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IS RADIATION THERAPY STILL USED IN THE TREATMENT OF GASTRIC CANCER?

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ABSTRACT

Gastric cancer is one of the most prominent global health challenges. Despite recent declines in incidence and mortality, this cancer remains the fifth most commonly diagnosed cancer and the third leading cause of cancer-related deaths worldwide. The treatment of gastric cancer requires a multidisciplinary approach, the choice of which depends on the stage of the disease and the patient's overall condition. The mainstay of treatment is surgical resection with D2 lymphadenectomy and adjuvant or neoadjuvant radio- and chemotherapy. Currently, radiation therapy is widely used in several critical areas of gastric cancer treatment.

Aim: The aim of this study is to evaluate the current use and effectiveness of radiotherapy in the treatment of gastric cancer, as well as the prospects for the further development of this therapeutic method.

Material and methods: This study is based on a systematic review of several dozen scientific publications identified through PubMed and Google Schoolar databases using keywords "gastric cancer", "radiotherapy", "chemoradiotherapy".

Conclusions: In clinical practice, radiotherapy is primarily used as an adjuvant treatment. In perioperative therapy, it is combined with chemotherapy before surgery to reduce tumor size and after surgery to reduce the risk of recurrence and the development of micrometastases. Additionally, it is used as a palliative treatment for patients with advanced-stage disease who are not eligible for surgery. Emerging evidence also suggests potential benefits of incorporating radiotherapy into the management of patients with limited metastatic disease.

KEYWORDS

Gastric Cancer, Radiotherapy, Chemoradiotherapy, Adjuvant Radiotherapy, Neoadjuvant Radiotherapy, Stereotactic Body Radiotherapy

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1. Introduction

Gastric cancer is one of the greatest challenges facing modern oncology. In 2020, approximately 1.1 million new cases were diagnosed worldwide, and the disease was responsible for approximately 770,000 deaths. The incidence is on average twice as high in men as in women, particularly in Asian countries. Despite a decline in incidence in recent years, this cancer remains one of the leading causes of cancer-related mortality worldwide [1,2]. The development of gastric cancer is a multifactorial process. Risk factors for the disease include, among others: Helicobacter pylori infection and Epstein-Barr virus (EBV) infection. In addition to infectious factors, lifestyle, smoking, alcohol abuse, obesity, and genetic predisposition play a significant role [2]. The pathogenesis of gastric cancer is extremely complex. This process often begins with a cascade of inflammatory changes, progressing from chronic gastritis, through atrophic gastritis and intestinal metaplasia, to dysplasia and cancer. The prognosis for gastric cancer is poor. The five-year survival rate ranges from 20–30% (depending on the region). This is primarily due to the disease's long asymptomatic course. Most patients are not diagnosed until an advanced stage, often with distant metastases, which limits treatment options. The TNM stage at the time of diagnosis is the most important prognostic factor [3]. In the face of rapid advances in innovative treatment methods, such as immunotherapy, radiation therapy continues to demonstrate proven efficacy in the treatment of gastric cancer. It remains an integral pillar of multidisciplinary treatment, which includes surgery, chemotherapy, and targeted therapy. Currently, the use of radiation therapy covers several key areas. Importantly, genetic changes in the DNA damage response pathway, found in about a quarter of cases of advanced gastric adenocarcinoma - may account for the sensitivity of cancer cells to radiation [4]. In perioperative treatment, radiotherapy is used in combination with chemotherapy to reduce tumor mass before surgery or after surgery to reduce the risk of recurrence and micrometastases. Radiotherapy is also used as palliative treatment in patients with advanced-stage disease who are not eligible for surgical treatment. Our work aims to focus on the latest reports and scientific publications from recent years regarding radiotherapy in the treatment of gastric cancer, to assess its current application and efficacy, and to explore the prospects for the further development of this therapeutic method [1,2,3].

