The Laryngoscope

Cost-Effectiveness of Surgery Versus Organ Preservation in Advanced Laryngeal Cancer

Ann-Jean C. C. Beck, MD; Wim H. van Harten, MD, PhD; Michiel W. M. van den Brekel, MD, PhD; Arash Navran, MD; Valesca P. Retèl, PhD

Objective: Treatment decision-making for patients with laryngeal cancer consists of a complex trade-off between survival and quality of life. For decision makers on coverage and guidelines, costs come in addition to this equation. Our aim was to perform a cost-effectiveness analysis of surgery (laryngectomy with or without radiotherapy) versus organ preservation (OP: radiotherapy, chemo- and/or bioradiation) in advanced laryngeal cancer patients from a healthcare perspective.

Methods: A cost-effectiveness analysis was conducted using a Markov model. For each modality, data on survival and quality-adjusted life years (QALYs) were sourced from relevant articles in agreement with experts, and national benchmark cost prices were included regarding treatment, follow-up, adverse events, and rehabilitation.

Results: Total QALYs of the surgical approach (6.59) were substantially higher compared to the OP approach (5.44). Total lifetime costs were higher for the surgical approach compared to the OP approach, namely €95,881 versus €47,233. The surgical approach was therefore more effective and more costly compared to OP, resulting in an incremental cost-effectiveness ratio of €42,383/QALY.

Conclusion: Based on current literature, surgical treatment was cost-effective compared to OP in advanced laryngeal cancer within most willingness-to-pay thresholds. The study provides information on the survival adjusted for quality of life in combination with costs of two different approaches for advanced laryngeal cancer, relevant for patients, physicians, and policy makers. As financial toxicity is a relevant aspect in this population, collection of real-world data on country-specific costs and utilities is strongly recommended to enable further generalization.

Key Words: Laryngeal carcinoma, total laryngectomy, organ preservation, cost-effectiveness analysis, quality of life.

Level of Evidence: N/A.

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INTRODUCTION

Worldwide, the incidence of laryngeal cancer is estimated to be 177,000 and accounts for 94,000 deaths per year.[1] Cancer of the larynx is accountable for approximately one-third of the head and neck cancers (HNCs).[2] The disease and treatment have a detrimental impact on a patient's life and often patients have to cope with significant morbidity after treatment.[3]

In laryngeal cancer, choosing the right individual treatment is dependent on multiple aspects including patient-related (e.g., age, comorbidity) and treatment-related factors (e.g., intensity, duration, toxicity). This is especially difficult when treatment options have similar survival rates. In example, most studies on patients with T3 laryngeal carcinoma do not report significant differences in overall survival (OS) between surgery and organ preserving (OP) modalities.[4] Not only survival outcomes, but also treatment effects on quality of life (QoL) and physical and psychosocial functioning are crucial in decision-making.[5] In advanced laryngeal cancer patients, no significant differences in QoL outcome were reported between treatment with either total laryngectomy or chemoradiation. However, they do have different toxicities (e.g., the chemoradiation group had more problems with dry mouth whereas the laryngectomy group suffered from disturbances in smell, use of painkillers and taste and coughing).[3] In addition, most long-term QoL studies in laryngectomy patients report that these patients have a relatively high overall QoL due to factors such as adequate counseling and coping.[6,7] Overall, the tradeoff between treatment-related QoL and survival outcomes makes selecting a treatment challenging for the patient and physician. Combining QoL and survival in one effectiveness outcome such as the quality-adjusted life years (QALY) outcome could be relevant information in clinical practice.

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In a cost-effectiveness analysis, all these relevant aspects are combined in the trade-off. This information can serve as input for guideline development, optimization of treatment choices in individual decision-making, and at a political level, in the decision whether or not to reimburse certain treatments. Taking into account costs for the total treatment trajectory—including costs for treatment of adverse events (AE) and rehabilitation into—is necessary, especially nowadays due to growing numbers of cancer survivors and healthcare costs as a whole. Medical expenses, in terms of financial toxicity, impact this financially strained population for whom coverage is not always assured.[8] The literature on cost-effectiveness research in the laryngeal cancer field is scarce. Morton et al. reported on cost-effectiveness in 1997 showing the trade-off between the modalities of guidelines at that time.[9] A cost-minimization study evaluating total laryngectomy with radiotherapy (RT) versus induction chemotherapy and RT resulted in cost savings in the surgery group.[10] This study only focused on short-term AE. In addition, economic burden was reported in two studies, with substantially high (outpatient) chemoradiation costs in the United States.[11,12]

Currently, a complete overview of patients' survival, detailed AE, function (QoL), and cost data is lacking in literature. Using a cost-effectiveness model, all relevant information available in literature could be combined, and (cost-)effectiveness outcomes could be used as relevant information to support clinical and policy decision-making.

