World J Surg (2021) 45:2752–2758
https://doi.org/10.1007/s00268-021-06172-7

World Journal of Surgery

ORIGINAL SCIENTIFIC REPORT

Outcomes of Tracheal Resections in Well-Differentiated Thyroid Cancer—A case series and meta-analysis

Anton Warshavsky[1] · Roni Rosen[1] · Narin Nard-Carmel[1] · Nidal Muhanna[1] · Omer Ungar[1] · Avraham Abergel[1] · Dan M. Fliss[1] · Gilad Horowitz[1]

Accepted: 2 May 2021 / Published online: 22 May 2021

Abstract

Background Tracheal invasion in thyroid cancer is a well-known form of advanced disease. There is an ongoing controversy over outcomes of tracheal shaving in this situation. The aim of this study was to compare the results of tracheal shaving to radical resections in patients with low-volume tracheal involvement.

Methods An institutional case series and a meta-analysis was conducted. All studies that included patients diagnosed with well-differentiated thyroid cancer (WDTC) and tracheal invasion were analyzed. Patients with low-volume tracheal invasion (according to the Shin classification) were extracted from the various studies and subsequently included in this study. The outcomes of tracheal shaving and radical resection were consolidated and compared. All recurrences and mortality over 10 years of follow-up were calculated using the Kaplan–Meier method.

Results Institutional case series included 22 patients diagnosed with WDTC and tracheal invasion that underwent resection. There was one case of recurrence (4.5%) during the follow-up period and no mortality. The meta-analysis yielded a total of 284 patients from six studies who met the inclusion criteria. The 10-year overall survival was 82.4% for the shave group and 80.8% for the resection group. The combined Kaplan–Meier curves revealed no statistically significant difference between the two techniques (hazard ratio [HR] = 0.86, P = .768). The combined 10-year local control rate of the shave group was 90.2%.

Conclusions The outcomes of tracheal shaving in low-volume invasion are similar to more aggressive forms of tracheal resections. Shave resection is oncologically safe in carefully selected WDTC patients demonstrating minimal tracheal invasion.

Introduction

Thyroid cancer that invades the tracheal cartilage represents a surgical dilemma in terms of how aggressive the resection should be. Fortunately, the extent of tracheal invasion in thyroid cancer is mostly superficial. [1] Although aggressive tracheal resections in these patients may prolong survival, the associated morbidity remains significant. [2]

Surgical techniques for treating tracheal invasion range from shaving the trachea to various forms of tracheal resection (i.e., window resection and circumferential resection with end-to-end anastomosis). [3] Tracheal

Anton Warshavsky and Roni Rosen have contributed equally.

✉ Gilad Horowitz
giladhorowitz@gmail.com

1 The Department of Otolaryngology, Head & Neck Surgery and Maxillofacial Surgery, Tel-Aviv 'Sourasky' Medical Center, 'Sackler' School of Medicine, Tel-Aviv University, 6 Weizmann Street, 6423906 Tel-Aviv, Israel

shaving is defined as the sharp removal of all gross disease from the surface of the trachea while leaving the mucosa intact, and it is commonly performed for tumors with minimal invasion of the perichondrium. [4, 5] Tracheal shaving harbors a high risk of microscopic residual disease, and although complete resection is feasible, it is difficult to perform. [6–8].

Not surprisingly, the outcomes of shave resections for tracheal invasion by well-differentiated thyroid cancer (WDTC) have been controversial. [9] A number of studies reported similar survival and local control rates for shave resections compared to more aggressive tracheal resections in carefully selected patients. [10–12] That finding has been called into question by others who demonstrated worse outcomes for tracheal shaving. [13, 14] Therefore, the extent of tracheal resection necessary to achieve the best outcomes while avoiding untoward morbidity remains controversial. The aim of this study was to compare the outcomes of tracheal shaving to radical resections in WDTC patients with minimal tracheal involvement.

