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Review Article

Postoperative Microbial Infections in Esophageal Cancer: Epidemiology, Diagnosis, and Management

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Abstract

This review synthesizes current evidence on postoperative microbial infections after esophageal cancer surgery, covering epidemiology, pathogen spectrum (bacteria, fungi, viruses), risk factors, clinical manifestations, diagnostic approaches, and evidence-based management emphasizing antimicrobial prophylaxis and microbiome-targeted prevention to reduce morbidity and improve long-term survival.

Keywords: Postoperative infection; Esophageal cancer; Microbiome; Antimicrobial prophylaxis; Fungal infection; Immunonutrition

Abbreviations

PI: Postoperative Infection; SSI: Surgical Site Infection; UAT: Upper Alimentary Tract; ABPC/SBT: Ampicillin/Sulbactam; CEZ: Cefazolin; NLR: Neutrophil-To-Lymphocyte Ratio; SIRS: Systemic Inflammatory Response Syndrome

Epidemiology and Risk Factors of Postoperative Microbial Infections in Esophageal Cancer

Incidence and Distribution Patterns

Postoperative microbial infections (PIs) represent a significant complication following esophageal cancer surgery, with a notable impact on patient morbidity and mortality. The incidence of PIs after esophagectomy varies across studies but generally remains high. For instance, Lin et al. (2023) reported an overall PI incidence of 28.3% in a cohort of 902 esophageal tumor patients, highlighting the substantial burden of infections in this population [1]. Similarly, Dan et al. (2025) found a comparable incidence rate of 29.6% among 747 patients aged 60 years and older undergoing radical esophagectomy [2]. These findings underscore that nearly one-third of patients undergoing esophageal cancer surgery develop postoperative infections, emphasizing the clinical importance of this complication.

The distribution of infection types post-esophagectomy is diverse, with pulmonary infections, surgical site infections (SSIs), and anastomotic leaks being among the most frequently reported. Wan et al. (2021) analyzed data from the International Surgical Outcomes Study (ISOS) involving over 44,000 patients undergoing elective surgery, including cancer surgeries, and found that superficial SSIs accounted for 32.7% of infections, pneumonia for 17.6%, and urinary tract infections for 16.9% [3]. Specifically, in esophageal cancer surgery, pneumonia and anastomotic leakage are prominent infectious complications. Kataoka et al. (2016) reported pneumonia incidence of 14% and anastomotic leakage of 14% among 152 patients undergoing transthoracic esophagectomy, with pneumonia being significantly associated with worse overall survival [4]. Moreover, Yamashita et al. (2016) identified severe pulmonary infection as an independent prognostic factor for poor cancer-specific survival in esophageal squamous cell carcinoma patients receiving preoperative chemotherapy followed by surgery [5].

The microbial spectrum involved in postoperative infections after esophageal cancer surgery is complex. Sharpe et al. (1992) demonstrated that pathogenic organisms present in the upper alimentary tract at the time of surgery correlated with those causing postoperative infections in 66% of cases, indicating the endogenous flora as a significant source of infection [6]. Additionally, Heuker et al. (2020) found that yeast infections occurred in 7.3% of post-esophagectomy patients, with diabetes mellitus identified as a significant risk factor for fungal infections, which were associated with increased morbidity and mortality [7]. The presence of polymicrobial infections, including gram-positive and gram-negative bacteria, as well as fungi, complicates the management of postoperative infections in this setting. Emerging evidence also suggests that alterations in the esophageal and intestinal microbiota may influence postoperative infection risk and oncologic outcomes. Maruyama et al. (2022)

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reported that the presence of Proteus mirabilis in preoperative fecal microbiota was associated with higher systemic inflammation and increased postoperative pneumonia incidence, whereas Bacillus species correlated with favorable prognosis and better response to preoperative treatment [8]. Furthermore, the esophageal microbiome's role in carcinogenesis and treatment response is increasingly recognized, with dysbiosis potentially contributing to infection susceptibility post-surgery [9,10].

In summary, postoperative microbial infections after esophageal cancer surgery occur in approximately 28-30% of patients, with pneumonia, surgical site infections, and anastomotic leaks being the most common. The infections are often polymicrobial, involving bacteria from the patient's own upper gastrointestinal tract flora and occasionally fungi. These infections not only increase morbidity but also adversely affect long-term survival outcomes.

Patient- and Procedure-Related Risk Factors

Multiple patient- and procedure-related factors contribute to the risk of postoperative microbial infections in esophageal cancer surgery. Smoking has been consistently identified as a significant modifiable risk factor. Both Lin et al. (2023) and Dan et al. (2025) found smoking to be independently associated with increased postoperative infection risk, emphasizing the need for smoking cessation interventions preoperatively [1,2]. Prolonged preoperative hospital stays also emerged as a risk factor, likely reflecting increased exposure to nosocomial pathogens and patient frailty [1].

Advanced age is another important risk factor. Dan et al. (2025) specifically studied patients aged 60 years and older and highlighted that elderly patients are at considerable risk for postoperative infections, particularly when combined with modifiable factors such as smoking and hyperglycemia [2]. Gallis (1988) reviewed infections in elderly cancer patients, noting that age-related immune senescence and comorbidities contribute to increased infection susceptibility [11].

Diabetes mellitus is associated with a higher incidence of postoperative infections, including fungal infections. Heuker et al. (2020) reported a significantly increased incidence of yeast infections in diabetic patients after esophagectomy, which correlated with worse clinical outcomes [7]. Hyperglycemia, both preoperative and postoperative, has been linked to infection risk, as elevated blood glucose impairs immune function and wound healing [2].

