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Surgical site infections in oral cavity carcinoma: predictive factors, microbiological trends, and clinical implications—experience of a major Italian medical center

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Objective. Surgical site infections (SSI) are a common but clinically significant postoperative complication in oral squamous cell carcinoma (OSCC) surgery with center-specific microbiology. This study aimed to quantify SSI incidence, identify independent predictors as a pre-ERAS baseline, with an exploratory estimate of ERAS impact.

Study Design. Retrospective cohort at a major Italian center, including 575 adults undergoing OSCC resection. SSI were defined per Centers for Disease Control and Prevention (CDC/NHSN) criteria with a 30-day surveillance window. Cultures/susceptibility testing were obtained when infection was suspected. Multivariable logistic regression with Lasso and Cox models estimated odds and hazard ratios; receiver operating characteristic analyses assessed discrimination.

Results. SSI occurred in 24.3% patients with a median onset 7 days. Independent predictors were age per 10 years, smoking, alcohol use, and radical neck dissection (RND) as supported by Cox estimates. Exploratorily, the ERAS period (late-2022 onward) was associated with lower SSI hazard. Microbiology was predominantly polymicrobial (71.4%), led by *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Conclusion. s: Age, smoking, alcohol use, and RND predict SSI. ERAS pathway was introduced in 2022. Future prospective studies are needed to improve outcomes, considering that microbiological findings and resistance rates reflect the local ecology of a tertiary Italian center and may differ in other settings. (Oral Surg Oral Med Oral Pathol Oral Radiol 2025;000:1−10)

Head and neck cancer surgery for oral squamous cell carcinoma (OSCC) often requires complex reconstruction to restore function and aesthetics. Following tumor resection, microvascular free flaps and pedicled flaps are among the most used reconstructive techniques.[1] Despite advances in surgical techniques and perioperative management, surgical site infections (SSI) remain a common but clinically significant postoperative complication, affecting postoperative recovery, length of hospital stay, and overall morbidity.[2]

Reported SSI rates in head and neck oncology range from 3% to 61%, influenced by factors such as comorbidities, tumor stage, and surgical approach.[3] Recent reviews focusing on OSCC have indicated variability in SSI incidence, reflecting differences in patient populations and perioperative protocols.[4,5] Known risk factors include a high American Society of Anesthesiologists (ASA) score, prolonged surgical duration, perioperative blood transfusions, prior radiation therapy, and extended hospital stays.[6]

Recent studies suggest that inadequate Gram-negative coverage in prophylactic antibiotic regimens is associated with an increased risk of SSI following microvascular reconstruction.[2] In addition, malnutrition, hypoalbuminemia, and a high platelet-to-lymphocyte ratio have been implicated as predictors of poor postoperative outcomes.[4]

Given the existing literature, factors such as advanced age, smoking, and alcohol consumption have been repeatedly associated with compromised immune function and delayed wound healing. In addition, the extent of surgical trauma has been implicated in increasing SSI risk. Emerging data on the prevalence of multidrug-resistant organisms underscore the need

Statement of Clinical Relevance

Surgical site infections after oral squamous cell carcinoma surgery are common and linked to modifiable risks like smoking and alcohol; targeted preoperative interventions may reduce infection rates and improve patient outcomes.

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for a comprehensive evaluation of both patient-related and surgical factors, including the microbiological spectrum of SSI, to inform and optimize prophylactic strategies.[4,7]

Evidence on the microbiologic spectrum of SSI in OSCC—and how it should guide prophylaxis—remains limited. We therefore quantified SSI incidence, identified independent risk factors, and characterized causative organisms to inform empiric management. Our institutional ERAS pathway for major head and neck surgery was introduced in late 2022; this cohort precedes implementation and aims to serve as a pre-ERAS baseline for a planned, adequately powered pre/post ERAS comparison.

MATERIALS AND METHODS

Study design and population

This retrospective observational study adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines. The study analyzed a hospital database of patients admitted for surgical treatment of OSCC at the Maxillofacial Surgery Department of the University Hospital of Marche, Ancona, Italy, between January 2009 and January 2024; therefore, the microbiological profile and antimicrobial resistance rates reported represent the local ecology during the study period.

The inclusion criteria were: (1) patients aged ≥18 years with histologically confirmed OSCC who underwent tumor resection (with or without neck dissection) and (2) those with complete medical records, including perioperative details. Patients were consecutively enrolled to minimize selection bias. The exclusion criteria were: (1) previous maxillofacial malignancies treated with surgery, radiotherapy, or chemotherapy; (2) incomplete or missing perioperative data on key parameters (e.g., surgical duration or antibiotic prophylaxis details); and (3) patients who withdrew consent. TNM stage, ASA physical-status score, and prior radiotherapy were extracted and considered as potential confounders. ERAS components for head and neck were rolled out at our institution from late 2022: the current dataset predominantly reflects pre-ERAS practice, which is analyzed as a baseline cohort.

