



Safety of Non-robotic Transoral Surgeries for Pharyngolaryngeal Cancer: A Risk Factor Analysis of Complications Using Nationwide Claims Data

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ABSTRACT

Background. Non-robotic transoral surgery (NRTOS) is the mainstream approach for pharyngolaryngeal cancer resection in Japan, whereas the da Vinci surgical system is not widely used. NRTOS employs reusable instruments, resulting in significantly lower costs than those of transoral robotic surgery (TORS). Given the comparable oncological outcomes, this study aimed to investigate the risk factors for complications and mortality following NRTOS as an alternative to TORS.

Patients and Methods. This retrospective cohort study utilized Japanese claims data from diagnosis procedure combination and receipt databases. Data from patients who underwent NRTOS between April 2020 and December 2022 were collected. The primary outcomes were postoperative bleeding, dysphagia, and laryngopharyngeal edema.

Results. Among the 336 included patients, 88.7% were male, with a median age of 72 years. The incidence rates of bleeding, dysphagia, and laryngopharyngeal edema after NRTOS were 3.3%, 4.2%, and 8.0%, respectively. Univariate logistic regression analysis revealed that history of hypertension [odds ratio (OR): 9.82, 95% confidence interval (CI): 1.24–77.50] was a possible risk factor for postoperative bleeding, while a disease stage $\geq$ T2 (OR: 5.37, 95% CI:

1.52–19.00), a body mass index < 18.5 kg/m² (OR: 5.51, 95% CI: 1.46–20.80), and concurrent neck dissection with NRTOS (OR: 10.20, 95% CI: 3.26–32.10) were risk factors for postoperative dysphagia. No variables were identified as risk factors for laryngopharyngeal edema. Only one patient (0.3%) died during this study.

Conclusions. NRTOS demonstrated relatively low complication and mortality rates, establishing it as a safe technique for pharyngolaryngeal cancer resection.

Keywords Complication · Laryngeal cancer · Pharyngeal cancer · Risk factor · Transoral surgery · Transoral robotic surgery

Endoscopic transoral surgeries have become popular worldwide as minimally invasive approaches for pharyngolaryngeal cancer resection, with several countries using the da Vinci surgical system (Intuitive Surgical, Sunnyvale, CA) to perform transoral robotic surgery (TORS) since 2005.¹ However, in Japan, transoral surgeries that do not utilize the da Vinci surgical system, such as endoscopic laryngopharyngeal surgery (ELPS),² transoral videolaryngoscopic surgery (TOVS),³ and end-flexible-rigidoscopic transoral surgery (E-TOS),^{4,5} are more common (Fig. 1 and Supplementary Text 1). Despite TORS recently gaining insurance coverage in Japan in April 2022, these unique surgical procedures and transoral laser microsurgery,⁶ collectively referred to as non-robotic transoral surgery (NRTOS), remain the primary approach for pharyngolaryngeal cancer resection in Japan. And the oncologic outcomes and safety of NRTOS are comparable to those of TORS.^{2–5}

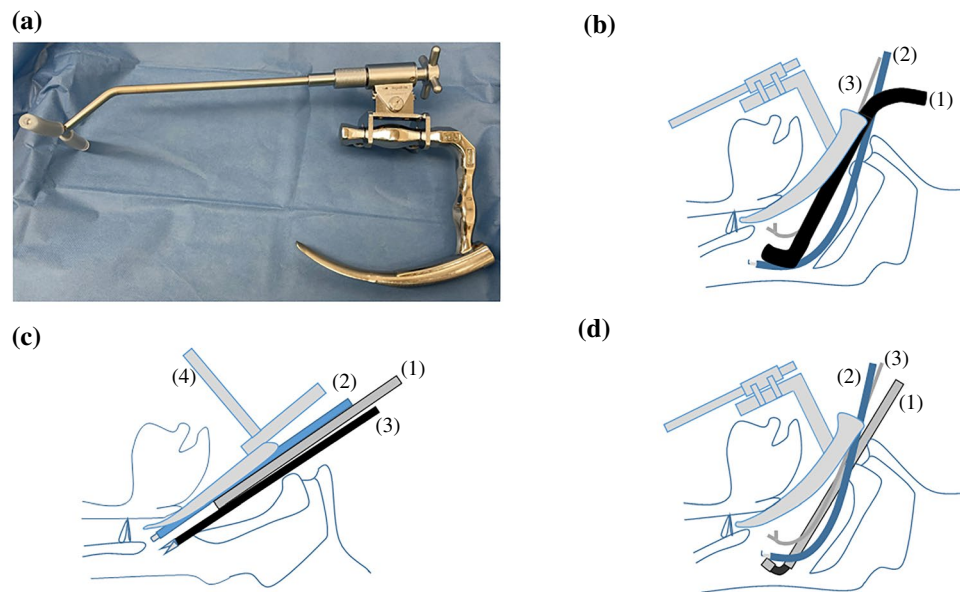


FIG. 1 A curved retractor and schema for each procedure of the non-robotic Japanese transoral surgery. **a** A curved rigid laryngopharyngeal retractor with the holder (Nagashima Medical Instruments, Tokyo, Japan). This original curved retractor is used in ELPS and E-TOS. **b** A scheme of ELPS. The surgical instruments used in ELPS include (1) a gastrointestinal endoscope, (2) a curved electric knife, and (3) curved forceps. **c** A scheme of TOVS. The surgical instruments used in TOVS include (1) a straight rigid endoscope, (2)