Therefore, the aim of this study is to evaluate the cost-effectiveness of surgery, comprising of total laryngectomy with or without postoperative RT, compared to organ preservation (OP), consisting of RT, chemoradiation (CRT with Cisplatin) and bioradiation (BRT with Cetuximab), including short and long-term AE in advanced (stages 3 and 4) laryngeal cancer.

MATERIALS AND METHODS

Patient Groups

Two patient groups were compared in the model: patients with advanced (stages 3 and 4) laryngeal cancer treated with curative intent with surgery with or without RT versus OP (RT/CRT/BRT). Weighted averages were applied to patients with or without treatment with RT (surgery group) and patients treated with RT, CRT, or BRT (OP group). For the surgery group, this means that a proportion of patients—in accordance to literature—received postoperative RT. This portion of patients had additional costs related (e.g., RT treatment, follow-up, and treatment of RT-specific AE [fibrosis]). As the model input data derived from literature—including the survival-specific data—was not available for stages 3 and 4 separately, we could not build separate models based on stage.

The study was assessed and approved by the Medical Ethical Committee of the Netherlands Cancer Institute (NKI-AVL) registration number: METC18.0916/P18CEA).

Model Description

A Markov decision model was developed from a healthcare perspective including three mutually exclusive health states: disease-free survival, progression of disease (POD), and death (due to laryngeal cancer or other causes) (Fig. 1). By means of Monte Carlo simulation, a hypothetical cohort of 5000 patients was simulated with a lifetime horizon using a 1-year cycle time. The survival data (progression of disease), cost data, and treatment regimens were based on the Dutch perspective.

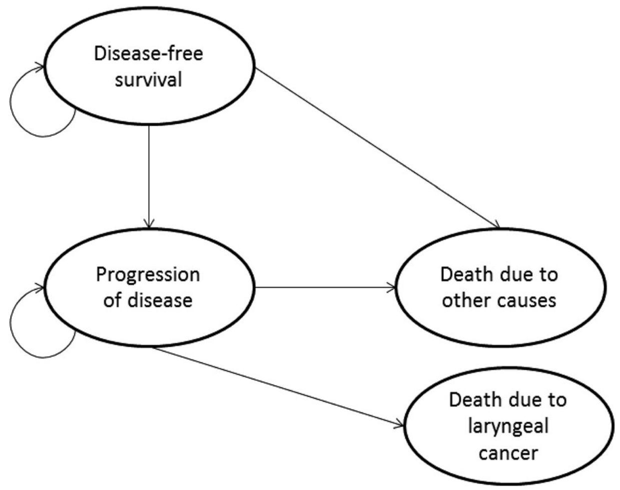

Fig. 1. Health states of the Markov model.

Input Data

The input parameters were obtained from various key international articles, carefully selected on relevant criteria in consensus with a group of experts. An overview of the input parameters is shown in Table I. Detailed information on the methods regarding the input data is provided in full text in Appendix S1.

The relevant criteria were: tumor group ([at least] inclusion of advanced laryngeal cancer), sample size (at least 50 per subgroup [except for five subgroups; see "sample size" in Appendix S2]), availability of AE/QoL data using a (validated) measurement tool (e.g., EuroQol five-dimensional questionnaire [EQ-5D]),[13] time point of assessment of AE/QoL (preferably at least 6 months post-treatment) and quality of the study (e.g., [randomized] controlled trial) to obtain comparable input data. Literature-based input data comprised of survival data, (primary and secondary) treatment probabilities and most incidental long-term AE.

The health effects, expressed in QALYs, were calculated by multiplying the life years gained times the associated EQ-5D utilities, and sourced from literature.

When literature was not sufficient or available regarding probabilities for the BRT group, they were assumed to be similar to the CRT group based on expert elicitation. Also, the probability of managing fibrosis for postoperative RT and RT group was assumed to be similar to CRT and BRT, respectively, by the experts.

All literature-based input data were confirmed and assessed for generalizability with a panel of experts in the HNC field consisting of head and neck surgeons, radiotherapist, medical oncologist, speech-language pathologist, physiotherapist, dietician, physician assistant, and nurse specialists. Additional information on the specifications (e.g. sample size, tumor group, time point of measurement) of the included articles and sourcing of the probabilities is provided in Appendix S2.

