Original Article

Characteristics and impact of postoperative surgical site infection on increased antibiotic duration among patients with laryngocarcinoma: a retrospective cohort study

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Background: Whether increased antibiotic duration is necessary for surgical site infection (SSI) in patients after neck surgery is unclear. We investigated the characteristics of SSI, and the impact of SSI on increased antibiotic duration among patients with laryngocarcinoma (LC).

Methods: A retrospective cohort study including consecutive LC patients ≥18 years, undergoing surgery without remote metastasis was conducted from October 2015 to February 2022 in the Department of Otolaryngology-Head and Neck Surgery, Chengdu Second People's Hospital. SSI was defined according to current guidelines. Patients were stratified into 3 groups including no-infection, lower respiratory tract infection (LRTI) and SSI. Patient characteristics was recorded. Patients were followed up until discharge. A multiple linear regression model including SSI and other factors including age, sex, comorbidity and antibiotic treatments was performed to explore the impact of SSI on increased antibiotic duration among LC patients with postoperative infection.

Results: A total of 88 patients were included, with 26 (29.5%) in no-infection group, 38 (43.2%) in LRTI group, and 24 (27.3%) in SSI group. Laryngocutaneous fistula occurred in 8 (33.3%) patients with SSI. Thirteen (34.2%) patients in LRTI group and 9 (37.5%) patients in SSI group experienced postoperative infection within 2 days after surgery, and antibiotic susceptibility tests were performed in 18 (47.4%) and 12 (50.0%) patients in LRTI and SSI group, respectively (P>0.05 for both). Levofloxacin and cefoperazone-sulbactam were the most commonly used antibiotics for postoperative infection in both LRTI and SSI groups (P>0.05 for both), irrespective of antibiotic susceptibility tests or not. The postoperative antibiotic duration in SSI group was significantly longer than that in LRTI group (13.62±4.28 days in SSI *vs.* 11.22±3.64 days in LRTI, P=0.021). A multiple linear regression analysis including SSI, age, sex, diabetes, antibiotic susceptibility test and hypoalbuminemia showed that, SSI was independently associated with increased antibiotic duration with LRTI as the reference among LC patients diagnosed [regression coefficient β=3.02, 95% confidence interval (CI): 1.01–5.03, P=0.004], whereas antibiotic susceptibility test was not (P=0.467).

Conclusions: SSI may be independently associated with increased postoperative antibiotic duration in patients with LC with or without antibiotic susceptibility test.

Keywords: Surgical site infection (SSI); laryngocarcinoma (LC); antibiotic duration; surgery

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Introduction

As a common malignant tumor of the head and neck, laryngocarcinoma (LC) is newly diagnosed in approximately 200,000 patients per year, with a gradually increasing trend (1). Besides leading to cancer-related death, LC seriously devastates patient quality of life with a series of clinical symptoms such as hoarseness, sore throat, and malnutrition, especially after neck cancer surgery (2-4). Although an individualized treatment strategy devised in consultation with a multi-disciplinary team (MDT) is now highly recommended, neck cancer surgery is still one of the preliminary therapeutic regimens for patients with LC. Due to the complexity and enlarged incision area of neck cancer surgery, diminishing postoperative complications and promoting wound healing remains an inescapable issue for improving patient survival benefit (4-7).

Postoperative infection is a prevalent complication after surgery for patients with neck cancer, especially that of surgical site infection (SSI) (5,8,9). Due to the violation of laryngeal surfaces and exposure to abundant bacteria, patients are prone to SSI after clean-contaminated neck cancer surgery (10,11). According to multiple studies, the rate of SSI after head and neck surgery varies from 4% to 40%, and SSI is substantially associated with increased mortality (12-15). The clinical characteristics of SSI are widely acknowledged, SSI was associated with multiple baseline characteristics, including surgical location, smoking or alcohol habits, comorbidities and surgical procedures (16,17). However, the risk factors and impact of SSI on prognosis among patients with LC are scarcely identified. Additionally, in order to avoid the occurrence of SSI, prophylactic antibiotics as a routine strategy after head and neck oncology surgery have also been explored by several randomized controlled trials (RCTs) (11,18,19). Meanwhile, whether increased antibiotic duration is necessary for SSI treatment among patients after neck surgery remains controversial (20,21). We therefore aimed to conduct an observational study to evaluate the characteristics of SSI, and the impact of SSI on increased antibiotic duration specifically among post-surgical LC patients, in order to unveil the link of SSI and antibiotic strategy and guide post-procedural management. We present the following article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2539/rc).

