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HEAD AND NECK

Long-term outcomes and cost-effectiveness of a magnet-based valve voice prosthesis for endoprosthesis leakage treatment

Miguel Mayo-Yáñez[1,2,3] · Carlos Chiesa-Estomba[3,4] · Jérôme R. Lechien[3,5,6] · Christian Calvo-Henríquez[2,3,7] · Luigi A. Vaira[3,8] · Irma Cabo-Varela[1]

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Abstract

Purpose Tracheoesophageal speech is considered the gold standard for rehabilitation following total laryngectomy. The main reason of voice prosthesis failure is the endoprosthesis leakage. Provox ActiValve® incorporates a magnet-based valve system to achieve active closure of the valve to treat these leakages, with the drawback of being significantly more expensive. The aim of the study was to compare the Provox Vega® and Provox ActiValve® duration and costs in patients with replacements increase due to endoprosthetic leakage.

Methods Prospective case-crossover study in laryngectomized patients with Provox Vega® and endoprosthesis leakage to whom a Provox ActiValve® was placed. Survival and possible factors that affect voice prosthesis were studied using Kaplan–Meier curves and Cox Proportional Hazards Regression. Cost-effectiveness analysis from the perspective of the Spanish Public National Health System with incremental cost-effectiveness calculation was performed.

Results A total of 159 prostheses were evaluated. The most frequent reason for replacement was the endoprosthesis leakage ($N = 129$; 83.77%) in both models. The mean duration-time of Provox Vega® was 44.77 ± 2.82 days (CI 95%, 39.18–50.35; median 36 days), and 317.34 ± 116.8 days (CI 95% 86.66–548; median 286 days) for the Provox ActiValve® ($p < 0.000$). For every replacement not made thanks to the Provox ActiValve® there was saving of 133.97€

Conclusions The Provox ActiValve® is a cost-effective solution in patients with increased prosthesis replacements due to endoprosthetic leakage, reducing the number of changes and cost compared to Provox Vega®.

Keywords Tracheoesophageal voice prosthesis · Endoprosthesis leakage · Device duration · Laryngectomy · Provox ActiValve · Provox Vega

✉ Miguel Mayo-Yáñez
miguel.mayo.yanez@sergas.es

1 Otorhinolaryngology-Head and Neck Surgery Department, Complexo Hospitalario Universitario A Coruña (CHUAC), As Xubias 84, 15006 A Coruña, Galicia, Spain

2 Clinical Research in Medicine, International Center for Doctorate and Advanced Studies (CIEDUS), Universidade de Santiago de Compostela (USC), 15782 Santiago de Compostela, Galicia, Spain

3 Young-Otolaryngologists of the International Federations of Oto-Rhino-Laryngological Societies (YO-IFOS) Study Group, Paris, France

4 Otorhinolaryngology-Head and Neck Surgery Department, Hospital Universitario Donostia, 20014 Donostia, Euskadi, Spain

5 Otolaryngology Department, Elsan Hospital, Paris, France

6 Otorhinolaryngology and Head and Neck Surgery Department, Foch Hospital, Paris Saclay University, Paris, France

7 Otorhinolaryngology-Head and Neck Surgery Department, Complexo Hospitalario Universitario Santiago de Compostela (CHUS), 15706 Santiago de Compostela, Galicia, Spain

8 Maxillofacial Surgery Operative Unit, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Introduction

Tracheoesophageal voice is considered the treatment of choice to rehabilitate patients following total laryngectomy [1]. The continuous development and sophistication of voice prosthesis (VP) has made it possible to obtain a significant better outcomes for fundamental frequency, maximum phonation time and intensity compared to esophageal or electrolarynx speech [2]. The VP are not permanent implants and need to be replaced, usually after a period of 2–3 months.[3]