National cost prices were linked to the 2018 Dutch diagnosis-related groups (DRGs) (sub)codes (Table I).[14] Costs for medication and nutritional support were calculated with online prices.[15,16]

TABLE I.
Model Input Parameters per Year.

Probabilities (range 0–1)	Mean	SE	Distribution	Source
Survival				
Progression of disease—Surgery	0.133	0.043	Beta	See Appendix S2
Progression of disease —OP	0.176		Beta	See Appendix S2
RT	0.178	0.038		
CRT	0.163	0.081		
BRT	0.163	0.081		
Death due to laryngeal cancer*	0.249	0.022	Beta	See Appendix S2
Treatment probabilities—surgery				
PORT (1 cycle)†	0.797	0.012	Beta	See Appendix S2
Secondary treatment (curative) of recurrent disease (1 cycle)	0.125	0.042	Beta	See Appendix S2
Secondary treatment (palliative) of recurrent disease* (1 cycle)	0.300	0.034	Beta	See Appendix S2
Treatment probabilities—OP				
Secondary treatment (curative) of recurrent disease (1 cycle)	0.164	0.033	Beta	See Appendix S2
Adverse events—surgery				
Dysphagia—oral supplements (continuous cycles)	0.417	0.081	Beta	See Appendix S2
Fibrosis (2 cycles)	0.069	0.033	Beta	See Appendix S2
Hypothyroidism (continuous cycles)	0.108	0.050	Beta	See Appendix S2
Neopharyngeal spasm (1 cycle)	0.124	0.029	Beta	See Appendix S2
Neopharyngeal stenosis (3 cycles)	0.233	0.019	Beta	See Appendix S2
Tracheostomal stenosis (1 cycle)	0.130	0.023	Beta	See Appendix S2
Adverse events—OP				
Dysfunctional larynx—total laryngectomy (1 cycle)	0.041		Beta	See Appendix S2
RT	0.041	0.018		
CRT	0.041	0.018		
BRT	0.041	0.018		
Dysfunctional larynx—tracheostomy (1 cycle)	0.020		Beta	See Appendix S2
RT	0.020	0.013		
CRT	0.020	0.013		
BRT	0.020	0.013		
Dysphagia—oral supplements (1 cycle)	0.336		Beta	See Appendix S2
RT	0.335	0.032		
CRT	0.327	0.063		
BRT	0.394	0.034		
Dysphagia—tube feeding (1 cycle)	0.132		Beta	See Appendix S2
RT	0.100	0.013		
CRT	0.330	0.026		
BRT	0.239	0.062		
Fibrosis (2 cycles)	0.024		Beta	See Appendix S2
RT	0.018	0.018		
CRT	0.069	0.033		
BRT	0.018	0.018		
Hypothyroidism (continuous cycles)	0.086		Beta	See Appendix S2
RT	0.086	0.027		
CRT	0.086	0.027		
BRT	0.086	0.027		
Laryngeal edema (1 cycle)	0.074		Beta	See Appendix S2
RT	0.074	0.031		
CRT	0.074	0.031		
BRT	0.074	0.031		

(Continues)

