Mini-review

Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in the treatment of gastric cancer with peritoneal carcinomatosis---A mini-review

Lynne M. Ellison, D.O., M.T.; Itzhak Avital, M.D., FACS; Alexander Stojadinovic, M.D., FACS; Yan-Gao Man, M.D., Ph.D.

Bon Secours Cancer Institute, Bon Secours Health System, Richmond, VA

New Approaches combating Cancer & Aging 2014; 1: 46-54

Corresponding authors: Itzhak Avital, M.D., FACS; Professor of Surgery, Executive Director, Bon Secours Cancer Institute, Bon Secours Health System, Virginia, USA. Phone: 804- 221-7364; Email address: itzhakavital@gmail.com.

This is an open-access article distributed under the terms of the International Standard Serial Number (2372-7837) and the International Union for Difficult-to-treat-Diseases (www/iudd.org). Reproduction is permitted for personal or noncommercial use, provided that the article is in whole, unmodified, and properly cited.

Received: 10-21-2014. Accepted: 10-30-2014. Published: 11-11-2014

Abstract

Although gastric cancer with peritoneal carcinomatosis is associated with poor prognosis and is generally treated with palliative systemic therapy, recent studies have shown that cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) may prove to be an efficacious treatment option. In addition to revie the natural history of gastric cancer with peritoneal carcinomatosis, this mini-review examines literature looking at the efficacy of CRS and HIPEC as compared to chemotherapy and surgical options. Both randomized and non-randomized studies were summarized with the emphasis focused on overall survival. In summary, CRS and HIPEC is indeed a promising treatment option for gastric cancer with peritoneal carcinomatosis and large randomized clinical trials are warranted.

Introduction

Although the incidence of gastric cancer has decreased over the years, it is the fifth leading cause of cancer worldwide after lung, breast, colorectal, and prostate cancer and it is the third most common cause of cancer deaths worldwide after lung and liver cancer [1, 2]. Gastric cancer accounted for 10% of the total cancer related deaths and 8% of the total cancer cases in 2008 with over 70% of new cases and deaths occurring in developing countries [3]. Asia and Eastern Europe have the highest rates of disease [4]. The overall 5-year survival for gastric cancer is approximately 15-20% and the survival rate drops steeply as the staging progresses [4]. When localized to the stomach the 5-year survival is approximately 55%, but by stage IV the 5-year overall survival decreases to 4% [4].

Peritoneal carcinomatosis arising from gastric cancer is generally associated with poor prognosis. Risk factors found to be significantly associated with peritoneal carcinomatosis in literature include tumor stage T3/T4 [5-9], age ≤60 years [9], histologic type

小综述

癌组织减灭术和腹腔温热化疗在治疗胃癌腹膜转移中的作用---小综述

Lynne M. Ellison, D.O., M.T.; Itzhak Avital, 医学博士, Alexander Stojadinovic，医学博士；满延高，医-哲学博士

美国 Bon Secours 癌症研究院与医疗系统, 维吉尼亚

新法抗癌抗衰杂志 2014 年第 1 期第 46-54 页

通讯作者： Itzhak Avital，医学博士，外科教授，所长 美国 Bon Secours 癌症研究院与医疗系统, 维吉尼亚；电话：804-221-7364；E-mail：itzhakavital@gmail.com

本刊为网上杂志,国际标准序列号为:2373-2806. 本刊为国际抗疑难杂症联盟(www.iudd.org) 的学术刊物. 在保证如实完整反映本刊所发论文的前提下,任何个人与非商业团体可免费下载任一文章的全文或章节。

收稿：2014-10-1。接受：2014-10-20。发表：2014-10-22

摘要

虽然胃癌合并腹膜转移预后较差，且一般使用姑息性全身治疗，但最近的研究表明：癌组织减灭术（CRS） 和腹腔温热化疗 （HIPEC）可能是有效的治疗选择。本文除回顾胃癌合并腹膜腔转移的自然历史外，还检阅了关于 CRS 和 HIPEC 的有效性，并与化学疗法和外科手术方案作对比，总结随机化与非随机化研究结果，重点讨论总体生存率。总之，CRS 和 HIPEC 这两种方法，对胃癌合并腹膜腔内转移确实是有希望的治疗方案，但尚需大规模随机临床试验。

导言

尽管胃癌的发病率近年来有所下降，但它仍然是世界上继肺癌、乳癌、结肠直肠癌和前列腺癌之后第五位领先的癌瘤，而且是世界上继肺癌和肝癌之后第三位的最普遍的癌症死因【1，2】。据统计，在 2008 年，胃癌约占整个与癌症相关死亡人数的 10%，和整个发生癌症病例人数的 8%。超过 70% 的胃癌新病例人数和死亡人数发生在发展中国家【3】，在亚洲和东欧，则此病占据最高比例【4】。胃癌的五年存活率约为 15-20%，而在其进展期则更为低下【4】。当胃癌仅局限于胃时，其五年存活率约为 55%，但若於第 IV 期胃癌，其五年存活率则降为 4% 【4】。

