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Predicting Lymph Node Invasion in Prostate Cancer – Validating the Briganti Nomogram and Developing a Novel Machine Learning based Nomogram for UK Clinical Practice

Ranya Vardini Kumar

rvk25@cam.ac.uk

University of Cambridge

Prakrit Raj Kumar

University Hospitals Coventry and Warwickshire NHS Trust

Cristian Ilie

Norfolk and Norwich University Hospital

Amit Patel

Oxford University Hospitals NHS Trust

Vivekanandan Kumar

Norfolk and Norwich University Hospital

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Abstract

Introduction

According to EAU guidelines, the indication for extended pelvic lymph-node dissection(ePLND) at the time of radical-prostatectomy (RP) should be based on validated nomograms. The Briganti 2017(B17) nomogram is considered the most appropriate to predict lymph-node invasion (LNI) in our cohort because most patients were diagnosed via systematic biopsies. We aim to perform the first UK-based external validation of B17 and improve its accuracy using machine learning approaches through development of an updated UK-tailored Briganti Nomogram 2025 (UKB25).

Methods

From a retrospective cohort of 1551 prostate cancer patients who underwent RP, 286 had ePLND between 2010 and 2021 in a tertiary referral centre. The B17 variables - preoperative PSA; clinical stage; biopsy Gleason grade group; percentage of positive cores with highest-grade PCa; and percentage of positive cores with lower grade PCa - were analysed with univariate and multivariate logistic-regression models predicting LNI. All variables with an OR > 1 were included in the subsequent model. The UKB25 nomogram was developed using penalised logistic-regression of the Briganti variables with elastic-net-regularisation. An optimal threshold was selected to maximise accuracy without increasing false negative rate. Performance metrics were compared between UKB25 and retrospective application of the B17 nomogram.

Results

Of 286 patients, 23(8.0%) had LNI. Application of the B17 nomogram, with a 7% threshold, to our population results in 8.7% of patients below the cut-off having LNI. This is unsatisfactory as per Briganti's definition.

Instead, using a 5.8% cutoff, the refined machine-learning-based UKB25 nomogram outperforms the Briganti 2017 nomogram in classification accuracy (McNemar's test statistic $\chi 2 = 34.2$, $p < 0.001$). Importantly, UKB25 would have spared 52 patients from unnecessary ePLND (162 vs 214) with a lower rate of missed LNI (4.2%), thereby enhancing specificity (38.4% vs 18.6%) and PPV (11.9% vs 8.9%), while maintaining NPV (99% vs 96.1%), sensitivity (95.6% vs 91.3%) and area under ROC (0.785 vs 0.763).

Conclusions

Although the B17 predicts LNI reliably in other populations, its accuracy is limited in the UK. The updated UKB25 nomogram shows superior predictive performance in the UK, reducing the number of unnecessary ePLNDs by one quarter without missing additional LNI-positive patients. Further external validation is warranted.

Introduction

In prostate cancer the strongest predictor of disease progression to metastatic disease is lymph node involvement. Identification of lymph node involvement (LNI) at radical prostatectomy helps in planning adjuvant and salvage treatments to improve outcome for those patients. Prevalence of LNI varies from 1.1% to 26% in contemporary series[1]. Pelvic lymph node dissection (PLND) remains the most accurate method of staging LNI at radical prostatectomy[2] despite the availably of newer imaging techniques like MRI and PET-CT. However, its clinical application is limited by prolonged operative time, a 10–20% complication rate, and significant healthcare costs[3]. Given the heterogeneity of LNI risk, predictive models such as the Briganti 2012/2017[4] and MSKCC nomograms[5] have been developed to guide patient selection. Current European Association of Urology (EAU) guidelines recommend the use of such tools to inform the indication for PLND[6, 7].

The therapeutic value of PLND is debated. In patients with LNI-positive disease, the role of adjuvant therapy remains unclear, and recent systematic reviews suggest that effective salvage treatment after biochemical recurrence may neutralise survival differences between LNI-positive and LNI-negative cohorts[8]. These observations challenge the routine use of PLND and highlight the need to either refine patient selection or improve predictive accuracy. For example, in his own cohort, applying the Briganti 2017 nomogram at a 7% threshold would subject 66% of patients to the risks of PLND without conferring therapeutic benefit[4].

Prospective trials in the United Kingdom are currently evaluating the role of PLND in high-risk disease, although these are powered to detect only modest differences in biochemical recurrence and will require a decade to reach mature outcomes[9]. Consequently, there is a pressing need for a predictive model adapted to the UK population.

All currently EAU-recommended models suffer from the limitations associated with standard logistic regression techniques, namely their inability to capture non-linear, high-dimensional or interaction effects. This explains their poorer predictive accuracy relative to Machine Learning models for the prediction of LNI in prostate cancer patients[10]. Furthermore, their data dependence often limits their generalisability: thus, a recent systematic review confirmed the Briganti nomogram performed inferiorly in external validation cohorts compared to its original population[4, 11, 12]. Instead, Machine Learning automatically models complex interactions, accounting for the collinearity often present in medical datasets[13]. Along with k-fold cross-validation, this increases model accuracy and generalisability. However, there are no ML-based models to date, trained, even partly, on a UK population, which predict LNI.