Ethical approval

The study was conducted in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. To ensure patient confidentiality, all personal identifiers were removed or coded during data collection, and access to sensitive information was restricted to authorized personnel only. All the procedures followed the ethical standard of IRB—CET Marche, and the study was approved with protocol 116/2025. The research complied with European GDPR (General Data Protection Regulation) and Italian privacy laws.

SSI definition and prophylaxis

Variables collected for each patient included age and sex, tumor location and staging, surgical approach, and reconstructive technique. Focus was given to the incidence of SSI, microbiological characteristics, and their association with potential risk factors, including comorbidities, perioperative management, and antibiotic prophylaxis. Postoperative SSI diagnosis followed the Centers for Disease Control and Prevention/National Healthcare Safety Network (CDC/NHSN) criteria.[8] As prosthetic material is rarely used in OSCC surgery, we adopted the 30-day surveillance window recommended for procedures without implanted hardware, capturing most clinically significant incisional and organ-space SSI reported in head-and-neck oncology series while maintaining methodological comparability with prior studies.[9]

SSI were defined according to CDC criteria as any infections occurring within 30 days after surgery at or near the incision site, accompanied by clinical signs such as purulent discharge, pain, redness, or swelling, and with microbiological culture confirmation.[10]

The standard prophylactic antibiotic regimen for oral cancer surgery involves a combination of cefazolin (2 g IV) and metronidazole (500 mg IV). The first dose was administered within 30 to 60 min before the surgical incision, and additional doses were repeated intraoperatively depending on the duration of the procedure. Prophylaxis was continued for 24 h postoperatively in the absence of complications. In cases of β-lactam allergy, clindamycin (600-900 mg IV every 8 h) was substituted, and metronidazole was maintained for anaerobic coverage. Skin preparation was performed using povidone-iodine, and all procedures followed a standardized protocol to minimize contamination. The oral hygiene protocol included supragingival scaling 48 h preoperatively and 0.20% chlorhexidine three times daily postoperatively.[11]

Surgical protocol

Defects ≤3 cm in any dimension, with an intact mandible and no skin breach, were closed primarily or with a pedicled regional flap (submental, pectoralis major, or temporalis) according to the institutional "reconstructive ladder." Free microvascular tissue transfer was preferred when the defect (1) exceeded 3 cm, (2) involved composite bone-soft-tissue loss, or (3) required three-dimensional contouring (tongue base, floor-of-mouth, or oropharynx). Contraindications for free flaps were severe vascular comorbidities

(ASA ≥ IV), non-reconstructible cervical vessels, or patient refusal.

To minimize bacterial load and the risk of tumor cell implantation, the surgeons replaced gloves and instruments after completing tumor resection during each surgery. Therefore, maintaining normothermia was prioritized during microvascular free flap reconstruction.[10,12,13]

All surgical procedures were performed by experienced maxillofacial surgeons to ensure consistency in the treatment approach and minimize variability in outcomes associated with trainees or less experienced operators.[14]

Given the retrospective nature of the study, follow-up was not standardized; however, all postoperative infections were assessed within a 30-day period. Wound swabs or aspirates were collected from patients with suspected SSI and analyzed by the microbiology laboratory. Samples underwent Gram staining, culture, and antibiotic sensitivity testing using a standardized disk diffusion protocol. Organisms were identified to the species level, and the presence of multidrug-resistant strains (e.g., methicillin-resistant *Staphylococcus aureus* [MRSA] and carbapenem-resistant *Pseudomonas*) was recorded.

Statistical analysis

Data are summarized using counts and percentages for categorical variables and means ± standard deviations or medians with interquartile ranges (IQRs) for continuous variables. Group comparisons were performed using the chi-square or Fisher's exact test for categorical data, the independent-samples t-test for normally distributed data, and the Mann−Whitney U test for non-normally distributed data. For comparisons involving >2 groups, one-way analysis of variance (ANOVA) or the Kruskal−Wallis test was applied.