Highlight box

Key findings

- Surgical site infection (SSI) may be independently associated with the increased postoperative antibiotic duration in patients diagnosed with laryngocarcinoma (LC) undergoing surgery, irrespective conducting antibiotic susceptibility test or not.

What is known and what is new?

- Postoperative infection is a prevalent complication after surgery for patients with neck cancer, especially that of SSI, which is substantially associated with increased mortality.
- Our study further demonstrates that SSI is significantly associated with the increased postoperative antibiotic duration among patients diagnosed with LC undergoing surgery with or without antibiotic susceptibility test, qualifying SSI as an independent predictor of antibiotic duration.

What is the implication, and what should change now?

- Preventing the occurrence of SSI is important to not only improve the prognosis of patients with LC, but also decrease the duration of antibiotic treatment during hospitalization.

Methods

Population and endpoints

This single-center, retrospective observational study was conducted to identify the risk factors of SSI and its impact on increased antibiotic duration after surgery. We included consecutive patients diagnosed with LC undergoing surgery from October 2015 to February 2022 in the Department of Otolaryngology-Head and Neck Surgery, Chengdu Second People's Hospital, Chengdu, China. This study was approved by the Ethics Committee of Chengdu Second People's Hospital (No. 2022230), and complied with principles of the Declaration of Helsinki (as revised in 2013). Individual consent for this retrospective analysis was waived. The inclusion criteria were as follows: age ≥18 years; pathologically diagnosed with LC; surgical indications for total- or hemi-laryngectomy; no remote metastasis; life expectation >3 months; provision of written informed consent. The major exclusion criteria

were as follows: remote metastasis or involvement of important organs or tissues; pregnancy; participation in other ongoing clinical trials. There were 2 objectives prespecified in this observational study: objective 1 was to identify the characteristics of postoperative SSI occurrence in patients with LC, and the endpoint for objective 1 was the occurrence of SSI; objective 2 was to explore the impact of SSI on postoperative antibiotic duration during hospitalization among patients with postoperative infection, and the endpoint for objective 2 was the duration of antibiotic treatment.

Study design, data collection, and follow-up

SSI was defined in accordance with the Centers for Disease Control and Prevention (CDC) National Nosocomial Infections Surveillance (NNIS) system and Johnson's criteria (22), as well as physician's discretion. An incisional SSI was defined as infection occurring at the site of an incision with existence of at least 1 of the following: purulent drainage; spontaneous dehiscence or deliberate opening of the incision with pain, tenderness, localized swelling, redness, or heat; or detection of an organism in a culture of fluid from the incision. Space SSI was defined as purulent discharge from drains or an abscess without evidence of clinical anastomotic leakage. Leakage or fistula were defined as clinically evident leakage from anastomotic sites or laryngocutaneous fistula. Considering that lower respiratory tract infection (LRTI) is also a common postoperative infection type among patients with LC (23), we classified the participants into 3 groups: without postoperative infection, postoperative LRTI, and SSI, in order to properly identify the risk factors of SSI. Total- or hemi-laryngectomy procedures were performed in accordance with standard practices and the surgeon's discretion. For patients in the LRTI group or SSI group, postoperative antibiotic durations with or without antibiotic sensitivity tests were recorded. Baseline clinical characteristics, procedural characteristics, and antibiotic treatments were obtained from the hospital's information system. All collected data were screened, rectified, and then recorded in a dedicated database. Participants were routinely followed up until discharge.

