

Peritoneal carcinomatosis index and overall survival in patients taken to cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy

Índice de carcinomatosis peritoneal y supervivencia global en pacientes llevados a cirugía citorreductora más quimioterapia intraperitoneal hipertérmica

Horacio N. López-Basave^{1*}, Flavia Morales-Vázquez², Ángel Herrera-Gómez³, Gerardo Miranda-Devora¹, Alejandro E. Padilla-Rosciano¹, Carolina Castillo-Morales¹, César A. Paleta-Torres¹, and Ezequiel Vázquez-Cortes¹

¹Departamento de Gastroenterología; ²Departamento de Ginecología Oncológica; ³Subdirección de Cirugía. Instituto Nacional de Cancerología, Mexico City, Mexico

Abstract

Background: The peritoneal carcinomatosis (PC) due to gastrointestinal or gynecological cancer has increased its incidence. It has a worse prognosis compared to other sites of metastasis. The peritoneal carcinomatosis index (PCI) establishes overall survival in patients with gastrointestinal or gynecological tumors and carcinomatosis. **Objective:** To evaluate the relationship of PCI to overall survival (OS) and recurrence-free survival (RFS) in patients treated with cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC). **Method:** A descriptive, retrospective study of 80 charts of patients with CP was conducted. We included patients with colon, ovarian, appendicular, pseudomyxoma and gastric tumors with CP treated with CRS plus HIPEC. The OS and RFS were determined according to the type of adenocarcinoma and the degree of differentiation. The OS and RFS were determined in months in patients with PCI > 15 PCI as well as in patients with PCI < 15 considering the tumor of origin. **Results:** Patients with ovarian tumors and pseudomyxoma with PCI < 15 presented OS > 70 months, compared to patients with gastric tumors (4 months). **Conclusions:** The PCI and histology are predictors of OS. Patients with ovarian tumors and PCI < 15 have higher OS, similar to pseudomyxomas. RFS was also higher in patients with PCI < 15.

Keywords: Peritoneal carcinomatosis. Cytoreduction. HIPEC.

Resumen

Antecedentes: La incidencia de carcinomatosis peritoneal (CP) secundaria a cáncer gastrointestinal o ginecológico ha aumentado y tiene peor pronóstico en comparación con otros sitios de metástasis. El índice de carcinomatosis peritoneal (ICP) establece la supervivencia global en pacientes con tumores gastrointestinales o ginecológicos y carcinomatosis. **Objetivo:** Evaluar la relación del ICP con la supervivencia global (SG) y la supervivencia libre de recurrencia (SLR) en pacientes tratados con cirugía citorreductora (CCR) más quimioterapia intraperitoneal e hipertemia (HIPEC). **Método:** Estudio descriptivo, retrospectivo, de 80 expedientes de pacientes con CP. Se incluyeron tumores de colon, ovario, apendicular, pseudomixomas y gástricos con CP tratados con CRS + HIPEC. Se determinaron la SG y la SLR de acuerdo con el tipo de adenocarcinoma y el grado de diferenciación, en meses, en pacientes con ICP > 15 y con ICP < 15 considerando el tumor de origen.

*Correspondence:

Horacio N. López-Basave
E-mail: lobohnoe@gmail.com

Date of reception: 12-05-2022

Date of acceptance: 20-07-2022

DOI: 10.24875/CIRUE.M22000512

Cir Cir (Eng). 2023;91(2):189-193

Contents available at PubMed

www.cirugiaycirujanos.com

2444-0507/© 2022 Academia Mexicana de Cirugía. Published by Permanyer. This is an open access article under the terms of the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Resultados: Los pacientes con tumores de ovario y pseudomixoma con ICP < 15 tenían una SG > 70 meses, frente a 4 meses con tumores gástricos. **Conclusiones:** El ICP y la histología son predictores de la SG. Las pacientes con tumores ováricos con ICP < 15 tienen mayor SG, igual que los pseudomixomas. La SLR fue mayor en los pacientes con ICP < 15.

Palabras clave: Carcinomatosis peritoneal. Citorreducción. HIPEC.

Introduction

The presence of peritoneal carcinomatosis (PC) due to GI and ovarian tumors has increased in recent years. It represents advanced disease, has a grim prognosis^{1,2}, and limited therapeutic options compared to other sites of metastasis^{3,4}. PC mainly originates from GI, gynecological, and peritoneal tumors^{1,2}. The presence of a tumor in the peritoneum is associated with a poor prognosis, indicating advanced clinical stage, disease progression, or recurrence of GI or gynecological tumors.

PC identified as locoregional tumor disease has led to a modified approach, with patients undergoing radical cytoreductive surgery (CRS), along with hyperthermic intraperitoneal chemotherapy (HIPEC). CRS removes macroscopic tumors, while HIPEC treats microscopic residual disease. These treatments are complex and associated with high morbidity and mortality rates.

