**Name of Journal:** *World Journal of Surgical Procedures*

**Manuscript NO:** 45382

**Manuscript Type:** EDITORIAL

**Can hyperthermic intraperitoneal chemotherapy effectively control gastric cancer-associated peritoneal carcinomatosis?**

Chiu CC *et al.* Hyperthermic chemotherapy for gastric cancer

Chong-Chi Chiu, Chao-Jung Tsao, Jhi-Joung Wang, Yutaka Yonemura

**Chong-Chi Chiu,** Department of General Surgery, Chi Mei Medical Center, Tainan City 73657, Taiwan

**Chong-Chi Chiu,** Department of Electrical Engineering, Southern Taiwan University of Science and Technology, Tainan City 710, Taiwan

**Chao-Jung Tsao,** Department of Oncology, Chi Mei Medical Center, Tainan City 73657, Taiwan

**Jhi-Joung Wang,** Department of Medical Research, Chi Mei Medical Center, Tainan City 73657, Taiwan

**Yutaka Yonemura,** Peritoneal Surface Malignancy Center, Kishiwada Tokushukai Hospital, Kishiwada, Osaka 596-8522, Japan

**ORCID number:** Chong-Chi Chiu (0000-0002-1696-2648); Chao-Jung Tsao (0000-0002-1656-3831); Jhi-Joung Wang (0000-0002-4028-5624); Yutaka Yonemura (0000-0001-5796-9603).

**Author contributions:** All authors participated in the writing and editing of the manuscript.

**Supported by** grant from Chi Mei Medical Center, Taiwan, No. CLFHR10606.

**Conflict-of-interest statement:** All authors declare no competing financial interests.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

**Manuscript source:** Invited Manuscript

**Corresponding author: Yutaka Yonemura, PhD, Surgeon,** Peritoneal Surface Malignancy Center, Kishiwada Tokushukai Hospital, 4-27-1 Kamori-Cho, Kishiwada, Osaka 596-8522, Japan. yutakayonemura57@gmail.com

**Telephone:** +81-072-4459915

**Received:** December 25, 2018

**Peer-review started:** December 25, 2018

**First decision:** March 5, 2019

**Revised:** March 11, 2019

**Accepted:** April 19, 2019

**Article in press:** April 19, 2019

**Published online:** May 21, 2019

**Abstract**

Gastric cancer-associated peritoneal carcinomatosis leads to a poor prognosis and low quality of life. The current systemic chemotherapy processes cannot effectively improve survival. Hyperthermic intraperitoneal chemotherapy (HIPEC) has been used as an alternative treatment to control this disease through recurrence prevention, definitive therapeutic modality, and symptom palliation. Although HIPEC has been demonstrated to yield favorable results mainly in some Asian studies, widespread adoption of this treatment is still debatable before larger prospective randomized controlled clinical trials confirm its effectiveness.

**Key words:** Hyperthermic intraperitoneal chemotherapy; Gastric cancer; Peritoneal carcinomatosis

**© The Author(s) 2019.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Peritoneal carcinomatosis associated with gastric cancer leads to poor clinical outcomes and low quality of life. Hyperthermic intraperitoneal chemotherapy can potentially be used for the control of this disease.

**Citation:** Chiu CC, Tsao CJ, Wang JJ, Yonemura Y. Can hyperthermic intraperitoneal chemotherapy effectively control gastric cancer-associated peritoneal carcinomatosis? *World J Surg Proced* 2019; 9(1): 7-11

**URL:** https://www.wjgnet.com/2219-2832/full/v9/i1/7. htm

**DOI:** https://dx.doi.org/10.5412/wjsp.v9.i1.7

**INTRODUCTION**

Peritoneal carcinomatosis (PC) of gastric cancer origin refers to the spreading of gastric tumor cells in the peritoneum[1]. PC is characterized by extremely poor prognosis with a residual lifespan of approximately 3-7 mo[2-5]. Therefore, the median survival of patients with PC treated with systemic chemotherapy is 9.5-12 mo[6,7]. In addition, intractable ascites may severely affect the quality of life and lead to particularly painful sensations and life-threatening consequences in these patients[8,9].

