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ORIGINAL ARTICLE

Postlaryngectomy prosthetic voice rehabilitation outcomes in a consecutive cohort of 232 patients over a 13-year period

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Abstract

Background: With the increasing necessity for total laryngectomy (TL) after prior (chemo)radiotherapy, prosthetic vocal rehabilitation outcomes might have changed.

Methods: Retrospective cohort study including all patients laryngectomized between 2000 and 2012 with a voice prosthesis (VP) in the Netherlands Cancer Institute.

Results: Median device lifetimes of the standard Provox2 and Vega VPs are 63 and 66 days, respectively, and for the problem-solving ActiValve Light and Strong VPs 143 and 186 days, respectively. In multivariable analysis, salvage TL and TL for a dysfunctional larynx (compared to primary TL) were associated with a shorter device lifetime. Almost half of the patients (48%) experienced tracheoesophageal puncture tract-related problems, and this concerned 12% of all VP replacements.

Conclusions: Compared to historical cohorts, device lifetimes of regular Provox2 and Vega voice prostheses have decreased. Complications are not occurring more frequently but affect more patients. Nevertheless, the clinical reliability and validity of prosthetic voice rehabilitation is still sound.

KEYWORDS

complication management, device lifetime, total laryngectomy, voice prosthesis, voice rehabilitation

1 | INTRODUCTION

Since the first total laryngectomy (TL) for cancer, performed by Theodore Billroth in 1873, voice restoration has been considered the leading postlaryngectomy rehabilitation challenge.[1] The three main methods for restoring oral communication are esophageal, electrolarynx, and tracheoesophageal (TE) prosthetic speech. In 1973, Mozolewski et al[2] were the first to publish the results of a prosthetic device used in

24 patients, and in 1980, Singer and Blom[3] introduced the first commercial voice prosthesis (VP). With a success rate of around 90%, TE prosthetic speech has now become the method of choice for voice rehabilitation in most countries with an adequate health care insurance system.[4]

Besides the original Blom-Singer VP (InHealth Technologies, Carpinteria, CA, USA), a variety of prosthetic devices have been developed, for example, in the Netherlands, the Groningen button, the Nijdam VP, and Provox VPs (Atos Medical AB, Hörby, Sweden).[3,5–7] Median and/or mean device lifetime of these VPs have been reported to be around 3-6 months, and

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the main reason for replacement reportedly is transprosthetic leakage.[4,7] These studies have, however, been conducted in a time where primary TL was the gold standard in advanced larynx and hypopharynx cancer treatment. With the increasing use of radiotherapy (RT) and the introduction of chemoradiotherapy (CRT) in the 1990s, we have observed a decrease in primary TL and an increase in (C)RT as primary treatment modalities.[8] This has, however, also led to an increase in salvage TLs after failed (C)RT, which have been associated with more TE wall (TEP tract)-related problems and possibly a lower device lifetime of VPs.[9–11]

In 2000, Op de Coul et al[4] published the long-term results of voice rehabilitation with the first Provox VPs in the Netherlands Cancer Institute. Since then, several new generations of VPs have been developed, aimed at improving patient comfort, by, for example, improving airflow characteristics and replacement tools (Provox Vega), and at reducing biofilm overgrowth or inadvertent opening of the valve during swallowing or breathing (Provox ActiValve).[6,12–15] These new VP's have, however, not been extensively evaluated yet in a long-term fashion. Thus, in an era with an increasing necessity for salvage surgery and with the development of several new generations of VPs, the aim of this study was to evaluate our experience with the consistent use of several generations of VPs for voice rehabilitation in a large cohort of consecutively treated patients with TL. Our main outcome measures were the median device lifetime of the various VPs used in the study period, possible correlations with patient, tumor and treatment characteristics, indications for device-related and TEP tract-related VP replacement, and solutions for complications.

2 | METHODS

2.1 | Patient selection

We conducted a retrospective cohort study of all patients laryngectomized between January 2000 and December 2012 and in regular follow-up for voice rehabilitation in our hospital (n = 242). Patients, who never had a VP (n = 3) and patients whose medical files were (partially) missing were excluded (n = 7). This left 232 patients for further analysis.

We considered the following parameters: sex, age at TL, primary tumor site, TNM classification, primary treatment, indication for TL (primary, salvage, second primary, and dysfunctional larynx), surgical characteristics (eg, neck dissection and flap reconstruction), driving distance to the hospital, and survival status. To assess the driving distance in minutes by car to the hospital, we used Google Maps software and the postal codes of the patients. For each VP replacement, the following data were collected: date of insertion and replacement or removal, type and size of the VP, the reason for replacement or removal, and use of a washer for periprosthetic leakage. Last date of follow-up was set at

January 05, 2017. This study does not fall under the scope of the Medical Research Involving Human Subjects Act, which was confirmed by the institutional review board (MREC 17.0793).