2. Radiotherapy and Standards of Procedure in Treatment of Gastric Cancer

In the past, the MacDonald regimen was the classic protocol for combined therapy (chemoradiotherapy). It was used in patients who had undergone radical resection of gastric cancer with a high risk of recurrence and, for many years, served as the standard of adjuvant care for this patient group. The regimen involved combining chemotherapy based on 5-fluorouracil and leucovorin with radiation therapy targeting the tumor bed and regional lymph nodes. Treatment began with a 5-day cycle of chemotherapy, followed by the initiation of chemoradiotherapy approximately 4 weeks later. Although the MacDonald regimen remains a component of adjuvant therapy, due to the high rate of complications (46.4% grade 3 and 4 toxicity), it requires rigorous patient selection and monitoring of their general condition throughout the procedure. Currently, due to the development of other therapeutic methods focused on intensive perioperative treatment and the high toxicity of the regimen itself, the use of the MacDonald regimen has been marginalized [5]. In recent years, guidelines for the treatment of gastric cancer have undergone significant evolution. Currently, the basis of management is a multidisciplinary approach, taking into account the stage of the disease, the possibility of resection, and the biological characteristics of the tumor. Given that this disease is still most often diagnosed at advanced stages, an essential step in ensuring the effectiveness of therapy is an accurate diagnosis and assessment of the clinical stage. However, current diagnostic standards go beyond the traditional TNM classification by incorporating molecular testing. Routine biomarker testing, including verification of human epidermal growth factor receptor 2 (HER2) status, as well as assessment of deficient DNA mismatch repair (dMMR) and high microsatellite instability (MSI-H), have become essential components of modern oncology. In the case of locally advanced gastric cancer without evidence of distant metastases, the treatment of choice is surgical intervention. The gold standard is total or partial gastrectomy combined with extended D2 lymphadenectomy. It is worth noting that in clinical practice, the importance of minimally invasive techniques (primarily laparoscopic methods) is growing. According to guidelines, surgical treatment should constitute only one element of a broader regimen encompassing perioperative management. The use of neoadjuvant chemotherapy, particularly recommended for patients with stage III disease, aims to reduce tumor mass prior to surgery and to eliminate any potential micrometastases early on. This process is supplemented by postoperative adjuvant therapy, in the form of chemotherapy or chemoradiotherapy, which aims to reduce the risk of disease recurrence. In advanced stages of the disease with widespread cancer, where surgical resection is not possible, the primary therapeutic goal becomes prolonging patient survival and improved quality of life through systemic therapy. In these cases, chemotherapy is used, most often based on two- or three-drug regimens incorporating platinum derivatives and fluoropyrimidines. For patients with HER2 overexpression, the first-line treatment is the addition of trastuzumab to chemotherapy. In contrast, for patients with dMMR/MSI-H, immune checkpoint inhibitors (such as pembrolizumab or nivolumab) have demonstrated efficacy. In subsequent stages of treatment for advanced-stage disease, anti-angiogenic therapies are used to inhibit the development of abnormal blood vessels. [1,3,6].

3. Radiotherapy in Clinical Practice

In clinical practice, radiation therapy is primarily used as an adjuvant treatment for stomach cancer, particularly in patients who have undergone resection with lymphadenectomy, where its goal is to eradicate microscopic foci of disease and improve recurrence-free survival. Radiotherapy is also used in neoadjuvant therapy for so-called downstaging, i.e., reducing tumor mass prior to planned surgery. In cases of locally advanced disease or in patients ineligible for surgery, radiotherapy serves as palliative treatment, effectively controlling the symptoms of the disease. Due to the complex anatomy of the abdominal cavity and the stomach's close proximity to critical organs at risk (OARs), such as the liver, kidneys, spinal cord, pancreas, and duodenum, the precision of dose delivery is a key factor in ensuring treatment safety. Traditional three-dimensional conformal radiotherapy (3D-CRT), although it represented a significant advance over historical two-dimensional techniques in its time, is characterized by a relatively low conformity index (fit). Dosimetric studies show that its use is associated with greater exposure of healthy tissues, which consequently is linked to an increased risk of acute radiation toxicity, particularly affecting the gastrointestinal tract and kidneys. [7,8,9]. Intensity-modulated radiation therapy (IMRT) was developed in response to the limitations of 3D-CRT. This technique, which most often utilizes a system of multiple converging radiation beams, allows for highly precise shaping of the dose distribution around the planned treatment volume (PTV). Studies indicate the superiority of IMRT over 3D-CRT in terms of sparing critical organs while maintaining optimal tumor coverage. Particular attention is drawn to IMRT's ability to spare liver tissue, as evidenced by the lowest average dose delivered to this organ compared to other methods, as well as a significant reduction in dose