Materials and methods

Literature search

We carried out a methodical and comprehensive search for all relevant publications in the English literature between January 1970 and August 2019 in the electronic databases: 'Embase,' 'PubMed' and 'Google Scholar,' using the key terms: 'Thyroid Cancer,' 'Well-Differentiated,' 'Locally Advanced,' 'Trachea,' 'Tracheal Invasion,' 'Surgical Management,' 'Shave,' 'Resection,' 'Window Resection,' 'Circumferential Resection,' and 'Tracheal Shaving versus Resection.' Some terms were also used in combination. The reference section of each article was searched for additional potentially relevant publications.

Study eligibility criteria

All studies that included outcomes of WDTC patients with tracheal invasion were eligible for inclusion in this meta-analysis. The specific inclusion criteria for the study were: (1) both prospective and retrospective cohorts, as well as any randomized controlled trials, case–control studies, case studies, and case reports; (2) study populations with the histopathologic diagnosis of WDTC, including papillary thyroid carcinoma and follicular carcinoma; (3) patients with superficial tracheal invasion including those with disease abutting but not invading the external perichondrium (in accordance with type I invasion of the Shin classification [15]) and (4) patients with invasion between the rings of the cartilage or invasion causing minor cartilage destruction (in accordance with type II invasion of the Shin classification [15]).

Exclusion criteria were: (1) Medullary thyroid carcinoma and other undifferentiated tumors; (2) Reports including mixed histology in which case differentiation was not possible; (3) patients with submucosal and intraluminal disease involvement (in accordance with type III and IV invasion of the Shin classification [15]); (4) poorly defined surgical techniques for carrying out tracheal resection; and (5) unreported outcomes.

Case series

Patients treated at the Tel-Aviv 'Sourasky' Medical Center (TASMC) between January 1, 2006, and December 31, 2015, fulfilling the inclusion criteria were identified from the institutional electronic database. Institutional research ethics board approval was obtained prior to study initiation. (IRB TLV-704–16). Demographic, clinical, pathologic, and radiologic data on all included patients was analyzed. All inclusion and exclusion criteria defined for the meta-analysis were also applied to the current case series. Tracheal invasion was confirmed on final histological results and margin status reported as negative resection margins (R0), microscopic involvement (R1) and gross disease (R2). Outcome measures were recorded and matched to the meta-analysis requirements.

Data extraction

Information on study design, patient characteristics, primary tumor treatment, sample size, and average follow-up time was retrieved from the selected papers. Data were initially extracted and evaluated by the 2 principal investigators (A.W. and R.R.) and thereafter rechecked and confirmed by two other investigators (N.C-N. and G.H.). Data on the type of resection, pathology, postoperative therapy, and survival rates were recorded (Table 1). Since most of the available studies were retrospective and observational, we followed the guidelines for meta-analyses of observational studies. [16].

Statistical analysis

The statistical method described by Parmar et al [17] was applied to derive the number of patients censored and the patients who had recurrences (events) in each year of follow-up from the original Kaplan–Meier (K–M) curves. K–M curves were recalculated for each study and compared

Table 1 Clinical and demographic characteristics

Sex (male)	6 (27.3%)
Age at surgery	54 ± 17.98
Airway symptoms at presentation	1 (4.5%)
Vocal cord paralysis	0
Preoperative suspicious of tracheal invasion	1 (4.5%)
Positive microscopic margins	6 (27.3%)
Radioactive iodine treatment	15 (68.2%)
EBRT	1 (4.5%)
Chemotherapy	0
Recurrence	1 (4.5%)
MCI total cumulative dosage	183 ± 76.7
LOFU (months)	54.4 ± 35.8

MCI millicurie iodine, *EBRT* external beam radiation treatment, *LOFU* length of follow-up

with the original K–M curves in order to evaluate the statistical estimation.

