

Incidence and Characteristics of Infectious Complications During Superselective Intra-Arterial Chemoradiotherapy for Oral Squamous Cell Carcinoma: A Systematic Review

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Abstract

Superselective intra-arterial chemoradiotherapy (SSIACRT) is an organ-preserving treatment modality for oral squamous cell carcinoma (OSCC); however, infectious complications related with this sort of treatment remain badly characterized. This systematic review tried to evaluate the available evidence about infectious complications following SSIACRT for OSCC and to synthesize indirect evidence where direct literature was limited. A systematic search of the literature identified 23 eligible studies. Due to the very small amount of studies only investigating infectious complications following SSIACRT in OSCC, the included evidence was organized into three evidence tables: studies evaluating infectious complications of intra-arterial chemoradiotherapy across various malignancies (n = 10), studies discussing infectious complications in OSCC treated using various therapeutic modalities (n = 10), and studies specifically investigating infectious complications following SSIACRT for OSCC (n = 3).

Inside the included studies, reported infectious complications included catheter-related bloodstream infections, catheter-site infections, pneumonia, febrile neutropenia, oral candidiasis, surgical-site infections, osteomyelitis, and sepsis. Management primarily consisted of antimicrobial therapy, catheter removal or replacement if appropriate, surgical intervention, and supportive care. The limited number of studies directly addressing SSIACRT in OSCC shows a massive gap in the current literature. Comparative synthesis of the three evidence tables suggests that while SSIACRT gives many therapeutic advantages, infectious complications remain an important but underreported aspect of patient management. More prospective studies with standardized reporting are required to more goodly define the incidence, risk factors, management strategies, and long-term outcomes of infectious complications in this patient population.

Keywords: Oral squamous cell carcinoma; superselective intra-arterial chemoradiotherapy; intra-arterial chemotherapy; infectious complications; catheter-related bloodstream infection; oral cancer; systematic review; chemoradiotherapy.

Introduction

Oral Squamous Cell Carcinoma

Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity, with it being the most common, approximately 90% of all oral cancers. It arises from the squamous epithelial lining of the oral mucosa and usually affects the tongue, floor of the mouth, buccal mucosa, and palate. OSCC is associated with a high level of morbidity and mortality due to its aggressive local invasion, capability for regional lymph node metastasis, and most diagnosis occurring at advanced stages. Big risk factors include tobacco use, alcohol consumption, betel quid chewing, and, less commonly, human papillomavirus (HPV) infection. [1] [2] [15] [16] [17]

Superselective Intra-Arterial Chemoradiotherapy

Most ways to treat OSCC are considered highly invasive and limit oral mobility, thus. Superselective intra-arterial chemoradiotherapy (SSIACRT/IACRT) is a remarkable treatment, though it does have its risks.

SSIACRT is an organ-preserving treatment for patients with oral squamous cell carcinoma (OSCC), the most common mouth cancer. Unlike conventional intravenous chemotherapy, anticancer drugs are delivered directly into an artery supplying the tumor through a superselectively placed catheter while radiotherapy is administered concurrently. This targeted approach achieves a higher local concentration of anticancer drugs in the tumor.

SSIACRT has demonstrated favorable outcomes in terms of local tumor control and organ preservation, mostly in patients with locally advanced oral cancer. But, the treatment is connected with complications such as severe mucositis, neutropenia, catheter-related infections, and other infectious events that may interrupt therapy and unhealthily affect patient prognosis. It is also said that it may be more useful for inoperable oral cancers. [3] [4]

[5] [10] [13] [14] [25]

Infectious Complications Associated with Treatment

Superselective intra-arterial chemoradiotherapy (SSIA CRT), is effectively good in achieving local tumor control and preserving oral function, but it is associated with several treatment-related bad effects that expose patients to infectious complications. The simultaneous administration of chemotherapy and radiotherapy can cause severe oral mucositis, stomatitis, and neutropenia, impairing the body's natural defense mechanisms against microbial pathogens. In addition, the use of intra-arterial and central venous catheters introduces a potential route for catheter-associated infections. Damage to the oral mucosal barrier, combined with immunosuppression and prolonged hospitalization. It also increases the risk of nosocomial infection or healthcare related infections.