In the past, these patients have been considered incurable and only received palliative systemic chemotherapy without surgical resection[10,11]. However, systemic chemotherapy, even with targeted agents, has yielded poor responses[12] due to the presence of the “plasma–peritoneal barrier,” which separates organs inside the peritoneum from intravenous chemotherapeutic drugs[13]. Notably, in the 1980s, a new concept of a “locoregional disease” in patients with PC led to the identification of a new treatment strategy, cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC)[1]. After complete CRS of macroscopic tumor resection, intraperitoneal chemotherapy (IC) is performed to maximize the dosage and contact time of chemotherapeutic drugs delivered to intraperitoneal microscopic-free tumor cells while minimizing systemic toxicity. Prolonged drug retention in the peritoneal cavity and clearance from the systemic circulation are considered crucial attributes for the intraperitoneal approach[14,15]. Heat has also been proven to be synergistic with the antitumoral effects of chemotherapeutic agents (*e.g.*, mitomycin C, cisplatin, and oxaliplatin)[16,17]. Moreover, the addition of extensive intraoperative peritoneal lavage followed by IC with cisplatin yielded significant improvements in 5-year survival in a Japanese gastric cancer study[18]. The principle underlying this effect is that the use of a large amount of diluent inside the peritoneum before HIPEC could diminish a majority of free tumor cells, and the combined action of physical injury caused by heat and the chemotherapeutic toxin demolishes the remaining tumor cells[19].

HIPEC has been used in three aspects of gastric cancer management. First, it has been used as an adjuvant approach following curative CRS to extend lifespan and reduce the rate of intraperitoneal recurrence in many Asian randomized clinical trials[19]. Second, CRS followed by HIPEC is the sole therapeutic modality in PC management, leading to long-term survival in well-selected patients. Third, HIPEC has been demonstrated to effectively palliate massive ascites and alleviate the need and frequency of paracentesis.

**A METHOD OF RECURRENCE PREVENTION**

HIPEC is the most appealing prophylactic treatment of gastric cancer for those with a high risk of recurrence in the peritoneum after curative CRS[19]. According to the “tumor cell entrapment hypothesis” proposed by Dr. Sugarbaker, perioperative IC including peroperative HIPEC with or without early postoperative intraperitoneal chemotherapy (EPIC) should be performed to eradicate possible tumor cells released into the peritoneal cavity during cancer resection, transection of lymphatic channels or in cases with close resection margins, and tumor-contaminated blood spillage[20]. Several meta-analyses of prophylactic IC for carcinomatosis prevention have been published. Sun *et al*[21] stated a substantial extent of lifespan after HIPEC despite the use of different chemotherapeutic drugs (mitomycin C or 5-fluorouracil) and irrespective of whether adjuvant intravenous chemotherapy was applied. Mi *et al*[22] reported that HIPEC could reduce the 5-year recurrence rate in the peritoneum even with six different combinations of chemotherapeutic drugs (5-fluorouracil, mitomycin C, cisplatin, cisplatin and 5-fluorouracil, cisplatin and mitomycin C, mitomycin C and 5-fluorouracil). However, neither of these studies demonstrated increased postoperative morbidity after HIPEC[21,22]. Huang e*t al*[23] and Yan *et al*[24] demonstrated a higher incidence of postoperative neutropenia and abscess formation after HIPEC with four different combinations of chemotherapeutic drugs (5-fluorouracil, mitomycin C, cisplatin and mitomycin C, mitomycin C and 5-fluorouracil) but with no effect on mortality rate. Moreover, sole prophylactic HIPEC or HIPEC combined with EPIC yielded survival benefits. Yonemura *et al*[25]reported a 5-year survival rate reaching 42% in a study group comprising 15 Cy+/P0 patients with combined cisplatin and mitomycin C regimen. Grossly, this prophylaxis strategy in patients with nodal metastasis or serosal invasion has been proven effective and safe. Nevertheless, a large percentage of these randomized clinical trials were conducted in Asian countries, and clinical trials in Western countries were scant[19].

**A DEFINITIVE THERAPEUTIC MODALITY**

In 1996, Yonemura *et al*[5] reported a 5-year-survival rate of 11% in a study of treatment with HIPEC using regimen of cisplatin and mitomycin C and etoposide, after CRS in 83 patients with PC. The first study of the West reported in 1999 was a phase Ⅱ study of 42 patients receiving HIPEC with mitomycin C regimen. Sayag-Beaujard *et al*[26]reported an overall median survival of 10.3 mo and a 5-year survival rate of 8%. However, a low tumor load (peritoneal cancer index, PCI) and complete cytoreduction [completeness of cytoreduction (CC) score = 0] would lead to ideal survival. One 49-patient study by Glehen *et al*[27] published in 2004 showed that the median survival reached 21.3 mo and 5-year survival rate increased to 29.4% after CC-0/1 resection and HIPEC with mitomycin C regimen. This improvement in clinical outcomes demonstrated the significance of proper patient selection and technical progress in complete cytoreduction as experience increased.

