Surgical strategy for patients with papillary thyroid carcinoma invading the trachea: a comparison of tracheal sleeve resection with end-to-end anastomosis and window resection with tracheocutaneous fistula

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Background: Sleeve resection with end-to-end anastomosis (Procedure A) and window resection with a tracheocutaneous fistula (Procedure B) are the major surgical procedures for patients with papillary thyroid carcinoma (PTC) exhibiting transluminal tracheal invasion. For each procedure, the indications, postoperative course, and treatment results were examined retrospectively.

Methods: Of 1,456 patients with PTC (maximum tumor diameter >1 cm) who received initial treatment between 1993 and 2013, we reviewed 51 patients. Of these 51 cases, 45 showed full-layer tracheal invasion, and 6 did not reach the tracheal mucosa, but required full-layer tracheal resection. Twenty-four patients underwent Procedure A, and 27 patients underwent Procedure B.

Results: Regarding surgical procedure selection, Procedure B was selected significantly more frequently than Procedure A for cases with preoperative recurrent laryngeal nerve (RLN) palsy, tumor invasion of the esophagus, clinical lymph node metastasis, or a large number of resected tracheal rings. Postoperative airway-related complications were not significantly different between the procedures, but decreased with the use of intraoperative neuromonitoring (IONM). The postoperative hospital stay was significantly longer for Procedure B than for Procedure A. In addition, the rate of a permanent postoperative tracheostoma was higher with Procedure B than with Procedure A. Local recurrence-free survival (LRFS) and cause-specific survival (CSS) did not differ significantly between the two procedures.

Conclusions: Certain patients may benefit from Procedure A with IONM in terms of a shorter hospital stay and avoiding the need for a permanent tracheostoma. Although Procedure B was indicated for patients with more advanced disease than Procedure A, treatment outcomes were similar.

Keywords: Papillary thyroid carcinoma (PTC); tracheal infiltration; sleeve resection with end-to-end anastomosis; window resection with tracheocutaneous fistula

Introduction

Background

Papillary thyroid carcinoma (PTC) sometimes invades the larynx, trachea, hypopharynx, and esophagus. According to Brauckhoff, widely invasive extrathyroidal thyroid cancer invading the aerodigestive tract, including the larynx, trachea, hypopharynx, and/or esophagus, occurs in 1–8% of patients with thyroid cancer (1). Furthermore, according to Matsumoto *et al.*, tracheal invasion by well-differentiated thyroid carcinoma is infrequent, occurring at a rate of 3.4–13% (2-7).

The depth of invasion represents an important prognostic factor in such cases (8-11). Patients with transluminal tracheal invasion show worse outcomes in terms of disease-free and cause-specific survivals (CSS) than those with superficial invasion, and they require full-layer tracheal resection for local control (11).

Rationale and knowledge gap

We compared two surgical approaches for PTC with full-layer tracheal invasion. One was sleeve resection with end-to-end anastomosis (Procedure A), and the other was window resection with a tracheocutaneous fistula (Procedure B). Each procedure has specific advantages and disadvantages in terms of curability and different postoperative complications. In Procedure A, the trachea is resected circumferentially. After resection, end-to-end anastomosis can be completed in one stage, and the airway lumen is covered by normal tracheal mucosa. In contrast, Procedure B is a technique in which all layers of the tracheal wall invaded by thyroid cancer are resected with a safety margin. In general, there was no postoperative tracheostoma with sleeve resection for Procedure A.

However, in Procedure A, neck lengthening must be avoided after surgery (12-15). Moreover, the risk of fatal complications, such as tracheal suture failure, is a concern. On the other hand, there is no risk of tracheal suture failure with Procedure B, but once a tracheocutaneous fistula is constructed, primary closure of the fistula may be difficult in some cases, requiring reconstruction using various techniques. Thus, although the fatal postoperative complications of Procedure A are more frequent than those of Procedure B, Procedure B is not less invasive because it requires separate surgery to close the tracheocutaneous fistula. The surgical procedure was decided based on the patient's general condition and tumor status.

Current guidelines do not provide specific guidance on the resection of tracheal invasion. Therefore, criteria for selection of the surgical approach in patients with tracheal invasion have not been established for either Procedure A or B.

Objective

This retrospective study investigated the following factors for the two procedures in PTC patients with tracheal invasion: (I) background characteristics of the patients and tumors; (II) postoperative course including airway-related complications, length of hospital stay, need for tracheostoma, and probability of tracheostoma closure; and (III) treatment outcomes including local recurrence-free survival (LRFS) and CSS. Eight patients who underwent total laryngectomy were excluded. The aim of the study was to elucidate the appropriate criteria for procedure selection in each patient. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-23-171/rc).

