

Risk factors for surgical site infection after major oral oncological surgery: the experience of a tertiary referral hospital in China

Menghan Shi^{1,2}, Zhengxue Han¹,
Lizheng Qin¹ , Ming Su¹, Yanbin Liu¹,
Man Li¹, Long Cheng¹, Xin Huang¹  and
Zheng Sun²

Abstract

Objective: To identify risk factors associated with surgical site infection (SSI) after major oral oncological surgery.

Methods: This retrospective study reviewed data from patients that underwent major surgery for oral cancer at a tertiary referral hospital in China between January 2005 and July 2016. SSI was diagnosed within 30 days. Demographic, cancer-related, preoperative, perioperative and postoperative data were analysed using descriptive statistics and univariate and multivariate analyses of the risk factors for SSI.

Results: A total of 786 patients were enrolled, of whom 125 had SSI (15.9%), which were all incisional. Independent risk factors for SSI, identified by multivariate analysis, were diabetes mellitus (odds ratio [OR] 2.147, 95% confidence interval [CI] 1.240, 3.642), prior radiotherapy

¹Department of Oral and Maxillofacial Surgery, Beijing Stomatological Hospital & School of Stomatology, Capital Medical University, Beijing, China

²Department of Oral Medicine, Beijing Stomatological Hospital & School of Stomatology, Capital Medical University, Beijing, China

Corresponding authors:

Xin Huang, Department of Oral and Maxillofacial Surgery, Beijing Stomatological Hospital & School of Stomatology, Capital Medical University, 4 Tiantanxili, Dongcheng District, Beijing 100050, China.

Zheng Sun, Beijing Stomatological Hospital & School of Stomatology, Capital Medical University, 4 Tiantanxili Street, Dongcheng District, Beijing 100050, China.

Emails: huangxin@ccmu.edu.cn; sunzheng12@vip.126.com



(OR 4.595, 95% CI 1.293, 17.317) and oral–neck communication (OR 2.838, 95% CI 1.263, 7.604); and factors reflecting large extent resections were tracheostomy (OR 2.235, 95% CI 1.435, 3.525), anterolateral thigh flap (OR 1.971, 95% CI 1.103, 3.448) and latissimus dorsi flap (OR 4.178, 95% CI 1.325, 13.189).

Conclusions: Multiple risk factors were associated with SSI after major oral oncological surgery. To minimize SSI risk, surgeons managing oral cancer patients should have a better understanding of the risk factors, including diabetes mellitus, prior radiotherapy, tracheostomy, oral–neck communication and flap reconstruction.

Keywords

Surgical site infection, major surgery, oral cancer, risk factor

Date received: 5 February 2020; accepted: 1 July 2020

Introduction

Surgical site infection (SSI), defined as an infection in a surgical wound within 30 days after the procedure, is a common postoperative complication of major oral oncological surgery.^{1,2} Multiple factors contribute to the process of infection in which microbes interact with the host.³ The incidence rate of SSI after major surgery was reported to range between 10% and 45% in oral cancer patients.^{4–10} Clinical symptoms of SSI include tenseness, pain, fever, pus discharge and wound dehiscence.^{11,12} Once SSI occurs, it delays healing and results in the postponement of adjuvant therapy administration, which may increase the risk of tumour recurrence and mortality rate.^{13–15} Significant functional morbidities, such as language and swallowing dysfunction, poor cosmetic results and poor quality of life, may consequently occur.¹⁵ Additionally, SSI prolongs hospitalization and increases healthcare expenditure.¹⁵

Aseptic surgery and preoperative antimicrobial prophylaxis are key measures for preventing SSI.^{2,16,17} However, the incidence of SSI remains high, even if the principle of sterilization was strictly followed

during the operation and antibiotics were preoperatively administered.^{4–10} Unfortunately, there is still no consensus about the selection of antibiotics and the duration of antibiotic therapy. Therefore, identifying the risk factors for SSI is critical for developing proper preventive and therapeutic strategies.

Many risk factors have been reported in previous studies. For example, diabetes mellitus, smoking, prior radiotherapy, prior surgery, prior chemotherapy, poor American Society of Anesthesiologists physical status score, hypoalbuminaemia, perioperative blood transfusion, tracheotomy, clean-contaminated wounds, length of preoperative hospital stay, lymph node metastasis and reconstruction with myocutaneous flaps or microvascular-free flaps were observed to be associated with SSI.^{8,9,13,15,18,19} However, due to the differences in study design, patient population and sample size, some discrepancies remain in the literature. This study aimed to identify the risk factors associated with SSI after major surgery for oral cancer through a retrospective study of cases within 11 years at a tertiary referral hospital in China.

