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Outcomes of tracheoesophageal puncture in twice-radiated patients☆

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ABSTRACT

Objective: Previous research has demonstrated the safety of tracheoesophageal puncture voice prosthesis (TEP) placement in radiated patients; however, there is a growing population of twice-radiated patients with limited research on the outcomes of TEP-placement in this cohort.

Methods: After Institutional Review Board approval, a retrospective review of 80 patients that underwent TEP from 2006 to 2017 at a single institution was conducted, of which 16 patients underwent two courses of radiation. Outcome measures include TEP removal, complication and duration of usage.

Results: Half of twice-radiated patients had ultimate removal of their voice prosthesis with removal occurring at a median of 24.9 months after placement. Reasons for prosthesis removal included widening tracheoesophageal fistula, local recurrence, and dysphagia/esophageal stenosis. Nearly one-third of these patients required surgical intervention for closure of a widening fistula. In contrast, only 17% of once-radiated patients had their prosthesis removed with removal occurring at a median of 28.1 months. This was statistically fewer than the twice-radiated group ($p = 0.02$). Reasons for removal included patient preference, persistent leakage, recurrence of disease, enlarging tracheoesophageal fistula, poor voice, and dysphagia. Eleven percent of once-radiated patients required surgical intervention for TEP-related complications ($p = 0.057$).

Conclusion: In the twice-radiated patient cohort, there is a higher rate of TEP removal and need for surgical intervention for a voice prosthesis-related complication as compared to a once-radiated cohort.

1. Introduction

Tracheoesophageal puncture (TEP) is a method of restoring voice in post-laryngectomy patients. A tract is created between the posterior tracheal wall and esophagus, and a one-way valve voice prosthesis is inserted to allow exhaled air to enter the esophagus creating mucosal vibrations to generate speech. The relative simplicity of performing a TEP, the ease of which patients can learn how to use the voice prosthesis, the excellent voice outcomes, and the low complication rates have made TEP the preferred method of voice restoration [1–3]. The procedure can be performed at the same time of total laryngectomy (primary) or in a delayed fashion (secondary) in the operating room or in the office [4]. A recent meta-analysis concludes that the outcomes of primary and secondary TEP are similar in terms of voice outcomes and complication rate [5].

Many laryngeal cancers are treated with definitive radiation; however, recurrence leads to surgical salvage procedures, the mainstay of which is the total laryngectomy. Surgical salvage is associated with higher complication rates including pharyngocutaneous fistula, tissue necrosis, and wound breakdown [6,7]. In patients presenting with an advanced-stage recurrent laryngeal cancer, dual-modality treatment is indicated which may include a second course of radiation for these previously-radiated patients. Intensity Modulated Radiation Therapy (IMRT) administered to patients who have previously undergone radiation has been demonstrated to be an effective treatment method for recurrent head and neck tumors and limits radiation to surrounding structures, however treatment toxicity and morbidity remains high [8]. In addition to radiation toxicity, re-irradiation has been shown to lead to poor wound healing, as evidenced in the high postoperative complication rates including wound infection and wound dehiscence in twice-radiated microvascular free flap patients [9].

The effect of radiation on the success of a voice prosthesis has been studied after primary and secondary TEP. Many conclude that the presence of radiation does not increase complications nor diminish

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speech outcomes [10–13]. However, there is an increasing population of twice-radiated patients and currently no literature describing TEP in this patient population. The objective of this study is to describe the outcomes of TEP in a single-institution's cohort of twice-radiated patients and compare them to a cohort of once-radiated patients.

2. Materials and methods

After Institutional Review Board approval, medical charts were queried for patients undergoing TEP procedure by CPT code 31611 from 2006 to 2017 at University Hospitals Cleveland Medical Center. Records without adequate follow up (> 2 visits), inadequate documentation, and those not receiving any radiation therapy were excluded. Eighty patients who underwent TEP were included for retrospective chart review: 64 underwent one course of radiation ("once-radiated") and 16 underwent two courses of radiation ("twice-radiated"). Variables included for analysis are age at TEP, radiation timing and dose, surgery type, presence of flap reconstruction, and adjuvant chemotherapy. The primary outcome was voice prosthesis removal. Secondary outcomes included surgical intervention for TEP-related complication and the duration of voice prosthesis utilization. A two-sample *t*-test was used to compare incidence of voice prosthesis removal between the twice-radiated and once-radiated patients. The small sample size of the twice-radiated patients precluded multivariate analysis or survival analysis.