The data from all studies were consolidated, and combined K–M curves were calculated for recurrences and mortality over 10 years of follow-up. The log-rank test was used to compare between surgical methods, and univariate cox regression models were used to estimate the hazard ratio (HR). All statistical tests were two-tailed, and a P value < 0.05 was considered significant. The statistical analysis was calculated using the SPSS software (IBM SPSS Statistics for Windows, Version 25, IBM corp., Armonk, NY, USA, 2017).

Results

Study selection

The search strategy identified 71 papers published from 1970 to 2019. Those papers were selected and transferred into EndNote (Thomson Reuters®), and replicates were removed. The various phases of assessing the abstracts and reasons for exclusion from the meta-analysis are depicted in Fig. 1. Five retrospective studies eventually met the inclusion criteria. All cases from the Tel-Aviv 'Sourasky' Medical Center that met the inclusion criteria were also incorporated into the study (Table 1), yielding a total of 284 patients from six studies who were subsequently included in the meta-analysis (Table 2).

TASMC results

Twenty-two patients diagnosed with WDTC had minimal tracheal invasion (Shin I and II; see study eligibility criteria), all treated with a tracheal shave. One patient was suspected preoperatively for tracheal invasion and underwent a tracheoscopy to rule out intraluminal involvement. All other 21 patients had tracheal invasion diagnosed only at the time of surgery. The patients included 16 females (72.7%) and six males (27.3%) with a median age of 52, IQR [43–65.75]. The median follow-up time was 48.7 months IQR [22.0–86.7]. The final pathological results revealed that 16 patients (72.7%) had an R0 resection and that the remaining six patients (27.3%) had positive microscopic margins (R1). One patient suffered a tracheal perforation and a temporary unilateral vocal cord paralysis necessitating revision surgery. The perforation was patched using a strap muscle local flap, and the patient decannulated a few days later.

Postoperative RAI treatment was recommended to 17 patients but delivered only in 15 cases (68.2%) after two patients declined treatment. The RAI overall dosage range was 50–300 mCi (mean 183 ± 76.7 mCi) given in one or two treatments. One patient underwent radiation therapy. There was one case of recurrence (4.5%) during the follow-up period—a lateral neck disease diagnosed one-year post-RAI treatment (surgically salvaged), and no cases of mortality. The baseline clinical and treatment details of the cohort are listed in Table1.

Meta-analysis results

Overall survival (OS) rates were compared between the two surgical techniques, tracheal shave (shave group) and tracheal resection (resection group). The 10-year OS rate for the shave group was 82.4% (3.9% std. error) and 80.8% (9.5% std. error) for the resection group. The combined K–M curves revealed no statistical difference between the two techniques (HR = 0.86 [95% confidence interval [CI] 0.29–2.50], $p = 0.768$). (see Fig. 2) Due to the lack of data on recurrences in the resection group, local control (LC) values were calculated only for the shave group; one-hundred and fifty-five patients from four studies were included, and the 10-year LC rate was 90.2% (2.7% std. error). (see Fig. 3).

