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Clinical outcomes of palliative 3-dimensional conformal external beam gastric radiotherapy: single center experience

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ABSTRACT

Aim: Patients diagnosed with locally advanced and/or metastatic gastric cancer and who cannot undergo surgery may need palliative treatment during their follow-up. There is scarce data about outcomes of palliative gastric radiotherapy (RT). In this study, we aimed to investigate the effect of 3-D external beam RT on oncological outcomes, as a non-invasive method.

Material and Method: From 2013 to 2017, sixteen gastric cancer patients treated with palliative external RT in our institutional clinic were evaluated. Only patients who received palliative gastric radiotherapy for obstruction, pain and bleeding were analyzed, and patients who had previously received RT to the abdomen or who were given RT for adjuvant purposes were not included in the analysis.

Results: Seven patients (43%) were not able to finish the planned palliative course. Thirty Gray with 10 fractions was the most planned RT schedule. Almost half of the patients (%56) received chemotherapy before RT. Overall survival was found to be median 2 months. Median survival was better in patients who were able to receive 28 Gy bioequivalent dose (4 vs 0.3 months, p≤0.00). Purpose of palliation also found to be a significant factor on survival. Patients who were referred for pain have found to be better survival rather than bleeding and obstruction (13 vs 0.7 months, p=0.03).

Conclusion: External radiotherapy is an easily applicable and effective method for palliation in gastric cancer patients. Early referral for radiotherapy in patients who need palliation may increase oncological outcomes. It has been observed that the prognosis is worse in patients who received palliative radiotherapy due to gastric bleeding and obstruction.

Keywords: Gastric cancer, radiotherapy, gastrointestinal hemorrhage

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INTRODUCTION

Gastric cancer is the third most common cancer worldwide and also fifth in Turkey (1). 5-year overall survival is approximately 20% (2,3). Some patients still may not be approached curatively despite the improvements and new technologies in imaging, surgery and adjuvant therapies. Patients who could not have gastrectomy or locally recurred during the follow-up may need palliation for the local disease during follow-up.

Palliative radiotherapy is a non-invasive, easily applicable and successive approach that has been used for many sites, diseases and conditions like pain, obstructive symptoms and bleeding. Despite the common use of radiotherapy for gastric palliation, there is scarce data in the literature on that topic.

In this study, we tried to evaluate palliative radiotherapy outcomes in patients who were referred for symptomatic local disease, such as bleeding, pain and obstruction, as a non-invasive approach.

MATERIAL AND METHOD

All the medical records between 2013 and 2017 at Ankara Traininig and Research Hospital Radiation Oncology Department were reviewed retrospectively in which patients diagnosed with gastric cancer who were referred for palliative radiotherapy (RT) with any symptoms were included in this study. This study has been initiated after ethical approval taken from Ankara City Hospital No: 1 Clinical Researches Ethics Committee (Date: 25.08.2021, Decision No: E1-21-1954). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

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We excluded the patients who were evaluated in a definitive setting for medically inoperable newly diagnosed patients. Data was collected from the institutional registry and our local radiation oncology database. Patients who had undergone prior RT were excluded. Sixteen metastatic patients who had been treated with palliative gastric RT were included in the current study. Overall survival was calculated from the first day of radiotherapy to death. Patient characteristics were shown in **Table 1**.

Table 1. Patient Characteristics	
Median Age n, (Min-Max)	63 (12-85)
Sex n, (%)	
Female	3 (19)
Male	13 (81)
Histopathology n, (%)	
Adeno Ca	14 (88%)
Malign Epithelial Tm	2 (12%)
Metastatic Spread n,(%)	
One site	8 (50%)
At Least Two Sites	7 (44%)
Unknown	1 (6%)
Symptom n,(%)	
Bleeding	10 (62%)
Obstruction	3 (19%)
Pain	3 (19%)
Median RT Dosage (Min-Max)	4250 cGy (180-4000)
Chemotherapy before RT n, (%)	
Yes	9 (56%)
No	7 (44%)

3-dimensional conformal radiotherapy was used for all treatments. The target volume was the whole stomach and 0.5-1 cm planning target volume margins were added for setup errors and organ movements. Most of the patients were male and the most common RT protocol was 30 Gy in 10 fractions daily. α/β value was taken as 10 for bioequivalent dose (BED10) calculations.

Statistical analysis was performed using the SPSS software version 24 (IBM, Armonk, NY). Categorical data were given as numbers and proportions, Median and minimum-maximum levels were used for non-normally distributed quantitative variables. All tests were two-sided and a 0.05 p-value or less was considered statistically significant. Overall survivals were calculated from the first day of RT to death with the Kaplan-Meier estimation method. Log-rank statistics were used for analyzing the effect of symptom type, metastatic burden and RT dose on survival.

