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Keynote 8: 29-07 14.00-14.30

Postlaryngectomy Rehabilitation in this Era of Increasing Organ Preservation Treatment

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Disclosure Statement

- The Netherlands Cancer Institute receives a Research Grant (RG) from Atos Medical Sweden, which contributes to the existing infrastructure for health-related quality of life research of the department of Head and Neck Oncology and Surgery
- All reported research, including studies carried out in relation to this RG, has been approved by the institutional Medical Ethical Review Board

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Postlaryngectomy Rehabilitation in this Era of Increasing Organ Preservation Treatment

At the last WCLC in 1994

- TL was still the preferred treatment option for advanced larynx cancer, although the first organ preservation studies (VA and EORTC) started a paradigm shift
- Tracheoesophageal voice rehabilitation was well on its way to become the gold standard for restoring oral communication after TL, 21 and 14 years after the publication of functioning voice prostheses by Mozolewski in Poland (1973) and Singer and Blom (1979)

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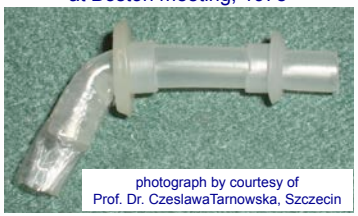
Start of present prosthetic voice rehabilitation history*

Mozolewski 1973*, presented at Boston meeting, 1978



photograph by courtesy of Prof. Dr. CzeslawaTarnowska, Szczecin

* Mozolewski E, Zietek E, Jach K. Surgical rehabilitation of voice and speech after laryngectomy. Pol Med Sci Hist Bull. 1973;15: 373-377

Singer-Blom 1980**

** Singer MI, Blom ED. An endoscopic technique for restoration of voice after laryngectomy. Ann ORL. 1980; 89: 529-533.

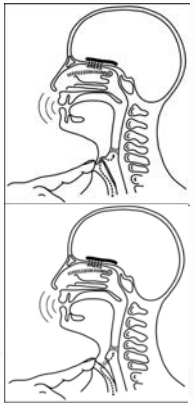
*Bień S et al. Laryngoscope. 2008; Hilgers, van den Brekel. 2008/15; 5th/6th edition Cummings' textbook)

VP development in the first decade/eighties

- Difference in preference of type of VP :
  - non-indwelling BI-S/Panje devices (USA/UK/Australia)
  - indwelling devices (Groningen/Traissac/Nijdam/Provox) in Europe
- Difference in TEP approach
  - primary TEP + direct VP fit (Groningen/Provox)
  - primary TEP + stenting + delayed VP insertion (BI-S)
- Focus on perceptual, acoustic and clinical research showing better voice quality and easier acquisition of TE than of E speech
- Identification of hypertonicity pathophysiology as main reason for failing to acquire fluent TE (and probably also E) speech (Singer-Blom, 1981)
- First identification of complex biofilm formation (bacteria + yeast) as major culprit of decreased VP device life (Mahieu et al. 1986)

Postlaryngectomy surgical and prosthetic vocal rehabilitation in the Netherlands Cancer Institute

- Staffieri's procedure[1] 1979-80
- Non-indwelling prostheses: to be handled by the patient
  - Blom-Singer[2] 1980
  - Panje[3] 1980
- Indwelling prostheses: to be handled by the clinician
  - Groningen[4] 1980-88
  - Provox[5] 1988-



[1] Staffieri et al. Laryngol Rhinol Otol (Stuttg). 1978
[2] Singer and Blom. Ann Otol Rhinol Laryngol 1980
[3] Panje Ann Otol Rhinol Laryngol. 1981
[4] Annyas et al. Clin Otolaryngol Allied Sci. 1984
[5] Hilgers & Schouwenburg. Laryngoscope 1990

Rationale for preference of indwelling voice prostheses in Europe (e.g. Groningen, Provox) instead of non-indwelling devices in USA/UK/Australia (e.g. Blom-Singer, Panje)

