ORIGINAL ARTICLE

The cost-effectiveness of radiofrequency ablation for Barrett's esophagus with low-grade dysplasia: results from a randomized controlled trial (SURF trial)

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Background and Aims: The Surveillance versus Radiofrequency Ablation (SURF) trial randomized 136 patients with Barrett's esophagus (BE) containing low-grade dysplasia (LGD), to receive radiofrequency ablation (ablation, n = 68) or endoscopic surveillance (control, n = 68). Ablation reduced the risk of neoplastic progression to high-grade dysplasia and esophageal adenocarcinoma (EAC) by 25% over 3 years (1.5% for ablation vs 26.5% for control). We performed a cost-effectiveness analysis from a provider perspective alongside this trial.

Methods: Patients were followed for 3 years to quantify their use of health care services, including therapeutic and surveillance endoscopies, treatment of adverse events, and medication. Costs for treatment of progression were analyzed separately. Incremental cost-effectiveness ratios (ICER) were calculated by dividing the difference in costs (excluding and including the downstream costs for treatment of progression) by the difference in prevented events of progression. Bootstrap analysis (1000 samples) was used to construct 95% confidence intervals (CIs).

Results: Patients who underwent ablation generated mean costs of U.S.$13,503 during the trial versus $2236 for controls (difference $11,267; 95% CI, $9996-$12,378), with an ICER per prevented event of progression of $45,066. Including the costs for treatment of progression, ablation patients generated mean costs of $13,523 versus $4,930 for controls (difference $8593; 95% CI, $6881-$10,153) with an ICER of $34,373. Based on the various ICER estimates derived from the bootstrap analysis, one can be reasonably certain (>75%) that ablation is efficient at a willingness to pay of $51,664 per prevented event of progression or $40,915 including downstream costs of progression.

Conclusions: Ablation for patients with confirmed BE-LGD is more effective and more expensive than endoscopic surveillance in reducing the risk of progression to high-grade dysplasia/EAC. The increase in costs of ablation can be justified to avoid a serious event such as neoplastic progression. At a willingness to pay of $40,915 per prevented event of progression, one can be reasonably certain that ablation is efficient. (www.trialregister.nl number: NTR 1198.) (Gastrointest Endosc 2017;■:1-10.)

Abbreviations: BE, Barrett's esophagus; CI, confidence interval; EAC, esophageal adenocarcinoma; ICER, incremental cost-effectiveness ratio; LGD, low-grade dysplasia; SURF trial, Surveillance versus Radiofrequency Ablation trial; QALY, quality-adjusted life-year.

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INTRODUCTION

The incidence of esophageal adenocarcinoma (EAC) continues to increase significantly in the western world.[1,2] Malignant degeneration in Barrett's esophagus (BE), the most important precursor for development of EAC, is thought to occur in a step-wise fashion: from non-dysplastic intestinal metaplasia to low-grade dysplasia (LGD), then high-grade dysplasia, and eventually adenocarcinoma.[3,4] Depending on the presence and severity of dysplasia, patients with BE either undergo endoscopic surveillance or treatment.[4]

Radiofrequency ablation is an established endoscopic technique for eradication of BE with and without dysplasia, and is associated with an acceptable safety profile and, more importantly, a reduced risk of neoplastic progression.[5-8] Ablation, if necessary combined with endoscopic resection of visible abnormalities, is considered the management strategy of choice for patients with BE with high-grade dysplasia and early cancer.[9,10] The optimal management strategy for patients with LGD is less well established.

A recent study indicated that endoscopic surveillance of patients with BE is neither cost-effective nor preventative.[11] Ablation of LGD may therefore be clinically useful if neoplastic progression can be reduced at an acceptable cost profile. Using a BE disease model, we previously analyzed the cost-effectiveness of ablation treatment for patients with BE with and without dysplasia.[12,13] This analysis suggested that ablation might be cost-effective for LGD if the disease is confirmed and stable.[13] However, as with any modeling study, the validity of these results is limited by the uncertainty of the model inputs: data on the natural history of LGD were scarce; and all simulations were based on a hypothetical cohort of 50-year-old otherwise healthy individuals. For medical decision making with regard to LGD in BE, more robust cost-effectiveness data are necessary.