Nutritional status and systemic inflammation also influence infection risk. Maruyama et al. (2022) found that patients with unfavorable gut microbiota profiles had higher systemic inflammation scores and increased pneumonia incidence post-esophagectomy [8]. Similarly, Ruzzenente et al. (2022) identified elevated neutrophil-to-lymphocyte ratio as an independent preoperative risk factor for surgical infectious complications in hepatobiliary cancer surgery, which may be extrapolated to esophageal cancer given the shared inflammatory pathways [12].

Regarding procedural factors, longer operative time and increased blood loss have been associated with higher infection rates. Kataoka et al. (2016) demonstrated that longer operation duration and greater intraoperative blood loss correlated with increased severe postoperative complications, including infections[5]. The extent of lymphadenectomy also influences infection risk; three-field lymphadenectomy was linked to higher incidence of severe complications in the same study [5]. Morita et al. (2011) suggested that a two-stage operation might reduce critical postoperative complications in high-risk patients by limiting surgical stress and allowing recovery between stages [13].

Preoperative chemotherapy and chemoradiotherapy, while improving oncologic outcomes, may increase infection risk due to immunosuppression and tissue toxicity. Yamashita et al. (2016) found that severe postoperative infectious complications were associated with worse prognosis in patients undergoing preoperative chemotherapy followed by surgery [5]. Stiles et al. (2009) reported that persistent nodal disease after neoadjuvant therapy predicted survival, but postoperative infections could further compromise outcomes[14].

Other patient-related factors include comorbidities such as chronic pulmonary disease, liver dysfunction, and poor performance status, which have been implicated in increased postoperative infection risk [13], [15]. Preoperative anemia and higher American Society of Anesthesiologists (ASA) grade have also been associated with increased infection rates in surgical oncology patients [3].

Infectious complications are often polymicrobial, involving both gram-positive and gram-negative bacteria. Vos et al. (2015) reported that postoperative infections following tumor resections frequently involved polymicrobial flora, with gram-negative bacteria more common in soft tissue tumors and non-prosthesis-associated infections, and staphylococci predominant in bone tumors [16]. This polymicrobial nature complicates empirical antibiotic selection and necessitates careful microbiological surveillance [12].

In conclusion, patient-related factors such as smoking, advanced age, diabetes mellitus, nutritional and inflammatory status, and comorbidities, along with procedure-related factors including operative time, extent of surgery, and neoadjuvant therapies, significantly influence the risk of postoperative microbial infections in esophageal cancer surgery. Recognition and modification of these factors where possible are essential to reduce infection incidence and improve patient outcomes.

Spectrum of Common Microbial Pathogens After Esophagectomy

Bacterial Infections

Postoperative bacterial infections represent a significant complication following esophagectomy for esophageal cancer, contributing to increased morbidity and mortality.

The bacterial spectrum involved in these infections is diverse, often reflecting the endogenous flora of the upper gastrointestinal tract and the perioperative environment.

A large retrospective study involving 747 patients undergoing radical esophagectomy revealed an overall postoperative infection incidence of 29.6%, with bacterial infections constituting a major proportion of these cases. Independent risk factors identified included smoking, prolonged surgical duration, and elevated postoperative blood glucose levels, particularly in patients aged 60 years and older

[2]. This highlights the importance of patient-related and procedural factors in the development of bacterial infections post-esophagectomy.

The upper alimentary tract (UAT) harbors a complex microbiota, and its disruption during surgery predisposes to infection. A prospective study of 138 patients undergoing major esophageal surgery demonstrated that 61% had pathogenic organisms cultured directly from stomach or esophageal contents at the time of operation. Postoperative infections, predominantly pleuropulmonary and wound infections, were closely correlated (66% of cases) with pathogens isolated from UAT contents, underscoring the relevance of intraoperative microbial sampling to guide antibiotic prophylaxis [6]. Common pathogens isolated include gram-positive cocci such as Staphylococcus species and gram-negative bacilli, reflecting the polymicrobial nature of these infections.

Further characterization of the esophageal microbiota in esophageal cancer patients before and after esophagectomy showed a significant reduction in microbial diversity postoperatively, with an increased abundance of potentially pathogenic bacteria such as Fusobacteria [17]. This dysbiosis may contribute to susceptibility to bacterial infections after surgery.

In terms of clinical outcomes, fecal microbiota analysis in 783 patients undergoing oncologic esophagectomy identified specific bacterial species associated with postoperative complications. The presence of Proteus mirabilis was linked to higher systemic inflammation and increased incidence of postoperative pneumonia, while Bacillus species correlated with better prognosis and lower inflammation scores[8]. These findings suggest that gut microbial composition may influence postoperative infection risk and patient outcomes.

Regarding antimicrobial prophylaxis, a quasi-experimental study comparing cefazolin (CEZ) and ampicillin/sulbactam (ABPC/SBT) in 356 patients undergoing thoracoscopic esophagectomy found that ABPC/SBT significantly reduced the incidence of early-onset postoperative pneumonia (3.8% vs. 13.6%, P = 0.006) and shortened hospital stay without increasing Clostridioides difficile infections or multidrug-resistant organisms [18]. This evidence supports the use of broad-spectrum antibiotics covering both gram-positive and gram-negative bacteria to prevent postoperative bacterial infections effectively.