TABLE I.
Continued

Probabilities (range 0–1)	Mean	SE	Distribution	Source	
Pneumonia (continuous cycles)	0.117		Beta	See Appendix S2	
RT	0.100	0.007			
CRT	0.213	0.023			
BRT	0.213	0.023			
Frequencies (range > 0)	**Mean**	**SE**	**Distribution**		
Treatment-related frequencies—surgery					
Yearly number of voice prosthesis replacements	5.214	0.665	Gamma		
Health effects (utility values, range 0–1)	**Mean**	**SE**	**Distribution**	**Source**	
Utility DFS—Surgery	0.890	0.020	Beta	17	
Utility DFS—OP	0.846		Beta		
RT	0.847	0.024		18	
CRT	0.840	0.011		19	
BRT	0.840	0.011		EE	
Disutility Progression	0.130	0.070	Beta	18	
Costs (€)	**Mean**	**SE**	**Distribution**	**Source**	**Content diagnostics/treatment**
Treatment costs—surgery					
Total laryngectomy	16,692	2129	Gamma	14	
PORT	6678	852	Gamma	14	
ICU (per day)	2325	297	Gamma	14	
Total costs Surgery	24,339		Gamma	14	
Diagnostics progression of disease*	345	44	Gamma	14	Laryngoscopy, CT scan of the head and neck, ultrasound of the neck with FNAC, PET-CT (only in patients treated with curative intention)
Secondary treatment (curative) of recurrent disease	1459	186	Gamma	14	Neck dissection
Secondary treatment (palliative) of recurrent disease*	40,659	5,186	Gamma	14,15	Chemotherapy (Carboplatin) or immunotherapy (Nivolumab) with tracheostomy placement in a portion of the patients
Treatment costs—OP					
RT	9246	1,179	Gamma	14	
CRT	11,408	1,455	Gamma	14,15	
BRT	20,970	2,675	Gamma	14,15	
Diagnostics	1453	185	Gamma	14	Laryngoscopy, CT scan of the head and neck, chest x-ray, OPT, ultrasound of the neck with FNAC, PET-CT, examination under general anesthetics (including 1-day admission)
Total costs OP	11,311		Gamma	14	
Secondary treatment (curative) of recurrent disease	22,997	2,933	Gamma	14	Total laryngectomy and flap reconstruction (including 1 ICU day)
Treatment-related costs—surgery					
Voice prosthesis replacements first year (total)	3281	418	Gamma	14	
Voice prosthesis replacements FU (costs per replacement)	778	99	Gamma	14	
FU consultation specialist year 0*	63	8	Gamma	14	
FU consultation specialist year 1	216	28	Gamma	14	
FU consultation specialist year 2	171	22	Gamma	14	
FU consultation specialist year 3–5	108	14	Gamma	14	
Treatment-related costs—OP					
FU consultation specialist year 1	206	26	Gamma	14	
FU consultation specialist year 2	143	18	Gamma	14	
FU consultation specialist year 3–5	103	13	Gamma	14	

(Continues)

TABLE I.
Continued

Probabilities (range 0–1)	Mean	SE	Distribution	Source	
Adverse events costs—surgery					
Dysphagia—oral supplements	3048	389	Gamma	14,16	VFSE, consultation speech-language pathologist and dietician, oral supplements (every 3 mo)
Fibrosis*,‡	153	19	Gamma	14	Consultation physiotherapist (every 4 mo)
Hypothyroidism FU year 1–5*	489	62	Gamma	14,15	Consultation internist, Thyrax supplementation (every 6 mo)
Hypothyroidism FU after 5 years*	244	31	Gamma	14,15	Consultation internist, Thyrax supplementation (every 12 mo)
Neopharyngeal spasm	283	36	Gamma	14,15	Consultation head and neck surgeon, Botox injection
Neopharyngeal stenosis	2565	327	Gamma	14	VFSE, dilatation
Tracheostomal stenosis	4104	523	Gamma	14	Stomaplasty
Adverse events costs—OP					
Dysfunctional larynx—total laryngectomy	16,692	2,129	Gamma	14	Total laryngectomy
Dysfunctional larynx—tracheostomy	2013	257	Gamma	14	Tracheostomy and PRG placement
Dysphagia—oral supplements	1327	169	Gamma	14,16	VFSE, consultation speech-language pathologist and dietician, oral supplements (6 mo max)
Dysphagia—tube feeding	6973	889	Gamma	14, hospital costs	VFSE, PRG placement, consultation speech-language pathologist and dietician, tube feeding (12 mo)
Laryngeal edema	1460	186	Gamma	14	Tracheostomy placement
Pneumonia	3063	391	Gamma	14	Antibiotics during hospital admission
Rehabilitation—Surgery	4091	522	Gamma	14	Outpatient clinic healthcare providers (e.g, speech-language pathologist, physiotherapist, occupational therapist), diagnostics (e.g., blood count. x-ray)
Rehabilitation—OP	1588		Gamma	14	Outpatient clinic healthcare providers (e.g., speech-language pathologist, physiotherapist, occupational therapist), diagnostics (e.g., blood count. x-ray)
RT	1146	146			
CRT	4091	522			
BRT	4091	522			

The table includes the probabilities, health effects ([dis]utilities) and costs used in the model to obtain the deterministic model outcomes. Treatment probabilities, adverse events, utilities, treatment(–related) costs, adverse events costs and rehabilitation are provided for the surgery and organ preservation group separately. To conduct the simulations, random numbers were drawn for each parameter from the beta (probabilities/utilities) and gamma (costs/frequencies) to account for the uncertainty within the parameters.

Probabilities and costs for OP are weighted averages. Survival rates were converted to one-year probabilities with the formulas: rate = –(ln[1-probability])/time and 1-year probability = 1-exp(–rate*1).[20]

The number of simulation cycles applied to the AE is provided between brackets.