In the recently published SURF (Surveillance versus Radiofrequency Ablation) trial, standard endoscopic surveillance was compared with radiofrequency ablation in the prevention of neoplastic progression in patients with BE with a confirmed diagnosis of LGD. The SURF trial was closed before all patients reached the projected 3 years of follow-up because of the superiority of ablation for the primary endpoint.[14] In the trial, ablation resulted in eradication of BE and dysplasia in about 90% of patients and only a limited number of adverse events were observed. The present study was performed alongside the SURF trial and is the first trial-based cost-effectiveness analysis of ablation compared with endoscopic surveillance for the management of patients with BE with LGD. This analysis was performed from the perspective of a Dutch hospital provider taking into account the associated costs and events of neoplastic progression during the 3 years of the trial.

METHODS

Patient population and the SURF study protocol

The methods and results of the SURF trial have been described in detail elsewhere (www.trialregister.nl, NTR 1198).[14] In brief, 136 patients (116 male, mean age 63 years) were recruited between June 2007 and June 2011 from 9 centers in the Netherlands, Belgium, United Kingdom, and Ireland. Patients with confirmed LGD in BE were randomized to receive radiofrequency ablation (ablation) or endoscopic surveillance (control). In all patients, the LGD diagnosis was confirmed once by one of the pathologists from a central panel of expert pathologists before inclusion. In the ablation group, patients were treated with the circumferential or focal radiofrequency ablation catheter until complete endoscopic and histologic eradication of BE was achieved. If BE epithelium persisted after the maximum number of ablations was reached (maximum 2 circumferential and 3 focal sessions), a single session of endoscopic resection or argon plasma coagulation was permitted.[14] The first follow-up endoscopy with biopsy was scheduled 3 months after the last therapeutic endoscopy, with subsequent follow-up performed annually. In the control group, patients underwent surveillance endoscopy with biopsy at 6 and 12 months within the first year, with subsequent follow-up performed annually. The primary outcome of interest was the occurrence of high-grade dysplasia or EAC (defined as neoplastic progression) at any time during the 3 years after randomization. Patients who showed neoplastic progression were treated per standards for high-grade dysplasia/EAC.

Clinical outcomes of the SURF trial

Sixty-eight patients were randomized to ablation and 68 patients to the control group. Within 3 years, 1.5% (n = 1) of the patients in the ablation group had neoplastic progression compared with 26.5% (n = 18) of patients in the control group. Ablation significantly reduced the risk of neoplastic progression by 25.0% (95% confidence interval [CI], 14.1-35.9).

Design of the economic study

This prospective cost-effectiveness analysis was developed from a Dutch hospital provider perspective, and compared radiofrequency ablation against endoscopic surveillance alongside the SURF trial. All authors had access to the study data and reviewed and approved the final manuscript.

Volumes of used resources

Major use of health care resources from the randomization date until the end of follow-up (restricted to 36 months) was gathered principally from the study database.

TABLE 1. Prices and sources used to value resource use

	Unit costs (U.S.$)	Source
Therapeutic and surveillance endoscopies		Academic Medical Hospital ledger 2012
Therapeutic endoscopy*	398.64	
HALO 360 ablation catheter (Medtronic, Minneapolis, Minn)	3201.12	
HALO 360 sizing balloon	981.14	
Guidewire for HALO 360 procedure	117.19	
HALO 90 ablation catheter	1967.55	
Argon plasma coagulation	323.74	
Endoscopic resection	323.74	
Histologic assessment of endoscopic resection	235.06	
Histologic assessment of biopsies	176.68	
Surveillance/follow-up endoscopy	398.64	
Daycare after sedation with propofol (day)	362.99	Dutch guideline for costing[23]
Consultation by telephone	40.67	
Medication†		www.medicijnkosten.nl
Esomeprazole (at 40 mg twice daily for 3 months)	38.30	
Ranitidine (for 2 weeks after RFA)	4.97	
Sucralfate (4 times a day for 2 weeks after RFA)	13.59	
Adverse events and surgical treatment of neoplastic progression		Academic Medical Hospital ledger 2012
Endoscopy for bleeding	713.37	
Endoscopy with dilatation	713.37	
Hospital stay (per day)		Dutch guideline for costing[23]
Consultation at outpatient department	831.56	Dutch guideline for costing[23]
Radiography of the abdomen	61.55	
Radiography of the thorax	61.55	
CT thorax	186.95	
Esophagectomy (surgery)	7739.58	
Endoscopy EUS	1114.27	
Echo abdomen	128.50	

RFA, Radiofrequency ablation.
*Therapeutic endoscopy costs were derived from unit costs of combined procedures (argon plasma coagulation/endoscopic resection). Subunit costs of the combined procedure were costs for therapeutic endoscopy plus the costs for argon plasma coagulation/endoscopic resection/RFA.
†For every unit cost, $8 was added for prescription costs of medication.