However, the patients may face risks of complications and mortality. Gill *et al*[28]summarized the results of ten studies and demonstrated a complication risk of 21.5% and average mortality rate of 4.8%. Common complications included ileus, anastomotic leakage, intra-abdominal abscess, digestive fistula, and hematologic toxicity[28-31]. Therefore, appropriate selection of candidates for this treatment is essential. During preoperative evaluation, a low PCI score and low CC score are essential prognostic factors. Moreover, preoperative PCI scores indirectly forecast the possibility of complete cytoreduction during operation. Yonemura *et al*[32]demonstrated complete cytoreduction of 86%, 39%, and 7% in their patients when the PCI score was ≤ 6, >7, and > 13, individually. Suitable indications of CRS and HIPEC for gastric cancer-related PC should include younger age (< 60 years), low PCI scores (lower than 10 points), no para-aortic lymph node involvement, no distant metastasis, and a high possibility of complete cytoreduction[27,30,32-34].

**A METHOD OF SYMPTOM PALLIATION**

For symptomatic patients with malignant ascites and complete cytoreduction deemed impossible[19], many oncologists have suggested performing HIPEC to relieve the symptoms caused by ascites related to PC[35]. Yonemura *et al*[36] and Fujimoto *et al*[37] advocated effective resolution of ascites in patients after HIPEC treatment. In addition, some studies have reported the successful use of laparoscopic HIPEC to palliate the ascites-related symptoms, to reduce the frequency of repeated paracentesis, and to avoid any significant morbidity or mortality[38]. Moreover, laparoscopic HIPEC could shorten the operation time and length of admission[39,40].

**PERSPECTIVE**

In the past two decades, the use of CRS and HIPEC in gastric cancer-related PC management has been debatable. Although preliminary data from Asian studies were scrutinized with considerable skepticism, indications of HIPEC in PC treatment remain elusive. Additional large prospective randomized controlled clinical trials are warranted to achieve consensus regarding the use of HIPEC as a gold standard.

**REFERENCES**

1 **Dehal A**, Smith JJ, Nash GM. Cytoreductive surgery and intraperitoneal chemotherapy: an evidence-based review-past, present and future. *J Gastrointest Oncol* 2016; **7**: 143-157 [PMID: 26941992 DOI: 10.3978/j.issn.2078-6891.2015.112]

2 **Thomassen I**, van Gestel YR, van Ramshorst B, Luyer MD, Bosscha K, Nienhuijs SW, Lemmens VE, de Hingh IH. Peritoneal carcinomatosis of gastric origin: a population-based study on incidence, survival and risk factors. *Int J Cancer* 2014; **134**: 622-628 [PMID: 23832847 DOI: 10.1002/ijc.28373]

3 **Yoo CH**, Noh SH, Shin DW, Choi SH, Min JS. Recurrence following curative resection for gastric carcinoma. *Br J Surg* 2000; **87**: 236-242 [PMID: 10671934 DOI: 10.1046/j.1365-2168.2000.01360.x]

4 **Sadeghi B**, Arvieux C, Glehen O, Beaujard AC, Rivoire M, Baulieux J, Fontaumard E, Brachet A, Caillot JL, Faure JL, Porcheron J, Peix JL, François Y, Vignal J, Gilly FN. Peritoneal carcinomatosis from non-gynecologic malignancies: results of the EVOCAPE 1 multicentric prospective study. *Cancer* 2000; **88**: 358-363 [PMID: 10640968]

5 **Yonemura Y**, Fujimura T, Nishimura G, FallaR, Sawa T, Katayama K, Tsugawa K, Fushida S, Miyazaki I, Tanaka M, Endou Y, Sasaki T. Effects of intraoperative chemohyperthermia in patients with gastric cancer with peritoneal dissemination. *Surgery* 1996; **119**: 437-444 [PMID: 8644010]