Potential predictors of SSI ($P < .1$ in univariate analysis) were entered into a multivariate logistic regression model. To improve interpretability and numerical stability, age was scaled by dividing by 10 (i.e., one unit = 10 years) before entry into the model so that the resulting coefficients and odds ratios (ORs) represented the effect per decade. ORs with 95% confidence intervals (CIs) were calculated. Receiver operating characteristic (ROC) analyses were conducted for continuous variables to identify optimal cutoffs. Due to the limited number of events compared to the number of candidate predictors, least absolute shrinkage and selection operator (Lasso) regularization was employed to the multivariate logistic regression to mitigate potential multicollinearity and overfitting. Notably, TNM stage and prior radiotherapy did not remain significant after Lasso regularization, suggesting that radical neck dissection (RND) may capture the excess risk associated with advanced disease extent. A post-hoc power calculation was performed in G*Power 3.1.9.7 (two-tailed, $\alpha = 0.05$) assuming a baseline SSI incidence of 12% and an OR of 2.0 (effect size $w = 0.22$). With a sample size of 575, the achieved statistical power was 81% ($\beta = 0.19$). The final number of participants ($n = 575$) was determined by record completeness and inclusion criteria. Overall, missing data did not exceed 6% for any variables, allowing for complete-case approach ($n = 541$). Based on our observed baseline SSI rate (24.3%), we estimated the sample size required to detect a 10% point absolute reduction (to 14.3%) with $\alpha = 0.05$ and 80% power. Using a two-proportion normal approximation, this requires ∼244 patients per group (total ≈488). The 12% baseline incidence for the post-hoc power computation reflects published estimates in comparable OSCC cohorts; our observed 24.3% rate was used only for the prospective pre/post-ERAS sample-size scenario.

Time-to-event analysis: We additionally analyzed infection-free survival up to postoperative day 30. Time origin was the date of index surgery; events were the first SSI recorded within 30 days; patients without SSI were censored at discharge or day 30, whichever came first. Survival curves were estimated with the Kaplan−Meier method and compared with the log-rank test. We fitted Cox proportional-hazards models including age (scaled per 10-year increase), smoking, alcohol consumption, neck-dissection type (radical vs selective/modified radical), and flap type (pedicled vs free) as covariates. Hazard ratios (HRs) with 95% CIs are reported.

In a prespecified sensitivity analysis, we added an indicator for the ERAS period (implemented at our unit in late 2022).

To address potential confounding in the association between RND and SSI, multivariable models were also adjusted for AJCC T stage (T1 vs T2-T4), N category, and prior radiotherapy (yes/no), in addition to age, smoking, alcohol, and flap type. Multicollinearity was assessed using variance-inflation factors (VIF) and condition indices (all VIFs < 2; condition index <15). Pre-specified interaction terms (RND × T stage; RND × prior radiotherapy) were tested and were non-significant. Sensitivity analyses included (1) restriction to T3-T4 tumors, (2) exclusion of patients with prior radiotherapy, and (3) inverse-probability-of-treatment weighting (IPTW) using a propensity score for RND (age, sex, subsite, T/N, prior radiotherapy, flap type, smoking, alcohol). For robustness to unmeasured confounding, we calculated the E-value for the RND HR.

Statistical significance was set at $P < .05$.

All analyses were performed in jamovi (v2.x; The jamovi project), using R packages survival and glmnet.

RESULTS

A total of 575 patients were included in this study. The mean age was 63.4 ± 10.7 years, with a predominance of males (65.2%). The most common risk factors identified were smoking (58.3%) and alcohol consumption (47.8%).

Reconstruction was predominantly performed using free flaps (53.9%), most often the anterolateral thigh (47.5%), radial forearm (34.4%), or fibular flap (18.1%). Pedicled flaps (46.1%) primarily included the pectoralis major myocutaneous (45.3%), temporalis muscle (28.3%), and submental island (26.4%). Neck dissections were selective (57.4%), modified radical (29.6%), or radical (13.0%).

Overall, 140 patients (24.3%) developed SSI, with a median time to diagnosis of 7 days postoperatively (IQR: 5-10 days). The mean hospital stay was significantly longer in patients with SSI (23.1 ± 6.5 days) than those without infections (14.6 ± 4.2 days; $P < .001$).

Patients who developed SSI were significantly older than those who did not (67.8 ± 9.3 vs 61.2 ± 10.5 years; $P = .002$). Smoking was found to be a significant predictor of SSI, with 78.6% of infected patients having a history of smoking compared to 51.2% of non-infected patients ($P = .013$). Similarly, alcohol consumption was associated with a higher incidence of SSI (67.9% vs 42.3%; $P = .019$).

Among surgical variables, patients who underwent free flap reconstruction had a lower rate of SSI (18.5%) than those who underwent pedicled flap reconstruction (31.5%), but this difference was not statistically significant ($P = .064$). However, RND was associated with a significantly higher risk of SSI (40.0%) than were selective and modified radical dissections ($P = .003$) (Table I).