All routine procedures as part of ablation treatment and endoscopic surveillance during the 3-year follow-up of the trial were taken into account. The left column of Table 1 shows the volumes that were collected; a detailed description is included in Appendix 1 (available online at www.giejournal.org).

Unit costs

All unit costs and their sources for major health care components and procedures are shown in Table 1; a detailed description is included in Appendix 1. All unit costs are expressed in U.S. dollars with 2012 to 2013 as the base year period. Unit costs stemming from other calendar years were price indexed using the national general consumer price indices as published by Statistics Netherlands (access date, October 2013).[15]

Costs

Costs were calculated as the summed product of volumes of health care resources used and their respective unit costs. Costs were aggregated and summarized in the following time periods: 0 to 12 months (year 1), 13 to 24 months (year 2), and 25 to 36 months (year 3). Annual discount rates of 3% for the costs were applied to the second and the third year to account for time preference.

For each of the 136 patients, subcosts were based on all procedures performed during the trial before any neoplastic progression, and total costs were calculated by also taking into account the downstream costs for treatment of neoplastic progression. The cost analysis was based on health care resources used from randomization until 3 years of follow-up within the trial, or the closing date of the trial (May 8, 2014).

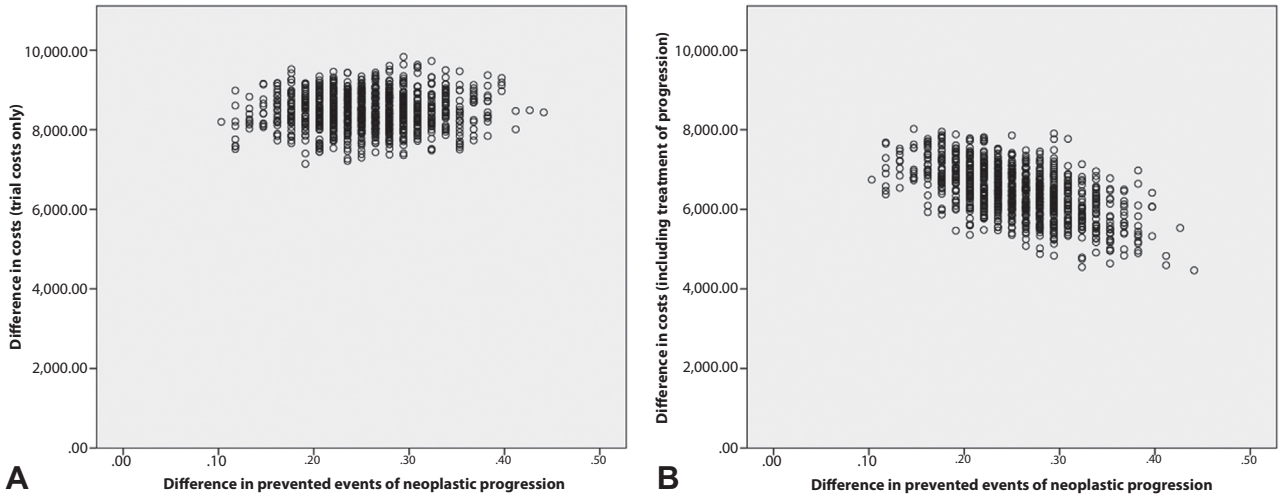

Figure 1. Cost-effectiveness plane showing the mean differences in costs between ablation and control after 1000 bootstrap replications. The y axis shows the differences in mean subcosts before neoplastic progression (**A**) and the total costs including downstream costs for treatment of neoplastic progression (**B**). The x axis shows the differences in prevented events of neoplastic progression. Ablation was more effective at a higher cost.

Analysis

The incremental costs per prevented patient with neoplastic progression were estimated for ablation against control and were calculated as the difference in costs divided by the difference in prevented events of neoplastic progression. The difference in costs was calculated excluding (subcosts) and including (total costs) the costs of treatment of neoplastic progression.