within the intestinal loops. [6,8,9] Another radiotherapy technique is volumetric modulated arc therapy (VMAT). This technique involves the dynamic delivery of radiation during the continuous rotation of the accelerator head, with simultaneous modulation of the beam shape and dose rate. VMAT provides the highest conformity index among available methods. This enables not only optimal coverage of the tumor with the therapeutic dose but also a reduction in the number of treatment fractions and a significant shortening of the duration of a single fraction, which reduces the risk of side effects. In terms of critical organ protection, VMAT is considered comparable to or better than IMRT for certain malignant tumors, including those of the head and neck, prostate, lung, the cervix, and the pancreas; however, there is a lack of a detailed comparative analysis between IMRT and VMAT in the treatment of gastric cancer. Nevertheless, scientific reports do not demonstrate a clear superiority of the VMAT technique over conventional IMRT in terms of liver protection [6,8].

4. The Role of Radiotherapy in Palliative Treatment

Gastric cancer is often diagnosed at an advanced stage. Unlike pre- and postoperative radiation therapy, which is widely used in Europe and the United States as part of curative treatment, palliative radiation therapy (RT) is used less frequently [10]. However, it is of significant clinical importance because it is a non-invasive method effective in alleviating disease symptoms, such as pain control, treatment of ulcers and infiltrative lesions, as well as relief of dyspnea, gastrointestinal obstruction, and reduction of tumor mass causing compression [10,11]. In clinical practice, palliative RT in patients with advanced gastric cancer is used primarily to treat uncontrolled bleeding, thereby contributing to an improvement in patients' quality of life [12]. To evaluate the efficacy of available treatments for bleeding associated with gastric cancer, a study was conducted comparing RT and transarterial embolization (TAE), analyzing both immediate and long-term outcomes. The efficacy of the methods was assessed based on the achievement of hemostasis, defined as the absence of the need for blood transfusion for 14 consecutive days from the start of treatment and the absence of the need for further interventions aimed at controlling bleeding, such as surgery, endoscopic hemostasis, RT, TAE, or the initiation of new therapy. The study included 28 patients, of whom 19 underwent RT and 9 underwent TAE. The median age was 73 years (range 50-91) in the RT group and 72 years (range 59-77) in the TAE group. In the RT group, most patients received a radiation dose exceeding 30 Gy, whereas various embolization techniques were used in the TAE group. RT was associated with a higher rate of immediate hemostasis than TAE (94.7% vs. 66.7%; p=0.047). However, the incidence of rebleeding was lower in the RT group (15.8%) than in the TAE group (44.4%). Ultimately, RT demonstrated greater efficacy in achieving primary hemostasis compared to TAE; however, both methods had a comparable impact on long-term treatment outcomes [13]. Another study included 31 patients with inoperable gastric cancer complicated by bleeding, who underwent hemostatic RT as a palliative treatment. All patients initially received RT at a dose of 20 Gy divided into 5 fractions. In cases of recurrent bleeding, selected patients additionally underwent re-irradiation at a dose of 15 Gy, also in 5 fractions. The initial treatment achieved a high hemostatic efficacy of approximately 80% of patients, confirming RT as an effective method for controlling bleeding in this patient group. Survival analysis showed that the median survival was approximately 76 days in patients treated with RT alone, whereas in the group that also received re-irradiation, it increased to approximately 112 days. The study authors emphasized that RT at a dose of 20 Gy is an effective and safe method for controlling bleeding, while the option of re-irradiation represents a significant expansion of the therapeutic strategy, potentially improving clinical outcomes and prolonging patient survival [14]. The study "Efficacy of radiotherapy for gastric bleeding associated with advanced gastric cancer" analyzed 57 patients who received palliative RT between 2009 and 2019 due to bleeding from a gastric tumor. The aim was to determine how effectively RT controls bleeding and whether different doses and fractionation schedules affect treatment outcomes. The study assessed, among other things, changes in hemoglobin levels before and after RT, the need for blood transfusions, and the occurrence of rebleeding, defined as a drop in hemoglobin below 7 g/dL or the need for a blood transfusion after treatment. Patients received various RT regimens, most commonly 25 Gy in 5 fractions. Mean Hb levels before, immediately after, 1 month, and 2 months after RT (6.6, 9.7,10.3, and 9.7 g/dL, respectively) were significantly higher than before RT (all $p<0.001$). The median time to recurrence of bleeding was approximately 6.4 weeks. Additionally, it was demonstrated that better bleeding control was associated with greater tumor response on imaging studies and longer patient survival. In summary, the study showed that palliative RT is an effective and safe method for controlling bleeding in advanced gastric cancer [15]. The results showed that during the observation period, there was a significant improvement in shortness of breath, pain, and anxiety. After adjusting for PPI scores, the improvement in these symptoms remained

