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Research Paper

Combining imaging and laparoscopy for the staging of peritoneal metastases: A retrospective cohort pilot study

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ABSTRACT

Background: Peritoneal cancer (PC) staging work-up is challenging. Current gold standard is the Peritoneal Cancer Index (PCI) performed during laparotomy (LT). Accurate and less invasive alternatives, such as computed tomography (CT) or diagnostic laparoscopy (LS), are needed to avoid unnecessary laparotomies. Despite inherent limitations, these modalities have improved over time. Combination of both CT and laparoscopy for PCI evaluation might come close to laparotomy.

Objective: To analyze the accuracy, agreement and reliability of combined PCI (PCI^{CT+LS}) evaluation of CT (PCI^{CT}) and laparoscopy (PCI^{LS}) compared to laparotomy (PCI^{LT}) in patients eligible for cytoreductive surgery.

Methods: A single-center retrospective pilot study of consecutive patients with PC irrespective of etiology, between February 2017 and May 2019. All included patients had sequential PCI staging with CT, laparoscopy and laparotomy. PCI was prospectively documented via a web-based form. Agreement and reliability were analyzed, using weighted-kappa and intraclass correlation respectively (ICC).

Results: Out of 220 patients, 25 had all three modalities of staging. Accuracy of PCI^{CT+LS} (76%) was highest between the 3 modalities in middle-PCI group (PCI 10 to 20), which was the group with the lowest accuracy (44–67%). Compared to laparotomy, reliability of combined CT + LS was the highest (ICC 0.91; 95% CI 0.81–0.96; $p < 0.001$).

Conclusions: The combination of CT with laparoscopy as combined PCI displayed the highest overall accuracy observed by group, as well as excellent reliability. CT is currently the preoperative reference imaging which may be enhanced by laparoscopy as a mandatory procedure selection of eligible candidates for CRS.

1. Introduction

The last three decades showed a complete change of paradigm in the management of peritoneal cancer (PC), from strictly palliative to curative approach. Improved radiological diagnosis, preoperative laparoscopy and coordinated management between oncology and surgery have considerably improved outcomes [1–3].

Despite these improvements, the Peritoneal Cancer Index (PCI), proposed by Sugarbaker, performed during laparotomy is still the gold standard staging for a thorough assessment of peritoneal implant's extent and remains a major survival prognostic factor [4–8]. Accurate and less invasive alternatives, like Computed Tomography (CT) or diagnostic laparoscopy, are however needed, to avoid unnecessary invasive laparotomies.

Nevertheless, assessing the true extent of PC is challenging. Computed tomography (CT) is currently the primary imaging modality of choice in the evaluation of malignant peritoneal disease [1]. CT limits of detection are PC deposits measuring less than 5 mm and those in specific anatomical locations (e.g. pelvis, small bowel's peritoneum, mesentery, lesser omentum) [2,4,9]. Although sensitivity is good, especially in expert hands, the limits of CT remain the size, the location and the expertise of the radiologist [10]. Laparoscopy over CT offers several advantages: direct visualization and biopsy assessment of PC nodules; monitoring of intraperitoneal chemotherapeutic agents and a promising therapeutic advantage.

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On the other hand, laparoscopy is invasive, with incidence of complications depending on the number and extent of previous surgeries [4,11–14]. The combination of CT and laparoscopy diagnostic advantages for PCI evaluation before cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) was barely studied [15].

The aim of the present pilot study was to compare combined PCI (PCI^{CT+LS}) evaluation of CT (PCI^{CT}) and laparoscopy (PCI^{LS}) versus the reference PCI laparotomy (PCI^{LT}) in patients eligible for cytoreductive surgery.

2. Materials and methods

2.1. Patients

This single center retrospective pilot cohort study of 220 consecutive patients with PC irrespective of etiology, was conducted between February 2017 and May 2019, in a swiss referring center. Eligibility criteria were: adult patients with peritoneal cancer with limited extraperitoneal metastatic extent (up to 3 liver metastasis); approval at multidisciplinary meeting for CRS and HIPEC; signed surgical informed consent. Twenty-five patients met the criteria and matched the following sequence: 1° pre-operative CT, 2° diagnostic LS, 3° LT for CRS.