Logistic regression analysis with Lasso regularization identified the following significant predictors: Age (OR = 1.18 per 10-year increase, 95% CI: 1.03-1.35, $P = .008$); smoking history (OR = 2.68, 95% CI: 1.35-5.32, $P = .006$); alcohol consumption (OR = 2.43, 95% CI: 1.21-4.90, $P = .013$); RND (OR = 3.12, 95% CI: 1.58-6.14, $P = .002$).

No significant associations were found between infection risk and type of reconstruction (free vs pedicled flap) or duration of surgery. The multivariable model achieved an area under the curve (AUC) of 0.79 (95% CI 0.75-0.83), outperforming age alone (AUC 0.72) and neutrophil count (AUC 0.68; both $P < .01$).

ROC analysis was conducted to determine the optimal cutoff values for continuous variables associated with SSI. The AUC for age was 0.72, with an optimal threshold of 65 years, indicating that patients older than this age had a higher probability of developing an SSI ($P < .01$). Similarly, the AUC for neutrophil count was 0.68, with an optimal cutoff of 5.2×10^9/L,

Table I. Demographic, clinical, and surgical characteristics associated with surgical site infections (SSIs)

Variable	*Overall* (N = *575)*	*No SSI* (n = *435)*	*SSI* (n = *140)*	*Univariate* P *value*	*Multivariate OR (95% CI)*	*Multivariate* P *value*
Age, years (mean ± SD)	63.4 ± 10.7	61.2 ± 10.5	67.8 ± 9.3	.002	1.18 (1.03-1.35)*	.008
Sex, male	65.2%	–	–	.20†	Not retained‡	–
Smoking history	58.3%	51.2%	78.6%	.013	2.68 (1.35-5.32)	.006
Alcohol consumption	47.8%	42.3%	67.9%	.019	2.43 (1.21-4.90)	.013
Type of flap reconstruction	Free flap (53.9%) Pedicled flap (46.1%)	81.5% free flap 68.5% pedicled flap	18.5% free flap 31.5% pedicled flap	.064	Not retained‡	–
Neck dissection type	Selective (57.4%) Modified radical (29.6%) Radical (13.0%)	SSI rate: Selective: 20.9% Modified radical: 21.2% Radical: 40.0%	–	.003	3.12 (1.58-6.14)§	.002
Hospital stay, days (mean ± SD)	–	14.6 ± 4.2	23.1 ± 6.5	<.001	Not applicable‖	–

SSI, surgical site infection; *OR*, odds ratio; *CI*, confidence interval; *SD*, standard deviation.
*Per additional 10-year increase in age.
†Sex distribution was not significantly different between groups in univariate analysis.
‡Variable was not retained in the final multivariate logistic regression model ($P > .1$ in univariate analysis or removed by regularization).
§Reference group includes patients undergoing selective or modified radical neck dissection.
‖Length of hospital stay was considered an outcome variable (consequence of SSI), not a predictor in the logistic regression model.

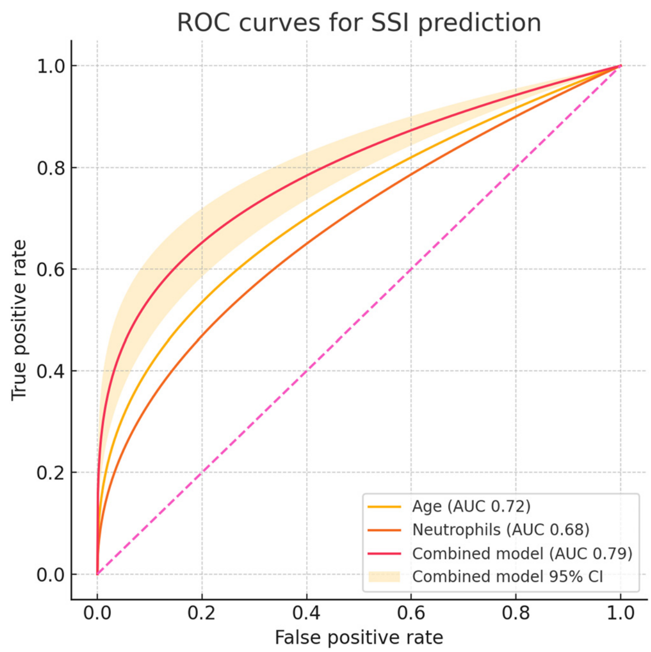

Fig. 1. ROC curve for SSI prediction. "Receiver operating characteristic (ROC) curve illustrating the predictive performance of age and neutrophil count for the occurrence of surgical site infections (SSI). The area under the curve (AUC) values indicate the discriminatory ability of each predictor, with age (AUC = 0.72) and neutrophil count (AUC = 0.68) demonstrating moderate predictive value. The diagonal dashed line represents a random classifier (AUC = 0.50)."

suggesting a potential role of inflammatory markers in predicting SSI risk (Figure 1).