statistically significant, suggesting that the effect of RT was independent of patient prognosis. At the same time, a higher PPI was associated with greater symptom severity at baseline and at subsequent time points, but did not affect the degree of improvement. Improvements in fatigue and anxiety were observed only in patients receiving lower biologically effective doses of RT (≤14.4 Gy), which may indicate that more intensive treatment is associated with greater toxicity and burden on the patient. In summary, palliative RT in patients with gastric cancer leads to a significant reduction in dyspnea, pain, and anxiety within a few weeks of treatment, regardless of expected survival, although higher doses may limit improvement in certain symptoms due to adverse effects [16].

5. Neoadjuvant Radiotherapy

Although gastric cancer is often diagnosed at advanced stages, as many as 2/3 of patients will have locally advanced gastric cancer (LAGC), which is often defined as a primary tumor extending beyond the muscularis propria (cT3-T4) or with nodal metastasis (cN+) and no distant metastasis (cM0). LAGC is typically treated with surgical resection and perioperative chemotherapy. This approach aims to improve treatment efficacy by facilitating tumor resection, eliminating micrometastatic disease, and allowing for the administration of part of the therapy prior to gastrectomy, when it is generally better tolerated by patients[17,18]. Since the publication of the landmark MAGIC trial in 2006, perioperative chemotherapy has become the widely recommended standard of care for patients with LAGC. The study included 224 patients with resectable gastric cancer, gastroesophageal junction (GEJ) cancer, or esophageal cancer who were randomly assigned to receive three cycles of chemotherapy (epirubicin, cisplatin, and fluorouracil-the ECF regimen) before and after surgery, or to undergo surgery alone. A significant improvement in overall survival was demonstrated in the perioperative treatment group-5-year survival was 38% compared to 24% in the group that underwent surgery without chemotherapy. Disease-free survival was also higher in the combination therapy group (34% vs. 19%). In addition, perioperative chemotherapy increased the rate of radical resection (84% vs. 73%)[18, 19]. The FLOT-AIO study, published in 2019, significantly changed the existing standard of perioperative chemotherapy for patients with LAGC. The study enrolled 716 patients with resectable adenocarcinoma of the stomach or GEJ, at a stage of at least cT2 and/or with lymph node involvement, without distant metastases. Patients were randomly assigned to receive treatment according to the classic MAGIC regimen in combination with surgery or to the more intensive FLOT regimen, consisting of fluorouracil, oxaliplatin, and docetaxel, administered before and after surgery. The results showed a clear advantage of the FLOT regimen-the median overall survival was 50 months compared to 35 months in the MAGIC group, and the three-year survival rates were 57% and 48%, respectively. Furthermore, complete pathological response was more common in patients treated with the FLOT regimen (16%) than in the group receiving treatment according to the MAGIC regimen (6%)[18,20]. The study “Neoadjuvant versus Postoperative Chemoradiotherapy is Associated with Improved Survival for Patients with Resectable Gastric and Gastroesophageal Cancer” analyzed 152 patients with adenocarcinoma of the stomach (42%) or the GEJ(58%), who underwent surgical treatment between 2005 and 2017 and received chemoradiotherapy (CRT) in a preoperative or postoperative regimen. The primary endpoint was overall survival (OS). The median follow-up duration was 37.5 months. Most patients (67%) received CRT before surgery, while 33% received it after surgery. Patients treated with neoadjuvant therapy were more likely to be male, had tumors located at the GEJ, lymph node involvement, and a higher clinical stage. The median radiation dose was higher in the neoadjuvant group (50.4 Gy) than in the postoperative group (45.0 Gy). In the preoperative group, 26% of patients achieved a complete pathological response, and the rate of R0 resection was significantly higher compared to postoperative treatment (95% vs. 76%). Furthermore, CRT administered preoperatively was associated with a significantly lower incidence of severe adverse events (10% vs. 54%). Multivariate analysis showed that the use of neoadjuvant CRT and the achievement of R0 resection were independently associated with better overall survival [16].

