Long-term results of conversion surgery for advanced gastric cancer

Ann. Ital. Chir., 2023 94, 5: 454-459
pii: S0003469X23037946

Murat Kalin*, Ozgul Duzgun**

**Department of General Surgery, University of Health Sciences, Umraniye Training and Research Hospital, Istanbul, Turkey*
***Department of Surgical Oncology, University of Health Sciences, İstanbul Umraniye Training and Research Hospital, Istanbul, Turkey*

Long-term results of conversion surgery for advanced gastric cancer

AIM: *Upon this topic, randomized trials regarding gastrectomized and combination therapy with gastrectomy and chemotherapy have been made and survival has been prolonged to 15 months. In this study, we aimed to present our results by retrospectively classifying them according to Yoshida classification in stage 4 gastric cancer patients who have been operated in the last 5 years.*
METHODS: *The datas of 102 cases were collected prospectively and analyzed retrospectively between years 2016 and 2021. All cases were classified according to Yoshida classification.*
RESULTS: *22 (%21,5) cases in category 1, 35 (%34,3) cases in category 2, 30 (%29,4) cases in category 3 and 15 (%14,7) cases in category 4. Overall survival rate of 1,3 and 5 year period in category 1 patients were %90, %50 and %25 respectively. Mean survival time was 24 months. In category 2, overall survival rate of 1,3 and 5 years was %90, %50 and %25 respectively. Mean survival time was 18 months. In category 3, overall survival rate of 1,3 and 5 years was %50, %10 and %0 respectively. Mean survival time was 12 months. Lastly, in category 4, overall survival rate of 1,3 and 5 years was %40, %0 ve %0 respectively and mean survival time was 9 months.*
CONCLUSION: *We found that gastric cancer tumors without peritoneal involvement and responding to effective chemotherapy had longer survival and disease-free survival after conversion surgery.*

KEY WORDS: Gastric Cancer, Yoshida Classification, Conversion Surgery

Introduction

According to 2020 Globocan datas, gastric cancer is the fifth most common cancer around the world and fourth in mortality [1]. Along with the advancements in chemotherapy, standart treatment modality has been developed and reported in Japan and NCCN guidelines regarding gastric cancer [2,3]. Upon this topic, randomized trials regarding gastrectomized and combination therapy with gastrectomy and chemotherapy have been made and survival has been prolonged to 15 months [4]. In Regatta study, it is reported that combination of surgery and chemotherapy does not have a statistically important efficacy. However, in Japan and Italy series, longer period of overall survival and disease-free survival is reported when R0 resection is achieved [5-7].

Conversion therapy of Yoshida and classification of surgery has changed the view of perspective to this patient group [8]. According to this classificaiton, the range of patient survival changes from total cure to palliative care. Patients has been classified in 4 groups according to computed tomography, clinical stage and macroscopic peritoneal involvement. Category 1 has been described as patients without macroscopic peritoneal involvement. Marginal resectable cases has been described as category 2, patients with peritoneal involvement and potentially unresectable has been described as category 3 and last-

Pervenuto in Redazione Febbraio 2022. Accettato per la pubblicazione Maggio 2022
Correspondence to: Ozgul Duzgun, MD, Ass. Prof. of Surgical Oncology, University of Health Sciences, stanbul Umraniye Training and Research Hospital, Department of Surgical Oncology, Istanbul, Turkey (e-mail: ozgulduzgun@gmail.com)

ly, non curable metastatic cases has been described as category 4. Upon this calassification, treatment option of category 1 patients is described as surgery, category 2 patients are directed to neoadjuvant chemotherapy. Treatment option for category 3 and 4 patients vary according to other organ involvements. Treatment option for this patient group is a combination therapy of chemotherapy, molecular target treatment, and intraperitoneal chemotherapy. After the combination therapy, if the tumour becomes technically resectable, volume reduction surgery becomes an option. If the combination therapy has not been effective, treatment continues with palliative chemotherapy. In this study, we aimed to present our results by retrospectively classifying them according to Yoshida classification in stage 4 gastric cancer patients who have been operated in the last 5 years.