Bootstrap analysis was performed to mimic the results that would be gained if 1000 trials identical to the SURF trial were performed. This expresses the variability within the original study sample and can be used to construct bias-corrected and accelerated percentile CIs.[16] Bootstrap analysis of subcosts, total costs, and the proportion of patients with neoplastic progression was performed in each group with bootstrap resampling, drawing 1000 samples of the same size as the original groups (both n = 68) and with replacement. After pairing the samples from both groups, differences in (sub)total costs and in proportional events of neoplastic progression were calculated. Each cost difference was divided by the difference in proportional events of neoplastic progression from the same pair of samples to generate an incremental cost-effectiveness ratio (ICER) for the extra costs incurred to prevent events of neoplastic progression for patients randomized to ablation compared with control. The distribution of the various ICER estimates after 1000 bootstrap replications are graphically presented by a scatter plot on the cost-effectiveness plane. The horizontal axis divides the plane according to incremental cost (positive above, negative below), and the vertical axis divides the plane according to incremental effect (positive to the right, negative to the left). This divides the incremental cost-effectiveness plane into 4 quadrants through the origin. The north-east quadrant as shown in Figure 1 represents the situation where ablation may be cost-effective depending on the willingness-to-pay threshold.

Societal willingness to pay

The individual ICER estimates were used to construct cost-effectiveness acceptability curves, in order to assess the cost-effectiveness of ablation, by plotting the proportion of cost-effect pairs that are cost-effective for a given willingness-to-pay threshold. This proportion is identifiable from the cost-effectiveness plane (Fig. 1) as the proportion of points falling to the south and east of a ray through the origin with the slope equal to the willingness-to-pay value. The x axis indicates various amounts of willingness-to-pay thresholds to prevent events of neoplastic progression. The y axis indicates the probability of ablation being cost-effective, which is defined as the proportion of ICER estimates below the chosen willingness-to-pay level. At a chosen level of willingness to pay, the probability of ablation being cost-effective should at least be 0.75 to provide reasonable confidence for Dutch health care policy makers that offering ablation to Dutch patients is efficient. How much society should be willing to pay to prevent neoplastic progression is open to public debate, and to bring that discussion forward and decide on reimbursement for ablation for the studied indication, the willingness-to-pay value corresponding to the 0.75 probability of ablation being cost-effective was reported.

RESULTS

Patients

Supplementary Table 1 (available online at www.giejournal.org) shows the baseline characteristics of our study participants. Both groups were comparable at baseline.[14]

TABLE 2. Volumes (mean) and costs (mean) per patient of routine procedures during the trial

	Ablation (n = 68)			Control (n = 68)			Cost difference	
	Volume (mean)	Costs ($)	n	Volume (mean)	Costs ($)	n	$	95% CI
Therapeutic endoscopy		10,962			0		10,962	9746 to 12,010
Therapeutic endoscopy	3.43	1335	68					
HALO 360 catheters	1.13	3624	59					
HALO 360 sizing balloon + guidewire	1.07	1177	59					
HALO 90	2.15	4224	65					
Argon plasma coagulation	0.24	76	15					
Endoscopic resection	0.12	39	7					
Endoscopic resection during RFA	0.10	40	6					
Daycare after sedation with propofol (day)	0.53	186	16					
Consultation by telephone	4.53	184	68					
Histologic assessment of endoscopic resection	0.12	28	7					
Histologic assessment of biopsies	0.28	49	19					
Surveillance endoscopy		1605			1852		−247	−419 to −68
Surveillance/follow-up endoscopy total	3.01	964	68	2.56	1151	67		
Histologic assessment total	3.00	432	68	2.52	519	67		
Consultation by telephone total	3.22	112	68	2.82	129	192		
Sedation with propofol	0.15	97	6	0.26	53	14		
Medication		587			384		203	160 to 247
Ranitidine + sucralfate (2 weeks after RFA)	3.10	108	68	0.00	0	0		
Esomeprazole	10.36	479	68	8.32	384	68		
Treatment of adverse events		349			0		349	33 to 927
Endoscopy for bleeding	0.02	11	1					
Endoscopy with dilatation	0.22	157	8					
Hospital stay (in days)	0.21	172	1					
Consultation by telephone	0.13	5	7					
Radiography of the thorax	0.02	1	1					
CT thorax	0.015	3	1					
Subtotal (costs during the trial)		13,503			2236		11,267	9996 to 12,378

Mean volumes were averaged for 68 patients. n = number of patients who underwent procedure.
CI, confidence interval; *RFA*, radiofrequency ablation.

Total volumes and mean costs per patient

Table 2 shows the volumes and mean costs of hospital care, endoscopic procedures, and other resources during the trial before any neoplastic progression (subcosts) by study group. Patients randomized to ablation generated mean costs of $13,503 during the trial; patients randomized to control generated mean costs of $2236 (cost difference $11,267; 95% CI, $9996-$12,378). Therapeutic endoscopies were the main cost drivers in the ablation group; costs differed therefore between the 2 groups: $10,962 versus $0, respectively. Surveillance endoscopies (surveillance and follow-up procedures) were the main cost drivers in the control group: $1605 versus $1852, respectively. Costs for medication and treatment of adverse events were both higher in the ablation group than in the control group: $587 versus $384 and $349 versus $0, respectively.