2.2 | Statistical analysis

We consistently have described the results both on device level and on patient level. Descriptive analysis was used to summarize device and patient characteristics. Overall survival (OS) of the study population was calculated from time of TL to date of last follow-up (FU) or death, using Kaplan Meier analysis.

The main outcome measure of this study was the device lifetime of the VPs in days, measured as the time from insertion of the VP to the date of removal. Kaplan Meier analyses were used to assess the median device lifetimes. Lifetimes of the VPs ongoing at the end of the observation period were right censored as were lifetimes of VPs that were still in situ when the patient was lost to follow-up or died.

To assess the influence of several factors on the in situ time of the VPs, we used Cox proportional hazard models, with the replacement of the VP as the event of interest. For estimating the influence of *VP characteristics*, all analyzed VPs are treated as individual observations, with in situ time counted in days since insertion. However, in our Cox-model regressing the in situ time of the VP on the VP characteristic of interest, we stratify by patient. Hence, the underlying assumption is that VPs in different patients may have different baseline hazards for replacement (depending on the patient), while the effect of the VP characteristic (eg, ActiValve vs normal) on this hazard is the same across patients.

For estimating the influence of *patient and treatment characteristics* (eg, age), we address the fact that each patient can have multiple events (ie, VP replacements) by adopting the "Cox models for counting processes" framework of Andersen and Gill.[16] This means that the times of insertion and replacement of each VP are measured in days since the insertion of the *first* VP of the patient using it, thus ensuring that at every time point each of the 232 patients contributes at most one VP to the estimation of the relative hazards of replacement at that time point. In both type of models, VPs are censored if they were still in situ either at January 5th, 2017 or at the date of death or lost to follow-up of the patient.

Logistic regression analysis was used to identify patient and treatment characteristics that correlate with the patient having at least one VP replacement as a result of hypertrophy or infection. In the univariable analyses, a significance level of 10% (two sided) was used to determine whether a variable would be considered for inclusion in the multivariable models. Patient characteristics considered (both for their relation to device lifetime as for their relation to hypertrophy/infection) were age at time of TL, sex, (C)RT, origin of tumor, TNM classification, indication for TL, pharyngectomy,

reconstruction, neck dissection, and driving distance to the hospital. Moreover, an additional variable was used, which was based on whether or not a patient ever required an Acti-Valve during follow-up. Variables with known correlations between them (eg, TNM classification and indication for TL) were barred from entering the multivariate models together. SPSS Statistics 20.0 (IBM, Armonk, NY) and R-3.2 were used to conduct the analyses.[17]

3 | RESULTS

3.1 | Patient characteristics

Patient, tumor, and treatment details of the 232 patients in this study are summarized in Table 1. Mean age was 64 years (SD 10.8), the majority of patients had a larynx tumor (72%) and 68% had prior (chemo)radiotherapy. Only 12 patients (5%) did not receive RT somewhere during the course of their disease. The median OS was 35.9 months (95% CI 29.7-67.8). At the end of the study period, 53 patients were still alive with the VP in situ, 7 patients were alive without a VP in situ, 141 patients were deceased with the VP in situ, and 9 patients were deceased without the VP in situ. The remaining 22 were lost to follow-up with their VP in situ. Thus, in total, in 16 (7%) patients, the VP was definitively removed. Median follow-up time was 127 months (95% CI 117-144).

3.2 | Device lifetime

In total, 3319 VPs were used during the entire study period. VPs with an in situ time of 0 days (n = 92) were excluded from analysis because these mainly concerned replacements because of immediately noticed sizing errors. We excluded VPs replaced for developmental study purposes (n = 86), and sporadically used following types of VPs: Provox Vega XtraSeal (n = 16; introduced at the end of the study period), Provox1 (n = 4), and Provox ActiValve XtraStrong (n = 4), leaving 3117 VPs for the univariable and multivariable device lifetime analysis. During follow-up, 39 of the 232 patients never required VP replacement (17%): 33 died before any VP replacement was required, 5 were lost to follow-up with the first VP in situ, and in 1 patient, the first VP was removed shortly after the surgery because of a too wide TEP tract. This tract became a permanent voicing fistula, which the (gastric-feeding-tube dependent) patient refused to have closed because of her good voice.

The overall median device lifetime of the VPs used in the study period (ie, the regular Provox2 [n = 1664], Vega [n = 1136] prostheses, and the problem solving Provox ActiValve Light [n = 171] and Strong [n = 121]) together was 70 days (95% CI 67-73). The remaining 25 VPs were of "unknown type" (median device lifetime 66 days; 95% CI 27-106). Between the two regular VPs, there were no

significant differences: Provox2 (median 63 days, 95% CI 61-68) and Vega (median 66 days, 95% CI 63-71). The median device lifetime of the ActiValve VPs was significantly longer than that of the regular VPs: ActiValve Light 143 days (95% CI 111-211) and ActiValve Strong 186 days (95% CI 132-245; P value between regular VPs and both ActiValve VPs <.0001; see Figure 1 for the Kaplan-Meier curves).

