

Treatment options in synchronous peritoneal metastasis from gastric cancer: A retrospective cohort analysis

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Abstract

Gastric cancer (GC) is a common malignancy and one of the leading causes of cancer related death. Peritoneal metastases (PM) are not uncommon and then prognosis is poor. Treatment options in these cases are not standardized. The use of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) represents an option in selected patients.

We retrospectively analyzed our prospectively collected peritoneal surface malignancy database and assessed patients with synchronous peritoneal metastases from gastric primary based on peritoneal cancer index (PCI).

Over a 16 year period, 600 such patients were identified. They were divided into 5 treatment groups based on their PCI. Surgical morbidity ranged from 5 to 22% and mortality from 1.4 to 3.8%. Overall survival was 7.3 months (range 3.9-14.8). PCI was an independent factor for increased overall survival and the most important factor for treatment decision making.

Generally, patients with GC associated PM have poor prognosis. CRS and HIPEC can offer a survival benefit in carefully selected patients. Long-term survival was observed in patients with $PCI \leq 7$. Non-surgical approach can be equally effective for more advanced disease and palliative chemotherapy can offer a better quality of life.

Keywords: Gastric cancer; Peritoneal metastases; HIPEC; Cytoreductive surgery

1. Introduction

Gastric cancer (GC) represents the 5th most common type of malignancy in the world and the 3rd leading cause of cancer related death [1]. The peritoneum is the most common site of metastasis and the primary site of recurrence after radical surgery in 60% of all recurrences [2]. Peritoneal metastases (PM) are associated with a median overall survival (OS) of 3-4 months [3].

While standard of care treatment for primary gastric cancer includes neo-adjuvant and adjuvant chemotherapy, radical surgery and in certain cases radiotherapy, treatment options for peritoneal disease are limited and not standardized. The use of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC), neo-adjuvant chemotherapy (NAC) or neo-adjuvant intraperitoneal chemotherapy (NIPC) has been proposed but remains controversial [4, 5].

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The aim of this study was to retrospectively investigate the survival outcomes of different treatment options in our cohort of GC patients with synchronous PM in an analysis based on the stage of peritoneal cancer index (PCI). [6]

2. Material and methods

During a 16 year period (2005-2021), 5,500 consecutive patients with peritoneal metastases from various primaries were registered in our prospectively collected database. The age of the patients enrolled, ranged from 24 to 87 years with a median age of 55.4±8.2 years. The primary source and timing of diagnosis are described in Table 1.

Table 1 Type of primary cancer site analysis

Primary cancer site	N	Synchronous PM	Metachronous PM
Ovarian	2880	1140	1740
Mesothelioma	319	n/a	n/a
Pseudomyxoma	401	n/a	n/a
Colorectal	803	310	493
Gastric	807	600	207
Endometrial	100	33	67
Cervical	50	14	36
Rare*	140	48	92
Total	5500	2145	2635

PM: peritoneal metastasis; *: Hepatopancreatobiliary: 48, sarcoma:67, Breast:11, Lung:4, NETs:8, Unknown primary:2

A retrospective treatment analysis was performed on 600 GC patients with synchronous peritoneal metastases. We conducted an analysis of clinical and morphological prognostic factors and assessed the efficacy of conventional treatment (palliative surgery, palliative chemotherapy and best supportive care), based on peritoneal dissemination as described by PCI.

The diagnosis of GC in all patients was verified morphologically prior to onset of treatment. The assessment of the extend of intraperitoneal dissemination and its staging was conducted with the use of PCI. PCI was calculated as described by Sugarbaker et al [6]. The staging was performed during laparoscopy, laparotomy or palliative surgery. In patients who did not underwent surgical staging, this was conducted based on radiological findings (computed tomography).

The patients were divided into 5 groups according to mean PCI and received treatment as decided by the multi-disciplinary meeting.

- Group A (n=86) included patients with a mean PCI of 4.5±3.8. These patients received cytoreductive surgery and HIPEC after neo-adjuvant systemic chemotherapy followed by adjuvant chemotherapy.
- Group B (n=24) with a mean PCI of 10.4±4.6 underwent palliative surgery (CC1-CC2) and HIPEC after neo-adjuvant chemotherapy followed by post-operative chemotherapy
- Group C (n=340) with a mean PCI of 17.2±8.7 received neo-adjuvant chemotherapy followed by palliative surgery and postoperative chemotherapy.
- Group D (n=20) with a mean PCI of 20.3±9.8 received systemic chemotherapy and Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC)
- Group E (n=130) with a mean PCI of 25.4±9.9 received palliative chemotherapy and best supportive care.

Survival outcomes of the 5 groups were compared using median overall survival with log-rank coefficient.

3. Results

Post-operative morbidity recorded using the Clavien-Dindo score was documented in 22%, 16%, 12.3% and 5% of patients in Group A to D, respectively (Table 2). Median follow up was 54.6 months. Overall survival for the whole cohort of 600 patients was 7.3 months (95% CI 3.9-14.8). (Table 2)

Table 2 Survival and surgical morbidity and mortality

Group	Median Survival (months)	Morbidity (%)	Mortality (%)
A	13.6±1.8	22	3.8
B	7.3±1.3	16	4.4
C	6.7±1.1	12.3	3.1
D	5.9±0.8	5	1.4
E	5.6±1.6	-	-

In multivariate analysis, PCI was an independent factor for increased overall survival and the most important factor for treatment decision making. Median OS of patients with PCI 4-10 was 9.7 months and 1-year survival was 65%. Median OS of patients with PCI 11-20 was 4.3 months with 1-year survival of 10%. Finally, PCI >20 had 0% 1-year survival.