Statistical analysis

Patient baseline and procedural characteristics were compared between the non-infection group, LRTI group, and SSI group. Continuous variables were presented with mean ± standard deviation (SD) and were compared using *t*-test. Categorical variables were presented as counts (%) and were compared via χ^2 test or Fisher's exact test, as appropriate. Missing data was imputed using respective median values. Multinomial logistic regression for objective 1 was used to evaluate characteristics of SSI, with a tripartite-ordered outcome variable classified into no infection, LRTI, and SSI. Baseline and procedural variables of all included patients were included in the logistic regression model. For objective 2, which was explore the association between SSI and antibiotic duration, a multiple linear regression model was performed with the antibiotic duration as a continuous outcome variable. In the multiple linear regression model specifically focusing on patients in the LRTI or SSI group, antibiotic susceptibility tests and type of postoperative infection (LRTI or SSI) as well as other baseline variables were included. β regression coefficient from multiple linear regression was used as the effect size to reflect the degree of correlation between included factors and antibiotic duration (positive correlation if $\beta>0$, and vice versa). Variance inflation factor (VIF) was calculated to determine the existence of multicollinearity, and the P value of VIF <0.1 indicated positive multicollinearity. A two-sided P value <0.05 was considered statistically significant, except for VIF (for which <0.1 was significant). All data were analyzed using the software SPSS 25.0 (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics

A total of 88 patients with LC undergoing surgery were included in this observational study. LRTI and SSI occurred in 38 (43.2%) and 24 (27.3%) patients, respectively (*Figure 1*). Laryngocutaneous fistula occurred in 8 (33.3%) participants in the SSI group. Preoperative infection occurred in 7 (21.1%) and 6 (25.0%) participants in the LRTI and SSI group, respectively (P=0.490). A total of 13 (34.2%) participants in the LRTI group and 9 (37.5%) participants in the SSI group experienced postoperative infection within 2 days after surgery. Antibiotic susceptibility tests were performed in 18 (47.4%) and 13 (50.0%) participants in the LRTI and SSI groups, respectively. Levofloxacin and cefoperazone-sulbactam were the most commonly used antibiotics for postoperative infection, irrespective of whether antibiotic susceptibility

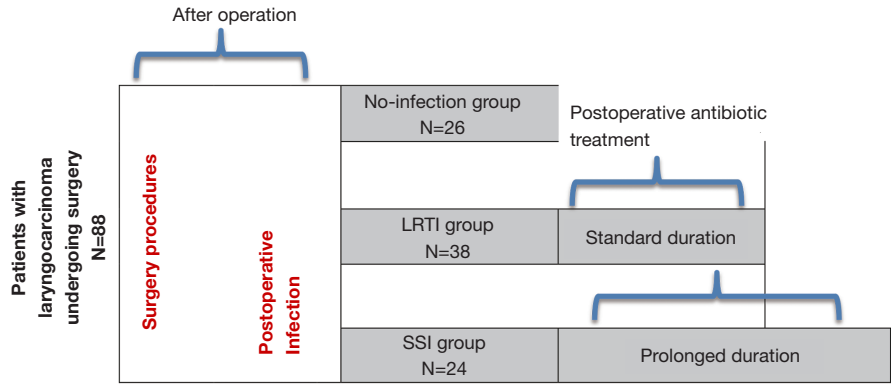

Figure 1 Graphical abstract. The condensed abstract of this observational study. The 88 included patients with laryngocarcinoma undergoing surgery were divided into 3 groups including no-infection, LRTI, and SSI. After analysis, SSI was independently associated with increased postoperative antibiotic duration in comparison with LRTI. LRTI, lower respiratory tract infection; SSI, surgical site infection.

tests had been conducted or not (*Table 1*). No significant differences were found in the proportion of antibiotic susceptibility tests, duration from surgery to infection, and antibiotic types between the LRTI and SSI groups (P>0.05 for all), but the postoperative antibiotic duration in the SSI group was significantly longer than that in LRTI group (13.62±4.28 days in SSI *vs.* 11.22±3.64 days in LRTI, P=0.021, *Table 1*). Patients in the SSI group had significantly higher rates of diabetes mellitus (DM) (62.5% in SSI *vs.* 31.6% in LRTI *vs.* 19.2% in the no-infection group, P=0.008) and hypoalbuminemia (58.3% in SSI *vs.* 29.0% in the LRTI *vs.* 26.9% in the no-infection group, P=0.032) than those in the no-infection group and LRTI group (*Table 1*). Other baseline and procedural characteristics were similar between the 2 groups (*Table 1*).