The indication for using the "problem solving" Acti-Valve in our institution was a device lifetime of less than 2 months of the regular VPs.[14,18] There were 69 (30%) patients, who received at least one ActiValve during follow-up, and 163 (70%) patients, who never required an Acti-Valve. The median device lifetime of regular Provox2 and Vega VPs in the "non-ActiValve group" was 90 days (95% CI 84-96) and in the "ActiValve group" 54 days (95% CI 50-57; P value between groups < .0001; see Figure 1B). Of the 69 patients who ever received an ActiValve, 17 (25%) never had a TEP-tract-related problem, 33 (48%) had a TEP-tract-related problem prior to the first ActiValve insertion, and 19 (28%) developed such a problem after their first Acti-Valve insertion. The median time after TL of the first replacement required for a TEP-tract-related problem was 980 days (95% CI 718-1568), and the median time after TL to the first ActiValve insertion was 695 days (95% CI 537-1194).

Univariable and multivariable analyses for associations between device lifetime and clinical parameters are found in Table 2; in this analysis, a hazard ratio (HR) > 1 indicates a shorter device lifetime and a HR < 1 indicates a longer device lifetime. In univariable analysis, compared to a primary TL, salvage TL had a HR of 1.29 (95% CI 1.19-1.41; P < .0001), and TL for a dysfunctional larynx a HR of 1.26 (95% CI 1.10-1.45, P = 0.001). No significant difference in device lifetime was observed between patients with a primary TL and those with TL for a second primary. The median driving distance to the hospital by car was 26 minutes (range 7-124 minutes). There was a significant association between driving distance and device lifetime. Among the standard VPs, every extra 15 minutes driving time resulted in a HR of 0.92 (95% CI 0.90-0.94, P < .0001) in which a HR < 1 indicates a longer device lifetime. This effect was more profound in the standard VPs exchanged for TEP-tract related indications for replacements than for device related indications for replacement, a HR of 0.94 (95% CI 0.88-0.99, P = .047) and a HR of 0.97 (95% CI 0.95-0.99, P = .015) respectively. Multivariable analysis was carried out with the variables age at TL, indication for TL (primary, salvage, second primary, or dysfunctional) and driving distance to the hospital in minutes. This analysis confirmed that both driving distance and indication for TL were significantly associated with device lifetime. Every 15 minutes, increase in driving time reduced the hazard of VP replacement by a HR of 0.90 (95% CI 0.88-0.92, P < .0001).

TABLE 1 Patient, tumor and treatment details of all patients

	Number of patients (%)
Sex	
Men	185 (79%)
Women	48 (21%)
Mean age	63.5 (SD 10.8)
TNM classification	
Tis	2 (1%)
T1	34 (15%)
T2	51 (22%)
T3	49 (21%)
T4	88 (38%)
Tx	8 (3%)
N0	143 (62%)
N1	28 (12%)
N2	51 (22%)
N3	6 (3%)
Nx	4 (2%)
M0	232 (100%)
M1	0 (0%)
Primary tumor site	
Larynx	167 (72%)
Hypopharynx	31 (13%)
Oropharynx	21 (9%)
Miscellaneous	13 (6%)
Primary treatment	
RT	119 (51%)
CRT	38 (16%)
Other[a]	2 (0.9%)
TL with postoperative RT	58 (25%)
TL with postoperative CRT	5 (2%)
TL without postoperative (C)RT	10 (4.3%)
Indication TL	
Primary TL	73 (32%)
Salvage TL	107 (46%)
TL for second primary	28 (12%)
TL for dysfunctional larynx	24 (10%)
Pharyngectomy	
No (standard laryngectomy)	158 (68%)
Near total	47 (20%)
Circumferential	23 (10%)
Unknown	4 (2%)
Neck dissection during TL	
No	64 (28%)
Unilateral during TL	53 (23%)
Bilateral during TL	103 (44%)
Unknown	12 (5%)
Reconstruction	
No (primary closure)	143 (61%)
PM flap for reconstruction lumen	46 (20%)
PM flap for reinforcement	15 (6%)
FRFF	9 (4%)
Gastric pull-up	9 (4%)

(*Continues*)

TABLE 1 (Continued)

	Number of patients (%)
ALT	5 (2%)
LD	1 (0.4%)
Unknown	4 (2%)

Abbreviations: ALT, Antero-lateral thigh flap; CCRT, concomitant chemoradiation; FRFF, Free radial forearm flap; LD, Latissimus dorsi flap; PM, pectoralis major muscle; RT, radiotherapy; TL, total laryngectomy.
[a]One patient underwent CO2 laser therapy prior to TL and one patient was treated for thyroid cancer with radioactive iodine therapy.