RESULTS

Patient Characteristics

In this single-center study, 16 patients were found referring to our institution for palliative gastric RT. None of the patients has prior RT history. The median age was found 63 (12-85) and 13 (81%) patients were male. All patients except one were metastatic at the time of diagnosis and no patient underwent gastrectomy before RT. Eight patients had a single metastatic disease at the time of diagnosis and the remaining seven patients had multiple metastases. While the tumor site was widespread in more than one region of the stomach in nine patients, 6 patients had a single localization. Adenocarcinoma was found as common histology and bleeding was the major referring symptom. Three thousand cGy in ten fractions was the most commonly used regimen. Chemotherapy has already begun for progression in 9 patients (56%) before palliative RT with minimal or nil response.

Outcomes

All the patients were dead, and any censored data did not exist at the time of the analysis. Median overall survival (OS) was found at 2 months for the whole cohort. After the beginning of radiotherapy, only 7 (43%) patients were able to finish the planned palliative RT schedule. The median BED10 value was 28.8 Gy. Overall survival was statistically better for those who were able to receive 2800 cGy biologically equivalent dose (p≤0.00) (**Figure 1**).

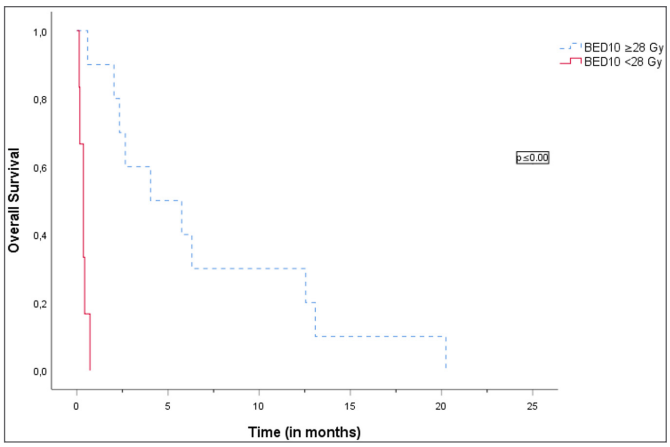

Figure 1. Kaplan-Meier Curves based on the Bioequivalent Radiotherapy Doses for α/β=10

In terms of symptom and number of metastases, OS was found worse in patients irradiated for bleeding and obstructive symptoms rather than pain (13 vs 0.7 months, p=0.03) (**Figure 2**). We also found overall survival as 5.7 months in patients with one distant metastasis and 0.6 months for multiple (p≤0.01) (**Figure 3**). We could not find any effect of previously applied chemotherapy on survival outcomes.

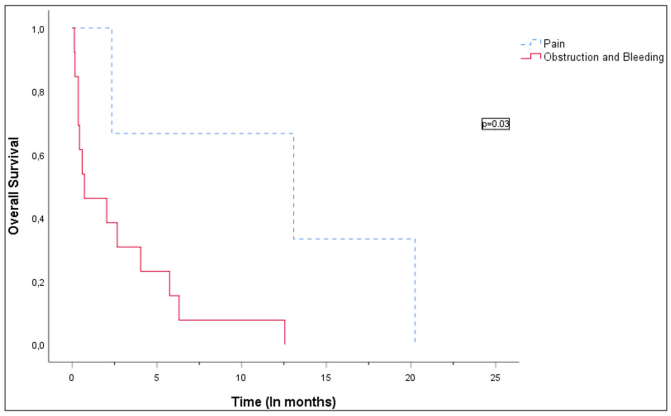

Figure 2. Kaplan-Meier Curves according to the symptoms

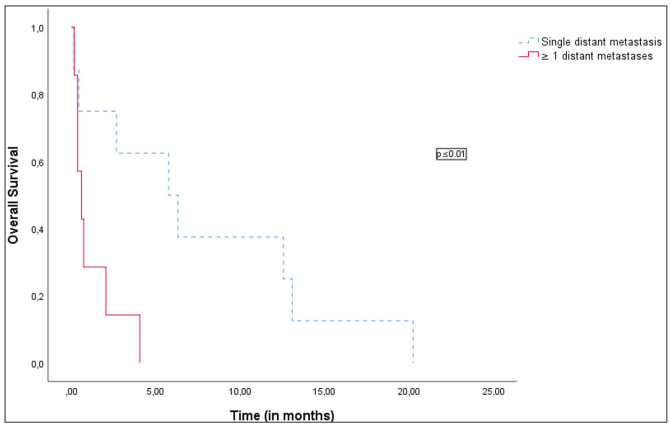

Figure 3. Kaplan-Meier curves according to the number of distant metastasis sites.

DISCUSSION

This report demonstrates that palliative radiotherapy is an effective, non-invasive approach, especially in patients referred for pain when given over 2800 cGy BED dose.