Table 3 shows the volumes and costs of hospital care, endoscopic procedures, and other resources for treatment of neoplastic progression by study group. Patients randomized to ablation generated mean costs of $20; patients randomized to control generated mean costs of $2693. The main cost drivers were therapeutic endoscopies and surgical treatment of neoplastic progression.

Table 4 shows the mean total costs per patient, taking into account the costs for treatment of neoplastic progression. The mean total costs per patient randomized to ablation amounted to $13,523 versus $4930 for control (cost difference, $8593; 95% CI, $6881-$10,153).

TABLE 3. Volumes (mean) and costs (mean) per patient generated for treatment of neoplastic progression

	Ablation (n = 68)			Control (n = 68)			Cost difference	
	Volume (mean)	Costs ($)	n	Volume (mean)	Costs ($)	n	U.S.$	95% CI
Endoscopic therapy after neoplastic progression		17			2177		−2160	−3171 to −1314
Therapeutic endoscopy				0.66	251	16		
HALO 360 catheters				0.21	642	13		
HALO 360 sizing balloon + guidewire				0.21	220	13		
HALO 90				0.28	536	11		
Endoscopic resection				0.16	51	9		
Outpatient care after sedation (day)				0.22	77	11		
Consultation by telephone	0.03	1	1	1.31	52	17		
Histological assessment of endoscopic resection				0.15	33	8		
Histological assessment of biopsies	0.03	5	1	0.57	97	14		
Hospital stay after endoscopic therapy				0.04	35	2		
Surveillance/follow-up endoscopy after neoplastic progression	0.03	11	1	0.49	183	13		
Surgical treatment of neoplastic progression		0			332		−332	−866 to −1
Consultation at outpatient department				0.02	5	1		
Esophagectomy				0.02	114	1		
Hospital stay (per day)				0.15	122	1		
Radiography of the abdomen				0.02	1	1		
Radiography of the thorax				0.02	1	1		
Echo abdomen				0.02	1	1		
Endoscopy EUS				0.07	82	2		
Endoscopy with dilatation				0.03	21	1		
Medication after neoplastic progression		3			75		−72	−112 to −37
Ranitidine + sucralfate (2 weeks after RFA)					4	5		
Esomeprazole	0.06	2	1	1.53	71	16		
Treatment of adverse events after neoplastic progression		0			109		−109	−209 to −9
Endoscopy with dilatation				0.03	21	2		
Radiography of the abdomen				0.03	1	2		
Consultation by telephone				0.04	1	3		
Hospital stay (per day)				0.03	85	7		
Subtotal (costs for treatment of neoplastic progression)		20			2693		−2673	−3865 to −1669

Mean volumes were averaged for 68 patients. N = number of patients who underwent procedure.
CI, confidence interval; *RFA*, radiofrequency ablation.

Cost-effectiveness ratios

On a per patient level, the reduction in risk of neoplastic progression of 25% for the ablation group resulted in an ICER of $11,267/0.25 = $45,068 (95% CI, $31,020-$82,625) per prevented event of neoplastic progression. When taking into account the costs for treatment of neoplastic progression, the average ICER dropped to $8593/0.25 = $34,372 (95% CI, $30,521-$69,004) per prevented event of neoplastic progression. The variability surrounding this estimate is illustrated in a cost-effectiveness plane (Fig. 1), which is derived from the bootstrap replications. The results from the bootstrapping procedure show that 100% of the bootstraps generated higher costs with more events of neoplastic progression prevented in case of ablation.

The probability of ablation being cost-effective increased with increasing willingness to pay as shown in Figure 2. If society would be willing to pay at least $51,664 per prevented event of neoplastic progression, or at least $40,915 when taking into account the downstream costs for treatment of neoplastic progression, then reimbursement of ablation is efficient in at least 75% of the patients with the indication.

TABLE 4. Total costs (mean) per patient excluding and including the downstream costs for treatment of neoplastic progression

	Ablation (n = 68)	Control (n = 68)	Difference (95% CI)	ICER (95% CI)
Events (%)	1.5	26.5	25.0 (14.1-35.9)	
Subcosts before neoplastic progression ($)	13,503	2236	11,267 (9996-12,378)	45,068 (31,021-82,625)
Total costs including treatment of neoplastic progression ($)	13,523	4930	8593 (6881-10,153)	34,372 (30,521-69,004)

ICER, Incremental cost-effectiveness ratio.