3. Results

Eighty patients were identified and included for analysis. Ninety-nine percent ($n = 79$) of TEPs were performed secondarily. Sixty-four (80%) patients received one course of radiation therapy, whereas 16 (20%) were twice-radiated. Table 1 demonstrates the clinical characteristics of patients undergoing TEP. There were no statistically significant differences in age at the time of TEP, treatment with adjuvant chemotherapy, or presence of reconstruction with free or local flap. Patients that received two courses of radiation underwent TEP at a median of 7 months after the second course of radiation (range 2–84 months). Three patients underwent TEP before the second course of radiation and maintained the prosthesis throughout the treatment course. The median duration of time between surgery and TEP was 8 (ranges 1–86) months for twice-radiated patients.

Of the sixteen twice-radiated patients, eight (50%) had ultimate removal of their voice prosthesis with removal occurring at median of 24.9 (0.7–122.2) months after placement. Fifty-percent ($n = 4$) of those patients had the TEP removed more than two years after placement. Reasons for prosthesis removal included widening tracheoesophageal fistula ($n = 5$), local recurrence ($n = 2$), and dysphagia/esophageal stenosis ($n = 1$). One patient required a re-puncture in the clinic setting. Five patients (31%) required surgical intervention for closure of a widening fistula. The twice-radiated patients that did not have their voice prosthesis removed have a median follow up time of 41 (13.8–58.8) months.

Of the sixty-four once-radiated patients, TEP was performed at a median 12 months after radiation completion (range 0–230 months) and at a median of 5 (range 0–15) months after surgery. Twelve patients (19%) had their prosthesis removed with removal occurring at a median of 28.1 (0.3–104.8) months. This was statistically fewer than the twice-radiated group ($p = 0.02$). Four of these patients maintained the TEP for > 2 years. Reasons for removal included patient preference ($n = 4$), persistent leakage ($n = 2$), recurrence (n = 2), enlarging tracheoesophageal fistula ($n = 1$), poor voice (n = 1), and dysphagia (n = 1). Seven patients (11%) required surgical intervention for TEP-related complications ($p = 0.057$). Table 2 describes the clinical characteristics of all patients who underwent eventual voice prosthesis removal. Once-radiated patients that did not have their TEP removed have a median follow up time of 28.5 months.

Twelve (75%) of the twice-radiated patients and 46 (72%) of the once-radiated patients underwent flap reconstruction at that time of total laryngectomy. The documentation was insufficient to determine the exact placement of the prosthesis in relationship to the free flap tissue.

4. Discussion

The aim of this study was to investigate the outcomes of twice-radiated patients who undergo TEP. Half of these patients ultimately had the voice prosthesis removed and a quarter required surgical intervention for a widening tracheoesophageal fistula. The rate of prosthesis removal was significantly higher and the rate of surgical intervention was double in the twice-radiated cohort compared to the once-radiated cohort. Previous studies have validated the safety of TEP in radiated patients with no significant difference in complication rates between radiated and non-radiated patients undergoing TEP [10,13]. Our voice prosthesis removal rate in the once-radiated patients cohort (17%) was similar to rates reported in the literature (13%) [13].

Although one course of radiation does not seem to pose a significant threat of TEP failure, two courses of radiation in our population did result in a higher incidence of TEP failure. The pathophysiological effects of radiation and its impact on wound healing are well known. Fibrosis and loss of normal secretory functions are major side effects, both of which can have a tremendous impact on proper functioning of mucosa surrounding the prosthesis site. Radiation induces increased vascular permeability that allows for fibrin deposition, subsequent collagen formation, and eventual fibrosis. Salivary tissue is particularly sensitive to radiation. The tissue degenerates after small doses of radiation which leads to markedly diminished salivary output [15]. These effects of radiation on tissue are thought to be dose-dependent [14].

The high rate of voice prosthesis-failure in the twice-radiated cohort is likely related to the cumulative effects of the radiation and the poor wound healing properties of the radiated tissue. The most common cause of TEP removal was a widening tracheoesophageal fistula. Fibrosis corrupts the elastic properties of the skin and thus affects the skin's ability to create a tight seal around a foreign body such as a TEP prosthesis. Fibrosis has been shown to occur as early as 4 to 12 weeks after a single dose of 15 to 25 Gy and 36 to 48 weeks after lower doses of 5 to 10 Gy [16]. Irradiated fibroblasts demonstrate greater growth

Table 1
Clincal characteristics of patients undergoing TEP.