The objectives of this study are two-fold:

1. To perform the first UK-based external validation of the Briganti nomogram.
2. To refine the Briganti model using machine learning approaches for application to the UK population.

Materials and Methods

Patient Population

Data from an existing cohort of 1551 consecutive prostate cancer patients, who underwent minimally invasive radical prostatectomy by four experienced surgeons between 2010 and 2021 in a UK tertiary referral centre, were retrospectively analysed. 286 patients underwent extended pelvic lymph node dissection (ePLND). Decision for ePLND was based on clinical judgement, incorporating pre-operative characteristics, lymph node findings on staging MRI and patient-specific data [Figure 1].

Most patients underwent MRI for local staging, with high-risk patients undergoing an abdominal contrast-enhanced CT and bone scintigraphy in addition. A prostate biopsy was obtained by either TRUS-guided systematic (pre-2017) or transperineal biopsy (post-2017).

Inclusion criteria:

1. Male aged over 18, with prostate cancer who had radical prostatectomy and extended Pelvic lymph node dissection

Exclusion criteria

1. Patients with concomitant malignancy
2. Patients with missing data for any of the predictor or outcome variables

Surgical Technique

ePLND was performed at the time of radical prostatectomy. The ePLND template consisted of excision of fibro-fatty tissue along the external iliac vein, with the distal limit at the femoral canal and the deep circumflex vein. Posteromedially, the lymphatic tissue surrounding the obturator nerve, obturator vessels and the internal iliac artery was completely removed. Laterally, all lymphatic tissue overlying the external iliac artery up to the genitofemoral nerve was cleared. Proximally, dissection was performed up to the ureteric crossing of iliac vessels.

Statistical Analysis

Comparison of descriptive statistics between LNI-positive and LNI-negative groups was performed by Mann Whitney U (continuous variables) or Chi Squared/Fisher's Exact tests (categorical variables). All statistical tests were two-tailed with a significance level of 0.05 and performed using the R statistical package V4.2.3. This study followed the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) statement[14, 15] [Appendix 1].

External Validation of the Briganti Nomogram

We retrospectively applied the Briganti 2017 nomogram – using the original reported model coefficients with the intercept - to each patient to estimate the probability of lymph node involvement (LNI) based on clinical variables. The Briganti 2017 variables, detailed below, were analysed with univariate and multivariate (MVA) logistic regression models predicting lymph node involvement (LNI), in order to determine each variable's predictive ability. All variables with an OR > 1 were included in subsequent analyses.

UKB25 Nomogram Development

The UKB25 nomogram was generated using penalised logistic regression with elastic net regularisation. The predictors included the Briganti variables:

1. Preoperative serum prostate-specific antigen (PSA) [linear continuous]
2. Clinical stage (based on digital rectal examination (DRE) and/or imaging) [categorical: T1/T2/T3]
3. Biopsy Gleason Grade Group [categorical: 1–5]
4. Percentage of positive cores with highest-grade prostate cancer [linear continuous]
5. Percentage of positive cores with lower- grade prostate cancer [linear continuous].

Interaction terms were not addressed in the prediction model. The binary outcome was presence of LNI, as determined by pathological analysis of postoperative ePLND specimens.

Elastic net regression – a classical machine learning technique - combines the advantages of both ridge ($\ell 2$) and lasso ($\ell 1$) penalties: ridge shrinkage stabilizes coefficient estimates, while the lasso component encourages sparsity and performs variable selection.

Model Training and Testing

Model training used 10-fold cross-validation, to prevent overfitting and provide more generalisable estimates of model performance. An optimal parameter set for the mixing (α) and regularization (λ) parameters was selected to maximise AUC, averaged across resamples. To ensure reproducibility, the set.seed(123) function was used to set a random seed. No fold was observed to contain zero outcome events. Thereafter, the final penalised logistic regression model was refitted on the full dataset using the tuned penalty parameters.

To facilitate clinical implementation, an online risk calculator was developed using the final model coefficients to estimate the probability of lymph node invasion [Appendix 2]. The coefficients and intercept are reported in [Appendix 3].

Discrimination ability was evaluated by plotting the receiver operating characteristic (ROC) curve and calculating the corresponding AUC from the final model's predicted probabilities. DeLong's test was used

to determine if the AUCs of the UKB25 and Briganti 2017 nomograms were significantly different. Calibration was assessed using out-of-fold predicted probabilities, with the calibration slope and intercept reported.

Threshold Optimisation

Various thresholds of the UKB25 nomogram were systematically tested for their F1 score. The optimal threshold was determined as the one which maximises the F1 score, without increasing the number of false negatives beyond that of the Briganti nomogram. To determine the clinical implications of the UKB25 and Briganti nomograms with their respective recommended thresholds, confusion matrices were drawn. McNemar's test compared the two models' classification accuracy and quantified their relative performance with an Odds Ratio.