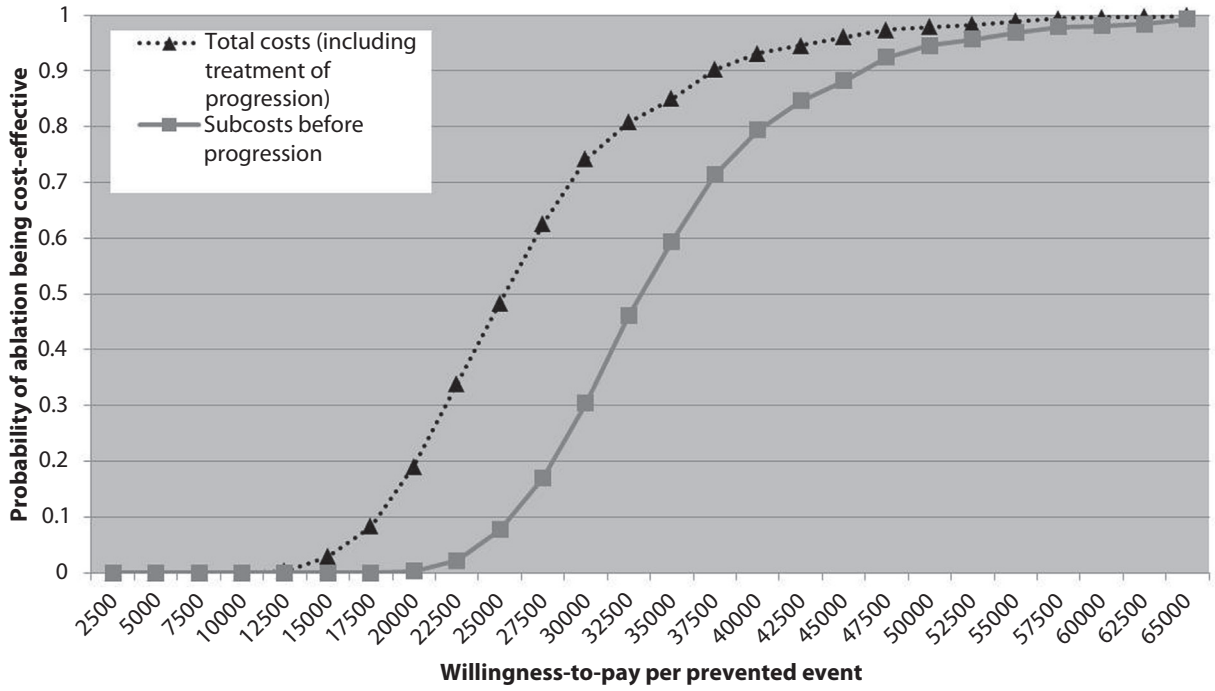

Figure 2. Probability of ablation being cost-effective, defined as the proportion of the incremental cost-effect pairs that are cost-effective for a given willingness-to-pay threshold.

DISCUSSION

The SURF trial demonstrated that, in patients with a confirmed diagnosis of LGD, ablation resulted in a reduced risk of neoplastic progression compared with standard endoscopic surveillance: during 3 years of follow-up, 1.5% of patients in the ablation group had neoplastic progression versus 26.5% of patients in the control group.[14] The current accompanying cost-effectiveness analysis shows that ablation is more expensive than endoscopic surveillance, resulting in a mean cost difference of $11,267 (95% CI, $9996-$12,378) or a mean cost difference of $8593 (95% CI, $6881-$10,153) when taking into account the downstream costs for treatment of neoplastic progression. The costs for treatment of neoplastic progression are also the most important determinant of the cost difference between the 2 groups. The ICER of the extra cost per prevented event of neoplastic progression was $45,068, or $34,372 when the costs for treatment of neoplastic progression were included. Furthermore, at a willingness to pay of $51,664 per prevented event of neoplastic progression, or $40,915 when taking into account the downstream costs of treatment of neoplastic progression, the probability of ablation being efficient equals 75%, which may provide a reasonable level of confidence for health care policy making.

