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Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for gastric cancer with peritoneal metastases at an Australian centre

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Abstract

Introduction Gastric cancer is a major cause of cancer mortality, with poorer prognosis in the presence of peritoneal metastases as low as 2.8–9 months. Systemic therapy has a limited role. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have been shown to improve survival. This study evaluates survival of patients with gastric cancer and peritoneal metastases (GCPM) undergoing CRS and HIPEC at an Australian centre.

Methods A retrospective analysis was conducted on a prospectively collected database of patients who underwent CRS and HIPEC for GCPM from January 2009 to December 2023. Data included demographics, perioperative factors, histopathology and survival.

Results Twenty-four patients were identified, with median postoperative overall survival of 11.7 months (95% CI 8.6–34.2 months). Most patients had poorly differentiated adenocarcinoma ($n = 23$, 96%), with 14 (58%) exhibiting signet cell pathology. 62% ($n = 15$) received preoperative chemotherapy. Median PCI was 5, with a CC score of 0 in 96% of patients ($n = 23$). Clavien-Dindo III/IV morbidity was noted in 8 patients (33%) with no perioperative mortality. No survival differences were found between those with signet cell pathology and those without (10.6 vs. 11.7 months, $p = 0.83$), nor between those receiving preoperative chemotherapy and those who did not (11.7 vs. 10.6 months, $p = 0.60$). Age, sex, PCI, CC and tumour markers demonstrated correlations with survival in linear regression, but no individual factor significantly influenced outcomes.

Conclusion CRS and HIPEC for low volume GCPM should be considered in select patients.

Keywords Cytoreductive surgery, Hyperthermic intraperitoneal chemotherapy, Gastric cancer, Peritoneal disease

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Introduction

Gastric cancer represents the fifth most common cancer and the fourth most common cause of cancer related death worldwide [1]. Overall survival is poor and malignancy can disseminate rapidly through lymphatic, haematogenous or intra-abdominal spread. Intra-abdominal spread is of particular concern given free cancer cells are found in up to 40% of what would otherwise appear to be Stage II or III disease, with significantly impact on survival [2]. The presence of macroscopic disease (peritoneal carcinomatosis), occurring in about 20–30% of those with gastric cancer, confers the poorest prognosis of a median overall survival of as low as 2.8–9 months [1, 3–5]. As many as 40–60% of patients treated with a curative gastrectomy and adjuvant chemotherapy will develop isolated peritoneal recurrence [6].

Treatment of gastric cancer with peritoneal metastases (GCPM) is a complex and evolving field. Traditionally, the presence of peritoneal disease has been recognised as a factor in treatment failure with poor penetrance of systemic chemotherapy. The REGATTA trial, a large multinational randomised controlled trial comparing cytoreduction and adjuvant chemotherapy to adjuvant chemotherapy alone for incurable gastric cancer (including the presence of peritoneal disease) found no benefit of gastrectomy and recommended against surgical intervention, but peritoneal disease was not removed at time of operation [7]. In trials evaluating cytoreduction (the removal of all macroscopic disease and affected organs [8]) alone for gastric cancer with peritoneal disease, it has generally been found that patients with poorly differentiated carcinoma or signet cell pathology do not have a benefit of surgical intervention even for extremely low peritoneal carcinoma index (PCI) scores [9]. There is a growing body of literature into the role of cytoreductive surgery (CRS) and intraperitoneal chemotherapy, which includes hyperthermic intraperitoneal chemotherapy (HIPEC) and early post-operative intraperitoneal chemotherapy (EPIC) [3]. HIPEC applies intraperitoneal chemotherapy at time of operation which can penetrate malignancy through diffusion, with only 2–3 mm of spread into tissues, allowing higher concentrations of chemotherapy agents to be delivered to cancer cells than what could be delivered through a systemic approach and hyperthermia which enhances chemosensitivity of tumour cells [10]. For GCPM, CRS and HIPEC in particular has shown significant survival benefits with demonstration of long-term survival (beyond five years), not seen in this cohort previously [11, 12]. The largest prospective trial, GASTRIPEC-I, was conducted randomising 105 patients to CRS or CRS and HIPEC, however only 50 of the 105 patients underwent surgery due to disease progression or death. They found no benefit of HIPEC compared to CRS and HIPEC but included all

PCI subgroups, with 53.3% ($n=56$) of patients having a PCI of greater than 7, with most identified literature showing survival benefits below this level [6]. Due to limited numbers, they were unable to examine for benefit in those with lower PCI groups [13]. Three other randomised controlled trials have been performed which all found benefits with addition of HIPEC as well as significant heterogeneity of inclusion criteria [14–16].

Our unit is a high-volume CRS and HIPEC unit based in Sydney Australia and a major referral centre for peritoneal carcinomatosis, including gastric cancer. There have been no Australian results published within the limited literature of outcomes for CRS and HIPEC in gastric cancer, and overall, worldwide limited reporting. We aim to report the postoperative overall survival of patients with GCPM undergoing CRS and HIPEC at the highest volume peritoneal malignancy centre in Australia.

Methods

This manuscript and trial were conducted in accordance with the revised 2013 Declaration of Helsinki. Ethics approval was granted by the South Eastern Local Health District Ethics committee, under ethical approval code QAQI/18/078.