Endoprosthesis leakage is the most frequently reported indication for replacing these devices [3–5]. One of the possible causes is an inadvertent opening of the valve during swallowing and/or deep inhalation. This phenomenon can be observed by anterograde inspection of the prosthesis via the stoma, while the patient is swallowing or inhaling deeply. Most probably both maneuvers cause an "under-pressure" in the esophagus, either by swallowing as such, or by the creation of a negative intra-thoracic pressure during deep inhalation [6]. These observations have stimulated the development of a special problem-solving VP, involving a change towards magnet-based valve system to achieve active closure of the valve. This feature result in a resistance against the inadvertent opening of the valve caused by an under-pressure during swallowing and/or deep inhalation. An example of this is the Provox ActiValve® (Atos Medical®, Hörby, Sweden) [7], which has been shown to significantly increase device life over traditional indwelling devices [4, 5, 8]. While the Provox Vega® is one-way valve made out of medical-grade silicone rubber and a radiopaque fluoroplastic optimized to improve airflow characteristics, the Provox ActiValve® contains a valve made of Candida-resistant Teflon-like fluoroplastic and magnets that allow to actively close [7].

Despite its good results, one of the barriers to adopt the Provox ActiValve® is the fact that it is significantly more expensive than traditional VP [5, 9]. To date, studies have compared the Provox ActiValve® with the Provox 2® or models from other brands [4, 5, 8, 9], but there is no cost and/or outcome analysis against the standard VP at present for vocal rehabilitation, the Provox Vega® [10]. The aim of the study is to compare the Provox Vega® and Provox ActiValve® duration in patients with a replacements increase due to endoprosthetic leakage and to analyze the costs of using this type of VP.

Methods

Study design

A prospective cross-over observational study was conducted. In the study, subjects acted as their own control to limit bias and provide a valid control interval. These studies, which focus on the moment in which the event occurs, try to answer the question of whether there has been something unusual that has favoured the event. For which, only cases are selected and the exposures are compared immediately before of the event with those of other previous moments, which serve as control. In this way, controlling all those confounding factors that remain stable throughout the study and avoiding biases in the selection of controls [11].

Patients were recruited from the departments of an Otorhinolaryngology—Head and Neck Surgery Department of a tertiary hospital. All laryngectomized patients are under prospective follow-up in a database in which VP changes and failure causes are collected (Fig. 1) [3, 12]. The selection of the volunteer participants, all of them users of Provox Vega®, was through they fulfilled the following criteria: were

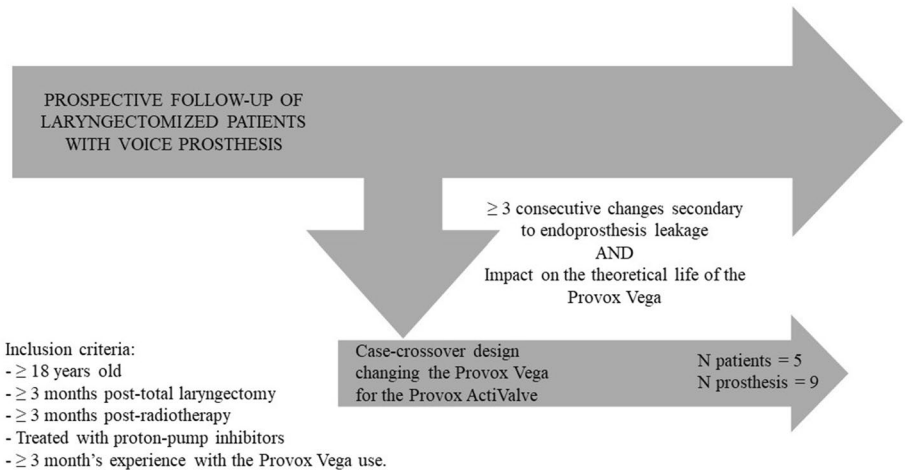

Fig. 1 Scheme of patient selection

over 18 years, at least 3 month post-total laryngectomy, at least 3 month post-radiotherapy or chemotherapy in the case of having received this type of treatment, at least 3 years of follow-up, being treated with proton–pump inhibitors, and had at least 3 month experience with the Provox Vega® use. Subjects were excluded on the basis of prior medical problems preventing Provox use, recurrent or metastatic disease, use of another phonation method instead of the VP, functional incapacity to clean the VP independently, inability to understand or provide informed consent, impaired cognitive ability, or regular use of any type of cannula. This research involved human participants and was approved by the Hospital's Ethics Committee. Informed consent was obtained from all individual participants included in the study.