The predictive value of age for device lifetime differed significantly between indications for TL. Using a subsequent cox-model with an interaction term between indication and age, we find the following effects of aging. Within patients with a primary TL or a salvage TL, elder patients tend to have longer device lifetimes than younger patients: HR per 10 years age increase 0.91 (95% CI 0.86-0.97, $P = .002$) and 0.95 (95% CI 0.90-0.99, $P = 0.03$), respectively, in line with what we found in the univariable analysis. For patients with a TL for a dysfunctional larynx however younger age corresponds with better device lifetime: HR per 10 years increase in age 1.21 (95% CI 1.02-1.42, $P = .03$). For patients with a second primary, there is no significant relation: HR 0.99 (95% CI 0.89-1.11, $P = .87$).

3.3 | Reasons for replacement

Reasons for replacement were assessed for 3133 VPs (the 3117 aforementioned VPs plus the 16 XtraSeal VPs, used to solve periprosthetic leakage issues; see Table 3). Patients could have multiple indications for replacement of their VP; therefore, the numbers add up to 3201 indications in 3133 VP replacements. The main reason for replacement was transprosthetic leakage: 1806 times (58%) in 174 patients (75%). For 368 VPs (12%) in 119 patients (51%), the indication for replacement was not documented; 113 of these 119 (95%) had previous replacements for transprosthetic leakage, and the reporting suggested that these replacements were quite likely standard replacements for transprosthetic leakage. This would total the replacements for transprosthetic leakage at 70%. Periprosthetic leakage was noted 266 times (9%) in 101 patients (44%). Periprosthetic leakage immediately solved by downsizing or by keeping the same size occurred in 154 VP replacements (58% of the 266 replacements for periprosthetic leakage) in 74 of the 101 patients experiencing this problem, see Figure 2. These replacements were not considered to be due to a TEP tract-related complication, but merely a result of the subsiding of the postsurgical TEP tract tissue swelling or gradual thinning of the trachea-esophageal wall.

3.4 | TEP tract-related reasons for replacement

The following issues were considered complicated TEP tract-related reasons for VP replacement or removal: Periprosthetic
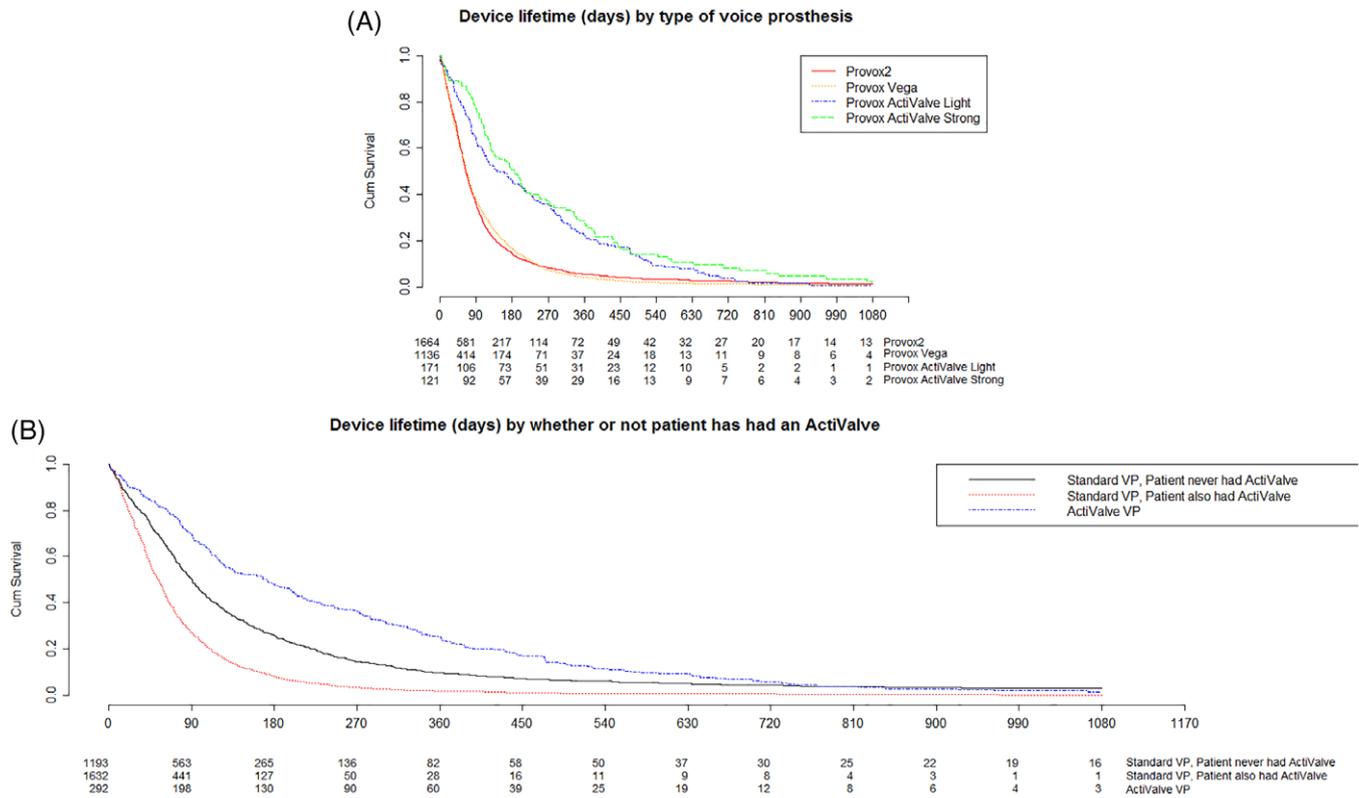
FIGURE 1 A) Kaplan Meier curve of device lifetime analyzed separately for the different VPs. B) The device lifetime for the standard VPs (Provox2 and Vega) grouped by whether or not these patients have ever had an ActiValve VP during follow-up and the device lifetime of the ActiValve VPs together [Color figure can be viewed at wileyonlinelibrary.com]

