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Optimizing the risk threshold of lymph node involvement for performing extended pelvic lymph node dissection in prostate cancer patients: a cost-effectiveness analysis

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Abstract

Background: Extended pelvic lymph node dissection (ePLND) may be omitted in prostate cancer (CaP) patients with a low predicted risk of lymph node involvement (LNI). The aim of the current study was to quantify the cost-effectiveness of using different risk thresholds for predicted LNI in CaP patients to inform decision making on omitting ePLND.

Methods: Five different thresholds (2%, 5%, 10%, 20%, and 100%) used in practice for performing ePLND were compared using a decision analytic cohort model with the 100% threshold (i.e., no ePLND) as reference. Compared outcomes consisted of quality-adjusted life years (QALYs) and costs. Baseline characteristics for the hypothetical cohort were based on an actual Dutch patient cohort containing 925 patients who underwent ePLND with risks of LNI predicted by the Memorial Sloan Kettering Cancer Center web-calculator. The best strategy was selected based on the incremental cost effectiveness ratio when applying a willingness to pay (WTP) threshold of €20,000 per QALY gained. Probabilistic sensitivity analysis was performed with Monte Carlo simulation to assess the robustness of the results.

Results: Costs and health outcomes were lowest (€4,858 and 6.04 QALYs) for the 100% threshold, and highest (€10,939 and 6.21 QALYs) for the 2% threshold, respectively. The incremental cost effectiveness ratio for the 2%, 5%, 10%, and 20% threshold compared with the first threshold above (i.e., 5%, 10%, 20%, and 100%) were €189,222/QALY, €130,689/QALY, €51,920/QALY, and €23,187/QALY respectively. Applying a WTP threshold of €20.000 the probabilities for the 2%, 5%, 10%, 20%, and 100% threshold strategies being cost-effective were 0.0%, 0.3%, 4.9%, 30.3%, and 64.5% respectively.

Conclusion: Applying a WTP threshold of €20.000, completely omitting ePLND in CaP patients is cost-effective compared to other risk-based strategies. However, applying a 20% threshold for probable LNI to the Briganti 2012 nomogram or the Memorial Sloan Kettering Cancer Center web-calculator, may be a feasible alternative, in particular when higher WTP values are considered.

Introduction

Extended Pelvic lymph node dissection (ePLND) in patients with prostate carcinoma (PCa) is still the most accurate staging method for lymph node involvement (LNI) [1,2]. However, the value of ePLND in the treatment of pelvic lymph node metastasis is an ongoing topic of debate for

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several years [3]. A recent systematic review suggested that there is no evidence for any beneficial therapeutic effect of the procedure [4]. Still, prospective randomized trials on the potential benefit of ePLND on PCa outcomes are lacking. Therefore, omitting ePLND in PCa patients with low predicted risk of LNI, that is, below a certain risk threshold based on prediction models, may be advised. Applying such a risk threshold can prevent unnecessary complications in node negative patients, and reduce health care expenditure [5]. The ePLND is generally performed as part of a radical prostatectomy (RP), or is performed as a standalone procedure prior to radiotherapy. Having 1 or more positive lymph nodes worsens the prognosis of the disease [6]. Selecting those patients expected to benefit most from ePLND is the crux regarding its controversy, and the key to its efficient and beneficial use.

Several tools have been developed to predict the risk of LNI in PCa patients, supporting urologists in the decision to perform or omit ePLND. Predictions are made based on prostate specific antigen, primary and secondary Gleason scores, clinical T-stage, and either percentage of positive biopsy cores or amount of positive and negative biopsy cores taken [7−9]. Several guidelines recommend to base the decision to perform ePLND on the predicted risk of LNI. However, these guidelines recommend usage of different prediction tools: either the Briganti nomogram, Memorial Sloan Kettering Cancer Center (MSKCC) nomogram, Partin Tables or the Roach formula [7−10]. These 4 tools predict a different risk for the same patient, and consequently their recommended risk threshold to perform ePLND also varies between 2% (National Comprehensive Cancer Network guideline), 5% (European Association of Urology (EAU) guideline), and 10% (Dutch guideline) risk of LNI. As a result, it remains difficult for urologists to assess whether a patient might benefit from ePLND or not. This may result in differences in patient management across hospitals and urological practices, and thus differences in both quality and costs of care [11].