2.2. Compliance with ethical and reporting standards

This study was conducted in compliance with international standards for research practice and reporting. Written informed consent was obtained from included patients. All data was deidentified and anonymized prior to analysis. Retrospective analysis was approved by the local institutional review board (CER-VD 2019–00747), which was conducted in compliance with the STROBE criteria (www.strobe-statement.org) and in line with the STROCSS criteria [16].

2.3. PCI documentation

Since February 2017, surgical PCI was prospectively documented via a standardized website http://www.e-promise.org/[17]. PCI^{CT} was recorded following the same procedure by an expert peritoneal cancer radiologist. Due to heterogeneity of scanning parameters (patients CT were addressed to our referring by Picture Archiving and Communication System, PACS), those parameters can be summarized by the standard values for multidetector CT, with 1.25 mm slice thickness, reconstruction interval between 0.8 and 1 mm, arterial and portal phase acquisition. A single surgeon in charge of the surgery documented prospectively the PCI^{LS} and PCI^{LT} with ePromise, after each surgery. For the purpose of this study, a combined PCI^{CT+LS} score was determined corresponding to the highest score for each of the 13 areas in the two modalities. To quantify PCI, a score of 0–3 points was assigned to each region depending on the size of the implants. Zero, if there was no lesion; 1, for lesions less than or equal to 0.5 cm; 2, for lesions between 0.5 and 5 cm; 3, for lesions >5 cm, confluent or adherent to surrounding organs. The maximum score is 39 points for 13 regions according to Sugarbaker [4]. Completeness of cytoreduction (CCR) score was reported for every patient.

2.4. Statistical analysis

The distribution of cancer types was described by median and interquartile range. Wilcoxon signed rank test was used for median ordinal data, as non-parametric test. Student *t*-test was used for the descriptive quantitative data, as parametric test. Welch's *t*-test was used as parametric test for data where assumption of variance homogeneity was not met. This assumption was assessed with Levene's test. A threshold of $p < 0.05$ was defined as statistically significant.

Diagnostic characteristics were calculated for global PCI for each modality (CT, LS and CT + LS). Receiver Operator Characteristic (ROC) curves and area under curves were analyzed for PC detection. Sensitivity, specificity and predictive values with interval of confidence of 95% were assessed, PCI^{LT} was considered as gold standard. McNemar's test was calculated for accuracy comparison for each modality compared to laparotomy. Diagnostic statistics were assessed with ROC curves for the three categories of size. Accuracy and rate of over- and underestimation were assessed for three groups of PCI; low-PCI, 0 to 9; middle-PCI, 10 to 20; high-PCI, 21 to 39.

Interobserver agreement between modalities was assessed by calculating the interclass correlation coefficient (ICC) for PCI (continuous scale). Agreement for each region was calculated using weighted Cohen's kappa (WCK) (categorial variables). Statistical analysis was performed using SPSS (IBM SPSS Statistics for MacOS, version 26 (IBM Corp., Armonk, N.Y., USA)).

Agreement between PCI^{CT}, PCI^{LS}, PCI^{CT+LS} and PCI^{LT} regarding peritoneal cancer categorization for each region was assessed using WCK statistic. Kappa values below 0.4 represent poor agreement; values between 0.4 and 0.75 indicate fair to good agreement; values of 0.75 and higher represent excellent agreement [18].

Agreement regarding PCI between modalities was assessed using ICC. ICC estimates and their 95% confident intervals were calculated based on a multiple-raters, absolute-agreement, 2-way mixed-effects model. ICC values less than 0.5 are indicative of poor reliability, values between 0.5 and 0.75 indicate moderate reliability, values between 0.75 and 0.9 indicate good reliability, and values greater than 0.90 indicate excellent reliability [19].

A graphical representation of agreement was done with Bland-Altman plots, then linear regression was calculated to assess the presence of bias of proportionality between tested modality and the reference. The existence of proportional bias indicates that modalities are not equally suitable across the range of measurements (PCI 0 to 39).