Polymicrobial growth was identified in 71.4% of infected sites. *S. aureus* (42.9%) and *Pseudomonas aeruginosa* (35.7%) were the most frequently isolated pathogens; multidrug-resistant strains occurred in 28.6% of cases, including MRSA (17.9%) and carbapenem-resistant *P. aeruginosa* (10.7%). *P. aeruginosa* was more prevalent after pedicled flap reconstruction, whereas *S. aureus* predominated after free flaps reconstruction (Figure 2).

Figure 3 displays Kaplan−Meier curves on the subset with complete daily follow-up ($n = 115$), while HRs come from the adjusted Cox model on the analysis set. With this models, hazard-ratio estimates were broadly consistent with the logistic-regression ORs. Age (per 10 years), smoking, alcohol consumption, and RND were independently associated with shorter infection-free survival (Table II). Kaplan−Meier curves, by neck dissection type, showed early separation within the first postoperative week, in line with the observed median onset at day 7. In an exploratory model including an indicator for the ERAS period (late 2022 onward), the ERAS indicator was associated with a lower instantaneous risk of SSI. Using the observed counts as effect-size summary for the pre-ERAS baseline, we derived exact ORs with 95% CIs (Fisher's exact *P*) for key predictors (Table III).

Given the limited post-implementation sample, this analysis should be interpreted cautiously.

The adjusted RND effect was stable across sensitivity analyses (Table IV): T3-T4-only cohort HR 2.67 (95% CI 1.21-5.89), exclusion of prior radiotherapy HR 2.83 (95% CI 1.14-7.01), and IPTW HR 2.95 (95% CI 1.46-5.96). No evidence of problematic collinearity was detected (all VIFs < 2; condition index <15), and interaction terms RND × T stage and RND × prior radiotherapy were non-significant. The *E*-value for the main RND HR (2.61) was ≈4.6, indicating that an unmeasured confounder would need a risk-ratio association of ∼4.6 with both exposure and outcome, beyond measured covariates, to fully explain the findings.

DISCUSSION

SSI represents a common but clinically significant postoperative complication in patients undergoing surgical treatment for OSCC, impacting postoperative recovery, increasing length of stay in the hospital, and potentially affecting oncological outcomes. The overall SSI rate observed in this study (24.3%) falls within the range reported in the literature, which varies from 10% to 50% depending on patient selection, surgical complexity, and perioperative management.[15,16] Specifically, the impact of advanced age, smoking history, and alcohol consumption corroborate earlier reports linking these factors with compromised wound healing

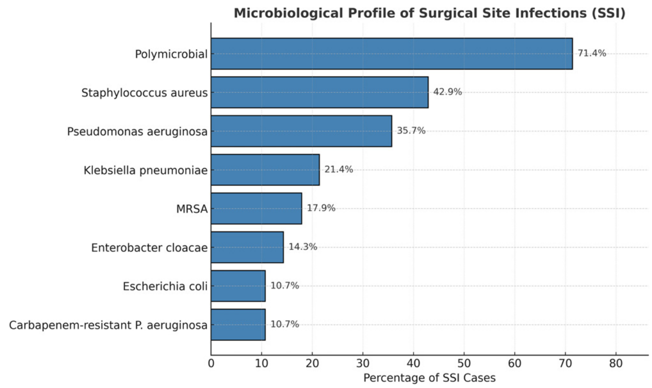

Fig. 2. Horizontal bar chart representing the microbiological profile of surgical site infections (SSI) in oral squamous cell carcinoma (OSCC) patients. The most common pathogens were *Staphylococcus aureus* (42.9%)—including methicillin-resistant strains (MRSA, 17.9%)—and *Pseudomonas aeruginosa* (35.7%), with 10.7% being carbapenem-resistant. Polymicrobial infections were observed in 71.4% of SSI cases. Percentages exceed 100% because 71.4% of SSI cultures were polymicrobial.