a straight electric knife, (3) straight forceps, (4) a Feyh–Kastenbauer, Weinstein–O’Malley retractor (Olympus Corp., Tokyo, Japan). **d** A scheme of E-TOS. The surgical instruments used in E-TOS include (1) a flexible-tip rigid endoscope, (2) a curved electric knife, and (3) curved forceps. *ELPS* endoscopic laryngo-pharyngeal surgery, *E-TOS* end-flexible-rigidoscopic transoral surgery, *TOVS* transoral videolaryngoscopic surgery

NRTOS offers several advantages over TORS. First, the curved retractor (Nagashima Medical Instruments, Tokyo, Japan) used in ELPS² and E-TOS^{4,5} can effectively expose the surgical field in the hypopharynx. This is in contrast to the Feyh–Kastenbauer–Weinstein–O’Malley retractor (Olympus Corp., Tokyo, Japan) used in TORS, which exhibits limited ability in effectively exposing the surgical field within the hypopharyngeal lumen. Since most reports of TORS-related outcomes and postoperative complications involved patients with oropharyngeal cancer,^{7–11} this advantage has led to a high proportion of patients with hypopharyngeal cancer being treated with these approaches, as reported in a previous study on the oncological outcomes of NRTOS.⁵ Second, the forceps used in NRTOS are thinner than those of the robotic arm used in TORS and reduce the interference between the endoscopic instrument and forceps, allowing the surgeon to resect the primary cancer in a wider working space.^{2–5} Lastly, since NRTOS uses reusable instruments, with the exception of the electric knife, the initial and maintenance cost and cost per surgery are substantially lower than those of TORS. The costs of initial equipment required, annual maintenance, and additional equipment required per surgery are approximately 120,000, 8650, and 50 US dollars (USD), respectively, for E-TOS, and approximately 2,400,000, 130,000, and 1000 USD, respectively, for TORS.⁵ E-TOS is less expensive than TORS and is easier to

implement at facilities with/without the da Vinci Surgical System.⁵

While understanding the risk factors for postoperative NRTOS-related complications and mortality is crucial for surgical decision-making and patient counseling, no nationwide studies have investigated these risk factors in Japan. Therefore, this study aimed to investigate the risk factors for postoperative complications and mortality following NRTOS using Japanese claims data.

PATIENTS AND METHODS

Data Source

This retrospective cohort study extracted data from two claims databases that track outpatient and inpatient visits at contracted medical institutions across Japan, provided by two commercial vendors in Japan. The first database, provided by JMDC Inc. (JMDC, Tokyo, Japan), contained diagnosis procedure combination data of over 550 hospitals under contract with JMDC, with 17 million registered patients as of 2022. The second database, maintained by the Health, Clinic, and Education Information Evaluation Institute (HCEI) with support from Real World Data, Co., Ltd. (RWD, Kyoto, Japan), contained electronic medical records, receipts, and diagnosis procedure combination

data from 225 medical institutions under contract with the HCEI, with 24.4 million registered patients as of 2022. These databases included patient characteristics, such as age and sex, clinical diagnostic names coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th edition (ICD-10), medical and pharmacy claims data, and medical procedures coded using the Japan-specific standard procedure codes (K-codes). This study was approved by the ethics committee of the Graduate School of Medicine, Kyoto University (January 5, 2023, R3791). The requirement for obtaining informed consent was waived owing to the secondary nature of the analysis and use of anonymized patient data.

Study Cohort

In Japan, NRTOS for pharyngeal and laryngeal cancer resection has been covered under the insurance codes K374-2 and K394-2-1, respectively, since April 1, 2020. Before this, the same codes (K374 and K394-1) were assigned for transcervical open surgery. Additionally, TORS has been covered by insurance in Japan since April 1, 2022 and assigned the same K-codes as NRTOS, although each surgical procedure can be distinguished. Thus, the present study included patients treated with NRTOS between April 1, 2020 and December 31, 2022. Patients who underwent multiple NRTOS procedures during the study period were considered as individual cases, while those who underwent TORS during the same period were excluded.