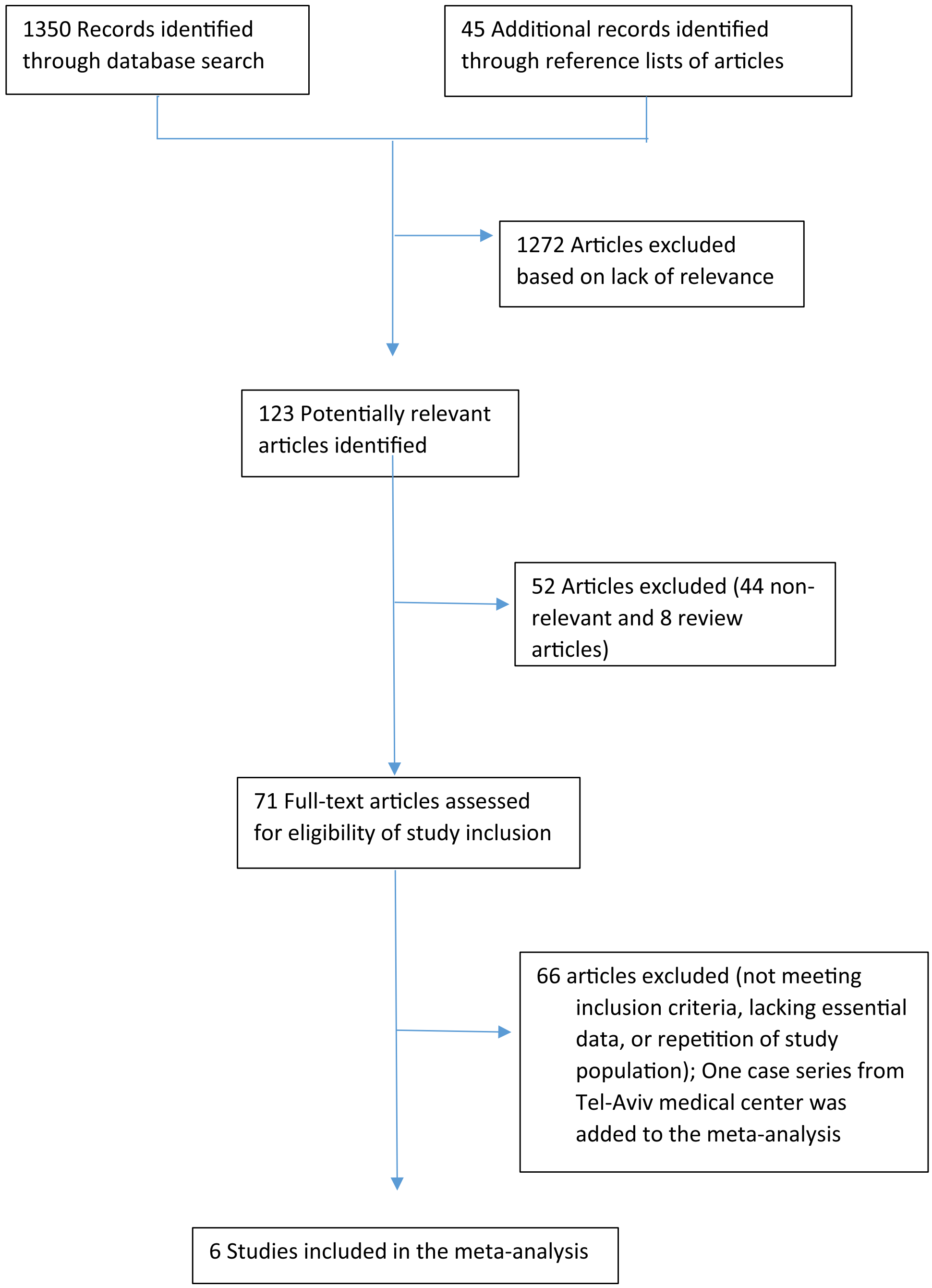

Fig. 1 Article selection flowchart

Discussion

Tracheal invasion of WDTC is regarded as a rarity, and the number of publications on the subject is sparse. This paper demonstrates similar outcomes for shave and tracheal resections for carefully selected patients with WDTC presenting with tracheal invasion. Meta-analyses of the cumulative data show similar 10-year OS ($\sim$ 80%) for both groups. The 10-year LC rate in the shave group was roughly 10%.