leakage not immediately solved by downsizing, TEP tract hypertrophy/infection, spontaneous VP loss, and need for shrinking and/or surgical closure of the TEP tract. The median device lifetime of VPs replaced due to TEP-tract related reasons was 48 days, which was significantly lower than replacement due to device related problems in which a median of 67 days could be observed ($P = .006$). However, the number of VPs replaced for TEP-tract related problems was only 371 whereas the number of VPs replaced for device related problems were 2540.

- Periprosthetic leakage not immediately solved by downsizing or keeping the same size occurred in 96 instances (36% of the 266 replacements for periprosthetic leakage) in 51 patients (22%). Twenty-five of 51 patients (49%) experienced this problem more than once. More details about VP replacement because of periprosthetic leakage and effects are summarized in Figure 2.
- Replacement of VP because of TEP tract hypertrophy/infection occurred 177 (6%) times in 70 patients (30%). In 60% of these patients, this occurred more than once. In 137 of 177 (77%) hypertrophy/infection-related replacements, a longer VP (n = 93) or a VP with the same/shorter size (n = 44) was successfully inserted. In 24 replacements (14%), this solution was not successful. Temporary removal of the VP because of hypertrophy/infection was needed 5 times (3%) with success n = 3, patient deceased n = 1, unsuccessful n = 1. The short-

term result of insertion of a longer VP or a VP with the same/shorter size was untraceable in nine replacements. Five patients died, three VPs were still in situ at final date of data collection and data was missing in one patient. In two patients, the outcome was unknown as they were lost to follow-up after replacement for hypertrophy/infection. In multivariable analysis of the relation between patient and treatment characteristics and hypertrophy/infection, the only significant relation found was that patients ever needing an ActiValve had a significant higher risk for also having TEP tract hypertrophy/infection (OR 5.02, 95% CI 2.72-9.25, $P < .0001$).

- VPs replaced because of spontaneous loss occurred 93 (3%) times in 41 (18%) patients. Twenty of these 41 patients experienced this problem more than once. In three patients, the VP was lost in the lower airway and had to be removed endoscopically. In two of these patients, this happened during a dilatation procedure for a pharyngeal stenosis.
- Shrinking of TEP was a reason for VP removal 34 (1%) times in 22 (10%) patients (in 13 patients once, in 6 patients twice, and in 3 patients three times). Shrinkage of the TEP-tract entails removal of the VP to allow for natural shrinkage of its diameter. This is usually applied for a few days in which the patient requires a cuffed cannula to prevent aspiration and a feeding tube.
- Lastly, nine (0.3%) VPs, in seven (3%) patients, were removed because of definitive closure of TEP tract (two