A retrospective case series was undertaken with extraction from the Saint George Hospital Peritonectomy database, a prospectively collected database, for all patients who underwent CRS and HIPEC for gastric cancer with macroscopic peritoneal metastases from 1st January 2009 to December 31st 2023.

Patient selection

All patients with gastric cancer and peritoneal disease (including peritoneal recurrence and those presenting with obstruction) referred to the unit undergo computed tomography (CT) imaging of the chest, abdomen and pelvis and blood work including carcinoembryonic antigen (CEA), cancer antigen 125 (CA125), cancer antigen 19.9 (CA19.9) and alpha-fetoprotein (AFP). Whole-body positron emission tomography (PET) or magnetic resonance imaging (MRI) is used to further evaluate for the presence of lung or liver lesions. Diagnostic laparoscopy is also performed to evaluate the volume of peritoneal disease, if not already done so at time of referral.

All patients are then discussed at a multidisciplinary meeting including allied health, oncology, palliative care, anaesthetists and surgical oncologists and a decision made regarding best supportive care, chemotherapy, immunotherapy or CRS and HIPEC. Typically, this depends on patients age with a guide of less than 75 years and functional status with an Eastern Cooperative Oncology Group (ECOG) score of two or less. In our institution, we do not offer CRS and HIPEC for patients with a PCI of greater than 7 on staging laparoscopy, in

keeping with most identified literature showing survival benefits with CRS and HIPEC at this cutoff level [6]. Patients must also have no distal metastatic disease. In recent years, we.

Intraoperative process

CRS and HIPEC is performed following the principles first established by Sugarbaker [8]. PCI was calculated at the beginning of the operation to describe the volume and distribution of peritoneal disease, and the completeness of cytoreduction (CC) was recorded at the end of the procedure to describe the macroscopic clearance of visible disease [17]. Specifically for gastrectomy, a D2 lymphadenectomy was performed. After cytoreduction was completed, HIPEC was administered using the open technique. The abdomen was primed with fluid and heated to 41.5 degrees Celsius, before chemotherapy was cycled through the abdomen for 90 min. The solutions used for priming was originally Dianeal PD4 (1.5%) Peritoneal Dialysis Solution, switched with Plasmalyte 148 in later years. Chemotherapy agents used within our unit for gastric cancer included cisplatin (120mg/m²) with addition of mitomycin (MMC) (30mg/m²) or doxorubicin (15/m²). Sodium thiosulfate was additionally used

after 2018 for renal protection. Three abdominal drains are left at the end of the operation, one near the upper anastomoses post gastrectomy, one in the subhepatic space and one in the pelvis.

Postoperative process

All patients are taken to the intensive care unit intubated and extubated the following day if appropriate to do so. Total parental nutrition is utilised given the expected ileus after CRS and HIPEC and weaned as gut function progresses, as monitored by nasogastric outputs and patient clinical signs of flatus or bowel movements. All patients undertake drain lipase and amylase analysis on day three. Patients are stepped down to the ward when appropriate to do so and undergo physiotherapy until cleared for discharge. At time of discharge, all patients are referred back to their referring oncologist for review for further systemic therapy.

Data collection

Demographic information including age and sex were extracted. Clinical information regarding date of operation, PCI score, CC score, histological grading of disease, HIPEC agent used and death dates were recorded. Deaths were cross-referenced against the births, deaths, and marriages registry to ensure accurate death dates were recorded. For alive patients, date of last clinical follow-up was used in calculations for survival, with overall survival (OS) was defined as time from surgery to death or last clinical follow-up. The 8th of September 2024 was used for a censor date for alive patients.

Data analysis

All statistical analysis and figures were generated using Jamovi version 2.5 (The jamovi project (2024) [Computer Software]. Retrieved from <https://www.jamovi.org>). Kaplan-Meier survival curves were generated for median OS. Multivariable and linear regression were used to correct for cofounders for impact on survival. The level of significance (p) was set to 0.05.

Results

There were 24 patients identified who underwent CRS and HIPEC for gastric cancer with peritoneal metastases between January 1st 2009 and December 31st 2023, 20 of which (83.3%) were index operation and four (16.7%) for peritoneal recurrence after previous surgical intervention. Median follow-up time was 42.2 months. Fourteen (58%) patients had their procedure from 2019 onwards. Mean age was 52.5 years (SD= 10.6 years) with an overall slight female preponderance (n= 13, 54%). Median ASA was 3 (Interquartile range (IQR) 2–4). Median values of the tumour markers are reported in Table 1. Of the 24 patients, 15 (62%) received preoperative chemotherapy;

Table 1 Baseline demographic data for patients undergoing cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for gastric cancer (n = 24)

Category	Values
Age mean (SD)	52.5 (10.6)
Sex	
Female n (%)	13 (54)
ASA median, range	3 (2–4)
ASA 2 n (%)	7 (29)
ASA 3 n (%)	15 (63)
ASA 4 n (%)	2 (8)
Tumour markers median (IQR)	
AFP (n = 16) kIU/L	2.0 (2.0–4.0)
CA125 (n = 23) kU/L	13.0 (10.0–27.0)
CA199(n = 22) kU/L	15.5 (5.5–27.0)
CEA (n = 23) ug/L	2.0 (1.0–4.0)
Preoperative chemotherapy treatment n (%)	15 (62)
Fluorouracil, Leucovorin, Oxaliplatin and Docetaxel (FLOT)	11 (46)
Leucovorin calcium (folinic acid), Fluorouracil and Oxaliplatin (FOLFOX)	2 (8)
Epirubicin, Oxaliplatin and Capecitabine (EOX)	1 (4)
Epirubicin, Cisplatin and Capecitabine (ECX)	1 (4)
Immunotherapy n (%)	1 (4)
Nivolumab	1 (4)