Material and Methods

In this study, the datas of 102 cases were collected prospectively and analyzed retrospectively between years 2016 and 2021 in Umraniye Research and Training Hospital, Surgical Oncology Clinic. Study permission numbered 2021/318 was granted from ethical committee of Umraniye Research and Training Hospital.In this study, the groups involved were patients younger than 70 years who were previously operated and received chemotherapy, patients classified in Eastern Cooperative Oncology Group (ECOG) 3 and patients with ASA score of 1-3. All of the patients were treated with chemotherapy regimen consisting of FLOT regimen consisting of docetaxel (60 mg/m^2), oxaliplatin (85 mg/m^2), leucovorin (200 mg/m^2), and 5-fluorouracil (2,600 mg/m^2 as a 24 hr infusion). Cisplatin 75 mg/Body Surface Area (BSA) ve Doxorubicin 15 mg/BSA 60 minutes in 43 degrees was applied as Hiperthermic intraperitoneal chemotherapy (HIPEC) medical regimen. R0 resection is described as no macroscopic residual tumour after surgery, R1 resection is described as microscopic residual tumour, R2 resection is described as macroscopic residual tumour. Total gastrectomy and lymph node resection of involved lymph nodes (16a1, 16a2, 16b1, 16b2) and additional organ resections were involved in the operation. HIPEC was added to cases with R0 resection. All cases were classified according to Yoshida classification.

Statistical analyses

The data obtained from raw data were recorded to IBM SPSS Statistics 22 (IBM SPSS) software and analyzed. The numerical data obtained were summarized in tables as arithmetic mean, ± standard deviation, minimum, maximum and range values. The nominal and ordinal data were evaluated as frequency and percentages. Finally, overall survival was calculated by using Kaplan-Meier survival analysis available in the same software.

Results

In 5 year survival period, 102 cases in this study was treated according to conversion therapy described by Yoshida. 55 (53.9 %) of these cases were male and 47 (%46.1) of the cases were female. Average age of male patients was 58 (34-70) and average age of female patients was 58 (34-70). Average BSA of the cases was 176 (154-202). Upon all the cases, 62 (%60,7) patients were classified as ASA I, 29 (%28,4) patients were ASA II and 11 (% 10,8) patients were ASA III. ECOG performance status was 0 for 70 (%68,6) patients and 1 for 32 (%31,4) patients. None of the cases were operated nor received chemotherapy due to gastric cancer previously.

Regarding tumour location, tumour was located at the antrum in 34 (%33,3) cases, at corpus in 30 (%29,4) cases. In 13 (%12,7)cases linitis plastica was detected. Isolated liver metastasis was detected in 10 (%9,8) cases, paraaortic 16a2-b1 lymph node metastasis was detected in12 (%11,7) cases and peritoneal metastasis was detected in 80 (%78,4) cases (Table I). The The patients

TABLE I - *Demographic Datas*

Demographic Variables	Patients (N:102) (%)
Age	
Mean	57
Range	32-70
Gender	
Male	55(%53,9)
female	47(%46,1)
ECOG score	
0	70(%68,6)
1	32(%31,4)
Liver Metastasis	
yes	10(%9,8)
no	92 (%90,1)
PALN Metastasis	
yes	12(%11,7)
no	90 (%88,2)
Peritoneal Metastasis	
yes	80 (%78,4)
no	22 (%21,5)
Tumor Location	
Antrum	34(%33,3)
Corpus	25(%24,5)
Cardia	30(%29,4)
Linitisplastica	13(%12,7)
ASA score	
1	62(%60,7)
2	29 (%28,4)
3	11(%10,8)

Abb: ECOG: Eastern Cooperative Oncology Group; PALN: Paraaortic Lymph nodes

TABLE II - *Yoshida classification*

Yoshida classification	Patients N (%)
Category 1	22 (%21,5)
Category 2	35 (%34,3)
Category 3	30 (%29,4)
Category 4	15 (%14,7)