In 1995, Sugarbaker et al.^{5,6} introduced the Peritoneal Carcinomatosis Index (PCI), a scoring system that quantifies PC to compare overall survival (OS) and recurrence-free survival (RFS) across different studies^{4,7}. PCI has prognostic relevance regardless of the origin of PC⁸. Former studies have demonstrated that patients with higher PCI have lower survival rates and worse outcomes compared to those with PCIs < 15^{2,4,9,10}. Various PCI cut-off values have been described, such as < 10^{9,11}, < 11¹², and < 15⁴, and they are related to OS.

For a long time, CRS and HIPEC have been the first-line therapy for PC, showing improved clinical outcomes in selected patients compared to systemic chemotherapy and cytoreductive surgery alone. Various drugs have been used, being platinum and mitomycin C the most widely used. However, none of these drugs has been established as the standard treatment^{1,2,9}. Patients who achieve R0 cytoreduction and PCI < 15 tend to have better survival rates.

Other factors, in addition to the presence of PC, affect survival in patients with GI tract cancer, including high PCI, the presence of signet ring cells, the mucinous component¹⁰, a low Eastern Cooperative

Oncology Group (ECOG) score¹, postoperative complications¹¹, the presence of comorbidity, poor nutritional status, high body mass index, and metastatic disease outside the peritoneum¹⁰.

Method

This was a descriptive, retrospective, case-series study that reviewed a total of 80 health records from patients with PC from February 2008 through August 2020 at the Department of Gastro-Surgery of Instituto Nacional de Cancerología, Mexico City, Mexico.

The study aimed to evaluate the PCI and its relationship with OS in patients who underwent combined CRS and HIPEC for PC at a referral center in Mexico.

The study included 80 patients of both sexes aged 18 to 75 years with resectable peritoneal disease. Patients with extraperitoneal disease or renal or cardiac comorbidities were excluded. Diagnoses included colon, ovarian, appendix, gastric adenocarcinomas, and pseudomyxomas with PC treated with CRS and HIPEC. Patients who achieved R0 cytoreduction with PCI < 15 were considered.

OS and RFS were determined based on the histological type (moderately differentiated adenocarcinoma, mucinous type, and well-differentiated adenocarcinoma). PCI, OS, and RFS were evaluated, and PCI was determined according to Sugarbaker's classification.

OS was calculated from the first surgery plus HIPEC until the patient's death or the last health record available, recorded in months. RFS was also recorded in months and represented the time until disease recurrence was first reported. Information was obtained from the follow-up data from the Department of Gastro-Surgery database.

Results

Sixty-three out of the 80 patients from the study (78.75%) were men, and the mean age was 52 years (range, 20-78 years). The mean PCI score was 7

points (range, 0-32); the mean OS, 39.59 months; and the mean RFS, 39.22 months.

Out of the 80 patients studied, 36% had colorectal origin, 34% ovarian origin, 14% appendicular origin, 8% pseudomyxoma origin, and the rest had gastric origin (Table 1).

Regarding the histological type, 48% were moderately differentiated adenocarcinomas, 28% mucinous adenocarcinomas, and 24% well-differentiated adenocarcinomas (Table 2).

A comparison of the OS was made based on the different histological types. This comparison revealed an OS of 35.17 months for mucinous adenocarcinoma, 30.86 months for well-differentiated adenocarcinoma, and a lower OS in patients with moderately differentiated adenocarcinoma (Table 3). Appendiceal tumors had a better survival rate (63.3 months [range, 3 to 108 months]).

The highest RFS was reported for tumors of appendicular origin and pseudomyxomas (in both cases > 50 months). Gastric adenocarcinomas had the worst RFS of all (4 months [Table 4]).

To compare OS based on PCI, patients were divided into 2 groups: PCI < 15 and PCI > 15; the OS was 42.6 months and 13.7 months, respectively.

For appendicular tumors, the OS with PCI < 15 was 65.36 months, and with PCI > 15, 41 months.

There were no patients with pseudomyxoma and gastric cancer with PCI > 15. With PCI < 15, the OS for pseudomyxoma was 75.8 months, and for gastric cancer, 4 months. In patients with colorectal cancer and PCI < 15, the OS was 28.13 months, and with PCI > 15, 10.1 months. It is in ovarian cancer, where the largest difference was seen, with an OS of 8 months in patients with PCI > 15 and 70 months in those with PCI < 15 (Table 5). Patients who achieved complete cytoreduction (R0) had PCI < 15, while those who did not achieve complete cytoreduction (R1) had PCI > 15.

The mean OS for appendicular tumors was 65.3 months, 53 months for ovarian cancer, 51.4 months for pseudomyxoma, 24.4 months for colorectal cancer, and 4 months for gastric cancer (the worst OS).

