Comparison between Chemotherapy and Chemoradiotherapy in Esophageal Cancer Treatment: Efficacy, Safety, and Controversial Issues

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Abstract: Esophageal cancer is a highly prevalent malignant tumor of the digestive system, with cases in China accounting for more than half of the global total. Chemotherapy and chemoradiotherapy are important treatment modalities for this disease. This study compared the efficacy, safety, and clinical controversies of the two approaches. In terms of efficacy, chemoradiotherapy showed significantly better performance than chemotherapy alone in local control rate (2-year rate: 70% vs. 40% for chemotherapy alone), distant metastasis rate (3-year rate: 35% vs. 50% for chemotherapy alone), and survival rate (5-year rate: 30% vs. 15% for chemotherapy alone), which is attributed to the synergistic effect of radiotherapy and chemotherapy. Regarding safety, both treatments are associated with adverse reactions, but chemoradiotherapy, due to the superimposition of adverse effects from radiotherapy and chemotherapy, not only causes common chemotherapy-related adverse reactions such as myelosuppression (leukopenia rate: 50%-70%) and gastrointestinal reactions (nausea and vomiting rate: 70%-80%) but also leads to radiotherapy-specific adverse reactions like radiation esophagitis (incidence rate: 60%-80%), resulting in a more severe impact on patients' quality of life. Clinical controversies mainly focus on the selection of treatment regimens (which needs to consider patients' physical status, tumor stage, and pathological type), the optimal timing and sequence of chemoradiotherapy (concurrent chemoradiotherapy has better efficacy but greater adverse reactions, while sequential chemoradiotherapy shows the opposite characteristics), the management and risk assessment of treatment-related complications (e.g., the incidence rate of esophageal fistula is 5.3%, and preoperative assessment of patients' nutritional status and cardiopulmonary function is required), and the follow-up and quality of life improvement for long-term survivors. In clinical practice, the pros and cons of chemotherapy and chemoradiotherapy should be balanced, and personalized treatment plans should be formulated based on patients' specific conditions to improve prognosis.

1. Introduction

Esophageal cancer, a common malignant tumor of the digestive system, poses a serious threat to human health. Globally, its incidence and mortality rates are notable. According to the 2020 Global Cancer Burden Data released by the International Agency for Research on Cancer (IARC) of the World Health Organization, there were approximately 604,000 new cases and 544,000 deaths of esophageal cancer worldwide that year, ranking 7th and 6th among all malignant tumors in terms of incidence and mortality, respectively[1].

China is a country with a high incidence of esophageal cancer, where the number of new cases and deaths accounts for more than half of the global total. In 2020, there were 324,000 new cases and 301,000 deaths of esophageal cancer in China[2]. The incidence of esophageal cancer shows obvious geographical variations, with higher rates in Hebei, Henan, Fujian, Sichuan, and other provinces[3]. For instance, Cixian County in Hebei Province and Linxian County in Henan Province are high-incidence areas worldwide. In terms of gender distribution, the incidence rate in males is higher than that in females, with a male-to-female ratio of approximately 1.6:1. This may be related to bad living habits of males, such as long-term smoking and alcohol consumption. Meanwhile, dietary habits of

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Chinese people, such as preference for hot food, fast eating speed, and consumption of pickled food in some regions, also increase the risk of developing esophageal cancer. The high incidence and mortality rates of esophageal cancer not only impose a heavy physical and mental burden on patients and their families but also exert enormous pressure on social medical resources.

In the treatment of esophageal cancer, chemotherapy and chemoradiotherapy are important therapeutic approaches. Chemotherapy inhibits the growth and division of tumor cells by using chemical drugs and plays a certain role in the comprehensive treatment of esophageal cancer. For early-stage esophageal cancer, chemotherapy can be used as an adjuvant treatment for surgery to help reduce tumor volume and improve the success rate of surgical resection. For advanced esophageal cancer, chemotherapy serves as one of the main treatment methods, aiming to prolong patients' survival and improve their quality of life. Common chemotherapeutic drugs include cisplatin, 5-fluorouracil, paclitaxel, etc.[4], which exert anti-tumor effects through different mechanisms of action. Chemoradiotherapy, on the other hand, combines radiotherapy and chemotherapy. Radiotherapy mainly irradiates local tumors and kills tumor cells with high-energy rays, while chemotherapy focuses on systemic treatment. The combination of the two can complement each other, effectively controlling local tumors and preventing systemic metastasis. However, these two treatment methods differ in terms of efficacy, safety, and other aspects, and there are still many controversial issues in their clinical application, which urgently require in-depth research and discussion.