6 **Shirao K**, Boku N, Yamada Y, Yamaguchi K, Doi T, Goto M, Nasu J, Denda T, Hamamoto Y, Takashima A, Fukuda H, Ohtsu A; Gastrointestinal Oncology Study Group of the Japan Clinical Oncology Group. Randomized Phase III study of 5-fluorouracil continuous infusion vs. sequential methotrexate and 5-fluorouracil therapy in far advanced gastric cancer with peritoneal metastasis (JCOG0106). *Jpn J Clin Oncol* 2013; **43**: 972-980 [PMID: 24014884 DOI: 10.1093/jjco/hyt114]

7 **Hong SH**, Shin YR, Roh SY, Jeon EK, Song KY, Park CH, Jeon HM, Hong YS. Treatment outcomes of systemic chemotherapy for peritoneal carcinomatosis arising from gastric cancer with no measurable disease: retrospective analysis from a single center. *Gastric Cancer* 2013; **16**: 290-300 [PMID: 22898806 DOI: 10.1007/s10120-012-0182-1]

8 **McQuellon RP**, Loggie BW, Fleming RA, Russell GB, Lehman AB, Rambo TD. Quality of life after intraperitoneal hyperthermic chemotherapy (IPHC) for peritoneal carcinomatosis. *Eur J Surg Oncol* 2001; **27**: 65-73 [PMID: 11237495 DOI: 10.1053/ejso.2000.1033]

9 **Garofalo A**, Valle M, Garcia J, Sugarbaker PH. Laparoscopic intraperitoneal hyperthermic chemotherapy for palliation of debilitating malignant ascites. *Eur J Surg Oncol* 2006; **32**: 682-685 [PMID: 16631341 DOI: 10.1016/j.ejso.2006.03.014]

10 **Koizumi W**, Narahara H, Hara T, Takagane A, Akiya T, Takagi M, Miyashita K, Nishizaki T, Kobayashi O, Takiyama W, Toh Y, Nagaie T, Takagi S, Yamamura Y, Yanaoka K, Orita H, Takeuchi M. S-1 plus cisplatin versus S-1 alone for first-line treatment of advanced gastric cancer (SPIRITS trial): a phase III trial. *Lancet Oncol* 2008; **9**: 215-221 [PMID: 18282805 DOI: 10.1016/S1470-2045(08)70035-4]

11 **Sakata Y**, Ohtsu A, Horikoshi N, Sugimachi K, Mitachi Y, Taguchi T. Late phase II study of novel oral fluoropyrimidine anticancer drug S-1 (1 M tegafur-0.4 M gimestat-1 M otastat potassium) in advanced gastric cancer patients. *Eur J Cancer* 1998; **34**: 1715-1720 [PMID: 9893658]

12 **Yonemura Y**, Endou Y, Sasaki T, Hirano M, Mizumoto A, Matsuda T, Takao N, Ichinose M, Miura M, Li Y. Surgical treatment for peritoneal carcinomatosis from gastric cancer. *Eur J Surg Oncol* 2010; **36**: 1131-1138 [PMID: 20933363 DOI: 10.1016/j.ejso.2010.09.006]

13 **Jacquet P**, Sugarbaker PH. Peritoneal-plasma barrier. *Cancer Treat Res* 1996; **82**: 53-63 [PMID: 8849943]

14 **Dedrick RL**, Myers CE, Bungay PM, DeVita VT Jr. Pharmacokinetic rationale for peritoneal drug administration in the treatment of ovarian cancer. *Cancer Treat Rep* 1978; **62**: 1-11 [PMID: 626987]

15 **Markman M**. Intraperitoneal antineoplastic drug delivery: rationale and results. *Lancet Oncol* 2003; **4**: 277-283 [PMID: 12732164]

16 **Detroz B**, Laurent S, Honoré P, Blaffart F, Limet R, Meurisse M. Rationale for hyperthermic intraperitoneal chemotherapy (HIPEC) in the treatment or prevention of peritoneal carcinomatosis. *Acta Chir Belg* 2004; **104**: 377-383 [PMID: 15469146]

17 **González-Moreno S**, González-Bayón LA, Ortega-Pérez G. Hyperthermic intraperitoneal chemotherapy: Rationale and technique. *World J Gastrointest Oncol* 2010; **2**: 68-75 [PMID: 21160924 DOI: 10.4251/wjgo.v2.i2.68]

18 **Kuramoto M**, Shimada S, Ikeshima S, Matsuo A, Yagi Y, Matsuda M, Yonemura Y, Baba H. Extensive intraoperative peritoneal lavage as a standard prophylactic strategy for peritoneal recurrence in patients with gastric carcinoma. *Ann Surg* 2009; **250**: 242-246 [PMID: 19638909 DOI: 10.1097/SLA.0b013e3181b0c80e]

