Hemostatic effect of palliative radiation therapy for bleeding from unresectable gastric cancer: A case series of seven patients

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Abstract

The hemostatic effect of palliative radiation therapy (RT) for unresectable gastric cancer is unclear. We performed palliative RT (20 Gy in 5 fractions or 30 Gy in 10 fractions) in 7 consecutive patients with bleeding. The number of blood transfusions decreased significantly post-RT, supporting the hemostatic effect of palliative RT.

CASE REPORT for Clinical Case Reports

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Abstract

The hemostatic effect of palliative radiation therapy (RT) for unresectable gastric cancer is unclear. We performed palliative RT (20 Gy in 5 fractions or 30 Gy in 10 fractions) in 7 consecutive patients with bleeding. The number of blood transfusions decreased significantly post-RT, supporting the hemostatic effect of palliative RT.

(50 words = 50 words)

KEYWORDS

gastric cancer, radiation therapy, hemostasis, palliation

1 | INTRODUCTION

Advanced gastric cancer induces various symptoms, such as bleeding, anorexia, obstruction, and pain. In particular, bleeding from gastric cancer not only compromises the quality of life but also results in a life-threatening condition (1).

Palliative treatment options for bleeding from advanced gastric cancer include surgery, endoscopic hemostasis, transcatheter embolotherapy, and radiation therapy (RT) (1). Surgery is an effective treatment for bleeding from gastric cancer; however, it is eligible only for patients with a good performance status (PS) (2). Conversely, endoscopic hemostasis, transcatheter embolotherapy, and RT can be administered even to inoperable patients.

The rate of successful hemostasis by endoscopic treatment and that by embolotherapy is reported to be 31%–100% (3–5) and 40%–100% (1), respectively. Hemostatic RT is not used as commonly as those treatments (6). There have been several studies reporting the efficacy of RT on hemostasis as being approximately 50%–80% (1). However, the dose and fractionation have varied widely among studies, ranging from 8 Gy in 1 fraction to 60 Gy in 30 fractions, making the efficacy of this treatment obscure. In the clinical setting, the most commonly used dose-fractionation includes 20 Gy in 5 fractions and 30 Gy in 10 fractions.

We retrospectively analyzed the efficacy of palliative RT on hemostasis in seven patients with unresectable gastric cancer treated using dose-fractionations.

2 | CASE SERIES

Patients with pathologically-confirmed unresectable gastric cancer who met the following criteria were retrospectively analyzed: (i) bleeding from gastric cancer confirmed by endoscopic or bleeding signs as hematemesis or melena; (ii) treated with palliative RT for hemostatic purposes at Sano Kosei General Hospital between April 2019 and December 2021; and (iii) followed for at least two months post-RT. As a result, 7 patients were considered eligible for the analysis, and the median follow-up period was 5 (range, 2–9) months (**Table 1**).

All patients were treated with external-beam three-dimensional conformal RT using 10 MV-photons. Treatment planning was performed using Monaco (Elekta Co., Ltd., Stockholm, Sweden). The clinical target volume was defined as the gross tumor volume with 5-mm outward margins identified by computed tomography (**Figure 1**). Using a Synergy irradiator (Elekta), 3 and 4 patients received a total of 20 Gy in 5 fractions and 30 Gy in 10 fractions, respectively, in a 5-fractions-per-week schedule. No patients received re-irradiation for gastric cancer.

Notably, compared to 2 months before RT, the number of blood transfusions was significantly decreased in the 2 months after RT (2.42 ± 1.72 vs. 0.14 ± 0.38 , p = 0.0121 assessed by the paired *t*-test) (**Table 2**). In three-quarters of the 30-Gy patients, hemoglobin levels increased after irradiation. In contrast, the hemoglobin levels in the 20-Gy patients continuously increased in only 1 case (**Figure 2**). No adverse events of Grade [?]3 as assessed by the Common Terminology Criteria for Adverse Event (version 4.0) were observed in any patients.

3 | DISCUSSION

Our data indicate that RT of 20 Gy in 5 fractions and 30 Gy in 10 fractions can prevent a rapid decline in the hemoglobin level and reduce the frequency of blood transfusion. From this perspective, palliative RT can contribute to improving the quality of life of patients with advanced gastric cancer with bleeding.