This study aims to comprehensively and systematically compare the efficacy of chemotherapy and chemoradiotherapy in the treatment of esophageal cancer, and analyze their impacts on patients' survival, tumor remission, and other aspects; evaluate their safety, and explore the adverse reactions caused during the treatment process and their impacts on patients' quality of life; and deeply analyze the current controversial issues regarding chemotherapy and chemoradiotherapy in clinical application, such as the selection of treatment timing and the optimization of treatment regimens. It is expected to provide comprehensive and scientific reference for clinicians in the selection of esophageal cancer treatment regimens, so as to improve the treatment effect of esophageal cancer and enhance patients' prognosis and quality of life.

2. Comparison of Efficacy between Chemotherapy and Chemoradiotherapy in the Treatment of Esophageal Cancer

2.1. Comparison of Local Control Rate

Numerous clinical studies have demonstrated that chemoradiotherapy is significantly superior to chemotherapy alone in terms of the local control rate of esophageal cancer. A randomized controlled study involving patients with locally advanced esophageal cancer showed that the chemoradiotherapy group adopted a concurrent chemoradiotherapy mode, with a chemotherapy regimen of cisplatin combined with 5-fluorouracil and intensity-modulated radiation therapy (IMRT) at a total dose of 60 Gy, achieving a 2-year local control rate of 70%[5]. In contrast, the chemotherapy-alone group received the same chemotherapy regimen for 6 cycles, with a 2-year local control rate of only 40%.

The ability of chemoradiotherapy to improve the local control rate is primarily attributed to the synergistic effect of radiotherapy and chemotherapy. Radiotherapy acts directly on tumor cells through high-energy rays, damaging their DNA structure and inducing tumor cell death. Chemotherapeutic drugs not only inhibit the growth and division of tumor cells but also exert a radiosensitizing effect. For example, cisplatin can inhibit the DNA damage repair mechanism of tumor cells[6], preventing the effective repair of DNA double-strand breaks caused by radiotherapy and thereby enhancing the killing effect of radiotherapy on tumor cells. Some chemotherapeutic drugs, such as paclitaxel, can arrest tumor cells in the G2/M phase, which is sensitive to radiotherapy, thereby increasing the radiosensitivity of tumor cells. The combination of the two approaches attacks tumor cells from different perspectives, more effectively controlling the growth and spread of local tumors and improving the local control rate.

2.2. Comparison of Distant Metastasis Rate

Clinical research data indicate that chemoradiotherapy has a significant advantage in reducing the distant metastasis rate of esophageal cancer. A study on patients with advanced esophageal cancer compared the distant metastasis rates between chemoradiotherapy and chemotherapy alone. The chemoradiotherapy group adopted a sequential chemoradiotherapy mode: first receiving 3 cycles of chemotherapy with a regimen of paclitaxel combined with cisplatin, followed by radiotherapy at a dose of 60 Gy. The chemotherapy-alone group received the same chemotherapy regimen for 6 cycles. The results showed that the 3-year distant metastasis rate of the chemoradiotherapy group was 35%, while that of the chemotherapy-alone group was as high as 50%[7].

The mechanism by which chemoradiotherapy reduces the distant metastasis rate mainly lies in its integration of the systemic therapeutic effect of chemotherapy and the local control effect of radiotherapy. Chemotherapeutic drugs can enter the bloodstream and eliminate potential micrometastases throughout the body. Radiotherapy, by controlling the growth of local tumors, reduces the likelihood of tumor cells metastasizing to distant sites. Additionally, radiotherapy can modify the tumor microenvironment and inhibit tumor angiogenesis, thereby reducing the chance of tumor cells entering the bloodstream and developing distant metastases. This comprehensive effect of chemoradiotherapy effectively lowers the distant metastasis rate of esophageal cancer.

2.3. Comparison of Survival Rate

In terms of survival rate, chemoradiotherapy also demonstrates a significant advantage over chemotherapy alone in the treatment of esophageal cancer. A long-term follow-up study on esophageal cancer patients showed that the chemoradiotherapy group adopted a concurrent chemoradiotherapy mode, with a chemotherapy regimen of cisplatin combined with fluorouracil and radiotherapy at a dose of 60-66 Gy. The 1-year, 3-year, and 5-year survival rates were 75%, 45%, and 30%, respectively. In contrast, the chemotherapy-alone group received the same chemotherapy regimen for 6 cycles, with 1-year, 3-year, and 5-year survival rates of 60%, 30%, and 15%, respectively[8].

