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Intraoperative macroscopic tumour consistency is associated with overall survival after cytoreductive surgery and intraperitoneal chemotherapy for appendiceal adenocarcinoma with peritoneal metastases: A retrospective observational study

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ABSTRACT

Background: This study examines the impact of intraoperative macroscopic tumour consistency on short-term and long-term outcomes after cytoreductive surgery (CRS) with intraperitoneal chemotherapy (IPC) for appendiceal adenocarcinoma with peritoneal metastases.
Methods: Macroscopic intraoperative tumour consistency was classified in three groups as soft (jelly-like geltatinous tumours), hard (hard tumour nodules without gelatinous features) and intermediate (both soft and hard features). In-hospital mortality, major morbidity, intensive care unit (ICU), high dependency unit (HDU) and total hospital stay, disease-free survival (DFS) and overall survival (OS) were compared.
Results: The three groups had similar perioperative short-term outcomes. Patients with soft, intermediate and hard tumours revealed differences in OS ($p < 0.001$) and DFS ($p = 0.03$). Multivariable analysis revealed a shorter OS for patients with hard versus soft tumours (HR for hard tumours = 4.43, 95%CI 2.19 −9.00).
Conclusions: Intraoperative macroscopic tumour consistency may be used as a prognostic marker for survival in patients with appendiceal adenocarcinoma with peritoneal metastases.

Introduction

Primary appendiceal carcinoma is relatively rare and affects less than 0.5% of patients with gastrointestinal tract neoplasms, 20% of whom also suffer from peritoneal metastases.[1] It is usually an incidental finding when seen at its early stages. In its advanced stages, tumour perforation and peritoneal seeding can lead to formation of peritoneal metastases (PM).[2] The previous approach of debulking surgery only led to a 5-year survival rate of 6% for patients with Dukes stage D appendiceal adenocarcinoma.[3] In the last two decades, cytoreductive surgery (CRS) combined with intraperitoneal chemotherapy (IPC) has revolutionised the treatment for high-grade appendiceal tumours with isolated peritoneal metastases and is one of the most important factors in improving 5-year survival to 59% for this group of patients.[2]

Peritoneal dissemination of appendiceal adenocarcinoma is not a homogenous disease.[1,4] Multiple series have evaluated the impact of histological factors on survival outcomes and established that histopathological subtype is one of the most important prognostic factors in appendiceal tumours with peritoneal metastases who undergo CRS and IPC.[1,5,6] The specific subgroup of appendiceal adenocarcinomas, according to the classification by Carr et al., has a highly variable intraoperative macroscopic presentation.[7] Soft

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tumours present mainly as gelatinous masses that are quite easily removed during surgery. Hard tumours, on the other hand, usually present as firm, infiltrative masses or nodules that are not easily removed, and require resection and/or ablation to achieve elimination. Intermediate tumours consist of both soft and hard textural components.[8]

As microscopic features of tumours play such an important role in prognosis, whether intraoperative macroscopic tumour consistency also affects long-term survival is worth examining.[9] In addition, it may also affect short-term postoperative outcomes. Hard tumours may require a more extensive surgery which may therefore influence postoperative mortality and morbidity. Hence, the aim of this study was to determine the impact of intraoperative macroscopic tumour consistency on short-term postoperative outcomes and long-term survival outcomes in patients with appendiceal adenocarcinoma with peritoneal dissemination treated by CRS and IPC. We hypothesised that soft tumours were associated with favourable short-term postoperative outcomes and long-term survival outcomes compared to other groups.

Materials and METHODS

Study design

This was a retrospective observational study of prospectively collected data of consecutive patients with peritoneal dissemination of appendiceal adenocarcinoma who underwent CRS and IPC by a single surgical team at St George Hospital, Sydney, Australia between January 1996 and May 2017. A signed informed consent for anonymised prospective data was obtained from all included patients.

Patients

This study included all consecutive patients who underwent complete CRS with IPC for histologically confirmed appendiceal adenocarcinoma with peritoneal metastases, with complete data on macroscopic tumour consistency.[10]. Histopathology diagnosis was extracted from the histological pathology report. The intraoperative macroscopic tumour consistency of the patients was classified by the operating surgeons in three groups. It was retrospectively extracted from operative notes.

Treatment

Preoperative management

All patients underwent preoperative investigations which have been described in our previous paper.[11]

Cytoreductive surgery (CRS)

After laparotomy, an initial assessment of the volume and extent of disease was recorded using peritoneal cancer index (PCI), as described by Jacquet and Sugarbaker.[10] CRS was performed using Sugarbaker's technique.[12]

Hyperthermic intraperitoneal chemotherapy (HIPEC)

After complete or near-complete CRS, HIPEC with oxaliplatin was performed as previously described. HIPEC with mitomycin C (MMC), as previously described, was only performed in patients with previous toxicility to oxaliplatin or in patients with an intraoperative macroscopic appearance of a low-grade appendiceal mucinous neoplasm, since MMC is the standard drug for this disease.[13]

Early postoperative intraperitoneal chemotherapy (EPIC)

EPIC is not routinely performed in patients with peritoneal metastasis of an appendiceal adenocarcinoma. However, in our centre, there are several circumstances that EPIC was used: a lack of availability of HIPEC (e.g. emergency), contraindication to oxaliplatin or MMC, or a macroscopic appearance of abundant areas of low-grade disease or pseudomyxoma peritonei[14]

Postoperative management

All patients were followed two-four weeks following discharge, then three monthly for two years and six-monthly until the 5-year mark with clinical examination, measurement of relevant tumour markers, and assessment of thoracoabdominopelvic CT scans. After 5 years, patients continue to be followed up by either the surgical team or medical oncologist.