The FU consultations with specialists refer to the head and neck surgeon and radiotherapist.

All treatments include diagnostics (except for primary OP treatment), treatment, hospital admission (if applicable), medication use, consultations healthcare providers including specialists, acute complications and the first outpatient consultation. The content of diagnostics for the OP group, treatments of AE, secondary treatments and rehabilitation care are specified in the content column.

*Similar between Surgery and OP group.

†The proportion of patients receiving RT in the surgery group. The additional costs related to RT treatment, FU and AE are included in the total costs for the surgery group based on this proportion (through a weighted average).

‡Only applies to patients with postoperative RT.

BRT = bioradiation; CRT = chemoradiation; CT-scan = *Computed Tomography* scan; EE = expert elicitation; FNAC = fine needle aspiration cytology; FU = follow-up; OP = organ preservation; OPT = panoramic radiograph; PET-CT = Positron emission tomography–*computed tomography*; PORT = postoperative radiotherapy; PRG = percutaneous radiologic gastrostomy; RT = radiotherapy; SE = standard error; VFSE = video fluoroscopic swallowing exam; x-ray = electromagnetic radiation.

Deterministic Analysis

The incremental cost-effectiveness ratio (ICER) was used as a primary outcome. The ICER is calculated by dividing the difference in total lifetime costs of both strategies by the QALY difference. The ICER is expressed in costs per QALY gained. The willingness-to-pay (WTP) threshold reflects how much the Dutch

TABLE II. Model outcomes of cost-effectiveness of the analysis surgery compared to organ preservation in advanced laryngeal cancer from a healthcare perspective.				
Treatment modality	Costs (€)	QoL (QALY)	Survival (LY)	ICER (€/QALY)
Surgery	95,881	6.59	7.80	
OP	47,233	5.44	6.89	
Increments	48,647	1.15	0.91	
Surgery compared to OP				42,383

BRT = bioradiotherapy; CRT = chemoradiation; ICER = incremental cost-effectiveness ratio; LY = life year; OP = organ preservation; QALY = quality-adjusted life year; QoL = quality of life; RT = radiotherapy.

population is willing to pay for a gain in effect (QALY), and is situated at €80,000 currently in the Netherlands.[21]

A discount rate of 4% and 1.5% was applied to the costs and health outcomes respectively according to Dutch guidelines.[22]

Probabilistic Sensitivity Analysis

Uncertainty within the input probabilities was handled probabilistically through distributions for each of the parameters (Table I). Random numbers were drawn from the distributions to simulate the outcomes of 5000 patients. The simulations were visualized by a cost-effectiveness (CE) plane, consisting of four quadrants, in which the incremental costs (y-axis) and QALYs (x-axis) indicate whether the treatment in question is more or less costly or effective compared to usual care. The cost-effectiveness acceptability curve (CEAC) displays the probability (y-axis) of a strategy being cost-effective (ie, the highest net monetary benefit) at the various thresholds in costs/QALY (x-axis).[20,23]

The analysis was performed in Microsoft Excel version 2010 (Microsoft, Redmond, WA).

Sensitivity Analyses

A tornado diagram was constructed to show the sensitivity of uncertain parameters and for identification of most influential parameters on the ICER, costs and QALYs. Margins of ±20% were applied to obtain the parameter ranges. Specific scenario analysis were performed for: 1) rehabilitation care, because this type of care is provided but is not (yet) standardized, and 2) the number of cycles of chemotherapy because these may be discontinued due to AE including nephrotoxicity (Appendix S3).

RESULTS

Mean Results

Over the lifetime period, the surgical approach was more effective but more costly than the OP group (Table II). In the surgery versus OP group, the LY and QALY gain were 0.91 (7.80 vs. 6.89) and 1.15 (6.59 vs. 5.44), respectively. The total lifetime healthcare costs per patient were higher with the surgical approach (€95,881) compared to OP (€47,233).