There are two main reasons why chemoradiotherapy can improve the survival rate. On one hand, it achieves more sustained and comprehensive tumor control: radiotherapy controls local tumors, while chemotherapy eliminates systemic micrometastases, reducing the risk of tumor recurrence and metastasis and thus prolonging patients' survival. On the other hand, although chemoradiotherapy is associated with relatively more adverse reactions, most patients can tolerate it through appropriate supportive care and dose adjustments, ensuring the smooth progress of treatment. In contrast, chemotherapy alone has a relatively weaker effect on local tumor control, which easily leads to local recurrence and thereby affects patients' survival rate.

Patients' tolerance and compliance with treatment also impact the survival rate. Although chemoradiotherapy causes more significant initial adverse reactions, with the advancement of treatment technology and the improvement of supportive care, patients' tolerance has gradually increased. Patients who can complete the full course of treatment as scheduled are more likely to achieve better therapeutic effects and higher survival rates. For chemotherapy alone, if patients develop drug resistance or severe adverse reactions leading to treatment interruption, the survival rate will also be affected.

3. Comparison of Safety between Chemotherapy and Chemoradiotherapy in the Treatment of Esophageal Cancer

3.1. Comparison of Types and Incidence Rates of Adverse Reactions

Both chemotherapy and chemoradiotherapy can induce a variety of adverse reactions in the treatment of esophageal cancer, and the incidence rate of adverse reactions in chemoradiotherapy is usually higher. Common adverse reactions of chemotherapy include myelosuppression, gastrointestinal reactions, and impairment of liver and kidney function.

In terms of myelosuppression, approximately 50%-70% of patients experience varying degrees of

leukopenia, and 20%-30% of patients develop thrombocytopenia. This is because chemotherapeutic drugs not only inhibit the growth of tumor cells but also suppress bone marrow hematopoietic stem cells, thereby affecting the production of blood cells. Gastrointestinal reactions are also relatively common: the incidence rate of nausea and vomiting can reach 70%-80%, and the incidence rate of diarrhea is about 30%-40%. Chemotherapeutic drugs irritate the gastrointestinal mucosa, leading to disorders of gastrointestinal peristalsis and abnormal secretion of digestive juices, which in turn trigger these symptoms.

In addition to chemotherapy-related adverse reactions, chemoradiotherapy can also cause radiotherapy-specific adverse reactions, such as radiation esophagitis and radiation pneumonitis. The incidence rate of radiation esophagitis can be as high as 60%-80%[9], typically occurring when the radiotherapy dose reaches 20-30 Gy. Its pathogenesis lies in the fact that radiotherapy damages the epithelial cells of the esophageal mucosa, causing an inflammatory response; patients may experience symptoms such as odynophagia (painful swallowing) and aggravated dysphagia (difficulty swallowing). The incidence rate of radiation pneumonitis ranges from 10% to 30%[10], mostly occurring 1-3 months after radiotherapy. Radiotherapy irradiates normal lung tissues, resulting in inflammation and fibrosis of the lung tissue; patients often present with symptoms including cough, expectoration, fever, and dyspnea (difficulty breathing).

The high incidence rate of adverse reactions in chemoradiotherapy is mainly due to the superimposition of adverse effects from radiotherapy and chemotherapy. The damage to normal tissues caused by radiotherapy reduces the body's tolerance to chemotherapeutic drugs, further exacerbating adverse reactions. Moreover, chemotherapeutic drugs may interfere with the repair of tissues damaged by radiotherapy, leading to an increase in the severity and duration of adverse reactions.

3.2. Impact of Adverse Reactions on Patients' Quality of Life

Adverse reactions of both chemotherapy and chemoradiotherapy have a significant multi-faceted impact on patients' quality of life, and the impact of chemoradiotherapy is more severe.

Adverse reactions caused by chemotherapy, such as severe nausea and vomiting, prevent patients from eating normally, resulting in insufficient nutrient intake, weight loss, and physical weakness. Long-term gastrointestinal reactions can also cause psychological anxiety and fear in patients, affecting their emotional state. Leukopenia caused by myelosuppression increases the risk of infection in patients; once an infection occurs, patients require long-term hospitalization, which restricts their range of activities and affects their daily lives.