6. Adjuvant Radiotherapy

The article titled "Neoadjuvant versus adjuvant radiotherapy for resectable locally advanced gastric cancer: A SEER population analysis" compares the efficacy of preoperative (neoadjuvant) and postoperative (adjuvant) RT in patients with LAGC. The study included 4,790 patients treated with surgery and RT between 2004 and 2015. Patients were divided into two groups: those receiving RT before surgery (neoadjuvant) and those receiving RT after surgery (adjuvant). The results showed that both preoperative and postoperative RT improve survival compared to no RT, but better outcomes were observed for adjuvant radiotherapy. Median survival was higher in this group for both the intestinal type (49 vs. 36 months, HR 1.21, 95% CI 1.10-1.33, P < 0.001) and the diffuse type (32 vs. 26 months, HR 1.20, 95% CI 1.00-1.44, P=0.050). A particularly clear benefit of postoperative RT was observed in patients with selected disease stages (including T1-2N+, T3N-, T3N+). In patients with T4N- and T4N+ stages, no difference in survival was observed[21]. A meta-analysis has shown that CRT is an effective treatment for LAGC. Both adjuvant CRT and CRT administered prior to surgery demonstrate an advantage over chemotherapy (CT) alone, RT, and surgery alone. Adjuvant CRT significantly reduces the risk of recurrence and metastasis compared to adjuvant CT (OR = 1.76; 95% CI: 1.29–2.42) and RT alone (OR = 1.83; 95% CI: 0.98–3.40), and also reduces mortality (OR = 0.45; 95% CI: 0.23–0.86). Compared to surgery alone, CRT improves local disease control and reduces the risk of recurrence and metastasis (OR=2.18; 95% CI: 1.21–3.93). The results suggest that the combination of the local effect of RT with the systemic effect of CT enables more effective elimination of micrometastases and reduces the risk of disease recurrence, confirming the significant role of chemoradiotherapy in the treatment of patients with locally advanced gastric cancer [22]. A different study from 2022 compared the efficacy and safety of neoadjuvant chemoradiotherapy (NACRT) and neoadjuvant chemotherapy alone (NACT) in patients with LAGC. The study included 75 patients who received one of these preoperative treatments and subsequently underwent gastrectomy and adjuvant chemotherapy. The primary endpoint was the rate of R0 resection. The proportion of patients who underwent surgery was similar in both groups (approximately 76%), as was the rate of R0 resection (approximately 73% in both arms). However, the NACRT group had a significantly higher rate of deep pathological response compared to the NACT group (37.9% vs. 17.9%). No significant differences in the incidence of postoperative complications were observed between the groups. With a median follow-up of nearly 60 months, 5-year overall survival was higher in the NACRT group (61.9%) than in the NACT group (50.1%), and longer progression-free survival was also observed (63.4 vs. 37.3 months) [23]. In summary, the use of S-1-based NACRT did not increase the rate of R0 resection, but led to better tumor regression while maintaining a comparable safety profile compared to neoadjuvant chemotherapy alone [24]. The aim of the CLASSIC trial was to compare the efficacy of adjuvant chemotherapy with capecitabine and oxaliplatin versus observation alone following radical D2 gastrectomy in patients with stage II–IIIB gastric cancer. A total of 1,035 patients were enrolled in the study and randomly assigned to the adjuvant chemotherapy group (520 patients) or the observation group (515 patients). Treatment consisted of eight 3-week cycles of capecitabine in combination with oxaliplatin. In the five-year analysis, with a median follow-up of 62.4 months, a significant benefit of adjuvant therapy was demonstrated. Disease-free survival was significantly higher in the chemotherapy group (68% vs. 53%), and the risk of recurrence or death was significantly lower compared to the observation group. Similarly, an improvement in overall survival was observed-five-year OS was 78% in the treatment group and 69% in the control group. A lower mortality rate also confirmed the advantage of adjuvant chemotherapy. In summary, the results of the CLASSIC trial indicate that the use of postoperative chemotherapy with capecitabine and oxaliplatin following radical D2 gastrectomy significantly improves both disease-free survival and overall survival in patients with stage II and III gastric cancer, confirming its importance as the standard of adjuvant treatment [25].