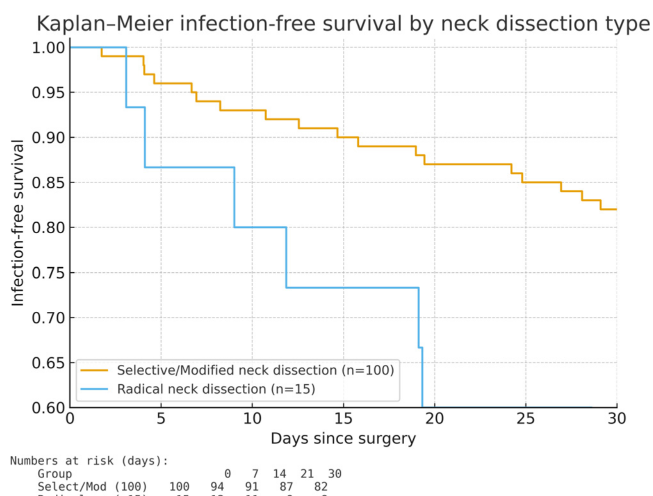

Fig. 3. Kaplan−Meier infection-free survival. Displayed on the time-to-event subset with complete daily data (n = 115). Kaplan−Meier curves depicting infection-free survival over the first 30 postoperative days, stratified by neck dissection type (radical, n = 15; selective/modified radical, n = 100). Surgical-site infection (SSI) was defined per CDC criteria. Groups differed significantly by log-rank test (P = .003). Early curve separation mirrors the cohort's median SSI onset at postoperative day 7.

Table II. Cox proportional hazards model for time to surgical site infection (30-day window)

Predictor	*HR*	*95% CI*	P *value*	*Notes*
Age (per 10 years)	1.18	1.02-1.37	.029	
Smoking (yes vs no)	2.12	1.11-4.04	.023	
Alcohol (yes vs no)	1.85	1.00-3.43	.049	
Neck dissection: radical vs selective/ modified	2.61	1.30-5.23	.006	
ERAS period (late-2022 onward)	0.66	0.37-1.19	.170	Exploratory

Model mutually adjusted for age, smoking, alcohol, and neck dissection type; ERAS term added as an exploratory covariate.
HR, hazard ratio; *CI*, confidence interval; *ERAS*, Enhanced Recovery After Surgery.

and immune response[2,3] and reinforce previous evidence that preoperative health status plays a crucial role in postoperative infection risk.[17]

In practical terms, identifying a neutrophil count cutoff presents an opportunity for more individualized perioperative surveillance. Patients exceeding this threshold, whether preoperatively or in the immediate postoperative period, may benefit from intensified monitoring of infection markers, consideration of a broader or extended antibiotic regimen (within an antibiotic stewardship framework), and additional immunonutritional support.

Patients undergoing RND experienced a significantly higher rate of SSI (40%) than did selective or modified radical dissections (P = .003). This suggests that increased surgical trauma, lymphatic disruption,

Table III. Effect sizes for key predictors of SSI

Predictor (exposed vs reference)	*Exposed events/total*	*Reference events/total*	*Odds ratio*	*95% CI*	*Fisher* P
Smoking: Yes vs no	22/28 (78.6%)	45/87 (51.7%)	3.544	1.369-9.185	.007
Alcohol: Yes vs no	19/28 (67.9%)	37/87 (42.5%)	2.973	1.210-7.307	.016
Flap type: Pedicled vs free	17/53 (32.1%)	11/61 (18.0%)	2.397	1.020-5.637	.043
Neck dissection: Radical vs selective/modified	6/15 (40.0%)	22/100 (22.0%)	2.419	0.818-7.156	.111

Counts for flap type exclude one primary closure (total 114). Unadjusted exact odds ratios on the time-to-event display subset show a significant association for pedicled vs free flaps; this effect was not retained after multivariable adjustment in the full cohort.

Table IV. Robustness of the association between radical neck dissection and 30-day SSI in Cox models

Model specification	*Adjustments/population*	*HR for RND (95% CI)*	P *value*
Main adjusted model	Age (per 10 years), smoking, alcohol, flap type, T stage, N category, prior radiotherapy	2.61 (1.32-5.15)	.006
T3-T4 only	Same covariates; restricted to T3-T4	2.67 (1.21-5.89)	.015
Excluding prior radiotherapy	Same covariates; prior RT excluded	2.83 (1.14-7.01)	.025
IPTW (propensity for RND)	Weighted for age, sex, subsite, T/N, prior RT, flap type, smoking, alcohol	2.95 (1.46-5.96)	.003

No significant interactions were detected for RND × T stage or RND × prior RT. Diagnostics showed VIFs < 2 and condition index <15.
HR, hazard ratio; *RND*, radical neck dissection; *RT*, radiotherapy; *IPTW*, inverse-probability-of-treatment weighting.

and prolonged operative time contribute to a greater likelihood of postoperative infections. As TNM stage and prior radiotherapy were controlled for in the multivariable model, the observed effect of radical dissection appears to be independent of these factors.