Variables

Tumour consistency was dividided into three groups. Group I included soft tumours which were defined as resemblance to pseudomyxoma peritonei (PMP), gelatinous tumour. Group Ii included hard tumours which were defined as hard nodules and there were no gelatinous features. Group III included Intermediate tumours which contain both soft and hard features.

Age was calculated based on date of birth and date of surgery. Definition of appendiceal adenocarcinoma with signet cells was signet cells represented more than 50% of the cancer. Operation time was recorded from the first cut of skin to closure of laparotomy wound. Transfusion units were defined as number of units of packed red blood cells transfused during operation. Preoperative tumour makers including CEA, CA19-9, CA125 were collected as part of routine preoperative work-up.

Perioperative complications were graded based on the Clavien-Dindo Classification (CDC) of surgical complications.[15] Hospital mortality was defined as death that occurred during the same hospital admission for CRS. Major morbidity was defined as CDC grade III or IV. Hospital stay was calculated based on the date of surgery to date of discharge from hospital. Intensive care unit (ICU) stay was calculated on the date of surgery to the date of discharge from ICU. High dependency unit (HDU) stay was calculated on the date of surgery to the date of discharge from HDU.

Statistical methods

All statistical analyses were performed using SPSS for Windows version 22 (IBM Corporation, New York, USA) and R Statistical Packages.[16] A significant difference was defined as a p-value <0.05. Continuous baseline variables (e.g. age, PCI) and outcome variables (e.g. hospital days) were compared between patients with soft, intermediate, and hard tumours by using analysis of variance test or Kruskal-Wallis test for non-normally distributed continuous variables. Categorical baseline variables (e.g. signet ring cell histology) and categorical outcome variables (e.g. major morbidity, postoperative mortality) were compared between the three groups by using the Chi-square test or Fisher' exact test where appropriate. Age, PCI, operation duration and number of transfusion units were reported as mean with standard deviation (SD). Tumour markers, ICU, HDU and total length of stay were reported with median with range.

Median survival was calculated based on the date of surgery to last time of contact or death in months. Disease-free survival was calculated based on the date of surgery to date of recurrence of disease detected. Overall survival and disease-free survival were compared between the three groups by using the log-rank test. The cut-offs for tumour markers for Cox regression analysis were the

medians of serum tumour markers of this study cohort. A multivariable Cox regression analysis was used to calculate a hazard ratio (HR) with 95% confidence interval (CI) for the risk of death of patients with hard, intermediate and soft tumours after adjusted for all potential variables. In this analysis, adjustment was made for variables including tumour consistency, presence of signet ring cells, age, PCI, operation duration, number of units of blood transfusion, tumour markers and use of EPIC. All factors in background characteristics of this study group were included due to potential confounding impacts on these factors, contributing to insignificance in bivariate analysis.

Subgroup analyses

In each tumour consistency group, survival outcomes were further analysed among three PCI groups. PCI has been established as an important prognostic indicator in peritoneal metastases from gastrointestinal cancer.[17] Thus, PCI was divided equally to three groups (0–10, 11–20, >20). In addition, subgroup analysis was also performed based on use of EPIC in addition to HIPEC. There is emerging evidence on potential benefit of use of EPIC in appendiceal adenocarcinoma with peritoneal metastasis.[2,11,18]

Results

Descriptive characteristics

192 patients formed the cohort of this study (Fig. 1), of which 93 patients had soft (48.4%), 78 had hard (40.6%) and 21 patients had intermediate tumour consistency (10.9%). Patients demographic features are summarised in Table 1.

Comparison of baseline characteristics

Patients with soft, intermediate, and hard tumours showed baseline difference in PCI ($p < 0.001$), incidence of signet ring cell histopathology ($p < 0.001$), operation hours ($p = 0.01$), transfusion units ($p = 0.03$) and use of EPIC ($p < 0.001$). Other baseline characteristics were similar between groups (Table 1).

Comparison of short-term postoperative outcomes

Patients with soft, intermediate and hard tumours had similar postoperative mortality ($p = 0.18$), major morbidity ($p = 0.42$), ICU stay ($p = 0.63$), HDU stay ($p = 0.28$), and total length of hospital stay ($p = 0.44$) (Table 2).

Survival outcomes

The median overall survival (OS) was 59 months (95% CI = 55–102) with a 1–, 3– and 5–year OS of 88.6%, 68.0% and 49.5%, respectively. On univariable analysis, patients with soft, intermediate and hard tumours revealed differences in OS ($p < 0.001$) and disease-free survival ($p = 0.03$) (Fig. 2).

After adjustment for age, PCI, the presence of signet ring cells, operating time, numbers of units of packed blood cell units transfused, preoperative serum tumour marker levels as well as the use of EPIC, multivariable analysis revealed a shorter overall survival for aptients with a hard versus soft intraoperative macroscopic tumour consistency (adjusted HR for hard tumours 4.43, 95%CI 2.19–9.00) (Table 3), whereas a similar risk of death was observed for patients with a soft versus intermediate intraoperative macroscopic tumour consistency (adjusted HR = 1.31, 95%CI 0.53–3.29, Table 3).

