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# Gastric Cancer Patients Receiving Maintenance Hemodialysis After Surgery With and Without Postoperative Chemotherapy: A Case Series of 6

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**Background:** The management of gastric cancer patients who received gastrectomy and/or postoperative chemotherapy is of high importance. However, the safety and efficacy of chemotherapy in hemodialysis patients have not been established. In this study, we report 6 cases of hemodialysis patients who underwent gastrectomy for gastric cancer.

**Case Presentation:** The presented cases included 5 men and 1 woman, with a mean age of 66.3 years (range, 59–74 years). All patients underwent standard laparotomy, with 3 of 6 patients (50%) experiencing postoperative complications. Three patients who did not experience any postoperative complications could receive subsequent chemotherapy. S-1 chemotherapy regimen and uracil and tegafur chemotherapy regimen were administered to 1 and 2 patients, respectively. These 3 patients did not experience any chemotherapy-related side effects. Among the 4 patients who received a diagnosis of pathologic stages II to III, 2 patients treated with postoperative chemotherapy achieved better prognoses than those who did not receive chemotherapy (mean, 25.5 versus 5.0 months).

**Discussion and Conclusion:** Hemodialysis patients with gastric cancer who received gastrectomy exhibited a high morbidity rate. Postoperative chemotherapy can be performed immediately after surgery in patients who do not experience postoperative complications. S-1 regimen and uracil and tegafur regimen could be administered safely in hemodialysis patients. Postoperative chemotherapy may lead to a good prognosis in gastric cancer patients receiving hemodialysis.

*Key words:* Hemodialysis – Gastric cancer – Gastrectomy – Complication – Chemotherapy

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More than 2.35 million patients received hemodialysis or peritoneal dialysis worldwide in 2012.[1] In Japan, more than 310,000 patients were administered dialysis treatment by the end of 2012, with the number of hemodialysis (HD) patients steadily increasing.[2] Among all dialysis patients, the leading cause of death is cardiac failure, followed by infectious disease, with malignant tumors being the third leading cause of death, accounting for 9.1% of fatalities among such patients.[2] Patients with end-stage renal disease have a high risk of cancer.[3] The growing number of patients on long-term HD is likely to lead to an increase in the number of HD patients who require surgery.[4] In addition, HD patients are at increased risk for postoperative complications, according to previous studies.[5,6] The morbidity and mortality rates of HD patients who undergo abdominal surgery range from 39.0% to 41.8% and 5.7% to 24.0%, respectively.[6–9]

Gastric cancer is the fifth most common cancer and is the third leading cause of cancer death worldwide.[10] In a previous study, we described 36 HD patients who underwent abdominal surgery for various gastrointestinal diseases, including gastric cancer.[6] Of these 36 patients, 8 had received a diagnosis of gastric cancer. It is important to carefully manage patients with gastric cancer who undergo gastrectomy. In addition, it is also important to manage patients who are treated with postoperative chemotherapy. However, the safety and efficacy of chemotherapy in HD patients have not been established. In this study, we report on 6 of the 8 previously described HD patients with gastric cancer.[6] Of these 8 patients, 2 were excluded from this study because of postoperative complications and loss to follow-up. All 6 study patients underwent gastrectomy for gastric cancer at the Department of Surgery, Juntendo Shizuoka Hospital, between November 2003 and December 2011. A total of 3 of the 6 patients received postoperative chemotherapy. S-1 was administered to 1 patient and uracil and tegafur (UFT) was employed for the 2 other patients. This case series was not research that required approval by the Institutional Review Board of Juntendo Shizuoka Hospital. Written informed consent was obtained from the patients for the publication of this case report.

## Case Presentation

The clinical presentation and characteristics of the study patients are shown in Table 1. The patients included 5 men and 1 woman, with a mean age of 66.3 years (range, 59.0–74.0 years). The underlying renal disease was diabetic nephropathy in 3 patients, nephrosclerosis in 2 patients, and glomerulonephritis in 1 patient. The patients had received HD for a mean of 5.4 years before surgery (range, 0.5–10.0 years). Preoperative performance status was evaluated according to the Eastern Cooperative Oncology Group criteria.[11] One of the 6 patients had a performance status of 2, and the other patients had performance status scores of 0. The mean body mass index was 20.4 $kg/m^2$ (range, 13.8–24.9 $kg/m^2$). All patients had coexisting disorders, including hypertension in 4 patients; diabetes mellitus in 3 patients; and cerebrovascular disease, angina pectoris, and chronic hepatitis in 1 patient each. All patients underwent standard laparotomy. Surgical procedures included distal gastrectomy in 3 patients, distal gastrectomy and radiofrequency ablation for gastric cancer and liver metastasis in 2 patients, and total gastrectomy in 1 patient. According to the 2010 Japanese gastric cancer treatment guidelines,[12] lymph node dissection involved D1 or D1+ lymphadenectomy in 5 patients and D2 lymphadenectomy in 1 patient. Histologically, the tumors were diagnosed as differentiated and undifferentiated in 3 and 3 patients, respectively. According to the Japanese classification of gastric carcinoma,[13] tumors were pathologically staged as IIA in 1 patient, IIB in 2 patients, IIIC in 1 patient, and IV in 2 patients.