- Advantages
  - Designed to be inserted immediately at TEP, allowing primary placement
  - No replacement required by patient
  - Shorter learning curve and little dexterity needed for daily care
  - More robust design: longer device life
  - With increasing age (loss of dexterity/visual acuity) still applicable
- Disadvantage
  - Patients stays dependent of clinician, but non-indwelling device patients also regularly require clinician's help and device aspirations are more frequent than with indwelling devices

* Hancock K, Houghton B, Van As-Brooks CJ, Coman W. First clinical experience with a new non-indwelling voice prosthesis (Provox NID) for voice rehabilitation after total laryngectomy. Acta Otolaryngol. 2005; 125: 981-90

Postlaryngectomy Rehabilitation in this Era of Increasing Organ Preservation Treatment

- Since 1994, focus on organ preservation. RTOG 91-11: adding CT to RT in stage III-IV larynx cancer preserves more larynges than RT alone, but does not improve survival and increases toxicity and complications rates in salvage surgery

Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. Forastiere et al. N Engl J Med. 2003; Long-Term Results RTOG 91-11: A Comparison of Three Nonsurgical Treatment Strategies to Preserve the Larynx in Patients With Locally Advanced Larynx Cancer. Forastiere et al. J Clin Oncol. 2013; Weber et. Al. Arch Otolaryngol Head Neck Surg 2003

- Somewhat neglected: the preceding VA study* had shown significant better survival for T4N0 with TL, reason to exclude this patient category from RTOG 91-11

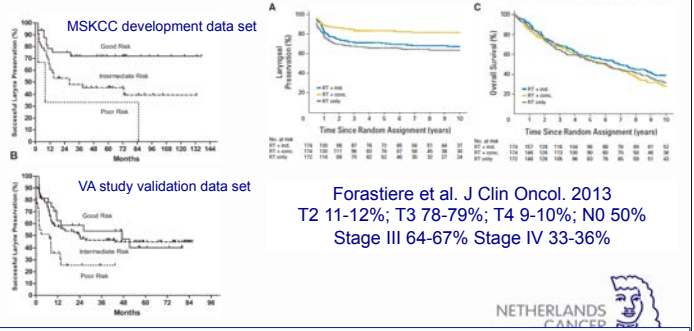
*Veterans Affairs Laryngeal Cancer Group study. N Engl J Med. 1991; 324: 1685-90

- Moreover, it became all too obvious that organ preservation is not synonymous with function preservation

E.g.; Machtay et al. J Clin Oncol 2008. RTOG 91-11, 97-03, and 99-14 (43% severe complications); Theunissen et al. Otolaryngol Head Neck Surg 2012 (11% of TLs in 10-years for dysfunctional larynx)

And is larynx preservation the relevant outcome/success parameter of that study for the organ preservation discussion?

TALK Score: Development and Validation of a Prognostic Model for Predicting Larynx Preservation Outcome. Sherman et al. Laryngoscope 2012



Forastiere et al. J Clin Oncol. 2013
T2 11-12%; T3 78-79%; T4 9-10%; N0 50%
Stage III 64-67% Stage IV 33-36%

TALK = **T4** (1) – Albumen (< 4mg/dL=1) – alcohol/Liquor (≥6 units=1) – Karnofsky (<80=1)
Larynx preserving probability: TALK score 0 = Good Risk; 1-2 = Intermediate Risk; 3-4 = Poor Risk
3-year larynx preservation rates by TALK score: 65% (0), **41% (1–2)**, and 6% (3–4), P < .0001

Postlaryngectomy Rehabilitation in this Era of Increasing Organ Preservation Treatment

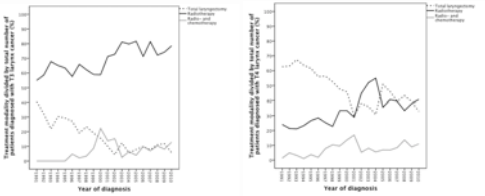
- In the mean time more and more evidence is collected that T4 disease has a significant better prognosis/overall survival with TL + postoperative RT …….