Polymicrobial infections are common in surgical oncology patients, with gram-negative bacteria frequently isolated in soft tissue tumor resections and staphylococci predominating in bone tumor surgeries. This pattern may be extrapolated to esophageal cancer surgery, where a combination of broad-spectrum and antistaphylococcal antibiotics is recommended for empirical therapy [16].

The emergence of multidrug-resistant organisms further complicates management, necessitating careful microbiological surveillance and tailored antibiotic regimens [12].

The use of synbiotics (a combination of probiotics and prebiotics) perioperatively has been investigated as a strategy to modulate intestinal microflora and reduce postoperative infections. A randomized controlled trial involving 70 esophageal cancer patients undergoing esophagectomy demonstrated that synbiotic administration increased beneficial bacteria counts, decreased harmful bacteria, and elevated organic acid concentrations in the gut. Although the reduction in infection rate did not reach statistical significance (10% vs. 29.4%, P = 0.0676), the duration of systemic inflammatory response syndrome (SIRS) was significantly shorter, and abdominal symptoms were less frequent in the synbiotic group [19]. These findings suggest a potential role for synbiotics in improving postoperative outcomes by restoring microbial balance and enhancing barrier function.

In summary, bacterial infections after esophagectomy are predominantly polymicrobial, involving both gram-positive and gram-negative organisms derived from the upper gastrointestinal tract flora. Risk factors include patient comorbidities, surgical factors, and microbial dysbiosis.

Empirical antibiotic prophylaxis with broad-spectrum agents such as ampicillin/sulbactam is effective in reducing early postoperative pneumonia. Adjunctive strategies like synbiotic administration may further modulate the gut microbiota to decrease infection risk and inflammatory responses.

Fungal Infections

Fungal infections, particularly those caused by yeast species, represent a notable subset of postoperative infections following esophagectomy, although their incidence and clinical impact have been less extensively characterized compared to bacterial infections.

A retrospective analysis of 565 patients who underwent esophagectomy reported a 7.3% incidence of yeast infections postoperatively. Patients with diabetes mellitus were at significantly higher risk for developing these infections. Those affected exhibited higher Acute Physiology and Chronic Health Evaluation (APACHE) II scores, increased rates of intensive care unit readmission, prolonged hospital stays, and elevated mortality rates. One-year survival was significantly lower in patients with yeast infections, especially when diabetes mellitus and yeast-positive pleural effusion were present [7]. These data underscore the clinical significance of fungal infections in this patient population and suggest that diabetes is an important predisposing factor.

The pathogenesis of fungal infections post-esophagectomy may be linked to the disruption of mucosal barriers and immune suppression associated with major surgery and cancer. The role of antifungal prophylaxis remains unclear, and further prospective studies are warranted to evaluate its potential benefits in high-risk patients. Fungal pathogens have also been implicated in the etiology of esophageal cancer itself, with certain fungi producing mutagenic and carcinogenic effects. Although the mechanisms remain to be fully elucidated, fungi such as Candida species may contribute to esophageal mucosal damage and carcinogenesis [20]. This etiological association highlights the importance of monitoring fungal colonization and infection in esophageal cancer patients, particularly in the postoperative setting.

Viral Infections

Viral infections in the postoperative period after esophagectomy are less commonly reported but remain a concern due to their potential impact on patient outcomes.

Certain viruses, including human papillomavirus (HPV), herpes simplex virus (HSV), cytomegalovirus (CMV), and Epstein-Barr virus (EBV), have been implicated in the pathogenesis of esophageal cancer and are known to infect esophageal epithelium. While their direct role in postoperative infections is not well defined, these viruses may contribute to immunosuppression or mucosal injury, thereby predisposing patients to secondary infections [20].

Laboratory diagnosis of viral infections in cancer patients is challenging due to the wide differential diagnosis and often negative conventional tests. Advances in molecular diagnostics have improved sensitivity and turnaround time, facilitating earlier detection and management of viral infections in this vulnerable population [21]. However, the clinical significance of viral detection must be carefully interpreted in the context of the patient's overall condition.

In conclusion, while bacterial pathogens remain the predominant cause of postoperative infections after esophagectomy, fungal and viral infections also contribute to the infectious spectrum. Recognition of these pathogens and their risk factors is essential for optimizing perioperative management and improving patient outcomes.

Clinical Manifestations and Complications

Respiratory Tract Infections

Respiratory tract infections, particularly postoperative pneumonia, represent one of the most frequent and severe complications following esophagectomy for esophageal cancer.

The International Surgical Outcomes Study (ISOS) reported that pneumonia accounted for 17.6% of postoperative infections after elective surgeries, including cancer resections, highlighting its clinical significance[3]. In esophageal cancer patients, pneumonia incidence ranges around 14%, as observed in the JCOG9907 trial, where 22 out of 152 patients developed pneumonia post-esophagectomy [4]. This complication is associated with increased mortality and prolonged hospital stay. Specifically, patients with postoperative pneumonia had a hazard ratio (HR) of 1.82 (95% CI: 1.01–3.29) for overall survival (OS) reduction, indicating a significant negative impact on prognosis [4].

The pathogenesis of postoperative pulmonary infections is multifactorial, involving aspiration, impaired mucociliary clearance, and immunosuppression. Recent microbiological analyses have revealed a correlation between gut microbiota alterations and pulmonary infections after upper gastrointestinal cancer surgery. A nested case-control study in gastric cancer patients demonstrated that enrichment of Klebsiella, Enterobacter, and other intestinal bacteria during postoperative pulmonary infection regulated lipopolysaccharide synthesis pathways, contributing to infection progression. Additionally, disruption of short-chain fatty acid (SCFA) synthesis pathways was implicated in modulating inflammatory responses, suggesting a gut-lung axis in postoperative pneumonia pathophysiology [22].