SD=Standard deviation. ASA=American Society of Anaesthesiologist score. AFP=alphafetoprotein. CA125=Cancer antigen 125. CA199=Cancer antigen 199. CEA=CarcinoEmbryonic Antigen

11 (46%) Fluorouracil, Leucovorin, Oxaliplatin and Docetaxel (FLOT), two (8%) Leucovorin calcium (folinic acid), Fluorouracil and Oxaliplatin (FOLFOX), one (4%) Epirubicin, Oxaliplatin and Capecitabine (EOX) and one (4%) Epirubicin, Cisplatin and Capecitabine (ECX). There was one patient (4%) who received immunotherapy (nivolumab) in addition to FOLFOX (Table 1). Of the cohort, 13/14 patients (93%) from 2019 onwards received preoperative chemotherapy, with FLOT the only chemotherapy agent used. In those who did not receive chemotherapy, data was available for six of the nine, with three predating available records. These six presented with symptoms of intestinal obstruction and received operative intervention without chemotherapy.

Perioperative and admission related data is presented in Table 2. The median PCI was 5 (IQR 3–8), with a median CC score of 0. One patient had a PCI of 39 and we achieved a CC score of 1. The original pathology was thought to be appendiceal adenocarcinoma. The majority of patients ($n=22$, 92%) received cisplatin and mitomycin C HIPEC, with one patient receiving cisplatin and doxorubicin (4%) and the patient with presumed appendiceal

adenocarcinoma received mitomycin C alone. The predominant histopathology ($n=23$, 96%) was poorly differentiated adenocarcinoma, with one patient having moderately differentiated adenocarcinoma (4%). Signet cell pathology was identified in 14 of 23 poorly differentiated adenocarcinoma patients (61%) and was not present in the patient with moderately differentiated adenocarcinoma. Diffuse type was identified in 19 patients (79%), intestinal type in three (13%) and mixed type in two (8%). The median length of stay was 22.5 days (IQR 18–29.25 days) with a median Intensive Care Unit length of stay of 2.5 days (IQR 1.72–4.0 days). Sixteen patients (67%) experience a grade 1 or 2 Clavien-Dindo morbidity and eight patients (33%) experienced grade 3 or 4 Clavien-Dindo morbidity.

Cytoreductive procedures are reported in Supplementary 1. The most frequently resected organ was the omentum and stomach with all 24 patients (100%) having omentectomy and gastrectomy; 12 (50%) patients had a subtotal gastrectomy and 12 (50%) patients had a total gastrectomy. Of the total gastrectomies, four (33%) were completion total gastrectomies after previous subtotal gastrectomy. The most frequent procedures following this were cholecystectomy ($n=14$, 58%), colonic resections ($n=14$, 58%), oophorectomy ($n=12$, 50%), splenectomy ($n=11$, 46%), diaphragm interventions ($n=10$, 42%) including bilateral stripping in 8 patients, right stripping in one and a left sided resection in one, liver interventions ($n=7$, 29%), pancreas interventions ($n=6$, 25%), small bowel resection ($n=5$, 21%) and hysterectomy ($n=2$, 8%).

Overall survival after CRS and HIPEC for gastric cancer with peritoneal metastases is displayed in Fig. 1, with a median length of survival of 11.7 months (95% CI 8.6–34.2 months, range 3.0 months– 55.1 months). Overall survival at 1, 2 and 3 years was 42.5%, 37.8% and 18.9% respectively. There was no significant difference in survival in patients with and without signet cell pathology (Fig. 2), at 10.6 months v 11.7 months respectively ($p=0.83$). Similarly, there was no survival difference in patients who received preoperative chemotherapy compared with those that did not (11.7 months vs. 10.6 months median survival, $p=0.60$) (Fig. 3). Linear regression was performed examining survival with coefficients of age, sex, ASA, tumour markers, HIPEC agent, PCI and signet pathology, with strong correlation demonstrated with an R^2 of 0.802. Within this, posthoc omnibus ANOVA revealed no individual component to be significantly affecting survival (Table 3).

Discussion

This study described the clinical outcomes of 24 patients with GCPM treated with CRS and HIPEC, showing a postoperative median survival of 11.7 months and

Table 2 Perioperative and admission related data for patients undergoing cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for gastric cancer ($n=24$)

Category	Values
PCI median (IQR)	5 (3–8)
CC score median (IQR)	0 (0)
0 n (%)	23 (96)
1 n (%)	1 (4)
HIPEC agent n (%)	
Cisplatin + doxorubicin	1 (4)
Cisplatin + MMC	22 (92)
MMC	1 (4)
Histopathology n (%)	
Moderately differentiated	1 (4)
Poorly differentiated	23 (96)
(Signet cell subtype)	14 (61)
Lauren classification	
Diffuse type	19 (79)
Intestinal type	3 (13)
Mixed type	2 (8)
Clavien-Dindo median (IQR) Morbidity grade median (IQR)	2 (2–3)
1 n (%)	1 (4)
2 n (%)	15 (63)
3 n (%)	6 (25)
4 n (%)	2 (8)
ICU length of stay	2.5 (1.75–4.0)
Total length of stay median (IQR) days	22.5 (18–29.25)