Methods

A total of 1,456 patients with PTC (maximum tumor diameter >1 cm) underwent initial surgery between 1993

Highlight box

Key findings
- Sleeve resection with end-to-end anastomosis (Procedure A) is an ideal airway reconstruction procedure because, after tracheal resection, airway reconstruction is completed in one step.
- On the other hand, window resection with a tracheocutaneous fistula (Procedure B) was indicated for cases with more advanced progression than Procedure A, but the treatment results were similar.

What is known and what is new?
- Procudure A and procedure B are the major surgical procedures for patients with papillary thyroid carcinoma exhibiting transluminal tracheal invasion, and studies have compared them.
- However, no studies have investigated indications, which is the novelty of this study.

What is the implication, and what should change now?
- In this study, we described the indication related to surgical procedure selection, but there is a bias because it was a retrospective study of a small number of cases.
- Further prospective studies are needed for validation.

and 2013 at the Cancer Institute Hospital, Japanese Foundation for Cancer Research, a tertiary oncology referral center in Tokyo, Japan. The postoperative clinical follow-up period was until 2020. We reviewed the medical records of 51 patients (3.5%) who had full-layer resection of the trachea. Regarding the measurements and data collected, computed tomography (CT), ultrasonography (US), laryngoscopy, and surgical findings, were used to measure the extent of tracheal infiltration. Postoperative radioactive iodine (RAI) uptake was also used as a reference for postoperative evaluation of distant metastases. Recurrent laryngeal nerve (RLN) palsy was assessed by laryngoscopy. For postoperative follow-up, US and CT were performed every year. The survival period was defined as the interval from the date of surgery to the date of final confirmation of survival or the date of death. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of Cancer Institute Hospital (No. 2013–1128), and individual consent for this retrospective analysis was waived.

Of the 51 patients, 24 underwent sleeve resection with end-to-end anastomosis (Procedure A), and 27 underwent window resection with a tracheocutaneous fistula (Procedure B). Forty-five patients had transluminal tracheal invasion (Ex3), and 6 patients showed submucosal tracheal invasion (Ex2) (11). The participants were 14 men and 37 women (male-to-female ratio, 1:3.8). Age at the time of initial surgery ranged from 27 to 83 years (mean ± standard deviation: 65.5±11.2 years), and the observation period after surgery ranged from 2.0 to 22.0 years (mean ± standard deviation: 10.2±4.9 years).

In Procedure A, the trachea is resected circumferentially. After resection, end-to-end anastomosis can be completed in one stage, and the airway lumen is covered by normal tracheal mucosa. In contrast, Procedure B is a technique wherein all layers of the tracheal wall invaded by thyroid cancer are resected with a safety margin. In patients undergoing Procedure B, in which the resection range is limited or only the posterior membranous tracheal wall is preserved, the tracheal wall can be sutured primarily without requiring a tracheostomy or tracheocutaneous fistula (2). However, in our facility, a tracheocutaneous fistula was created in all patients. For Ex2 or Ex3 cases, the surgical procedure was determined by the surgeon, considering the extent of tracheal resection (longitudinal and lateral directions) and the presence or absence of bilateral RLN palsy. We defined Procedure A as an end-to-end anastomosis without a tracheostomy and Procedure B

as a tracheocutaneous fistula.

This study analyzed the relationship between patient and tumor characteristics and the choice of procedures. We also studied characteristics of the postoperative course such as airway-related complications, duration of hospital stay, and the presence or absence of a transient or permanent tracheostoma for each procedure. We had been using intraoperative neuromonitoring (IONM) of the RLN since 2007. As for the analysis of postoperative complications, we compared complication rates before and after the introduction of IONM. Treatment outcomes including local recurrence-free survival (around the site of tracheal resection) and CSS rates were also investigated and compared between Procedures A and B.

Statistical analysis

Statistical analysis was performed using SPSS Statistics 27 (IBM, Armonk, NY, USA). Comparisons between groups were performed by Fisher's exact test for categorical data and Student's t-test for continuous variables, as appropriate. Survival curves were determined by the Kaplan-Meier method and compared with the log-rank test. Multivariate analysis was conducted by multiple regression analysis for continuous data and logistic regression analysis for categorical data. Values of P<0.05 were considered significant, and values of P that were ≥0.05 but <0.1 were regarded as reflecting a tendency.