Yoshida categories for stage IV gastric cancer

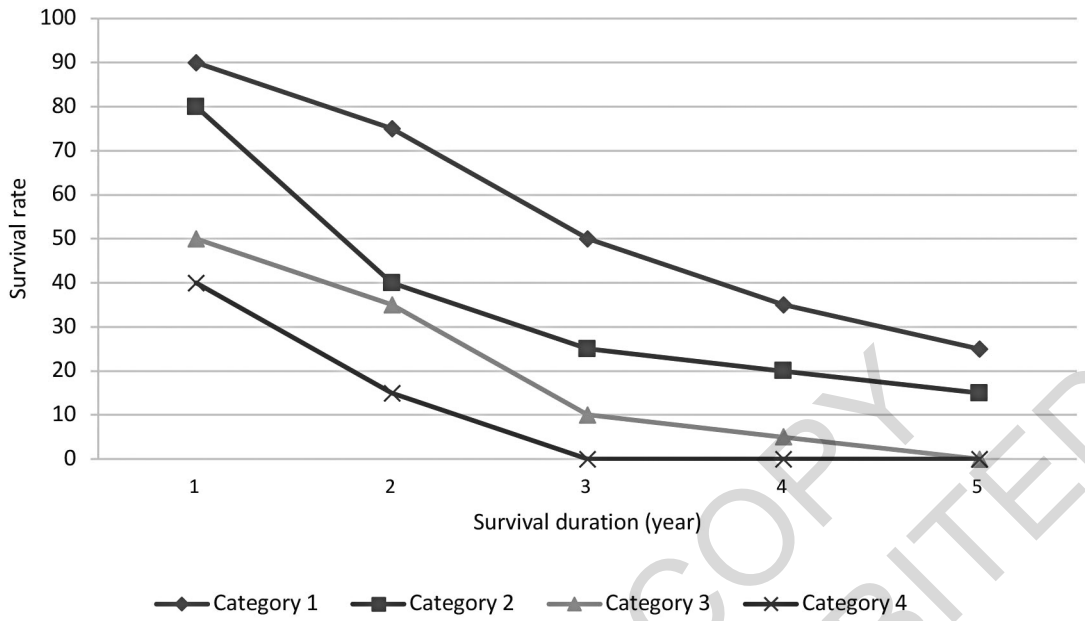
TABLE III - *Clavien-Dindo complication classification*

Clavien-Dindo classification	Patients N(%)
3a	
Intraabdominal abscess	
Pleural effusion	
Esophagojejunal anastomosis leak	322
3b	
Evisceration	
Jejunojejunostomy leak	21
5	
Mortality	1

were categorized and treated according to the algoritm Yoshida described. 22 (%21,5) cases in category 1, 35 (%34,3) cases in category 2, 30 (%29,4) cases in category 3 and 15 (%14,7) cases in category 4 (Table II). All of the cases were evaluated in multidisciplinary tumour council and 14 (%13,7) patients in category 1 were operated. These patients were directed to medical oncology department for adjuvant therapy. Other 8 (%7,8) cases were operated after the neoadjuvant chemotherapy. R0 resection was applied to all cases in category 1. 12 (%11,7) patients in category 2 were operated, however, 7 (%6.7) of these cases were evaluated as unresectable cancer peroperatively and the surgery was terminated. These patients were directed to chemotherapy. Among these 7 patients, 2 (%1,96) of them refused oncologic chemotherapy and decided upon alternative medical treatment. Among the polyclinic controls of these 2 cases, the the tumour was progressed and they were categorized as category 4. The other 5 (%4,9) patients were operated and R0 complete resection was applied. Twenty three (%22.5) patients in category 2 were evaluated after the intensive chemotherapy and 15 (%14,7) of these patients were operated due to their sufficient response to chemotherapy. R0 resection was applied to 10 (%9,8) , R1 resection was applied to 3 (%2,9) of these patients. R0 resection could not be applied to 2 (%1,96) patients and therefore volume reduction surgery was applied. Eight (%7.8) of the patients in category 2 were re-directed to chemotherapy since they were not suitable for surgery. After the chemotherapy, R0 resection was applied to 3 (%2,94) of these cases and volume reduction surgery was applied to 5 (%4,9) of these cases. Among the 30 patients in category 3, volume reduction surgery was applied to 17 (%16,6) of these cases and 13 (%12,7) of these cases were not evaluated as suitable for surgery and directed to palliative chemotherapy. Out of 15 patients in category 4, volume reduction surgery was applied to 2 (%1,96) of these patients after they have become technically resectable. Palliative chemotherapy was decided for 13(%12,7) of these cases. Only 5 (%4,9) of these patients accepted chemotherapy and the other 8 (%7,8) of these patients didn't accept chemotherapy due to intolerance. FLOT regimen was applied as the chemotherapy protocole. If the FLOT regimen was not tolerated due to toxic reaction, then it was replaced by XELOX (oxaliplatin 130 mg/m^2 on day 1; xeloda 1,000 mg/m^2 twice a day, on day 1-14), SOX (oxaliplatin 130 mg/m^2 on day 1; tegafur 40 mg/m^2 twice a day, on day 1-14), or FOLFOX6 (oxaliplatin 85 mg/m^2, leucovorin 200 mg/m^2 on, and 5-fluorouracil 2,600 mg/m^2) regimens. FLOT therapy regimen was tolerated by 90% of the patients. In category 1, 11 (%10,7) patients had a .The number of patients with peritoneal carsinomatosis index (PCI) score less than 6 was 11 (%10,7) in category 1, 23 (%22,5) in category 2. HIPEC was applied to all of the 34 (%33,3) of these patients. Completeness of cytoreduction score was 0 after the surgical operation. Total gastrectomy and D2 lymph node disection and isolated liver metastasectomy and/or paraaortic 16a2-b1 lymph node dissection was applied to cases in category 1. Paraaortic 16a1-b2 lymph node dissection was added to category 2 patients. Mean average operation time was 6 (4-10) hours. Blood loss was 300 cc (150-2000). Average day of stay at the intensive care unit was 1 day (0-5) and the mean average day of stay at the inpatient service was 9 days (7-28 days)