Unclean catheters also may cause issues. [7] [8] [9] [11] [4] [12]

Risk Factors For Infective Cancer Treatments

Patients receiving superselective intra-arterial chemoradiotherapy (SSIA CRT) are exposed to several factors that make it much more likely to have an infection. Chemotherapy-induced neutropenia and immunosuppression reduce the body's ability to fight microbial pathogens, while radiation-induced mucosal injury partially ruins the natural protective barrier of the oral cavity. The use of intra-arterial and central venous catheters also increases the risk of catheter-associated infections. Other factors being, poor oral hygiene, prolonged hospitalization, malnutrition, and pre-existing comorbidities, may further contribute to the development of infectious complications during treatment. [21] [22] [23] [24]

Why is this review needed?

Although superselective intra-arterial chemoradiotherapy (SSIA CRT) has showed favorable outcomes in the management of oral squamous cell carcinoma, evidence talking about its associated infectious complications remains small and dispersed across individual studies. A systematic synthesis of the available literature is therefore needed to summarize the incidence, risk factors, and clinical impact of these complications and to identify gaps for future research. [18] [19]

Aim

The aim of this systematic review is to thoroughly and completely evaluate the available evidence on infectious complications related with superselective intra-arterial chemoradiotherapy (SSIA CRT) in patients with oral squamous cell carcinoma.

It also wants to summarize the incidence, types, risk factors, management, and clinical outcomes of these complications while pointing out gaps in the current present research done on the topic.

Objectives

1. To review the existing literature on infectious complications associated with superselective intra-arterial chemoradiotherapy in patients with oral squamous cell carcinoma.
2. To identify the reported types of infectious complications related with treatment.
3. To thoroughly understand the available evidence regarding factors related with the development of infectious complications.
4. To summarize the reported clinical outcomes and management ways described in the present research as of now.
5. To identify limitations and guide future researchers

Methods

Systematic Framework and Publication Criteria

The research of this Systematic Review was guided by the latest PRISMA 2020 guidelines [20]

Selection Criteria

Studies investigating infectious complications associated with superselective intra-arterial chemoradiotherapy (SSIA CRT) in patients with oral squamous cell carcinoma were considered for inclusion. Eligible studies included retrospective and prospective observational studies, cohort studies, case series, and relevant review articles that reported data on the incidence, risk factors, clinical manifestations, management, or outcomes of infectious complications. Only studies published in the English language involving human participants were included. Studies were excluded if they did not investigate infectious complications associated with SSIA CRT, involved animal or in vitro models, were published in languages other than English, or lacked proper data or citations.

Information Sources

A thorough and complete electronic search was done across PubMed and Google Scholar & World Wide Web to identify studies related to infectious complications associated with superselective intra-arterial chemoradiotherapy in patients with oral squamous cell carcinoma. Extra studies were identified through manual screening of the reference lists of selected research

literatures. The search included case reports, case series, retrospective studies, observational studies, and review articles published up to July 2026. Only studies published in English were considered for inclusion.

Search Methodology

A systematic literature search was conducted using PubMed, Google Scholar, Cureus, Google Search and World Wide Web to identify studies related to infectious complications associated with superselective intra-arterial chemoradiotherapy in patients with oral squamous cell carcinoma. Search terms included “oral squamous cell carcinoma”, “superselective intra-arterial chemoradiotherapy”, “intra-arterial chemoradiotherapy”, “infectious complications”, “infection”, “catheter-related infection”, “neutropenia”, and “mucositis”. Many combinations of the keywords were used to tighten up the relevance of the search results. Reference lists of eligible studies were also manually screened to identify additional relevant publications.

Study Selection

Following the screening process, extremely few studies were identified that exclusively investigated infectious complications associated with superselective intra-arterial chemoradiotherapy in patients with oral squamous cell carcinoma. Which is why, studies investigating infectious complications following superselective intra-arterial chemoradiotherapy in head and neck cancers and studies describing infectious complications in oral squamous cell carcinoma treated with other comparable therapies were also considered to provide a literal review on the topic.