Comparative Description of Models

In comparison to the Briganti 2017 nomogram, the UKB25 utilises:

1. A UK sample (cf. Briganti's Italian population) – to enhance applicability to the UK population.
2. Machine learning techniques, including elastic net regularisation and cross-validation (cf. simple logistic regression model of Briganti 2017) – improves model generalisability by shrinking unstable coeffficients, reducing overfitting in the setting of limited events, and selecting the optimal bias-variance trade-off based on out-of-sample performance.

Ethical Approval

The project protocol was processed through the NHS Health Research Authority, and the report stated this project is not considered 'Research'. As such, this study was exempt from an institutional review board ethical approval, which is the case with similar publications pertaining to retrospective data obtained during routine care.

No external funding was involved.

Results

Baseline Characteristics

Of 286 patients who underwent radical prostatectomy with ePLND, only 23 (8.0%) had lymph node invasion (LNI) [Table 1]. the LNI-positive population was significantly younger than the LNI-negative patients, perhaps reflective of the more rigorous disease progression in the former (61.7 vs 65.1 years; p=0.049).

LNI-positive group compared to the LNI-negative group had higher PSA of 4.7ng/ml (p=0.009). more cT3 (17.5% vs3.0% (p<0.001). Biopsy characteristics, namely number and percentage of positive cores, were significantly different between LNI-positive and LNI-negative individuals (p=0.026 and 0.030 respectively).

Following pathological examination of RP and ePLND specimens of pN1 patients, 100% were classified as T3, 95.7% had a primary Gleason grade ≥4 and 95.7% had a Gleason grade group ≥3 (vs. 63.9%, 70.3% and 73.4% of pN0 respectively; p<0.001, 0.010 and 0.036). In LNI-positive patients, a greater number of nodes were removed (p=0.033) and more were positive (p<0.001) compared to LNI-negative patients.

Patients were monitored for a mean of 4.5 years, which was equivalent in both cohorts. Post-operative and latest PSA levels were undetectable in 258 (90.2%) and 230 (80.4%) patients respectively. Whilst fewer LNI-positive patients had undetectable PSA on both occurrences compared to LNI-negative patients (p=0.006, 0.003), there was no significant difference in their survival (p=0.896). 11 deaths were reported in the cohort, of which 3 were prostate cancer specific.

External Validation of the Briganti 2017 Nomogram

The eligibility criteria, demographics, outcome and predictors were similar between our cohort and the original Briganti 2017 cohort [Table 2].

The Briganti 2017 nomogram with a 7% threshold indicates ePLND for 82.2% of our patients (n=235). Furthermore, it results in 8.7% of patients below the cut-off having LNI (n=2/23). This is unsatisfactory as per Briganti's definition (1.5% LNI rate). Thus, there is a call for a model which limits the number of unnecessary ePLNDs, without missing more patients with LNI.

Univariate and multivariate models predicting LNI

A univariate and multivariate logistic regression analysis was performed to determine which of the Briganti variables are significant predictors of LNI in our cohort [Table 3]. In the univariate analysis, preoperative PSA; cT3; and percentage of positive cores with highest-grade PCa were statistically significant predictors for the presence of lymph node metastases (p=0.004, 0.004, 0.044). A patient classified as cT3 had a nearly 7 times greater odds of LNI than a cT1 patient (OR = 6.711). Whilst the most accurate predictor of LNI was PSA level (AUC = 66.3%), no single variable predicted LNI with sufficient accuracy.

The multivariate analysis showed that all factors were associated with higher odds of LNI (OR>1); thus, all the Briganti variables were incorporated in our UKB25 model. Of these factors, preoperative PSA, clinical stage T3 and biopsy Gleason grade group ≥4 were independent predictors (p=0.003, 0.026, 0.015). Patients with a Gleason grade group of ≥4 were 10 times more likely to have LNI (OR = 10.504).

Calibration

There is no evidence of systemic miscalibration (calibration intercept 0.46, *p=0.54*) on average, but the risk distribution is compressed (calibration slope 1.20, *p<0.001*) as expected with penalised models.

Comparison of UKB25 and Briganti 2017 Nomograms

The UKB25 nomogram, with an optimal threshold of 5.8%, outperforms the Briganti 2017 nomogram in classification accuracy (McNemar's test statistic c2 = 37.0, p<0.001)[Table 4]. UKB25 showed a higher paired accuracy than Briganti 2017 (difference 0.185, 95% CI 0.133-0.241). UKB25 is 6.3 times more likely to be correct, when the two models disagree (OR = 6.3, 95% CI 3.6 - 14.4).

The specificity of the UKB25 nomogram is more than double that of the Briganti nomogram (38.4% vs 18.6%) [Table 5]. The UKB25 nomogram offers a higher positive predictive value (PPV) (11.9 vs 8.9%), with no significant difference in negative predictive value (NPV) (99.0% vs 96.1%), sensitivity (95.6% vs 91.3%) and area under the Receiver Operating Characteristic curve (AUC) (0.785 vs 0.763, p=0.778) [Figure 2].