There is an ongoing debate in the literature on the superior type of resection and outcomes in tracheal invasion by WDTC. One possible explanation for these inconsistencies may be attributed to different invasion patterns (according to Shin types) among the studies. Excellent local control rates may be anticipated in patients with Shin I and II undergoing shave resections, whereas that approach may lead to macroscopic residual disease and high recurrence rates among patients with Shin types III and IV. [18] With that being said, a recently published

Table 2 Study data, demographics, resection types and postoperative therapy

Study	Design	Year of accrual	Sample size (*n*)	Age range (*y*)	Male/ female (*n*)	Shave (*n*)	Resection (*n*)	EBRT (*n*)	RAI (*n*)	Chemotherapy (*n*)
Czaja et al., [11]	Retrospective	1940–1995	109*	N/A	N/A	75	34	Majority	Majority	N/A
Bayles et al., [28]	Retrospective	1977–1997	13*	24–83	N/A	8	5	1	13	1
Nishida et al., [12]	Retrospective	1970–1994	15*	50–70	1/14	13	2	N/A	0	N/A
Tsukahara et al., [29]	Retrospective	1994–2005	18*	29–89	9/9	18	0	0	5	N/A
Ito et al.,[30]	Retrospective	1987–2004	107	40–67	15/92	107	0	Minority #	4	N/A
TASMC case series	Retrospective	2006–2015	22	24–88	5/17	22	0	0	15	0

EBRT external beam radiation therapy; *RAI* radioactive iodine; *N/A* not applicable; *TASMC* Tel-Aviv 'Sourasky' Medical Centre;

*Sample size extracted for analysis

Suspicious for positive margins

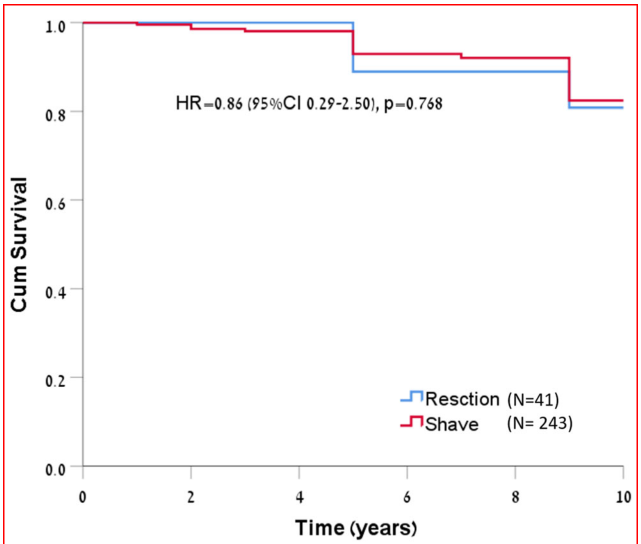

Fig. 2 Overall survival rates of the 'tracheal shave' (Shave) and 'tracheal resection' (Resection) groups

paper on definitive surgery for locally advanced WDTC observed that disease extent and surgical extent were not associated with either LC or OS. [19] Positive microscopic margins (R1) in locally advanced thyroid cancer are rather prevalent and are not necessarily attributed to the type of resection. A recently published paper reported similar negative and microscopically involved resection margins in all types of tracheal resection. [20] Various studies have shown that positive microscopic margins do not portend worse outcomes in WDTC patients. [21, 22] With that being said, a recent study on T4a patients showed higher rates of failures in R1 resections, despite being regional or distant. [23] An important variable that may affect outcomes of high-risk patients is the volume of the treating center; Patients treated at low-volume centers have higher rates of incomplete resection and compromised outcomes. [24] In an investigation on tracheal invasion from WDTC, Moritani [25] suggested that distant metastasis occurred frequently (despite good locoregional control) and that this was the leading cause of death. The results of the current meta-analysis support the notion that local recurrences are probably not the cause of death but rather poor regional and distant control. This conclusion is derived from the discrepancies between local recurrences and OS in the shave groups in which there was a 90% 10-year LC rate while the OS was as low as 65%.

One of the possible explanations for the similar results for the various resection techniques is adjuvant treatment. Many patients included in the meta-analysis had undergone radioactive iodine (RAI) treatment and occasionally radiotherapy in an attempt to ablate residual disease. This may explain the results; the vast majority of patients are well controlled with the use of postoperative treatment (and suppression). Radiotherapy is theoretically reserved for poorly controlled disease. [26].