起源于胃癌的腹膜腔内癌，一般来讲都预后不良。在文献中可见与腹膜腔内癌瘤明显相关的危险因子包括：T3/T4 期【5-9】，年龄在 ≤ 60, [9], 癌组织类型（包含印戒细胞特征）【6,10】,

(including signet-ring cell features) [6, 10], nodal invasion [7, 8], vascular invasion [6], ascites [5], liver metastasis [5], and female gender [10]. The median survival rates for peritoneal carcinomatosis range from 1-9 months with no survival at 5 years [11].

淋巴结扩散【7,8】，血管扩散【6】，腹水【5】，肝转移【5】，以及女性【10】。胃癌腹膜转移的中位存活期约 1-9 个月，而五年存活期则为零【11】。

Recently, Thomassen and colleagues [10] did a population based study to look at the morbidity and mortality among patients with peritoneal carcinomatosis of gastric origin and found the median survival of patients with peritoneal metastasis to be 4 months as compared to 14 months in patients without metastasis. Out of the 5,220 patients studied, 39% of them presented with metastatic disease and 35% of them had peritoneal carcinomatosis [10]. Similarly, Sadeghi and colleagues [5] found the overall survival was 3.1 months and over half were diagnosed with peritoneal carcinomatosis at the time of primary gastric cancer diagnosis in their prospective trial.

近来 Thomassen 及其同事【10】研究了一群起源于胃癌的腹膜腔癌瘤病人中的发病率和死亡率，发现合并有腹膜腔转移癌病人的中位存活期约 4 个月，而没有伴发腹膜腔转移癌者其中位存活期则为 14 个月。在 5,220 名研究病人中，39%病人伴有转移癌，而其中 35%病人伴有腹膜腔转移癌【10】。同样，Sadeghi 及其同事在一前瞻性研究中【5】发现：胃癌合并腹膜转移的总生存期为 3.1 个月。此研究超过一半的病人在原发性胃癌诊断时已经伴有腹膜腔转移癌。

Surgery along with adjuvant chemotherapy or chemoradiation has been the mainstay treatment of non-metastatic gastric cancer over the years with palliative systemic chemotherapy being the standard of care in advanced or recurrent gastric cancer. Within the last three decades, there has been an increasing interest in cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in treating advanced gastric carcinoma with peritoneal carcinomatosis with the goal of killing any residual microscopic disease that may be present after completely removing the macroscopic disease. The intent of this article is to review literature dealing with treatments for gastric cancer with peritoneal carcinomatosis including chemotherapy, surgery, and hyperthermic intraperitoneal chemotherapy.

外科手术合并辅助的化学疗法或化学放射疗法多年来一直是治疗不合并转移癌的胃癌的主要手段，而姑息性系统化疗已作为进展期或再发性胃癌的一个常规治疗方法。在过去三十年里，以癌组织减灭术和腹腔温热化疗治疗晚期胃癌腹膜转移的兴趣已日趋增加. 其目的在于杀死外科手术后可能残留的微观疾病。本文的意图是：回顾有关胃癌合并腹膜腔内转移癌瘤治疗的文献，包括化疗，外科手术，以及腹腔温热化疗。

Chemotherapy and Surgery

Palliative chemotherapy is the standard of care in advanced or recurrent gastric cancer. Wagner and colleagues [12] published a systematic review in 2010 that evaluated the effect of chemotherapy in patients with advanced gastric cancer as compared to best supportive care. They found a 6.7 month improvement in median survival (from 4.3 months to 11 months) in the chemotherapy group when compared to the best supportive care [12]. In 2013, GASTRIC (Global Advanced/Adjuvant Stomach Tumor Research International Collaboration) [13] did a meta-analysis on the efficacy of chemotherapy on overall survival and progression-free survival in advanced/recurrent gastric cancer. When comparing the experimental chemotherapy arms with the corresponding control arms the hazard ratio was 0.88 and 0.81 in regards to overall survival and progression-free survival. These hazard ratios equated to a median overall survival difference of 3 weeks (37.6 and 34.4 median in weeks) and a progression-free survival difference of 4 weeks (20.4 and 16.4 median in weeks). The GASTRIC study exemplified how chemotherapy in addition to standard regimens has yielded minimal improvement in overall survival and progression-free intervals with no certain chemotherapy regimen emerging as a better standard [13]. Although