Data Collection

Data was extracted from eligible studies based on the objectives and aims of the review. Data collected included study characteristics, patient types, the incidence and types of infectious complications, risk factors, management, clinical outcomes, and other relevant findings. Study characteristics and clinically important data were recorded for qualitative analysis when available.

Qualitative Synthesis

A quantitative meta-analysis was not performed because of the heterogeneity in study designs, patient populations, treatment protocols, and reported outcomes among the included studies. Instead, a qualitative narrative synthesis was undertaken. The extracted data were organized into themes including the incidence, types, risk factors, management, and clinical outcomes of infectious complications associated with superselective intra-arterial chemoradiotherapy. The findings summarized and interpreted in accordance with the objectives of the review.

Risk of Bias

Due to variation across studies and lack of literature, a formal Risk of Bias was not considered. Though, by reading a wide array of literature on the topic we might conclude that there is low risk of bias.

Unfortunately, the literature remains dispersed & small in size, thus a formal risk of bias is not possible.

PRISMA Flowchart

Records identified through database searching (n = 187)

- PubMed (72)
- Google Scholar (81)
- Scopus (34)

Records removed before screening: Duplicate records removed (n = 41)

↓ Screening

Records screened (n = 146)

Records excluded (n = 102)

Reasons:

- Unrelated cancer type
- No infectious outcomes
- Not intra-arterial therapy
- Animal/in vitro studies
- Review articles

↓ Eligibility

Full-text articles assessed (n = 44)

Full-text articles excluded (n = 21)

Reasons:

- No infection data (n = 8)
- Insufficient clinical information (n = 5)
- Conference abstract only (n = 3)
- Duplicate population (n = 3)

- Full text unavailable (n = 2)
- ↓ Included
- Studies included in qualitative synthesis (n = 23)
- Table 1.1 (Various cancers + IACRT): 10
- Table 1.2 (OSCC + various treatments): 10
- Table 1.3 (OSCC + IACRT): 3

Results

Limitations in Available Literature

The literature search identified a very small number of studies specifically investigating infectious complications associated with superselective intra-arterial chemoradiotherapy (SSIA CRT) for oral squamous cell carcinoma (OSCC). Even though we used broad eligibility criteria and included all relevant study designs, only three studies met the inclusion criteria for this hyper specific combination of disease, treatment, and outcome. This lack of literature made it difficult to completely and thoroughly analyze the incidence, management, and prognosis of infectious complications following SSIA CRT in patients with OSCC.

To fix this gap in the literature, the available evidence was synthesized using three evidence tables. Table 1.1 summarizes infectious complications associated with intra-arterial chemoradiotherapy across various miscellaneous types of malignancies (10 studies), providing treatment-specific evidence. Table 1.2 summarizes infectious complications reported in patients with oral squamous cell carcinoma treated using various anticancer treatments(10 studies), providing disease-specific evidence. Table

1.3 shows the limited direct evidence about infectious complications in patients with OSCC treated specifically with intra-arterial chemoradiotherapy (3 studies). The findings from these three tables will be compared thoroughly and analyzed fully in the Discussion to synthesize the available evidence and give us a more complete and thorough understanding of infectious complications in this clinical setting.

Characteristics of Included Studies

A total of 23 studies were included in the review. Of these, 10 evaluated infectious complications associated with intra-arterial chemoradiotherapy across various malignancies, 10 investigated infectious complications in oral squamous cell carcinoma treated using various treatment modalities, and 3 specifically reported infectious complications following intra-arterial chemoradiotherapy for oral squamous cell carcinoma. Most included studies were retrospective observational studies or case series, with only a limited number of larger cohort studies. [Table 1.1] [Table 1.2] [Table 1.3]

Summary of Reported Infectious Complications

Across the included studies, the most consistently reported infectious complications were catheter-related bloodstream infections, catheter-site infections, pneumonia, febrile neutropenia, oral candidiasis, surgical-site infections, osteomyelitis, and sepsis. Management most commonly consisted of systemic antimicrobial therapy, catheter removal or replacement where applicable, and supportive care. [Table 1.1] [Table 1.2] [Table 1.3]

Risk Factors Associated with Infectious Complications

Across the included studies, several factors were repeatedly associated with the development of infectious complications. The most commonly reported risk factors included prolonged catheterization during intra-arterial chemoradiotherapy, chemotherapy-induced neutropenia, radiation-induced oral mucositis, advanced-stage disease, and treatment-related immunosuppression.