3. Results

3.1. Demographics

Twenty-five patients met all the eligibility criteria with peritoneal disease mainly from colorectal and ovarian origin (see in Appendix, Table A1; Flowchart of patients' eligibility; Table A2 for baseline demographics). Peritoneal metastases characteristics are detailed in Table 1. Mean delay between PCI^{CT} and PCI^{LS} was 27 days (interquartile range (IQR): 26 days). Median delay for the subsequent step (PCI^{LS} to PCI^{LT}) was 92 days (IQR: 119 days). Overall median PCI between CT and LS were similar ($p = 0.48$) (Table 1). For the purpose of the study, only the initial work-up CT-scan was considered for PCI^{CT}, because of an important heterogeneity of neoadjuvant chemotherapy. It was decided to choose the first CT-scan which was displayed at the multidisciplinary meeting, thus initiating a CRS and HIPEC. Further preoperative imaging that were undergone were not been considered.

3.2. Neoadjuvant chemotherapy

Between initial CT-scan (PCI^{CT}) and surgery (PCI^{LT}), 17 patients (68%) had neoadjuvant chemotherapy (NACT); 4 patients (16%) finished their NACT prior to this interval; 4 patients (16%) had no NACT. The mean delay to surgery after the last chemotherapy was

Table 1
Peritoneal metastases characteristics.

Type of cancer	Median PCI (IQ range)				
	n (%)	CT	LS	LT	$p^{CT\ vs\ LS}$
Colorectal	9 (36)	3 (5)	3 (11)	7 (9)	0.81
Ovarian	6 (24)	29 (25)	26 (22)	33 (19)	0.66
Appendix	4 (16)	17 (12)	12 (–)	20 (–)	0.75
Gastric	3 (12)	12 (–)	9 (–)	14 (–)	0.99
Other	3 (12)	11 (–)	12 (–)	14 (–)	0.50
Overall	**25**	**9 (19)**	**12 (39)**	**14 (38)**	**0.48**

IQR: interquartile range; n: number of patients; CT: computed tomography; LS: laparoscopy; LT: laparotomy.
$p^{CT\ vs\ LS}$: Wilcoxon matched-pairs signed rank test was conducted for median CT versus LS.

43.5 days (SD 32.9) in 17 patients (68%) and 121.0 days (SD 114.2) in 4 patients, those who completed NACT prior PCI^{CT}. The two NACT groups were compared, there was no statistical difference ($p = 0.269$).

3.3. Surgical data

Median operating time was 373 min (IQR: 200 min), with a median of 3 resected organs (IQR: 3) and 200 ml of blood loss (IQR: 285 ml). Four (17%) patients had their primary resected during the CRS.

3.4. Diagnostic characteristic and accuracy

The diagnostic characteristics for each modality were described in Table 2 (see details of the receiver operating characteristic (ROC curve) in appendix Fig. A1). The PCI's combined modality (PCI^{CT+LS}) accuracy was not different to laparotomy ($p = 0.72$). Area under curve for PCI^{CT}, PCI^{LS} and PCI^{CT+LS} were 0.81; 0.77; 0.79 respectively, with $p < 0.001$ for all values. Sensitivity/specificity for lesions > 5 cm was 93/73; 88/60; 85/80 respectively for PCI^{CT}, PCI^{LS} and PCI^{CT+LS} (see details for ROC curve of diagnostic performances and for each lesion size in appendix, Table. A3, Fig. A1 and A2).

To summarize, PCI^{CT+LS} had higher sensitivity than individual modalities with similar accuracy to laparotomy. Accuracy, rate of over- and underestimation were assessed for each group of PCI in Table 3. Accuracy of PCI^{CT+LS} (76.4%) was the highest between the 3 modalities in middle-PCI group, which was the group with the lowest accuracy performances (44.4–66.7%). Nearly a quarter (26.9%) of the patients had an underestimated PCI, half of them (55.6%) were in the middle-PCI group. On the other hand, overestimation rate was low (0–12.5%), which was only observed in low-PCI group.

3.5. Agreement and reliability analysis

Agreement for each region was described using WCK-values (Fig. 1). PCI^{CT} showed the best agreement for central, right and upper regions including distal small bowel ($p < 0.001$). PCI^{LS} had the best agreement for central, both flanks and proximal small bowel ($p < 0.001$). The combined modality PCI^{CT+LS} showed almost the same agreement than PCI^{CT} including the right upper region and the small bowel ($p < 0.001$). Pelvis and left iliac fossa showed both the lowest agreement value for all modalities ($p^{CT} = 0.01$; $pLS = 0.18$; $p^{CT+LS} = 0.05$).