- Veterans Affairs Laryngeal Cancer Group study. N Engl J Med. 1991; 324: 1685-90. TLE vs CRT: survival 68% vs. 60% (P = .0098)
- Carvalho AL et al. Int J Cancer 2005; 114: 806-816: downward trend for survival of larynx cancer contrary to trends in other HN sites
- Hoffman et al., Laryngoscope 2006; 116: 1-13. Similar finding as Carvalho 2005
- Chen, Halpern. Arch Otolaryngol Head Neck Surg 2007; 133: 1270-76. **HR for Death TLE 1, RT 1.6, CRT 1.3 (P < .001)** (SEERS database; N>7000)
- Dziegielewski et al. J Otolaryngol Head Neck Surg. 2012; 41 Suppl 1:S56-64 (Alberta Cancer Registry, Canada/tertiary care centers …)
- Grover S et al. Int J Radiat Oncol Biol Phys. 2015. National Cancer Database, T4a (N=969) TL or CRT: overall survival CRT < TL (HR 1.31, 95% CI 1.10-1.57). PM. Patients treated in high case-volume facilities were more likely to receive TL

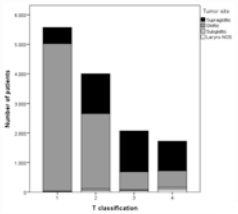
AJ Timmermans, BAC van Dijk PhD, LIH Overbeek, MLF van Velthuysen, H. van Tinteren, FJM Hilgers, MWM van den Brekel.

Trends in treatment and survival of advanced larynx cancer: a 20-year population-based study in the Netherlands.
Head Neck 2015, in press

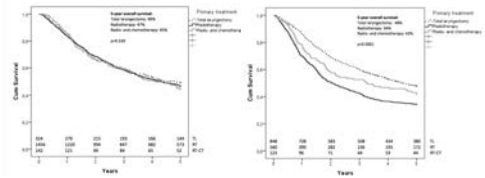
Time trends for therapy T3 (N=2072) and T4 (N=1722)



T1-4: N = 14,080



5-year overall survival T3 and T4 according to therapy



T3 vs T4: Hazard Ratio for Death 1 vs 1.21 (95% CI: 1.11-1.32; p<0.001)
T4: Hazard Ratio for Death TL+RT=1; CRT=1.27; RT=1.50 (p=0.04/p<0.0001)

Postlaryngectomy Rehabilitation in this Era of Increasing Organ Preservation Treatment

- Moreover, patients still might priorities survival over organ preservation (i.e. time-trade off studies*)

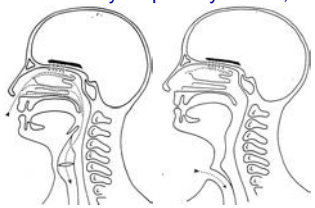
*Otto et al. Ann ORL. 1997. Impact of a laryngectomy on quality of life: perspective of the patient versus that of the health care provider.
Conclusion: % of HCPs who believed patients would trade survival for "voice box" time substantially higher than patients would. Only a minority of patients would trade survival for 'voice box' time (despite their poor rehabilitation level in the mid nineties)

*Hamilton et al. Head Neck. 2015. Quality compared to quantity of life in laryngeal cancer: A time trade-off study. "In many individuals, larynx conservation may not be the primary consideration in treatment preference."

- This means that TL is here to stay, also while T4 CT+RT still has to be considered experimental treatment, which after proper counseling should be offered only on patient's specific request, or in the course of a clinical trial

But this also means that during counseling the patient should be offered a comprehensive postlaryngectomy rehabilitation program ……..