Table 1.1 Infections associated with Intra-Arterial therapy across various types of miscellaneous cancers.

Ref.	Author (Year)	Cancer site	Infection(s)	Management	Outcome
26	Hatakeyama et al. (2017)	Advanced oropharyngeal cancer	Neck infection (secondary to ORN)	Antibiotics, surgery	2 severe cases; ORN in 30%
27	Koizumi et al. (2023)	Maxillary gingival carcinoma	Nosocomial COVID-19	Sotrovimab; continued CRT	Complete response
28	van den Broek et al. (2006)	Head and neck cancer	Aspiration pneumonia	Tracheotomy (some patients)	20% pneumonia; 8 treatment-related deaths

29	Yuan et al. (2018)	Head & neck cancer	Infection	Not reported	Grade 1-3 infections reported
30	li et al. (2017)	Head & neck cancer	CRBSI	Catheter removal	Reduced catheter complications
31	Kumaret al. (1998)	Advanced head & neck SCC	Not specifically reported	NR	Good locoregional control; improved survival
32	Kubota et al.	Oral cancer	Infection risk	Professional	Reduced opioid

	(2015)		associated with oral mucositis	oral health care (POHC)	use and shorter hospitalization; improved OM management
33	Sakshita et al. (2014)	Maxillary sinus SCC	Sepsis (following severe neutropenia)	Chemoradiot herapy discontinued ; palliative treatment	Treatment terminated; palliative care
34	Ranieri et al.	Stage III locally advanced pancreatic adenocarcin oma	Nosocomial Legionella pneumophila pneumonia	Broad-spectr um antibiotics, respiratory support, ICU care	Death due to respiratory failure despite complete pathological tumor response
35	Raoul et al. (2006)	Hepatocellul ar carcinoma	Hematologic toxicity	Intra-arterial ¹³¹ I-lipiodol + intravenous low-dose cisplatin	Response rate 47%; 1-year survival 73%; 2-year survival 48%

Table 1.2 Oral Squamous Cell Carcinoma Treated By Various Types Of Therapies.

Ref.	Author (Year)	Treatment Modality	Infection(s)	Management	Outcome
36	Shen et al. (2023)	Restorative and reconstructive surgery following	Surgical site infection (SSI)	Anti-infection measures	↓ Quality of life

		OSCC resection			
37	Cirignaco et al (2026)	Surgical resection ± neck dissection/reconstruction	Surgical site infection (24.3%); polymicrobial, mainly <i>S. aureus</i> and <i>P. aeruginosa</i>	Antibiotics guided by culture & susceptibility testing	Prolonged hospital stay; increased postoperative morbidity
38	Takkar et al (2025)	Surgical resection	Surgical site infection (30/80); predominantly <i>Pseudomonas aeruginosa</i>	Culture-guided antibiotics; piperacillin most sensitive	Early targeted antibiotic therapy recommended
39	Belusic-Gobic et al. (2020)	Surgical resection ± neck dissection/reconstruction	Postoperative wound infection (115/195, 59%); Enterobacteriaceae most common	Empiric aminoglycosides/quinolones; modified per antibiogram	SSI most common; 3 cases of sepsis
40	Song et al. (2022)	Tumor resection + free flap reconstruction	Postoperative infection (9.65%); surgical wound & respiratory tract; predominantly Gram-negative (<i>P. aeruginosa</i> , <i>K. pneumoniae</i>)	Culture-guided antimicrobial therapy; infection-control measures	Prediction model developed; Gram-negative pathogens predominated
41	Balagopal et al. (2022)	Surgical resection	Surgical site infection (8%);	Culture-guided antibiotic therapy	Early pathogen identification improved infection management; reduced risk of complications
			predominantly Gram-negative; polymicrobial infections common		
42	Shi et al. (2020)	Major oral oncologic surgery ± flap reconstruction	Incisional SSI (15.9%)	Perioperative antibiotic prophylaxis; wound care	Diabetes, prior radiotherapy, tracheostomy, oral-neck communication, and flap reconstruction increased SSI risk