After the surgery, Clavien-Dindo 3a-b complication was reported in 10 (%9,8) cases. Clavien Dindo complication grade 3a was reported in 7 cases. Intraabdominal abscess was detected in 3 cases, pleuvral effusion was detected in 2 cases and esophagojejunostomy anastomosis leakage was detected in 2 cases. These complications were managed by placing percutaneous drainage catheter by interventional radiology and by placing cover capped stent by gastroenterology respectively. Clavien-Dindo grade 3b complication was detected in 3 cases. Evisceration was detected in 2 cases and jejunojejunostomy anastomosis leakage was detected in 1 case. The case with jejunojejunostomy anastomosis leakage was accepted exitus in 20th day postoperatively. None other mortality was observed during the first 30 day period postoperatively (Table III).

Overall survival rate of 1,3 and 5 year period in category 1 patients were %90, %50 and %25 respectively. Mean survival time was 24 months. In category 2, overall survival rate of 1,3 and 5 years was %90, %50 and %25 respectively. Mean survival time was 18 months.



	1-year OS	3-year OS	5-year OS	MST (months)
Category 1	90 %	50 %	25 %	24
Category 2	60 %	25 %	15 %	18
Category 3	50 %	10 %	0 %	12
Category 4	40 %	0 %	0 %	9

Fig. 1: Overall Survival

In category 3, overall survival rate of 1,3 and 5 years was %50, %10 and %0 respectively. Mean survival time was 12 months. Lastly, in category 4, overall survival rate of 1,3 and 5 years was %40 ,%0 ve %0 respectively and mean survival time was 9 months (Fig. 1).

Discussion

It is widely accepted that primary treatment for metastatic gastric cancer, is chemotherapy and surgery has no role in the treatment unless the tumour is obstructive or bleeding [9]. Peritoneum, liver and paraaortic lymph node (16a2b1 and 16a1b2) stations are the most common isolated metastatic sites for gastric cancer. In the literature, it is reported that gastric cancer metastasis could be seen nearly in all organs [10]. It is reported that peritoneal metastasis is a bad prognostic factor whereas liver and paraaortic lymph node metastasis have a better prognostic value due to R0 resectability of these metastasis.[11] During recent years, with advancements in chemotherapy with multi agent protocols and new anticancer treatments, chemotherapy response has become successfull and chance of macroscopic resection has been a light of hope. FLOT therapy has been a popular treatment option in the west whereas docetaxel, cisplatin, and S-1 (DCS) therapy has been a popular treatment option in far east. Efficacy of these treatment has been proved. In HER-2 + cases, transtuzumab has been added to the treatment protocole and better results are reported [12,13]. REGATTA study showed that addition of chemotherapy to gastrectomy has no superiority over just chemotherapy regarding survival. However, this study showed that stage IV patients can benefit from surgery in terms of survival only when this is radical. These results were obtained by analysing the retrospective series of grade IV unresectable patients who were treated by induction chemotherapy followed by surgery [14]. In randomized phase 3 CheckMate 649 study, first line nivolumab plus chemotherapy was compared with just chemotherapy. It is shown that with additional nivolumab therapy, survey has been prolonged to 15 months compared to 11 months of survival with just chemotherapy [4]. More than 20 years ago, Nakajima et al has showed that unresectable gastric cancer could become resectable after intense chemotherapy and reported that this has a benefit over prolonged survival rate [15]. From that date to recent years multiple number of studies were made. This treatment protocole defined as conversion surgery or conversion therapy has provided an overall survival period