Patients and methods

Patient population and study design

This retrospective study reviewed the medical records of consecutive patients that underwent major surgery for oral cancer in the Department of Oral and Maxillofacial Surgery, Beijing Stomatological Hospital & School of Stomatology, Capital Medical University, Beijing, China between January 2005 and July 2016. All patients received perioperative antibiotic therapy and had their surgical sites were disinfected with povidone-iodine. All surgeries were performed by the same group of qualified oral surgeons (Z.H., L.Q. & X.H.) with at least 10 years of experience in this field. Surgical procedures included the following: excision of the tumour, neck dissection, and flap reconstruction, if required. In some cases, two or more of these procedures may have been simultaneously performed. The flaps were used to reconstruct tissue defects arising from tumour resection. In our institute, surgeons commonly utilize a radial forearm flap for small soft tissue defects and an anterolateral thigh flap for large soft tissue defects. Patients undergoing mandibulectomies for large mandibular defects underwent fibula osteoseptocutaneous flap reconstructions. Latissimus dorsi flap and pectoralis major pedicled flap were used only when the condition of the commonly preferred flap was poor or flap necrosis was observed. The pectoralis major flap was the only pedicled flap; all others were free flaps. All wounds were categorized into Class I to Class IV according to the Centers for Disease Control (CDC) Surgical Wound Classification.^{20,21} This study exclusively included Class I (clean) and Class II (clean-contaminated) wounds; Class III (contaminated) and Class IV (dirty-infected) wounds were excluded.

Patients whose medical records were incomplete were also excluded.

This retrospective study was conducted in accordance with ethical principles, including those of the World Medical Association Declaration of Helsinki (2002 version). The study was approved by the Institutional Review Board of the Beijing Stomatological Hospital (no. CMUSH-IRB-KJ-YJ-2017-11). Written or verbal consent was obtained from all study participants or their legally authorized representatives.

Study outcomes

Patients were assigned to the following two groups: those with SSI and those without SSI. According to the CDC National Nosocomial Infections Surveillance system and Johnson's criteria, SSI was defined as an infection related to an operative procedure, occurring at or near the surgical incision site within 30 days after the procedure.^{11,22–25} Superficial or deep incisional SSI was diagnosed if there was purulent drainage from the incision, spontaneous wound dehiscence, a wound that required opening by surgeons because of signs or symptoms of infection (pain, tenderness, localized swelling, redness or heat) or a positive result from the bacterial culture of the drainage fluid. Space SSI was diagnosed if there was purulent discharge from drains or an abscess without evidence of anastomotic leakage. From medical records, the following five types of clinical data were collected: demographic data, cancer-related data, preoperative assessment, perioperative assessment and postoperative assessment. The clinical endpoint was the diagnosis of SSI within 30 days after surgery.

Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics for Windows,

version 19.0 (IBM Corp., Armonk, NY, USA). A two-sided Fisher's exact test was used to analyse the differences between categorical variables, whereas the Mann-Whitney *U*-test was used to compare continuous variables (age, body mass index [BMI], preoperative hospital stay, operation time, intravenous fluid, blood loss, 4-day drainage). Based on the World Health Organization recommendation in Asian populations, the BMI categories were defined as follows: underweight (BMI < 18.5 kg/m²), normal weight (BMI 18.5–23.0 kg/m²) and overweight/obese (BMI ≥ 23 kg/m²).²⁶ Preoperative laboratory test results of blood cell analyses were defined according to parameters issued by the Ministry of Health of China in 2012 as follows: red blood cells (RBC) (men: normal ≥ 4.3–≤ 5.8 × 10¹² per l, low < 4.3 × 10¹² per l, high > 5.8 × 10¹² per l; women: normal ≥ 3.8–≤ 5.1 × 10¹² per l, low < 3.8 × 10¹² per l, high > 5.1 × 10¹² per l); white blood cells (WBC) (normal ≥ 3.5–≤ 9.5 × 10⁹ per l, low < 3.5 × 10⁹ per l, high > 9.5 × 10⁹ per l); haemoglobin (men: normal ≥ 130–≤ 175 g/l, low < 130 g/l, high > 175 g/l; women: normal ≥ 115–≤ 150 g/l, low < 115 g/l, high > 150 g/l); albumin (normal ≥ 40–≤ 55 g/l, low < 40 g/l, high > 55 g/l). A forward stepwise multivariate logistic regression model was used to identify the independent risk factors associated with SSI. A *P*-value < 0.05 was considered statistically significant.

Results

Of 786 patients that underwent major surgery for oral cancer, 125 (15.90%) developed SSI, which were all incisional SSI. As shown in Table 1, the most common pathological diagnosis was epidermoid carcinoma (*n* = 735, 93.51%). There were 387 patients (49.24%) with lymph node metastasis. Primary tumours were localized in the

tongue (*n* = 305, 38.80%), gingiva (*n* = 199, 25.32%) and buccal region (*n* = 112, 14.25%). However, no association was found between pathological diagnosis, metastasis or tumour site and SSI on univariate analysis.

The analysis of demographic data showed positive associations between the male sex (*P* = 0.038), age (≤ 58.5 years, *P* = 0.016) and diabetes mellitus (*P* = 0.008) with SSI (Table 2). Other patient-related factors, such as BMI, tobacco smoking, alcohol consumption and other comorbidities, were not significantly associated with SSI.