TABLE 2 Univariate and multivariate analysis for device lifetime

	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Age (per 10 years increase)	0.96	0.93-0.99	.013*	0.94	0.91-0.98	<.001*
Age (per 10 increase) within patients with indication for:						
Primary TL				0.91	0.86–0.97	.002 ‡
Salvage TL				0.95	0.90–0.99	.03 ‡
Second primary				0.99	0.89–1.11	.87 ‡
Dysfunctional larynx				1.21	1.02–1.42	.03 ‡
Sex (ref = male)	0.9998	0.90-1.11	0.996			
Origin tumor (ref = larynx)						
Hypopharynx	0.84	0.73-0.97	.020*			
Oropharynx	0.98	0.86-1.12	.79			
Micellaneous	1.25	1.08-1.45	.003*			
T-classification (ref = T1)						
T2	0.95	0.85-1.07	.42			
T3	1.03	0.92-1.15	.65			
T4	0.78	0.70-0.87	<.001*			
N-classification (ref = N0)						
N1	0.92	0.80-1.06	.24			
N2	1.05	0.95-1.15	.35			
N3	0.55	0.40-0.74	<.001*			
Indication TL (ref = primary TL)						
Salvage TL	1.29	1.19–1.41	<.001*	1.38	1.26-1.50	<.001 †
Second primary	1.06	0.94-1.21	.33	1.28	1.13-1.46	<.001 †
Dysfunctional larynx	1.26	1.10-1.45	.001*	1.31	1.14-1.51	<.001 †
Pharyngectomy type (ref = partial)						
Near total	0.91	0.82-1.00	.04*			
Circumferential	0.95	0.81-1.10	.49			
(Neo)-adjuvant treatment (ref = RT)						
None	0.86	0.72-1.03	.10			
CRT	0.93	0.84-1.04	.19			
Driving time to hospital (in minutes for standard VPs)						
Per 15 min increase	0.92	0.90-0.94	<.001*	0.90	0.88–0.92	<.001 ‡

Abbreviations: HR, hazard ratio; ref, reference variable. Note: HR > 1 means a shorter device lifetime; HR < 1 means a longer device lifetime. Note that in the multivariate analysis, we present the results from two multivariate models: We first constructed a simple model containing age at TL, indication for TL, and driving distance to the hospital (marked with †). In a subsequent cox model, we have used an interaction term between indication and age, to assess the effect of aging (marked with ‡).
*P value <.05.

patients had a secondary puncture and surgical closure for a second time). Four of the seven patients had earlier shrinking of TEP. In the remaining three patients, closure of TEP was performed because of severe dysphagia/stenosis, failure of speech rehabilitation, and severe hypertrophy/infection.

4 | DISCUSSION

The main outcome measure of this single institution study was the median device lifetime of all the VPs used during a 13-year assessment period in 232 consecutive TL patients. For the regular VPs Provox2 and Vega, this was 63 and 66 days, respectively, and for the problem-solving ActiValve Light and Strong VPs, this was 143 and 186 days,

respectively. The finding that the device lifetime of the regular VPs in the patients never requiring an ActiValve compared to those patients having required at least one such device is significantly longer (90 and 54 days, respectively) and is a logical consequence of the fact that ActiValve VPs are indicated for patients with a (too) short device lifetime.

The main indication for replacement, transprosthetic leakage, was reported in 58% of all replacements. In 12% of replacements, the exact reason was not reported, but the way of reporting suggested that these also were standard replacements for transprosthetic leakage. Thus, the actual incidence of transprosthetic leakage most likely is 70%, which is only slightly lower than the 73% reported in the earlier study from our Institute.[4]

The observed median device lifetime of 2 months for the regular VP is noticeably lower than observed in our

TABLE 3 Indications for replacement of 3133 VPs in 232 patients

Indication for replacement	VP, N (%)[a]	Patients, N (%)[a]
Transprosthetic leakage	1805 (58%)	174 (75%)
No reason reported	368 (12%)	119 (51%)
Inaccurate size	214 (7%)	112 (48%)
Voice problems	85 (3%)	49 (21%)
Dirty VP	31 (1%)	19 (8%)
Request patient	18 (0.6%)	12 (5%)
Logistic reasons	16 (0.5%)	14 (6%)
Increased pressure	16 (0.5%)	15 (7%)
Study purposes	56 (2%)	37 (16%)
Miscellaneous[b]	13 (0.4%)	12 (5%)
Periprosthetic leakage	266 (9%)	101 (44%)
Hypertrophy/infection	177 (6%)	70 (30%)
Spontaneous VP loss	93 (3%)	41 (18%)
Shrinking TEP	34 (1%)	22 (10%)
Closure TEP tract	9 (0.3%)	7 (3%)

[a] Patients could have multiple indications for replacement of their VP; therefore, the numbers add up to 3201 indications in 3133 VP replacements. Sometimes, it was difficult to determine the main indication for VP replacement, for example, in case of transprosthetic leakage and periprosthetic leakage, both are equally compulsory indications, and therefore both mentioned in this table. During follow-up, 39 patients never required VP replacement.