Reliability between each modality and PCI^{LT} was defined with ICC-values. Reliability of PCI^{CT}, PCI^{LS} and PCI^{CT+LS} were 0.88 (95% CI = 0.53–0.96; $p < 0.001$), 0.85 (95% CI = 0.66–0.93; $p < 0.001$), and 0.91 (95% CI = 0.81–0.96; $p < 0.001$), respectively.

Bland-Altman plots were analyzed for the agreement depending of the amount of carcinosis (Fig. A3 in Appendix). PCI^{CT}, PCI^{LS} and PCI^{CT+LS} mean difference with PCI^{LT} was respectively 3.5 (±4.2); 2.6 (±6.0); 1.4 (±4.8). Mean difference = 0 corresponds to perfect concordance. Linear regression analysis was performed and did not show proportionality bias between the tested modality and the reference PCI^{LT} ($p^{CT\ \mathbf{vs}\ LT} = 0.70$; $p^{LS\ \mathbf{vs}\ LT} = 0.58$; $p^{CT+LS\ \mathbf{vs}\ LT} = 0.67$).

Table 2
Diagnostic characteristics for each modality.

	CT	LS	CT + LS
Sensitivity, % (95% CI)	71 (64–77)	75 (67–79)	84 (75–86)
Specificity, % (95% CI)	90 (83–94)	78 (69–84)	74 (65–81)
PPV, % (95% CI)	91 (85–95)	84 (77–89)	83 (77–88)
NPV, % (95% CI)	67 (59–74)	65 (57–72)	72 (63–79)

CT: computed tomography; LS: laparoscopy; CT + LS: combined modality; PPV: predictive positive value; NPV: negative predictive value; 95% CI: 95% confidence interval.

Table 3
Mean accuracy and under-/overestimation rate for PCI staging.

Accuracy, %	CT	LS	CT + LS
Overall	73.1	69.0	76.4
L-PCI (n = 8)	100	87.5	87.5
M-PCI (n = 9)	44.4	44.4	66.7
H–PCI (n = 9)	75.0	75.0	75.0
Underestimation, %			
Overall	26.9	26.9	19.4
M-PCI (n = 9)	55.6	55.6	33.3
H–PCI (n = 9)	25.0	25.0	25.0
Overestimation, %			
Overall	0.0	4.2	4.2
L-PCI (n = 8)	0.0	12.5	12.5
M-PCI (n = 9)	0.0	0.0	0.0
P-value[a]	<0.001	0.01	0.72

CT: computed tomography; LS: laparoscopy; CT + LS: combined modality; L-PCI: low-PCI group, 0 to 9; M-PCI: middle-PCI group, 10 to 20; H–PCI: high-PCI group, 21 to 39.
[a] P-value defined after McNemar's test, compared with laparotomy (gold standard).

3.6. Cytoreduction completeness

Complete cytoreduction (CC-0 or CC-1 for ovarian, appendix and pseudomyxoma origin) was achieved in 16 patients (64%), with subsequent HIPEC in 13 patients (52%). HIPEC regimens were based on oxaliplatin (61.5%); mitomycin-c (30.8%) and cisplatin-doxorubicin (7.7%). Uncomplete cytoreduction (CC-2 to CC-3) was done in 6 patients (24%) with mean PCI 24.7; range 8–33, including cancer from gastric (2), appendix (1), colon (1) and ovarian (2) origin. Three patients (12%) had overly extensive disease (diffuse micronodular involvement of the small bowel serosal surface), with mean PCI 25; range 3–39, leading to open-close surgery, with the placement in one patient of peritoneal catheter for ascites drainage.

4. Discussion

This retrospective pilot study with prospectively acquired PCI documentation shows high agreement between the combined modality (PCI^{CT+LS}) and the reference PCI (PCI^{LT}). This combined modality showed high values of sensitivity and specificity comparable to CT and LS, individually. As suspected, the highest overall accuracy observed by group of PCI was also observed for the combined modality.