One of the main caveats of this study is that we could not calculate the exact disease-specific survival (DSS) outcomes. DSS could not be extrapolated since most of the studies did not report the cause of death. Given the recognized flaws in reporting OS, DSS is an important outcome measure, especially when comparing disease control between therapeutic approaches. [27] Another shortcoming that bears mentioning is the lack of molecular analysis in

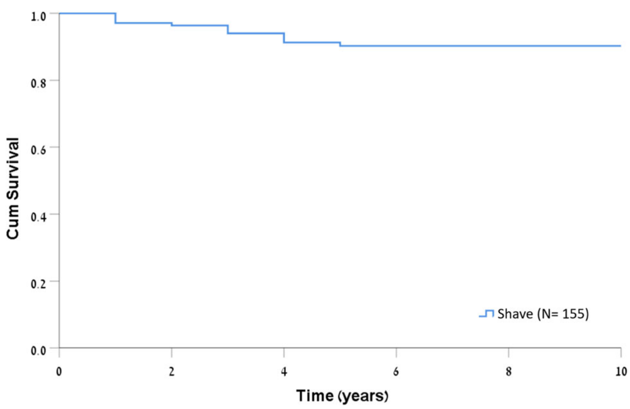

Fig. 3 Local control (LC)—"tracheal shave" (Shave)

our cohort that could shed some light on the outcomes. Other caveats of this study are the relatively small numbers of patients in the various series, the retrospective nature of all the studies, and the small proportion of studies with head-to-head comparison of the various surgical techniques.

Conclusion

The outcomes of tracheal shaving in low-volume invasion of WDTC are similar to more aggressive forms of tracheal resections. Shave resection is oncologically safe in carefully selected WDTC patients with minimal tracheal invasion.

Declaration

Conflict of interest The author declares there is no conflict of interest.