Beyond the main demographic and behavioral factors, we also recorded several common comorbidities (hypertension, diabetes, and cardiac conditions) and preoperative neutrophil counts as potential risk factors for SSI. However, certain parameters, particularly those related to nutritional status (e.g., body mass index, serum albumin levels), were not consistently available in the medical records. Despite these gaps, previous studies have indicated that malnutrition and hypoalbuminemia increase the risk of infectious complications, compromise flap vitality, and may affect long-term rehabilitation.[18]

The impact of flap type on infection rates remains controversial. Some studies suggest that free flaps provide superior vascularization and reduce the risk of infection.[2,19,20] Although free flap reconstruction showed a trend toward lower SSI rates compared to pedicled flaps (18.5% vs 31.5%, $P = .064$), this difference did not reach statistical significance and contrasts with findings by Goyal et al.,[15] who reported lower infection rates in free flap reconstructions compared to pedicled flaps. This lack of statistical significance may partly reflect limited power in subgroup analyses, and fewer patients received certain pedicled flaps, thereby reducing the sample size for these groups. Similarly, differences in surgical duration did not reach statistical significance, despite previous literature suggesting otherwise. One possible explanation is the relatively standardized approach and surgical expertise at our centre, which may reduce variability in operative times and outcomes.

Multidrug-resistant organisms, including MRSA and carbapenem-resistant *P. aeruginosa*, were detected in 17.9% and 10.7%, respectively. This raises concerns regarding antimicrobial stewardship and the need for targeted prophylactic strategies.[2]

A practical approach may involve reviewing institutional antibiograms to guide empirical coverage and considering nasal swab screening for MRSA in high-risk patients. Given the high prevalence of multidrug-resistant organisms observed in the analyzed cohort, personalized antibiotic strategies are paramount for optimizing perioperative infection control. Standard prophylactic regimens, often restricted to agents like cefazolin and metronidazole, may be insufficient in centers facing significant rates of MRSA or carbapenem-resistant Gram-negative bacteria. Patients with additional risk factors for multidrug-resistant organisms (e.g., prior hospitalization, recent antibiotic therapy, multiple comorbidities) may benefit from broadened or targeted prophylaxis guided by local surveillance data. However, the indiscriminate use of broad-spectrum antibiotics can contribute to escalating resistance; thus, careful patient selection and ongoing microbiological monitoring are essential to refine prophylaxis choices and ensure that coverage is escalated or de-escalated based on culture results and local resistance patterns.[21]

This study employed ROC analysis to determine optimal cutoff values for age and neutrophil count as predictors of SSI: neutrophil count ($\times 10^9$ L^{-1}) was defined as the last complete blood count obtained within 24 h before skin incision (median sampling time

8 h pre-op; IQR 5-14 h). The identified threshold of 65 years for age and 5.2×10^9/L for neutrophil count supports previous research indicating that systemic inflammation and immune competence significantly influence infection susceptibility.[3] However, the Cochran−Armitage test failed to demonstrate a significant trend between the cumulative number of risk factors and infection risk (P = .773), suggesting that specific individual factors may exert a stronger effect than an overall accumulation of risk variables.

Although the total sample (n = 575) was suitable for descriptive evaluation of SSI, certain subgroups contained fewer participants: for instance, only 13% of patients underwent RND, and a smaller proportion received less-common flap types. This limited the statistical power for subgroup comparisons, potentially explaining why some differences, despite being clinically relevant in magnitude (such as the disparity in SSI rates between pedicled and free flaps), did not achieve statistical significance.

Reporting HRs complements ORs by incorporating the timing of events. In our cohort, most SSI occurred within the first 10 days, and the Cox model confirmed the same independent risk factors identified by logistic regression. The exploratory ERAS term suggested a protective effect; a larger post-implementation sample and an interrupted time-series design will allow a more definitive estimate.