IQR=Interquartile range. CC=Completion of Cytoreduction. PCI=Peritoneal Carcinomatosis Index. HIPEC=Hyperthermic IntraPeritoneal Chemotherapy. MMC=Mitomycin C. ICU=Intensive care unit

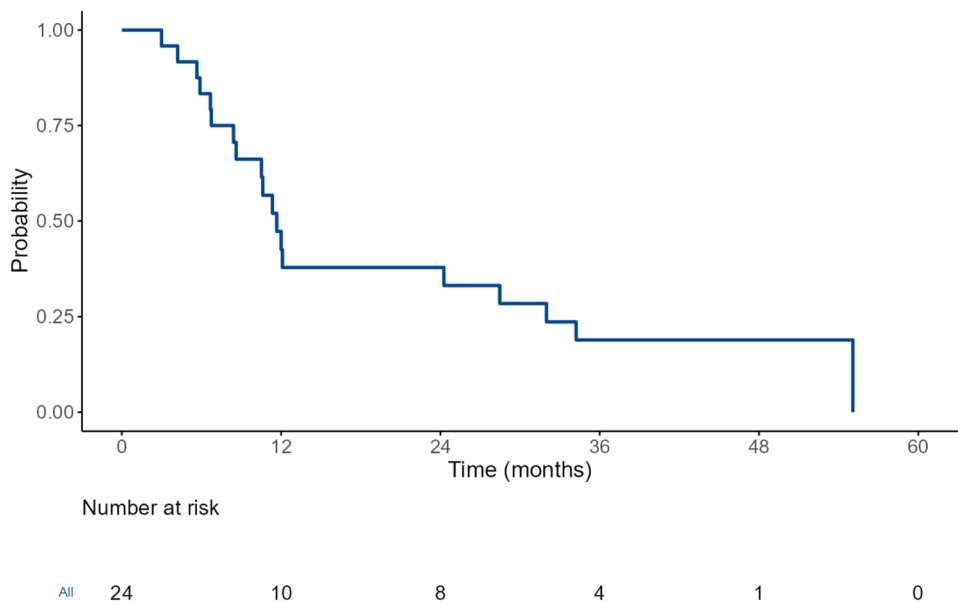


Fig. 1 Survival curve post cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for gastric cancer with peritoneal disease ($n=24$). Median survival of 11.7 months (95th Confidence intervals 8.6–34.2 months)

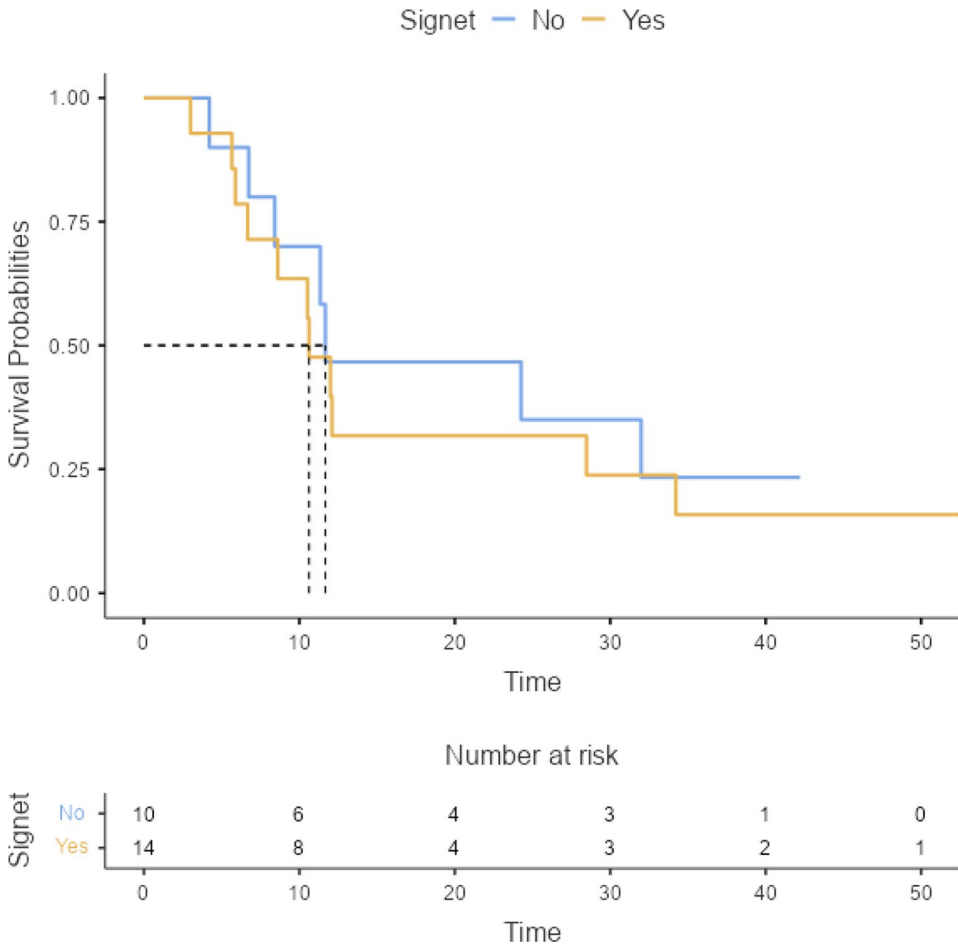


Fig. 2 Survival curve post cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for gastric cancer with peritoneal disease as split by signet cell pathology ($n=24$). Median survival of 11.7 months for non-signet cell pathology v 10.6 months for signet cell pathology ($p=0.83$)