The complications associated with NRTOS were identified using the following ICD-10 codes: bleeding (T81.0, R58, R04.1, and R57.1), dysphagia (F50.9, R13, and J39.8), laryngopharyngeal edema (J38.4), fistula formation (K22.3), subcutaneous emphysema (T797), aspiration pneumonia (J690), pharyngoesophageal stricture (K22.2 and J39.2), and airway stricture (J98.8 and J38.0). Pharyngoesophageal and airway strictures occurring during wound epithelialization were defined according to the ICD-10 codes assigned within 90 days after surgery, considering the timing of stenosis formation during the wound healing process, which typically lasts approximately 3 months. All other postoperative complications were defined according to the ICD-10 codes assigned within 30 days after surgery. Owing to the fact that several patients were assigned ICD-10 codes for dysphagia on the basis of only on the results of postoperative swallowing function tests, we defined postoperative dysphagia according to the use of nasogastric tube feeding and/or swallowing function training, alongside the presence of the relevant ICD-10 codes.

Outcomes

The primary outcomes were postoperative bleeding, dysphagia, and laryngopharyngeal edema. The secondary outcomes were the presence of other complications, such as fistula formation, subcutaneous emphysema, aspiration pneumonia, pharyngoesophageal stricture, and airway stricture. The post hoc analysis comprised the following postoperative measures: in-hospital or 30-day mortality, the composite outcome of complications (bleeding, dysphagia, laryngopharyngeal edema, fistula formation, subcutaneous emphysema, aspiration pneumonia, pharyngoesophageal stricture, and airway stricture) occurring within 30 days, the timing of complication occurrence, the proportion of patients readmitted within 30 days after NRTOS, the proportion of patients who received multiple NRTOS for the same disease name, and the proportion of patients who received postoperative radiation/chemoradiation therapy.

Statistical Analyses

Patient characteristics were summarized using medians [interquartile range (IQRs)] for continuous variables and proportions for categorical variables. The explanatory variables were patient characteristics, primary site, T classification, perioperative use of anticoagulants, previous radiotherapy or surgery to the primary site, concurrent neck dissection (CND) with NRTOS, and comorbidities.^{7–16} Since the Japan Gerontological Society and the Japan Geriatrics Society define 75 years and older as elderly, age was categorized into < 75 years and ≥ 75 years.¹⁷ Staging was based on the T classification and categorized as either < T2 or ≥ T2. Patients were grouped on the basis of their body mass index (BMI) according to the definition provided by the Japan Society for the Study of Obesity: low body weight, BMI < 18.5 kg/m²; standard weight, 18.5 kg/m² ≤ BMI < 25 kg/m²; and obesity, BMI ≥ 25 kg/m².¹⁸ Univariate and multivariate logistic regression analyses were conducted to evaluate the association between each complication and the variables. Complete-case analysis only included data records without missing values. Multivariate logistic regression analysis was not performed, except for laryngopharyngeal edema and composite outcome, owing to an insufficient number of events. Multivariate analysis of postoperative laryngopharyngeal edema was adjusted for two relevant variables: previous radiotherapy to the primary site and CND. Multivariate analysis of composite outcome was adjusted for age, T classification, BMI, previous radiotherapy to the primary site, and CND. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. All statistical analyses were conducted using R software, version 4.20, particularly the “RcmdrPlugin.EZR, version 1.61” package.¹⁹ A two-sided *p* level of 0.05 was considered significant.

Sensitivity Analysis

To verify the robustness of our results using complete-case analysis, we performed a sensitivity analysis using multiple imputations for T classification, BMI, and smoking history. Multiple imputation, an established general analytical technique for handling data containing missing values,^{20–22} was performed with 20 imputations using SAS (version 9.4; SAS Institute).

RESULTS

Patient Characteristics

Overall, 336 patients [median (IQR) age: 72 (64–78) years; 298 (88.7%) male individuals] were included in this study (Table 1). The most common primary site was the hypopharynx (39%). Missing values exceeded 1% for T classification (26.5%), BMI (6.3%), and smoking history (11.9%).

Bleeding

Postoperative bleeding occurred in 11 (3.3%) patients, with 4 (36.4%) of these patients requiring surgical hemostasis, 2 (18.2%) requiring blood transfusion, and 1 (9.1%) requiring tracheotomy to secure airway during bleeding events. Among these patients, a history of hypertension was the only significant risk factor associated with postoperative bleeding (OR: 9.82, 95% CI: 1.24–77.50, $p = 0.03$) (Table 2).

Dysphagia

Postoperative dysphagia occurred in 14 (4.2%) patients, with 10 (71.4%) of these patients receiving nasogastric tube feeding for a median (IQR) of 8 (5–12) days during hospitalization. The risk factors significantly associated with postoperative dysphagia were a disease stage of $\geq T2$ (OR: 5.37, 95% CI: 1.52–19.00, $p = 0.009$), a BMI of ≤ 18.5 kg/m² (OR: 5.51, 95% CI: 1.46–20.80, $p = 0.01$), and CND (OR: 10.20, 95% CI: 3.26–32.10, $p < 0.001$) (Table 3).

Laryngopharyngeal Edema

Laryngopharyngeal edema developed in 27 (8.0%) patients. Only one patient required tracheostomy, while the others responded well to conservative treatment, such as intravenous steroid infusion. Univariate analysis did not identify any significant risk factors for laryngopharyngeal edema (Table 4). Multivariate analysis of previous radiotherapy to the primary site and CND was performed, although no significant differences were found.