The impact of adverse reactions from chemoradiotherapy on patients' quality of life is more extensive and severe. Odynophagia caused by radiation esophagitis brings great pain to patients during eating, seriously impairing their eating experience and nutrient intake. Patients may reduce their food intake due to fear of pain, leading to malnutrition and further weakening of physical resistance. Dyspnea caused by radiation pneumonitis limits patients' ability to perform daily activities; they are unable to engage in normal physical activities, and even simple actions such as walking and dressing can leave them out of breath. Patients' sleep quality is also severely affected: frequent coughing and dyspnea at night interrupt their sleep, resulting in poor mental state and a sharp decline in quality of life. Additionally, chemoradiotherapy may cause adverse reactions such as skin damage and fatigue in patients. Collectively, these adverse reactions cause immense physical and mental suffering to patients and significantly reduce their quality of life.

4. Controversial Issues in Chemotherapy and Chemoradiotherapy for Esophageal Cancer Treatment

4.1. Basis for Selection of Treatment Regimens

In the treatment of esophageal cancer, the selection of treatment regimens requires comprehensive consideration of multiple factors such as patients' physical status, tumor stage, and pathological type, all of which play a crucial role in the decision-making of treatment regimens.

Patients' physical status serves as the foundation for selecting treatment regimens. Patients with poor general conditions, such as severe cardiopulmonary dysfunction, hepatic and renal insufficiency, or malnutrition, may not tolerate the high intensity and high incidence of adverse reactions of chemoradiotherapy. For patients with severely impaired cardiopulmonary function, radiotherapy may further increase the burden on the heart and lungs, while the metabolism of chemotherapeutic drugs can also add to the burden on the liver and kidneys, potentially leading to organ failure. Patients with malnutrition have poor physical resistance, making it difficult for them to withstand the adverse reactions of chemoradiotherapy, which in turn affects treatment efficacy and prognosis. For such patients, chemotherapy alone may be a more appropriate option, and the dosage and regimen of chemotherapeutic drugs can be adjusted according to their specific conditions to reduce treatment risks. In contrast, patients with good physical status and high performance status scores are more likely to tolerate chemoradiotherapy, thereby achieving better treatment outcomes.

Tumor stage is one of the key factors determining the treatment regimen. For patients with early-stage esophageal cancer, where the tumor is localized, surgical resection is the main treatment modality. For some early-stage patients who are ineligible for surgical resection, or to reduce the risk of postoperative recurrence, chemotherapy or chemoradiotherapy can be selected. For early-stage patients with good physical status, chemoradiotherapy may have advantages in local control and reducing the risk of recurrence. For patients with advanced esophageal cancer, the tumor has a wide range of invasion, and the risks of local progression and distant metastasis increase. At this stage, chemoradiotherapy is usually the main treatment option to improve local control rate, reduce distant metastasis rate, and prolong patients' survival. However, for some patients with advanced cancer who have extensive distant metastasis and poor physical status, chemotherapy may focus more on palliative treatment to relieve symptoms and improve quality of life.

Pathological type also plays an important role in the selection of treatment regimens. Esophageal squamous cell carcinoma and esophageal adenocarcinoma differ in biological behavior and sensitivity to treatment. Esophageal squamous cell carcinoma is relatively sensitive to radiotherapy, so chemoradiotherapy may yield better results. Multiple studies have shown that concurrent chemoradiotherapy can effectively improve the local control rate and survival rate in the treatment of esophageal squamous cell carcinoma[11]. The treatment of esophageal adenocarcinoma places more emphasis on the role of chemotherapy, and some chemotherapy regimens have shown good efficacy in its treatment. However, with the deepening of research, the application of chemoradiotherapy in esophageal adenocarcinoma is gradually increasing, and the specific treatment regimen needs to be selected based on the patient's individual situation.

4.2. Optimal Timing and Sequence of Chemoradiotherapy

Chemoradiotherapy for esophageal cancer mainly includes two modes: concurrent chemoradiotherapy and sequential chemoradiotherapy. Each mode has its own advantages and disadvantages, and the selection of the optimal timing and sequence needs to comprehensively consider factors such as the local condition of the tumor and the patient's tolerance.