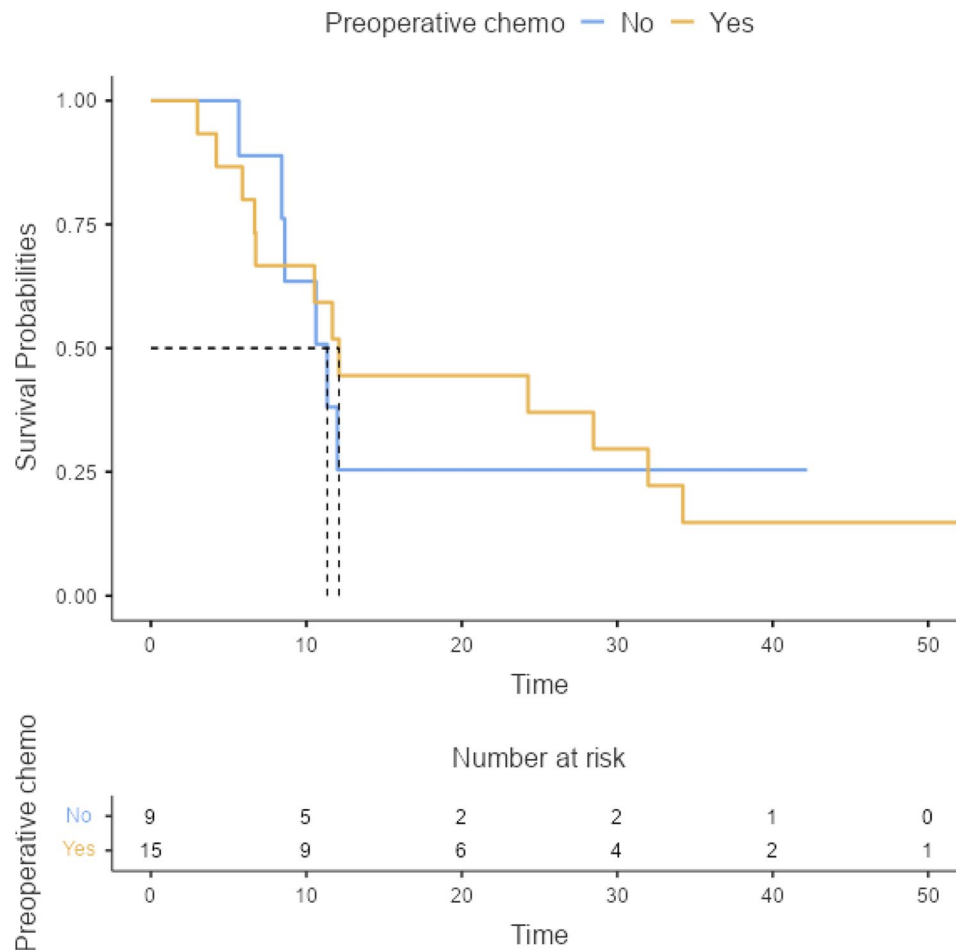


Fig. 3 Survival curve post cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for gastric cancer with peritoneal disease as split by preoperative chemotherapy treatment ($n=24$). Survival Curve. Median survival of 11.7 months for those who received preoperative chemotherapy treatment v 10.6 months for those who did not ($p=0.60$)

Table 3 Omnibus ANOVA testing after linear regression for factors impacting survival after cytoreductive surgery and HIPEC for gastric cancer with peritoneal metastases ($R^2=0.862$)

	Sum of Squares	df	Mean Square	F	p
Age at operation	1221.59	1	1221.59	5.93	0.072
ASA	14.66	1	14.66	0.07	0.803
PCI	40.09	1	40.09	0.19	0.682
Signet pathology	628.50	1	628.50	3.05	0.156
AFP	110.39	1	110.39	0.54	0.505
CA125	392.26	1	392.26	1.90	0.240
CA199	75.00	1	75.00	0.36	0.579
CEA	683.01	1	683.01	3.32	0.143
Sex	118.71	1	118.71	0.58	0.490
HIPEC agent	291.92	1	291.92	1.42	0.300
Residuals	823.88	4	205.97		

ASA=American Society of Anaesthesiologist score. PCI=Peritoneal Carcinomatosis Index. AFP=alphafetoprotein. CA125=Cancer antigen 125. CA199=Cancer antigen 199. CEA=CarcinoEmbryonic Antigen. HIPEC=Hyperthermic IntraPEritoneal Chemotherapy

achieving complete cytoreduction in 96% of patients (with the only patient not achieving completeness of cytoreduction a high-volume gastric cancer thought to be appendiceal in origin). To our knowledge, this is the only available Australian series and first to include peritoneal recurrence.