[b] Miscellaneous: replacements for Provox course (n = 7), second primary in the stoma region (n = 2), surgical revision of the tracheostoma (n = 2), secondary puncture (n = 1), and severe tracheitis (n = 1).

historical cohort.[4] This is in line with a recent study by Lewin et al[11] who showed a median device lifetime of 61 days and a study by Kress et al,[19] who observed a median of 74 days (including ActiValve VPs, which figure in our cohort was 70 days). Interestingly, if we compare the device lifetime of the non-ActiValve group of 90 days with that of our institutional historic cohort of 89 days, there is no clinically relevant difference.[4] The increase in device lifetime for the ActiValve VPs as compared to the regular VPs is, besides the active magnetic closure mechanism counteracting underpressure in the esophagus, probably also a result of the fluoroplastic material used in the ActiValve VPs, which are insusceptible to destruction by Candida species. Microbial biofilm formation on the valve by different Candida species is thought to be the main reason for transprosthetic leakage.[15]

The increasing number of TLs after prior (chemo)radiotherapy since 1990 (68% in the present study and 45% in our historical cohort[4]), which has a profound effect on the TEP-tract, seems a likely explanation for the shorter device lifetime found in our study population. However, just like in the study of Lewin et al[11] there was no significant effect of the extent of surgery or RT on device lifetime in the multivariable analysis. On the other hand, we did find an association with the indication for TL, with the primary TL patients having a longer device lifetime than salvage TL patients. In our previous study, we found such a difference between nonradiated patients and patients ever receiving RT[4]; but, in the present study, the number of nonirradiated patients was too low for meaningful statistical analysis.

Another explanation for the shorter device lifetime found in recent studies might be the ease of replacement. In the study performed by Op de Coul et al,[4] the uncomfortable method of retrograde placement was still used. With the introduction of the Provox2 in 1997 anterograde replacement became available. This has lowered the threshold for patients to ask for a replacement in case of minor leakage, which they otherwise might have accepted somewhat longer.[20,21]

Despite the increasing number of TLs performed after prior (C)RT since 1990 the clinical reliability and validity of
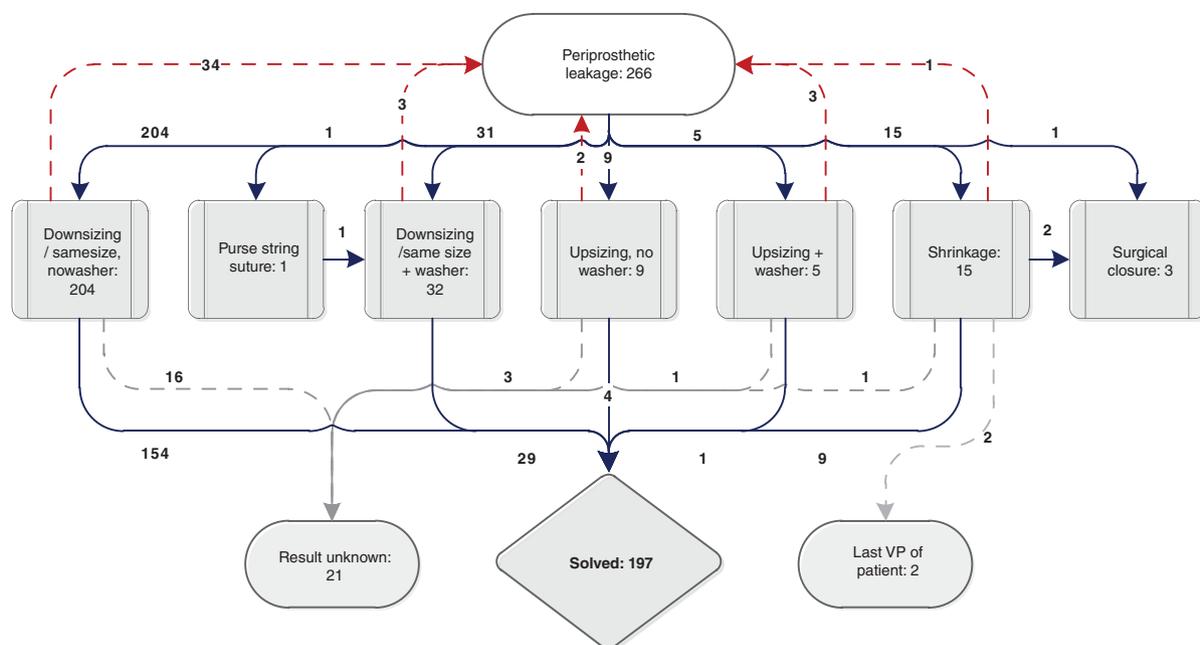

FIGURE 2 This figure illustrates the complex pathways of VP problem solving, in this case, periprosthetic leakage. As can be seen in this figure, 204 VPs were replaced with either the same or a smaller size, which was effective in 154 and not effective in 34 replacements. The result was undocumented for 16 VPs. The 34 VPs entered the flowchart again. Finally, it resulted in three surgical closures [Color figure can be viewed at wileyonlinelibrary.com]

prosthetic voice rehabilitation is still sound. In the present cohort with a median follow-up time of over 10 years 7% of the patients were not able to keep their VP, and this figure was 5% with a median follow-up time of over 6 years in our historical cohort.[4] This figure compares favorably with the 12% after 1 year in a recent study from Germany.[22]