	Twice-radiated ($n = 16$)	Once-radiated ($n = 64$)	p
Age at time of TEP [mean, (range)]	60 (43–76) years	63 (44–79) years	0.47
Free flap reconstruction	11 (69%)	39 (61%)	
Local flap reconstruction	1 (6%)	6 (9%)	
No flap reconstruction	4 (25%)	18 (28%)	
Chemotherapy	11 (69%)	31 (48%)	0.14
Duration between surgery and TEP [median. (range)]	8 (1–86) months	5 (0–15) months	
Duration between radiation and TEP [median, (range)]	7 (2–84) months	12 (1 − 230) months	
TEP Removal	8 (50%)	11 (17%)	0.02*

Table 2
Characteristics of Patients with TEP removal.

	Reason for removal (n [%])	Post-laryngectomy reconstruction (n)	Chemo-therapy (n)	Duration of use prior to removal (months)
Twice-radiated 8 (50%)	Leakage/enlarging TE fistula 5 (62.5%)	Free flap 2 Local flap 1 Primary closure 2	4	25.3
	Recurrence 2 (25%)	Free flap 1 Primary closure 1	2	7.6
	Dysphagia/Esophageal stenosis 1 (12.5%)	Primary closure 1	1	122.1
Once-radiated 11 (17%)	Leakage/enlarging TE fistula 3 (27.5%)	Free flap 3	3	31.3
	Recurrence 2 (18%)	Free flap 2	2	9.1
	Dysphagia/Esophageal stenosis 1 (9%)	Primary closure 1	1	10.5
	Patient preference 4 (36.5%)	Free flap 3 Primary closure 1	1	38.4
	Poor voice 1 (9%)	Primary closure 1	unknown	44.3

potential than fibroblasts from normal dermis and or in surgical scars [17]. This establishes a direct relationship between radiation dose and degree of fibrosis.

Of the five twice-radiated patients with an enlarging tracheoesophageal fistula, voice prosthesis removal occurred at an average of 31.5 months; two of these patients had post-laryngectomy free flap reconstruction, one a local flap, and two primary closure. The small sample size in this study prevents further analysis of the impact of post-laryngectomy reconstruction on incidence of complications and documentation was not sufficient to discern if voice prostheses were placed through flap tissue or through native radiated tissue.

Despite the higher rate of voice prosthesis removal in the twice-radiated cohort, the duration of use before removal was similar for both groups: 24.9 months for twice-radiated versus 28.1 months for once-radiated. For the patients that did not have their prosthesis removed within the study timeframe, the average follow-up time was 22 and 28.9 months for the twice-radiated and once-radiated cohorts, respectively. Interestingly, half of the twice-radiated patients maintained the voice prosthesis for over two years and the longest duration of use was 122 months when the TEP was discontinued due to esophageal stenosis. This demonstrates that despite high rates of removal, patients may benefit from the voice prosthesis for a significant amount of time prior to removal.

The major limitations of this study include its retrospective nature and small sample size, which precludes further statistical testing. A standardized metric of voice outcome was not regularly used, so data on the effect of twice-radiation on voice quality was not available. A major variable that was not reported in this study was the total radiation dose. This is due to the lack of detailed radiation records when the patient receives radiation at an outside institution and/or at a time prior to electronic medical records. However, the assumption is made that those treated with definitive radiation receive 60–70 Gy and those treated with adjuvant radiation receive 50–60 Gy, thus twice radiated patients receive approximately double the cumulative dose of radiation than those in the once-radiated cohort. Another variable that was not considered in our study was acid reflux; radiated laryngectomy patients with known reflux have higher failure rates of speech rehabilitation [18]. Further analysis regarding the nature of TEP in relation to free flap reconstruction may provide additional insight into this subject.

5. Conclusions

Twice-radiated patients have a significantly higher incidence of voice-prosthesis removal compared to once-radiated patients. Approximately one quarter of twice-radiated patients presented with an enlarging tracheoesophageal fistula that required surgical intervention. Despite the high rates of voice prosthesis removal, half of our twice-radiated patient cohort received benefit from the voice prosthesis for greater than two years. Although the average duration of TEP utilization before prosthesis removal was similar between the once-radiated and twice-radiated cohorts, the associated inconvenience of frequent follow ups, poor functioning, and return to the operating room may affect the quality of life prior to ultimate removal of the prosthesis in the twice-radiated cohort. Alternative means of communication may be more beneficial for this high-risk patient population. If TEP and voice prosthesis is strongly desired, appropriate pre-procedure counseling detailing the high rate of complications is critical.