化学疗法和外科手术

姑息化疗是治疗晚期或复发性胃癌组织的标准方法。Wagner 及其同事【12】在 2010 年发表了一系统性回顾文章，评价了化疗对晚期胃癌病人的疗效，并与最佳支持疗法作了对比 。他们发现，与最佳支持疗法相比较，化疗组的中间存活期（从 4.3 个月至 11 个月）提高 6.7 个月【12】。2013 年，全球晚期/辅助胃癌研究国际联盟（GASTRIC【13】分析了化疗对晚期/再发性胃癌整个存活期和静止存活期的影响。当实验性化疗与相应对照组比较时，其总的存活期和静止期存活期的机迁比例分别为 0.88 和 0.81。这些机迁比等同于 3 周 (37.6 和 34.4 周) 中位数的总体生存差异和 4 周（ 20.4 和 16.4 周） 的静止生存期差异。全球晚期/辅助胃癌研究国际联盟的研究报告说明：标准治疗方案加化疗对胃癌合并腹膜腔内转移病人总存活期和静止存活期的改善极微：目前没有一

chemotherapy is the mainstay treatment for advanced gastric cancer, there does not seem to be any set consensus on the overall efficacy of treatment.

种化疗制剂可望成为一个更好的疗法【13】。虽然化疗是晚期胃癌的主要治疗手段，但它的总体疗效，目前缺乏共识。

The outcome of surgical intervention is often predicated by the progression of the gastric cancer. Hioki and colleagues [14] found that gastrectomy increased survival in patients with metastasis to adjacent peritoneum (P1) and few scattered metastasis to adjacent peritoneum (P2) but not in patients with numerous distant peritoneal metastasis (P3). They found that the overall survival in P1, P2, and P3 groups were 18 months, 15 months, and 9 months, respectively. Furthermore, the 1-year survival was found to be 64.7%, 69.2%, and 35.2%, respectively [14]. However, Kim and colleagues [9] found that there was no significant trend of improved survival after surgical management of HIPEC.

胃癌的分期可以预测手术的结果. Hioki 及其同事【14】发现：在只有局灶腹膜转移（P1）和少数 P2 病例，胃全切可提高病人的存活率，但对广泛转移（P3）的病人，则无改善作用。他们发现，P1、P2 和 P3 病人组的存活期，分别为 18 个月、15 个月和 9 个月。此外，病人的一年存活率分别为 64.7%、69.2% 和 35.2%【14】。但是，Kim 及其同事【9】发现，腹膜腔内温热化疗（HIPEC）和外科手术对胃癌腹膜转移病人的存活期并没有明显的改善。

Currently, there are no large randomized studies examining the efficacy of surgery and systemic therapy versus systemic therapy alone in patients with advanced metastatic gastric cancer. The GYMSSA trial will be conducted by the National Cancer Institute and will compare gastrectomy with metastectomy plus systemic therapy versus systemic chemotherapy alone in metastatic gastric cancer patients [15]. This trial will highlight whether or not there is a benefit to aggressive surgical intervention in addition to the current chemotherapeutic standard of care.

目前，没有大的随机的研究，审查手术加全身疗法与单独的全身疗法在治疗晚期转移性胃癌患者的 疗效。美国国家癌症研究所将推出 GYMSSA 试用疗法，比较胃全切加系统性治疗和单独的全身疗法在治疗晚期转移性胃癌患者的 疗效 结果。这一试验将揭示是否广泛外科清除手术加现代标准化疗法较传统的疗法有优越性。

Table 1. Comparison of median survival times of chemotherapy versus surgery
表 1. 化疗与外科手术中间存活时间的比较

Treatment 治疗	Patient number 病人数量	Median survival Experimental 实验组中间存活时间	Median Survival Control 对照组中间存活时间	P P 值
Chemotherapy 化疗	103[12]	11 months (月)	4.3 months (月)	0.19
	4214[13]	9.4 months (月)	8.6 months (月)	<0.0001
Surgery 外科手术	101[14]	11 months (月)	None provided 未提供	<0.001

CRS + HIPEC versus chemotherapy

Hultman and colleagues [16] compared systemic chemotherapy followed by CRS and intraperitoneal chemotherapy compared to systemic chemotherapy only and found the mean overall survival in the experimental group was 20.5 months as compared to 11.1 months in the control group.