Subgroup analysis

Due to the impact of macroscopic tumour consistency on patient survival and as our analysis showed that 58.1% of patients with soft tumours received EPIC, a posthoc analysis stratified by use of EPIC was performed. Patients with soft and intermediate tumours that received EPIC additionally to HIPEC had significantly greater survival times than those who received HIPEC alone ($p < 0.001$, Fig. 3). Subgroup analysis revealed that the use of EPIC in addition to HIPEC is associated with a significant improvement in OS in patients with soft tumours ($p = 0.005$), whereas no such effect could be observed in patients with intermediate tumours ($p = 0.06$) nor those with hard tumours ($p = 0.329$) (Fig. 4).

When stratifying by tumour consistency according to PCI (0–10, 10–20, >20) we found that PCI was not a prognostic factor in patients with soft tumours ($p = 0.21$) nor those with intermediate tumours ($p = 0.85$), whereas patients with hard tumours and high PCI values had markedly worse overall survival ($p = 0.002$) (Fig. 5).

Discussion

To our knowledge, this is the first study evaluating the prognostic impact of the macroscopic appearance of peritoneal dissemination of appendiceal adenocarcinoma. We found that patients with macroscopically soft appendiceal adenocarcinoma have significantly improved overall and recurrence-free survival rates compared to patients with hard tumours. We also found that the differences in survival may be explained by the significantly higher rates of signet ring cell histology in patients with macroscopically hard tumours. Equally, the survival benefit of soft tumours may further be explained by an increased rate of as well as susceptibility to EPIC with 5-FU. Whilst external validation of these findings is still necessary, we believe that the assessment of macroscopic consistency in conjunction with PCI may provide valuable information aiding the intraoperative and postoperative decision-making processes in these patients.

To date, studies evaluating prognostic factors in appendiceal adenocarcinoma have focused on patient characteristics and microscopic tumour features.[1,2,5,6,19] In a multi-institutional analysis of 2298 patients with peritoneal metastases of appendiceal origin who underwent CRS+/-IPC, Chua et al. identified prior systemic chemotherapy, higher PCI, and debulking surgery as independent predictors of a poorer survival.[2] The negative impact of a higher volume of disease has been reported for a variety of cancers treated by CRS/HIPEC.[20–22] Low-grade appendiceal mucinous neoplasms (LAMNs) have superior survival outcomes compared to patients with peritoneal dissemination of appendiceal adenocarcinoma and patient survival is not as dependent on PCI as it is in other tumours including appendiceal adenocarcinoma.[13,23] Intriguingly, we found that in patients with macroscopically soft tumours, PCI did not have a significant negative impact on patient outcomes, whereas in patients with hard tumours and a higher disease volume did poorly. Taken together, as our data suggests an increased susceptibility of soft appendiceal adenocarcinoma tumours to EPIC and knowing that EPIC has a beneficial effect on LAMN patient survival,[14] this raises the question about whether soft appendiceal adenocarcinoma tumours behave similarly to LAMNs.

Upon analysis of histologic features, we found that patients with macroscopically hard tumours had a significantly higher proportion of signet ring cells compared to patients with soft tumours. The presence of signet ring cells is a recognised negative prognostic factor in appendiceal tumours.[1,24] The presence of signet ring cells affects mucins produced although their contribution to the macroscopic tumour consistency is currently unknown. However, the structure of a signet ring cell and its intracellular mucin plays an