Overall survival who needs palliation in advanced gastric cancer is generally poor. It varies from 2.1 to 5.2 months in different case series despite the good responses, especially for bleeding (4-11). In most published studies on this topic, the patient population includes both metastatic and non-metastatic patient groups. Only metastatic patients were examined in the studies of Hashimoto (5) and Kondoh et al. (10) like the current study. In these studies, which included 19 and 15 patients, overall survival was found to be 3.4 months and 2.1 months, respectively. In our relatively but comparable small series with 16 metastatic patients, overall survival was found to be 2 months, and in this sense, it was found to be similar to the published data. The total applied radiation dose also seems to have a role in outcomes. In the study of Mitsuashi et al. (12) from Japan, where the incidence of gastric cancer is high, survival analysis was performed according to palliative RT dose. Here, doses with BED10 value above and below 39 Gy were compared and no contribution to survival was determined. The effect of palliative radiotherapy dose on survival was also evaluated in our study. The survival of patients who could receive 2800 cGy or higher bioequivalent dose (BED10) was found to be 4 months. Survival was found to be 0.3 months in patients who couldn't receive BED10 2800 cGy and this difference was significantly high (p=.0). When patients receiving less than 2800 cGy were examined, it was found that most of these patients were not able to receive the intended dose. This may be due to the initiation of palliative treatment with another non-invasive method, chemotherapy, in patients with gastric cancer who needs palliation. To start palliation with chemotherapy as first-line treatment may delay the start of radiotherapy. Additionally, systemic side effects of chemotherapy, which can continue during radiotherapy, may have a negative impact on outcomes in this group of patients. Therefore, early referral of patients who require palliative gastric radiotherapy may lead to the administration of planned palliative doses, which may increase oncological outcomes and palliation rates. In our series, only half of the patients were able to finish the complete planned course of RT.

Invasive procedures like endoscopic laser coagulation, gastrectomy and non-invasive palliative chemotherapy are the alternative approaches for palliation (13-16) and need better performance status. This may explain the use of RT in patients with poorer performance status and relatively low survival rates in our trial.

As we examined the relationship between the symptomatic reason for palliative RT and survival, significantly worse results were found in patients irradiated for bleeding and obstructive symptoms like less than a month. Patients who received palliative RT due to pain had a survival of approximately one year despite metastatic state. Therefore, even though the bleeding control was achieved, a lower survival rate with palliative RT has been observed for bleeding, and a relatively good survival rate of 13 months was found for pain.

Although some studies (11,12,17) have shown that radiotherapy is an effective method for bleeding, our data also shows the positive contribution of palliative RT on pain relief. In a series of 115 patients, Tey et al. (9) reported that 80.6% of patients had bleeding control, 45.5% had pain control, and 51.2% had obstruction palliation with palliative RT in the metastatic and non-metastatic patient group. There are also publications that have a relatively low 50% hemorrhagic response rate. Duration time for bleeding control varies between 1.5 and 11.4 months in the literature. Although the number of patients who underwent palliation due to pain and

obstruction were less, response rates were found 67% for pain and 68% for obstruction in other relatively small series (18). In a case series, three year long term symptom control for obstruction has also been reported (19).

In this study, the number of metastatic sites was also found to be a negative prognostic factor. While the survival rate was 5.7 in patients with metastases in a single metastatic site or organ other than primary cancer, survival was found to be 0.6 months in patients with more than a site. This result showed that, as expected, the cancer spread and survival were also inversely proportional in gastric cancer patients who needed palliation.

Chemotherapy can also be used concurrently with or without RT for palliation in gastric cancer (15). The role of concomitant chemotherapy with palliative radiotherapy has not been determined well. Fifty-six percent of our patients received chemotherapy. In the study by Asakura et al. (7), it was found that chemo radiotherapy may lead to a decrease in the re-bleeding events. Chemotherapy with concomitant radiotherapy is also the main treatment modality in advanced unresectable gastroesophageal junction and esophageal cancer and adding chemotherapy to radiotherapy in this group of patients improves survival (20, 21). Whilst, in a phase 3 study by the Trans-Tasman Radiation Oncology Group examining the contribution of adding chemotherapy to palliative radiotherapy in patients with esophageal cancer, it was found that while chemotherapy increasing toxicity, it did not change oncologic outcomes (22). In the current study, no difference in survival was found in the group receiving chemotherapy compared to those who received not.

CONCLUSION

External radiotherapy is an effective and easy applicable method for palliation in gastric cancer patients. Oncological outcomes may be improved with early radiotherapy initiation and higher bioequivalent RT doses. Current study demonstrated that the referral symptom for palliation has an impact on the oncologic outcome. Better results were shown in patients who received radiotherapy for pain compared to bleeding and obstruction. Prospective randomized studies are needed for further results.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara City Hospital No: 1 Clinical Researches Ethics committee (Date: 25.08.2021, Decision No: E1-21-1954)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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