In the last two decades studies showed overall PCI sensitivity for CT-scan between 60 and 93%, with 60–94% accuracy, which are

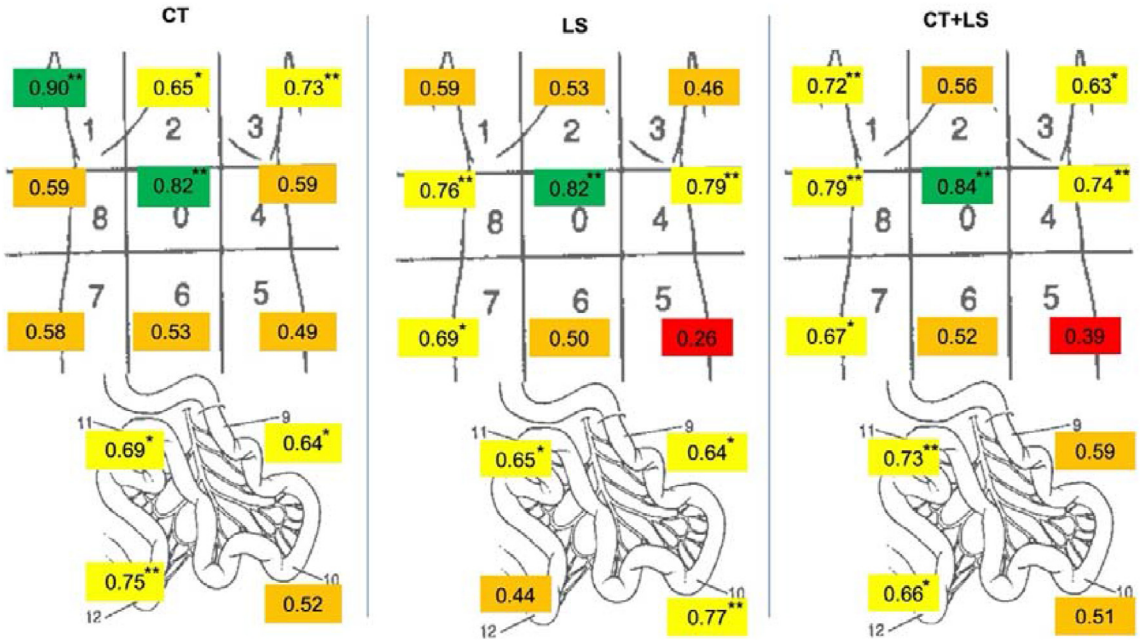

Fig. 1. Agreement with laparotomy (weighted Cohen's kappa) for each modality, by area. CT: computed tomography; LS: laparoscopy; CT + LS: combined modality. Kappa-value scale of agreement: 0.20 to 0.40 (red) = fair; 0.41 to 0.60 (orange) = moderate; 0.61 to 0.80 (yellow) = substantial; 0.81 to 0.99 (green) = near perfect agreement. *p < 0.01. **p < 0.001. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

consistent with the present study [9,20–22]. Though PCI^{CT+LS} had the highest accuracy observed, unexpectedly PPV was higher for PCI^{CT}. We assumed this was a statistical effect due to the calculation method for PPV, as binary variable for all patients vs categorial variable for low-/mid-/high-groups. PCI^{CT+LS} estimation accuracy appeared to be better with middle-PCI group (67%) and showed the lowest rate of underestimation (19%) among the modalities analyzed. This is particularly important as this is the pivotal group of patients, in whom an underestimation of PCI can put a patient in a poor prognostic factor situation; e.g. in the case of a PCI >20 for colorectal cancer, or a PCI >7 for gastric cancer [14,20,21]. In addition, underestimation is particularly important to consider in the case of micronodular but diffuse involvement of mesentery root in a patient with a PCI initially considered as eligible for surgery. Underestimation of PCI by laparoscopy was reported to occur in 1–37% of patients which is consistent with the findings of the present study (overall 27%) [3,22–25].

The size and particular site of lesion is the limiting factor for both modalities. In most series, CT detection sensitivity for lesion under 5 cm showed 9–28%, which is lower than the range of the present study showing 47–68% [9,19].

Agreement between modalities and the reference PCI was excellent, with PCI^{CT+LS} showing the highest reliability (ICC = 0.91). In their evaluation of agreement of CT compared to surgical reference other authors described an agreement between 0.48 and 0.8 [9,26,27].