Results

Patient and tumor characteristics for each procedure are shown in *Table 1*. Age, sex, tumor size, presence of distant metastasis, circumference, and presence of cricoid resection did not differ significantly between groups. Preoperative RLN palsy, tumor invasion of the esophagus, and clinical lymph node metastasis were significantly more frequent in Procedure B. The number of resected tracheal rings was significantly greater in Procedure B. For Procedure A, ≤4 rings were resected in 23 cases (96%), whereas 10 cases (37%) in Procedure B underwent resection of ≥5 rings.

Postoperative airway-related complications were seen in 5 cases (21%) with Procedure A and in 1 case (4%) with Procedure B (P=0.07). These complications are summarized in *Table 2*, comparing before and after the introduction of IONM. Although no significant differences were seen, the frequency of airway-related complications dropped from 5 cases (15%) to 1 case (6%) after the use of IONM (P=0.34).

Table 1 Patient and tumor characteristics, and surgical procedures

Characteristics	Procedure A (n=24)	Procedure B (n=27)	P
Age (years)	61.0±13.4 [27–81]	67.4±8.6 [50–83]	0.08
Sex			0.36
Male	5 [21]	9 [33]	
Female	19 [79]	18 [67]	
Tumor size			0.05
<40 mm	15 [63]	9 [33]	
≥40 mm	9 [38]	18 [67]	
Preoperative RLN palsy			0.002 (– vs. +)
No	19 [79]	9 [33]	
Unilateral	5 [21]	17 [63]	
Bilateral	0 [0]	1 [4]	
Invasion of the esophagus			5×10^{-4}
Absent	20 [83]	9 [33]	
Present	4 [17]	18 [67]	
Lymph node metastasis			0.02 (N0 vs. N1)
N0	13 [54]	6 [22]	
N1a	4 [17]	4 [15]	
N1b	7 [29]	17 [63]	
Distant metastasis			0.36
M0	19 [79]	18 [67]	
M1	5 [21]	9 [33]	
Number of resected tracheal rings	3.0±1.1 [1–5]	4.4±1.5 [2–9]	4×10^{-4}
Circumference			0.57
<1/3 lap	16 [67]	15 [56]	
≥1/3 lap	8 [33]	12 [44]	
Cricoid resection			0.20
Absent	21 [88]	20 [74]	
Present	3 [12]	7 [26]	

Data are shown as mean ± standard deviation [range] or number [percentage]. Procedure A: sleeve resection with end-to-end anastomosis; Procedure B: window resection with tracheostomy. RLN, recurrent laryngeal nerve.

Table 2 Postoperative airway-related complications for each procedure before and after introduction of IONM

Procedure	Before introduction of IONM (n=34)	After introduction of IONM (n=17)
Procedure A (n=24)	4/15 patients (27%): reintubation for subglottal stenosis (n=1); postoperative tracheostomy for bilateral RLN palsy (n=2); resuturing due to tracheal suture failure (n=1)	1/9 patients (11%): tracheal suture failure and anastomotic stenosis due to granulation (n=1)
Procedure B (n=27)	1/19 patients (5%): tracheal stenosis due to granulation (n=1)	0/8 patients (0%)

Procedure A: sleeve resection with end-to-end anastomosis; Procedure B: window resection with tracheostomy. IONM, intraoperative neuromonitoring; RLN, recurrent laryngeal nerve.

Table 3 Risk factors for longer postoperative hospital stay

Risk factors	Shorter hospital stay (≤20 days) (n=27)	Longer hospital stay (≥21 days) (n=24)	P
Age			0.03
<65 years	17 [63]	8 [33]	
≥65 years	10 [37]	16 [67]	
Sex			0.76
Male	8 [30]	6 [25]	
Female	19 [70]	18 [75]	
Tumor size (mm)	36.1±12.0 [15–61]	50.0±18.7 [22–100]	0.006
Number of resected tracheal rings	3.0±1.1 [1–5]	4.6±1.4 [3–9]	$<1\times10^{-4}$
Postoperative airway-related complication			0.40
Absent	25 [93]	20 [83]	
Present	2 [7]	4 [17]	
Postoperative RLN palsy			0.005 (– *vs.* +)
No	12 [44]	2 [8]	
Unilateral	13 [48]	14 [58]	
Bilateral	2 [7]	8 [33]	
Surgical procedure			$<1\times10^{-4}$
A	21 [78]	3 [13]	
B	6 [22]	21 [88]	

Data are shown as mean ± standard deviation [range] or number [percentage]. Procedure A: sleeve resection with end-to-end anastomosis, Procedure B: window resection with tracheostomy. RLN, recurrent laryngeal nerve.