癌组织减灭术和腹腔温热化疗与化疗的比较

Hultman 及其同事【16】比较了全身性化疗加癌组织减灭术加腹腔温热化疗与单纯的全身性化疗后发现，在实验组的平均总存活期为 20.5 个月，而对照组的平均总存活期为 11.1 个月。

Table 2. Comparison of average and median survival times of CRS + HIPEC + EPIC VS chemotherapy
表 2. CRS+HIPEC+EPIC 与化疗的平均存活期和中间存活期的比较

Treatment 治疗	Patient number 病人数量	Average survival 平均存活期	P P 值	Median survival 中间存活期	P P 值
Chemotherapy 化疗	10 [16]	11.1 months (月)	Not provided 未提供	10.4 months (月)	Not provided 未提供
CRS + HIPEC 癌组织减灭术+腹腔温热化疗	7 [16]	20.5 months (月)	Not provided 未提供	15.3 months	Not provided 未提供

CRS + HIPEC versus surgery

If intraperitoneal free cancer cells are present after curative surgery in advanced gastric patients that the 5-year survival rate is only 15.4% as compared to 49.4% if no intraperitoneal cancer cells are found [17]. Furthermore, Kuramoto and colleagues [18] found that extensive intraoperative peritoneal lavage followed by intraperitoneal chemotherapy (EIPL-IPC) significantly increased the 5-year survival rate on patients with intraperitoneal free cancer cells without overt peritoneal metastasis as compared to surgery plus intraperitoneal chemotherapy and surgery alone groups. The 5-year survival rate was 43.8%, 4.6%, and 0% in the EIPL-IPC, IPC, and surgery alone groups, respectively [18]. The goal of HIPEC in killing off microscopic tumor cells that may be present after CRS is a promising treatment modality for gastric cancer with peritoneal carcinomatosis.

There are a limited amount of randomized trials on CRS and HIPEC. Yang and colleagues [19] completed a randomized phase III study and found the median survival for the CRS + HIPEC group was 11.0 months as compared to 6.5 months in the CRS alone group. Yonemura and colleagues [20] did a prospective randomized study on 139 patients with advanced gastric cancer that were treated with either chemohyperthermic peritoneal perfusion and surgery, chemonormothermic peritoneal perfusion and surgery, or surgery alone. They found that the overall 5 year survival rates for CHPP, CNPP and surgery alone groups were 61%, 43%, and 42% respectively [20]. Fujimura and colleagues [21] did a randomized study that showed improved survival in patients receiving continuous hyperthermic peritoneal perfusion or continuous normothermic peritoneal perfusion as compared to the gastric surgery without perfusion group. Furthermore, the significant differences in the survival curves shows that peritoneal perfusion, whether hyperthermic or normothermic, is an effective procedure for preventing peritoneal recurrence [21]. Yu and colleagues [22] did a prospective randomized trial which showed that gastric resection plus early postoperative intraperitoneal chemotherapy improved overall 5-year survival compared to surgery only in patients with stage IV gastric cancer (28% and 5%, respectively) [22].

There are many nonrandomized studies dealing with CRS and HIPEC. Fujimoto and colleagues [23] did a nonrandomized study that found increased survival rate for gastric cancer patients with peritoneal carcinomatosis receiving intraperitoneal hyperthermic chemoperfusion and aggressive surgery as compared to surgery alone. Hirose and colleagues [24] did a nonrandomized study looking at the efficacy of continuous hyperthermic peritoneal perfusion with surgery as compared to surgery alone by a multivariate regression analysis. The continuous hyperthermic peritoneal perfusion group had a higher median survival time and the 1-year survival rate as compared to the control group: 11 months and 44.4% versus 6 months and 15.8%, respectively [24]. Similarly, Yonemura et al. [25] found the median survival of 11.5 months in his patients that received cytoreduction and intraperitoneal hyperthermic chemotherapy. Glehen et al. [26] found the median survival of patients receiving CRS followed by

癌组织减灭术和腹腔温热化疗与手术的比较

若晚期胃癌病人经有疗效的外科手术后腹膜腔内出现游离分散的癌细胞者，其五年存活率仅为 15.4%，而腹膜腔内未见癌细胞者，其五年存活率则为 49.4% 【17】。此外，Kuramoto 及其同事【18】发现，对腹膜腔内伴有分离散在的癌细胞但未合并明显转移的病人，在手术中广泛腹膜腔灌洗后作腹膜腔内化疗（EIPC-IPC），其五年存活率比对照的手术+腹膜腔内化疗（IPC）组和单纯外科手术组有明显提高。在 EIPC-IPC 组、IPC 组和单纯外科手术组，其五年存活率分别为 43.8%、4.6%和 0%【18】。腹腔温热化疗（HIPEC）的目的在于截杀手术（CRS）后可能残余的显微镜下可见的癌瘤细胞，这是胃癌合并腹膜腔转移癌症人一个很有希望的治疗方式 。