By using the UKB25 nomogram instead of the B17 nomogram, the number of unnecessary ePLNDs would decrease from 214 to 162. Hence, 52 unnecessary ePLNDs would be avoided (24.3% decrease). Moreover, no additional patients with LNI would be missed (n=1/23 UKB25 vs n=2/23 Briganti). Missing LNI by reducing ePLNDs can have adverse consequences, which is not the case in this population. However, robust safeguards are required, including strict postoperative surveillance, predefined PSA thresholds for intervention, access to modern imaging modalities, and timely salvage interventions, to mitigate potential adverse outcomes.

Discussion

This report presents the first validation of the Briganti 2017 nomogram (B17) in a UK population[4]. Our findings show that B17 demonstrates suboptimal accuracy, with the missed lymph node involvement (LNI) rate being 8.7%. We introduce our novel UKB25 nomogram, which aims to identify groups at high risk of LNI who would benefit from extended pelvic lymph node dissection (ePLND). The model has a higher classification accuracy, reduces 52 unnecessary extended pelvic lymph node dissections (ePLNDs), and decreases rates of missed LNI when compared with the original B17 nomogram.

Several external validations of the B17 nomogram have reported variable concordance. In a French cohort[16], its application demonstrated low accuracy in the intermediate-risk group, with an AUC of 53.1%, a lymph node–positive rate of 9.5% (27/285) and missed LNI rate of 8.9%. Validation in a Polish cohort[17] produced mixed results, with a higher LNI rate of 23% (53/222). Using a 7% cut-off, the B17 nomogram missed 19% (10/53) of LNIs, compared with only 1.5% in the internal validation cohort—an outcome considered suboptimal. Nonetheless, both papers did not propose any alternative model. The variability in LNI rate and the predictive significance of clinical variables between populations necessitates population-specific models. Similar to the findings of other countries, our results confirm

poor applicability of B17 to the UK. Instead, our UKB25 nomogram is found to be a superior model for the UK population.

ePLND provides accurate staging and prognostic information. However, a recent systematic review of pelvic lymph node dissection (PLND) at radical prostatectomy concluded that it is associated with poor intra- and perioperative outcomes in 19.8% of patients, without clear therapeutic benefit. Furthermore, two randomized controlled trials failed to demonstrate any advantage of an extended approach over a limited PLND in terms of early oncologic outcomes[8]. Therefore, ePLND should be reserved for patients with the highest likelihood of benefit whilst minimising the risk of missing LNI. Our nomogram, an AI-powered model adapted to the UK population and based on the key parameters of the Briganti 2017 tool, substantially reduces the number of ePLND procedures required without increasing the risk of missed LNI (4% vs 8.7%).

Given the effectiveness of adjuvant and salvage therapies, there is increasing debate about whether ePLND should be avoided altogether at the time of radical prostatectomy. Available adjuvant options include LHRH agonists/antagonists, androgen receptor–targeted therapy, external beam radiotherapy, and stereotactic ablative radiotherapy. While these approaches may improve survival, their side-effect profiles can significantly impact quality of life and contribute to non-cancer-related mortality. By contrast, ePLND, although associated with perioperative morbidity, carries less than 5% long-term morbidity and should therefore be considered a first-line option.

Notably, we report for the first time in UK that patients with LNI have a higher rate of biochemical failure, both immediate post-operatively and at 5-year follow-up. Despite this, cancer-specific mortality was observed in none of 23 LN-positive patients, compared with 3 of 263 LN-negative patients which may be due to effective salvage therapies.

Our study has certain limitations. Whilst our events-per-variable ratio of approximately 3.3 is below traditional thresholds for unpenalized logistic regression, penalised regression with shrinkage was used to reduce overfitting. Moreover, it is comparable to other cohorts, including the original cohort of Briganti 2017[4, 16, 17]. Recent methodological work has demonstrated that acceptable predictive performance and stable coefficient estimates may be achieved at lower EPV when shrinkage methods and pre-specified predictors are employed[18].

Secondly, this is a retrospective series spanning predominantly the pre-MRI targeted era, with some cases from the early MRI-targeted era. Hence there is a suggestion that nomograms including MRI may have a better predictive accuracy. However, the Briganti 2022 (B22) nomogram[19], which included MRI data in the nomogram, demonstrated superior performance only in patients with positive MRI-targeted biopsies and, therefore, is not directly applicable to our cohort. The explanation provided for the need of B22 is that multiple positive cores from targeted biopsies may artificially inflate the estimated risk of LNI. However, in our series, the proportion of patients who underwent a targeted biopsy is smaller and, within this sub-group, the number of cores per target was also fewer, reducing the impact of this inflation. Moreover, the performance of the B17 nomogram in the non–MRI-targeted group was also

suboptimal in our UK population. Hence, there is a need for a model with greater applicability to UK population. By utilising clinical variables with biopsy characteristics alone, we improve generalisability of our model to healthcare settings across the world, where more expensive tests such as PSMA-PET and MRI are not accessible[20-22]. Furthermore, it improves cost-efficiency, thereby limiting the burden on public healthcare systems, such as the NHS.

Although novel imaging techniques such as PSMA PET-CT have shown promise, their sensitivity and specificity remain insufficient to serve as standalone guides for PLND during radical prostatectomy[23]. Current NICE guidelines in the United Kingdom do not endorse PSMA PET for primary staging, primarily due to its limited therapeutic impact and considerable cost implications. In this context, the UKB25 nomogram provides a pragmatic interim solution until more reliable imaging modalities become available.