Table 4 Multivariate analysis of risk factors for longer postoperative hospital stay

Risk factor	Coefficient value (B)	Standard error	Significance	Exp(B)
Age at time of surgery (≥65 years)	1.398	0.856	0.103	4.047
Tumor diameter (≥40 mm)	0.757	0.832	0.363	2.133
Number of resected tracheal rings (≥5)	2.079	1.347	0.123	7.997
Postoperative RLN palsy (+)	0.325	1.222	0.790	1.384
Surgical procedure (B)	2.678	0.962	0.005	14.560

Procedure B: window resection with tracheostomy. RLN, recurrent laryngeal nerve.

Postoperative complications other than airway complications were postoperative infection in 4 patients (Procedure A: 0, Procedure B: 4), dysphagia in 11 patients (Procedure A: 1, Procedure B: 10), bleeding in 1 patient (Procedure A: 1, Procedure B: 0), and chyle in 1 patient (Procedure A: 0, Procedure B: 1).

The length of postoperative hospital stay was significantly longer for Procedure B (median, 45.5 days; range, 9–192 days) than for Procedure A (median, 10.5 days; range, 7–69 days, $P<1\times10^{-4}$). On univariate analysis, longer hospital stay (≥21 days) was related to older age, larger tumor size, greater number of resected tracheal rings, postoperative RLN palsy, and Procedure B (*Table 3*). On multivariate regression analysis, Procedure B was found to be an independent risk

Table 5 Risk factors for permanent tracheostoma

Risk factors	Transient (n=20)	Permanent (n=10)	P
Age (years)	67.6±8.1 [51–83]	66.9±9.3 [50–80]	0.83
Sex			1.00
Male	7 [35]	3 [30]	
Female	13 [65]	7 [70]	
Tumor diameter (mm)	46.5±19.4 [22–100]	50.4±13.67 [31-78]	0.58
Number of resected tracheal rings	4.1±1.5 [2–9]	4.9±1.1 [3-6]	0.046
Postoperative airway complication			0.58
Absent	18 [90]	8 [80]	
Present	2 [10]	2 [20]	
Postoperative RLN palsy			0.045
No	2 [10]	0	
Unilateral	14 [70]	4 [40]	
Bilateral	4 [20]	6 [60]	
Surgical procedure			1.00
A	2 [10]	1 [10]	
B	18 [90]	9 [90]	

Data are shown as mean ± standard deviation [range] or number [percentage]. Procedure A: sleeve resection with end-to-end anastomosis, Procedure B: window resection with tracheostomy. RLN, recurrent laryngeal nerve.

factor for longer hospital stay (*Table 4*).

Among patients who underwent Procedure A, 3 (12.5%) required postoperative tracheostoma, but only 1 (4%) was permanent. On the other hand, all patients who underwent Procedure B had a tracheocutaneous fistula, of which 9 (33%) were permanent (18 were temporary). Of these patients, 4 had postoperative permanent bilateral RLN palsy, and tracheostoma could not be closed due to airway stenosis. Three patients did not want tracheal closure due to dyspnea, and 3 failed tracheal stoma closure. In three patients whose fistula failed to close, there was a large tracheal stoma, and the fistula was closed with a deltopectoral flap, but the fistula was perforated again.

In addition, for patients with postoperative permanent RLN palsy, those with no recurrence for more than 1 year after surgery and who were in good general condition underwent phonosurgery at other hospitals only if they wished. Even if phonosurgery was performed, tracheostoma closure was associated with risks, so there were cases in which the tracheostomy was not closed, and cases in which the tracheostomy was re-opened after closure.

For patients requiring temporary tracheostomy, time

to stoma closure ranged from 15 to 4,099 days (mean 384 days). A small fistula may close spontaneously merely following removal of the tracheal canula. Fistulas that were difficult to close spontaneously were sutured, or localized skin flaps were used. The case that took 4,099 days had a recurrence of the stoma and delayed closure.

Univariate analysis of risk factors for permanent tracheostoma identified larger number of tracheal rings and postoperative bilateral RLN palsy as significant factors (*Table 5*). On multivariate logistic regression analysis, resection of ≥5 tracheal rings and postoperative bilateral RLN palsy were independent risk factors for a permanent tracheostoma (*Table 6*).