Antimicrobial prophylaxis plays a critical role in preventing early-onset pneumonia after esophagectomy. A retrospective analysis comparing cefazolin (CEZ) and ampicillin/sulbactam (ABPC/SBT) prophylaxis in 356 patients undergoing thoracoscopic esophagectomy found that ABPC/SBT significantly reduced early-onset pneumonia incidence (3.8% vs. 13.6%, P=0.006) and shortened postoperative hospital stay (median 17 vs.20 days, P<0.001). Multivariate analysis confirmed the superiority of ABPC/SBT with an odds ratio of 0.20 for early pneumonia prevention [18]. These findings support the selection of appropriate perioperative antibiotics to mitigate respiratory infections.

Furthermore, the presence of specific gut microbes has been associated with postoperative pulmonary complications. For instance, Proteus mirabilis detection in fecal samples correlated with increased postoperative pneumonia incidence and systemic inflammation, whereas Bacillus species were linked to favorable outcomes and lower inflammation scores [8].

This suggests that preoperative gut microbiota profiling might inform risk stratification and targeted interventions.

Yeast infections, although less common, also contribute to respiratory complications post-esophagectomy. A retrospective study of 565 patients reported a 7.3% incidence of yeast infections, with higher rates in diabetic patients. These infections were associated with increased intensive care unit readmissions, prolonged hospitalization, and higher mortality, underscoring the need for vigilance and possibly antifungal prophylaxis in high-risk groups [7].

In summary, respiratory tract infections after esophageal cancer surgery are prevalent and significantly impact patient outcomes. The interplay between altered microbiota, immune response, and perioperative management strategies such as antibiotic prophylaxis is critical in their prevention and control.

Anastomotic and Wound Infections

Anastomotic leakage and surgical wound infections remain major postoperative complications following esophagectomy, contributing to morbidity and mortality. The ISOS study identified superficial surgical-site infections as the most frequent postoperative infection (32.7%), with wound infections constituting a significant proportion of complications [3]. In esophageal cancer surgery, anastomotic leakage incidence is approximately 14%, as reported in the JCOG9907 trial, with 21 patients experiencing leakage among 152 analyzed [4]. Although leakage did not significantly affect overall survival (HR 1.06, 95% CI: 0.52–2.13), it remains a critical clinical concern due to associated morbidity.

Risk factors for surgical wound infections include technical aspects of the operation such as bleeding, devitalized tissue, and the use of drains, as well as patient-related factors like obesity and diabetes mellitus [23]. The presence of multidrug-resistant organisms in perioperative cultures has been linked to increased surgical site infections and worse short-term outcomes, emphasizing the importance of microbiological surveillance [12]. For example, in patients undergoing surgery for perihilar cholangiocarcinoma, preoperative factors such as neutrophil-to-lymphocyte ratio ≥3.4, endoscopic sphincterotomy, and acute cholangitis were independent predictors of infectious complications [12].

Management of anastomotic and wound infections has evolved with advances in endoscopic and radiologic techniques. Endoscopic vacuum therapy and stent placement have improved nonoperative management success rates, while embolization techniques aid in

controlling bleeding complications [24]. Early recognition through clinical signs and imaging is essential. Postoperative imaging modalities, including computed tomography (CT), are crucial for detecting anastomotic leaks and associated mediastinitis, guiding timely intervention [25].

A two-stage surgical approach has been revisited for high-risk esophageal cancer patients to reduce postoperative complications. In a comparative study, patients undergoing a two-stage operation (esophagectomy followed by delayed reconstruction) had a morbidity rate of 29.6%, comparable to 32.2% in simultaneous resection and reconstruction controls. Notably, no in-hospital deaths occurred in the two-stage group, and survival rates were similar between groups, suggesting this approach may mitigate critical postoperative complications including anastomotic issues [13].

The microbiological flora of the upper alimentary tract is a significant source of pathogens responsible for postoperative infections. A prospective study involving 138 patients found that 61% had pathogenic organisms in the stomach or esophagus at surgery, with a 20.3% preoperative sputum colonization rate. Importantly, 66% of postoperative infections were caused by pathogens identified in the upper alimentary tract contents, underscoring the relevance of intraoperative cultures to guide antibiotic therapy [6].

In conclusion, anastomotic and wound infections after esophagectomy are influenced by surgical technique, patient factors, and microbial flora. Advances in diagnostic and therapeutic modalities, along with tailored perioperative management, are essential to improve outcomes.

Systemic and Catheter-Related Infections

Systemic infections, including bloodstream infections and catheter-related infections, constitute significant postoperative complications in esophageal cancer patients. These infections contribute to increased morbidity, prolonged hospitalization, and can adversely affect oncologic outcomes.

Cancer patients are predisposed to infections due to immunosuppression from malignancy and treatments. Laboratory diagnosis of infections in this population is challenging, as conventional methods often yield negative results despite clinical suspicion. Novel diagnostic techniques with enhanced sensitivity and rapid turnaround times are emerging, yet interpretation of clinical significance remains complex [21]. Accurate and timely identification of pathogens is critical for appropriate antimicrobial therapy.