This is a UK-specific model derived from a single centre, selection bias and era effects (limited PSMA PET and MRI-targeted biopsy) may affect transportability. Hence a future multi-centre validation is needed.

Conclusion

The Briganti 2017 nomogram sub-optimally predicts the need to perform ePLND at radical prostatectomy in the UK population. Our novel UKB25 nomogram demonstrates superior accuracy, by reducing the number of ePLNDs performed by one quarter without missing additional lymph node positive patients. We recommend further external validation before incorporation into routine clinical practice.

Declarations

Ethical Approval

The project protocol was processed through the NHS Health Research Authority, and the report stated this project is not considered ‘Research’. As such, this study was exempt from an institutional review board ethical approval, which is the case with similar publications pertaining to retrospective data obtained during routine care.

Author Contribution

Authorship Contribution FormManuscript title: A novel machine learning based nomogram to predict Lymph Node Invasion in Prostate Cancer— Updating the Briganti Nomogram for UK Clinical Practice We, the undersigned authors, certify that we have made substantial contributions to the work as outlined below, and approve the final version of the manuscript for submission.conception and design of the

work; RVK, PRK, VKThe acquisition, analysis,interpretation of data; RVK, PRK, AP, VKThe creation of new software used in the work; RVK, PRK, VKDraft the work: RVK, PRK, VKsubstantial revision: RVK, PRK, AP, CI, VKApproved the submitted version: RVK, PRK, AP, CI, VK**Funding:** : None**Conflicts of Interest:**: noneEach author meets the ICMJE authorship criteria:1. Substantial contributions to conception, design, data acquisition, analysis, or interpretation.2. Drafting or critical revision of the manuscript for important intellectual content.3. Final approval of the version to be published.4. Agreement to be accountable for all aspects of the work.Signatures:Ranya V Kumar (Author 1, 21/01/2026)Prakrit Raj Kumar (Author 2, 21/01/2026)Amit Patel(Author 3, 21/01/2026)Cristian P Ilie(Author 4, 21/01/2026)Vivekanandan Kumar (Author 5, 21/01/2026)

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Tables

Table 1: Patient descriptive characteristics (n=286)

Variable	Overall	pN0	pN1	*p value*
Patients				
[N (%)]	286	263 (92.0)	23 (8.0)	
Age [years]				*0.049**
Mean (median)	64.8 (66)	65.1 (66)	61.7 (62)	
IQR	61 - 69	61 – 69	55 - 69	
PSA level [ng/mL]				*0.009**
Mean (median)	12.4 (10.3)	12.0 (10.1)	16.7 (15.3)	
IQR	7.0 - 16.4	7.0 – 15.8	9.6 – 23.4	
Clinical stage [N (%)]				*<0.001**
T1c	199 (69.6)	189 (66.1)	10 (3.5)	
T2	75 (26.2)	66 (23.1)	9 (3.1)	
T3	12 (4.2)	8 (2.8)	4 (1.4)	
Biopsy				
Primary Gleason grade [N (%)]				*0.084*
£3	82 (28.7)	79 (30.0)	3 (1.0)	
³4	204 (71.3)	184 (70.0)	20 (7.0)	
Secondary Gleason grade [N (%)]				*0.511*
£3	79 (27.6)	74 (25.9)	5 (1.7)	
³4	207 (72.4)	189 (66.1)	18 (6.3)	
Gleason Grade Group [N (%)]				*0.199*
£2	60 (21.0)	58 (20.3)	2 (0.7)	

3	74 (25.9)	69 (24.1)	5 (1.7)	
³4	152 (53.1)	136 (47.6)	16 (5.6)	
No. of total cores				*0.912*
Mean (median)	19.7 (19)	19.6 (19)	20.2 (15)	
IQR	12 - 27	12 – 26	11 - 28	
No. of positive cores				*0.026**
Mean (median)	7.5 (7)	7.3 (6)	9.2 (8)	
IQR	4 - 10	4 - 10	6 - 11	
Percentage of positive cores [%]				*0.030**
Mean (median)	43.4 (38.1)	42.3 (37.5)	56.3 (50.0)	
IQR	25.0 - 56.4	25.0 – 54.6	32.1 – 87.5	
Percentage of positive cores with highest-grade PCa [%]				*0.236*
Mean (median)	32.7 (25.9)	31.8 (25.0)	42.8 (37.5)	
IQR	14.2 - 45.5	14.3 – 42.9	11.1 – 58.3	
Percentage of positive cores with lower-grade PCa [%]				*0.469*
Mean (median)	10.6 (0.0)	10.3 (0.0)	13.5 (8.3)	
IQR	0.0 - 17.7	0.0 – 16.7	0.0 – 22.5	
Clinical Risk Classification [N (%)]				*0.215*
Low	1 (0.3)	1 (0.3)	0 (0.0)	
Intermediate	96 (33.6)	92 (32.2)	4 (1.4)	
High	189 (66.1)	170 (59.4)	19 (6.6)	
Radical Prostatectomy				