Postoperative outcomes including LRFS and CSS were compared between procedures. Neither rate differed significantly between procedures (*Figures 1,2*). Regarding LRFS, no significant differences were found. However, cases with older age at the time of surgery (≥65 years old) tended to show a higher recurrence rate. The 10-year CSS rate was significantly lower in older patients (≥65 years old) and patients with resection of a larger number of tracheal rings (≥5 tracheal rings) (*Tables 7,8*). In this cohort,

Table 6 Multivariate analysis of risk factors for permanent tracheostoma

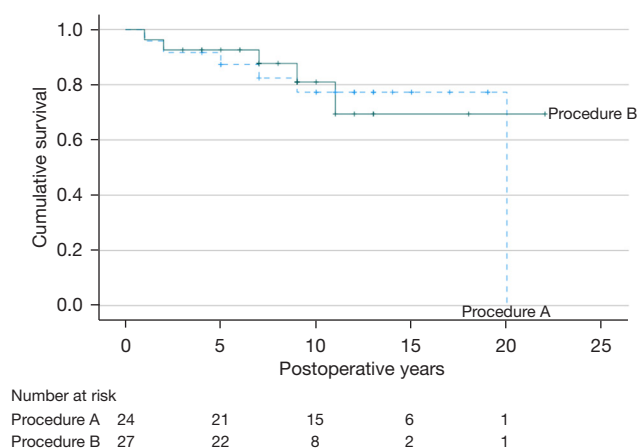| Risk factors	Coefficient value (B)	Standard error	Significance	Exp(B)
Age at time of surgery (≥65 years)	0.028	0.988	0.977	1.028
Number of resected tracheal rings (≥5)	1.951	0.984	0.047	7.036
Postoperative bilateral RLN palsy	1.960	0.985	0.047	7.102

RLN, recurrent laryngeal nerve.

Figure 1 LRFS for each procedure and number at risk. Procedure A is sleeve resection with end-to-end anastomosis, and Procedure B is window resection with tracheostomy (P=0.80; log-rank test). LRFS, local recurrence-free survival.
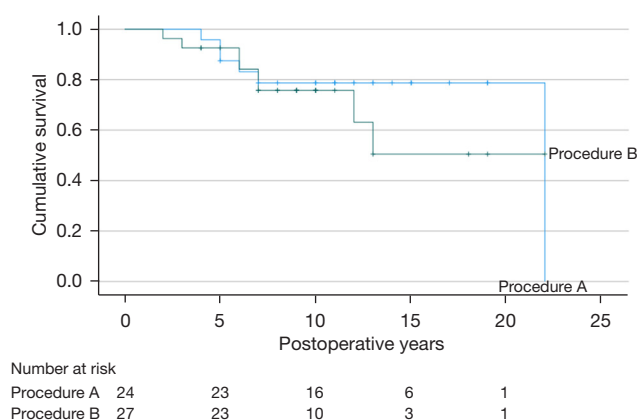
Figure 2 CSS for each procedure and number at risk. Procedure A is sleeve resection with end-to-end anastomosis, and Procedure B is window resection with tracheostomy (P=0.54; log-rank test). CSS, cause-specific survival.

14 patients died of the primary disease, with distant metastasis in 11 (79%) and local recurrence in 3 (21%).

Discussion

Strengths and limitations

We retrospectively examined the indications, postoperative clinical course, and treatment outcomes for 51 patients who underwent localized radical resection plus reconstruction surgery for full-layer tracheal infiltration. However, because it was a retrospective study with only 51 cases, bias existed in the choice of reconstruction method.

Specifically, the surgical method was determined subjectively by the operator, taking into consideration factors such as the operator's skill and the patient's background. In addition, other prognostic factors, such as patient complications, were not considered in this study when determining treatment plans.

Key findings and comparison with similar research

Procedure A was selected for cases without preoperative RLN palsy, esophageal infiltration, or clinical lymph node metastasis, and for cases with a small number of resected tracheal rings. Tsukahara *et al.* selected Procedure B for: (I) cases with bilateral RLN palsy; (II) cases requiring resection of ≥6 tracheal rings; (III) cases with bilateral neck dissection; (IV) cases in which extreme tension was applied to the part under the end-to-end anastomosis; and (V) cases with a low activity index, as seen in elderly persons (16).

According to Czaja *et al.*, in general, the limit of tracheal resection with primary anastomosis without a complete tracheal and laryngeal mobilization procedure is 5–6 cm of the trachea (8). In addition, Allen *et al.* reported