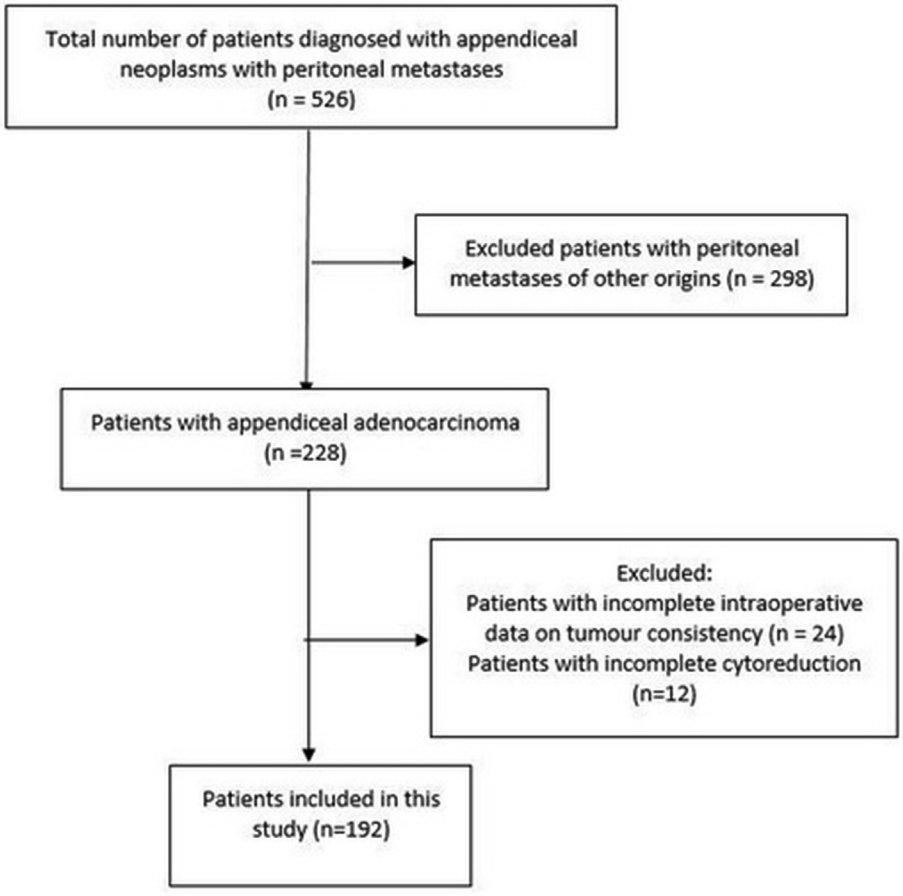

Fig. 1. Selection process.

important role in tumour resistance to chemotherapy. Mucins secreted in appendiceal adenocarcinoma are known to vary with regards compactness ranging from low (soft) to medium (intermediate) to high (very compact/hard)[8,25] and previous studies have shown that the macroscopic difference in consistency of mucin producing tumours (including appendiceal adenocarcinoma) may be explained by differences in cellular and biochemical composition including variations in different mucin glycoproteins (MUCs).[26] This latter aspect is of importance as expression of certain MUCs has been shown to be higher in hard mucin compared to soft tumours[26] including MUC5AC, which is a well-known negative prognostic factor in gastrointestinal malignancies.[27] Further studies evaluating the histologic and molecular properties of appendiceal adenocarcinoma with soft and hard mucin

Table 1
Description of baseline characteristics of all included patients and comparision of baseline characteristics between patients with soft, hard and intermediate tumours.

	All patients	Soft	Hard	Intermediate	*p-value*
Total n (%)	–	93.0 (48.4)	78.0 (40.6)	21.0(10.9)	
Sex, n (%)					0.98
Male	88.0 (45.8)	42.0 (45.2)	36.0 (46.1)	10.0 (47.6)	
Female	104.0 (54.2)	51.0 (54.8)	42.0 (53.9)	11.0 (52.4)	
Age (mean, SD)	55.0 (9.3)	57.0 (11.8)	53.0 (12.1)	53.0 (13.2)	0.14
PCI (mean, SD)	24.0 (12)	28.0 (10.6)	20.0 (11.4)	33.0 (10.9)	<0.001
Signet ring cells present, n (%)	81.0 (31.8)	16.0 (17.2)	38.0 (48.7)	7.0 (33.3)	<0.001
Operation hours (mean, SD)	9.5 (2.5)	10.0 (2.5)	9.0 (2.6)	10.0 (2.6)	0.01
Transfusion units (mean, SD)	7.0 (8.0)	9.0 (9.0)	5.0 (5.0)	9.0 (12.0)	0.03
Use of HIPEC, n (%)					0.48
Yes	183.0 (95.3)	87.0 (93.5)	76.0 (97.4)	20.0 (95.2)	
No	10.0 (4.7)	6.0 (6.5)	2.0 (2.6)	1.0 (4.8)	
Use of EPIC, n (%)					<0.001
Yes	82.0 (42.7)	54.0 (58.1)	19.0 (24.3)	9.0 (42.8)	
No	111.0 (57.3)	39.0 (41.9)	59.0 (59.4)	12.0 (57.2)	
CEA(mg/L) (median, range)	8.0 (0.9–1135.0)	20.0 (0.9–981.0)	3.0 (0.9–1135.0)	7.0 (1.0–227.0)	0.07
CA19-9 (U/mL) (median, range)	28.0 (0.9–13250.0)	82.0 (0.9–13250.0)	18.0 (0.9–9300.0)	21.0 (1.0–4120.0)	0.49
CA125 (U/mL) (median, range)	45.5 (3.0–1401.0)	76.0 (3.0–344.0)	83.0 (4.0–761.0)	165.0 (7.0–1401.0)	0.39

SD-standard deviation; HIPEC- hyperthermic intraperitoneal chemotherapy; EPIC- early postoperative intraperitoneal chemotherapy; CEA-carcinoembryonic antigen; CA 19-9-cancer antigen 19-9; CA125-cancer antigen 125.

Table 2
Comparison of short-term postoperative outcomes between patients with soft, hard, and intermediate tumours.

	All patients	Soft	Hard	Intermediate	*p-value*
Total n (%)	–	93.0 (48.4)	78.0 (40.6)	21.0(10.9)	
Hospital mortality, n (%)	4.0 (2.0)	0 (-)	4 (5.1)	0 (-)	0.18
Major morbidity (Grade III/IV), n (%)					0.42
Yes	96.0 (50.0)	58.0 (62.4)	28.0 (35.9)	10.0 (47.6)	
No	96.0 (50.0)	35.0 (37.6)	50.0 (64.1)	11.0 (52.4)	
ICU stay, days, median (range)	2.0 (0–71.0)	3.0 (1.0–71.0)	2.0 (0–60.0)	3.0 (1.0–52.0)	0.63
HDU stay, days, median, (range)	3.0 (0–39.0)	4.0 (0–22.0)	2.0 (0–21.0)	3.0 (0–39.0)	0.28
Total length of stay, days, median (range)	24.0 (7.0–306.0)	27.0 (10.0–119.0)	22.0 (7.0–153.0)	28.0 (9.0–306.0)	0.44

ICU- Intensive care unit; HDU- high dependency unit.