Although the recommended risk thresholds for the 4 prediction models are different, they are all derived based on a (perceived) optimal balance between the chance of false positive and of false negative classifications of patients. However, such thresholds do not account for the consequences of such false positive and of false negative classifications, based on subsequent patient management decisions, in terms of health outcomes and health care costs. In a cost-effectiveness analysis the optimal risk threshold for ePLND can be derived accounting for all relevant health and economic aspects.

A recent validation study assessed a total of 16 tools on their performance at predicting LNI in Dutch PCa patients [12]. The validation study demonstrated that the Briganti 2012 nomogram and the MSKCC web-calculator were best at predicting LNI. Currently, the cost-effectiveness of using different risk thresholds for ePLND is unknown. Therefore, the purpose of this study is to apply a cost-effectiveness analysis to identify the best risk threshold for the MSKCC web-calculator and the Briganti 2012 nomogram, from a set of 5 realistic threshold values, to inform decision making on performing ePLND in a Dutch healthcare context. The cost-effectiveness analysis of the MSKCC web-calculator is shown in the paper. The analysis of the Briganti 2012 nomogram is displayed in supplemental data S3 (scenario 2).

Methods

Target population

The proportion of patients with and without pathohistologically proven LNI above and below different risk thresholds applied in practice (e.g., 2%, 5%, 10%, and 20%) were derived from the recently performed validation study by Hueting et al. [12] and used as input in the decision analytic model. The derived proportions for the MSKCC web-calculator are displayed in Table 1. The population used for the validation study consisted of 1,001 Dutch PCa patients of which 925 were eligible for validating the MSKCC web-calculator. The number of patients with confirmed LNI that would have been missed when applying a 2%, 5%, 10%, 20% or 100% risk threshold to perform ePLND were 1 (0.1%), 12 (1.3%), 27 (2.9%), 72 (7.8%), and 276 (29.8%), respectively. On the other hand, unnecessary ePLND could have been spared in patients with confirmation of having no

Table 1
Model input per threshold based on a validation study of 925 Dutch patients in the MSKCC web-calculator

Threshold	Proportion of Patients With Predicted LNI Risk Exceeding the Threshold	Proportions of Patients With Predicted LNI Risk Below the Threshold	Proportion of Patients With Positive LNI Below Threshold[a]	Proportion of Patients With Positive LNI Above Threshold[a]
2%	0.96	0.04	0.001	0.30
5%	0.84	0.162	0.01	0.29
10%	0.66	0.345	0.03	0.27
20%	0.37	0.635	0.08	0.21
100%	0	1	0.30	0

Uncertainty for each probability was assessed using beta distribution.

[a] In the decision tree, for all five options, there are two branches. The branch not showing in this table is the complement of the shown probability for that branch.

LNI. Applying a 2%, 5%, 10%, 20%, or 100% risk threshold resulted in the safe omission of ePLND in 53 (5.7%), 177 (19.1%), 311 (33.6), 458 (49.5%), and 649 (70.2%) patients, respectively. The applied ePLND template included removal of the nodes overlying the internal and external iliac artery, nodes located within the obturator fossa, and optionally within the common iliac artery and presacral areas.

Model development

A decision tree was constructed to evaluate the cost-effectiveness of different risk thresholds for performing ePLND (Fig. 1). The development of the tree was based on published clinical guidelines [1,2,13]. Five strategies were compared; applying a 2%, 5%, 10%, 20%, and a 100% threshold to the predicted risk of LNI to guide application of ePLND. The 100% threshold represents the strategy in which no ePLND is performed in any patient (i.e., all patients will have a risk of LNI less than 100%) and was used as a reference strategy in the analysis. All patients in the decision tree underwent RP and based on their characteristics and predicted risk, and the selected risk threshold, they did or did not receive ePLND. The patients who received ePLND could experience complications from the procedure. Patients with histopathologically proven LNI received either observation, Adjuvant hormonal deprivation therapy (ADT) or a combination of ADT and adjuvant radiotherapy (ART) as indicated in the EAU guideline [1].

Probabilities of ePLND related complications, adjuvant treatment, quality of life values (utilities) for the health outcomes following with or without concomitant ePLND, and costs were derived from available literature. An overview of the probabilities, utilities, and costs used in the analysis, with respective evidence sources, is shown in Tables 1 and 2.