Risk factors of the occurrence of SSI

Univariable analyses were firstly conducted to select potential factors included in the subsequent multinomial logistic regression model. After analyses, age, sex, DM, hypoalbuminemia, and total-/hemi-laryngectomy were included in the logistic regression. Other factors, including infection characteristics, did not meet the statistical significance and were excluded from logistic regression (data not shown). After multivariable analyses, only DM was independently associated with the occurrence of SSI after surgery in patients with LC [odds ratio (OR): 3.80, 95% confidence interval (CI): 2.65–5.47, P=0.003, *Table 2*]. Age, sex, hypoalbuminemia, or total-/hemi-laryngectomy were not found to be independently associated with SSI (P>0.05 for all, *Table 2*).

Impact of SSI on postoperative antibiotic duration

Furthermore, we performed a multiple linear regression model to determine whether SSI was independently associated with increased postoperative antibiotic duration in 62 participants who were diagnosed with postoperative LRTI or SSI. After regression analysis, SSI was an independent predictor of increased antibiotic duration with LRTI as the reference (regression coefficient β=3.02, 95% CI: 1.01–5.03, P=0.004, *Table 3*), which indicated that the occurrence of SSI increased 3.02 days of the antibiotic duration in comparison with LRTI. Conversely, antibiotic susceptibility testing was not associated with antibiotic duration (β=–0.03, 95% CI: –2.45 to 3.65, P=0.467, *Table 3*). Additionally, hypoalbuminemia was found to be associated with increased postoperative antibiotic duration among patients with LC (β=2.36, 95% CI: 0.17–4.55, P=0.035, *Table 3*), which indicated that the presence of hypoalbuminemia increased antibiotic duration by 2.36 days in LC patients with postoperative infection. No multicollinearity was found in the established model with the VIF >0.1.

Discussion

This observational study explored the characteristics of SSI, and the impact of SSI on postoperative antibiotic duration in patients with LC after surgery. The results of this study showed that: (I) DM was an independent

Table 1 Patient characteristics

Characteristics	No-infection (N=26)	LRTI (N=38)	SSI (N=24)	P value
Age, years	60.46±11.79	62.56±12.37	65.54±9.48	0.285
Female	7 (26.9)	5 (13.2)	4 (16.7)	1.000
DM	5 (19.2)	12 (31.6)	15 (62.5)	0.017
Hypoalbuminemia	7 (26.9)	11 (28.9)	14 (58.3)	0.032
Smoking				0.220
None	12 (46.2)	15 (39.5)	10 (41.7)	
Current	9 (34.6)	16 (42.1)	9 (37.5)	
Former	5 (19.2)	7 (18.4)	5 (20.8)	
Total laryngectomy	10 (38.5)	12 (31.6)	7 (29.2)	0.958
Preoperative infection	NA	7 (18.4)	6 (25.0)	0.490
Duration from surgery to infection				0.463
≤2 days	NA	13 (34.2)	9 (37.5)	
>2 days	NA	25 (65.8)	15 (62.5)	
Laryngocutaneous fistula	NA	NA	8 (33.3)	
Postoperative antibiotic sensitivity test	NA	18 (47.4)	12 (50.0)	0.492
Antibiotics				
Levofloxacin	NA	24 (63.2)	15 (62.5)	0.958
Cefoperazone-sulbactam	NA	22 (57.9)	16 (66.7)	0.490
Others	NA	6 (15.8)	4 (16.7)	1.000
Postoperative antibiotic duration, days	NA	11.22±3.64	13.62±4.28	0.021

Values are mean ± SD or n (%). LRTI, lower respiratory tract infection; SSI, surgical site infection; DM, diabetes mellitus; NA, not available; SD, standard deviation.

Table 2 Multinomial logistic regression predicting occurrence of postoperative SSI in LC

Variables	OR (95% CI)	P value
Age	1.01 (0.97–1.07)	0.675
Female	0.68 (0.12–3.91)	0.664
DM	3.80 (2.65–5.47)	0.003
Hypoalbuminemia	1.25 (0.37–4.25)	0.717
Total-/hemi-laryngectomy	0.92 (0.63–1.35)	0.217

The multinomial logistic regression model of predicting the occurrence of SSI. A tripartite-ordered outcome variable (three covariates including no-infection, LRTI and SSI) was prespecified. SSI, surgical site infection; LC, laryngocarcinoma; OR, odds ratio; CI, confidence interval; DM, diabetes mellitus.