A systematic review analyzing antimicrobial resistance in cancer patients highlighted the heterogeneity of clinical outcome models and the urgent need for standardized protocols. Antimicrobial resistance complicates management of systemic infections, leading to higher mortality rates. Multidrug-resistant organisms are increasingly reported in bloodstream infections among cancer patients, necessitating vigilant surveillance and tailored antimicrobial stewardship [26].

In the context of esophageal cancer surgery, systemic infections may arise from surgical site contamination, translocation of gut flora, or catheter use. The presence of multidrug-resistant bacteria in perioperative cultures correlates with postoperative infections, including organ/space and incisional surgical site infections [12]. This association underscores the importance of microbiological monitoring and infection control measures.

Yeast infections, particularly candidemia, have been documented post-esophagectomy.

A retrospective analysis of 565 patients revealed a 7.3% incidence of yeast infections, with diabetic patients at higher risk. These infections were linked to increased intensive care unit readmissions, longer hospital stays, and elevated mortality. One-year survival was significantly lower in patients with yeast infections, emphasizing the need for early detection and management [7].

Perioperative interventions such as synbiotic administration have shown promise in modulating intestinal microflora and reducing systemic inflammatory responses. A randomized controlled trial involving 70 esophageal cancer patients undergoing esophagectomy demonstrated that synbiotics increased beneficial gut bacteria, decreased harmful bacteria, and reduced postoperative infection rates from 29.4% to 10%. Additionally, the duration of systemic inflammatory response syndrome (SIRS) was shorter in the synbiotic group (P=0.0057), suggesting a potential role in preventing systemic infections [19].

In summary, systemic and catheter-related infections after esophageal cancer surgery are influenced by host factors, microbial resistance patterns, and perioperative management. Enhanced diagnostic methods, microbiological surveillance, and preventive strategies such as synbiotic use may improve patient outcomes.

Diagnostic Strategies for Postoperative Microbial Infections

Clinical Assessment and Laboratory Evaluation

Postoperative microbial infections in esophageal cancer patients represent a significant clinical challenge due to their impact on morbidity and mortality. Early and accurate diagnosis is essential for effective management. Clinical assessment remains the cornerstone of initial evaluation, focusing on signs and symptoms such as fever, localized pain, erythema, purulent discharge, respiratory distress, and systemic inflammatory response indicators. Given the complexity of esophageal cancer surgery and the high risk of complications, a thorough clinical examination should be complemented by laboratory investigations to identify infection and guide therapy.

Laboratory evaluation typically includes complete blood counts, inflammatory markers such as C-reactive protein (CRP) and procalcitonin, and blood cultures. Elevated neutrophil-to-lymphocyte ratio (NLR) has been identified as a significant preoperative risk factor for postoperative infectious complications, with a threshold of ≥3.4 correlating with increased infection risk [12]. This parameter can serve as a useful biomarker in preoperative risk stratification. Microbiological cultures from surgical sites, sputum, pleural fluid, or drainage tubes are critical for identifying causative pathogens. A prospective study involving 138 patients undergoing major esophageal surgery demonstrated that 61% had pathogenic organisms cultured from the upper alimentary tract contents intraoperatively, and 66% of postoperative infections were caused by these same pathogens [6]. This finding underscores the importance of obtaining intraoperative

samples for microbiological analysis to tailor antibiotic regimens effectively.

Imaging studies play a complementary role in the diagnostic process. Computed tomography (CT) is recommended for initial postoperative imaging to detect complications such as abscesses, anastomotic leaks, or pleural effusions [25,26]. Endoscopic ultrasonography (EUS) and positron emission tomography (PET) are valuable for preoperative staging and monitoring therapeutic response but have limited roles in acute postoperative infection diagnosis [27]. However, flexible esophagoscopy is indispensable for assessing the extent of esophageal injury and infection, especially in cases complicated by esophageal perforation or anastomotic leakage [28].

The clinical presentation of postoperative infections can be variable, often overlapping with non-infectious postoperative inflammatory responses. Therefore, a combination of clinical, laboratory, and imaging findings is necessary to improve diagnostic accuracy. The use of inflammatory biomarkers such as procalcitonin has been suggested to differentiate bacterial infections from other causes of inflammation, although further validation in esophageal cancer postoperative settings is warranted [21].

In summary, clinical assessment combined with targeted laboratory evaluation, including inflammatory markers and microbiological cultures, forms the basis of diagnosing postoperative microbial infections in esophageal cancer patients. Imaging modalities, particularly CT and endoscopy, provide essential anatomical and functional information to confirm infection and guide management.

Microbiological Testing and Advanced Diagnostic Modalities

Microbiological testing is pivotal in the diagnosis and management of postoperative infections following esophageal cancer surgery. Traditional culture methods remain the standard for pathogen identification but are often limited by low sensitivity and prolonged turnaround times. Recent advances in molecular diagnostics and sequencing technologies have enhanced the detection of pathogens, including fastidious and unculturable organisms, thereby improving diagnostic yield.

The application of 16S rRNA gene sequencing and metagenomic analyses has revealed complex alterations in the microbiota associated with postoperative infections. For instance, a nested case-control study in gastric cancer patients demonstrated that postoperative pulmonary infections correlated with significant changes in gut microbiota composition, including enrichment of Klebsiella, Enterobacter, Ruminococcus, and Collinsella species [22]. These bacteria were implicated in modulating lipopolysaccharide synthesis pathways and short-chain fatty acid (SCFA) metabolism, which may influence inflammatory responses and infection susceptibility. Although this study focused on gastric cancer, the findings highlight the potential role of gut microbiota dysbiosis in postoperative infections, which may be extrapolated to esophageal cancer patients given the anatomical and physiological proximity.

