.143	
Proportion of positive cores in biopsy (continuous)	**1.01**	1.01, 1.02	**<0.001**	**0.5808**	**1.014**	1.011, 1.017	**<0.001**	
Gleason Grade Group on biopsy (Ref. GGG 1)	—	—		**0.5907**	—	—		
2	1.20	0.85, 1.75	0.3		1.42	0.99, 2.10	0.070	
3	**2.43**	1.72, 3.54	**<0.001**		**3.53**	2.46, 5.22	**<0.001**	
Number of intermediate-risk factors ≥2 (Ref. 1)	**1.92**	1.69, 2.18	**<0.001**	**0.5791**	**1.21**	1.03, 1.43	**0.025**	

*adjusted for prostate volume, PSA value, cTstage, number of positive biopsy cores, number of sampled biopsy cores, proportion of positive cores on biopsy, Gleason Grade Group on biopsy, number of intermediate-risk factors. **after 2000 bootstrap resamples for internal validation, 95% confidence interval 0.6890-0.7216.

Abbreviations: BMI = body mass index; CI = confidence interval; OR = odds ratio; PSA = prostate-specific antigen.

8. Figures

Figure 1 Study cohort selection

Abbreviations: BMI = body mass index; MK = Martini Klinik; PCa = prostate cancer; pN = pathologic lymph node stage at surgery; pT = pathologic tumor stage at surgery; RP = radical prostatectomy.

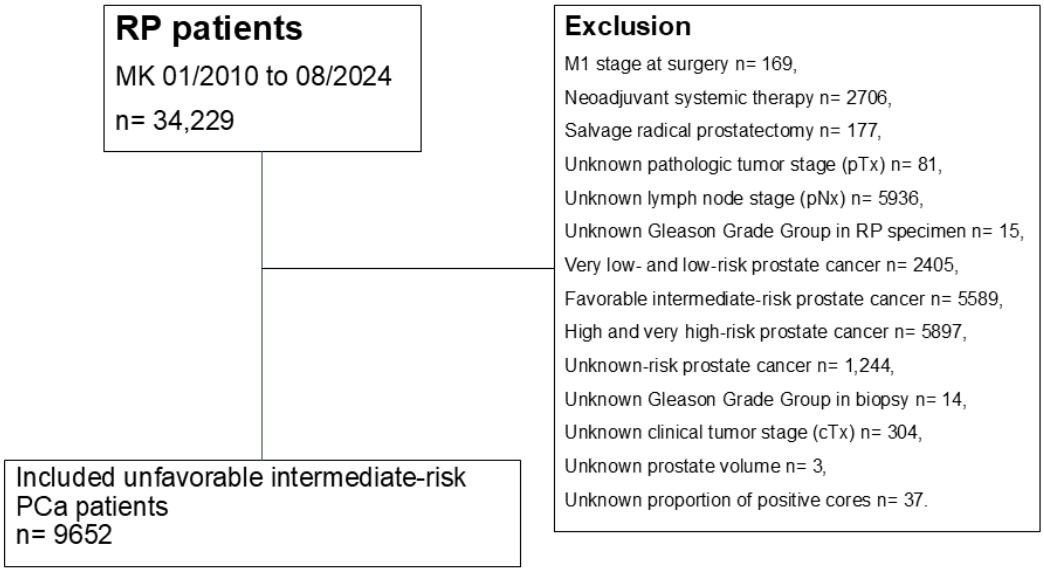


Figure 2 Heat map depicting the distribution of pathologic tumor stage (pT) and Gleason Grade Group (GGG) according to pathologic lymph node stage (pN) in radical prostatectomy specimen in 9652 unfavorable intermediate-risk prostate cancer patients treated with radical prostatectomy between 01/2010 and 08/2024. Gray overlay highlights patients with indication for adjuvant therapy after radical prostatectomy according to the current prostate cancer guidelines of the European Association of Urology (EAU 2026).

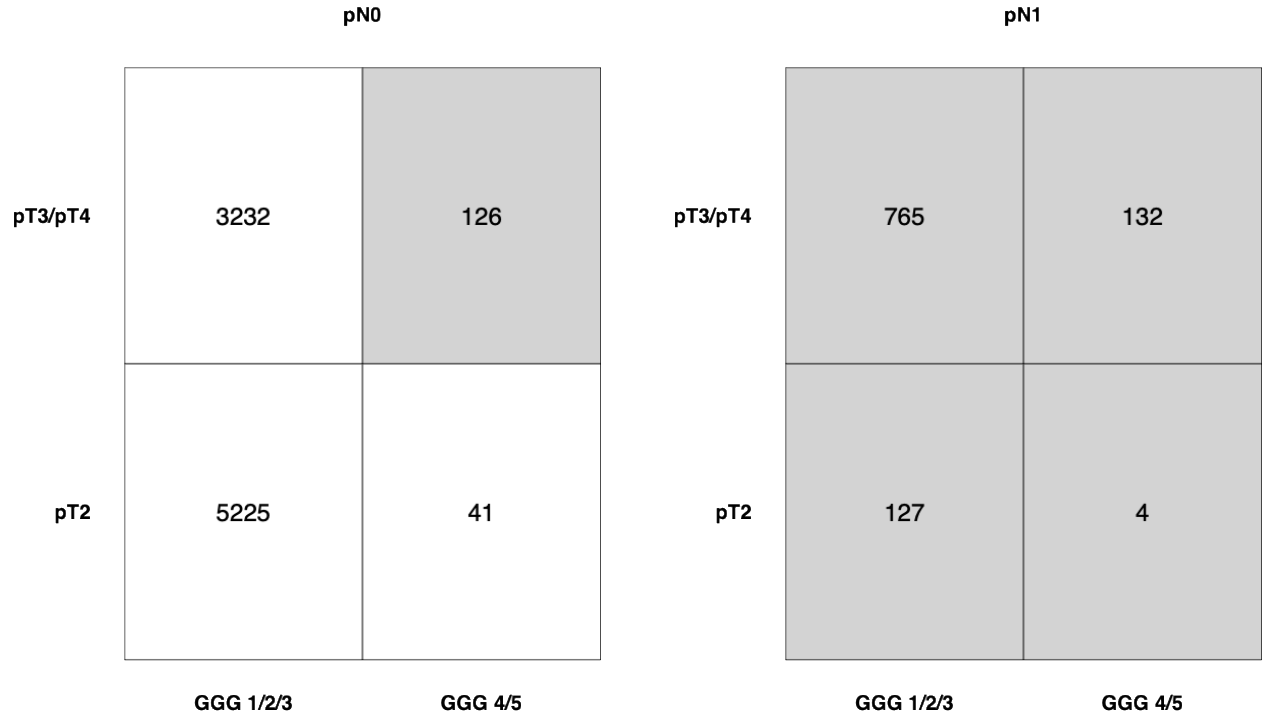


Figure 3 Nomogram addressing the indication of adjuvant radiation therapy after radical prostatectomy in 9652 NCCN unfavorable intermediate-risk prostate cancer patients.

Abbreviations: cT = clinical tumor stage; PSA = prostate-specific antigen.