19 **Seshadri RA**, Glehen O. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in gastric cancer. *World J Gastroenterol* 2016; **22**: 1114-1130 [PMID: 26811651 DOI: 10.3748/wjg.v22.i3.1114]

20 **Sugarbaker PH**. Peritoneal Metastases from Gastrointestinal Cancer. *Curr Oncol Rep* 2018; **20**: 62 [PMID: 29884974 DOI: 10.1007/s11912-018-0703-0]

21 **Sun J**, Song Y, Wang Z, Gao P, Chen X, Xu Y, Liang J, Xu H. Benefits of hyperthermic intraperitoneal chemotherapy for patients with serosal invasion in gastric cancer: a meta-analysis of the randomized controlled trials. *BMC Cancer* 2012; **12**: 526 [PMID: 23153379 DOI: 10.1186/1471-2407-12-526]

22 **Mi DH**, Li Z, Yang KH, Cao N, Lethaby A, Tian JH, Santesso N, Ma B, Chen YL, Liu YL. Surgery combined with intraoperative hyperthermic intraperitoneal chemotherapy (IHIC) for gastric cancer: a systematic review and meta-analysis of randomised controlled trials. *Int J Hyperthermia* 2013; **29**: 156-167 [PMID: 23418917 DOI: 10.3109/02656736.2013.768359]

23 **Huang JY**, Xu YY, Sun Z, Zhu Z, Song YX, Guo PT, You Y, Xu HM. Comparison different methods of intraoperative and intraperitoneal chemotherapy for patients with gastric cancer: a meta-analysis. *Asian Pac J Cancer Prev* 2012; **13**: 4379-4385 [PMID: 23167347]

24 **Yan TD**, Black D, Sugarbaker PH, Zhu J, Yonemura Y, Petrou G, Morris DL. A systematic review and meta-analysis of the randomized controlled trials on adjuvant intraperitoneal chemotherapy for resectable gastric cancer. *Ann Surg Oncol* 2007; **14**: 2702-2713 [PMID: 17653801 DOI: 10.1245/s10434-007-9487-4]

25 **Yonemura Y,** Shinbo M, Hagiwara A, Shimada S, Nakajima T, Ikeda S, Pkamura H, Hirano M, Mizuno M, Endou Y, Miura M, Mizumoto Y. Treatment for potentially curable gastric cancer patients with intraperitoneal free cancer cells. *Gastroenterological Surg* 2008; **31**: 802-812

26 **Sayag-Beaujard AC**, Francois Y, Glehen O, Sadeghi-Looyeh B, Bienvenu J, Panteix G, Garbit F, Grandclément E, Vignal J, Gilly FN. Intraperitoneal chemo-hyperthermia with mitomycin C for gastric cancer patients with peritoneal carcinomatosis. *Anticancer Res* 1999; **19**: 1375-1382 [PMID: 10365109]

27 **Glehen O**, Schreiber V, Cotte E, Sayag-Beaujard AC, Osinsky D, Freyer G, François Y, Vignal J, Gilly FN. Cytoreductive surgery and intraperitoneal chemohyperthermia for peritoneal carcinomatosis arising from gastric cancer. *Arch Surg* 2004; **139**: 20-26 [PMID: 14718269 DOI: 10.1001/archsurg.139.1.20]

28 **Gill RS**, Al-Adra DP, Nagendran J, Campbell S, Shi X, Haase E, Schiller D. Treatment of gastric cancer with peritoneal carcinomatosis by cytoreductive surgery and HIPEC: a systematic review of survival, mortality, and morbidity. *J Surg Oncol* 2011; **104**: 692-698 [PMID: 21713780 DOI: 10.1002/jso.22017]

29 **Yonemura Y**, Kawamura T, Bandou E, Takahashi S, Sawa T, Matsuki N. Treatment of peritoneal dissemination from gastric cancer by peritonectomy and chemohyperthermic peritoneal perfusion. *Br J Surg* 2005; **92**: 370-375 [PMID: 15739249 DOI: 10.1002/bjs.4695]

30 **Glehen O**, Gilly FN, Arvieux C, Cotte E, Boutitie F, Mansvelt B, Bereder JM, Lorimier G, Quenet F, Elias D; Association Française de Chirurgie. Peritoneal carcinomatosis from gastric cancer: a multi-institutional study of 159 patients treated by cytoreductive surgery combined with perioperative intraperitoneal chemotherapy. *Ann Surg Oncol* 2010; **17**: 2370-2377 [PMID: 20336386 DOI: 10.1245/s10434-010-1039-7]