The economic impact of radiofrequency ablation for eradication of BE with LGD has been addressed in a limited number of modeling studies.[12,13] Inadomi et al[12] compared different strategies, including endoscopic surveillance and radiofrequency ablation. In this analysis ablation for LGD was superior to endoscopic surveillance, although continued endoscopic follow-up after successful ablation was expensive. Recently, their Markov model was updated by Hur et al,[13] and only included radiofrequency ablation as an endoscopic treatment modality. Initial ablation for LGD was potentially cost-effective, with an ICER well below the willingness-to-pay threshold of $100,000/quality-adjusted life-year (QALY), compared with continued surveillance with radiofrequency ablation when high-grade

dysplasia was found. In this model, LGD was defined as a confirmed and stable (present on more than 1 endoscopy) disease. It should be noted that Hur et al were very conservative in selecting neoplastic progression rates for their model (0.19%-0.75% per year), whereas the annual neoplastic progression rate in the SURF trial was 11.8% per year. Because of the differences in patient populations and outcomes, it is not possible to compare the results of these 2 modeling studies with our patients. However, their results suggest that radiofrequency ablation is potentially cost-effective, depending on the selection of patients with LGD.

The current study provides the most direct evidence available concerning the cost-effectiveness of ablation as an integral part of a randomized trial investigating the optimal management strategy for confirmed LGD in BE. The reported costs, including the downstream costs for treatment of neoplastic progression, closely represent the nature of the endoscopic surveillance strategy, with endoscopic or surgical treatment when neoplastic progression is detected. In the SURF study, general quality-of-life data suitable for health evaluation were not obtained. It is therefore not possible to report cost-effectiveness in relation to QALYs. The use of QALYs is generally favored in economic studies because it enables comparison of interventions across different diseases and health conditions. However, the relatively short follow-up period of the SURF trial (<36 months) makes the chosen endpoint per avoided neoplastic progression relevant.

In our view, the increase in costs of ablation ($8593) in order to avoid an event such as progression to high-grade dysplasia and even EAC is justified. Ablation may therefore be recommended over endoscopic surveillance in patients with confirmed LGD, in particular because, in the future, the ICER for ablation as reported in this trial may decrease considerably for various reasons. First, in the SURF trial, most of the patients who progressed could be adequately treated by endoscopic means; however, one patient required esophagectomy for a poorly differentiated submucosal carcinoma, and a second patient required widespread endoscopic resection in 3 sessions for an extensive lesion.[14] The high number of patients in whom neoplasia was detected at an early and (endoscopically) curable stage reflects the strict quality criteria that were adhered to in the trial. In our view, endoscopic work-up, treatment, and follow-up of Barrett's neoplasia should therefore be restricted to centers with extensive expertise in this field. Under less optimal circumstances such as a community surveillance setting, neoplasia may progress to an advanced or incurable stage and hence be associated with higher rates of surgery or cancer-related death. This would increase the costs of the endoscopic surveillance strategy and favor the cost-effectiveness ratio for ablation. Second, in the control group of the SURF trial, patients underwent endoscopic surveillance at 6 and 12 months within the first year, with subsequent follow-up performed annually. Recent guidelines have recommended surveillance every 6 months instead of every 6 to 12 months for patients with confirmed LGD.[17] Implementing a surveillance interval of every 6 months will increase the costs of the endoscopic surveillance strategy compared with the current study. Third, this trial had a limited duration of observation (ie, restricted to 36 months). The cost-effectiveness of ablation is likely to be different when patients are evaluated over a longer period. One of the downsides of the radiofrequency ablation protocol are the high costs of therapy in the first year, which are mainly driven by the costs of disposables and the higher number of endoscopies. An increasing number of publications on the long-term efficacy show that radiofrequency ablation is durable in more than 90% of patients during follow-up.[6,18] The cost-effectiveness of ablation may therefore improve for a longer observation period if patients undergo follow-up endoscopies at a lower intensity after successful ablation compared with untreated patients. In opposition, any recurrence in the ablation arm after treatment could increase the costs for ablation, as re-treatment may be required. However, untreated patients may also still show neoplastic progression after the 36-month cut-off point as used in the current study. Fourth, the selection of patients with a reliable diagnosis of LGD remains difficult.[19-21] The observed rates of progression in our control group comports with the high progression rates from studies in which confirmation by an expert gastrointestinal pathologist was required. Even though a single confirmed diagnosis of LGD sufficed for inclusion in the SURF trial, 28% of patients in the control group had no dysplasia detected during follow-up. Other studies have reported similar rates of not reproducing the LGD diagnosis over time.[5,22] Treating such patients logically reduces the cost-effectiveness ratio given their lower risk of neoplastic progression. Insisting that a diagnosis of LGD is not only confirmed but also stable over time will improve the selection of patients for ablation and affect the cost-effectiveness of ablation.[13,17]