- The larynx is more than just a 'voice box': due to its central position in the respiratory tract, its removal requires rehabilitation of all three 'systems' depending on an intact airway/respiratory airflow, i.e.
  - vocal rehabilitation
  - pulmonary rehabilitation
  - olfactory rehabilitation



- Rehabilitation of laryngectomized patients requires a dedicated multidisciplinary team effort (HN surgeon, SLP, oncology nurse, patient counselor) for achieving optimal results and quality of life

Postlaryngectomy Rehabilitation in this Era of Increasing Organ Preservation Treatment

What does this mean for TE voice rehabilitation?

- Primary TEP does not increase postop complication rates; limiting surgical trauma is still important, though, because of increased tissue vulnerability post (C)RT
  - …….. a new surgical instrument (PVPS)/the case for primary TEP with direct fit/optimizing pulmonary rehab postop (+avoiding a cannula) …..
- In follow-up: pro-active complication prevention-treatment
  - Main TEP problems (widening – atrophy – hypertrophy) are comorbidity issues: reflux and PE segment stenosis …..
  - VP device life (material degradation: biofilm/under-pressure): instead of (unproven) medical solutions (Nystatine, Diflucan), technical solutions (ActiValve and/or customized/adapted VPs*) …..

*Kress et al. Laryngorhinootologie 2006
Hilgers et al. Laryngoscope 2008
Lewin JS, et al. Laryngoscope 2012

Medical device research is increasingly time consuming: from start research project to publication

- Provox: 1988 – 1990
  - Hilgers & Schouwenburg. Laryngoscope 1990
  - Hilgers, Cornelissen, Balm. Eur Arch ORL 1993
  - Hilgers, Balm. Clin Otolaryngol 1993
- Provox2: 1995 – 1997
  - Hilgers, Ackerstaff, Balm, Tan, Aaronson, Persson. Acta Otolaryngol 1997
  - Ackerstaff, Hilgers, Meeuwis, van der Velden, van den Hoogen, Marres, Vreeburg, Manni . Arch Otolaryngol HN Surg 1999
- Provox ActiValve: 1998 – 2003
  - Hilgers, Ackerstaff, Balm, vd Brekel, Tan, Persson. Acta Otolaryngol 2003
  - Soolsma, vd Brekel, Ackerstaff, Balm, Tan, Hilgers. Laryngoscope 2008
- Provox Vega/Smart Inserter: 2006 – 2010
  - Hilgers, Ackerstaff, van Rossum, Jacobi, Balm, Tan, van den Brekel. Acta Otolaryngol. 2010
  - Hilgers, Ackerstaff, Jacobi, Balm, Tan, van den Brekel. Laryngoscope 2010
- Provox Vega Puncture Set: 2008 – 2013
  - Hilgers, Lorenz, Maier, Meeuwis, Kerrebijn, Vander Poorten, Vinck, Quer, van den Brekel. Eur Arch ORL. 2013
  - Lorenz, Hilgers, Maier. HNO. 2013

Development and (pre-) clinical assessment of a novel surgical tool for primary and secondary tracheoesophageal puncture with immediate voice prosthesis insertion, the Provox Vega Puncture Set. Hilgers et al. Eur Arch ORL 2013; 270: 255-262

Provox Vega Puncture Set (PVPS), a novel, fully **disposable** set for primary and secondary TEP and immediate implantation of a Provox Vega voice prosthesis

TEP trauma limitation

- Annyas AA, Nijdam HF, Escajadillo JR, Mahieu HF, Leever H. Groningen prosthesis for voice rehabilitation after laryngectomy. Clin Otolaryngol Allied Sci. 1984; 9: 51-54
- Hilgers FJM, Schouwenburg PF. A new low-resistance, self-retaining prosthesis (Provox™) for voice rehabilitation after total laryngectomy. Laryngoscope 1990; 100: 1202-1207
- Deschler DG, Bunting GW, Lin DT, Emerick K, Rocco J. Evaluation of voice prosthesis placement at the time of primary tracheoesophageal puncture with total laryngectomy. Laryngoscope. 2009; 119: 1353-1357.