Advanced diagnostic modalities such as polymerase chain reaction (PCR)-based assays, multiplex pathogen panels, and next-generation sequencing (NGS) offer rapid and sensitive detection of bacterial, viral, and fungal pathogens. These techniques can identify multidrug-resistant organisms and mixed infections that are often missed by conventional cultures [21]. The integration of these molecular methods into clinical practice facilitates timely initiation of targeted antimicrobial therapy, which is crucial for improving outcomes.

Imaging techniques also contribute to the diagnostic process. Contrast-enhanced CT scans provide detailed visualization of postoperative anatomical changes, abscess formation, and fluid collections [25]. Magnetic resonance imaging (MRI) and contrast esophagography are useful adjuncts in specific scenarios, such as evaluating esophageal leaks or mediastinitis [28]. The combination of imaging and microbiological data enhances diagnostic accuracy and guides interventional procedures like drainage or surgical debridement.

Emerging research emphasizes the importance of the microbiome in esophageal cancer pathogenesis and postoperative infection risk. Dysbiosis of the esophageal, oral, and gut microbiota has been linked to tumor progression and impaired immune responses [29]. Understanding these microbial interactions may lead to novel diagnostic biomarkers and therapeutic targets. For example, certain oral pathogens such as Porphyromonas gingivalis and Fusobacterium nucleatum have been associated with inflammation and carcinogenesis, suggesting that their detection postoperatively could indicate infection risk or tumor recurrence [30].

In conclusion, microbiological testing for postoperative infections in esophageal cancer patients has evolved from conventional cultures to include advanced molecular diagnostics and microbiome analyses. These approaches, combined with imaging modalities, provide a comprehensive framework for accurate and timely diagnosis, enabling personalized management strategies to improve patient outcomes.

Current Approaches to Management and Treatment

Empirical and Targeted Antimicrobial Therapy

Postoperative microbial infections in esophageal cancer patients represent a significant clinical challenge, necessitating effective antimicrobial strategies to reduce morbidity and mortality. Empirical antimicrobial therapy is typically initiated promptly upon suspicion of infection, especially in the context of febrile neutropenia or clinical signs of infection, to cover the most likely pathogens before culture results are available. This approach has been shown to substantially reduce the clinical impact of infectious complications in cancer patients, as demonstrated by the European Organisation for Research and Treatment of Cancer International Antimicrobial Therapy Group (EORTC-IATG) studies, which established broad-spectrum antibiotic regimens as the standard for managing febrile neutropenia in oncologic settings [31].

In esophageal cancer surgery, the microbial spectrum of postoperative infections often includes both gram-positive and gram-negative bacteria, with polymicrobial infections being common. For instance, gram-negative bacteria are frequently isolated in early acute infections, while staphylococci predominate in certain

contexts such as bone tumor surgeries, suggesting the need for broad-spectrum coverage that includes both bacterial groups [16]. The choice of empirical antibiotics should therefore be guided by local microbiological data and resistance patterns to optimize efficacy and minimize the emergence of multidrug-resistant organisms.

A retrospective analysis comparing cefazolin (CEZ) and ampicillin/sulbactam (ABPC/SBT) as prophylactic agents in patients undergoing thoracoscopic esophagectomy revealed that ABPC/SBT significantly reduced the incidence of early-onset postoperative pneumonia (3.8% vs. 13.6%, P = 0.006) and shortened hospital stay (17 vs. 20 days, P < 0.001) without increasing Clostridioides difficile infections or multidrug-resistant organisms [18]. This evidence supports the preferential use of ABPC/SBT for antimicrobial prophylaxis in esophageal cancer surgery to prevent pulmonary infections, a common and severe postoperative complication.

Targeted antimicrobial therapy should be implemented once microbiological culture and sensitivity results are available. This approach allows for de-escalation from broad-spectrum agents to narrower-spectrum antibiotics, reducing the risk of resistance development and adverse effects. However, the increasing prevalence of antimicrobial resistance in cancer patients complicates treatment. A systematic review highlighted the heterogeneity in clinical outcomes related to resistant infections in cancer patients and emphasized the urgent need for standardized protocols to guide antimicrobial use [26].

In veterinary oncology, infections in cancer patients were predominantly caused by bacteria typical of the infection site, such as Escherichia coli and Staphylococcus pseudintermedius, underscoring the importance of site-specific empirical therapy [32]. Although this data is from veterinary medicine, it parallels human oncology in emphasizing the relevance of infection site and local flora in guiding empirical therapy.

The prevention and treatment of cancer-related infections require individualized risk assessment and incorporation of preventive measures, as outlined in the NCCN Clinical Practice Guidelines. These guidelines recommend stratifying patients based on infection risk and tailoring antimicrobial strategies accordingly to optimize outcomes [33]. In esophageal cancer patients, especially those undergoing preoperative chemotherapy, postoperative infectious complications, particularly pulmonary infections, have been associated with worse oncologic outcomes, highlighting the critical role of effective antimicrobial management [5].

In summary, current antimicrobial management in postoperative esophageal cancer patients involves prompt empirical broad-spectrum antibiotic therapy tailored to local microbiological patterns and patient risk factors, followed by targeted therapy based on culture results. Prophylactic regimens such as ABPC/SBT have demonstrated superiority in preventing early postoperative pneumonia. The rising challenge of antimicrobial resistance necessitates ongoing surveillance and adherence to evidence-based guidelines to optimize antimicrobial use and improve patient outcomes.