Table 7 Univariate analysis of LRFS of 51 patients

Characteristics	Total number of patients, n [%]	Patients showing progression, n [%]	Standard error	95% CI of LRFS, years	10-year LRFS, %	P by log-rank test
Age						0.06
<65 years	25 [49]	4 [16]	1.24	16.58–21.45	92	
≥65 years	26 [51]	7 [27]	1.56	10.93–17.05	61	
Sex						0.84
Male	14 [27]	3 [21]	2.31	12.87–21.94	86	
Female	37 [73]	8 [22]	1.19	14.36–19.02	77	
Tumor size						0.69
<40 mm	24 [47]	6 [25]	1.46	13.72–19.46	81	
≥40 mm	27 [53]	5 [19]	1.50	15.33–21.19	78	
Lymph node metastasis						0.90
Absent	20 [39]	5 [25]	1.55	13.82–19.90	76	
Present	31 [61]	6 [19]	1.49	15.00–20.83	82	
Distant metastasis						0.82
Absent	37 [73]	8 [22]	1.31	14.89–20.01	81	
Present	14 [27]	3 [21]	1.22	10.26–15.04	76	
Number of resected tracheal rings						0.55
<5 rings	40 [78]	10 [25]	1.25	14.62–19.55	77	
≥5 rings	11 [22]	1 [9]	0.95	10.13–13.87	91	
Surgical procedure						0.80
A	24 [47]	6 [25]	1.49	13.69–19.52	77	
B	27 [53]	5 [19]	1.75	14.17–21.03	81	

Procedure A: sleeve resection with end-to-end anastomosis; Procedure B: window resection with tracheostomy. LRFS, local-recurrence free survival; CI, confidence interval.

that the maximum range of tracheal resection that allows for simple end-to-end anastomosis is generally determined to be equivalent to seven rings of the trachea or a major axis of 5–6 cm (17).

Moreover, with respect to the required surgery for deeper wall invasion, Dralle classified six types of complete wall resection of the larynx and trachea. Window resection of the tracheal wall is used for types classified as having unilateral tumor invasion to a maximum extent of up to 2 cm vertically and within 1/4 of the horizontal circumference. Circular wall resection of the trachea is used for types with unilateral or bilateral wall tumor invasion >2 cm vertically and/or >1/4 of the horizontal circumference (1,18).

Airway complications tended to be more common with Procedure A, though none was fatal. The most serious complication of Procedure A is tracheal suture failure.

Tracheal suture failure leads to neck infection, abscess formation fistulizing into nearby vessels such as the common carotid artery, and massive bleeding (17). According to Rotolo et al., the postoperative complication rate in Procedure A was 15% to 39%, and the postoperative mortality rate was reported to be approximately 1.2% (19). In addition, Nakao reported that 4 of 40 patients who underwent Procedure A developed anastomotic failure (20). Wright et al. reported that 901 patients underwent Procedure A and anastomotic complications occurred in 81 patients (9%) (21).

The incidence of complications decreased with the introduction of IONM, which is considered essential for safe tracheal reconstruction. The usefulness of IONM

Table 8 Univariate analysis of CSS in 51 patients

Characteristics	Total number of patients, n [%]	Patients showing progression, n [%]	Standard error	95% CI of CSS, years	10-year CSS, %	P by log-rank test
Age						0.04
<65 years	25 [49]	5 [20]	1.40	16.47–22.00	92	
≥65 years	26 [51]	9 [35]	1.38	11.00–16.42	60	
Sex						0.17
Male	14 [27]	2 [14]	1.55	16.57–22.66	85	
Female	37 [73]	12 [32]	1.44	13.64–19.27	74	
Tumor size						0.95
<40 mm	24 [47]	7 [29]	1.65	14.43–20.89	73	
≥40 mm	27 [53]	7 [26]	1.73	13.08–19.87	81	
Lymph node metastasis						0.53
Absent	20 [39]	5 [25]	1.72	15.14–21.89	84	
Present	31 [61]	9 [29]	1.52	13.54–19.51	72	
Distant metastasis						0.88
Absent	37 [73]	10 [27]	1.33	15.00–20.22	74	
Present	14 [27]	4 [29]	0.98	10.67–14.53	86	
Number of resected tracheal rings						0.02
<5 rings	40 [78]	9 [22]	1.15	16.27–20.80	81	
≥5 rings	11 [22]	5 [45]	1.55	6.50–12.59	62	
Surgical procedure						0.54
A	24 [47]	6 [25]	1.54	15.47–21.49	79	
B	27 [53]	8 [30]	1.82	11.98–19.12	76	

Procedure A: sleeve resection with end-to-end anastomosis; Procedure B: window resection with tracheostomy. CSS, cause-specific survival; CI, confidence interval.

for RLN palsy can be predicted during surgery, and postoperative asphyxia due to bilateral RLN palsy can be prevented. Tsukahara has also reported on this (16).