Uncertainty Analysis

The CE plane shows that the majority of simulations (86%) is situated in the cost-effective quadrant (displayed northeast), which means that surgery is more effective and more costly (Fig. 2). The surgical approach is cost-effective

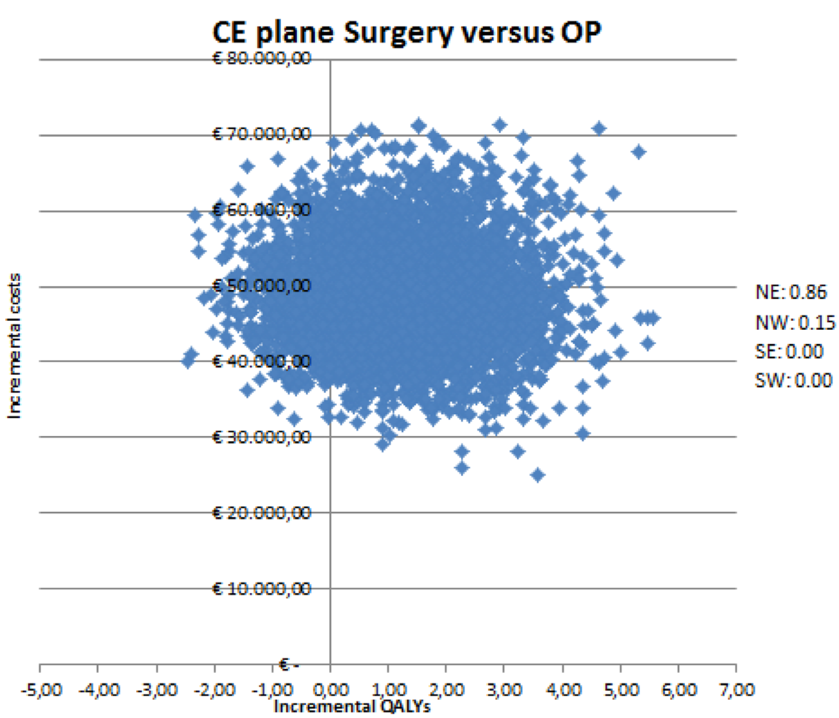

Fig. 2. Cost-effectiveness (CE) plane of surgery versus OP. The scatter dots each represent incremental costs and QALYs of the 5000 simulations. NE = northeast quadrant; NW = northwest quadrant (dominated); OP = organ preservation; SE = southeast quadrant (dominant); SW = southwest. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

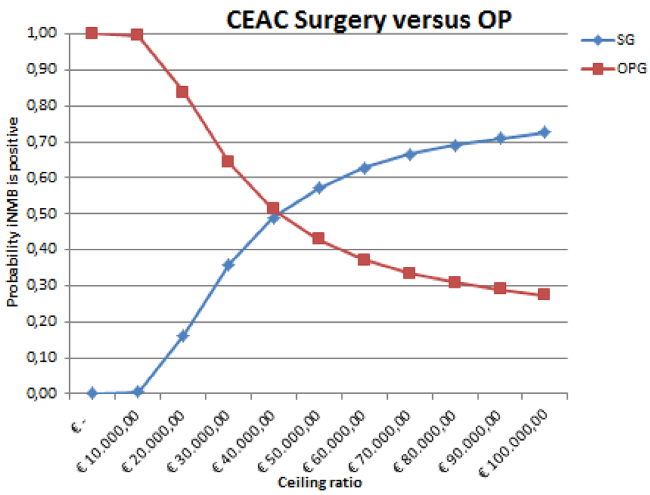

Fig. 3. Cost-effectiveness acceptability curves (CEAC) of surgery versus OP. The curve represents the probability of surgery being cost-effective at various willingness-to-pay thresholds (ceiling ratios). OP = organ preservation; OPG = organ preservation group; SG = surgery group. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

at a WTP threshold of more than €40,000 (Fig. 3). At the Dutch WTP threshold of €80,000/QALY, the surgical approach is cost-effective with a probability of 70%.

One-Way Sensitivity Analysis

The tornado diagrams in Fig. 4A–C show most influential input parameters (ranked most influential from top to bottom). The diagrams display the impact of changing a certain parameter in the model (±20%) on the ICER (Fig. 4A), incremental costs (Fig. 4B) and incremental QALYs (Fig. 4C).

Overall, model outcomes proved to be robust against parameter changes, as the surgical approach remained the most cost-effective approach. Taking into account costs for rehabilitation care and a reduction in systemic therapy costs through discontinuation of Cisplatin cycles did not impact the cost-effectiveness outcomes from the model.

DISCUSSION

Our results showed that the surgical approach was cost-effective compared to OP with an ICER of €42 383/QALY. Total QALYs of the surgical approach were higher compared to the OP approach; 6.59 and 5.44, respectively, which is substantial. We also see this in literature; this might be a result of coping well with and acceptance of the disability by laryngectomies.[3,7,24] Total lifetime costs were higher for the surgical approach (€95,881) compared to the OP approach (€47,233). For policy decision-making, taking the substantial higher QALY into account against the relative additional costs, it would be advised to make surgery the preferred choice of treatment for this population. On the individual- and shared decision-making level, the tornado diagram can give additional information when changing certain parameters.