In the decision analytic model, patients receiving either ADT or a combination of ADT+ART when having proven LNI have a survival benefit compared to patients who do not receive adjuvant treatment. However, there is a lack of substantial evidence for any treatment benefit in patients receiving ePLND compared to patients who did not receive ePLND. For this reason, we also analyzed a scenario in which the 10-year survival outcomes are similar for patients with positive LNI regardless of whether ePLND was performed. This scenario analysis was added in the supplementary data S3 (Scenarios 3 & 4). Due to lack of evidence, several assumptions were necessary to develop the decision analytic model. The assumptions made were outlined in supplementary data S4.

Outcomes

The strategies were compared in terms of health outcomes (Quality-Adjusted Life Years [QALYs]) and costs. One QALY equals 1 year in perfect health [14]. In the model, each strategy results in one of the end nodes, representing the consequences of (not) performing ePLND, experiencing complications, and receiving subsequent treatment. Expected health outcomes in QALYs were calculated using post RP survival data from available literature and is added as supplementary data S1 [6,15−19]. Survival outcomes were reported as progression free survival, biochemical recurrence, metastasized disease, and overall mortality. Reported outcomes were different between patients with and without LNI, and different in patients with LNI who received adjuvant treatment compared to patients with LNI who did not receive without adjuvant treatment. QALYs were calculated by multiplying the probability of these outcomes by its corresponding utility value and summing these values over the total time span of 10 years following RP. As available survival data from published papers were mostly limited to 10 year survival rates, a 10 year time horizon was applied to avoid data extrapolation. QALYs were discounted with 1.5% and costs with 4.0% each year according to the Dutch guideline to perform Health Economic evaluations [20]. The derived health outcomes and an example of the calculation of QALYs are presented in the supplementary data S1. In the calculation of QALYs

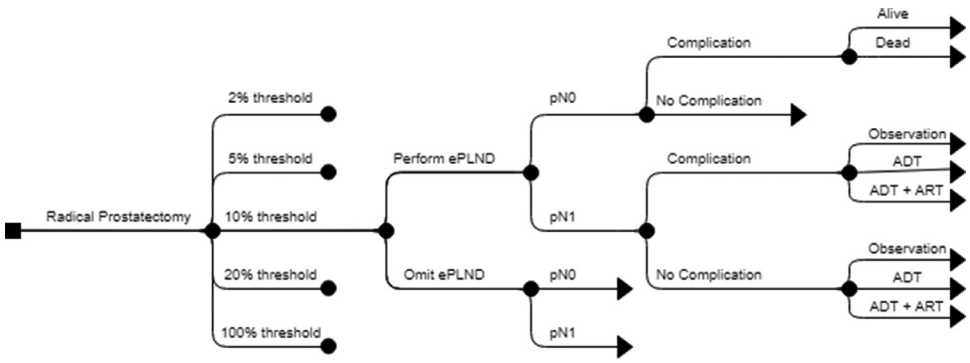

Fig. 1. Decision analytic model. The branches seen after 10% threshold are the same after each probability node next to the 2, 5, 20 and 100% thresholds with different inputs for performing and omitting ePLND. Complication in the tree exists of an initial probability of lymphoceles, deep venous thrombosis and pulmonary embolism with an enhanced probability of deep venous thrombosis and pulmonary embolism once lymphoceles occurred as displayed in the supplementary data. The 100% threshold regards the scenario in which no ePLND would be performed. Abbreviations: ADT = Adjuvant Hormonal Therapy, ART = Adjuvant Radiotherapy, LNI = Lymph Node Involvement, ePLND = Pelvic Lymph Node Dissection, RP = Radical Prostatectomy