The median PCI in our series of 5, and our unit considers a PCI of 7 to be the cut-off. This is line with most centres [6, 12] which identified significant survival benefit as split by above and below 7, but some recommend a PCI cut-off of up to 12 [13]. Of note, our series only contained patients with macroscopically visible disease. In the CYTO-CHIP series, the presence of positive peritoneal washings is considered evidence of peritoneal malignancy (a PCI 0) and were included in the GCPM cohorts. These made up 31% of the cytoreduction group and 8.2% of the CRS and HIPEC group [12]. It is unclear the significance of including those without evidence of macroscopic peritoneal disease and how this impacted the outcomes, but it is well studied that increasing PCI

in gastric cancer is correlated to worse survival [18]. The aim of CRS and achieving a completion of cytoreduction (in effect a PCI of 0) has clear survival benefits [13]. The current international classification systems for staging gastric cancer do not distinguish between the amount of peritoneal disease; in that a patient with only positive washings is classified similarly to a patient with a PCI of 39 [19]. There is need for further clarification and work into this area given the increased research into CRS and HIPEC for GCPM.

Our overall median survival was 11.7 months, with an overall survival of 42.5%, 37.8% and 18.9% at one, two and three years respectively. Survival in the literature for patients with GCPM is variable, reflective of the small numbers and heterogeneity of included patients. Overall, a large meta-analysis performed encompassing available literature looking at the treatment of GCPM with CRS and HIPEC showed a median overall survival of 11.1 months, which also included patients with positive peritoneal cytology [20]. Another study examining survival identified one-year survivals ranging from 29.5 – 96% and three-year survivals ranging from 5.9 – 80%, but this study included both treatment of gastric peritoneal disease as well as prophylactic HIPEC after resection of T4 gastric cancer [21]. It is important to note our series is limited to those with visible peritoneal disease and included treatment of patients who have had gastric cancer with peritoneal recurrence, who would otherwise not have been included in the above trials.

All patients with GCPM in our series received HIPEC. The most common HIPEC agent used in our series was Cisplatin and MMC in 22 (92%) patients. One patient received MMC alone as at the time of operation was thought to be of an appendiceal primary, and one patient received cisplatin and doxorubicin. This patient had their operation in 2009 and was the first patient in the series. The use of cisplatin and doxorubicin is a widely described regiment with good efficacy and prevention of recurrence compared to resection alone [22, 23]. Similarly, MMC in addition to cisplatin has also been shown to be an effective HIPEC agent for prevention of gastric cancer peritoneal recurrence and is the most commonly used additional agent. There is no convincing evidence of superiority of one drug over another [24, 25], but it is our unit's preference to use MMC due to some evidence of associated increased risk of systemic toxicity with doxorubicin over MMC [26].

In our cohort, 15 (62%) of patients received preoperative chemotherapy. This initially included EOX and ECX, which was switched to FLOT from 2016. One patient received FOLFOX from the referring oncologist. The use of FLOT as a neoadjuvant agent has been well described and has good evidence for benefit over other regimes in the perioperative treatment of patients with locally

advanced gastric cancer and limited metastatic disease [27–29]. While all studies excluded patients with distal peritoneal disease, AIO-FLOT3 included localised peritoneal disease (a P1 on the Japanese Research Society for Gastric Cancer system) visible on laparoscopy and not imaging. Of these 252 patients, a total of 3 patients had localised peritonectomy within this and as part of this group showed survival benefit [29]. There is also increasing interest into the role of pressurised intraperitoneal aerosol chemotherapy (PIPAC) as a neoadjuvant treatment for the downstaging of peritoneal disease, as well as the use of intraperitoneal chemotherapy infusions [30, 31]. The change of EOX and ECX to FLOT with new evidence available, as well as increasing technical familiarity with gastric cancer and CRS with HIPEC.

The majority of the patients in our cohort (96%, $n=23$) had poorly differentiated adenocarcinoma (G3), with 14 (61%) of these having signet cell subtype. This is in keeping with the literature as both poorly differentiated and signet cell pathology are frequently associated with peritoneal disease [4, 32]. While signet cell pathology is associated with worse prognosis in gastric cancer without peritoneal disease, in studies evaluating the utility of CRS and HIPEC for GCPM, patients with signet cell tumours do not have worse outcomes compared to those without signet cell pathology (HR 1.23, $p=0.624$) [6, 33]. In our cohort, subgroup analysis did not reveal a survival difference between those with signet cell pathology and those that without (10.6 v 11.7 months, $p=0.83$). This may be a reflection of the small numbers in our cohort. Our overall serious morbidity (Clavien-Dindo 3 or above) rate was 33% ($n=8$) with a median Clavien Dindo score of 2 and usually reflect the extent of the underlying cytoreductive component required.

The study period of this series spanned 15 years, but 15, or 58% of cases were performed in the last five years. This relative increase is reflective of the changing practice in the treatment of gastric cancer with increasing awareness of the role of CRS and HIPEC for patients with peritoneal disease. A summary of worldwide guidelines for GCPM currently generally do not recommend CRS and HIPEC outside of clinical trials, or not at all, with some referencing the REGATTA trial as evidence of no benefit of cytoreduction [34]. Limitations exist within the use of the REGATTA trial as evidence against CRS and HIPEC, including the design where peritoneal disease was not removed (in other words, not achieving cytoreduction). Importantly, the Peritoneal Surface Oncology Group International (PSOGI) does not have a guideline available regarding CRS with or without HIPEC for patients with GCPM.