All patients had an anterograde insertion of the vocal prosthesis, and speech was evaluated, while patients performed digital occlusion of the stoma via a heat and moisture exchanger device. The assessment of patients was made by an otolaryngologist and a speech therapist in relation to cause of leakage and related complications. The prostheses were prescribed and used in accordance with the manufacturer's recommendations, being the ActiValve use criteria an increase in the number of replacements of the Provox Vega® secondary to endoprosthesis leakage consecutively and having an impact on the theoretical life of the VP, based on previous literature [3, 10].

Statistical analysis

Statistical analysis was performed with Stata® 14.2 for Windows (StataCorp, College Station, TX, USA). Statistical tests were two-tailed with a 95% confidence interval. Normality was evaluated by the Kolmogorov–Smirnov test and variances using the Levene test. Quantitative variables were expressed as mean ± standard deviation (SD) and median. The comparison of means or medians between groups was performed using the Student's *t*, Mann–Whitney, ANOVA or Kruskal–Wallis test as appropriate. Qualitative variables were expressed as frequency and percentage. The differences between groups were evaluated by the chi-square test, Fisher's exact test or its variants as appropriate. Survival and possible factors that affect VP were studied using Kaplan–Meier curves and Cox Proportional-Hazards Regression with Schoenfeld residuals to test the possible assumptions. Duration of the VP ongoing at the end of the observation period were right censored as were duration of VPs that were still in situ when the patient was lost to follow-up or died. The model was conducted with the replacement of the VP as the event of interest. 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. Independent variables were: age, sex, type of puncture, pT-stage, pN-stage, tumor location, tumor stage, neck dissection or complementary treatment with radiotherapy or chemotherapy.

Cost-effectiveness analysis

The cost-effectiveness analysis (ACE) was carried out from the perspective of the Spanish Public National Health System for the year 2021 [13]. The cost of each Provox Vega® was 363€, and of each Provox ActiValve® was 1,757.47€. The effectiveness of the treatment was estimated based on the number of annual VP replacements and according to the follow-up length. This ratio was compared with the expected duration for Provox Vega® (2.94 changes per year) according to the existing literature [3, 12]. Finally the incremental cost-effectiveness (ICE) was obtained [13].

To be able to extrapolate the results to other settings/countries, the indirect costs of diagnosis and patient care were not considered, because each center uses a different care protocol (replacement only in scheduled consultation, possibility of emergency replacement, multidisciplinary assessment of the patient, etc.) that would distort the real effect of Provox ActiValve® use [14].

Results

Descriptive analysis

A total of 5 Caucasian men, with a mean follow-up of 5.24 years (range 4.04–6.57), were selected. The mean age was 63.84 ± 0.38 years. The majority of tracheoesophageal punctures (64.5%) were primary. The most frequent localization of the primary tumor was supraglottic with 3 (60%) patients, follow by glottic and hypopharyngeal ($N=1$;20%, each). Neck dissection was performed in all the patients, 20% unilateral and 80% bilateral, with bilateral functional dissection being the most frequently (75%). The 60% ($N=3$) of patients received adjuvant treatment with radiotherapy and 1 also with chemotherapy. In no case reconstruction with flap for pharyngeal closure was necessary.

Replacement reasons

A total of 159 prostheses were evaluated, 150 (94.34%) Provox Vega® and 9 (5.66%) Provox ActiValve®, with a total of 154 replacements (Table 1). The most frequent reason for replacement in both types of VP was an endoprosthesis leak ($N=129$; 83.77%). All replacement reasons were documented. Differences were found in the distribution of replacement reasons according to the type of prosthesis

Table 1 Prosthesis replacement reasons

	Total *N* (%)	Provox Vega *N* (%)	Provox ActiValve *N* (%)
Endoprosthetic	129 (83.77)	125 (85.62)	4 (50)
Periprosthetic	9 (5.84)	9 (6.16)	0
Extrusion	12 (7.79)	8 (5.48)	4 (50)
Fungic colonization	1 (0.65)	1 (0.68)	0
Peri + endoprosthetic	3 (1.95)	3 (2.05)	0
Total	154	146	8