Table 2
Input parameters of the model

Parameter	Mean	SD	Distribution	Source:
Utilities				
Biochemical recurrence	0.67	0.24	Beta	21
Metastatic disease	0.25	0.11	Beta	21
Orchiectomy	0.87	0.16	Beta	21
Hormonal injection	0.83	0.19	Beta	21
Adjuvant Radiotherapy[a]	0.73	0.3	Beta	21
Radiotherapy post 1st year[b]	Disutility -0.11		N.A.	23
DVT	0.84	0.09	Beta	27
PE	0.63	0.13	Beta	27
Age specific 60−69 years	0.84	0.18	Beta	24
Age specific 70−79 years	0.85	0.15	Beta	24
Probabilities				
Lymphocele	0.067	0.01	Beta	5
DVT[c]	0.019	0.004	Beta	5,28
PE[c]	0.015	0.006	Beta	5,28
Lymphocele & DVT[c]	0.082	0.032	Beta	5
Lymphocele & PE	0.028	0.019	Beta	5
DVT death	0.021	0.002	Beta	29
PE death	0.020	0.002	Beta	29
Observation	0.28	0.012	Beta	16
Adjuvant hormonal therapy	0.49	0.013	Beta	16
Adjuvant radiotherapy	0.23	0.011	Beta	16
Costs (€)				
PLND	5912	1066	Gamma	30
Orchiectomy	4342	269	Gamma	18
Hormonal injection	633	51	Gamma	30
Adjuvant radiotherapy	2133	166	Gamma	18
Yearly management of biochemical recurrent disease	1992	490	Gamma	31
Yearly management of metastasized disease	2394	611	Gamma	31
DVT	1187	259	Gamma	27
PE	4221	922	Gamma	27

Model input parameters.
Abbreviations: DVT: Deep venous thrombosis, ePLND: pelvic lymph node dissection, PE: Pulmonary embolism.
[a] Utility values for radical prostatectomy and adjuvant radiotherapy only accounted for the first year following treatment.
[b] Utility values accounted for the second year following treatment.
[c] Utility values for DVT and PE accounted for the first 18 months following treatment.

expected over a 10-year period, health outcomes were allowed to change over time. For instance it was found that the health state utility of RP was 0.67 for the first year following treatment, and increased to 0.90 for the second year following treatment [21,22].Comparable utilities were found for ART of which the utility value for the first year following treatment was 0.73 [21], and 0.89 for the second year [23]. Disease burden for thromboembolic events was taken into account in patients experiencing this complication for the first 18 months following treatment, by then, either the patient died from the event or would be completely cured. According to Versteegh et al. [24] the age specific utility of healthy individuals aged 60−69 years in the Netherlands is 0.84, and 0.85 for patients aged 70−79. These utilities were used as a ceiling value so that patients with PCa could not have a higher utility value than the average utility observed in healthy individuals of the same age.

The mean costs and corresponding standard errors of ePLND, ART & ADT were derived from pricelists (passantenprijslijsten) published by Dutch hospitals [30]. Annual management costs of biochemical recurrent disease and metastasized disease originate from a U.S. population described in 2012 and were converted from Dollars to Euros (conversion rate 1 USD = 0.765 Euro per December 2012) and adjusted to 2019 using the Dutch consumer price indices.

The 5 strategies were compared, amongst each other, using the incremental cost effectiveness ratio (ICER) in which the difference in mean costs is divided by the difference in mean QALYs achieved.

Analysis

To reflect uncertainty in the evidence used in the model all parameters were described with parametric distributions. Beta distributions were used for all utilities and probabilities. Gamma distributions were used for costs. Uncertainty in outcomes was then assessed by performing a probabilistic sensitivity analysis generating 5,000 samples. Results were visualized in the incremental cost-effectiveness plane using the 100% risk threshold strategy as a reference. ICERs were assessed by decreasing the threshold step-by-step to assess the additional costs of improving health outcomes by performing more and more ePLND procedures (20% vs. 100%, 10% vs. 20%, 5% vs. 10%, and 2% vs. 5%). The probabilities of strategies being cost-effective were visualized in a cost-effectiveness acceptability curve (CEAC). For decision making, a willingness to pay (WTP) of €20,000/QALY was applied, which is the lower bound of the WTP range applied in the Netherlands as advised by the national healthcare institute [25]. To inform decision makers from other countries with different WTP thresholds, a CEAC was displayed with thresholds ranging between €0/QALY and €100,000/QALY. The costs used in the analyses were derived from a health care perspective, using only direct and indirect medical costs. All analyses were performed using Microsoft Excel 2016.

Results

The decision analytic model is displayed in Fig. 1. The branches behind the first probability node (i.e., 5%

Table 3
Calculated Outcomes after 10 years following treatment

Health States	Average Calculated QALYs	Average Calculated Costs
Positive LNI without AT without ePLND	5.04	€ 8,640
Positive LNI without AT with ePLND	5.03	€ 14,653
Positive LNI with ADT[a]	5.85	€ 16,192
Positive LNI with ADT and ART[a]	5.77	€ 17,798
Negative LNI without ePLND	6.49	€ 3,823
Negative LNI with ePLND	6.48	€ 9,836

Calculated QALYs and Costs used for the outcomes in the decision tree. Calculations were added as supplementary data. Note: Costs can increase and QALYs can decrease based on the probability of DVT or PE occurring, these probabilities differ per threshold caused by different input probabilities.