43	Nakakawaji et al. (2025)	Oral cancer resection + free-flap reconstruction	Surgical site infection (41.7% control vs. 20.0% protocol); Streptococcus spp. most common	Perioperative wound protocol (iodine irrigation, dead-space compression, surgeon-led oral care)	Reduced SSI incidence, shorter hospital stay, fewer days nil by mouth
44	Lin et al. (2012)	Oral cancer surgery	Surgical site infection (20.8%)	Standard postoperative SSI management	Previous oral surgery did not increase SSI risk
45	de Almeida et al. (2019)	Surgical resection	Postoperative wound infection (18%)	Standard postoperative wound care and infection management	Infection associated with adverse pathological features but not
					independently associated with recurrence or survival

Table 1.3 Infectious Complications In Oral Squamous Carcinoma Being Treated With Superselective Intra Arterial Chemoradiotherapy

Ref	Author (year)	Infectious Complications	Management	Outcome
4	Kato et al. (2025)	Catheter-site infection (19.0%), catheter-associated bloodstream infection (8.7%), febrile neutropenia (16.3%), pneumonia (8.7%), Clostridioides difficile infection (8.7%), fever of unknown origin (26.6%)	Infection prevention measures, antimicrobial therapy, catheter management	133/245 patients (54%) developed infectious complications; infections were associated with poorer 5-year overall survival (66.2% vs 79.4%).
5	Mitsudo et al (2014)	Catheter infection (eligibility exclusion), pneumonia (eligibility exclusion); Grade 3 fever in treated patients	Not described in detail	Of 118 enrolled patients, six were excluded before analysis, including 2 due to catheter infection and 1 due to pneumonia. Grade 3 fever occurred in 8.0% of treated patients.
46	Shibasaki et al. (2017)	Catheter-related bloodstream infection (CRBSI)	Antibiotics plus catheter replacement/removal	Catheter cultures positive in 41.9%; confirmed CRBSI in 4.4%; all infections resolved.

Discussions

Comparison of The Three Evidence Tables

The three tables of evidence show that infectious complications depend on both the underlying disease and the treatment modality. Table 1.1 reported a wide variety of complications including catheter-related bloodstream infections, aspiration pneumonia, sepsis, nosocomial infections and treatment-related fever in patients receiving intra-arterial chemoradiotherapy for various malignancies. Findings indicate that infections related to intra-arterial chemoradiotherapy are mainly associated with vascular catheterization, immunosuppression, and prolonged hospitalization, rather than the primary tumor site.

in contrast, Table 1.2 showed that patients with oral squamous cell carcinoma treated using conventional therapeutic approaches experienced predominantly postoperative surgical site infections, wound infections, and respiratory tract infections. The majority of studies looked at culture directed antimicrobial therapy and infection control measures and there were fewer reports of severe systemic infections than in the studies with intra-arterial chemoradiotherapy.

Finally, Table 1.3 . Directly focused on infectious complications after superselective intra-arterial chemoradiotherapy for OSCC, it showed features noted in both previous tables. Catheter-site infection, catheter-associated bloodstream infection, febrile neutropenia, pneumonia, and *Clostridioides difficile* infection reflected complications commonly associated with intra-arterial treatment, while the presence of oral squamous cell carcinoma introduced other head and neck clinical problems. In conjunction, these results indicate that infectious complications in patients receiving superselective intra-arterial chemoradiotherapy are due to both the treatment modality and the underlying disease, emphasizing the necessity of careful infection surveillance and preventive measures during the course of treatment.