Pathological stage [N (%)]				*<0.001**
T2	94 (32.9)	94 (32.9)	0 (0)	
T3a	138 (48.3)	124 (43.4)	14 (4.9)	
T3b	53 (18.5)	44 (15.4)	9 (3.1)	
N/A	1 (0.3)	1 (0.3)	0 (0)	
Pathological Primary Gleason grade [N (%)]				*0.010**
£3	78 (27.3)	77 (26.9)	1 (0.3)	
³4	207 (72.4)	185 (64.7)	22 (7.7)	
N/A	1 (0.3)	1 (0.3)	0 (0.0)	
Pathological Secondary Gleason grade [N (%)]				*0.743*
£3	70 (24.5)	65 (22.7)	5 (1.7)	
³4	215 (75.2)	197 (68.9)	18 (6.3)	
N/A	1 (0.3)	1 (0.3)	0 (0.0)	
Pathological Gleason Grade Group [N (%)]				*0.036**
£2	70 (24.5)	69 (24.1)	1 (0.3)	
3	68 (23.8)	63 (22.0)	5 (1.7)	
³4	147 (51.4)	130 (45.5)	17 (5.9)	
N/A	1 (0.3)	1 (0.3)	0 (0.0)	
Extended Pelvic Lymph Node Dissection				
No. of removed and examined lymph nodes				*0.033**
Mean (median)	11.1 (10)	10.9 (10)	13.8 (12)	
IQR	7 - 14	7 – 14	9 – 16	
No. of positive lymph nodes in patients with LNI				*<0.001**

Mean (median)	0.2 (0)	0.0 (0)	1.8 (2)	
IQR	0 - 0	0 – 0	1 – 2	
Follow-up				
Duration [years] – Mean (median)	4.5 (4.4)	4.5 (4.5)	4.1 (4.0)	*0.294*
Post-operative PSA undetectable [N (%)]	258 (90.2)	241 (84.3)	17 (5.9)	*0.006**
Latest PSA undetectable [N (%)]	230 (80.4)	217 (75.9)	13 (4.5)	*0.003**
Deaths [N (%)]	11 (3.8)	10 (3.5)	1 (0.3)	*0.896*
Prostate Cancer-specific Deaths [N (%)]	3 (1.0)	3 (1.0)	0 (0.0)	*0.521*

** Indicates a* **statistically** *significant difference between pN0 and pN1 (p<0.05)*

Table 2: Comparative baseline data between UKB25 and B17 nomograms

Variable	Kumar, 2026	Briganti, 2017
Age [years]		
Median	66	65
IQR	61 - 69	60 - 70
PSA level [ng/mL]		
Median	10.3	6.2
IQR	7.0 - 16.4	4.6 - 8.3
Clinical stage [N (%)]		
T1c	69.6	55.0
T2	26.2	39.0
T3	4.2	6.2
Biopsy		
Gleason Grade Group [N (%)]		
£2	21.0	74.6
3	25.9	14.0
³4	53.1	11.7
Percentage of positive cores with highest-grade PCa [%]		
Median	25.9	29.4
IQR	14.2 - 45.5	14.3 – 50.0
Percentage of positive cores with lower-grade PCa [%]		
Median	0.0	27.7
IQR	0.0 - 17.7	16.6 – 41.6
Lymph Node Invasion		
Positive	8.0	11.6
Negative	92.0	88.4

Table 3: Therapeutic implications and performance characteristics of the UKB25 and Briganti 2017 nomograms

		UKB25	Briganti 2017	Comparison (UKB25 – Briganti)
Nomogram calculated probability of LNI (threshold) [%]		5.8	7	-
Patients in whom PLND is not recommended (below threshold) [N (%)]	Total	102 (35.7)	51 (17.8)	+ 51
	LN0	101 (35.3)	49 (17.1)	+ 52
	LN1a	**1 (0.3)**	**2 (0.7)**	**- 1**
Patients in whom PLND is recommended (above threshold) [N (%)]	Total	184 (64.3)	235 (82.2)	- 51
	LN0b	**162 (56.6)**	**214 (74.8)**	**- 52**
	LN1	22 (7.7)	21 (7.3)	+ 1
NPV [%, 95% CI]		99.0 (96.8 – 100.0)	96.1 (90.2 – 100.0)	+ 3.0 (0.0 – 7.7)
PPV [%, 95% CI]		11.9 (7.5 -16.9)	8.9 (5.5 – 12.7)	+ 3.0 (1.6 – 4.8) *
Sensitivity [%, 95% CI]		95.6 (85.0 - 100.0)	91.3 (78.3 – 100.0)	+ 4.4 (0.0 – 15.0)
Specificity [%, 95% CI]		38.4 (33.0 – 44.2)	18.6 (14.0 – 23.4)	+ 19.8 (14.0 – 25.6) *
AUROC [%, 95% CI]		78.5 (68.7 – 88.3)	76.3 (64.6 – 88.0)	+ 2.2

PLND: Pelvic Lymph Node Dissection; LN0: Patients without histologically confirmed Lymph Node Invasion; LN1: Patients with histologically confirmed Lymph Node Invasion; NPV: Negative Predictive Value; PPV: Positive Predictive Value; a: Number of potentially missed patients with LNI; b: Number of avoidable PLNDs

* Indicates a statistically significant difference between the two models. If the 95% CI of the difference did not include 0, the difference in the corresponding metric was considered statistically significant.