Abbreviations: ADT = Adjuvant hormonal therapy, ART = Adjuvant radiotherapy, AT = Adjuvant therapy, LNI = Lymph node involvement, ePLND = Pelvic lymph node dissection, QALY = Quality adjusted life year.

[a] PLND included

threshold) were defined identical for all risk thresholds, but not shown to improve visual clarity. Complications in the decision tree consist of lymphoceles (mean incidence: 6.7% ± 1.0%), DVT (1.9% ± 0.4%), and PE (1.5% ± 0.6%), with an increased probability of DVT (8.2% ± 3.2%) and PE (2.8% ± 1.9%) once lymphoceles occurred. Estimated outcomes in the model are displayed in Table 3, showing that the mean QALYs range from 5.0 to 6.8, and the mean costs range from €3,823 to €17.697. Differences in outcomes are caused by LNI and treatment received (ePLND, ADT, and ART), see supplementary data S1 for calculation. For all 5 strategies analyzed, utilities and costs assigned to health outcomes were identical, however, the probabilities of receiving ePLND, and proportion of patients with LNI receiving ePLND was different between strategies. The cost of management of biochemical recurrent and metastasized disease, and ADT injections were the only costs induced annually. Costs for these outcomes were multiplied by the probability of the outcome for each year and summed over 10 years. The treating physician has fewer options to personalize further treatment options in patients who did not receive ePLND, causing an increased risk of disease progression (i.e., biochemical recurrence, metastasized disease, and death) in patients with undetected LNI. In the supplementary data, costs have been converted to US Dollars to calculate the results.

Fig. 2 displays the results of the probabilistic sensitivity analysis for all 5 strategies. Displayed are incremental QALYs and incremental costs for the 2%, 5%, 10%, and 20% risk thresholds compared to the 100% risk threshold (reference). The majority of simulated samples are found in the northeast quadrant meaning that both costs and QALYs are higher for the 2%, 5%, 10%, and 20% thresholds compared to the 100% risk threshold.

The CEAC shows the probabilities of the 5 analyzed strategies being cost-effective for WTP thresholds between €0/QALY and €100,000/QALY (Fig. 3). The CEAC shows that the 100% strategy has the highest probability of being cost-effective when applying a €20,000/QALY WTP threshold. Probabilities for the 2%, 5%, 10%, 20%, and 100% strategies being cost-effective at this WTP threshold were 0.0%, 0.3%, 4.9%, 30.3%, and 64.5%, respectively.

The results of the analysis performed on the Briganti 2012 nomogram instead of the MSKCC web-calculator are presented in supplementary data S3: Scenario 2. The alternative scenario in which patients with confirmed LNI did not have any treatment benefit over patients with unidentified LNI are displayed in supplementary data S3: Scenario 3 and 4. The alternative scenario shows that the 100% threshold strategy is dominant over the other strategy thresholds.

Discussion

The purpose of this study was to identify the best threshold value for the Briganti 2012 nomogram and MSKCC web-calculator, from a set of 5 realistic threshold values, to perform or omit ePLND in prostate cancer patients using a cost-effectiveness analysis. When the risk threshold decreases from 100% to 2% health outcomes consistently improve and costs consistently increase. Applying a WTP of €20,000/QALY gained, decreasing the risk threshold from 100% to lower values would not be cost-effective, that is, would result in too limited health benefits to

Table 4
Results decision tree

Threshold	Average QALYs After 10 Years	Average Costs After 10 Years		ICER[a]	QALY Differences[a]	Cost Differences[a]
100%	6.05	€4,867				
20%	6.17	€ 7,357	20% vs. 100%:	€ 20,631	0.12	€ 2,490
10%	6.20	€ 9,178	10% vs. 20%:	€ 60,607	0.03	€ 1,821
5%	6.21	€ 10,300	5% vs. 10%:	€ 116,960	0.01	€ 1,122
2%	6.21	€ 11,050	2% vs. 5%:	€ 682,469	0	€ 750

Results of the five thresholds analyzed in the decision tree using a time horizon of 10 years. ICERS were calculated from top to bottom, displaying the ICER of each step taken. The 100% threshold regards the scenario in which no ePLND would be performed.