Regarding RFS, the group of appendicular origin had the highest mean (39.2 months), while for pseudomyxoma, the mean RFS was 36.8 months, 18.1 months for colorectal cancer, 10.8 months for ovarian cancer, again, gastric cancer showing the lowest RFS of all at 3.8 months.

Table 1. Overall characteristics of the population (n = 80)

Characteristics	
Age in years, mean (range)	52 (18-75)
Male, n (%)	17 (21.25)
Female, n (%)	63 (78.75)
Oncological origin	
Appendix, n (%)	11 (14)
Pseudomyxoma, n (%)	8 (10)
Ovarian, n (%)	27 (34)
Colorectal, n (%)	29 (36)
Stomach, n (%)	5 (6)

Table 2. Histopathological characteristics (n = 80)

Characteristics	
Histopathological type	
Well-differentiated adenocarcinoma, n (%)	23 (24%)
Moderately differentiated adenocarcinoma, n (%)	38 (48%)
Mucinous, n (%)	19 (28%)
Survival by histopathological type	
Well-differentiated adenocarcinoma, months	30.86
Moderately differentiated adenocarcinoma, months	19.57
Mucinous, months	35.17

Table 3. Mean overall survival by oncological origin (n = 80)

Oncological origin	Overall Survival, months (mean/range)
Appendicular	63.3 (3-108)
Pseudomyxoma	51.4 (7-107)
Ovarian	53 (4-125)
Colorectal	24.4 (0.109)
Gastric	4 (2-6)

Discussion

PC is a prognostic factor for survival in patients with some type of digestive or gynecological cancer. CRS + HIPEC increase the survival of patients with PC, regardless of its origin⁸.

Both RFS and OS were higher with PCI < 15, which is consistent with the medical literature available worldwide.

PCI serves as a long-term survival predictor, regardless of cancer type^{7,8}. Several studies have shown that a higher PCI is associated with worse long-term

Table 4. Mean recurrence-free survival by oncological origin (n = 80)

Oncological Origin	Recurrence-free survival, months Mean (range)
Appendix	39.2 (1-107)
Pseudomyxoma	36.8 (7-101)
Ovarian	10.8 (1-35)
Colorectal	18.1 (0-109)
Stomach	3.8 (1-6)

Table 5. Overall survival based on the Peritoneal Carcinomatosis Index (n = 80)

Oncological Origin	Overall Survival, months Mean
Appendicular	
> 15 points	41
< 15 points	65.36
Pseudomyxoma	
> 15 points	NA
< 15 points	75.8
Ovarian	
> 15 points	8
< 15 points	70
Colorectal	
> 15 points	10.1
< 15 points	28
Stomach	
> 15 points	NA
< 15 points	4

NA: not applicable.

prognosis. In our study, the PCI cut-off value with the highest OS was < 15^{4,7-9,11-13}.

Gastric adenocarcinoma had shorter OS and RFS. The presence of peritoneal carcinomatosis is associated with a poor prognosis.

The data reported in our study is consistent with what has been reported in the medical literature. In the studies conducted by Hotopp¹⁴, and Desiderio et al.¹⁵, the OS of patients with PC of gastric origin was 4 months, as it was the case with our study.

For patients with PC and PCI < 15, both the OS and RFS were higher. In these cases, patients underwent R0 cytoreduction. In our review, patients with colorectal tumors and PCI < 15 had an OS of 28.13 months (with PCI > 15, the OS was 10.1 months). For the entire group of patients with colorectal cancer, the RFS was 18.03 months. In Faron et al.'s study¹² with a PCI cut-off

value > 11, the OS was 41 months and RFS, 17.7 months, which is similar to the data reported in our study.

In the case of ovarian origin, Tentes et al.¹⁶ confirmed an OS of 80.2 months for patients with PCI < 10 (70 months in our study), whereas for the group with PCI > 10, they reported an OS of 38.8 months (ours was only 8 months); this difference may be attributed to the different PCI cut-off value. In the study conducted by Spiliotis¹⁷ involving 2 groups, group A included 60 patients treated with CRS + HIPEC + systemic chemotherapy, while group B included 60 patients treated only with CRS + systemic chemotherapy. The mean survival of group A was 26.7 months compared to 13.4 months from group B.

Patients with a PCI < 15 also appeared to have a longer OS, which confirms that survival is higher survival with lower PCI, as mentioned by Díaz-Gil et al.¹⁸, who noted an inversely proportional relationship between PCI and OS.

Conclusions

PC is a predictor of OS in patients, regardless of its origin. PCI has an inversely proportional relationship with OS and RFS in all patients with PC due to digestive or ovarian cancer.