Table 4: McNemar's Chi-Square Test Disagreements
McNemar's test statistic c2 = 34.2, p<0.001

		Briganti 2017 Nomogram Prediction		
		Incorrect	Correct	Total
UKB25 Nomogram Prediction	Incorrect	153	10	163
	Correct	63	60	123
	Total	216	70	286

Table 5: Univariate and multivariate logistic regression analyses predicting LNI from preoperative variables

Covariates	Univariate Analysis			Multivariable Analysis	
	OR (95% CI)	p value	AUC [%] (95% CI)	OR (95% CI)	p value
Preoperative PSA [ng/mL]	1.077 (1.024-1.134)	0.004**	0.663 (0.530-0.796)	1.095 (1.030-1.163)	0.0032**
Clinical Stage					
T2 vs T1	1.919 (0.768-4.583)	0.148	0.570 (0.465-0.675)	2.188 (0.778-6.051)	0.12964
T3 vs T1	6.711 (1.671-23.455)	0.004**	0.572 (0.492-0.652)	7.041 (1.151-41.719)	0.0304*
Biopsy Gleason Grade Group					
3 vs £2	0.781 (0.250-2.043)	0.638	0.522(0.432-0.613)	2.479 (0.434-20.883)	0.3371
³4 vs £2	2.134 (0.880-5.709)	0.106	0.589 (0.488-0.690)	10.504 (2.113-92.395)	0.0117*
Percentage of positive cores with highest-grade PCa	1.016 (1.000-1.031)	0.044**	0.575 (0.427-0.722)	1.015 (0.996-1.033)	0.1087
Percentage of positive cores with lower grade PCa	1.011 (0.985-1.033)	0.356	0.542 (0.418-0.666)	1.001 (0.996-1.033)	0.9445

OR = Odds Ratio; CI = Confidence Interval; AUC = Area under the Receiver Operating Characteristic curve *p<0.05; **p<0.01