Abbreviations: ICER = Incremental cost-effectiveness ratio, QALY = Quality adjusted life years.

[a] Compared with the row above.

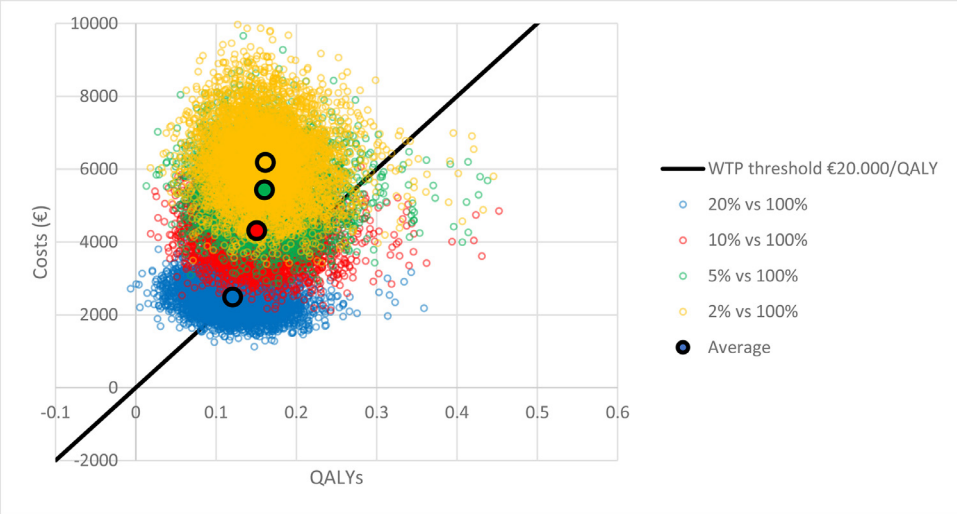

Fig. 2. Probabilistic sensitivity analysis using the 100% threshold as reference for comparison. The blue, red, green, and orange dots represent the 20%, 10%, 5% and 2% thresholds respectively. The plotted line represents a willingness to pay threshold of €20.000,- per QALY gained.

outweigh the additional costs. This implies that, from a health economic perspective, for this WTP value, and using these prediction models, ePLND should not be performed in this patient group. However, for higher WTP threshold values, for example, €30,000/QALY gained and higher, use of a 20% or 10% risk threshold has the highest probability of being cost-effective. Such threshold values may appear to be high compared to previous recommendations. This makes sense as evaluations only focusing on health outcomes will, in this case, always prefer low threshold values. The cost-effectiveness analysis enables to estimate the optimal threshold to perform or omit ePLND. However, the optimal threshold may be different from the best strategy identified here, as we choose to evaluate 5 plausible threshold values (based on current guideline recommendations) rather than evaluate all possible threshold values.

Our study had several limitations. In this evaluation it was assumed that patients receiving ePLND with histopathological proven LNI may consequently receive ADT or a combination of ADT and ART. However, currently there is no consensus on the most effective timing and treatment modality for administering ADT, which may lead to variation in healthcare outcomes and costs in practice. In addition, the reported outcomes in available literature were, with exception of 2 randomized controlled trials [15,26], solely based on retrospective data. Consequently, high quality evidence was not available for all input parameters of the decision analytic model. The decision analytic model was based on treatment recommendations from the EAU guideline1 in which 3 postoperative treatment strategies were discussed; observation, ADT, or a combination of ADT and ART. The strategies were substantiated by the long term survival data reported bij Touijer et al. [18]. However, in current clinical practice alternative treatment options may also be applied. In addition, certain urological methods may not support adjuvant treatment based on lymph node status, but are followed by postoperative procedures based on the presence of residual disease (i.e., reflected by (in) measurable prostate specific antigen levels). The discrepancy between guideline recommendations and clinical practice may be partly