Adjunctive and Supportive Measures

Adjunctive and supportive measures play a vital role in the comprehensive management of postoperative microbial infections in esophageal cancer patients. These measures aim to enhance host defenses, modulate the inflammatory response, and support nutritional status, thereby improving recovery and reducing infection-related complications.

Perioperative administration of synbiotics, which combine probiotics and prebiotics, has been investigated for its potential to modulate intestinal microflora and reduce postoperative infections in esophageal cancer patients undergoing esophagectomy. A prospective randomized controlled trial involving 70 patients demonstrated that synbiotic administration significantly increased beneficial bacteria counts and decreased harmful bacteria in the gut on postoperative day 7. This was accompanied by higher concentrations of total organic acids and acetic acid, lower intestinal pH, a trend toward reduced infection rates (10% vs. 29.4%, P = 0.0676), and a significantly shorter duration of systemic inflammatory response syndrome (SIRS) (P = 0.0057). Additionally, patients receiving synbiotics experienced fewer interruptions or reductions in enteral nutrition due to abdominal symptoms (6.7% vs. 29.4%, P = 0.0259) [19]. These findings suggest that synbiotics may suppress excessive inflammatory responses and improve gastrointestinal tolerance, contributing to better postoperative outcomes.

Probiotic therapy has also been explored as an adjunct in postoperative care for esophageal cancer patients. Although the beneficial effects remain somewhat controversial and warrant further investigation, some clinical studies indicate that probiotics can positively impact nutritional status and potentially reduce postoperative inflammation. This is particularly relevant given the high prevalence of malnutrition and gastrointestinal dysfunction in this patient population, which adversely affect prognosis [34]. The modulation of gut microbiota through probiotics may help restore barrier function and reduce colonization by pathogenic bacteria, thereby lowering infection risk.

Supportive care also encompasses meticulous perioperative management to prevent and promptly address common postoperative complications such as anastomotic leakage, pneumonia, and recurrent laryngeal nerve palsy. Advances in endoscopic techniques, including vacuum therapy and stent placement, as well as radiological interventions like embolization, have improved the management of these complications. Early recognition and appropriate treatment are essential to mitigate morbidity and mortality associated with postoperative infections [24].

Nutritional support is another critical component, as adequate nutrition enhances immune function and tissue repair. Tailored education for patients and their families regarding the postoperative course and potential complications can facilitate adherence to nutritional and supportive interventions, thereby improving recovery trajectories [35].

In cases of esophageal injury complicated by infection, such as following anterior cervical spine surgery, a multidisciplinary approach integrating surgical debridement, vascularized flap reinforcement, negative pressure wound therapy, and prolonged antibiotic administration is recommended. Imaging modalities including computed tomography (CT), magnetic resonance imaging

(MRI), and contrast esophagography are indispensable for assessing the extent of injury and infection. Innovative adjunctive therapies like hyperbaric oxygen therapy have shown promise in enhancing healing and reducing infection rates in these complex cases [28].

Overall, adjunctive and supportive measures complement antimicrobial therapy by addressing the multifactorial nature of postoperative infections in esophageal cancer patients. Strategies that modulate the gut microbiome, optimize nutritional status, and employ advanced diagnostic and therapeutic techniques contribute to improved management and outcomes in this vulnerable population.

Prevention Strategies and Future Directions

Infection Control and Perioperative Prophylaxis

Postoperative infections (PI) remain a significant challenge following esophageal cancer surgery, contributing to increased morbidity and mortality. Effective infection control and perioperative prophylaxis are critical components in reducing the incidence of these complications. Several studies have identified key risk factors and strategies to mitigate postoperative infections in this patient population.

Risk factors for PI after esophageal tumor surgery include smoking, prolonged preoperative hospital stays, advanced age, prolonged surgical duration, and elevated postoperative blood glucose levels. For instance, Lin et al. (2023) reported an overall PI incidence of 28.3% in a cohort of 902 esophageal tumor patients, with smoking and preoperative hospital stay identified as significant independent risk factors [1]. Similarly, Dan et al. (2025) found that in patients aged 60 years and older undergoing esophageal tumor surgery, smoking, longer operative times, and postoperative hyperglycemia were independently associated with increased PI risk [2].

The microbiological spectrum of postoperative infections predominantly involves endogenous flora from the upper alimentary tract. Sharpe et al. (1992) demonstrated a strong correlation between pathogens isolated from the upper alimentary tract during surgery and those responsible for postoperative infections, emphasizing the importance of targeted antimicrobial prophylaxis based on intraoperative cultures [6]. Moreover, yeast infections, particularly in diabetic patients, have been identified as notable contributors to postoperative morbidity and mortality, suggesting a potential role for antifungal prophylaxis in high-risk groups [7].

Perioperative antibiotic prophylaxis is a cornerstone in preventing surgical site infections and other postoperative infectious complications. According to the Canadian Infectious Disease Society guidelines, antibiotic prophylaxis should be administered intravenously immediately before surgery, with the choice of agent tailored to the expected pathogens, local antimicrobial susceptibility patterns, and pharmacokinetics of the drugs [36]. Nichols (1984) highlighted that appropriate surgical technique combined with well-chosen prophylactic antibiotics significantly reduces postoperative infections in gastrointestinal surgery [37]. In esophageal cancer surgery, antimicrobial regimens such as ampicillin/sulbactam have shown superiority over cefazolin in preventing early-onset pneumonia, a common and serious postoperative complication [18]. Higaki et al. (2021) reported a significantly lower incidence of early-onset pneumonia (3.8% vs. 13.6%, P=0.006) and shorter hospital stays in patients receiving ampicillin/sulbactam compared to cefazolin, without increased antimicrobial resistance [18].