References

1. Grillo HC, Zannini P (1986) Resectional management of airway invasion by thyroid carcinoma. Ann Thorac Surg 42(3):287–298
2. McCarty TM, Kuhn JA, Williams WL et al (1997) Surgical management of thyroid cancer invading the airway. Ann Surg Oncol 4(5):403–408
3. Grillo HC, Suen HC, Mathisen DJ, Wain JC (1992) Resectional management of thyroid carcinoma invading the airway. Ann Thorac Surg 54(1):3–10
4. Shindo ML, Caruana SM, Kandil E et al (2014) Management of invasive well-differentiated thyroid cancer: an American head and neck society consensus statement: AHNS consensus statement. Head Neck 36(10):1379–1390
5. Honings J, Stephen AE, Marres HA, Gaissert HA (2010) The management of thyroid carcinoma invading the larynx or trachea. Laryngoscope 120(4):682–689
6. Frazell EL, Foote FW Jr (1958) Papillary cancer of the thyroid. A review of 25 years of experience. Cancer 11(5):895–922
7. Mellière DJ, Yahia NEB, Becquemin JP, Lange F, Boulahdour H (1993) Thyroid carcinoma with tracheal or esophageal involvement: limited or maximal surgery? Surgery 113(2):166–172
8. Keum KC, Suh YG, Koom WS et al (2006) The role of postoperative external-beam radiotherapy in the management of patients with papillary thyroid cancer invading the trachea. International Journal of Radiation Oncology* Biology* Physics. 65(2):474–480
9. Chernichenko N, Shaha AR (2012) Role of tracheal resection in thyroid cancer. Curr Opin Oncol 24(1):29–34
10. Cody HS, Shah JP (1981) Locally invasive, well-differentiated thyroid cancer: 22 years' experience at Memorial Sloan-Kettering Cancer Center. Am J Surg 142(4):480–483
11. Czaja JM, McCaffrey TV (1997) The surgical management of laryngotracheal invasion by well-differentiated papillary thyroid carcinoma. Arch Otolaryngol-Head Neck Surg 123(5):484–490
12. Nishida T, Nakao K, Hamaji M (1997) Differentiated thyroid carcinoma with airway invasion: indication for tracheal resection based on the extent of cancer invasion. J Thorac Cardiovasc Surg 114(1):84–92
13. Park CS, Suh KW, Min JS (1993) Cartilage-shaving procedure for the control of tracheal cartilage invasion by thyroid carcinoma. Head Neck 15(4):289–291
14. Kasperbauer JL (2004) Locally advanced thyroid carcinoma. Annal Otol Rhinol Laryngol 113(9):749–753
15. Shin D-H, Mark EJ, Suen HC, Grillo HC (1993) Pathologic staging of papillary carcinoma of the thyroid with airway invasion based on the anatomic manner of extension to the trachea: a clinicopathologic study based on 22 patients who underwent thyroidectomy and airway resection. Hum Pathol 24(8):866–870
16. Moher D, Shamseer L, Clarke M et al (2015) Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Contr Found Appl 4(1):1
17. Parmar MK, Torri V, Stewart L (1998) Extracting summary statistics to perform meta-analyses of the published literature for survival endpoints. Stat Med 17(24):2815–2834
18. Hartl DM, Zago S, Leboulleux S et al (2014) Resection margins and prognosis in locally invasive thyroid cancer. Head Neck 36(7):1034–1038
19. Kim JW, Roh J-L, Gong G et al (2016) Treatment outcomes and risk factors for recurrence after definitive surgery of locally invasive well-differentiated papillary thyroid carcinoma. Thyroid 26(2):262–270
20. Kim BY, Choi JE, Lee E et al (2017) Prognostic factors for recurrence of locally advanced differentiated thyroid cancer. J Surg Oncol 116(7):877–883
21. Kluijfhout WP, Pasternak JD, Kwon JS et al (2016) Microscopic positive tumor margin does not increase the risk of recurrence in patients with T1–T2 well-differentiated thyroid cancer. Ann Surg Oncol 23(5):1446–1451
22. Wang LY, Ghossein R, Palmer FL et al (2015) Microscopic positive margins in differentiated thyroid cancer is not an independent predictor of local failure. Thyroid 25(9):993–998
23. Abraham E, Roshan D, Tran B et al (2019) Microscopic positive margins strongly predict reduced disease-free survival in pT4a papillary thyroid cancer. Head Neck 41(8):2549–2554
24. Youngwirth LM, Adam MA, Scheri RP, Roman SA, Sosa JA (2016) Patients treated at low-volume centers have higher rates of incomplete resection and compromised outcomes: analysis of 31,129 patients with papillary thyroid cancer. Ann Surg Oncol 23(2):403–409
25. Moritani S (2015) Surgical management of cricotracheal invasion by papillary thyroid carcinoma. Ann Surg Oncol 22(12):4002–4007

26. Kiess AP, Agrawal N, Brierley JD et al (2016) External-beam radiotherapy for differentiated thyroid cancer locoregional control: a statement of the American head and neck society. Head Neck 38(4):493–498
27. Burke HB (2018) Overall survival vs disease-specific survival. JAMA Oncol 4(4):586–586
28. Bayles SW, Kingdom TT, Carlson GW (1998) Management of thyroid carcinoma invading the aerodigestive tract. Laryngoscope 108(9):1402–1407
29. Tsukahara K, Sugitani I, Kawabata K (2009) Surgical management of tracheal shaving for papillary thyroid carcinoma with tracheal invasion. Acta Otolaryngol 129(12):1498–1502
30. Ito Y, Fukushima M, Yabuta T et al (2009) Local prognosis of patients with papillary thyroid carcinoma who were intra-operatively diagnosed as having minimal invasion of the trachea: a 17-year experience in a single institute. Asian J Surg 32(2):102–108