Acknowledgments

The authors wish to thank the team of the Gastroenterology Department and the Medical Society of Instituto Nacional de Cancerología, Mexico City, Mexico.

Funding

None declared.

Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

References

- Shaligram A. Management of peritoneal surface malignancies in laparoscopic era: a concise review. *Int J Surg Oncol (N Y)*. 2016;1:e05.
- Spiliotis J, Halkia E, de Bree E. Treatment of peritoneal surface malignancies with hyperthermic intraperitoneal chemotherapy — current perspectives. *Curr Oncol*. 2016;23:e266-75.
- Pamela K, Matthias Z, Reinhold KR, Julia P, Peter M, Alexander P, et al. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC): a single-center experience in Austria. *J Gastrointest Surg*. 2018;22:884-93.
- Huang Y, Alzahrani NA, Chua TC, Liauw W, Morris DL. Impacts of peritoneal cancer index on the survival outcomes of patients with colorectal peritoneal carcinomatosis. *Int J Surg*. 2016;32:65-70.
- Sugarbaker PH, Chang D, Koslowe P. Prognostic features of 51 colorectal with peritoneal carcinomatosis and 130 appendiceal cancer patients treated by cytoreductive surgery and intraperitoneal chemotherapy. *Ann Surg*. 1996;81:89-104.
- Harmon RL, Sugarbaker PH. Prognostic indicators in peritoneal carcinomatosis from gastrointestinal cancer. *Int Semin Surg Oncol*. 2005;2:1-10.
- Ng JL, Ong WS, Chia CS, Tan GHC, Soo KC, Teo MCC. Prognostic relevance of the peritoneal surface disease severity score compared to the peritoneal cancer index for colorectal peritoneal carcinomatosis. *Int J Surg Oncol*. 2016;2016:1-7.
- Solaini L, D'Acapito F, Passardi A, Framarini M, Tauceri F, Di Pietrantonio D, et al. Cytoreduction plus hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis in colorectal cancer patients: a single-center cohort study. *World J Surg Oncol*. 2019;17:1-6.
- Boerner T, Graichen A, Jeiter T, Zemann F, Renner P, März L, et al. CRS-HIPEC Prolongs survival but is not curative for patients with peritoneal carcinomatosis of gastric cancer. *Ann Surg Oncol*. 2016;23:3972-7.
- Massalou D, Benizri E, Chevallier A, Duranton-Tanneur V, Pedeutour F, Benchimol D, et al. Peritoneal carcinomatosis of colorectal cancer: novel clinical and molecular outcomes. *Am J Surg*. 2017;213:377-87.
- Llueca A, Escrig J, Serra-Rubert A, Gómez-Quiles L, Rivadulla I, Játiva-Porcar R, et al. Prognostic value of peritoneal cancer index in primary advanced ovarian cancer. *Eur J Surg Oncol*. 2018;44:163-9.
- Faron M, Macovei R, Goéré D, Honoré C, Benhaim L, Elias D. Linear relationship of peritoneal cancer index and survival in patients with peritoneal metastases from colorectal cancer. *Ann Surg Oncol*. 2016;23:114-9.
- Elias D, Gilly F, Boutitie F, Quenet F, Bereder J-M, Mansvelt B, et al. Peritoneal colorectal carcinomatosis treated with surgery and perioperative intraperitoneal chemotherapy: retrospective analysis of 523 patients from a multicentric French study. *J Clin Oncol*. 2010;28:63-8.
- Hotopp T. HIPEC and CRS in peritoneal metastatic gastric cancer — who really benefits? *Surg Oncol*. 2019;28:159-66.
- Desiderio J, Chao J, Melstrom L, Warner S, Tozzi F, Fong Y, et al. The thirty-year experience — a meta-analysis of randomized and high quality non-randomized studies of hyperthermic intraperitoneal chemotherapy (HIPEC) in the treatment of gastric cancer. *Eur J Cancer*. 2016;176:100-6.
- Tentes AAK, Tripsiannis G, Markakidis SK, Karanikiotis CN, Tzegas G, Georgiadis G, et al. Peritoneal cancer index: a prognostic indicator of survival in advanced ovarian cancer. *Eur J Surg Oncol*. 2003;29:69-73.
- Spiliotis J, Halkia E, Lianos E, Kalantzi N, Grivas A, Efsthathiou E, et al. Cytoreductive surgery and HIPEC in recurrent epithelial ovarian cancer: a prospective randomized phase iii study. *Ann Surg Oncol*. 2015;22:1570-5.
- Díaz-Gil D, Fintelmann FJ, Molaei S, Elmi A, Hedgire SS, Harsinghani MG. Prediction of 5-year survival in advanced-stage ovarian cancer patients based on computed tomography peritoneal carcinomatosis index. *Abdom Radiol*. 2016;41:2196-202.