Pro's and con's of primary tracheoesophageal puncture (TEP) with direct fit of an indwelling voice prosthesis, in stead of stenting with feeding tube and delayed fitting

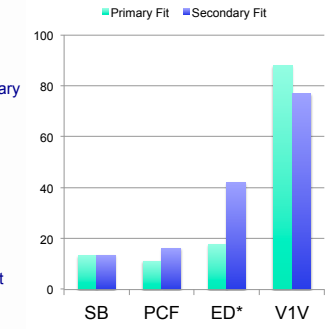
- Direct fit of VP:
  - Less traumatizing for TEP
    - First VP length mostly 8 mm, sometimes 10 mm
    - First VP length mostly 14-18 mm!
  - Supports/stabilizes party wall
  - Protects optimally against leakage (saliva, reflux)
  - Does not interfere with cannula or heat and moisture exchanger (HME)
  - Familiarizes patients rapidly with voice prosthesis and its daily maintenance (brush cleaning) through nurses
- No need for early postoperative prosthesis sizing and fitting, but immediate focus on voicing
- First replacement/fitting mostly months later, when most patients are in much better mental/physical shape

TEP: The Cleveland Clinic Experience

2009-2014; N=101; primary TEP 83, secondary TEP 18
Joann Kmiecik-Brian Burkey

Comparison of primary (N=45) vs secondary VP fit (N=38) in primary TEP (N=83)

- No significant differences for
  - Stomal breakdown (SB) (primary 13.3%, secondary 13.5%, p = 1.00)
  - Pharyngocutaneous fistula rate (PCF) (primary 11.1%, secondary 16.2%, p = 0.53)
  - Voice outcomes in any studied variable. Specifically, ability to voice at the first post-operative visit (V1V) was statistically similar between primary and secondary fitting (88% vs 77, p = 0.23)
- Significant difference for
  - Post-operative emergency department (ED) utilization significantly higher in secondary fit group (17.8% vs 42.1%, p = 0.03)



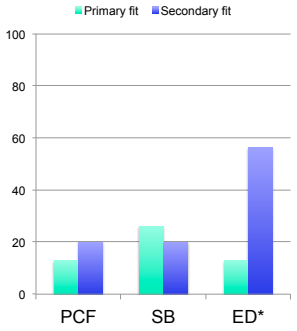
* p = 0.03

TEP: The Cleveland Clinic Experience

2009-2014; N=101; primary TEP 83, secondary TEP 18
Joann Kmiecik-Brian Burkey

Comparison of primary (N=45) vs secondary VP fit (N=38) in primary TEP (N=83)

- **After radiation failure**, no significant differences for
  - Stomal breakdown (SB) (primary 26.1%, secondary 20%, p = 1.00)
  - Pharyngocutaneous fistula rate (PCF) (primary 13%, secondary 20%, p = 0.66)
- Significant difference for
  - Post-operative emergency department (ED utilization significantly higher in secondary fit group (13% vs 56.3%, p < 0.01)
- Primary fit patients trended toward less pain (1.7 vs 2.7) (p = 0.18)



* p < 0.01

TEP: The Cleveland Clinic Experience

2009-2014; N=101; primary TEP 83, secondary TEP 18
Joann Kmiecik-Brian Burkey

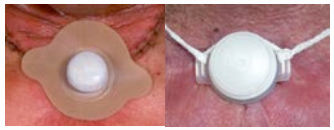
Conclusions

- While primary TEP with voice prosthesis placement is not commonly accepted in the United States, it has been adopted with good success at our institution since 2011
- This study provides clear evidence that it is a safe alternative to either secondary TEP or primary TEP with secondary prosthesis fitting
- While this study does not identify any voice-related benefits to primary TEP and fit, the decreased rate of post-operative ED visitation is quite robust
- While this study has obvious limitations and a controlled, prospective study would provide superior evidence, we offer compelling evidence that primary TEP and prosthesis fitting is a safe, efficacious strategy for voice rehabilitation following total laryngectomy