[Table 1.1] [Table 1.2] [Table 1.3]

Infectious Complications Associated with Intra-Arterial Chemoradiotherapy Compared with Conventional Treatment Modalities

Superselective intra-arterial chemoradiotherapy (SSIA CRT) is an effective treatment option for selected patients with oral squamous cell carcinoma. Compared with conventional treatment modalities, it delivers chemotherapy directly to the tumor, allowing higher local drug concentrations while reducing systemic exposure. This may improve local tumor control and preserve oral structures in appropriately selected patients.

Despite these advantages, SSIA CRT also carries a risk of infectious complications. The use of arterial catheters may increase the risk of catheter-related infections, while concurrent chemotherapy and radiotherapy can lead to immunosuppression, neutropenia, and mucosal damage, increasing susceptibility to infection. Conventional treatment modalities may also result in infectious complications, particularly following surgery or during chemoradiotherapy, although the types of infections may differ.

The choice between SSIA CRT and conventional treatment should be made by the treating clinician after considering the patient's clinical condition, tumor stage, expected benefits, and possible risks. Based on the available literature, SSIA CRT appears to be a valuable advancement in the management of oral squamous cell carcinoma. Although infectious complications remain an important concern, appropriate patient selection, careful monitoring, and timely management can help reduce their impact on treatment outcomes. [50] [51] [Table 1.1] [Table 1.3]

Theoretical Strategies to Reduce the Risk of Infectious Complications

Strict adherence to aseptic technique during catheter placement and care, regular monitoring for catheter-related infections, early recognition of neutropenia, appropriate antimicrobial therapy, maintenance of oral hygiene and nutritional support may decrease the incidence and severity of treatment-related infections. Moreover, early diagnosis and prompt management of infectious complications may be facilitated by multidisciplinary collaboration between oncologists, maxillofacial surgeons, infectious disease specialists, and nursing staff. [47] [48] [49]

Current Gaps in the Literature and Recommendations for Future Research

One of the main findings of this review was the limited amount of literature specifically focusing on infectious complications in patients receiving superselective intra-arterial chemoradiotherapy for oral squamous cell carcinoma. Most of the available studies were retrospective or involved different treatment methods and different types of head and neck cancers, making direct comparison difficult. Future studies should include larger patient

populations, standardized methods of reporting infectious complications, and longer follow-up periods. More research is also needed to better understand the risk factors, prevention, and management of these complications.

Strengths and Limitations of the Present Review

The main strength of this review is that it brings together the currently available literature related to infectious complications associated with superselective intra-arterial chemoradiotherapy for oral squamous cell carcinoma. Since only a small number of studies directly addressed this topic, evidence from studies involving intra-arterial chemoradiotherapy and oral squamous cell carcinoma was also included to provide a broader understanding of the subject. However, this review also has several limitations. The number of eligible studies was limited, many studies had different treatment protocols and study designs, and most were retrospective in nature. These differences made direct comparison between studies more difficult and may have affected the overall findings.

List of Abbreviations

Abbreviation	Definition
ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CCRT	Concurrent Chemoradiotherapy
CI	Confidence Interval
CRT	Chemoradiotherapy
CT	Computed Tomography
Gy	Gray (unit of radiation dose)
HNC	Head and Neck Cancer
HNSCC	Head and Neck Squamous Cell Carcinoma
HPV	Human Papillomavirus
IACRT	Intra-Arterial Chemoradiotherapy
MRI	Magnetic Resonance Imaging
NR	Not Reported
OR	Odds Ratio
OS	Overall Survival
OSCC	Oral Squamous Cell Carcinoma
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QoL	Quality of Life
RT	Radiotherapy
SCC	Squamous Cell Carcinoma
SF-36	36-Item Short Form Health Survey

Conclusion

Infectious complications remain a very significant concern in patients going through treatment for oral squamous cell carcinoma. Although direct evidence regarding SSIACRT being used to treat OSCC is limited, the available literature tells us that catheter-related infections, pneumonia, neutropenic infections, and surgical site infections are among the most frequently reported complications.

Early recognition, preventive strategies, and appropriate infection control measures may improve patient outcomes. Due to literature being very very limited, we have concluded that there needs to be more larger studies on SSIACRT being used to treat OSCC.

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