of 37-56 months compared to just chemotherapy [12,16]. Treatment modality of complicated grade 4 gastric cancer has gained a new dimension with conversion therapy algorithm defined by Yoshida and this algorithm standardized the treatment modality [8]. In the study consisting of 77 cases with grade 4 gastric cancer made by Yamaguchi and al, overall median survival was reported to be 41.3 months in conversion surgery with R0 resection and 21.2 months for R1-2 resection [17,18]. Kinoshita et all reported a 3 year survival rate of %92.9 for the treatment of gastrectomy following DCS chemotherapy protocole. They also reported that category I grade IV cancer patients are a good candidate for conversion gastrectomy following DCS treatment and they have a good prognosis [13]. Seung-Hoon Beom and all have reported a median overall survival of 26 months in their case series of 101 grade 4 IV gastric cancer patients. They also reported that the isolated liver metastasis have the best prognosis and have an overall survival of 49.2 months. As a conclusion,these studies showed that chemotherapy followed by gastrectomy have improved and contributed to overall survival. Complete response, decrease in CEA levels and complete macroscopic resections have been reported as good prognostic factors.[19] Solaini et al have reported peritoneal metastasis to be %84.4, lymph node metastasis to be %6.6 (n:3), and extensive liver involvement to be %8.8 (n:4) in their case series consisting of 45 cases. They have also reported a median follow up of 25 months and median overall survival from surgery was 15 months and 1-, 3- and 5-year survivals were 57.2, 36.1 and 24%, respectively. Median progression-free survival was 12 months with 1- and 3-year survival of 46.4 and 33.9%, respectively [20]. In our study, we observed a 1,3 and 5 year overall survival to be %90, %50 ve %20 respectively and a median survival time(MST) as 22 months in category I. In category II, we observed a 1,3 and 5 year overall survival to be %60, %25 ve %15 respectively and MST to be 16 months. In category III, we observed to be %50, %10, %0 ve MST as 12 months. Lastly in category 4, the values were %40, %0, %0 respectively and MST was 9 months. We observed that our data has corresponded with literature. Yoshida and Yamaguchi showed in their series peritoneal spread of gastric cancer is a poor prognostic factor and 3 year survey for these patients is around 35%. They showed that conversion therapy can be applied in these selected patients with grade 4 gastric cancer [8,17]. In our study, we treated the patients. In our case series, we applied CRS+HIPEC to 34 (11 of them was category I and 23 of them was category II) of our cases who had PCI score less than 6 and observed that this procedure can be done without extra morbidity and mortality. However, we detected that overall survival was lower in category II patients compared to category I patients. Arigami et al detected 3 year overall survival to be 55% in patients with peritoneal metastasis and 6% in patients without peritoneal metastasis in their stduy consisting of 93 cases [11]. We apply intraperitoneal cisplatin and doxorubicin combination in gastric peritoneal carcinomatosis. We think that in the near future, PD-1 inhibitor based therapies applied intavenously in Checkmate 649 study could have better results when used intraperitoneally.