N number

Table 2 Multivariate Cox Proportional-Hazards Regression final model

Variables	HR	SE	*p* value	95% CI	
Provox ActiValve	0.12	0.06	**< 0.001**	0.04	0.33
Type of puncture					
Primary	Reference				
Secondary	0.56	0.13	**0.013**	0.35	0.88
RT	2.14	0.61	**0.008**	1.22	3.73
Type of neck dissection					
Unilateral	Reference				
Bilateral	0.55	0.15	**0.026**	0.32	0.93
Age	0.94	0.02	**0.004**	0.90	0.98

Bold indicates statistically significant values

HR Hazard Ratio, *SE* Standard Error, *95% CI* 95% Confidence Interval, *VP* Voice prosthesis, *RT* radiotherapy treatment

($p = 0.008$) or the adjuvant treatment with radiotherapy ($p = 0.000$), but not depending on the type of puncture ($p = 0.461$).

Multivariate Cox Proportional-Hazards Regression analysis

After likelihood ratio test and confounding factors were identified. The final model included the type of prosthesis, the age, the complementary radiotherapy treatment, the type of puncture and the type of neck dissection variables (Table 2). The type of prosthesis ($p < 0.001$), with lower risk of replacement with the Provox ActiValve® (HR = 0.34;95% CI 0.2–0.56), the bilateral neck dissection ($p = 0.026$), the type of puncture ($p = 0.013$) and the patient's age ($p = 0.004$), seems to decrease the risk of VP replacement. The complementary treatment with radiotherapy increases the risk of VP replacement (HR = 2.14; $p = 0.008$).

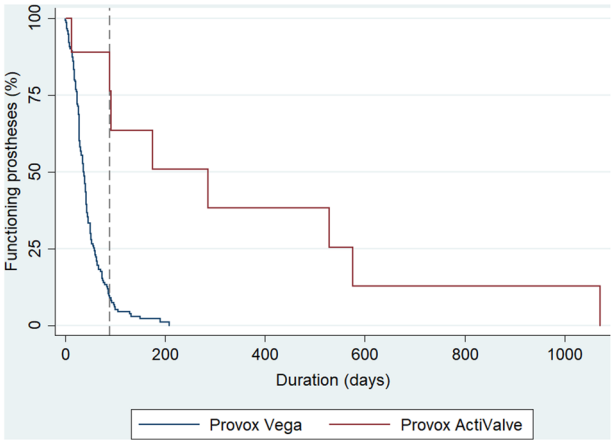

Fig. 2 Duration-time analysis based on prosthesis type. The dotted line marks the 3 month benchmark

Table 3 Cost-effectiveness analysis in Spanish Public National Health System

	Provox Vega	Provox ActiValve
Changes per year		
Predicted [3, 12]	2.94	2.94
Outcome	8.16	1.15
Effectiveness	−5.22	1.79
	7.01	
Price (€)		
Predicted [3, 12]	1067.60	5168.82
Outcome	2961.71	2022.84
Difference	1894.10	−3145.98
	−938.86	
Mean cost-effectiveness (MCE)	−567.60 €	1130.04 €
Incremental cost-effectiveness (ICE)	**−133.97** €	

Bold indicates statistically significant values

VP duration analysis

The mean duration-time of Provox Vega® was 44.77 ± 2.82 days (CI 95% 39.18–50.35; median 36 days), and 317.34 ± 116.8 days (CI 95% 86.66–548; median 286 days) for the Provox ActiValve® ($p < 0.000$). It was estimated that 92% (CI 95% 0.87–0.96) of the Provox Vega® failed within 90 days after being placed, compared to 33% (CI 95% 0.12–0.72) of the Provox ActiValve® (Fig. 2). Based on the results of the Cox model, a stratified survival analysis according to the complementary treatment with radiotherapy did not demonstrated differences in VP duration ($p = 0.437$).

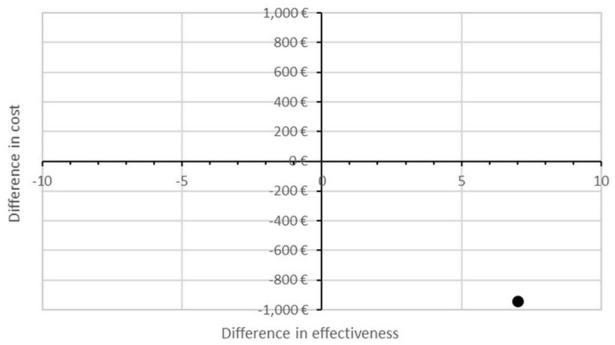

Fig. 3 Cost-effectiveness plane. Note the position of the Provox ActiValve® intervention in area II (more effective and less expensive interventions)