Three preoperative factors were positively correlated with SSI, namely prior radiotherapy (*P* = 0.001), weight loss ≥ 10% within 6 months prior to surgery (*P* = 0.006) and preoperative hospital stay > 9 days (*P* = 0.049) (Table 3). Prior chemotherapy, teeth cleaning, prior surgery for the same cancer, preoperative immunosuppression and preoperative laboratory test results (e.g. RBC count, WBC count, haemoglobin and albumin) were not significantly associated with SSI.

Regarding perioperative factors (Table 4), length of surgical procedure > 390 min (*P* < 0.001), intravenous infusion > 3500 ml (*P* < 0.001), blood loss > 500 ml (*P* < 0.001), blood transfusion (*P* = 0.007) and tracheostomy (*P* < 0.001) were associated with an increased incidence of SSI. Among these 786 patients, 443 (56.36%) underwent tumour excision with neck dissection and flap reconstruction. Type of operation, type of flap reconstruction, the extent of jawbone resection and oral-neck communication were all significantly associated with SSI (*P* < 0.001 for each comparison). However, the type of neck dissection was not a significant factor. Moreover, plate reconstruction (343 patients, 43.64%; *P* < 0.001) and clean-contaminated wound (706 patients, 89.82%; *P* = 0.010) were

Table 1. Tumour characteristics in patients ($n = 786$) that underwent major surgery for oral cancer that were grouped according to the development of surgical site infection (SSI).

Characteristic	SSI (+) $n = 125$		SSI (-) $n = 661$		Total $n = 786$	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Pathological diagnosis						
Epidermoid carcinoma	119	95.20	616	93.19	735	93.51
Adenocarcinoma	5	4.00	27	4.08	32	4.07
Mesenchymal carcinoma	1	0.80	9	1.36	10	1.27
Melanoma	0	0.00	6	0.91	6	0.76
Ameloblastic carcinoma	0	0.00	3	0.45	3	0.38
Lymph node metastasis						
Yes	64	51.20	323	48.87	387	49.24
No	61	48.80	338	51.13	399	50.76
Tumour site						
Tongue	48	38.40	257	38.88	305	38.80
Gingiva	30	24.00	169	25.57	199	25.32
Buccal	16	12.80	96	14.52	112	14.25
Floor of mouth	18	14.40	49	7.41	67	8.52
Jawbone	6	4.80	39	5.90	45	5.73
Lips	0	0.00	16	2.42	16	2.04
Palate	1	0.80	13	1.97	14	1.78
Submandibular	2	1.60	6	0.91	8	1.02
Retromolar region	2	1.60	6	0.91	8	1.02
Oropharynx	1	0.80	6	0.91	7	0.89
Parotid gland	1	0.80	4	0.61	5	0.64

No association was found between pathological diagnosis, lymph node metastasis or tumour site and SSI on univariate analysis ($P \geq 0.05$); two-sided Fisher's exact test.

significantly associated with higher rates of SSI on univariate analysis.

After surgery, significant associations were observed between SSI and the following characteristics: post-surgical hyperglycaemia ($P = 0.033$), flap failure ($P < 0.001$) and 4-day drainage ($P < 0.001$) (Table 5).

Forward stepwise multivariate logistic regression analysis revealed that independent risk factors for SSI were diabetes mellitus (odds ratio [OR] 2.147, 95% confidence interval [CI] 1.240, 3.642), prior radiotherapy (OR 4.595, 95% CI 1.293, 17.317), tracheostomy (OR 2.235, 95% CI 1.435, 3.525), perioperative oral-neck communication (OR 2.838, 95% CI 1.263, 7.604), reconstruction with an anterolateral thigh flap (OR 1.971, 95% CI 1.103, 3.448) and

reconstruction with a latissimus dorsi flap (OR 4.178, 95% CI 1.325, 13.189) (Table 6).

Discussion

Surgical site infection, as a serious complication after major surgery for oral cancer, causes delays in wound healing and adjuvant therapy, increases the chance of cancer recurrence and postoperative mortality, increases the expenditure of treatment and reduces the quality of life.¹⁵ In order to prevent SSI, it is critical to identify potential risk factors and take adequate preventive measures. However, many factors, such as different study population, sample size and research methodology,

Table 2. Demographic characteristics in patients ($n = 786$) that underwent major surgery for oral cancer that were grouped according to the development of surgical site infection (SSI).