Kinoshita et al reported Clavien Dindo Grade 3a complication as 14,5% in their study. These complications were as follows: pancreatic fistula, anastomosis leakage, ileus, intraabdominal abscess. In our study, we reported Clavien Dindo grade 3a complication as 6.8%. The complications in our study were as follows: inraabdominal abscess, pleural effusion, and esophagojejunostomy anastomotic leakage. In our study, 3 cases had Clavien Dindo grade 3b complication. These were evisceration and jejunojejunostomy anastomotic leakage. These cases were cases that received HIPEC. We think that increased intraabdominal pressure due to HIPEC and absence of Lambert sutures in jejunojejunostomy anastomotic line is the reason for these complications. In Kinoshita study, no mortality was detected, however 1 patient was considered exitus in our study, which is compatible with literature [13]. Yabusaki et al reported in their study that R0 resection is the main factor for curative surgery. Yabusaki reported that patients obtaining complete response/partial response (CR/PR) to chemotherapy as well as those with R0 resection and D2/D3 LN dissection had longer survival [21]. Fukuchi et al. also demonstrated that R0 resection as well as one non-curative factor was an independent significant predictor for overall survival in patients who underwent [22]. In our study, all of the patients in category I were treated by complete surgical resection and R0 resection was achieved. Regarding this, 1 year survival rate was 90% and 5 year survival rate was 20%. Limitations in our study was that it was a single centered retrospective study with small group of patients. We believe that heterogeneity of the metastatic lesions and potentially resectable category I patients consist a small part of this study which limits the study.

Riassunto

Su questo tema sono stati effettuati studi randomizzati a seguito della gastrectomia semplice e combinata con la chemioterapia, prolungando la sopravvivenza a 15 mesi. In questo studio, abbiamo mirato a presentare i nostri risultati classificandoli retrospettivamente secondo la classificazione di Yoshida considerando pazienti con carcinoma gastrico in stadio 4 che sono stati operati negli ultimi 5 anni.

Metodi: i dati di 102 casi sono stati raccolti in modo prospettico e analizzati retrospettivamente tra gli anni 2016 e 2021. Tutti i casi sono stati classificati secondo la classificazione Yoshida.

Risultati: 22 (%21,5) casi nella categoria 1, 35(%34,3) casi nella categoria 2, 30(%29,4) casi nella categoria 3 e 15(%14,7) casi nella categoria 4. Il tasso di sopravviven-

za globale del periodo di 1,3 e 5 anni nei pazienti di categoria 1 era rispettivamente del 90%,50% e 25%%25. Il tempo medio di sopravvivenza è stato di 24 mesi. Nella categoria 2, il tasso di sopravvivenza globale di 1,3 e 5 anni era rispettivamente del 90%,50% e 25%%25. Il tempo medio di sopravvivenza è stato di 18 mesi. Nella categoria 3, il tasso di sopravvivenza globale di 1,3 e 5 anni era rispettivamente % 50, % 10 e % 0. Il tempo medio di sopravvivenza è stato di 12 mesi. Infine, nella categoria 4, il tasso di sopravvivenza globale di 1,3 e 5 anni è stato rispettivamente di % 40,%0 e %0 e il tempo medio di sopravvivenza è stato di 9 mesi

CONCLUSIONI: Abbiamo scoperto che i tumori del cancro gastrico senza coinvolgimento peritoneale e che rispondevano a una chemioterapia efficace avevano una sopravvivenza più lunga e una sopravvivenza libera da malattia dopo l'intervento chirurgico di conversione (R0).

Conclusion

We believe that this treatment method may be effective in selected cases, at least promising in category 1 cases, after evaluation in multidisciplinary councils and conversion therapy applied in stage 4 patient group. We found that gastric cancer tumors without peritoneal involvement and responding to effective chemotherapy had longer survival and disease-free survival after conversion surgery. However, with the introduction of more effective chemotherapeutics, we need randomized controlled studies to await the results of cohort studies originating from the Far East.

Acknowledgments

We would like to express our gratitude to Pırılı Özcan who helped us during the writing of this manuscript.

References

1. Sung H, Ferlay J, Siegel RL, et al: *Global cancer statistics 2020: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries*. CA Cancer, J Clin, 2021; 71:209-49.

2. *Japanese gastric cancer treatment guidelines 2014 (ver. 4)*. Gastric Cancer, 2017; 20:1-19.

3. National Comprehensive Cancer Network NCCN, Clinical Practice Guidelines in Oncology (NCCN Guidelines). Gastric cancer, Version 2; 2021.