The length of hospital stay was significantly prolonged with Procedure B, especially in elderly patients, when the tumor was large, when multiple tracheal rings were resected, or postoperative RLN palsy developed (univariate analysis). However, multivariate analysis showed that Procedure B was an independent risk factor for long-term hospitalization. This was likely attributable to the large number of cases with more advanced conditions, rather than because of the surgical procedure itself.

Bilateral RLN palsy after surgery was a risk factor for permanent tracheostoma, as well as ≥5 resected tracheal rings. Moritani *et al.* also previously reported 76 cases of

full-layer tracheal invasion that all underwent window resection, finding that tracheocutaneous fistula closure was impossible in 46 cases (60%). They reported RLN palsy and resection of multiple tracheal rings as factors related to failure to close the tracheocutaneous fistula (22).

No differences in LRFS and CSS were seen according to the reconstruction method used in the present study. In addition, univariate analysis of each factor for LRFS and CSS showed that none of the factors was significant for LRFS. However, CSS for elderly patients and for patients with a large number of resected tracheal rings was poor. With Procedure B, patients were more often elderly and had advanced disease, including cases with large tumor size, infiltration to other organs, and lymph node metastases. Taking into consideration that Procedure A was selected for

patients with less advanced disease, Procedure B may offer higher curability.

Explanations of findings

Extrathyroidal infiltration is one of the most important prognostic risk factors for patients with PTC (17,23,24). In patients with full-layer tracheal infiltration, full-layer tracheal resection is needed for local control of the disease, but it is important to select the surgical method by taking into consideration curability, the patient's general condition, tumor status, and expected prognosis.

The present study of 51 patients with PTC suggested that Procedure A is better than Procedure B in terms of a shorter hospital stay and avoiding the need for a permanent tracheostoma.

Past reports have also indicated that Procedure A has the advantage of allowing reconstruction in one stage after full-layer resection of the trachea, and the tracheal lumen can be covered with normal tracheal mucosa. However, serious complications such as tracheal suture failure can occur (2,12,19-21,25,26). On the other hand, Procedure B was indicated more often for more advanced patients than Procedure A, although treatment outcomes were similar.

Implications and actions needed

In Procedure A, tracheal resection and primary reconstruction are feasible surgical procedures for patients with thyroid cancer with tracheal invasion, with good clinical outcomes. However, according to Etienne (27), primary tracheal resection with direct end-to-end anastomosis after release of the surrounding anatomical structures is insufficient when the length of trachea resected is greater than 50% in adults or 30% in children. Therefore, sleeve resection and end-to-end anastomosis cannot be performed in all cases, and it is necessary to select an appropriate surgical method for patients with tracheal invasion before surgery.

It is important for physicians to consider the patient's characteristics, degree of invasion, and postoperative complications when deciding the treatment plan.

This study had some limitations. As a retrospective study of only 51 cases, bias was present in the choice of reconstruction methods. The length of hospital stay in Japan is generally longer than in Western countries due to the national medical insurance system (28). Patients often remain hospitalized until tracheostoma closure or until

tracheostoma self-management becomes possible.

The present study also only evaluated the procedures in terms of patient benefit based on the length of hospital stay and the necessity for permanent tracheal stoma, whereas a prospective study should provide verification of any improvements in actual quality of life using valid scales, such as the EORTC QLQ-THY34 or ThyPRO.

Conclusions

The aim of this study was to elucidate appropriate criteria for surgical selection in each patient. It was found that Procedure A was selected significantly more often for patients with tracheal infiltration affecting <4 tracheal rings, no preoperative RLN palsy, and no esophageal invasion or lymph node metastasis.

Going forward, sample sizes need to be increased for verification, and further prospective studies should be conducted.

Acknowledgments

Footnote

2013–1128) and individual consent for this retrospective analysis was waived.