目前已有数量有限的 CRS 和 HIPEC 的随机性试验，Yang 其同事【19】完成了一组随机性 III 期研究，发现肿瘤细胞减灭术（CRS）+腹腔温热化疗（HIPEC）组的中间存活期为 11 个月，而对照的仅作癌组织减灭术组（CRS）的中间存活期仅为 6.5 个月。Yonemura 及其同事【20】对 139 例晚期胃癌病人应用腹腔温热化疗，腹膜腔内灌洗及外科手术组（CHPP），化疗加热器腹膜腔灌洗及外科手术组 （CNPP）或者仅作外科手术组者，作了前瞻性和随机性研究。他们发现，CHPP、CNPP 和单纯外科手术组，其总的五年存活率分别为 61%、43%和 42%【20】。Fujimura 及其同事【21】所作的随机性研究表明，近来接受连续性人工加热器腹膜腔灌洗或连续性正常加热器腹膜腔灌洗病人，其总的存活期比未作灌洗的胃部手术病人组有所改进。此外，在存活期曲线上的明显差别表明，无论是人工加热器或正常加热器的腹膜腔灌洗，都是预防腹膜腔癌瘤再发的一个有效的方法【21】。Yu 及其同事[22]所作的有希望的随机性试验表明，对第四期胃癌病人作胃切除术+早期手术后腹膜腔内化疗，其总的五年存活率比作单纯外科手术组病人有明显改进（前组为 28%，而后组为 5%）【22】。

对 CRS 和 HIPEC，现有许多非随机性研究。Fujimoto 及其同事【23】所作的非随机性研究发现，胃癌合并腹膜腔癌瘤病人接受腹腔温热化疗灌洗和外科手术者，其存活率比单纯外科手术者增高。Hirose 及其同事【24】通过多元回归分析对连续性腹腔温热化疗灌洗合并外科手术组，与对照单纯外科手术组的有效性观察，作了非随机性研究。其中连续性腹腔温热化疗腹膜腔灌洗组有较高的中间存活期（11 个月）和 1 年存活率（44.4%），而对照的外科手术组，则分别为 6 个月和 15.8%【24】。与此类似，Yonemura 等人【25】发现，在接受癌组织减灭术（CRS）和腹腔温热化疗（IPEC）组的中间存活期为 11 个月。Glehen 等人【26】发现，接受癌组织减灭术（CRS）和腹腔温热化疗（HIPEC）病人的中间存活期为 10.3 个月，而若获得 CCR-0 或 CCR-1

intraperitoneal chemotherapy to be 10.3 months with the median survival increasing to 21.3 months when CCR-0 or CCR-1 was obtained.

手术时，其中间存活期则可明显增加至 21.3 个月。

Table 3. Comparison of median survival times of CRS and HIPEC versus surgery alone.
表 3. 癌组织减灭术（CRS）加腹腔温热化疗（HIPEC）与单纯外科手术病人的中间存活期比较

Treatment 治疗	Patient number 病人数量	Median survival 中间存活期	P P 值
CRS + HIPEC 癌组织减灭术+腹腔温热化疗	34 [19]	11.0 months (月)	0.046
	17 [24]	11.0 months (月)	0.0455
	107[25]	11.5 months (月)	0.001
	49 [26]	10.3 months (月)	0.001
Surgery alone 单纯外科手术	34 [19]	6.5 months (月)	0.046
	20 [24]	6.0 months (月)	0.0455

Complete versus incomplete cytoreduction

Although CRS and HIPEC are promising treatment modalities for gastric cancer with peritoneal carcinomatosis, the success of the treatment is largely dependent on the resection status. Hall and colleagues [27] evaluated CRS and IPHC with peritoneal carcinomatosis from gastric cancer. The study investigated the outcomes of patients that either underwent gastric resection with CRS and IPHC with mitomycin C while the control group underwent radical gastrectomy without extended nodal resection. While the overall survival was similar between the experimental and control groups (7.8 months and 8.0 months, respectively), the overall survival times in the IPHC group was dependent on resection status. Within the IPHC group, a median survival time was 11.2 months if R0/R1 resection was completed as compared to 3.3 months if R2 resection was completed. Yonemura and colleagues [25] completed a retrospective study on 107 patients with peritoneal dissemination of gastric cancer who had intraoperative chemohyperthermic peritoneal perfusion after CRS to see whether or not completeness of cytoreduction or peritonectomy had an effect on overall survival and they found that the overall median survival was 11.5 months. The median survival was 15.5 months and 7.9 months in the complete and incomplete cytoreduction groups, respectively. The five year survival rate was 6.7% overall and in the peritonectomy group it was 27% [25]. Scaringi and colleagues [28] found a 23.4 month median survival in patients without demonstrable peritoneal carcinomtosis that received CRS + HIPEC while the peritoneal carcinomatosis group had a median survival of 6.6 months.