Fistula Formation, Subcutaneous Emphysema, and Aspiration Pneumonia

None of the assessed patients developed fistula formation, subcutaneous emphysema, or aspiration pneumonia following surgery.

Pharyngoesophageal Stricture and Airway Stricture

Pharyngoesophageal and airway strictures occurred in three (0.9%) and five (1.5%) patients, respectively (Supplementary Tables 1–2). None of the variables were identified as significant risk factors for these complications.

Mortality after NRTOS

Only one (0.3%) patient died after NRTOS in the present study (Table 1).

Composite Outcome

The composite outcome of complications occurring within 30 days after NRTOS was observed in 55 (16.4%) patients. Univariate logistic regression analysis revealed a significant association with CND (OR: 2.70, 95% CI: 1.15–6.33, $p = 0.02$); however, multivariate logistic regression analysis did not identify any significantly associated risk factors (Table 5).

Timing of Complication Occurrence after NRTOS

Bleeding, dysphagia, and laryngopharyngeal edema after NRTOS occurred during hospitalization in 90.9%, 100.0%, and 96.3% of patients, respectively. The median time of occurrence for all complications, except pharyngoesophageal stricture, was within 7 days (Supplementary Table 3).

The Proportion of Patients Readmitted within 30 Days after NRTOS

Three patients (0.9%) were readmitted within 30 days after surgery (17–25 days, median 21 days; Table 1).

The Proportion of Patients who Received Multiple NRTOS for the Same Disease Name

In this study, there were 11 patients (3.3%) who received multiple NRTOS for the same disease name (Table 1). No

TABLE 1 Characteristics of patients treated with NRTOS in this study

Characteristic	All patients (<i>N</i> = 336)
Age	
Median (IQR), years	72 (64–78)
Sex, no. (%)	
Male	298 (88.7)
Female	38 (11.3)
Primary site, no. (%)	
Pharynx	239 (71.1)
Hypopharynx	131 (39.0)
Oropharynx	104 (31.0)
Nasopharynx	2 (0.6)
Unidentified	2 (0.6)
Larynx	96 (28.6)
Supraglottis	17 (5.1)
Glottis	63 (18.8)
Subglottis	1 (0.3)
Unidentified	15 (4.5)
Unidentified	1 (0.3)
T classification, no. (%)	
Tis	69 (20.5)
T1	113 (33.6)
T2	52 (15.5)
T3	13 (3.9)
Unidentified	89 (26.5)
BMI, no. (%)	
BMI < 18.5 kg/m ²	31 (9.2)
18.5 ≤ BMI < 25 kg/m ²	229 (68.2)
25 ≤ BMI kg/m ²	55 (16.4)
Unidentified	21 (6.3)
Smoking history, no. (%)	
Smokers	210 (62.5)
Non-smokers	86 (25.6)
Unidentified	40 (11.9)
Perioperative anticoagulants, no. (%)	
Yes	52 (15.5)
No	283 (84.2)
Unidentified	1 (0.3)
Prior radiotherapy to the primary site, no. (%)	
Yes	23 (6.8)
No	313 (93.2)
Prior surgery to the primary site, no. (%)	
Yes	12 (3.6)
No	324 (96.4)
ND, no. (%)	
Yes	41 (12.2)
Concurrent ND with NRTOS	28 (8.3)
Planned ND	1 (0.3)
Previous or later history of ND	12 (3.6)
No	295 (87.8)
Comorbidity, no. (%)	
Hypertension	174 (51.8)

Table 1 (continued)

Characteristic	All patients (N = 336)
Hyperlipidemia	61 (18.2)
Diabetes mellitus	216 (64.3)
Pulmonary disease	91 (27.1)
Chronic obstructive pulmonary disease	24 (7.1)
Ischemic heart disease	91 (27.1)
Congestive heart disease	14 (4.2)
Chronic renal failure	7 (2.1)
Cerebrovascular disease	59 (17.6)
Surgery-related deaths	1 (0.3)
The proportion of patients readmitted within 30 days after NRTOS	3 (0.9)
The proportion of patients who received multiple NRTOS for the same disease name	11 (3.3)
Within 30 days of the previous NRTOS	0 (0.0)
The proportion of patients who received postoperative radiation/chemoradiation therapy	26 (7.7)
Radiation therapy	24 (7.1)
Chemoradiation therapy	2 (0.6)

*Percentages may not equal 100 because of rounding

NRTOS non-robotic transoral surgery, IQR interquartile range, BMI body mass index, ND neck dissection

patient received NRTOS within 30 days of the previous NRTOS (Table 1).

The Proportion of Patients who Received Postoperative Radiation/Chemoradiation Therapy

In total, 24(7.1%) and 2 (0.6%) patients received postoperative radiation therapy and chemoradiotherapy, respectively (Table 1).

Sensitivity Analysis

The results of multiple imputation were similar to those of the complete-case analysis (Supplementary Table 4). Multivariate logistic regression analysis for the composite outcome showed significant differences (OR: 1.71, 95% CI: 1.05–2.76, $p = 0.04$) for CND (Table 6).