Beyond antibiotics, modulation of the intestinal microbiota through probiotics and synbiotics has emerged as a promising adjunctive strategy. Jeppsson et al. (2011) reviewed 14 randomized clinical trials and found that perioperative administration of probiotics, mainly lactobacilli, in upper gastrointestinal surgeries resulted in a threefold reduction in postoperative infections and decreased postoperative inflammation [38]. Tanaka et al. (2012) conducted a prospective randomized controlled trial in esophageal cancer patients undergoing esophagectomy, demonstrating that perioperative synbiotics increased beneficial intestinal bacteria, reduced harmful bacteria, and lowered infection rates (10% vs. 29.4%, P=0.0676), alongside shortening the duration of systemic inflammatory response syndrome (SIRS) [19]. These findings suggest that synbiotics may help restore intestinal barrier function and modulate inflammatory responses, thereby reducing postoperative infectious complications.

In high-risk patients, surgical strategies such as two-stage operations have been revisited to minimize postoperative complications. Morita et al. (2011) compared two-stage esophagectomy with simultaneous resection and reconstruction, finding comparable morbidity rates but no in-hospital mortality in the two-stage group, indicating its safety and potential to prevent critical postoperative infections in selected patients [13].

In summary, infection control in esophageal cancer surgery involves a multifaceted approach: identification and modification of patient-related risk factors (e.g., smoking cessation, glycemic control), meticulous surgical technique, appropriate perioperative antibiotic prophylaxis tailored to local microbiological profiles, and adjunctive use of probiotics or synbiotics to maintain gut microbial balance. These strategies collectively contribute to reducing the incidence and severity of postoperative infections, thereby improving surgical outcomes.

Emerging Approaches and Research Perspectives

Recent advances in understanding the role of the microbiome and tumor microenvironment have opened new avenues for preventing and managing postoperative infections and improving overall outcomes in esophageal cancer.

The esophageal and gut microbiota have been increasingly recognized as influential factors in esophageal carcinogenesis and treatment response. Dysbiosis characterized by increased pathogenic bacteria such as Porphyromonas gingivalis and Fusobacterium nucleatum promotes chronic inflammation and immune suppression, facilitating tumor progression [29]. Moreover, alterations in microbiota composition can modulate systemic immunity and affect the efficacy of chemotherapy and immunotherapy [39]. These insights suggest that microbiome-targeted interventions could serve as novel preventive and therapeutic strategies.

Immunotherapy, particularly immune checkpoint inhibitors (ICIs) targeting PD-1/PD-L1 pathways, has shown promise in esophageal cancer treatment. However, response rates vary, and a

substantial proportion of patients remain unresponsive. Emerging evidence indicates that the tumor microenvironment (TME), including metabolic reprogramming and immune cell infiltration, critically influences immunotherapy outcomes [40]. Understanding the interplay between metabolic pathways and immune responses within the TME may enable the development of combination therapies that enhance immunotherapeutic efficacy.

Clinical trials are exploring multimodal approaches integrating surgery, chemotherapy, radiotherapy, targeted therapy, and immunotherapy. Waters et al. (2024) reviewed 21 clinical studies demonstrating that neoadjuvant chemoradiotherapy followed by surgery improves local disease control and survival compared to surgery alone, with immunotherapy emerging as a promising adjunct [41]. Kelly (2019) emphasized the need for personalized treatment strategies based on tumor histology and immune milieu to optimize patient selection for immunotherapy [42].

Microbiome profiling technologies, including next-generation sequencing, enable comprehensive characterization of esophageal microbial communities. Pandey et al. (2023) highlighted the association between specific bacterial taxa and tumorigenesis, as well as the potential of microbiome signatures to predict treatment response and immune-related adverse events [10]. These findings underscore the potential of microbiome-based biomarkers for early detection and personalized therapy.

Probiotic and synbiotic therapies continue to be investigated for their immunomodulatory and anti-inflammatory effects. Co et al. (2023) discussed the positive correlation between probiotic use and improved nutritional status and postoperative recovery in esophageal cancer patients, although further research is needed to clarify optimal strains, dosages, and treatment durations [34]. Additionally, fecal microbiota transplantation and dietary modifications represent emerging strategies to restore microbial balance and enhance treatment efficacy [29].

Advances in understanding the molecular and cellular components of the TME, including cancer-associated fibroblasts, myeloid-derived suppressor cells, and regulatory T cells, provide opportunities to develop targeted therapies that disrupt pro-tumorigenic signaling and enhance antitumor immunity [43]. Lin et al. (2016) emphasized the importance of integrating TME-targeting agents with existing modalities to improve outcomes in esophageal cancer [43].

Conclusion

In conclusion, emerging research highlights the critical role of the microbiome and tumor microenvironment in esophageal cancer pathogenesis, postoperative infection risk, and treatment response. Integrating microbiome modulation, immunotherapy, and TME-targeted strategies into multimodal treatment frameworks holds promise for improving patient outcomes. Ongoing clinical trials and translational studies are essential to validate these approaches and establish evidence-based protocols for prevention and management of postoperative infections in esophageal cancer.

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