The median survival was 15 months when curative CRS was performed versus the median survival of 3.9 months in the palliative group [28]. Similarly, Yang and colleagues [29] found that that the median survival of patients with PCI ≤ 20 undergoing CRS + HIPEC was 27.7 months while a PCI > 20 had a median survival of 6.4

彻底与不彻底癌组织减灭术的比较

虽然癌组织减灭术（CRS）和腹腔温热化疗（HIPEC）正在成为胃癌合并腹膜腔癌瘤病人有希望的治疗方式，其治疗效果主要取决于手术切除的状况。Hall 及其同事【27】评估了源自胃癌的腹膜内癌病人的 CRS 和 HIPEC 的治疗方法问题。该研究调查了接受合并 CRS 的胃全切术和应用丝裂霉素 C 的 IPHC 的治疗实验组，与接受胃全切术但未作广泛清扫术的对照组病人的结果 发现，虽然 此实验组与对照组之总存活期基本相似，分别为 7.8 个月和 8 个月，IPHC 实验组的总存活时间主要取决于手术切除的状况。在 IPHC 组，若完成 R0/R1 切除术，中间存活期为 11.2 个月。 若完成 R2 切除术，则中间存活期为 3.3 个月。Yonemura 及其同事【25】对 107 例胃癌合并腹膜腔扩散癌瘤病人作了回顾性研究，以便观察癌组织减灭术或腹膜腔清扫术的彻底程度是否对总的存活期产生影响的问题。他们发现其总的存活期为 11.5 个月，而完全的和不完全的癌组织减灭术组两者的总的存活期，分别为 15.5 个月和 7.9 个月。至于它们的五年存活率，则为 6.7%，而在腹膜腔摘除手术组为 27%【25】。Scaringi 及其同事【28】发现，未显示腹膜腔癌瘤病人接受 CRS+HIPEC 治疗者，其中间存活期为 23.4 个月，而显示有腹膜腔癌瘤者，其中间存活期为 6.6 个月。

接受癌组织减灭术(CRS) 病人的中间存活期为 15 个月，而在姑息治疗组，其中间存活期仅为 3.9 个月【28】。与此类似，Yang 及其同事【29】发现，用过 PCI≤20 和经历 CRS+HIPEC 治疗的病人，其中间存活期为 27.7 个月，而用过 PCI>20 者，其中间存活期为 6.4 个月。至于

months. The estimated median survival for patients with CCR-0, CCR-1, and CCR-2/3 were 43.4 months, 9.5 months, and 7.5 months, respectively [29]. Glehen and colleagues [30] did a retrospective multicenter study to evaluate the treatment of CRS combined with perioperative intraperitoneal chemotherapy for peritoneal carcinomatosis from gastric cancer. The study found a median survival time of 9.2 months with the median survival in months for completeness of CRS labeled CC-0, CC-1, and CC-2/3 were 15, 6, and 4, respectively [30].

CCR-0 手术、CCR-I 手术和 CCR-2/3 手术病人组，其估计的中间存活期，分别为 43.4 个月、9.5 个月和 7.5 个月【29】）。Glehen 及其同事【30】作过多中心回顾性研究，以评估 CRS 结合周期性手术腹膜腔内化疗对胃癌腹膜转移的治疗效果问题。研究发现：病人的总体中位存活率为 9.2 个月。但手术彻底度不同，存活率也各异：CC-0，CC-1 和 CC-2/3 的存活率分别为 15、 6 和 4 个月【30】。

Table 4. Comparison of median survival times on cytoreduction status
表 4. 癌组织减灭术（Cytoreduction）状况有关中间存活时间的比较

Treatment 治疗	Patient number 病人数量	Median survival 中间存活期	P P 值
R0	7 [27]	36.3 months (月)	0.05
R0/R1	12 [27]	11.2 months (月)	0.015
R2	19 [27]	3.3 months (月)	0.015
CCR-0	11 [29]	43.4 months (月)	0.001
	8 [28]	15.0 months (月)	0.007
	85 [30]	15 months (月)	<0.001
CCR-1	6 [29]	9.4 months (月)	0.001
	37 [30]	6.0 months (月)	<0.001
CCR-0 or CCR-1	25 [26]	21.3 months (月)	<0.01
CCR-2	24 [26]	6.6 months (月)	<0.01
	18 [28]	3.9 months (月)	0.007
CCR-2 or CCR-3	11 [29]	8.3 months (月)	0.001
	30 [30]	30.0 months (月)	<0.001
Complete Cytoreduction 彻底癌组织减灭术	47 [25]	15.5 months (月)	<0.001
Incomplete Cytoreduction 不彻底癌组织减灭术	60[25]	7.9 months (月)	<0.001