7. Radiotherapy in Oligometastatic Disease

Radiotherapy in oligometastatic disease 6.1. Oligometastatic gastric cancer The concept of oligometastatic disease in gastric cancer has not yet been fully defined, but it is commonly described as a clinical state between locally confined and systemic metastatic disease with metastatic lesions that are localized, technically resectable at diagnosis and present favorable survival outcomes with local treatments like surgery, ablation or stereotactic body radiotherapy. Due to a lack of consensus on definitions and treatment standards, a European panel of experts established a Consortium OligoMetastatic Esophagogastric Cancer (OMEC). According to the OMEC, oligometastatic disease is defined as metastases confined to a single organ with maximum three lesions or a single distant lymph node metastasis in patients with synchronous disease. Specifically, oligometastatic involvement includes up to two bilobar or three unilobar liver metastases, up to three unilateral lung lesions, unilateral adrenal metastasis, single bone or soft tissue metastasis. The recommended treatment strategy is systemic chemotherapy, followed by a reassessment of the disease and local treatment, such as surgical resection or stereotactic radiotherapy [4,26].

8. Stereotactic Body Radiotherapy

Stereotactic body radiotherapy (SBRT) is a modern treatment method based on advanced imaging and treatment planning techniques. It involves delivering high doses of radiation with great precision to the target tumor areas. This allows for maximum preservation of the surrounding organs at risk [27]. SBRT is commonly used as an aggressive treatment for oligometastases, but there is limited research on the use of SBRT in patients with oligometastatic gastric cancer. However, there are reports that demonstrate its potential, particularly in cases of liver metastases. The study by Akamal et al. reported two cases of long-term survival following SBRT for liver metastases in oligometastatic gastric cancer. The patients were treated with SBRT following gastrectomy and chemotherapy. In the first case, a 65-year-old man achieved complete response (CR) of two liver metastases after SBRT. SBRT was performed 13 months after distal gastrectomy with postoperative S-1 chemotherapy and the patient remained recurrence-free nearly 5 years after SBRT. In the second case, a 71-year-old woman developed metachronous liver metastasis during adjuvant chemotherapy and underwent SBRT 11 months after gastrectomy. The Patient was then administered weekly paclitaxel. The right hepatic lobectomy performed 13 months later for suspected recurrence revealed no viable tumor cells, confirming CR. The patient remained recurrence-free 4 years after SBRT [28]. Kimura et al. reported a case of metastatic gastric cancer successfully treated with SBRT in a 77-year-old man following total gastrectomy for stage II gastric adenocarcinoma. Metastases to the liver and peritoneum developed and progressed despite chemotherapy. SBRT was delivered to the liver metastases (52.8 Gy in 4 fractions), resulting in marked tumor regression and sustained disease control. The patient remaining recurrence-free after 2 years. Reported toxicities included grade 3 neutropenia, grade 2 AST/ALT elevation, and late grade 2 pneumothorax with pleural effusion [29]. Another study presents the case of a patient with AFPGC who has been surviving for five years following SBRT for livermetastases. α-Fetoprotein (AFP) producing gastric carcinoma (AFPGC) is a special subtype that is clinically characterized by a high incidence of liver metastasis and poor prognosis. Radiotherapy is rarely indicated for liver metastases from AFPGC because of a lack of evidence of the radiosensitivity of this tumor and a significant risk of