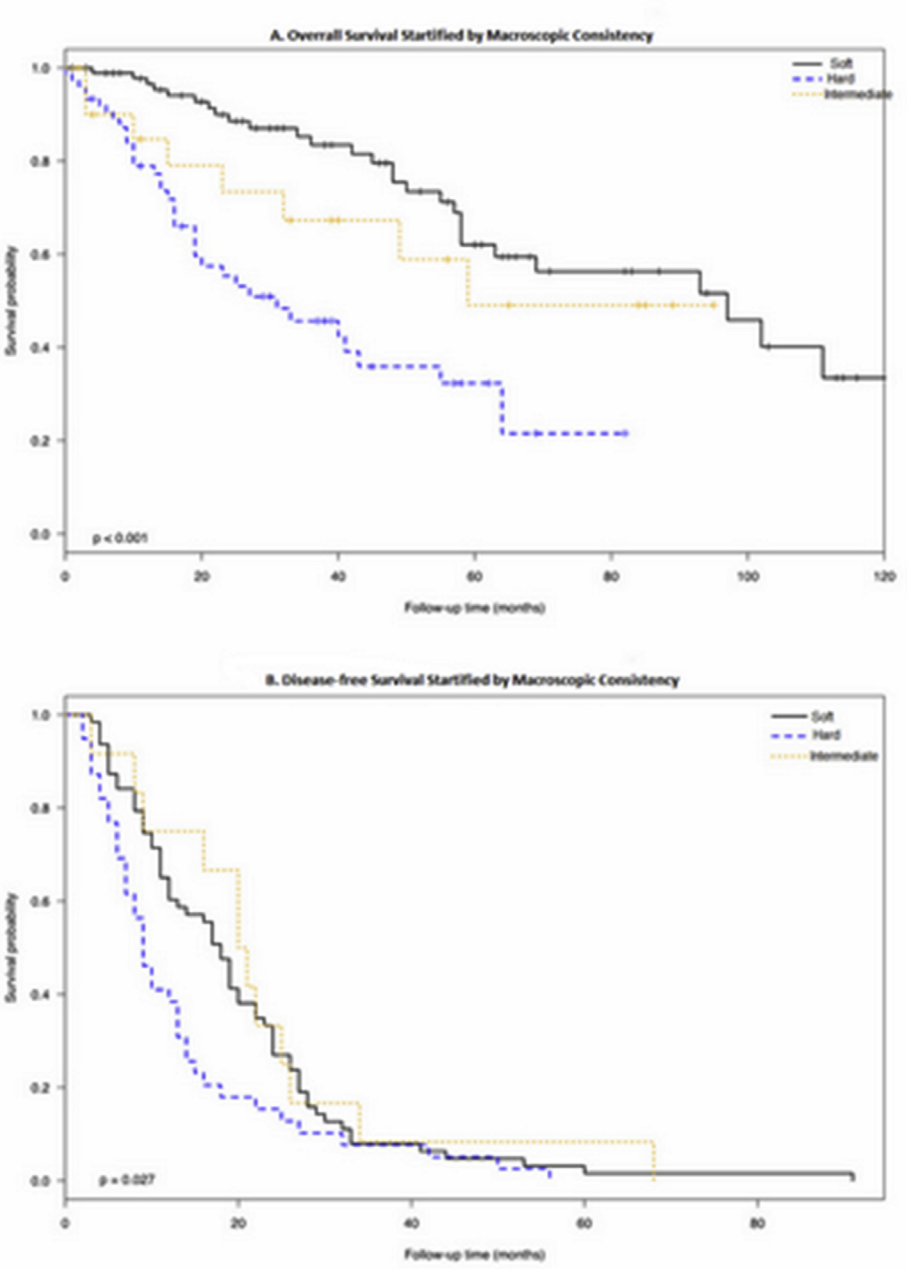

Fig. 2. 2A overall survival, 2B disease-free survival (n = 192).

Table 3
Univariable and multivariable Cox regression analysis of prognostic factors for overall survival.

	Univariable (HR, 95%CI)	*p-value*	Multivariable (HR, 95%CI)	*p-value*
Tumour texture				
Soft	Ref.		Ref.	*<0.001*
Hard	3.50 (2.06–5.94)	*<0.001*	4.43 (2.18–9.00)	
Intermeiate	1.61 (0.72–3.57)	*0.24*	1.31 (0.53–3.29)	
Signet ring cells				
Not present	Ref.	*<0.001*	Ref.	*0.002*
Present	3.49 (2.13–5.74)		2.88 (1.50–5.52)	
Age	0.99 (0.98–1.02)	*0.96*	1.01 (0.99–1.04)	*0.39*
PCI	1.01 (0.99–1.03)	0.43	0.98 (0.94–1.01)	0.20
Operation time (hours)	1.15 (1.06–1.27)	*0.002*	1.48 (1.26–1.74)	*<0.001*
Number of units of blood transfused	1.02 (0.99–1.04)	*0.12*	1.02 (0.98–1.06)	*0.32*
Preoperative serum CEA ≥8.0 mg/L				
No	Ref.	*0.27*	Ref.	*0.05*
Yes	0.76 (0.47–1.24)		0.46 (0.21–1.00)	
Preoperative serum CA19-9 ≥28.0 U/ml				
No	Ref.	*0.76*	Ref.	*0.027*
Yes	1.08 (0.66–1.77)		2.02 (1.08–3.76)	
Preoperative serum CA125 ≥ 45.5 U/ml				
No	Ref.	*0.11*	Ref.	*0.10*
Yes	1.50 (0.92–2.44)		1.81 (0.92–3.56)	
EPIC				
No	Ref.	*0.008*	Ref.	*0.03*
Yes	0.50 (0.30–0.83)		0.46 (0.23–0.92)	

compared to LAMNs, which is almost entirely MUC2 secreting may help elucidate the factors contributing to the current clinical observations.