Table 3 Multiple linear regression predicting postoperative antibiotic duration in LC

Variables	β coefficient (95% CI)	P value
Age	−0.02 (−0.11 to 0.06)	0.555
Female	−1.72 (−3.92 to 0.48)	0.129
Preoperative infection	0.60 (−2.45 to 3.65)	0.696
Antibiotic susceptibility test	−0.03 (−2.45 to 3.65)	0.467
DM	0.64 (−2.16 to 3.44)	0.649
Hypoalbuminemia	2.36 (0.17–4.55)	0.035
SSI (LRTI as the reference)	3.02 (1.01–5.03)	0.004

The results of multiple linear regression predicting postoperative antibiotic duration in patients with LC. β coefficient was the effect size of linear regression, reflecting the degree of correlation between variables and antibiotic duration. LC, laryngocarcinoma; CI, confidence interval; DM, diabetes mellitus; SSI, surgical site infection; LRTI, lower respiratory tract infection.

predictor of the occurrence of SSI after LC surgery; (II) compared with LRTI, SSI significantly increased the postoperative antibiotic duration by nearly 3.02 days during hospitalization, regardless of whether antibiotic susceptibility testing was conducted; (III) moreover, hypoalbuminemia was also associated with an increased antibiotic duration. The present study revealed the clinical features of SSI, and the negative impact of antibiotic regimens during hospitalization specifically among patients with LC.

Currently, reducing SSI is a critical issue for patients undergoing head and neck surgery, especially for those involving a clean-contaminated field (8). Although the risk factors of the occurrence of SSI are widely recognized (5,17), research specifically involving patients diagnosed with LC is rare. In our study, DM was found to be independently associated with the occurrence of SSI after surgery in patients with LC. DM is reported to be associated with increased postoperative complications including infection, and prognosis devastation by multiple studies (24-26). Indeed, poor wound healing complications are more common in diabetic patients (27), and it is well-known that the hyperglycemic state impedes wound healing. This result to some extent supported the credibility of our study.

A series of studies have explored antibiotic regimens for head and neck oncology surgery (10,18,28). Although prophylactic antibiotics are recommended to prevent postoperative infection, the optimal antibiotic duration has not yet been determined (20,21,29). In the present study, we determined the independent predictor of increased antibiotic duration after surgery among patients with LC. A multiple linear regression model was used in patients with postoperative infection. With LRTI as a reference, SSI was independently associated with an increased antibiotic duration, indicating that SSI is a kind of severe postoperative infection after LC surgery, and is more refractory than LRTI. Notably, the conduction of antibiotic susceptibility testing did not influence the postoperative antibiotic duration. This is partially because that the antibiotic empirical medications and susceptibility test-guided medications are currently similar, including cefoperazone-sulbactam, levofloxacin, piperacillin-sulbactam, and ceftriaxone, among others. Irrespective of antibiotic medication type, SSI did increase the duration of antibiotic use. To date, several RCTs have explored different antibiotic regimens for SSI after head and neck oncology surgery, such as cephalosporins, amoxicillin-clavulanate, gentamicin, and clindamycin (14,18,20,30). To sum up, therefore, pursuing novel effective antibiotics is of great significance to avoid the occurrence and diminish the impact of SSI.

There were several limitations to the present study. Firstly, although without overfitting in either multinomial logistic regression model or multiple linear regression, the sample size of 88 patients was relatively small. Secondly, this study only focused on patients with LC, whereas other types of neck cancer were not included in this study. Thirdly, only in-hospital data was shown, and long-term prognosis information after discharge was not demonstrated in our study due to the incomplete follow-up procedures. Out-of-hospital clinical outcomes of these patients will be subsequently reported in a future study.

Conclusions

This observational study demonstrated that, in comparison with LRTI, SSI significantly increased postoperative antibiotic duration in patients with LC, regardless of whether antibiotic susceptibility testing was conducted. The optimal antibiotic regimen of SSI is still warranted among patients with head and neck oncology undergoing surgery.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2539/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2539/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2539/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Ethics Committee of Chengdu Second People's Hospital (No. 2022230), and complied with

principles of the Declaration of Helsinki (as revised in 2013). Individual consent for this retrospective analysis was waived.

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