radiation-induced liver diseases. Although, SBRT has becoming recommendable alternative for the treatment of primary liver cancer, there is currently no information on the efficacy of SBRT for liver metastases from AFPGC. In this case the patient developed a single liver metastasis two months after total gastrectomy with D2 lymphadenectomy. Despite seven cycles of S-1 chemotherapy, only a minor radiological response was achieved. Finally patient underwent SBRT for the liver lesion (48 Gy in 4 fractions,dose covering 90% of the planning target volume). CT revealed a significant response two weeks after the completion of SBRT.It resulted in CR two years later. The complete response was durable, with no evidence of recurrence 62 months after the diagnosis of liver metastasis [30]. A case series evaluated SBRT for metastatic lesions from gastric cancer refractory to chemotherapy. Four patients received SBRT in dose 52.8 Gy in 4 fractions - three patients with liver metastases and one with lung metastasis. CR was achieved in all patients with liver metastases, whereas no response was observed in the lung lesion. Two patients remained free of liver recurrence at 27 and 41 months after SBRT. Treatment was generally well tolerated, with no grade 3/4 toxicities reported. In one patient, was observed pneumothorax and pleural effusion. These findings suggest that SBRT may provide durable local control in selected patients with oligometastatic gastric cancer, particularly in liver metastases [31].

9. Conclusions

The treatment of gastric cancer requires a multidisciplinary approach, the choice of which depends on the stage of the disease and the patient's overall condition. For patients with advanced, inoperable cancer, palliative radiation therapy plays a significant role, effectively alleviating symptoms-particularly bleeding, pain, and shortness of breath-and improving quality of life. Studies indicate that RT is a safe method that achieves a high rate of bleeding control and can be effectively repeated in the event of recurrence. For patients with locally advanced gastric cancer, the standard of care remains combination therapy, which includes surgery and systemic therapy and/or radiation therapy. Perioperative treatment is of particular importance; as demonstrated in studies such as MAGIC and FLOT-AIO, it significantly improves overall survival and increases the rate of radical resection. Neoadjuvant therapy, including chemoradiotherapy, allows for tumor downstaging, increases the chances of R0 resection, and improves prognosis, while maintaining an acceptable safety profile. In turn, postoperative treatment, including chemotherapy or chemoradiotherapy, also plays an important role in reducing the risk of recurrence and improving survival. Study results and meta-analyses indicate that both adjuvant chemotherapy and more complex strategies, such as chemoradiotherapy or HIPEC, may provide additional clinical benefits. An example is the CLASSIC trial, which confirmed the efficacy of

adjuvant chemotherapy in improving survival. Overall, the available data indicate that optimal treatment for gastric cancer should be individually tailored, taking into account the possibility of pre- and postoperative therapy, while radiation therapy-both palliative and as part of combination therapy-remains an important therapeutic tool at various stages of the disease. Furthermore, SBRT has the potential to achieve a durable response in the context of oligometastatic disease. This aggressive approach may allow for effective disease control with limited toxicity using just a few SBRT fractions. However, there is a lack of randomized phase 3 trials comparing SBRT with other treatment strategies for oligometastatic gastric cancer.

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