31 **Yang XJ**, Huang CQ, Suo T, Mei LJ, Yang GL, Cheng FL, Zhou YF, Xiong B, Yonemura Y, Li Y. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy improves survival of patients with peritoneal carcinomatosis from gastric cancer: final results of a phase III randomized clinical trial. *Ann Surg Oncol* 2011; **18**: 1575-1581 [PMID: 21431408 DOI: 10.1245/s10434-011-1631-5]

32 **Yonemura Y**, Elnemr A, Endou Y, Hirano M, Mizumoto A, Takao N, Ichinose M, Miura M, Li Y. Multidisciplinary therapy for treatment of patients with peritoneal carcinomatosis from gastric cancer. *World J Gastrointest Oncol* 2010; **2**: 85-97 [PMID: 21160926 DOI: 10.4251/wjgo.v2.i2.85]

33 **Bozzetti F**, Yu W, Baratti D, Kusamura S, Deraco M. Locoregional treatment of peritoneal carcinomatosis from gastric cancer. *J Surg Oncol* 2008; **98**: 273-276 [PMID: 18726891 DOI: 10.1002/jso.21052]

34 **Canbay E**, Mizumoto A, Ichinose M, Ishibashi H, Sako S, Hirano M, Takao N, Yonemura Y. Outcome data of patients with peritoneal carcinomatosis from gastric origin treated by a strategy of bidirectional chemotherapy prior to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in a single specialized center in Japan. *Ann Surg Oncol* 2014; **21**: 1147-1152 [PMID: 24356799 DOI: 10.1245/s10434-013-3443-2]

35 **Ni X**, Wu P, Wu J, Ji M, Tian B, Jiang Z, Sun Y, Xing X, Jiang J, Wu C. Hyperthermic intraperitoneal perfusion chemotherapy and response evaluation in patients with gastric cancer and malignant ascites. *Oncol Lett* 2017; **14**: 1691-1696 [PMID: 28789396 DOI: 10.3892/ol.2017.6342]

36 **Yonemura Y**, Fujimura T, Fushida S, Takegawa S, Kamata T, Katayama K, Kosaka T, Yamaguchi A, Miwa K, Miyazaki I. Hyperthermo-chemotherapy combined with cytoreductive surgery for the treatment of gastric cancer with peritoneal dissemination. *World J Surg* 1991; **15**: 530-535; discussion 535-536 [PMID: 1891941]

37 **Fujimoto S**, Shrestha RD, Kokubun M, Ohta M, Takahashi M, Kobayashi K, Kiuchi S, Okui K, Miyoshi T, Arimizu N. Intraperitoneal hyperthermic perfusion combined with surgery effective for gastric cancer patients with peritoneal seeding. *Ann Surg* 1988; **208**: 36-41 [PMID: 3133994]

38 **Facchiano E**, Scaringi S, Kianmanesh R, Sabate JM, Castel B, Flamant Y, Coffin B, Msika S. Laparoscopic hyperthermic intraperitoneal chemotherapy (HIPEC) for the treatment of malignant ascites secondary to unresectable peritoneal carcinomatosis from advanced gastric cancer. *Eur J Surg Oncol* 2008; **34**: 154-158 [PMID: 17640844 DOI: 10.1016/j.ejso.2007.05.015]

39 **Facchiano E**, Risio D, Kianmanesh R, Msika S. Laparoscopic hyperthermic intraperitoneal chemotherapy: indications, aims, and results: a systematic review of the literature. *Ann Surg Oncol* 2012; **19**: 2946-2950 [PMID: 22526907 DOI: 10.1245/s10434-012-2360-0]

40 **Valle M**, Van der Speeten K, Garofalo A. Laparoscopic hyperthermic intraperitoneal peroperative chemotherapy (HIPEC) in the management of refractory malignant ascites: A multi-institutional retrospective analysis in 52 patients. *J Surg Oncol* 2009; **100**: 331-334 [PMID: 19697441 DOI: 10.1002/jso.21321]

**P-Reviewer:** Yuan Y **S-Editor:** Cui LJ **L-Editor:** A **E-Editor:** Xing YX

**Specialty type:** Surgery

**Country of origin:** Taiwan

**Peer-review report classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0