Characteristic	SSI (+) $n = 125$		SSI (-) $n = 661$		Total $n = 786$		Statistical analysis ^{a,b}
	n	%	n	%	n	%	
Sex							$P = 0.038^a$
Male	84	67.20	377	57.03	461	58.65	
Female	41	32.80	284	42.97	325	41.35	
Mean age, years							$P = 0.016^b$
≤ 58.5	81	64.80	370	55.98	451	57.38	
> 58.5	44	35.20	291	44.02	335	42.62	
Body mass index, kg/m^2							NS
18.5–23.0	39	31.20	227	34.34	266	33.84	
< 18.5	8	6.40	23	3.48	31	3.94	
≥ 23	78	62.40	411	62.18	489	62.21	
Smoking							NS
Yes	44	35.20	197	29.80	241	30.66	
No	81	64.80	464	70.20	545	69.34	
Alcohol							NS
Yes	32	25.6	144	21.79	176	22.39	
No	93	74.4	517	78.21	610	77.61	
Hypertension							NS
Yes	35	28.00	207	31.32	242	30.79	
No	90	72.00	454	68.68	544	69.21	
Diabetes mellitus							$P = 0.008^a$
Yes	25	20.00	73	11.04	98	12.47	
No	100	80.00	588	88.96	688	87.53	
Cardiovascular disease							NS
Yes	13	10.40	82	12.41	95	12.09	
No	112	89.60	579	87.59	691	87.91	
Hyperlipidaemia							NS
Yes	0	0.00	8	1.21	8	1.02	
No	125	100.00	653	98.79	778	98.98	
Pulmonary disease							NS
Yes	2	1.60	18	2.72	20	2.54	
No	123	98.40	643	97.28	766	97.46	
Gastrointestinal disease							NS
Yes	3	2.40	4	0.61	7	0.89	
No	122	97.60	657	99.39	779	99.11	
Cerebrovascular disease							NS
Yes	4	3.20	20	3.03	24	3.05	
No	121	96.80	641	96.97	762	96.95	
Liver disease							NS
Yes	5	4.00	21	3.18	26	3.31	
No	120	96.00	640	96.82	760	96.69	
Thyroid disease							NS
Yes	1	0.80	5	0.76	6	0.76	
No	124	99.20	656	99.24	780	99.24	

^aTwo-sided Fisher's exact test; ^bMann–Whitney U -test; NS, no significant association ($P \geq 0.05$).

Table 3. Preoperative characteristics in patients ($n = 786$) that underwent major surgery for oral cancer that were grouped according to the development of surgical site infection (SSI).

Characteristic	SSI (+) $n = 125$		SSI (-) $n = 661$		Total $n = 786$		Statistical analysis ^{a,b}
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Prior radiotherapy							$P = 0.001^a$
Yes	7	5.60	5	0.76	12	1.53	
No	118	94.40	656	99.24	774	98.47	
Prior chemotherapy							NS
Yes	46	36.80	191	28.90	237	30.15	
No	79	63.20	470	71.10	549	69.85	
Teeth cleaning							NS
Yes	21	16.80	139	21.03	160	20.36	
No	104	83.20	522	78.97	626	79.64	
Previous surgery for the same neoplasia							NS
Yes	19	15.20	111	16.79	130	16.54	
No	106	84.80	550	83.21	656	83.46	
Weight loss $\geq 10\%$ in previous 6 months							$P = 0.006^a$
Yes	9	7.20	14	2.12	23	2.93	
No	116	92.80	647	97.88	763	97.07	
Immunosuppression							NS
Yes	0	0.00	2	0.30	2	0.25	
No	125	100.00	659	99.70	784	99.75	
Mean preoperative hospital stay, days							$P = 0.049^b$
≤ 9	73	58.40	417	63.09	490	62.34	
> 9	52	41.60	244	36.91	296	37.66	
Red blood cell count							NS
Normal	93	74.40	498	75.34	591	75.19	
Low	32	25.60	150	22.69	182	23.16	
High	0	0.00	13	1.97	13	1.65	
White blood cell count							NS
Normal	110	88.00	595	90.02	705	89.69	
Low	5	4.00	21	3.18	26	3.31	
High	10	8.00	45	6.81	55	7.00	
Haemoglobin							NS
Normal	98	78.40	542	82.00	640	81.42	
Low	24	19.20	106	16.04	130	16.54	
High	3	2.40	13	1.97	16	2.04	
Albumin							NS
Normal	71	56.80	415	62.78	486	61.83	
Low	54	43.20	243	36.76	297	37.79	
High	0	0.00	3	0.45	3	0.38	

^aTwo-sided Fisher's exact test; ^bMann-Whitney *U*-test; NS, no significant association ($P \geq 0.05$).

have contributed to discrepancies in previous research on the risk factors for SSI.^{8–10,13,15,18,19,27} There is a need to study specific patient populations.

This current study focused on patients that underwent major surgery for oral cancer, including cancer of the oral cavity and oropharynx, submandibular region and

Table 4. Perioperative characteristics in patients ($n=786$) that underwent major surgery for oral cancer that were grouped according to the development of surgical site infection (SSI).