Cost-effectiveness analysis

The annual replacement rates of the VP were 8.16 for the Provox Vega, and 1.15 for the Provox ActiValve® (Table 3). This represents an increase of 5.22 times the expected for the Provox Vega® and a decrease of 1.79 times in the case of the Provox ActiValve®. There was a 7.01 increase in effectiveness when using the Provox ActiValve® and a price difference of 938.86€ (Fig. 3). Therefore, for every replacement not made thanks to the Provox ActiValve® there was a saving of 133.97€ (ICE).

Discussion

The Provox Vega® offers a higher quality of voice (louder, longer phonation, better intelligibility and higher patient satisfaction) and durability in respect to its predecessors [1–3]. Despite this, the main cause of failure continues to be endoprosthetic leakage [15], which has caused the appearance of new solutions to reduce this problem. The aim of the study was to compare the device duration between the Provox Vega® and Provox ActiValve® in patients with endoprosthetic leakage problems and to evaluate the cost of its use possible. This study is the first one found in the literature that compares these two types of prostheses [4, 5, 8, 9, 15, 16].

Authors reported that the median device life-time of the Provox is between 66 and 75 days [3, 12, 16]. These results may be altered in certain patients with associated morbidities, such as complementary treatment with radiotherapy [17], or with an under-pressure during swallowing and/or deep inhalation [4, 5]. The influence of radiotherapy treatment has been widely studied over prosthetic device life and the onset of tracheoesophageal fistula-related pathologies, increasing the rigidity and decreasing the thickness of the tracheal wall, what could favour the appearance of this under-pressure.[17–19] The data found in our study does not differ in this sense, causing a decrease in the expected duration by half (36 days) and an endoprosthesis leakage. The most noteworthy of the results obtained is the mean-life time achieved with the Provox ActiValve®, assuming a day increase of 8 times without the need for replacement in patients with endoprosthetic leakage compared to the Provox Vega®, and reducing the expected costs in these patients. These results are consistent with previous ones in the literature [4, 5].

Considering the reasons for replacement of the Provox ActiValve®, it is noteworthy that 50% are due to extrusion, a cause usually relegated to a minimum percentage of the replacement causes [3, 16, 20, 21]. Analyzing the episodes, seems to be secondary to the VP long duration, which would cause a foreign body reaction, with the consequent inflammation of the fistula and extrusion of the VP or pressure lesion production. Other factors that seem to be associated with a lower risk of replacement are age or bilateral emptying. Both previously reported in the literature [3, 16].

The second most frequent cause of Provox Vega® replacement is the periprosthetic leak, but in a smaller proportion than in previous studies [3, 15, 16]. This suggests that the selection of patients in this study has been accurate, the main problem being endoprosthetic leakage. Other strengths of this study are that all the reasons of VP changes were collected, the ample time of follow-up, the prospective nature of the study, and the multidisciplinary and personalized assessment of the patients [3, 14, 22]. Among the limitations is the small number of participating patients or Provox ActiValve® used. This is explained by the strict criteria for the placement of this type of prosthesis, their long duration, and their high costs never before evaluated in patients with Provox Vega®. Another limitation lies in the use of the cost-effectiveness study, normally criticized for the parameters chosen as effectiveness rather than for the economic process carried out, due to the subjectivity found when defining measures of effectiveness [23]. It could be complement it in the future with a cost–utility study, to present the results in a widely known and used effectiveness unit, such as quality-adjusted life year [24]. Although an attempt has been made to mitigate this effect in the study, the results obtained can hardly be extrapolated according to the living conditions of each country.

Conclusion

This is the first study with a prospective case-crossover design assessing Provox Vega® and Provox ActiValve® with a large follow-up, a multivariate regression analysis and a cost-effectiveness analysis. The results proved the significant

differences in terms of prothesis duration between Provox Vega® and Provox ActiValve®, as well as its use is more effective and less expensive. These findings support the use of Provox ActiValve® in patients with increased prosthesis replacements due to endoprosthetic leakage, to reduce the number of changes and cost.

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