DISCUSSION

NRTOS has emerged as a cost-effective and minimally invasive transoral procedure that offers comparable outcomes to TORS and is also effective for hypopharyngeal cancer resection.^{2–5} Identifying postoperative complication rates and risk factors associated with NRTOS is critical for optimizing patient care. Although single-center and multi-center studies have been conducted,^{12–16} to the best of our knowledge, no nationwide survey has been performed. This study is the first to investigate risk factors for postoperative complications in NRTOS, as well as mortality using a

combination of diagnostic procedures and receipt databases registered throughout Japan.

Postoperative Bleeding

Several studies investigating the risk factors for bleeding following TORS in the oropharynx^{7–9} have reported a postoperative bleeding rate of 5.4–8.0%. However, in the present study, the bleeding rate after NRTOS was only 3.3%. While these previous studies reported prior irradiation, higher T stage, perioperative use of anticoagulants, advanced age, and tonsillar neoplasm as risk factors for postoperative bleeding, a history of hypertension emerged as the sole significant risk factor associated with postoperative bleeding in our univariate analysis (Table 2). Although some studies have reported a history of hypertension as a risk factor for postoperative bleeding in thyroidectomy,²³ carotid endarterectomy,²⁴ craniotomy,²⁵ and lumbar interbody fusion,²⁶ to the best of our knowledge, the present study is the first to report it as a risk factor for bleeding after transoral surgeries for pharyngolaryngeal cancer resection. In NRTOS, intraoperative hemostasis is often performed by cauterization of the bleeding site, not by ligation or clipping of the vessels. In addition, NRTOS does not involve transcervical arterial ligation,²⁷ which is often performed in TORS before resection of the primary site tumor to ligate the feeding vessel and may contribute to the high incidence of postoperative bleeding in patients with a history of hypertension after NRTOS.

Although the frequency of postoperative bleeding events in NRTOS was low, several patients required emergency procedures, such as surgical hemostasis (36.4%), blood

TABLE 2 Univariable logistic regression analysis of bleeding after NRTOS

No. (%)	11 (3.3)	<i>p</i> value
Variable	OR (95% CI)	
Age, years		
< 75	Reference	
75 ≤	1.44 (0.43–4.83)	0.55
Sex		
Female	Reference	
Male	0.56 (0.12–2.70)	0.47
Primary site		
Larynx	Reference	
Hypopharynx	0.50 (0.08–3.03)	0.45
Oropharynx	1.96 (0.48–8.06)	0.35
T classification		
Tis-T1	Reference	
T2-T3	1.42 (0.35–5.85)	0.63
BMI		
18.5 ≤ BMI < 25 kg/m ²	Reference	
< 18.5 kg/m ²	3.40 (0.83–13.90)	0.09
25 ≤ kg/m ²	NA	–
Smoking history		
Non-smokers	Reference	
Smokers	0.65 (0.18–2.26)	0.49
Perioperative anticoagulants		
No	Reference	
Yes	0.54 (0.07–4.27)	0.56
Prior radiotherapy to the primary site		
No	Reference	
Yes	1.38 (0.17–11.30)	0.77
Prior surgery at the primary site		
No	Reference	
Yes	NA	–
Concurrent neck dissection with NRTOS		
No	Reference	
Yes	1.10 (0.14–8.95)	0.93
Comorbidity		
Hypertension	9.82 (1.24–77.50)	0.03*
Diabetes mellitus	1.50 (0.39–5.76)	0.56
Ischemic heart disease	1.56 (0.45–5.47)	0.49
Congestive heart disease	2.40 (0.29–20.20)	0.42
Pulmonary disease	1.01 (0.26–3.89)	0.99
Chronic obstructive pulmonary disease	NA	–
Chronic renal failure	5.32 (0.58–48.40)	0.14

NRTOS non-robotic transoral surgery, OR odds ratio, 95% CI, 95% confidence interval, BMI body mass index, NA not applicable

transfusion (18.2%), or tracheostomy (9.1%). Thus, transcervical arterial ligation and/or transoral vascular ligation or clipping may be considered for patients with a history of hypertension to mitigate bleeding risk during NRTOS.