The current study has several limitations that need to be considered. One may argue that the current analysis is only applicable to centers in the Netherlands, although the cost calculations were performed in a European setting alongside the SURF trial. However, any provider can use our data on volumes of resources used to determine if ablation is cost-effective at their center. Unfortunately, because of the differences in payment systems between the United States and ours, our resources data cannot be used one on one to capture the results for a U.S. setting. Because this was not the intent nor within the scope of the current paper, a separate model and analysis would be needed. It is likely that both strategies will be more expensive in the United States because of the higher costs for medication and additional costs for

anesthesia care in comparison with the European setting. In addition, we conveniently chose a provider perspective for this cost-effectiveness analysis instead of a societal perspective based on readily available reliable costs and outcome data. We did not collect data on out-of-pocket expenses by patients, and costs of production loss due to sick leave from work, and general quality-of-life data suitable for health evaluation were not obtained. Further research should address these data requirements of a full economic evaluation from the societal perspective in order to enable priority setting in health care. However, the present analysis may support health care efficiency decisions within the field of oncologic gastroenterology.

CONCLUSIONS

This is the first cost-effectiveness analysis of ablation compared with endoscopic surveillance, based on the results from a large randomized trial. We demonstrate that ablation of patients with a confirmed diagnosis of LGD is more expensive than endoscopic surveillance, while significantly reducing the risk of neoplastic progression. The increase in costs of ablation ($8593) per patient can be justified to avoid a serious event such as neoplastic progression. At a willingness to pay of $40,915 per prevented event of progression, one can be reasonably certain (>75%) that ablation is efficient, which may be acceptable for society.

SURF study group

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APPENDIX 1

Volumes of resources used

Data on major use of health care resources from the randomization date until the end of follow-up (restricted to 36 months) were gathered principally from the study database. The case record forms were prospectively designed to capture all relevant information regarding the use of resources for the study procedures and for subsequent treatment of neoplastic progression. All recorded data were verified by independent study monitors who attended all study procedures.

Therapeutic endoscopies included the ablation procedure, endoscopic resection or argon plasma coagulation procedure, the use of disposables, histopathology analysis, consultation by telephone 3 days after any circumferential ablation and 2 weeks after each therapeutic endoscopy, and outpatient care after sedation with propofol. Surveillance endoscopies included surveillance endoscopy (control group) and the follow-up endoscopy (ablation group) with histopathology analysis, and consultation by telephone after 2 weeks. For adverse events during or after endoscopic procedures, the number of endoscopies for bleeding, dilatation, hospital stay (in days), consultations with the gastroenterology department, and radiology procedures were gathered from the case record form. The use of trial medication (ranitidine, sucralfate, and esomeprazole) was recorded. All medication was considered to be prescribed according to the trial protocol and to have been given at standard dosage. Treatment of neoplastic progression, the primary endpoint, included the volumes of diagnostic and therapeutic procedures, adverse events as described above, and surgery. Productivity losses related to any non-esophageal mortality or morbidity were not taken into account.

Unit costs

All unit costs and their sources for major health care components and procedures are shown in Table 1. Costs for the recruitment visit were not included as this was performed before randomization and patients were informed on both management strategies. Unit costs of therapeutic procedures and surveillance endoscopies were calculated from the 2012 financial accounts from the finance department of the Academic Medical Center Amsterdam. The unit costs of daycare admission were taken from the Dutch guideline for costing in health care research.[23] Expenditures for medication were priced according to the prices provided by the National Health Care Institute Netherlands (www.medicijnkosten.nl). For each unit cost of medication U.S.$8 was added for prescription costs. For costing purposes, we assumed that medication was prescribed according to the study protocol. We calculated the unit costs of esomeprazole per 3 months at a dosage of 40 mg twice daily, unit costs of ranitidine were calculated per 2 weeks at a dosage of 300 mg once daily, and unit costs of sucralfate were calculated per 2 weeks at a dosage of 1 g suspension 4 times a day. Unit costs for adverse events and surgical treatment of neoplastic progression were calculated from the 2012 financial accounts. The unit costs of a single hospital day (general ward) and the unit costs of a consultation at the outpatient department were taken from the Dutch guideline for costing in health care research.

SUPPLEMENTARY TABLE 1. Baseline characteristics of the patients

Characteristic	Ablation (n = 68)	Control (n = 68)
Age (years), mean ± standard deviation	63 ± 10	63 ± 9
Male sex, n (%)	55 (81)	61 (90)
White race, n (%)	66 (97)	66 (97)
Circumferential Barrett's esophagus, cm (range)	2 (0-6)	2 (1-4)
Maximum Barrett's esophagus, cm (range)	4 (2-8)	4 (3-6)