Figures

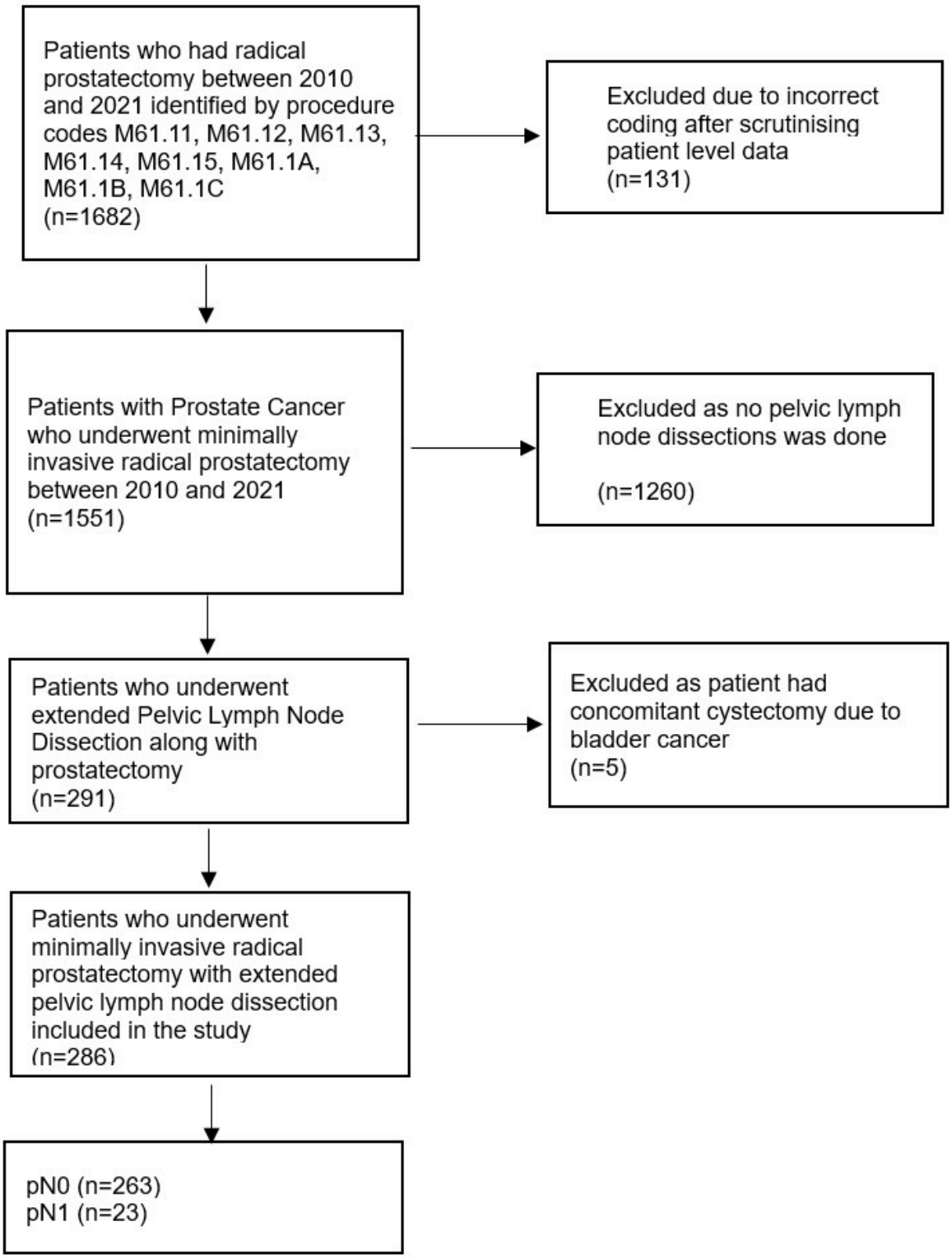


Figure 1

Patient inclusion flow chart

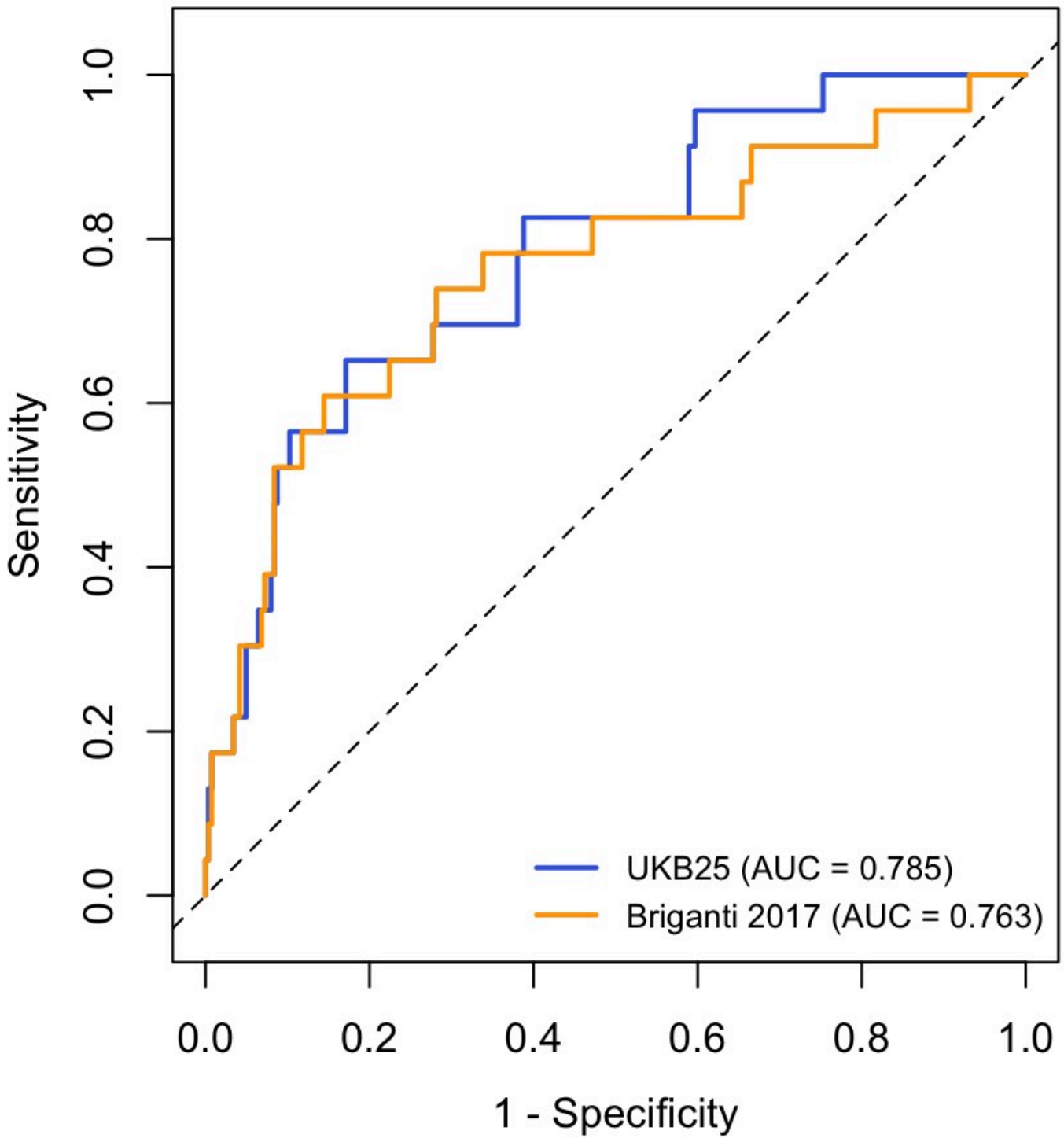


Figure 2

Receiver Operating Characteristic (ROC) curves of our novel UKB25 and the Briganti 2017 nomograms. AUC = Area under the ROC

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Appendices.docx
- Additionaldocument1UKB25calculator.xlsx