The advantage of concurrent chemoradiotherapy lies in the radiosensitizing effect of chemotherapeutic drugs, which can more effectively kill tumor cells and improve the local control rate. For example, cisplatin can inhibit the DNA damage repair mechanism of tumor cells, preventing the effective repair of DNA double-strand breaks caused by radiotherapy and thus enhancing the killing effect of radiotherapy on tumor cells. However, concurrent chemoradiotherapy imposes a heavier burden on the patient's body and is associated with relatively more adverse reactions, such as the simultaneous occurrence of chemotherapy-induced myelosuppression, gastrointestinal reactions, and radiotherapy-induced radiation esophagitis and radiation pneumonitis. Concurrent chemoradiotherapy may be a better choice for patients with good physical status, severe local tumor invasion, and an urgent need for local tumor control. For patients with locally advanced esophageal cancer, where the tumor invades surrounding tissues and urgent local lesion control is required, and the patient's physical status can tolerate the adverse reactions of concurrent chemoradiotherapy, this mode can more effectively control tumor growth and improve treatment efficacy.

The advantage of sequential chemoradiotherapy is that it can exert the advantages of chemotherapy and radiotherapy in sequence. Preceding chemotherapy can utilize the systemic effect of chemotherapeutic drugs to eliminate potential micrometastases and reduce tumor volume. Subsequent radiotherapy can then target the local tumor for precise treatment, improving the local control effect. The adverse reactions of sequential chemoradiotherapy are relatively more scattered compared with concurrent chemoradiotherapy, making it more tolerable for patients. However, sequential chemoradiotherapy has a relatively longer treatment cycle, which may increase the risk of tumor progression during treatment. It is a more suitable option for patients with poor physical status who cannot tolerate concurrent chemoradiotherapy. For elderly patients or those with poor underlying health conditions, sequential chemoradiotherapy allows patients to have a certain recovery period after chemotherapy before receiving radiotherapy, thereby reducing treatment risks[12].

The local condition of the tumor also affects the selection of the timing and sequence of chemoradiotherapy. For patients with large tumors that are closely associated with surrounding vital organs, prior chemotherapy to reduce the tumor size before radiotherapy helps improve the efficacy and safety of radiotherapy. For patients with relatively localized tumors but a risk of distant metastasis, a better strategy may be to first administer chemotherapy to control systemic micrometastases, followed by radiotherapy to control the local tumor.

4.3. Management of Treatment-Related Complications and Risk Assessment

During chemoradiotherapy for esophageal cancer, severe complications such as esophageal fistula and pulmonary infection may occur. Timely and effective management and preventive measures are crucial, and pre-treatment risk assessment is also indispensable.

Esophageal fistula is one of the relatively severe complications in chemoradiotherapy, with an incidence rate of approximately 5.3%[13]. Its pathogenesis mainly involves radiotherapy-induced damage to the esophageal mucosa and surrounding tissues, while chemotherapy further impairs tissue repair capacity, leading to perforation of the esophageal wall and the formation of an esophageal fistula. Once an esophageal fistula occurs, chemoradiotherapy should be immediately discontinued. For patients with esophagotracheal fistula or esophagobronchial fistula, the first priority is to ensure airway patency and prevent aspiration. Stent placement can be used to occlude the fistula, restore esophageal continuity, and reduce the entry of food or secretions into the respiratory tract. For patients with esophagomediastinal fistula or esophagopleural fistula, adequate drainage is necessary to prevent the aggravation of mediastinal infection or pleural infection. Meanwhile, nutritional support should be provided to the patient, either through nasogastric feeding or parenteral nutrition, to ensure sufficient nutrient intake and promote fistula healing.

Pulmonary infection is also a common and severe complication, whose incidence is related to factors such as the patient's age, underlying diseases, dosage and mode of chemoradiotherapy. Chemoradiotherapy can suppress the patient's immune system, resulting in decreased body resistance, and radiotherapy may damage normal lung tissue, increasing the risk of pulmonary infection. For patients with pulmonary infection, sputum culture and drug sensitivity testing should be performed in a timely manner, and sensitive antibiotics should be selected for treatment based on the test results. Respiratory management should be strengthened: patients should be encouraged to cough and expectorate, and sputum suction should be performed if necessary to maintain airway patency. Oxygen therapy should be administered to the patient to improve hypoxic conditions.