An interesting aspect of the present study is that we were able to analyze different types of VPs in the same patient over a prolonged period of time. This concerns the role of the special problem-solving VPs Provox ActiValve Light and Strong in comparison to the regular VPs (Provox2 and Vega). As mentioned before, the main reason to select an ActiValve somewhere during follow-up was a short device lifetime of the regular VP. Interestingly, however, this Acti-Valve cohort apparently also suffers significantly more from TEP tract hypertrophy/infection, as was found in the multi-variable analysis of these latter problems. The finding that in more than a quarter of these patients the TEP tract-related problems develop after the first ActiValve insertion is inter-esting. It might suggest that in some patients short device lifetime is also a sign of co-morbidity, just like TEP tract-related issues, that is, reflux and pharyngeal stenosis.[10,23,24] As these comorbidities are treatable, shortening of the device life might be a reason to start an intervention (dilatation or proton pump inhibitor (PPI) treatment). Especially of interest in this respect is the study of Lorenz et al,[25] where these authors found that device lifetime was significantly associated with reflux. Likewise, Boscolo-Rizzo et al[10] demonstrated a mean device lifetime of 127 days for patients with endoscopic evidence of gastroesophageal reflux disease vs 216 days for patients without. Because of the retrospective nature of our study, we were unable to reliably assess presence or absence of reflux in our cohort. However, this correlation between short device lifetime/ActiValve use and TEP tract-related problems suggests that a shortened device life-time (the first ActiValve was inserted after a median of 695 days, roughly two and a half years) as such already might be a sign of reflux. And if so, treatment with PPIs in patients not yet suffering from TEP tract-related problems could be considered to improve device lifetime before choosing an expensive specialty VP, such as the ActiValve. This comorbidity effect should be assessed in future studies, where confounding variables and possible shift in comorbidities and medication are prospectively documented.

Contrary to the decreasing device lifetime observed in our cohort and in other western countries, some studies from low-income countries report device lifetimes of up to 17-months average.[26] An explanation might be the financial challenges prosthetic voice rehabilitation imposes on patients. In our cohort, all patients received reimbursement for their VP, thus a socio-economic bias can be ruled out, similar to, for example, the study population of Kress et al. from Germany.[19] Therefore, we believe that, in the absence of economic issues, these results are more representative for the

actual device lifetime of VPs. Furthermore, the relatively close distance patients have to the nearest hospital, makes a visit for a replacement less of a burden in comparison to countries such as Australia, where this might be a delaying problem and indeed longer device lifetimes are observed.[27]

However, much to our surprise even in our cohort where patients live relatively close to the hospital with a median of 26 minutes driving time, we observed a highly significant relation between longer driving time to the hospital and lon-ger device lifetime for the standard VP. This effect was more profound in the TEP-tract related indications for replace-ments. This might suggest that patients recognize TEP-tract complications less easily than simple transprosthetic leakage as a reason to visit the hospital. Overall, with driving time to the hospital being a very significant factor in device lifetime, even in the multivariable analysis, when confirmed in other studies, distance to the hospital should to be taken into account when reporting device life times in future studies.

4.1 | Limitations

The previous study from our institute had a prospective char-acter, because before 2000, at each VP replacement, a special registration form was used to collect relevant data regarding reason for replacement and voice quality.[4] After 2000, how-ever, "registration" was done in the regular patient files. This led, as in many retrospective studies, to missing data and, for example, in 12% of cases, no reason for replacement was noted. In part, this problem could be solved by looking at the notes of the preceding and following replacement event. Another interesting piece of information missing in the pre-sent study is the voice quality assessment and use of VP for communication. This should be assessed in future studies.

5 | CONCLUSION

In conclusion, we report the results of prosthetic vocal reha-bilitation in a cohort of consecutively treated patients from one institute undergoing TL for any indication. Thereby it represents an unbiased and unselected study group and is one of the larger series in literature. In our cohort, we found an overall median device lifetime of 70 days. The median device lifetime of the regular Provox2 (63 days) and Vega (66 days) VPs was significantly shorter than that of the problem solving ActiValve Light (143 days) and Strong (186 days) VPs. The median device lifetime of the regular VPs was significantly longer in the cohort of patients never requiring an ActiValve (90 days) than that in the patients needing at least one ActiValve (54 days). This latter cohort also had a significantly higher risk for TEP tract-related problems (hypertrophy/infection). Main reason for replace-ment remained transprosthetic leakage (70%). However, with 12% of the replacements in almost half of the patients, TEP tract-related issues still form an important factor to take into

account when performing prosthetic voice rehabilitation. Fortunately, in most patients, these TEP tract problems can be solved. We found no difference in patients treated with RT vs those treated with chemoradiation. Despite the increased numbers of patients requiring TL for salvage, with 93% of the patients maintaining their VP long term, prosthetic voice rehabilitation is still a highly successful and manageable method to restore oral communication after TL.

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