The overall morbidity was 50% (3 of 6). Postoperative complications were assessed according to the Clavien-Dindo classification,[14] which included severe anemia that required a blood transfusion in 1 patient, shunt failure in 1 patient, catheter implantation for HD infection in 1 patient, and surgical wound infection in 1 patient. The mean duration of the patient postoperative hospital stay was 23.8 days (range, 15.0–40.0 days).

Regarding postoperative chemotherapy, S-1 was administered to 1 patient (patient 5), and UFT was employed in 2 cases (patients 2 and 6). S-1 was administered 11 times at a daily dose of 40 $mg/m^2$ after HD, followed by a period of rest, according to a method described in a previous report.[15] In patient 5, the S-1 chemotherapy did not cause any side effects. In patients 2 and 6, UFT was administered at daily doses of 300 mg/body and 200 mg/body, respectively. Neither of these patients presented chemotherapy-related side effects. The remaining 3 patients did not receive postoperative chemotherapy. One patient (patient 4) refused to undergo

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*Table 1 Patient characteristics*

| | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 | Patient 6 |
|---|---|---|---|---|---|---|
| Age, y | 70 | 63 | 74 | 59 | 66 | 66 |
| Sex | M | M | M | M | M | F |
| Cause of HD | DM | GN | NS | DM | NS | DM |
| Duration of HD, y | 1.5 | 10 | 5 | 6.5 | 9 | 0.5 |
| PS | 0 | 0 | 0 | 0 | 0 | 2 |
| BMI | 13.8 | 24 | 23 | 16.8 | 19.8 | 24.9 |
| Comorbidities | HT, DM | AP | HT | DM, CH | HT | DM, HT, CeVD |
| BUN, mg/dL | 42.9 | 29.1 | 30.5 | 19 | 28.8 | 60.1 |
| Creatinine, mg/dL | 6 | 8.9 | 7.9 | 7.4 | 7.2 | 5.2 |
| Hematocrit, % | 19 | 19.8 | 22.1 | 24.9 | 26.9 | 27.7 |
| TP, g/dL | 5.2 | 7.3 | 5.8 | 5.4 | 6.2 | 5.9 |
| Procedure | DGR, RFA | DGR, RFA | DGR | TGR | DGR | DGR |
| Node dissection | D1+ | D1 | D1+ | D1 | D2 | D1+ |
| Histology (type) | Undiff | Diff | Undiff | Undiff | Diff | Diff |
| TNM stage | T3N2M1HEP, IV | T3N1M1HEP, IV | T4aN3M0, IIIC | T4aN0M0, IIB | T2N1M0, IIA | T3N1M0, IIB |
| Complications | Severe anemia | None | Shunt failure, catheter infection | Surgical wound infection | None | None |
| Clavien-Dindo classification | II | | IIIa | IIIa | | |
| Length of postoperative hospital stay, d | 15 | 26 | 29 | 40 | 15 | 18 |
| Postoperative chemotherapy | None | UFT | None | None | S1 | UFT |
| Outcomes | Liver metastasis, death (2 mo) | Liver metastasis, death (7 mo) | Liver metastasis, death (7 mo) | NA, death (3 mo) | Liver metastasis, death (15 mo) | Alive (36 mo) |

AP, angina pectoris; BMI, body mass index; BUN, blood urea nitrogen; CeVD, cerebrovascular disease; CH, chronic hepatitis; DGR, distal gastrectomy; Diff, differentiated adenocarcinoma; DM, diabetes mellitus; GN, glomerulonephritis; HT, hypertension; NA, not available; NS, nephrosclerosis; PS, performance status; RFA, radiofrequency ablation; TGR, total gastrectomy; TP, total protein; Undiff, undifferentiated adenocarcinoma.

chemotherapy, and the remaining 2 patients (patients 1 and 3) did not recover sufficient physical strength after surgery.

Regarding long-term patient outcomes, the duration of the follow-up period ranged from 2 to 36 months, and the median overall survival time after surgery was 7 months. A total of 4 of the 6 patients (patients 1, 2, 3, and 5) experienced liver metastases. Two patients (patients 2 and 5) developed liver metastases shortly after surgery, despite receiving postoperative chemotherapy. One patient (patient 1) died of liver metastases 2 months after surgery, 2 patients (patients 2 and 3) died of liver metastases 7 months after surgery, and 1 patient (patient 5) died of liver metastases 15 months after surgery. Another patient (patient 4) died 3 months after surgery. However, no data regarding the cause of death for patient 4 were available. Therefore, of the 6 patients only 1 (patient 6) is currently alive without any evidence of disease.