Conclusion

Gastric cancer with peritoneal carcinomatosis has long been associated with a poor prognosis and is usually treated with palliative systemic chemotherapy. The state of the art treatment regimen including CRS and HIPEC has shown to increase overall survival rates. Gill and colleagues [31] did a systematic review looking of non-randomized, randomized, and prospective cohort trials regarding the effectiveness of CRS and HIPEC in patients with gastric cancer and peritoneal carcinomatosis and found the overall median survival was 7.9 months (range: 6.1-9.2 months) and 15 months if the patients had a completeness of cytoreduction scores of 0 or 1. They also found that the 1-year survival was 43% (range: 22-68%) [31]. Although there is a higher perioperative morbidity and mortality associated with CRS and HIPEC, patients should not be dissuaded because it has been

结论

胃癌合并的腹膜腔癌瘤长期以来认为是预后不良，而且通常是用姑息性系统性化疗治疗。包括癌组织减灭术（CRS）和腹腔温热化疗（HIPEC）在内的新技艺治疗方法的状况，已经表明能提高总的存活率。Gill 及其同事【31】，对胃癌合并腹膜腔转移癌瘤病人使用 CRS 和 HIPEC 的有效性，作了非随机性、随机性和前瞻性批次试用的系统性回顾，他们发现，若此类病人用彻底的癌组织减灭术 0 或 1 的等级时，其总的中间存活期分别为 7.9 个月（排列范围为 6.1 至 9.2 个月）和 15 个月，而一年的存活率为 43%（排列范围为 22%至 68%）【31】。虽然与 CRS 和 HIPEC 相关的周期性手术发病率和死亡率较高，但是不应该去劝阻这些病人拒绝使用，因为所发现的是，其手术后的生命质量与手术前者相类似，即有 6-12 个月的相似存活期。

found that the postoperative quality of life was similar to that of preoperative by 6-12 months [32] . Furthermore, knowing that resection status is an important prognostic factor it is imperative that only proficient surgeons conduct such aggressive therapy. CRS and HIPEC is a promising treatment option for patients with gastric cancer with peritoneal carcinomatosis.

此外，已知手术状况是一个重要的预后因素，而更为绝对必要的是，仅仅精通的外科医生们才能实施这类侵袭性治疗方法。因此癌组织减灭术(CRS)和腹膜腔内温热化疗（HIPEC），对胃癌合并腹膜腔转移癌瘤病人，确实是一个有希望前途的治疗方案。

Acknowledgement

The translation of this article from English to Chinese was made by Dr. Shizhang Shang of Georgetown University Medical School, Washington DC, USA, and typing was completed by Ms. Rui Gao of Maryland, USA. Journal of Cancer greatly appreciates their assistance.

鸣谢

此文的英文-中文翻译是由美国乔治城大 学医学院医学博士赏诗樟完成。中文打字由美国马利兰州高睿女士完成。( )杂志衷心感谢他(她)们的帮助。

References

1. Ferlay J SI, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 In. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr, accessed on 04/20/2014.
2. Bray F, Ren JS, Masuyer E, Ferlay J. Global estimates of cancer prevalence for 27 sites in the adult population in 2008. Int J Cancer 2013; 132: 1133-1145.
3. Jemal A, Bray F, Center MM et al. Global cancer statistics. CA Cancer J Clin 2011; 61: 69-90.
4. Edge SB, American Joint Committee on Cancer. AJCC cancer staging manual. New York: Springer 2010.
5. Sadeghi B, Arvieux C, Glehen O et al. Peritoneal carcinomatosis from non-gynecologic malignancies: results of the EVOCAPE 1 multicentric prospective study. Cancer 2000; 88: 358-363.
6. Fanelli MF, de Paiva TF, Jr., Silva MJ et al. Predictors of peritoneal carcinomatosis in patients with gastric cancer treated at a single institution in Brazil. J Surg Oncol 2009; 100: 452-455.
7. Tanaka T, Kumagai K, Shimizu K et al. Peritoneal metastasis in gastric cancer with particular reference to lymphatic advancement; extranodal invasion is a significant risk factor for peritoneal metastasis. J Surg Oncol 2000; 75: 165-171.
8. Roviello F, Marrelli D, de Manzoni G et al. Prospective study of peritoneal recurrence after curative surgery for gastric cancer. Br J Surg 2003; 90: 1113-1119.
9. Kim KW, Chow O, Parikh K et al. Peritoneal carcinomatosis in patients with gastric cancer, and the role for surgical resection, cytoreductive surgery, and hyperthermic intraperitoneal chemotherapy. Am J Surg 2014; 207: 78-83.
10. Thomassen I, van Gestel YR, van Ramshorst B et al. Peritoneal carcinomatosis of gastric origin: A population-based study on incidence, survival and risk factors. Int J Cancer 2013. Int J Cancer. 2014 Feb 1;134(3):622-8. doi: 10.1002/ijc.28373. Epub 2013 Aug
11. Bozzetti F, Yu W, Baratti D et al. Locoregional treatment of peritoneal carcinomatosis from gastric cancer. J Surg Oncol 2008; 98: 273-276.
12. Wagner AD, Unverzagt S, Grothe W et al. Chemotherapy for advanced gastric cancer. Cochrane Database Syst Rev 2010; Cd004064.
13. Group G, Oba K, Paoletti X et al. Role of chemotherapy for advanced/recurrent gastric cancer: an individual-patient-data meta-analysis. Eur J Cancer 2013; 49: 1565-1577.
14. Hioki M, Gotohda N, Konishi M et al. Predictive factors improving survival after gastrectomy in gastric