Limitations

This is a single centre study with overall low volume data over a longer period, reflective of the comparatively infrequent amounts of CRS and HIPEC performed for gastric cancer with peritoneal disease, at risk of Type 2 errors in our significance. There are similarly limitations in subgroups and multivariate analysis which may be underpowered to detect significance. There is heterogeneity in the patients which includes patients with primary disease as well as patients with peritoneal recurrence after initial gastrectomy. Some patients were unable to have preoperative chemotherapy due to obstruction, and types of therapy and length of therapy are not available. This series is a collection of patients that are carefully selected and CRS and HIPEC is only offered to patients with low volume PCI. The number of patients with peritoneal malignancy referred is not available for an indicator of the frequency CRS and HIPEC is offered at our unit. Our unit is a high-volume centre for peritoneal malignancies and outcomes may not be applicable to lower volume centres.

Conclusion

CRS and HIPEC for GCPM had a median postoperative OS of 11.7 months, with two thirds of patients experiencing minor morbidity only. CRS and HIPEC should be considered in GC with low volume PM (PCI < 7) in selected patients by a multidisciplinary team. Establishment of a consensus protocol for patient selection should be developed.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12957-025-03749-7>.

Supplementary Material 1

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Author contributions

R.H, N.D. and A.A. contributed to data collection and analysis. R.W, N.A, W.L. and D.M. provided significant and substantial revisions. All authors have reviewed the final manuscript.

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Data availability

Data from this study is not publicly available in order to protect patient privacy. Requests can be made to the corresponding author and an application made to the research team and local ethics board.

Declarations

Ethics approval

Ethics approval was granted by the South Eastern Local Health District Ethics committee, under ethical approval code QAQI/18/078.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Thomassen I, van Gestel YR, van Ramshorst B, Luyer MD, Bosscha K, Nienhuijs SW, et al. Peritoneal carcinomatosis of gastric origin: a population-based study on incidence, survival and risk factors. *Int J Cancer*. 2014;134(3):622–8.
2. Juhl H, Stritzel M, Wroblewski A, Henne-Bruns D, Kremer B, Schmiegel W, et al. Immunocytological detection of micrometastatic cells: comparative evaluation of findings in the peritoneal cavity and the bone marrow of gastric, colorectal and pancreatic cancer patients. *Int J Cancer*. 1994;57(3):330–5.
3. Gamboa AC, Winer JH. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for gastric cancer. *Cancers (Basel)*. 2019;11(11).
4. Ji L, Selleck MJ, Morgan JW, Xu J, Babcock BD, Shavlik D, et al. Gastric cancer peritoneal carcinomatosis risk score. *Ann Surg Oncol*. 2020;27(1):240–7.
5. Rijken A, Lurvink RJ, Luyer MDP, Nieuwenhuijzen GAP, van Erning FN, van Sandick JW, et al. The burden of peritoneal metastases from gastric cancer: A systematic review on the incidence. *Risk Factors Survival*. 2021;10(21):4882.
6. Manzanedo I, Pereira F, Pérez-Viejo E, Serrano Á. Gastric cancer with peritoneal metastases: current status and prospects for treatment. *Cancers (Basel)*. 2023;15(6).
7. Fujitani K, Yang HK, Mizusawa J, Kim YW, Terashima M, Han SU, et al. Gastrectomy plus chemotherapy versus chemotherapy alone for advanced gastric cancer with a single non-curative factor (REGATTA): a phase 3, randomised controlled trial. *Lancet Oncol*. 2016;17(3):309–18.
8. Sugarbaker PH. Peritonectomy procedures. *Ann Surg*. 1995;221(1):29–42.
9. Boerner T, Piso P. Cytoreductive surgery for peritoneal carcinomatosis from gastric cancer: technical details. *J Clin Med*. 2021;10(22).
10. Shen P, Stewart JHt, Levine EA. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal surface malignancy: overview and rationale. *Curr Probl Cancer*. 2009;33(3):125–41.
11. Badgwell BD. Don't call it a Comeback-HIPEC for gastric cancer. *Ann Surg Oncol*. 2022;29(12):7244–5.
12. Bonnot PE, Piessen G, Kepenekian V, Decullier E, Pocard M, Meunier B, et al. Cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy for gastric cancer with peritoneal metastases (CYTO-CHIP study): A propensity score analysis. *J Clin Oncol*. 2019;37(23):2028–40.
13. Coccolini F, Catena F, Glehen O, Yonemura Y, Sugarbaker PH, Piso P, et al. Complete versus incomplete cytoreduction in peritoneal carcinosis from gastric cancer, with consideration to PCI cut-off. Systematic review and meta-analysis. *Eur J Surg Oncol*. 2015;41(7):911–9.
14. Yang XJ, Huang CQ, Suo T, Mei LJ, Yang GL, Cheng FL, 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(6):1575–81.
15. Rudloff U, Langan RC, Mullinax JE, Beane JD, Steinberg SM, Beresnev T, et al. Impact of maximal cytoreductive surgery plus regional heated intraperitoneal chemotherapy (HIPEC) on outcome of patients with peritoneal carcinomatosis of gastric origin: results of the GYMSSA trial. *J Surg Oncol*. 2014;110(3):275–84.
16. Deng HJ, Wei ZG, Zhen L, Li GX, Uang XC, Qing SH. [Clinical application of perioperative continuous hyperthermic peritoneal perfusion chemotherapy for gastric cancer]. *Nan Fang Yi Ke Da Xue Xue Bao*. 2009;29(2):295–7.
17. Jacquet P, Sugarbaker PH. Clinical research methodologies in diagnosis and staging of patients with peritoneal carcinomatosis. *Cancer Treat Res*. 1996;82:359–74.
18. Ye Z, Yu P, Cao Y, Chai T, Huang S, Cheng X, et al. Prediction of peritoneal cancer index and prognosis in peritoneal metastasis of gastric cancer using NLR-PLR-DDI score: A retrospective study. *Cancer Manag Res*. 2022;14:177–87.
19. Washington K. 7th edition of the AJCC cancer staging manual: stomach. *Ann Surg Oncol*. 2010;17(12):3077–9.
20. Desiderio J, Chao J, Melstrom L, Warner S, Tozzi F, Fong Y, et al. The 30-year experience—A meta-analysis of randomised and high-quality non-randomised