The case for immediate pulmonary protection and rehabilitation

Randomized controlled trial on postoperative pulmonary humidification after total laryngectomy: External Humidification versus Heat and Moisture Exchanger. Mérol J, Charpiot A, Langagne T, Hémar P, Ackerstaff AH, Hilgers FJM. Laryngoscope 2011; 122: 275-281

vs

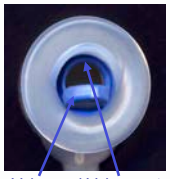


N=53; HME use shows significant

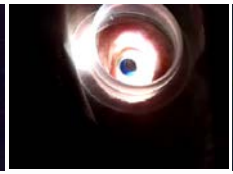
- Improved patient compliance (100% vs 42%)
- Reduced coughing (>5x daily 10% vs 42%)
- Reduced mucus expectoration/need for suctioning (2.5 vs 5.5)
- Less sleeping problems (17% vs 77%)
- Higher patient satisfaction (100% vs 11%)
- Reduced nursing time (20 min. vs 30 min.)
- Reduced daily costs (±$6 vs 15-60)

Easy oxygen application if needed

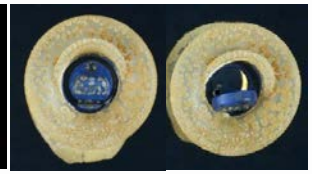
……VP device life issues (biofilm/under-pressure): technical rather than medical solution (Provox ActiValve*)



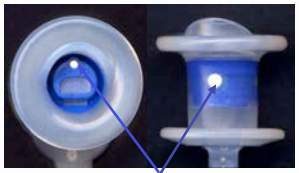
Valve and Valve seat made of fluoroplastic (Teflon-like) material



Spontaneous opening of valve during breathing, potentially counteracted by magnets



ActiValve in situ for 364 days; usual VP median 3 weeks

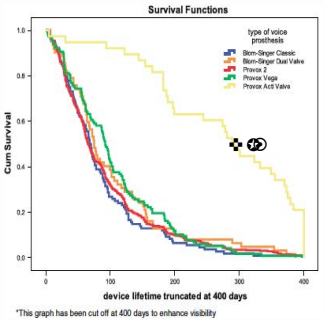


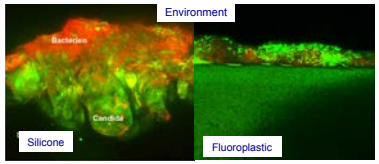
Magnets

A new problem-solving indwelling voice prosthesis, eliminating frequent candida- and 'under-pressure'- related replacements: Provox ActiValve. Hilgers FJM, Ackerstaff AH, Balm AJM, van den Brekel MWM, Tan IB, Persson JO. Acta Otolaryngol (Stockh) 2003; 123: 972-979

Silver oxide impregnation is not 'advantageous' enough

Provox ActiValve device life and 'biofilm' advantages





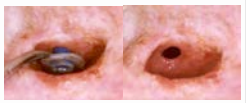
J Timmermans, H Harmsen, C Bus-Spoor, K Buijssen, C van As-Brooks, M de Goffau, R Tonk, M van den Brekel, F Hilgers, B van der Laan. Biofilm formation on the Provox® ActiValve: composition and ingrowth analyzed by Illumina paired-end RNA sequencing, fluorescence in situ hybridization and confocal laser scanning microscopy. Head Neck, online July 8 2015.