TABLE 3 Univariate logistic regression analysis for dysphagia after NRTOS

No. (%)	14 (4.2)	<i>p</i> value
Variable	OR (95% CI)	
Age, years		
< 75	Reference	
75 ≤	1.30 (0.44–3.83)	0.64
Sex		
Female	Reference	
Male	0.30 (0.09–0.99)	0.05
Primary site		
Larynx	Reference	
Hypopharynx	0.50 (0.08–3.03)	0.45
Oropharynx	3.03 (0.80–11.50)	0.10
T classification		
Tis-T1	Reference	
T2-T3	5.37 (1.52–19.00)	0.009*
BMI		
18.5 ≤ BMI < 25 kg/m ²	Reference	
< 18.5 kg/m ²	5.51 (1.46–20.80)	0.01*
25 ≤ kg/m ²	1.40 (0.28–7.14)	0.68
Smoking history		
Non-smokers	Reference	
Smokers	0.65 (0.18–2.26)	0.49
Perioperative anticoagulants		
No	Reference	
Yes	2.54 (0.75–8.57)	0.13
Prior radiotherapy to the primary site		
No	Reference	
Yes	2.39 (0.50–11.40)	0.27
Prior surgery to the primary site		
No	Reference	
Yes	NA	–
Concurrent neck dissection with NRTOS		
No	Reference	
Yes	10.20 (3.26–32.10)	< 0.001*
History of head and neck cancer		
No	Reference	
Yes	0.90 (0.28–2.94)	0.86
Comorbidity		
Pulmonary disease	1.52 (0.50–4.68)	0.46
Chronic obstructive pulmonary disease	NA	–
Cerebrovascular disease	0.78 (0.17–3.56)	0.74

NRTOS non-robotic transoral surgery, OR odds ratio, 95% CI 95% confidence interval, BMI body mass index, NA not applicable

Dysphagia

Previous single-center studies investigating the risk factors for dysphagia after transoral surgeries for

TABLE 4 Logistic regression analysis for laryngopharyngeal edema after NRTOS

No. (%)	27 (8.0)			
Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i> Value	OR (95% CI)	<i>p</i> value
Age, years				
< 75	Reference			
75 ≤	1.19 (0.54–2.67)	0.67		
Sex				
Female	Reference			
Male	0.53 (0.19–1.48)	0.22		
Primary site				
Larynx	Reference			
Hypopharynx	0.50 (0.08–3.03)	0.45		
Oropharynx	3.03 (0.80–11.50)	0.10		
T classification				
Tis-T1	Reference			
T2-T3	0.93 (0.32–2.66)	0.89		
BMI				
18.5 ≤ BMI<25 kg/m ²	Reference			
< 18.5 kg/m ²	NA	–		
25 ≤ kg/m ²	1.21 (0.47–3.17)	0.69		
Smoking history				
Non-smokers	Reference			
Smokers	1.55 (0.56–4.28)	0.40		
Perioperative anticoagulants				
No	Reference			
Yes	0.66 (0.19–2.28)	0.51		
Prior radiotherapy to the primary site				
No	Reference		Reference	
Yes	2.65 (0.83–8.46)	0.10	2.71 (0.85–8.67)	0.09
Prior surgery to the primary site				
No	Reference			
Yes	NA	–		
Concurrent neck dissection with NRTOS				
No	Reference		Reference	
Yes	1.42 (0.40–5.05)	0.59	1.50 (0.42–5.36)	0.54
History of head and neck cancer				
No	Reference			
Yes	1.37 (0.60–3.10)	0.46		
Comorbidity				
Diabetes mellitus	1.12 (0.49–2.58)	0.79		
Ischemic heart disease	0.59 (0.22–1.61)	0.30		
Congestive heart disease	0.88 (0.11–6.96)	0.90		
Pulmonary disease	0.94 (0.38–2.30)	0.89		
Chronic renal failure	NA	–		
Cerebrovascular disease		0.70		

NRTOS non-robotic transoral surgery, OR odds ratio, 95% CI 95% confidence interval, BMI body mass index, NA not applicable

pharyngolaryngeal cancer resection have reported rates of 4.7–9.5%,^{10,12–14} consistent with our finding of 4.2% in our study (Table 3). In previous studies, risk factors identified

by univariate analysis included a BMI of < 18.5 kg/m², previous radiotherapy, advanced age, smoking history, and a history of head and neck cancer. While significant

TABLE 5 Logistic regression analysis for composite outcomes of complications that occurred within 30 days after NRTOS

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i> Value	OR (95% CI)	<i>p</i> Value
No. (%) 55 (16.4)				
Age, years				
< 75	Reference		Reference	
75 ≤	1.28 (0.71–2.31)	0.41	1.24 (0.60–2.55)	0.56
Sex				
Female	Reference			
Male	0.50 (0.23–1.10)	0.08		
Primary site				
Larynx	Reference			
Hypopharynx	1.16 (0.56–2.41)	0.69		
Oropharynx	1.45 (0.69–3.05)	0.33		
T classification				
Tis-T1	Reference		Reference	
T2-T3	2.05 (1.01–4.15)	0.05	1.87 (0.87–4.00)	0.11
BMI				
18.5 ≤ BMI < 25 kg/m ²	Reference		Reference	
< 18.5 kg/m ²	1.25 (0.48–3.25)	0.65	1.39 (0.46–4.19)	0.56
25 ≤ kg/m ²	1.02 (0.46–2.25)	0.97	0.82 (0.31–2.11)	0.67
Smoking history				
Non-smokers	Reference			
Smokers	0.96 (0.49–1.89)	0.90		
Perioperative anticoagulants				
No	Reference			
Yes	0.94 (0.41–2.12)	0.88		
Prior radiotherapy to the primary site				
No	Reference		Reference	
Yes	2.42 (0.94–6.18)	0.07	1.36 (0.32–5.80)	0.68
Prior surgery to the primary site				
No	Reference			
Yes	NA	–		
Concurrent neck dissection with NRTOS				
No	Reference		Reference	
Yes	2.70 (1.15–6.33)	0.02*	2.16 (0.74–6.30)	0.16
Comorbidity				
Hypertension	1.79 (0.98–3.25)	0.06		
Hyperlipidemia	1.32 (0.65–2.69)	0.44		
Diabetes mellitus	1.59 (0.84–3.02)	0.16		
Ischemic heart disease	0.91 (0.47–1.75)	0.77		
Congestive heart disease	2.13 (0.64–7.04)	0.22		
Pulmonary disease	1.25 (0.67–2.35)	0.49		
Chronic obstructive pulmonary disease	0.44 (0.10–1.95)	0.28		
Chronic renal failure	2.08 (0.39–11.00)	0.39		
Cerebrovascular disease	0.64 (0.28–1.50)	0.31		