- studies of hyperthermic intraperitoneal chemotherapy in the treatment of gastric cancer. *Eur J Cancer*. 2017;79:1–14.
21. Patel M, Arora A, Mukherjee D, Mukherjee S. Effect of hyperthermic intraperitoneal chemotherapy on survival and recurrence rates in advanced gastric cancer: a systematic review and meta-analysis. *Int J Surg*. 2023;109(8):2435–50.
 22. Reutovich MY, Krasko OV, Sukonko OGJGO. Hyperthermic intraperitoneal chemotherapy in prevention of gastric cancer metachronous peritoneal metastases: a systematic review. 2020:55–S17.
 23. Reutovich MY, Krasko OV, Sukonko OG. Hyperthermic intraperitoneal chemotherapy in serosa-invasive gastric cancer patients. *Eur J Surg Oncol*. 2019;45(12):2405–11.
 24. Koga S, Hamazoe R, Maeta M, Shimizu N, Murakami A, Wakatsuki T. Prophylactic therapy for peritoneal recurrence of gastric cancer by continuous hyperthermic peritoneal perfusion with mitomycin C. *Cancer*. 1988;61(2):232–7.
 25. Van der Speeten K, Stuart OA, Mahteme H, Sugarbaker PH. Pharmacokinetic study of perioperative intravenous Ifosfamide. *Int J Surg Oncol*. 2011;2011:185092.
 26. Kusamura S, Baratti D, Younan R, Laterza B, Oliva GD, Costanzo P, et al. Impact of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy on systemic toxicity. *Ann Surg Oncol*. 2007;14(9):2550–8.
 27. Al-Batran SE, Hofheinz RD, Pauligk C, Kopp HG, Haag GM, Luley KB, et al. Histopathological regression after neoadjuvant docetaxel, oxaliplatin, fluorouracil, and leucovorin versus epirubicin, cisplatin, and fluorouracil or capecitabine in patients with resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4-AIO): results from the phase 2 part of a multicentre, open-label, randomised phase 2/3 trial. *Lancet Oncol*. 2016;17(12):1697–708.
 28. Al-Batran SE, Homann N, Pauligk C, Goetze TO, Meiler J, Kasper S, et al. Perioperative chemotherapy with fluorouracil plus leucovorin, oxaliplatin, and docetaxel versus fluorouracil or capecitabine plus cisplatin and epirubicin for locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4): a randomised, phase 2/3 trial. *Lancet*. 2019;393(10184):1948–57.
 29. Al-Batran SE, Homann N, Pauligk C, Illerhaus G, Martens UM, Stoecklmacher J, et al. Effect of neoadjuvant chemotherapy followed by surgical resection on survival in patients with limited metastatic gastric or gastroesophageal junction cancer: the AIO-FLOT3 trial. *JAMA Oncol*. 2017;3(9):1237–44.
 30. Ramalho-Vasconcelos F, Gomes R, Bouça-Machado R, Aral M, Nogueiro J, Bouça-Machado T et al. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) in the treatment of gastric cancer: feasibility, efficacy and Safety-A systematic review and Meta-Analysis. *J Clin Med*. 2024;13(11).
 31. Ishigami H, Fujiwara Y, Fukushima R, Nashimoto A, Yabusaki H, Imano M, et al. Phase III trial comparing intraperitoneal and intravenous Paclitaxel plus S-1 versus cisplatin plus S-1 in patients with gastric cancer with peritoneal metastasis: PHOENIX-GC trial. *J Clin Oncol*. 2018;36(19):1922–9.
 32. Pernot S, Voron T, Perkins G, Lagorce-Pages C, Berger A, Taieb J. Signet-ring cell carcinoma of the stomach: impact on prognosis and specific therapeutic challenge. *World J Gastroenterol*. 2015;21(40):11428–38.
 33. Rihuete Caro C, Manzanedo I, Pereira F, Carrion-Alvarez L, Serrano Á, Pérez-Viejo E. Cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with gastric cancer and peritoneal carcinomatosis. *Eur J Surg Oncol*. 2018;44(11):1805–10.
 34. Acs M, Piso P, Glockzin G. Peritoneal metastatic gastric cancer: local treatment options and recommendations. *Curr Oncol*. 2024;31(3):1445–59.

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