Characteristic	SSI (+) $n = 125$		SSI (-) $n = 661$		Total $n = 786$		Statistical analysis ^{a,b}
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Mean operation time, min							$P < 0.001^b$
≤ 390	36	28.80	338	51.13	374	47.58	
> 390	89	71.20	323	48.87	412	52.42	
Mean intravenous liquid, ml							$P < 0.001^b$
≤ 3500	44	35.20	386	58.40	430	54.71	
> 3500	81	64.80	275	41.60	356	45.29	
Mean blood loss, ml							$P < 0.001^b$
≤ 500	49	39.20	420	63.54	469	59.67	
> 500	76	60.80	241	36.46	317	40.33	
Transfusion							$P = 0.007^a$
Yes	13	10.40	27	4.08	40	5.09	
No	112	89.60	634	95.92	746	94.91	
Tracheostomy							$P < 0.001^a$
Yes	86	68.80	260	39.33	346	44.02	
No	39	31.20	401	60.67	440	55.98	
Type of operation							$P < 0.001^a$
Unilateral neck dissection	1	0.80	61	9.23	62	7.89	
Bilateral neck dissection	1	0.80	5	0.76	6	0.76	
Tumour excision with flap reconstruction	1	0.80	5	0.76	6	0.76	
Tumour excision with neck dissection	25	20.00	244	36.91	269	34.22	
Tumour excision with neck dissection and flap reconstruction	97	77.60	346	52.34	443	56.36	
Neck dissection							NS
No	1	0.80	4	0.61	5	0.64	
Selective	108	86.40	570	86.23	678	86.26	
Modified	3	2.40	19	2.87	22	2.80	
Radical	8	6.40	32	4.84	40	5.09	
Bilateral	5	4.00	36	5.45	41	5.22	
Flap reconstruction							$P < 0.001^a$
No	27	21.60	312	47.20	339	43.13	
Radial forearm flap	29	23.20	162	24.51	191	24.30	
Fibula osteoseptocutaneous flap	32	25.60	115	17.40	147	18.70	
Anterolateral thigh flap	23	18.40	50	7.56	73	9.29	
Latissimus dorsi flap	8	6.40	7	1.06	15	1.91	
Pectoralis major pedicled flap	6	4.80	15	2.27	21	2.67	
Plate reconstruction							$P < 0.001^a$
Yes	79	63.20	264	39.94	343	43.64	
No	46	36.80	397	60.06	443	56.36	

(continued)

Table 4. Continued.

Characteristic	SSI (+) n = 125		SSI (-) n = 661		Total n = 786		Statistical analysis ^{a,b}
	n	%	n	%	n	%	
Extent of jawbone resection							$P < 0.001^a$
No	25	20.00	272	41.15	297	37.79	
Block mandibulectomy	11	8.80	82	12.41	93	11.83	
Marginal mandibulectomy	25	20.00	91	13.77	116	14.76	
Segmental mandibulectomy	32	25.60	84	12.71	116	14.76	
Mandibulotomy	29	23.20	77	11.65	106	13.49	
Infrastructure maxillectomy	0	0.00	3	0.45	3	0.38	
Hemimandibulectomy	2	1.60	31	4.69	33	4.20	
Subtotal maxillectomy	1	0.80	20	3.03	21	2.67	
Total mandibulectomy	0	0.00	1	0.15	1	0.13	
Oral–neck communication							$P < 0.001^a$
Yes	119	95.20	531	80.33	650	82.70	
No	6	4.80	130	19.67	136	17.30	
Wound class							$P = 0.010^a$
Clean	5	4.00	75	11.35	80	10.18	
Clean-contaminated	120	96.00	586	88.65	706	89.82	

^aTwo-sided Fisher's exact test ; ^bMann–Whitney *U*-test; NS, no significant association ($P \geq 0.05$).

parotid gland. However, cancers in the larynx, thyroid, skin and other head and neck regions were excluded. In this current study population, the incidence of SSI was 15.9% and all were incisional SSI.

Diabetes mellitus has been identified as a risk factor for SSI by several studies using univariate analyses,^{15,28} multivariate analyses¹⁸ and meta-analyses.²⁹ In this current study, diabetes mellitus was demonstrated to be an independent risk factor for SSI. With multivariate analysis, the risk of developing SSI in patients with diabetes mellitus increased more than two-fold compared with those without diabetes mellitus. It is well established that diabetes mellitus causes microvasculopathy and immunosuppression, which interfere with wound healing.^{30,31} As such, the 2017 CDC guideline for the prevention of SSI recommends the implementation of perioperative glycaemic control with a blood glucose target level < 200 mg/dl for patients with or without diabetes mellitus.^{20,32}

Patients that underwent prior radiotherapy had a 58.33% (seven of 12 patients) chance of developing SSI in this current study, suggesting that prior radiotherapy is an independent risk factor for SSI. This observation was consistent with that of previous studies.^{5,15,33,34} As an adjuvant therapy for oral cancer, radiotherapy eliminates cancerous cells but also damages healthy cells, leading to problems with wound healing.¹⁴ These side-effects from radiation-induced DNA mutations, microvascular damage and soft tissue fibrosis reduce collagen deposition and angiogenesis during wound healing.^{14,15} Adverse effects tend to be protracted.³⁵ A previous study reported radiation complications associated with additional surgery later than 1 week after the initial reconstructive surgery.³⁵ This finding suggested that SSI, which results in the need to reopen the wound, should be identified as soon as possible to minimize radiation complications.³⁵

Table 5. Postoperative characteristics in patients ($n = 786$) that underwent major surgery for oral cancer that were grouped according to the development of surgical site infection (SSI).