4. Janjigian YY, Shitara K, Moehler M, et al: *First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (Check Mate 649): A randomised, open-label, phase 3*. Trial Lancet, 2021; 3:398(10294):27-40.

5. Ministrini S, Solaini L, Cipollari C, et al: *Surgical treatment of hepatic metastases from gastric cancer.* Updates Surg, 2018; 70:273-78.

6. Kodera Y: *Surgery with curative intent for stage IV gastric cancer: Is it a reality of illusion*? Ann Gastroenterol Surg, 2018; 2:339-47.

7. Kodera Y, Kobayashi D, Tanaka C, et al: *Gastric adenocarcinoma with para-aortic lymph node metastasis: A borderline resectable cancer?* Surg Today, 2015; 45:1082-90.

8. Yoshida K, Yamaguchi K, Okumura N, Tanahashi T, Kodera, Y: *Is conversion therapy possible in stage IV gastric cancer: The proposal of new biological categories of classification*. Gastric Cancer, 2016; 19:329-38.

9. Keränen I, Kylanpaa L, Udd M, et al: *Gastric outlet obstruction in gastric cancer: A comparison of three palliative method*s. J Surg Oncol, 2013; 108:537-41.

10. Guner A, Yildirim R: *Surgical management of metastatic gastric cancer: Moving beyond the guidelines.*Transl Gastroenterol Hepatol, 2019; 19:4-58.

11. Arigami T, Matsushita D, Okubo K, et al: *Clinic significance of conversion surgery for gastric cancer with peritoneal dissemination: A retrospective stualdy.* Oncology, 2020; 98(11):798-806.

12. Einama T, Abe H, Shichi S, et al: *Long-term survival and prognosis associated with conversion surgery in patients with metastatic gastric cancer.* Mol Clin Oncol, 2017; 6(2):163-66.

13. Kinoshita J, Fushida S, Tsukada T, et al: *Efficacy of conversion gastrectomy following docetaxel, cisplatin, and S-1 therapy in potentially resectable stage IV gastric cancer*. Eur J Surg Oncol, 2015; 41(10):1354-60.

14. Fujitani K, Yang HK, Mizusawa J, et al: *Regatta study investigators. Gastrectomy plus chemotherapy versuschemotherapy alone for advanced gastric cancer with a single non-curable factor (regatta*): *A phase 3, randomised controlled trial*. Lancet Oncol, 2016; 17:309-18.

15. Nakajima T, Ota K, Ishihara S, Oyama S, Nishi M, Ohashi Y, et al: *Combined intensive chemotherapy and radical surgery forincurable gastric cancer*. Ann Surg Oncol, 1997; 4:203-8.

16. Fukuchi M, Ishiguro T, Ogata K, Suzuki O, Kumagai Y, Ishibashi K, et al: *Prognostic role of conversion surgery for unresectable gastric cancer.* Ann Surg Oncol, 2015; 22:3618-24.

17. Yamaguchi K, Yoshida K, Tanahashi T, et al: *The long-term survival of stage IV gastric cancer patients with conversion therapy.* Gastric Cancer, 2018; 21:315-23.

18. Yamaguchi K, Yoshida K, Tanaka Y, et al: *Conversion therapy for stage IV gastric cancer-the present and future.* Transl Gastroenterol Hepatol, 2016; 1:50.

19. Beom SH, Choi YY, Baek SE, et al: *Multidisciplinary hemotherapy*. BMC Cancer, 2018; 18:1116.

20. Solaini L, Ministrini S, Bencivenga M, et al: *Conversion gastrectomy for stage IV unresectable gastric cancer: A GIRCG retrospective cohort study*. Gastric Cancer, 2019; 22:1285-293.

21. Yabusaki H, Nashimoto A, Matsuki A, Aizawa M: *Significance of surgical treatment in multimodal therapy for stage IV highly advanced gastric cancer.* Hepatogastroenterology, 2013; 60(122):377-81.

22. Fukuchi M, Ishiguro T, Ogata K, Suzuki O, Kumagai Y, Ishibashi K, Ishida H, Kuwano H, Mochiki E: *Prognostic role of conversion surgery for unresectable gastric cancer*. Ann Surg Oncol, 2015; 22(11):3618-24.