Compared to the existing literature, our findings on the QoL were similar.[9] However on the cost-side, we included much more detail on AE, which makes the trade-off more clear for both strategies.[9–12] Obviously, the costs of healthcare in different countries are difficult to compare. However, overall, the effects (e.g., survival in Western Europe) and the cost ratio between primary treatment costs of surgery and OP (RT) in the studies available in literature were in accordance to our study data.[9,10,25] This is an argument for international generalizability of our results in Western Europe. It should be acknowledged that, as the survival data, data on treatment regimens and costs are sourced from the Netherlands, this model will be most relevant to the Dutch perspective and countries in which the healthcare delivery models are similar. It could be valuable to source survival data from large studies (e.g., Surveillance, Epidemiology and End results [SEER-]) based in future cost-effectiveness analyses.[26] Additionally, access to large databases would facilitate precision of the estimates on survival data and improve quality of the model.

In this study, several limitations have to be considered. First, the input data was sourced from various controlled studies making it challenging to achieve comparability between modalities and contributes to the uncertainty of the outcomes. The input parameters sourced from the different studies were chosen based on a set of criteria and checked with an experienced panel in the field. However, we must emphasize that these results are heavily dependent on the choice of sources used for the input parameters. Access to large national databases with tumor-specific information would be helpful to overcome this. Second, it was difficult to find studies in literature reporting on AE data specifically to the laryngeal cancer population to estimate the exact AE differences between modalities. Third, the large uncertainty around the incremental QALYs captured in the CE plane resulted from the low sample sizes used in the literature. Fourth, with regard to the surgery group, we assumed that voice prosthesis use was applicable to the whole laryngectomy group because this is true for the majority of Dutch patients. However, from a worldwide perspective, use of the esophageal speech should also be included in a portion of patients.[27] This will result in lower costs for this patient population due to the lack of voice prosthesis replacements, whereas the QoL of these patients is lower compared to patients with voice prosthesis use.[28,29] This could lead to a more favorable cost-effectiveness ratio for surgery (lower ICER) in certain countries. Fifth, in the scenario analyses, the impact of the discontinuation of cisplatin cycles had an impact on the costs but did not lead to changes in effectiveness (survival and QoL). In future research, it would be advised to take this information into account whenever available, because survival changes could have an impact on relative effectiveness and cost-effectiveness outcomes. A strength of the study is that, to the best of our knowledge, this is the first study to evaluate the cost-effectiveness of surgery versus OP in HNC patients with a robust Markov model-based analysis using all relevant literature available regarding the indirect costs for AE treatments. The input parameters