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References

1. Brauckhoff M. Classification of aerodigestive tract invasion from thyroid cancer. Langenbecks Arch Surg 2014;399:209-16.
2. Matsumoto F, Ikeda K. Surgical Management of Tracheal Invasion by Well-Differentiated Thyroid Cancer. Cancers (Basel) 2021;13:797.
3. Sciuto R, Romano L, Rea S, et al. Natural history and clinical outcome of differentiated thyroid carcinoma: a retrospective analysis of 1503 patients treated at a single institution. Ann Oncol 2009;20:1728-35.
4. Hundahl SA, Cady B, Cunningham MP, et al. Initial results from a prospective cohort study of 5583 cases of thyroid carcinoma treated in the united states during 1996. U.S. and German Thyroid Cancer Study Group. An American College of Surgeons Commission on Cancer Patient Care Evaluation study. Cancer 2000;89:202-17.
5. Youngwirth LM, Adam MA, Scheri RP, et al. Extrathyroidal Extension Is Associated with Compromised Survival in Patients with Thyroid Cancer. Thyroid 2017;27:626-31.
6. Andersen PE, Kinsella J, Loree TR, et al. Differentiated carcinoma of the thyroid with extrathyroidal extension. Am J Surg 1995;170:467-70.
7. Kim H, Jung HJ, Lee SY, et al. Prognostic factors of locally invasive well-differentiated thyroid carcinoma involving the trachea. Eur Arch Otorhinolaryngol 2016;273:1919-26.
8. Czaja JM, McCaffrey TV. The surgical management of laryngotracheal invasion by well-differentiated papillary thyroid carcinoma. Arch Otolaryngol Head Neck Surg 1997;123:484-90.
9. Ishihara T, Kobayashi K, Kikuchi K, et al. Surgical treatment of advanced thyroid carcinoma invading the trachea. J Thorac Cardiovasc Surg 1991;102:717-20.
10. Nishida T, Nakao K, Hamaji M. Differentiated thyroid carcinoma with airway invasion: indication for tracheal resection based on the extent of cancer invasion. J Thorac Cardiovasc Surg 1997;114:84-92.
11. Hotomi M, Sugitani I, Toda K, et al. A novel definition of extrathyroidal invasion for patients with papillary thyroid carcinoma for predicting prognosis. World J Surg 2012;36:1231-40.
12. Hazama K, Miyoshi S, Akashi A, et al. Clinicopathological investigation of 20 cases of primary tracheal cancer. Eur J Cardiothorac Surg 2003;23:1-5.
13. Gerwat J, Bryce DP. The management of subglottic laryngeal stenosis by resection and direct anastomosis. Laryngoscope 1974;84:940-57.
14. Chen W, Zou S, Wang L, et al. Anastomosis in the absence of a suprahyoid release following circumferential sleeve resection is feasible in differentiated thyroid carcinoma patients with tracheal invasion. Oncol Lett 2017;14:2822-30.
15. Mutrie CJ, Eldaif SM, Rutledge CW, et al. Cervical tracheal resection: new lessons learned. Ann Thorac Surg 2011;91:1101-6; discussion 1106.
16. Tsukahara K, Sugitani I, Kawabata K. Tracheal resection with end-to-end anastomosis preserving paries membranaceus trachea for patients with papillary thyroid carcinoma. Acta Otolaryngol 2009;129:575-9.
17. Allen M, Spillinger A, Arianpour K, et al. Tracheal Resection in the Management of Thyroid Cancer: An Evidence-Based Approach. Laryngoscope. 2021;131:932-46.
18. Brauckhoff M, Dralle H. Extrathyroidal thyroid cancer: results of tracheal shaving and tracheal resection. Chirurg 2011;82:134-40.
19. Rotolo N, Cattoni M, Imperatori A. Complications from tracheal resection for thyroid carcinoma. Gland Surg 2017;6:574-8.
20. Nakao K, Kurozumi K, Nakahara M, et al. Resection and reconstruction of the airway in patients with advanced thyroid cancer. World J Surg 2004;28:1204-6.
21. Wright CD, Grillo HC, Wain JC, et al. Anastomotic complications after tracheal resection: prognostic factors and management. J Thorac Cardiovasc Surg 2004;128:731-9.
22. Moritani S. Window Resection for Intraluminal Cricotracheal Invasion by Papillary Thyroid Carcinoma. World J Surg 2017;41:1812-9.
23. Sugitani I, Kasai N, Fujimoto Y, et al. A novel classification

system for patients with PTC: addition of the new variables of large (3 cm or greater) nodal metastases and reclassification during the follow-up period. Surgery 2004;135:139-48.

24. Tsukahara K, Sugitani I, Kawabata K. Surgical management of tracheal shaving for papillary thyroid carcinoma with tracheal invasion. Acta Otolaryngol 2009;129:1498-502.

25. Gaissert HA, Honings J, Grillo HC, et al. Segmental laryngotracheal and tracheal resection for invasive thyroid carcinoma. Ann Thorac Surg 2007;83:1952-9.

26. Marulli G, Rizzardi G, Bortolotti L, et al. Single-staged laryngotracheal resection and reconstruction for benign strictures in adults. Interact Cardiovasc Thorac Surg 2008;7:227-30; discussion 230.

27. Etienne H, Fabre D, Gomez Caro A, et al. Tracheal replacement. Eur Respir J 2018;51:1702211.

28. Organisation for Economic Co-operation and Development. Health Care Utilization Statistics. Available online: https://www.oecd.org/els/health-systems/health-data.htm