This study highlights the need for comprehensive perioperative risk assessment in oral cancer patients undergoing surgery. Modifiable risk factors such as smoking and alcohol consumption should be addressed preoperatively through structured cessation programs to optimize outcomes.[22] Furthermore, personalized perioperative antibiotic prophylaxis should be considered to mitigate the risk posed by multidrug-resistant infections.[23-25] Future research should explore the integration of ERAS protocols, as emerging evidence suggests that ERAS strategies can improve surgical outcomes while reducing infection-related complications.[26]

In practice, ERAS programs for oral cancer surgery can include preoperative carbohydrate loading, avoidance of prolonged fasting, meticulous fluid management, and early mobilization. Equally important is establishing a structured smoking and alcohol cessation program for at least 2 to 4 weeks prior to surgery, whenever feasible, to improve tissue perfusion and immune function. A dedicated multidisciplinary team (including dietitians, anesthesiologists, and smoking cessation specialists) can facilitate adherence to these protocols, ultimately lowering postoperative SSI risk.

Reporting HRs complements ORs by incorporating timing: most SSIs accrued within 10 days, and Cox modelling confirmed the same independent risk factors. The exploratory ERAS-period term suggested a protective effect; however, a robust evaluation should account for implementation learning curves and secular trends.

This study has several limitations. First, the retrospective design limits the ability to establish causal relationships and introduces potential selection bias; data may also be missing or incomplete, as clinical documentation can vary over time. Second, as a single-centre study, the findings may not be generalizable to broader populations or different healthcare setting. Third, although standardized criteria were used for data collection, variations in clinical documentation, particularly in the classification of infection severity, could affect result reliability of these results. Our study did not monitor for infections beyond 30 days. Although the CDC/NHSN recommends extending follow-up to 90 days when prosthetic material is left in situ, this scenario is uncommon in OSCC surgery. Published reports indicate that 85%-95% of SSI manifest during the first postoperative month, consistent with our own median onset of 7 days (IQR 5-10). Given that late donor- or recipient-site infections could have been missed; hence, prospective 90-day surveillance is warranted in future studies. Fourth, several important relevant variables, especially those pertaining to nutritional and immunological status (serum albumin, body mass index, and advanced inflammatory markers such as C-reactive protein or lymphocyte subsets), were not consistently recorded. The absence of these data may have led us to underestimate or miss associations between malnutrition, immune function, and SSI risk. Fifth, because RND is preferentially performed in patients with advanced disease and prior irradiation, confounding is a major concern. We therefore adjusted for AJCC stage, nodal status, and prior radiotherapy, verified absence of problematic collinearity, and confirmed robustness in stratified, exclusion, and propensity-weighted analyses, all of which yielded consistent hazard-ratio estimates for RND. While residual confounding is still possible, the E-value (~5.7) suggests that an unmeasured factor would need a strong joint association with RND and SSI to explain the findings entirely. Mechanistically, the association may reflect greater operative complexity and lymphatic disruption with RND, which could plausibly increase SSI susceptibility. Sixth, the small sample sizes within certain subgroups reduce the statistical power for subgroup comparisons and warrant caution in generalizing these findings. Finally, we cannot exclude that unrecorded protocol deviations or evolving resistance patterns influenced late-period infection rates.

In conclusion, this study confirmed that advanced age, smoking history, alcohol consumption, and RND are independent risk factors for SSI in patients undergoing surgical treatment for OSCC. The profile of infections underscores the need for vigilant antimicrobial management and individualized perioperative prophylaxis as the microbiological and resistance patterns are center-specific and influenced by local antibiotic stewardship practices and referral case-mix. As such, external applicability requires consideration of local antibiograms and regional epidemiology. While ROC analysis supports the predictive value of specific patient factors, the lack of a significant cumulative risk trend suggests that targeted preventive strategies should focus on individual high-risk characteristics rather than a generalized risk-scoring system. By optimizing perioperative management and implementing personalized interventions, it could be possible to improve postoperative outcomes and reduce the burden of SSI in this patient population.

CONSENT TO PARTICIPATE

Informed consent was obtained from all individual participants included in the study.

INFORMED CONSENT

Patients signed informed consent regarding publishing their data and photographs.

DECLARATIONS OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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DATA AVAILABILITY STATEMENT

The data generated and analyzed during this study are not publicly available due to institutional and privacy policies, but are available from the corresponding author upon reasonable request.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Giulio Cirignaco: Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Pamela Rosettani:** Supervision, Formal analysis, Data curation. **Lisa Catarzi:** Writing – original draft, Investigation, Data curation. **Mariagrazia Paglianiti:** Methodology, Investigation, Data curation. **Enrico Betti:** Validation, Supervision. **Umberto Committeri:** Writing – review & editing, Supervision, Software, Data curation. **Luigi Angelo Vaira:** Validation, Supervision, Methodology. **Andrea Santarelli:** Validation, Supervision. **Giuseppe Consorti:** Writing – review & editing, Validation, Supervision, Formal analysis, Data curation, Conceptualization.

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