Characteristic	SSI (+) $n = 125$		SSI (-) $n = 661$		Total $n = 786$		Statistical analysis ^{a,b}
	n	%	n	%	n	%	
Haematomas							NS
Yes	7	5.60	23	3.48	30	3.82	
No	118	94.40	638	96.52	756	96.18	
Corticosteroid use							NS
Yes	117	93.60	612	92.59	729	92.75	
No	8	6.40	49	7.41	57	7.25	
Post-surgical hyperglycaemia							$P = 0.033^a$
Yes	17	13.60	49	7.41	66	8.40	
No	108	86.40	612	92.59	720	91.60	
Flap failure							$P < 0.001^a$
Yes	12	9.60	28	4.24	40	5.09	
No	113	90.40	633	95.76	746	94.91	
Other infections							NS
No	123	98.40	646	97.73	769	97.84	
Pneumonia	2	1.60	7	1.06	9	1.15	
Urinary tract infection	0	0.00	4	0.61	4	0.51	
Upper respiratory infection	0	0.00	4	0.61	4	0.51	
Mean drainage of day 1, ml							$P < 0.001^b$
≤ 200	60	48.00	450	68.08	510	64.89	
> 200	65	52.00	211	31.92	276	35.11	
Mean drainage of day 2, ml							$P < 0.001^b$
≤ 100	52	41.60	389	58.85	441	56.11	
> 100	73	58.40	272	41.15	345	43.89	
Mean drainage of day 3, ml							$P < 0.001^b$
≤ 80	79	63.20	532	80.48	611	77.74	
> 80	46	36.80	129	19.52	175	22.26	
Mean drainage of day 4, ml							$P < 0.001^b$
≤ 30	64	51.20	387	58.55	451	57.38	
> 30	61	48.80	274	41.45	335	42.62	
Mean total drainage of 4 days, ml							$P < 0.001^b$
≤ 380	51	40.80	393	59.46	444	56.49	
> 380	74	59.20	268	40.54	342	43.51	

^aTwo-sided Fisher's exact test; ^bMann-Whitney U -test; NS, no significant association ($P \geq 0.05$).

Tracheostomy is often used for patients with oral cancer to prevent asphyxia due to airway obstruction during or after surgery. Many previous investigations have shown that tracheostomy is significantly associated with SSI.^{13,15,27,36} In this current study, patients that underwent tracheostomy were two-times more likely to experience

SSI than those that did not. Potential contamination through tracheostomy may occur as a result of the exposure of the surgical wound to the skin or a permanent communication between the respiratory tract and the wound. Polymicrobial flora of the upper aerodigestive tract secretions that collect around a tracheostomy tube

Table 6. Forward stepwise multivariate logistic regression analysis of independent risk factors for surgical site infection in patients ($n = 786$) that underwent major surgery for oral cancer.

Risk factors	P-value	Odds ratio	95% confidence interval
Diabetes mellitus	$P = 0.005$	2.147	1.240, 3.642
Prior radiotherapy	$P = 0.018$	4.595	1.293, 17.317
Tracheostomy	$P < 0.001$	2.235	1.435, 3.525
Oral–neck communication	$P = 0.021$	2.838	1.263, 7.604
Anterolateral thigh flap	$P = 0.019$	1.971	1.103, 3.448
Latissimus dorsi flap	$P = 0.013$	4.178	1.325, 13.189

postoperatively may cause infection of neck wounds.^{12,22,37,38} In addition, tracheostomy tends to be used with a large oral cavity resection combined with mandibulotomy, indicating a complicated surgical process. Similarly, it tended to be involved in the formation of oral–neck communication, as mentioned below, increasing SSI incidence.

As a result of *en bloc* resection of the primary tumour and related lymphadenopathies, oral–neck communication has been proposed as a risk factor for SSI in the literature.³⁹ When the tumour involves the mouth floor, lower gingiva, the base of the tongue and unsafe lymph nodes in layers of the mouth floor musculature, the removal of mouth floor musculatures and lymphatic basins during the resection procedures results in a through-and-through defect connecting the oral cavity and neck. This orocutaneous communication is different from a fistula; it is surgically created for therapeutic reasons during the operation. These current data supported oral–neck communication as a significant risk factor for SSI. The incidence of SSI in patients with oral–neck communication was as high as 18.31% (119 of 650 patients) and multivariate analysis indicated that patients with oral–neck communication were approximately three-times more likely to develop SSIs than those without it. Perioperative oral–neck communication facilitates the growth of microorganisms in

the oral cavity and upper aerodigestive tract in a clean dissected neck, to generate postoperative SSI if the patient is unprotected by empiric prophylactic antibiotics.