cancer patients with peritoneal carcinomatosis. World J Surg 2010; 34: 555-562.

15. Kerkar SP, Kemp CD, Duffy A et al. The GYMSSA trial: a prospective randomized trial comparing gastrectomy, metastasectomy plus systemic therapy versus systemic therapy alone. Trials 2009; 10: 121
16. Hultman B, Lundkvist J, Glimelius B et al. Costs and clinical outcome of neoadjuvant systemic chemotherapy followed by cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in peritoneal carcinomatosis from gastric cancer. Acta Oncol 2012; 51: 112-121.
17. Ikeguchi M, Oka A, Tsujitani S et al. Relationship between area of serosal invasion and intraperitoneal free cancer cells in patients with gastric cancer. Anticancer Res 1994; 14: 2131-2134.
18. Kuramoto M, Shimada S, Ikeshima S et al. Extensive intraoperative peritoneal lavage as a standard prophylactic strategy for peritoneal recurrence in patients with gastric carcinoma. Ann Surg 2009; 250: 242-246.
19. Yang XJ, Huang CQ, Suo T et al. 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.
20. Yonemura Y, de Aretxabala X, Fujimura T et al. Intraoperative chemohyperthermic peritoneal perfusion as an adjuvant to gastric cancer: final results of a randomized controlled study. Hepatogastroenterology 2001; 48: 1776-1782.
21. Fujimura T, Yonemura Y, Muraoka K et al. Continuous hyperthermic peritoneal perfusion for the prevention of peritoneal recurrence of gastric cancer: randomized controlled study. World J Surg 1994; 18: 150-155.
22. Yu W, Whang I, Chung HY et al. Indications for early postoperative intraperitoneal chemotherapy of advanced gastric cancer: results of a prospective randomized trial. World J Surg 2001; 25: 985-990.
23. Fujimoto S, Takahashi M, Mutou T et al. Improved mortality rate of gastric carcinoma patients with peritoneal carcinomatosis treated with intraperitoneal hyperthermic chemoperfusion combined with surgery. Cancer 1997; 79: 884-891.
24. Hirose K, Katayama K, Iida A et al. Efficacy of continuous hyperthermic peritoneal perfusion for the prophylaxis and treatment of peritoneal metastasis of advanced gastric cancer: evaluation by multivariate regression analysis. Oncology 1999; 57: 106-114.
25. Yonemura Y, Kawamura T, Bandou E et al. Treatment of peritoneal dissemination from gastric cancer by peritonectomy and chemohyperthermic peritoneal perfusion. Br J Surg 2005; 92: 370-375.
26. Glehen O, Schreiber V, Cotte E et al. Cytoreductive surgery and intraperitoneal chemohyperthermia for peritoneal carcinomatosis arising from gastric cancer. Arch Surg 2004; 139: 20-26.
27. Hall JJ, Loggie BW, Shen P et al. Cytoreductive surgery with intraperitoneal hyperthermic chemotherapy for advanced gastric cancer. J Gastrointest Surg 2004; 8: 454-463.
28. Scaringi S, Kianmanesh R, Sabate JM et al. Advanced gastric cancer with or without peritoneal carcinomatosis treated with hyperthermic intraperitoneal chemotherapy: a single western center experience. Eur J Surg Oncol 2008; 34: 1246-1252.
29. Yang XJ, Li Y, Yonemura Y. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy to treat gastric cancer with ascites and/or peritoneal carcinomatosis: Results from a Chinese center. J Surg Oncol 2010; 101: 457-464.
30. Glehen O, Gilly FN, Arvieux C et al. 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.
31. Gill RS, Al-Adra DP, Nagendran J et al. 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.

32. Tsilimparis N, Bockelmann C, Raue W et al. Quality of life in patients after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: is it worth the risk? Ann Surg Oncol 2013; 20: 226-232.