✜ Kress P, Schäfer P, Schwerdtfeger FP, Rösler S. Are modern voice prostheses better? A lifetime comparison of 749 voice prostheses. Eur Arch ORL. 2014; 271:133-140

✪ Graville, Palmer, Andersen, Cohen. Determining the efficacy and cost-effectiveness of the ActiValve: results of a long-term prospective trial. Laryngoscope. 2011; 121: 769-776. Mean increase in device life > 500%: from a mean of 1.93 Month with Provox2 to 10,30 Month with ActiValve (N=11).

⊙ Soolsma, van den Brekel Ackerstaff, Balm, Tan, Hilgers. Long-term results of Provox ActiValve, solving the problem of frequent Candida- and 'under-pressure' -related voice prosthesis replacements (N=42). Laryngoscope 2008; 118: 252-257.

The main TEP problems (widening – atrophy – hypertrophy) are comorbidity issues: reflux and PE segment stenosis…



- There has been an unfortunate non-scientific discussion on the imaginary correlation between VP diameter and TEP widening, which has distracted for long from looking for the real culprits ……
- TEP widening is a co-morbidity issue: aside from possible causes like prolonged pistoning, previous (chemo-)radiotherapy, recurrent disease, poor thyroid function, poor nutrition, suboptimal TEP technique, most prominently that is **gastro-esophageal reflux**, and/or neoglottis stricture***; and not prosthesis diameter***

*** No correlation with voice prosthesis diameter**: Hutcheson et al. Head Neck 2011 (systematic review); Starmer et al. Otolaryngol Head Neck Surg. 2011; Hutcheson et al. Head Neck. 2012

**** Correlation with reflux**: Pattani et al. Laryngoscope 2008; Boscoli-Rizzo et al. Eur Arch ORL. 2008; Lorenz et al. HNO. 2009; Lorenz et al. Annals ORL. 2010; Lorenz et al. Eur Arch ORL. 2011; Lorenz et al. Head Neck 2015

*** A stenosis will result in an increased velocity of fluids, which increases the pressure and the risk of periprosthetic leakage; dilatation of the stenosis will very likely solve this!

Thus, think “co-morbidity” in case of periprosthetic leakage, and when simple prosthesis-downsizing fails

*Kress et al. Laryngorhinootologie 2006
Hilgers et al. Laryngoscope 2008
Lewin JS, et al. Laryngoscope 2012

(Removal of prosthesis for shrinkage of TEP tract (+ NG tube feeding ± cuffed cannula) is a not patient friendly option)

1. **Short-term**: application of thin (0.5 mm) silicon washer behind tracheal flange, or VP with enlarged esophageal flange, or both; in case of 17 or 20Fr VP, consider upsizing to next larger diameter
2. Submucosal purse string suture (3x0 vicryl)
3. Tissue augmentation with collagen or Bioplastique
4. In case of failure: surgical closure of the TEP

Long-term: PPI treatment and/or PE segment dilatation

Postlaryngectomy Rehabilitation in this Era of Increasing Organ Preservation Treatment - Conclusions

- TL remains the best chance for cure for T4 larynx cancer
- The advantages of tracheoesophageal voice in fluency and speed of acquisition, obvious from the start in the early eighties, are still outweighing possible disadvantages, despite the somewhat higher RT-related complication rates, in which comorbidity (reflux and pharyngeal stenosis) play an important role
- Recent material/technical developments and improvements are promising and contributing to the continued success of voice prostheses as the gold standard for restoring post-laryngectomy oral communication and more ……..

TE voicing 1 months post TL for recurrence post-RT

Example of progress in 30+ years of prosthetic voice rehabilitation

Cavalot AL, Schindler A, Juliani E, Schindler O, Cortesina G. Playing a brass instrument after total laryngectomy: a case report. Head Neck 2009; Physiology and prospects of bimanual tracheoesophageal brass instrument play. Hilgers FJM, Dirven R, Jacobi I, van den Brekel MWM. Acta Otorhinolaryngol Ital. 2015; 35: 202-207

Thank you for your attention

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