Flap reconstruction is frequently needed in oral cancer because of the resulting tissue defect after radical resection. In this current study, 43.13% (339 of 786 patients) underwent primary closure and all others received flap reconstructions. The most frequently used flap in this current study was a radial forearm flap, with fibula osteoseptocutaneous flap as the second and anterolateral thigh flap as the third. Previous literature reported that the frequency of SSI after reconstruction with a microvascular flap ranged from 26% to 48%.^{40,41} In this current study, latissimus dorsi flaps had the highest incidence of SSI (53.33%; eight of 15 patients), with anterolateral thigh flaps (31.51%; 23 of 73 patients) and pectoralis major flaps (28.57%; six of 21 patients) coming second and third, respectively. Even with multiple logistic regression modelling, flap reconstruction remained significantly related to SSI, and both anterolateral thigh and latissimus dorsi flaps were independent risk factors for SSI. Flap reconstruction often indicates a complex procedure, long surgery time, large tissue defect and high blood loss, which may all contribute to SSI.⁴² In our institute, reconstruction using latissimus dorsi flaps usually requires the turning over of patients

to prepare the flaps. Consequently, this prolongs the duration of surgery and increases blood loss and the chances of SSI occurrence. Previous research demonstrated a novel technique of harvesting the subscapular system of flaps, as well as latissimus dorsi flaps.⁴³ The authors used a supine position to prepare and drape, and the patient's arm was propped up using a bolster without the need for the patient to be rotated.⁴³ Ablation and harvesting can be simultaneously performed in this modified supine position to reduce the surgery time, thereby ensuring a low chance of developing SSI; however, the disadvantage is that it requires a two-team approach simultaneously.⁴³

Paradoxically, the univariate analysis revealed that younger patients (≤ 58.5 years) were more likely to develop SSI than older ones (> 58.5 years). This may be because older patients tend to experience systemic comorbidities, and consequently, are more likely to be excluded from surgery.

This current study had two limitations: (i) when patients were further classified into various categories, the sample size was occasionally insufficient in the subgroups to allow the generation of statistically powerful conclusions; (ii) some patients were excluded from this study due to incomplete medical record information.

In conclusion, several independent risk factors for SSI were identified among patients undergoing major surgery for oral cancer. These current data indicate that patients that have diabetes mellitus or underwent prior radiotherapy, tracheostomy, perioperative oral-neck communication caused by surgery and flap reconstruction were more susceptible to SSI. Therefore, patients with these risk factors may require close postoperative monitoring for possible SSI. In theory, better management of these risk factors would improve the surgical outcome for patients with oral cancer.

Declaration of conflicting interest


The authors declare that there are no conflicts of interest.

Funding

This work was supported by the Incubating Programme for Beijing Municipal Administration of Hospitals (grant number: pX2017061).

ORCID iDs

Lizheng Qin  <https://orcid.org/0000-0003-2384-7514>

Xin Huang  <https://orcid.org/0000-0003-0605-1055>

References

1. Haque M, McKimm J, Godman B, et al. Initiatives to reduce postoperative surgical site infections of the head and neck cancer surgery with a special emphasis on developing countries. *Expert Rev Anticancer Ther* 2019; 19: 81–92.
2. Young PY and Khadaroo RG. Surgical site infections. *Surg Clin North Am* 2014; 94: 1245–1264.
3. Candau-Alvarez A, Gil-Campos M, De la Torre-Aguilar MJ, et al. Early Modification in Drainage of Interleukin-1beta and Tumor Necrosis Factor-alpha Best Predicts Surgical-Site Infection After Cervical Neck Dissection for Oral Cancer. *J Oral Maxillofac Surg* 2015; 73: 1189–1198.
4. de Melo GM, Ribeiro KC, Kowalski LP, et al. Risk factors for postoperative complications in oral cancer and their prognostic implications. *Arch Otolaryngol Head Neck Surg* 2001; 127: 828–833.
5. Girod DA, McCulloch TM, Tsue TT, et al. Risk factors for complications in clean-contaminated head and neck surgical procedures. *Head Neck* 1995; 17: 7–13.
6. Grandis JR, Snyderman CH, Johnson JT, et al. Postoperative wound infection. A poor prognostic sign for patients with head and neck cancer. *Cancer* 1992; 70: 2166–2170.