NRTOS non-robotic transoral surgery, OR odds ratio, 95% CI 95% confidence interval, BMI body mass index, NA not applicable

differences were found in the incidence rates of a disease stage of ≥ T2, a BMI of < 18.5 kg/m², and CND, indicating that these events were possible risk factors for postoperative dysphagia; advanced age and a history of pulmonary

or cerebrovascular disease were not associated with postoperative dysphagia in our univariate analysis.^{10,12–14} Among the patients diagnosed with postoperative dysphagia in our study, 71.4% were provided nasogastric tube feeding for

TABLE 6 Logistic regression analysis with multiple imputation for composite outcomes of complications that occurred within 30 days after NRTOS

Variable	Univariate logistic regression		Multivariate logistic regression	
	OR (95% CI)	p Value	OR (95% CI)	p value
Age, years				
< 75			Reference	
75 ≤			1.14 (0.84–1.56)	0.41
T classification	Reference		Reference	
Tis-T1	1.30 (0.93–1.81)	0.15	1.16 (0.81–1.66)	0.44
T2-T3				
BMI	Reference		Reference	
18.5 ≤ BMI < 25 kg/m ²	1.31 (0.70–2.43)	0.41	1.38 (0.72–2.65)	0.34
< 18.5 kg/m ²	0.92 (0.53–1.60)	0.77	0.83 (0.44–1.51)	0.54
25 ≤ kg/m ²				
Smoking history				
Non-smokers	Reference			
Smokers	0.93 (0.67–1.30)	0.68		
Prior radiotherapy to the primary site				
No			Reference	
Yes			1.49 (0.91–2.43)	0.13
Concurrent neck dissection with NRTOS				
No			Reference	
Yes			1.71 (1.05–2.76)	0.04*

NRTOS non-robotic transoral surgery, OR odds ratio, 95% CI 95% confidence interval, BMI body mass index

a median (IQR) of 8 (5–12) days during hospitalization, which was 3 days longer than the duration reported for other patients in this study median (IQR): 5 (3–8) days]. However, this difference may have been underestimated, as some institutions routinely employ nasogastric tube feedings for a longer period after NRTOS (e.g., 5 days after E-TOS^{4,5,28}) to avoid damage to the resected wound surface. A prospective study of acute dysphagia after TORS reported that patients required tube feeding for an average of 15.6 days, with 98.0% of patients resuming transoral meal intake within 1 month after surgery.¹⁰ In this study, the duration of dysphagia after NRTOS was short, indicating that all patients resumed transoral meal intake, as the procedure code for tube feeding was not recorded at discharge.

Laryngopharyngeal Edema

No previous study has investigated the risk factors for laryngopharyngeal edema after transoral surgeries for pharyngolaryngeal cancer resection. Although a disease stage ≥ T2, previous radiotherapy or surgical treatment of the primary site, and CND were examined as potentially relevant explanatory variables, the univariate and multivariate logistic regression analysis did not reveal any significant risk factors for laryngopharyngeal edema (Table 4).

Fistula Formation, Subcutaneous Emphysema, and Aspiration Pneumonia

Although fistula formation, subcutaneous emphysema, and aspiration pneumonia were not observed during the study period, previous single-center¹⁵ and multicenter¹⁶ studies on NRTOS reported rates of 11.6 and 3.5% for subcutaneous emphysema development, respectively. Aspiration pneumonia was 10.3%.¹⁵

This discrepancy may be attributed to the fact that these studies spanned 2009–2015 and 2001–2012, respectively, encompassing the early period following NRTOS development, whereas the present study covered a much shorter duration.

Pharyngoesophageal Stricture and Airway Stricture

No previous study has investigated the risk factors for pharyngoesophageal and airway strictures after transoral surgeries for pharyngolaryngeal cancer resection. A disease stage ≥ T2, hypopharyngeal or laryngeal lesions, previous radiotherapy or surgical treatment of the primary site, CND, and a history of esophageal or hypopharyngeal cancers showed no significant associations with these complications (Supplementary Tables 1–2).