There have been several reports on RT for advanced gastric cancer with bleeding. Lee et al. analyzed hemoglobin and blood transfusion frequency after RT for 57 patients submitted to palliative RT for gastric bleeding (7). The authors reported that the mean hemoglobin levels before, immediately after, and one and two months after RT were significantly higher than before RT. No significant differences in re-bleeding rates were observed according to the total dose (17.5–45 Gy), fractional dose (1.8–5 Gy), or fraction number (4–25 fractions). Tey et al. investigated approximately 50 patients with advanced gastric cancer (8). In that study, the median survival duration was 85 days, and 80% of patients with bleeding responded to RT. Two patients (5%) had grade 3 anorexia and gastritis, but their symptoms resolved after a week. They received 36 Gy in 12 fractions, and the authors concluded that RT was effective and well-tolerated. In Japan, no guideline has yet been established for hemostatic RT for advanced gastric cancer. Taken together, these data indicate that RT at a total of 20–30 Gy is effective in alleviating bleeding from advanced gastric cancer.

The optimal dose for achieving hemostasis in cases of advanced gastric cancer is controversial, as a review by Tey et al. reported wide inter-study variations in dose fractionation (9). Fraction sizes ranged from 1.8 to 8 Gy, and total doses ranged from 8 Gy to 50 Gy, with the most common dose fraction regimen being 30 Gy in 10 fractions. The response to RT for bleeding ranged from 50% to 80.6%. The median duration of response ranged from 1.5 to 11.4 months. This review concluded that there was no marked difference in the response rate of bleeding between regimens with a high biological equivalent dose (BED) of [?]39 Gy versus those with a low BED of <39 Gy. Furthermore, low-BED regimens appear to be adequate for symptom palliation. The BED for 20 Gy in 5 fractions and for 30 Gy in 10 fractions, as was administered to the patients in our study, was 28 and 39 Gy, respectively. Although 30 Gy in 10 fractions is classified as a high BED of [?]39 Gy, no Grade [?]3 complications were observed in our study.

In summary, we report consecutive seven patients with gastric cancer with bleeding treated with palliative RT (20 Gy in 5 fractions or 30 Gy in 10 fractions). The number of blood transfusions decreased significantly post-RT, supporting the hemostatic effect of palliative RT.

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CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Y. Hisatake, T. Higashizawa and K. Teramoto treated the patients; N. Ota, A. Adachi, and T. Oike treated the patients, collected and analyzed the data, and wrote the manuscript; A. Adachi finalized the manuscript; Y. Okamura and T. Ohno: supervised the study.

INFORMED CONSENT

This study was approved by the Ethics Review Committee of Sano Kosei General Hospital (approval number: 202109). Written informed consent is declared. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

DATA AVAILABILITY STATEMENT

Raw data are not available, as restricted by the study protocol approved by the Ethics Review Committee of Sano Kosei General Hospital (approval number: 202109).

REFERENCES

1. Kawabata H, Hitomi M and Motoi S. Management of bleeding from unresectable gastric cancer. *Biomedicines.* 2009;7:54.

2. Thumurthy SG, Chaudry MA, Chau I, et al. Does surgery have a role in managing incurable gastric cancer? *Nat Rev Clin Oncol*.2015;12:676-682.

3. Koh KH, Kim K, Kwon DH, et al. The successful endoscopic hemostasis factors in bleeding from advanced gastric cancer. *Gastric Cancer*.2013:28;1489-1495.

4. Song IJ, Kim HJ, Cho SJ, et al. Clinical outcomes of endoscopic hemostasis for bleeding in patients with unresectable advanced gastric cancer. J Gastric Cancer. 2017:17;374-383

5. Kim YJ, Park JC, Kim EH, et al. Hemostatic powder application for control of acute upper gastrointestinal bleeding in patients with gastric malignancy. *Endosc Int Open.* 2018:6;E700-E705.

6. Kosugi T, Shikama N, Saito T, et al. Nationwide surgery in Japan of palliative radiotherapy for bleeding in gastrointestinal and genitourinary tumor patients. *World J Oncol.* 2016:29-33

7. Lee J, Byun HK, Koom WS, et al. Efficacy of radiotherapy for gastric bleeding associated with advanced gastric cancer. *Radiat Oncol*.2021;16:161.

8. Tey J, Zheng H, Soon YY, et al. Palliative radiotherapy in symptomatic locally advanced gastric cancer: A phase II trial. *Cancer Medicine*. 2019;8:1447-1458.

9. Tey J, Soon YY, Koh WY, et al. Palliative radiotherapy for gastric cancer: a systematic review and meta-analysis. *Oncotarget*.2017;8:25797-25805.

FIGURE LEGENDS

FIGURE 1. A representative image of the radiation therapy (RT) plan (Case #4). Solid magenta indicates the clinical target volume. Blue triangles show the wedge for beam intensity adjustment (45deg for each).

FIGURE 2. Kinetics of hemoglobin levels within two months pre- and post-radiation therapy (RT). Day 1 indicates the day of initiation of RT. Red arrows indicate blood transfusion.

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