Intraoperative assessment of tumour consistency is closely associated with our laboratory measurement of consistency index as measured by turbidity and viscosity.[8] In hard tumours, there is a significant reduction in the amount of glucose, lipid, thiol content but an increase in the content of sialic acid in hard mucin. Almost all soft mucin is glycoprotein, although it clearly does contain cancer cells, whereas hard mucins contain much more different material.[28] Our analysis of hard mucins demonstrated the importance of PCI in the prognosis of this group of patients. Given different biochemical properties and impacts of PCI, whether hard tumours behave more similarly to colorectal cancer (CRC) is worth investigating. The multicentre study conducted by Maillet et al. analysed the results of 231 patients with colorectal peritoneal metastases and

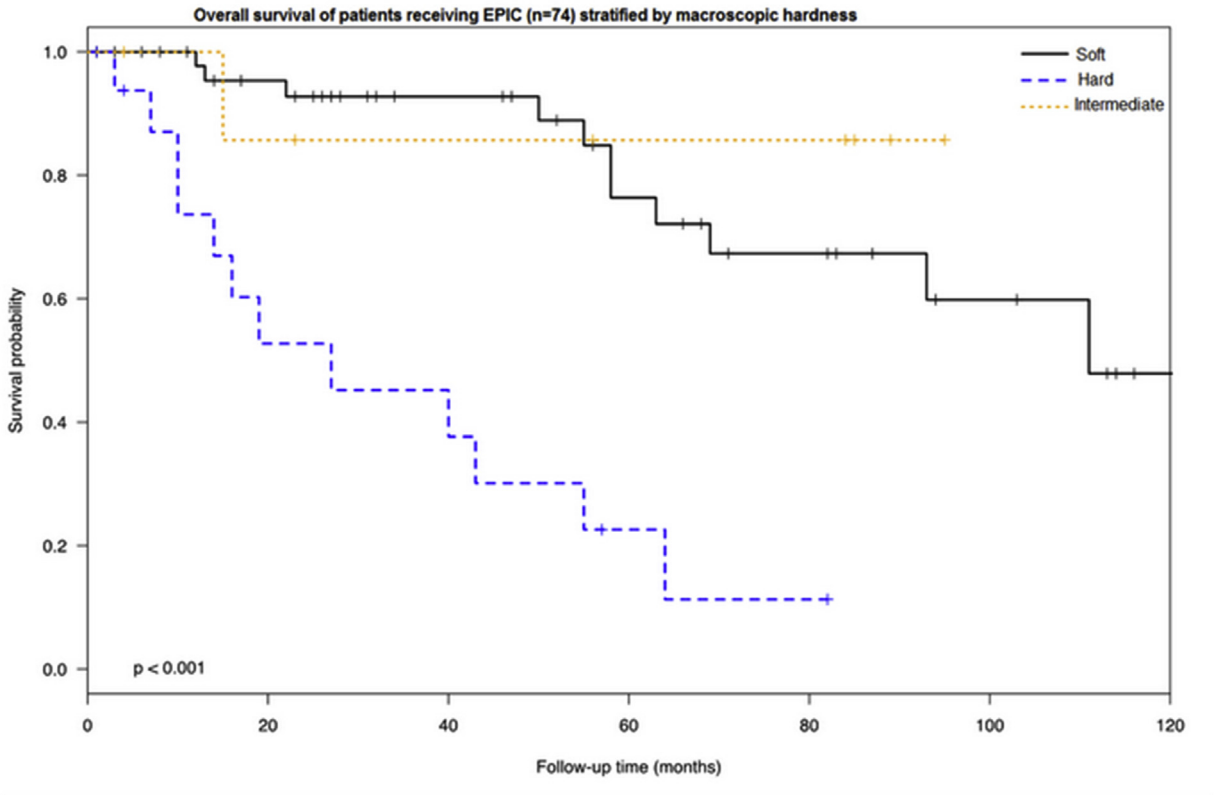

Fig. 3. Subgroup analysis of overall survival of patients receiving HIPEC+EPIC stratified by macroscopic tumour consistency.