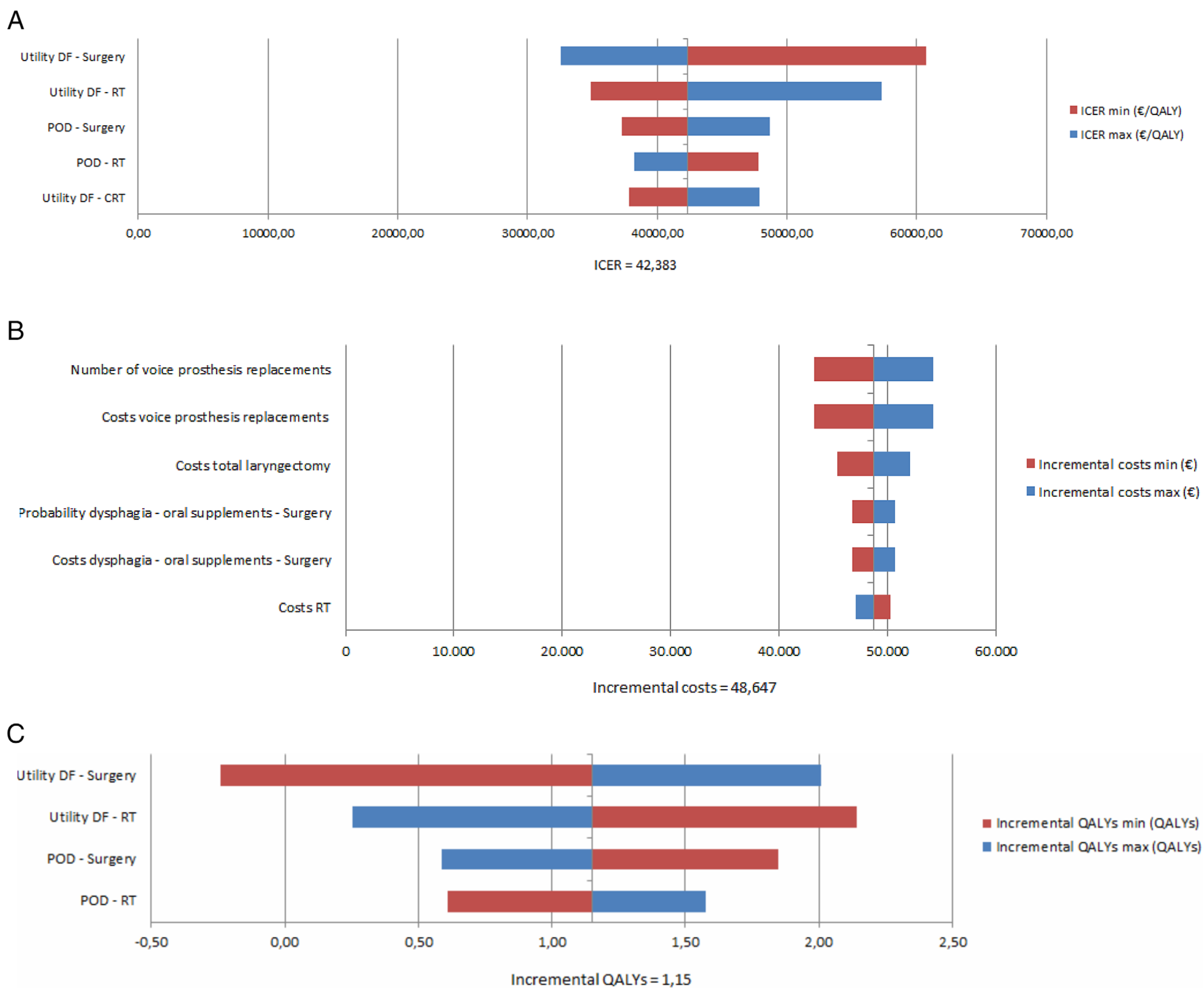

Fig. 4. Tornado diagrams including most influential input parameters incorporated in the model. For the input parameters, ran*20% were used to calculate the maximum and minimum (for the POD and utility values clinically relevant ranges of ±5% were applied). In the three figures, the influence of the parameters' maximum (blue bars) and minimum (red bars) on the ICER (A), incremental costs (B) and incremental QALYs (C) outcomes are visualized. The deterministic outcomes for the ICER (42,838), incremental costs (48,647) and QALYs (1.15) are displayed below the x-axis. CRT = chemoradiation; DF = disease-free; POD = progression of disease; RT = radiotherapy. (A) Influence on the incremental cost-effectiveness ratio (ICER). (B) Influence on the incremental costs. (C) Influence on the incremental quality adjusted life years (QALYs)* [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

were carefully selected from literature and were validated with a panel of clinical experts in the HNC field. Regarding the OP group, the parameters consisted of weighted averages calculated with individual data for each modality to enhance the precision of the estimates for the OP group. In addition, using the Dutch benchmark cost prices provided a good representation of the actual costs (in contrast to tariff prices).[14]

CONCLUSION

From this study, several research implications have to be considered for further research. From a patient perspective, preferably in a prospective study, it would be of value to collect and process data including the effects of rehabilitation, return to work, participation in society, and more specific data regarding AE specifically to laryngeal cancer patients to analyze this from a societal perspective. Methodologically, we encourage the development of HNC-specific utilities which would enhance the precision of QoL estimates in HNC patients (and decrease uncertainty as visualized in the tornado diagrams (Fig. 4).[30]

Practical implications that could come forth from this study are focused on clinical practice as well as policy-making. Nowadays, aside from patient's survival, there is increased focus on regaining QoL and daily activities after treatment.[31] Decision-making can vary among patients for which each case requires individual evaluation. Therefore, it is of great value to make adequate information available regarding QALY differences between surgery and OP treatments to facilitate the survival versus QoL tradeoff and improve shared, personalized decision-making. Presently a decision-aid for laryngeal cancer treatment is being developed[5] and implementing adequate QALY data in the tool could improve (objective) information provided to patients. Additionally, the uncertainty presented in the CEAC is mostly due to the higher surgery costs. It would be interesting to calculate possible scenarios resulting from the decision-aid, to get more insight into the cost-effectiveness based on patient preferences. Additionally, collection of country-specific costs will support additional analyses.

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