Pre-treatment risk assessment helps predict the risk of complication occurrence and enables the early implementation of preventive measures. Assessing the patient's nutritional status is an important part, which can be determined by measuring indicators such as body weight and serum protein levels. Patients with malnutrition have poor physical resistance and a higher risk of developing complications. For such patients, nutritional support should be provided before treatment to improve their nutritional status and enhance physical resistance. Assessing the patient's cardiopulmonary function is also crucial. Cardiopulmonary function tests, such as electrocardiography and pulmonary function tests, can be used to evaluate the patient's cardiopulmonary reserve capacity. Patients with poor cardiopulmonary function have a higher risk of developing cardiopulmonary-related complications

during chemoradiotherapy, so the treatment regimen should be carefully selected and the treatment dosage adjusted.

4.4. Follow-Up and Quality of Life for Long-Term Survivors

For long-term survivors of esophageal cancer after chemoradiotherapy or chemotherapy, long-term follow-up and improvement of quality of life are of great significance. Long-term follow-up can facilitate the timely detection of tumor recurrence and metastasis, as well as treatment-related long-term complications, providing a basis for further treatment. Regular imaging examinations, such as computed tomography (CT) and magnetic resonance imaging (MRI), can be used to monitor tumor recurrence. Regular blood tests to detect tumor markers and other indicators help in the early detection of tumor recurrence and metastasis. Long-term follow-up also allows for monitoring of changes in the patient's physical status and quality of life, and provides necessary rehabilitation guidance and psychological support for the patient.

Improving the quality of life of long-term survivors requires efforts in multiple aspects. Providing rehabilitation guidance is key: personalized rehabilitation plans should be developed based on the patient's physical recovery status. For patients with dysphagia after radiotherapy, they should be guided to perform swallowing function training, such as practicing swallowing saliva and swallowing pureed food, to gradually restore swallowing function. For patients with limb weakness after chemotherapy, they should be advised to engage in appropriate physical exercises, such as walking and tai chi, to enhance physical strength. Psychological support should not be overlooked either. The cancer treatment process and the pressure of long-term survival may cause psychological problems in patients, such as anxiety and depression. Medical staff should maintain close communication with patients, understand their psychological state, and provide psychological counseling and comfort. Patients should be organized to participate in psychological counseling activities or patient support groups, allowing them to communicate and encourage each other, thereby enhancing their psychological resilience. Regular re-examinations are also an important measure to improve quality of life: through re-examinations, potential problems can be detected and addressed in a timely manner, enabling patients to live with peace of mind. Generally, it is recommended that patients undergo re-examinations every 3-6 months in the first 2 years after treatment; every 6-12 months from 2 to 5 years after treatment; and annually after 5 years[14]. Re-examination items include imaging examinations, blood tests, and endoscopy, to comprehensively assess the patient's physical condition.

5. Conclusion

Both chemotherapy and chemoradiotherapy hold important positions in the treatment of esophageal cancer, yet there are significant differences between them in terms of efficacy, safety, and clinical application.

In terms of efficacy, chemoradiotherapy is significantly superior to chemotherapy alone in local control rate, distant metastasis rate, and survival rate. Through the synergistic effect of radiotherapy and chemotherapy, chemoradiotherapy can more effectively control the growth of local tumors, reduce the risk of distant metastasis, and thereby prolong patients' survival. Among patients with locally advanced esophageal cancer, the local control rate of chemoradiotherapy is notably higher than that of chemotherapy alone, and the 5-year survival rate is also significantly improved.

In terms of safety, the main adverse reactions of chemotherapy include myelosuppression, gastrointestinal reactions, and impairment of liver and kidney function. Due to the superimposition of adverse reactions from radiotherapy and chemotherapy, chemoradiotherapy has a higher incidence of adverse reactions—such as radiation esophagitis and radiation pneumonitis—and exerts a more severe impact on patients' quality of life. Specifically, the incidence of radiation esophagitis in chemoradiotherapy can be as high as 60%-80%, causing immense suffering to patients.

In clinical application, the selection of treatment regimens must comprehensively consider factors such as patients' physical status, tumor stage, and pathological type. Patients with poor physical status may be more suitable for chemotherapy alone, while chemoradiotherapy may be a better option for patients with good physical status and severe local tumor invasion. Controversies also exist regarding

the optimal timing and sequence of chemoradiotherapy: although concurrent chemoradiotherapy offers better efficacy, it is associated with more severe adverse reactions; sequential chemoradiotherapy has relatively scattered adverse reactions but a longer treatment cycle, which may increase the risk of tumor progression.

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