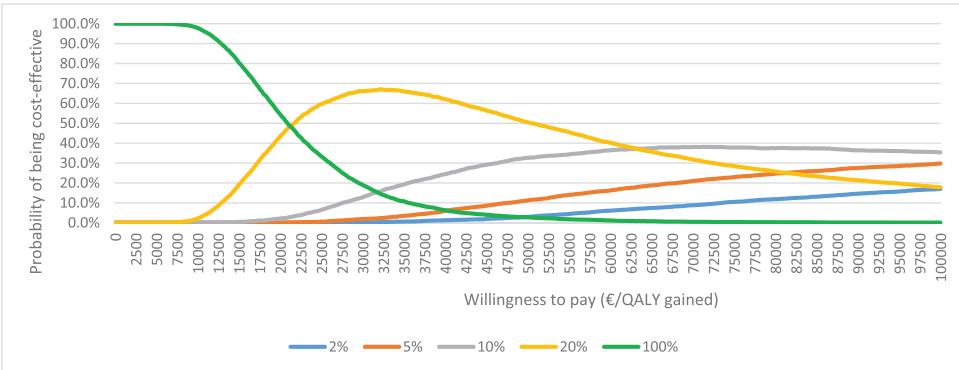

Fig. 3. Cost-effectiveness acceptability curve: Based on the disease burden, the willingness to pay (WTP) thresholds applied in the Netherlands are €20.000/QALY, €50.000/QALY, or €80.000/QALY. Applying a €20.000/QALY threshold, the 100% strategy has the highest probability (64%) of being cost-effective. The 100% threshold regards the scenario in which no ePLND would be performed.

explained by the fact that the outcomes of interest are often reported over 10-years after treatment. For instance, the fairly recent paper by Touijer et al. in 2018 reflects clinical decision making in patients who received treatment between 1988 and 2010 [18].

Certain complications caused by ePLND such as neurological, vascular, and ureteral damage could not be taken into account in the analysis since evidence was lacking regarding their impact on quality of life and costs. However, it is unlikely that these complications would have had a large impact on the outcomes, because their risk is lower than 1% [5]. In addition, anxiety or reassurance for (not) knowing whether cancer had spread to the pelvic lymph nodes may support the decision to perform ePLND and may also influence outcomes following RP with or without concomitant ePLND. Yet, anxiety and reassurance were not incorporated into the current analysis as evidence regarding effect size and duration is lacking.

The current analysis was performed using a hypothetic cohort for which the baseline characteristics were based on a cohort of Dutch prostate cancer patients who underwent ePLND. As the analysis focused on the Dutch health care setting, generalizability of the results to other health care settings may be limited, especially for settings in which the patient characteristics vary highly from Dutch prostate cancer patients (i.e., with more high risk prostate cancers). In addition, the applied WTP threshold of €20,000/QALY was used as recommended by the Dutch government. Other WTP thresholds may be used by other countries. Fig. 3 displays a range of feasible WTP thresholds to inform decision making in different health care settings.

The scenario in which the Briganti 2012 nomogram was assessed showed similar results as the MSKCC web-calculator (Supplement S3: Scenario 2). The analysis showed that applying a lower threshold (i.e., performing more ePLNDs) resulted in better health outcomes (e.g., higher QALYs). However, high-quality evidence to substantiate a beneficial therapeutic effect of ePLND is still lacking. Therefore, an alternative scenario was assessed in which patients with confirmed LNI did not experience any treatment benefit compared to patients with unidentified LNI (Supplement S3: Scenario 3&4). The results of this scenario showed that performing no more ePLND (i.e., applying a 100% threshold) is the dominant strategy compared to performing ePLND in patients with a risk above a 2%, 5%, 10%, or a 20% threshold, even for WTP thresholds up to €100,000 per QALY gained. Even in the absence of evidence supporting direct therapeutic value of ePLND a cost-effectiveness analysis may be valuable, for instance, to assess potential cost savings from ePLND, to identify the optimal risk threshold for providing ePLND, to inform policy makers on value-based aspects and trade-offs related to ePLND, or to guide future research on this topic. Until evidence on the true therapeutic value of ePLND becomes available, it remains unclear whether performing ePLND is cost-effective at all.

Conclusion

The current results suggest very limited value of ePLND in patients with risk of LNI less than 10%. Which risk would be "high enough" to consider ePLND is likely to be topic of further discussion, and part of the shared decision making process between clinicians and patients. However, finally, when new evidence on the actual therapeutic value of ePLND would become available, the presented analysis should be updated.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urolonc.2020.09.014.

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