Post Hoc Analysis

Mortality after NRTOS

In the present study, one (0.3%) patient died during hospitalization or within 30 days after NRTOS (Table 1). This patient was a 70-year-old woman who underwent NRTOS for lateral wall cancer of the oropharynx with multiple comorbidities, including hypertension, diabetes mellitus, valvular and ischemic heart disease, and cerebrovascular disease. The patient required ventilator management on postoperative day 5 and died 82 days after NRTOS. One single-center study investigating TORS-related mortality reported a mortality rate of 0.6% within 30 days after TORS, while another study reported TORS-related mortality rates of 0.1–3.3%.¹¹ Thus, the rate of TORS-related mortality is generally quite low. Nevertheless, although NRTOS can be considered a safe procedure, surgical guidelines should clearly address the potential for mortality.

Composite Outcomes

The multivariate analyses using complete-case analysis did not reveal any risk factors for postoperative complications following NRTOS (Table 5). However, multivariate analysis with multiple imputation highlighted CND (OR: 1.71, 95% CI: 1.05–2.76; $p = 0.04$) as a risk factor (Table 6). When performing CND with NRTOS, close monitoring of postoperative complications occurrence within 30 days after surgery is necessary.

Timing of Complication Occurrence after NRTOS

In this study, postoperative complications typically occurred early during hospitalization following NRTOS (Supplementary Table 3), likely prompting the early administration of interventions to treat each complication and contributing to the low mortality rate. Japan's robust social security system offers numerous benefits, including universal health insurance with a manageable copayment scheme (ranging from 10% to 30% of the medical expenses), a high-cost medical expense benefit system (monthly payments capped according to income), and full medical assistance provided to welfare recipients. This system supports aggressive treatment and health check-ups and potentially minimizes postoperative complications and mortality rates after NRTOS. Moreover, advancements in endoscopic diagnostic techniques in Japan, particularly those using narrow band imaging,^{29,30} facilitate the timely detection of carcinoma in situ and superficial cancer without muscle layer invasion, further contributing to the low complication rate after NRTOS.

The Proportion of Patients Readmitted within 30 Days after NRTOS

Among the three patients readmitted within 30 days after NRTOS, one was readmitted for postoperative bleeding on postoperative day (POD) 17, another for esophageal stricture on POD 21, and the third for airway stricture on POD 25. The patient with postoperative bleeding was admitted for observation only, while those with esophageal and airway strictures underwent endoscopic balloon dilatation and tracheostomy, respectively.

In a previous study of 5544 patients who underwent TORS for oropharyngeal cancer resection, the 30-day readmission rate was reported to be 17.5% ($n = 971$).³¹ In contrast, the readmission rate in this study was lower, at 0.9%. The low readmission rate following NRTOS may be attributed to Japan's comprehensive social security system, which supports careful postoperative management and discharge planning as discussed in the previous section.

The Proportion of Patients who Received Multiple NRTOS for the Same Disease Name and the Proportion of Patients who Received Postoperative Radiation/Chemoradiation Therapy

The dataset in this study is limited in that it does not include pathological findings, such as positive/close margins, perineural invasion, vascular invasion, lymphatic invasion, and extranodal extension, which are important factors in determining postoperative treatment. Accordingly, it is not possible to ascertain whether the patients who had undergone multiple surgeries for the same disease name or postoperative radiation/chemoradiation therapy were treated for positive/close margins or for other reasons.

Limitations

This study had some limitations. First, multivariate analysis to identify the risk factors of each complication after NRTOS could not be performed owing to the limited observation period and small number of events. Although univariate analysis showed significant associations between several variables and postoperative complications, the effect of confounding factors could not be excluded; thus, the risk factors identified in our analyses cannot be regarded as definite risk factors. Second, complications that did not require treatment may not have been assigned the appropriate diagnostic names in the receipts, possibly leading to an underestimation of the complication rate. Conversely, multiple diagnostic codes may have been assigned for proactive preventive treatments and comprehensive physical examinations to ensure patients could benefit from the Japanese social security system; therefore, the potential for overestimation cannot be ignored. Third, the retrospective design of this cohort study limits causal inference. Fourth, the datasets used in this study did not include

histopathologic or imaging findings, which limited the discussion of postoperative treatment.

Lastly, the two databases used in the present study were provided by commercial vendors and based on medical information data collected from contracted medical institutions across Japan but do not contain data on all NRTOS cases in Japan. Therefore, prospective, nationally representative studies leveraging larger datasets are needed to identify the definite risk factors for NRTOS-related complications.

CONCLUSIONS

NRTOS is a safe surgical procedure with low postoperative complications and mortality rates. Patients with a history of hypertension and those with a disease stage $\geq$ T2, a BMI of $\leq 18.5 \text{ kg/m}^2$, and CND exhibited an increased risk of postoperative bleeding and dysphagia, respectively. Patients who undergo CND with NRTOS should be closely monitored for postoperative complications within 30 days after NRTOS.

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