4. Discussion

Peritoneal surface malignancies (PSM) comprise a heterogenous group with significant variations in incidence, response to treatments and prognosis. Cytoreductive surgery is the essential component of curative treatment of PSM and aims to resect macroscopically visible tumour implants within the peritoneal cavity. Peritoneal metastases are relatively common in advanced stage gastric cancer and these patients have a poor prognosis despite systemic chemotherapy [7,8].

An analysis of outcomes in prospective trials suggested a survival benefit when adding HIPEC to CRS in carefully selected patients with localized PM and in some cases long-term survival can be achieved in patients with CC0 CRS and PCI<6 [9]. The results of our retrospective analysis are consistent with the above literature findings. In addition, our analysis has shown that the most important factor is the response to neoadjuvant chemotherapy which in our study was crucial for all synchronous PMs.

Another important topic is the role of palliative surgery in the presence of PM. In the recent REGATTA trial, palliative gastrectomy and systemic chemotherapy did not result in a significant survival benefit over chemotherapy alone [10]. Similarly, in our study there was no statistically significant difference in median OS between the 2 groups.

Interestingly, survival rates in neoadjuvant chemotherapy responders improved after palliative surgery [11].

5. Conclusion

In conclusion, patients with GC associated PM have poor prognosis. In this study, long-term survival was observed in patients with PCI≤7. Non-surgical approach can be equally effective for more advanced disease and palliative chemotherapy can offer a better quality of life.

Compliance with ethical standards

Disclosure of conflict of interest

All authors declare that there is no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

- [1] Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015 Mar 1, 136(5):E359-86.
- [2] Cortés-Guiral D, Hübner M, Alyami M, Bhatt A, Ceelen W, Glehen O, Lordick F, Ramsay R, Sgarbura O, Van Der Speeten K, Turaga KK, Chand M. Primary and metastatic peritoneal surface malignancies. *Nat Rev Dis Primers*. 2021 Dec 16, 7(1):91.
- [3] Yarema R, Ohorchak M, Hyrya P, Kovalchuk Y, Safiyan V, Karelin I, Ferneza S, Fetsych M, Matusyak M, Oliynyk Y, Fetsych T. Gastric cancer with peritoneal metastases: Efficiency of standard treatment methods. *World J Gastrointest Oncol*. 2020 May 15, 12(5):569-581.
- [4] Sugarbaker PH. Prevention and Treatment of Peritoneal Metastases from Gastric Cancer. *J Clin Med*. 2021 Apr 28, 10(9):1899.
- [5] Glehen O, Mohamed F, Gilly FN. Peritoneal carcinomatosis from digestive tract cancer: new management by cytoreductive surgery and intraperitoneal chemohyperthermia. *Lancet Oncol*. 2004 Apr, 5(4):219-28.
- [6] Harmon RL, Sugarbaker PH. Prognostic indicators in peritoneal carcinomatosis from gastrointestinal cancer. *Int Semin Surg Oncol*. 2005 Feb 8, 2(1):3.
- [7] Rosa F, Galiandro F, Ricci R, Di Miceli D, Longo F, Quero G, Tortorelli AP, Alfieri S. Survival advantage of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for advanced gastric cancer: experience from a Western tertiary referral center. *Langenbecks Arch Surg*. 2021 Sep, 406(6):1847-1857.
- [8] Mazurek M, Szlendak M, Forma A, Baj J, Maciejewski R, Roviello G, Marano L, Roviello F, Polom K, Sitarz R. Hyperthermic Intraperitoneal Chemotherapy in the Management of Gastric Cancer: A Narrative Review. *Int J Environ Res Public Health*. 2022 Jan 7, 19(2):681.
- [9] Brandl A, Yonemura Y, Glehen O, Sugarbaker P, Rau B. Long term survival in patients with peritoneal metastasised gastric cancer treated with cytoreductive surgery and HIPEC: A multi-institutional cohort from PSOGI. *Eur J Surg Oncol*. 2021 Jan, 47(1):172-180.
- [10] Fujitani K, Yang HK, Mizusawa J, Kim YW, Terashima M, Han SU, Iwasaki Y, Hyung WJ, Takagane A, Park DJ, Yoshikawa T, Hahn S, Nakamura K, Park CH, Kurokawa Y, Bang YJ, Park BJ, Sasako M, Tsujinaka T; REGATTA study investigators. Gastrectomy plus chemotherapy versus chemotherapy alone for advanced gastric cancer with a single non-curable factor (REGATTA): a phase 3, randomised controlled trial. *Lancet Oncol*. 2016 Mar, 17(3):309-318.
- [11] Chia DKA, So JBY. Recent Advances in Intra-peritoneal Chemotherapy for Gastric Cancer. *J Gastric Cancer*. 2020 Jun, 20(2):115-126.