## Discussion

In the present study, the overall morbidity rate was 50% (3 of 6). We started performing laparoscopic gastrectomy for gastric cancer at our institution beginning in 2011. Therefore, all patients underwent standard laparotomy in this study. Recently, laparoscopic surgery has been performed worldwide as a minimally invasive treatment for various cancers, including gastric cancer. However, in a previous study, HD patients were less likely to have a laparoscopic procedure because of a higher risk of mortality.[16]

Sasako *et al*[17] subsequently reported that postoperative adjuvant therapy with S-1 improved overall survival and relapse-free survival in patients with stages II and III gastric cancer who had undergone D2 gastrectomy. In the present study, the pathologic stage was IIA in 1 patient, IIB in 2, IIIC in 1, and IV in 2, with all patients initially recommended to receive chemotherapy; only 3 of the 6 patients actually received chemotherapy (patients 2, 5, and

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6). S-1 chemotherapy was administered to 1 patient, and UFT was employed in 2 patients. In 2007, 2 randomized control studies confirmed that postoperative adjuvant chemotherapy with UFT and S-1 had a significant survival benefit in patients with gastric cancer.[18,19] S-1 is an oral antitumor drug that combines 3 agents: tegafur, a prodrug of 5-fluorouracil; 5-chloro-2,4-dihydroxypyridine, a dihydropyrimidine dehydrogenase inhibitor; and potassium oxonate, which ameliorates gastrointestinal toxicities.[20] The plasma concentration of 5-fluorouracil is increased by the accumulation of 5-chloro-2,4-dihydroxypyridine in patients with renal dysfunction; therefore, it might lead to the occurrence of severe adverse events.[20] However, several studies have reported that adjusting S-1 doses based on the results of pharmacokinetics studies improves the safety and efficacy of treatment for advanced gastric cancer, even in maintenance for HD patients with chronic renal failure.[15,21,22] As for UFT, a previous report indicated that although the plasma 5-fluorouracil concentrations of HD patients treated with UFT were approximately double those seen in patients with normal renal function, no severe adverse reactions occurred in any of these patients.[23] The optimal doses of chemotherapy drugs for HD patients are uncertain, because there are few previous case reports about the use of chemotherapy to treat HD patients. In the present study, none of the patients who received chemotherapy experienced any related side effects. However, it was still uncertain whether the doses of chemotherapy agents used were appropriate.

In addition, based on the results of the SPIRITS[24] and JCOG9912[25] trials, S-1 plus cisplatin has been recommended as a first-line chemotherapy for patients with unresectable or recurrent gastric cancer, as well as those who underwent noncurative R2 resection. However, it is difficult to administer cisplatin to HD patients because it is not completely removed by the HD process.[26] Recently, oxaliplatin has been approved for use in patients with gastric cancer. In 2014, the CLASSIC trial reported its 5-year follow up data, which demonstrated that adjuvant treatment with capecitabine plus oxaliplatin after D2 gastrectomy was effective in patients with stages II and III gastric cancer.[27] It has been reported that the free platinum levels of patients who receive oxaliplatin treatment exhibit a bimodal pattern and that oxaliplatin can be used safely in HD patients with colon cancer without any dose reduction.[28] Therefore, it is expected that oxaliplatin will be used instead of cisplatin to treat HD patients with gastric cancer in the future.

In this study, postoperative chemotherapy could not be performed in 3 of the 6 patients (patients 1, 3, and 4). Notably, all of these patients experienced postoperative complications and experienced longer postoperative hospital stays than patients who did not experience postoperative complications (mean, 28.0 versus 19.7 days), suggesting that the occurrence of postoperative complications influenced decision-making regarding whether postoperative chemotherapy should be performed. All patients in the present study exhibited poor prognoses. Among the patients who received a diagnosis of pathologic stages II to III disease (patients 3–6), the patients who were treated with postoperative chemotherapy (patients 5 and 6) achieved better prognoses than those who did not receive chemotherapy (patients 3 and 4). In addition, as for the 2 patients who underwent distal gastrectomy and radiofrequency ablation for gastric cancer and liver metastasis (patients 1 and 2), the patient who was treated with postoperative chemotherapy (patient 2) exhibited a better prognosis than the patient (patient 1) who did not receive chemotherapy (7 versus 2 months). These results suggest that postoperative chemotherapy might influence the overall survival of HD patients with gastric cancer.

## Conclusions

Postoperative chemotherapy is feasible in patients immediately after surgery if no surgical complications have presented. Postoperative chemotherapy may lead to a good prognosis in HD patients with gastric cancer. S-1 and UFT chemotherapy regimens can be used safely in HD patients. However, further studies involving large patient cohorts are needed to establish guidelines for the perioperative treatment of HD patients with gastric cancer.

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