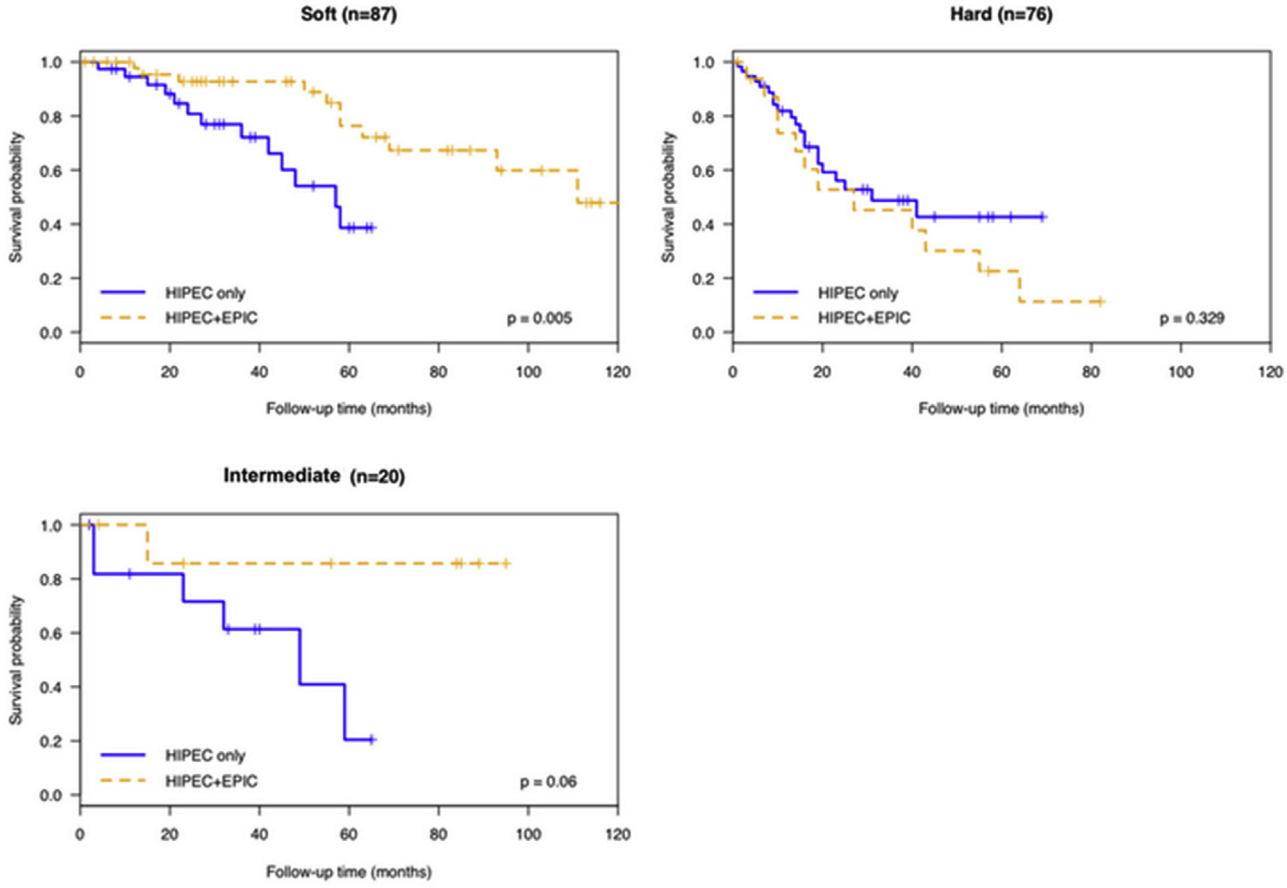

Fig. 4. Subgroup analysis of overall survival of patients stratified by macroscopic tumour consistency and use of EPIC in addition to HIPEC.

demonstrated a similar 5-year OS to that of our patients with hard mucin (34% vs. 32.3%).[29] However, a planned multicentre study with The Peritoneal Surface Oncology Group International will be conducted soon.

As mucins inhibit the efficacy of chemotherapeutic agents, acting as a protective barrier to cancer cells, our research group has been investigating the potential of applying Bromelain (Br) and N-Acetylcysteine (NAC) as a combination treatment in mucinous tumours. We found that Br/NAC therapy possesses mucolytic and mucoregulatory properties.[30] Both in-vivo and in-vitro studies have shown that this combination treatment can lead to a complete disintergration of soft mucin, whilst the dissolution was to a lesser extent (57% in vitro studies and 48.67% in vivo studies for intermediate (semi hard); 50% in in-vitro studies and 28.67% in in-vivo studies for hard mucin) in patient-derived LAMNs and appendiceal adenocarcinoma models.[8]

This drug combination may play dual roles including solubilisation of mucins and enhancement of cellular drug exposure by targeting their mucinous barrier.[8] It also inhibits cell cycle progression and induces cell death by activation of intrinsic and extrinsic caspase-dependent apoptotic pathways and inhibiting pro-survival pathways.[31] In addition, Br/NAC therapy significantly reduces the expression and production of mucins including MUC1, MUC2, MUC4, MUC5AC and MUC 16.Br/NAC therapy represents a potential treatment to improve the efficacy of the conventional therapies.[30] The chemosensitivity of 5-FU has been shown to be enhanced in combination with Br/NAC in in-vivo models of gastrointestinal cancer increasing penetration leading to possible dose reduction of chemotherapy and thus possible reduction of adverse effects.[8]

We found that use of EPIC, in addition to HIPEC, was an independent prognostic factor for superior survival in patients with appendiceal adenocarcinoma. Direct administration of high doses of chemotherapy to the region over a prolonged period leads to a high fraction of cell killing and a smaller possibility of drug resistance.[32] Although 5-FU has a very short half-life, this disadvantage may be overcome by EPIC as there is an extremely high intraperitoneal/intravenous AUC ratio for 5-FU resulting in approximately 250-fold greater exposure.[33] The large volume of EPIC (1L), and repeat administration, also allows for an adequate distribution of the drug to expose the entire peritoneal surface.[34] Rehydration of mucins through the intraperitoneal procedures (including CRS, HIPEC and EPIC) may also allow for improved penetration of the chemotherapies.