7. Legesse Laloto T, Hiko Gemedo D and Abdella SH. Incidence and predictors of surgical site infection in Ethiopia: prospective cohort. *BMC Infect Dis* 2017; 17: 119.
8. Lotfi CJ, Cavalcanti Rde C, Costa e Silva AM, et al. Risk factors for surgical-site infections in head and neck cancer surgery. *Otolaryngol Head Neck Surg* 2008; 138: 74–80.
9. Ogihara H, Takeuchi K and Majima Y. Risk factors of postoperative infection in head and neck surgery. *Auris Nasus Larynx* 2009; 36: 457–460.
10. Penel N, Fournier C, Lefebvre D, et al. Multivariate analysis of risk factors for wound infection in head and neck squamous cell carcinoma surgery with opening of mucosa. Study of 260 surgical procedures. *Oral Oncol* 2005; 41: 294–303.
11. Mazurek MJ, Rysz M, Jaworowski J, et al. Contamination of the surgical field in head and neck oncologic surgery. *Head Neck* 2014; 36: 1408–1412.
12. Simo R and French G. The use of prophylactic antibiotics in head and neck oncological surgery. *Curr Opin Otolaryngol Head Neck Surg* 2006; 14: 55–61.
13. Cunha TF, Soares Melancia TA, Zagalo Fernandes Ribeiro CM, et al. Risk factors for surgical site infection in cervico-facial oncological surgery. *J Craniomaxillofac Surg* 2012; 40: 443–448.
14. Dormand EL, Banwell PE and Goodacre TE. Radiotherapy and wound healing. *Int Wound J* 2005; 2: 112–127.
15. Lee DH, Kim SY, Nam SY, et al. Risk factors of surgical site infection in patients undergoing major oncological surgery for head and neck cancer. *Oral Oncol* 2011; 47: 528–531.
16. Barie PS and Eachempati SR. Surgical site infections. *Surg Clin North Am* 2005; 85: 1115–1135.
17. Mangram AJ, Horan TC, Pearson ML, et al. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 1999; 20: 250–280.
18. Liu SA, Wong YK, Poon CK, et al. Risk factors for wound infection after surgery in primary oral cavity cancer patients. *Laryngoscope* 2007; 117: 166–171.
19. Kamizono K, Sakuraba M, Nagamatsu S, et al. Statistical analysis of surgical site infection after head and neck reconstructive surgery. *Ann Surg Oncol* 2014; 21: 1700–1705.
20. Berrios-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. *JAMA Surg* 2017; 152: 784–791.
21. Chupp RE and Edhayan E. An effort to improve the accuracy of documented surgical wound classifications. *Am J Surg* 2018; 215: 515–517.
22. Brown BM, Johnson JT and Wagner RL. Etiologic factors in head and neck wound infections. *Laryngoscope* 1987; 97: 587–590.
23. Horan TC, Gaynes RP, Martone WJ, et al. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol* 1992; 13: 606–608.
24. Johnson JT, Myers EN, Thearle PB, et al. Antimicrobial prophylaxis for contaminated head and neck surgery. 1984. *Laryngoscope* 2015; 125: 275–280.
25. Minski M. Surgical Site Infection Coding Update. *J AHIMA* 2019; 90: 44–45.
26. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004; 363: 157–163.
27. Belusic-Gobic M, Car M, Juretic M, et al. Risk factors for wound infection after oral cancer surgery. *Oral Oncol* 2007; 43: 77–81.
28. Shigeishi H, Ohta K and Takechi M. Risk factors for postoperative complications following oral surgery. *J Appl Oral Sci* 2015; 23: 419–423.
29. Martin ET, Kaye KS, Knott C, et al. Diabetes and Risk of Surgical Site Infection: a Systematic Review and Meta-analysis. *Infect Control Hosp Epidemiol* 2016; 37: 88–99.
30. Jeffcoate WJ, Price P and Harding KG. Wound healing and treatments for people with diabetic foot ulcers. *Diabetes Metab Res Rev* 2004; 20: S78–S89.
31. Knapp S. Diabetes and infection: is there a link?—A mini-review. *Gerontology* 2013; 59: 99–104.

32. O'Hara LM, Thom KA and Preas MA. Update to the Centers for Disease Control and Prevention and the Healthcare Infection Control Practices Advisory Committee Guideline for the Prevention of Surgical Site Infection (2017): a summary, review, and strategies for implementation. *Am J Infect Control* 2018; 46: 602–609.
33. Son HJ, Roh JL, Choi SH, et al. Nutritional and hematologic markers as predictors of risk of surgical site infection in patients with head and neck cancer undergoing major oncologic surgery. *Head Neck* 2018; 40: 596–604.
34. Swift AC. Wound sepsis, chemoprophylaxis and major head and neck surgery. *Clin Otolaryngol Allied Sci* 1988; 13: 81–83.
35. Onoda S, Kimata Y, Sugiyama N, et al. Effects of radiation therapy on postoperative complications and adverse events in patients with head and neck reconstruction with flaps. *Microsurgery* 2014; 34: 516–521.
36. Coskun H, Erisen L and Basut O. Factors affecting wound infection rates in head and neck surgery. *Otolaryngol Head Neck Surg* 2000; 123: 328–333.
37. Cole RR, Robbins KT, Cohen JI, et al. A predictive model for wound sepsis in oncologic surgery of the head and neck. *Otolaryngol Head Neck Surg* 1987; 96: 165–171.
38. Robbins KT, Favrot S, Hanna D, et al. Risk of wound infection in patients with head and neck cancer. *Head Neck* 1990; 12: 143–148.
39. Lin SC, Chang TS, Yang KC, et al. Factors contributing to surgical site infection in patients with oral cancer undergoing microvascular free flap reconstruction. *Eur Arch Otorhinolaryngol* 2018; 275: 2101–2108.
40. Cloke DJ, Green JE, Khan AL, et al. Factors influencing the development of wound infection following free-flap reconstruction for intra-oral cancer. *Br J Plast Surg* 2004; 57: 556–560.
41. Karakida K, Aoki T, Ota Y, et al. Analysis of risk factors for surgical-site infections in 276 oral cancer surgeries with microvascular free-flap reconstructions at a single university hospital. *J Infect Chemother* 2010; 16: 334–339.
42. Mahieu R, Colletti G, Bonomo P, et al. Head and neck reconstruction with pedicled flaps in the free flap era. *Acta Otorhinolaryngol Ital* 2016; 36: 459–468.
43. Eskander A, Kang SY, Ozer E, et al. Supine positioning for the subscapular system of flaps: a pictorial essay. *Head Neck* 2018; 40: 1068–1072.