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References

[1] LaBruna A, Huo J, Klatsky I, Weiss MH. Tracheoesophageal puncture in irradiated patients. Ann Otol Rhinol Laryngol 1995;104(4):279–81.
[2] Silverman AH, Black MJ. Efficacy of primary tracheoesophageal puncture in laryngectomy rehabilitation. J Otolaryngol 1994;23(5):370–7.
[3] Shultz JR, Harrison J. Defining and predicting tracheoesophageal puncture success. Arch Otolaryngol Head Neck Surg 1992;118(8):811–6.
[4] LeBert B, McWhorter AJ, Kunduk M, et al. Secondary tracheoesophageal puncture with in-office transnasal esophagoscopy. Arch Otolaryngol Head Neck Surg 2009;135(12):1190–4. https://doi.org/10.1001/archoto.2009.166.
[5] Chakravarty PD, McMurran AEL, Banigo A, Shakeel M, Ah-See KW. Primary versus secondary tracheoesophageal puncture: systematic review and meta-analysis. J Laryngol Amp Otol 2018;132(1):14–21. https://doi.org/10.1017/S0022215117002390.
[6] Hasan Z, Dwivedi RC, Gunaratne DA, Virk SA, Palme CE, Riffat F. Systematic review and meta-analysis of the complications of salvage total laryngectomy. Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol 2017;43(1):42–51. https://doi.org/10.1016/j.ejso.2016.05.017.
[7] Weber RS, Berkey BA, Forastiere A, et al. Outcome of salvage total laryngectomy following organ preservation therapy: the radiation therapy oncology group trial 91-11. Arch Otolaryngol Neck Surg 2003;129(1):44–9. https://doi.org/10.1001/archotol.129.1.44.
[8] Takiar V, Garden AS, Ma D, et al. Reirradiation of head and neck cancers with intensity modulated radiation therapy: outcomes and analyses. Int J Radiat Oncol Biol Phys 2016;95(4):1117–31. https://doi.org/10.1016/j.ijrobp.2016.03.015.
[9] Clancy K, Melki S, Awan M, et al. Outcomes of microvascular free tissue transfer in twice-irradiated patients. Microsurgery 2017;37(6):574–80. https://doi.org/10.1002/micr.30154.
[10] Trudeau MD, Schuller DE, Hall DA. The effects of radiation on tracheoesophageal puncture. A retrospective study. Arch Otolaryngol Head Neck Surg 1989;115(9):1116–7.
[11] Mehle ME, Lavertu P, Meeker SS, Tucker HM, Wood BG. Complications of secondary tracheoesophageal puncture: the Cleveland Clinic Foundation experience. Otolaryngol–Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg 1992;106(2):189–92.
[12] Kao WW, Mohr RM, Kimmel CA, Getch C, Silverman C. The outcome and techniques of primary and secondary tracheoesophageal puncture. Arch Otolaryngol Head Neck Surg 1994;120(3):301–7.
[13] Serra A, Di Mauro P, Spataro D, Maiolino L, Cocuzza S. Post-laryngectomy voice rehabilitation with voice prosthesis: 15 years experience of the ENT Clinic of University of Catania. Retrospective data analysis and literature review. Acta

Otorhinolaryngol Ital Organo Uff Della Soc Ital Otorinolaringol E Chir Cerv-facc 2015;35(6):412–9. https://doi.org/10.14639/0392-100X-680.
[14] Tibbs MK. Wound healing following radiation therapy: a review. Radiother Oncol 1997;42(2):99–106. https://doi.org/10.1016/S0167-8140(96)01880-4.
[15] Cooper JS, Fu K, Marks J, Silverman S. Late effects of radiation therapy in the head and neck region. Int J Radiat Oncol Biol Phys 1995;31(5):1141–64. https://doi.org/10.1016/0360-3016(94)00421-G.
[16] Panizzon RG, Malkinson FD, Hanson WR, Schwartz DE. A one-year comparative study of post-irradiation collagen content and microscopic fibrosis in mouse skin. Br J Radiol Suppl 1986;19:54–7.
[17] Martin M, Remy J, Daburon F. In vitro growth potential of fibroblasts isolated from pigs with radiation-induced fibrosis. Int J Radiat Biol Relat Stud Phys Chem Med 1986;49(5):821–8.
[18] Cocuzza S, Bonfiglio M, Chiaramonte R, Serra A. Relationship between radiotherapy and gastroesophageal reflux disease in causing tracheoesophageal voice rehabilitation failure. J Voice Off J Voice Found 2014;28(2):245–9. https://doi.org/10.1016/j.jvoice.2013.08.008.