Limitations

This study was a retrospective analysis of a prospectively maintained patient cohort, leading to selection bias. The consistency assessment is subjective. A formal grading system, as reported in our recent laboratory work, should be validated. Subsequent validation of our findings using an objective scale may be necessary. In addition, we were willing to accept patients with a CC1 and soft tumour for the administration of EPIC. Different regimens of HIPEC and postoperative systematic chemotherapy may also affect our results. Additionally, there was no information on

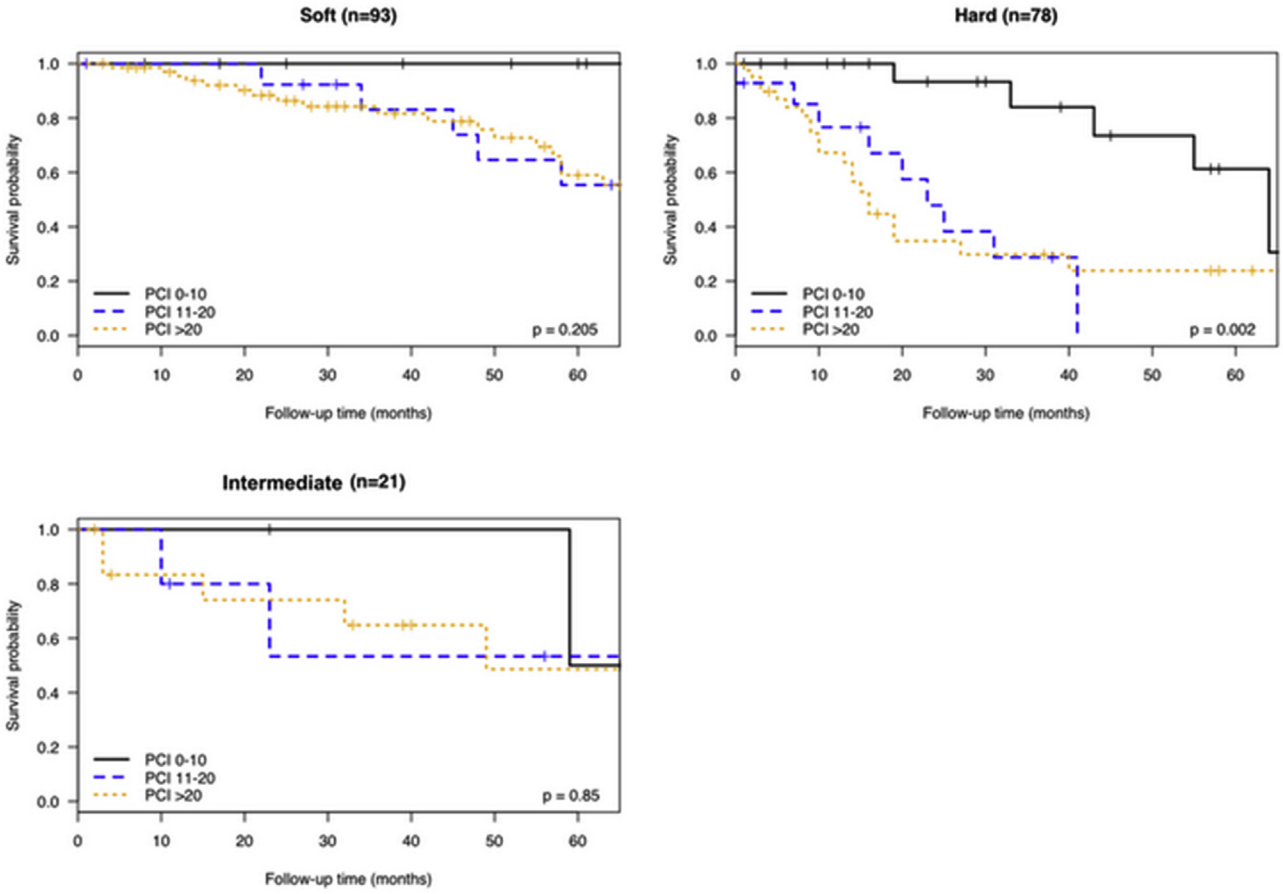

Fig. 5. Overall survival of patients stratified by macroscopic tumour consistency and PCI.

preoperative systematic chemotherapy available. Patients were also referred to our centre at the different stages of their disease. Furthermore, it was limited by our mortality and morbidity data. Our data was based on postoperative complications before the discharge. Our patients often come from different states or even countires. It was also difficult to determine the direct relationship between mortality and surgery after discharge.

Conclusions

In summary, intraoperative macroscopic tumour consistency may potentially be used as an intraoperative prognostic marker for survival outcomes of patients with PM of appendiceal adenocarcinoma as those with macroscopically soft tumour have a significantly longer OS. Additionally, the use of EPIC might be beneficial in patients with appendiceal adenocarcinoma, especially those with soft mucins. Further independent validation of our findings is necessary to further investigate the prognostic potential of intraoperative macroscopic tumour consistency and the role of EPIC in patients with soft appendiceal adenocarcinoma.

Disclosures

Nil.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2018.12.037.

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