Agreement by region was quite remarkable, with a clear demarcation of concordance performance by region. For CT-scanner, the upper hemi-abdomen and distal small bowel were the regions with the highest agreement. The central region and the right hypochondrium were the most reliable regions for PCI^{CT}, as shown in many studies of correlation between radiology and surgery [2,10,25,28,29]. For laparoscopy, the central region, flanks, right iliac fossa and proximal small bowel were the regions with the highest agreement. To date, the present study seems to be the only assessing specifically agreement of laparoscopy, CT and the combination of them. For this combined modality, agreement was the highest in the mid-abdominal region, both hypochondria and distal small bowel. The highest concordance values were in the central and both flanks.

In contrast, the left iliac fossa and pelvis were the least reliable regions for CT and laparoscopy. This may be explained by frequent tumor adhesions between visceral and parietal peritoneum in these regions (carcinosis from ovarian and colorectal origin) where PCI cannot be assessed, especially if the region is not accessible. The Bland-Altman plot showed in another fashion the agreement of PCI^{CT+LS} regardless of the extent of carcinosis.

A similar combination of imaging and laparoscopy as described in the present study, but with other imaging modalities like MRI or PET-CT need to be further investigated. Potentially more sensitive modality may contribute to better accuracy. Although PCI is a major predictor of resectability, it is also an imperfect predictor and an innovative combination with other parameters like cancer biology, histological subtype or mutation status deserves further investigations [30,31].

The limitations of the present study are the sample size, the retrospective design, its heterogeneity of histological types, with different morphologies, which make comparison and conclusions limited. The study timing was also challenging and a limitation that we have to mention. As patients were referred from various hospitals, limitation due to the various quality of imaging, the heterogeneity of neoadjuvant chemotherapy and the absence of restaging imaging for all patients have to be emphasized. Furthermore, a considerable period of time elapsed between imaging and CRS, which might have led to a significant tumor regression. Moreover, those limitations are the reflect of the real life in a referring center. Although the dedicated radiologist is an expert in peritoneal surface cancer, imaging quality may impact the accuracy and sensitivity of image reading. The PCI^{LS} and PCI^{LT} documentation by the same surgeon allowed us homogeneity in measurement and avoided inter-individual variability, with the possible counterpart of a possible bias that can be evoked. Unless there were two experienced surgeons in peritoneal cancer, the best approach would have been a documentation by two different persons.

5. Conclusions

In the present pilot study, the combination of CT-scan with laparoscopy as combined PCI showed the highest overall accuracy observed by group of PCI, as well as excellent reliability with the gold-standard. Those performance may be biased by the size-depending sensitivity. This combined modality however, may improve accuracy of preoperative PCI, and therefore the prediction of resectability with less invasive methods. CT-scan is currently the preoperative reference imaging, which may be enhanced by laparoscopy as mandatory procedure to select eligible candidates for CRS.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

Ethical approval was given by the local institutional review board (Commission cantonale (VD) d'Ethique sur la Recherche humaine – Switzerland) with the judgement's reference number CER-VD 2019–00747.

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Author contribution

CRediT authorship contribution statement:
Amaniel Kefleyesus and Martin **Hübner:** conceptualization, methodology, data analysis and interpretation, editing final version and supervision; **Amaniel Kefleyesus:** software, statistical analysis and writing-original draft preparation; **Amaniel Kefleyesus, Martin Hübner, Clarisse Dromain, Daniel Clerc, Hugo Teixeira:** data acquisition and curation; **All authors:** final review. **All authors** have read and agreed to the published version of the manuscript.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Guarantor

Martin Hübner is the guarantor of the submitted study.

Research Registration Number

1. Name of the registry: Research Registry
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3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/register-now#home/registrationdetails/5fca0c15e91f82001db9fd0c

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijso.2020.12.011.

References

[1] Yan TD, Morris DL, Shigeki K, Dario B, Marcello D. Preoperative investigations in the management of peritoneal surface malignancy with cytoreductive surgery and perioperative intraperitoneal chemotherapy: expert consensus statement. J Surg Oncol 2008;98:224–7. https://doi.org/10.1002/jso.21069.
[2] Koh JL, Yan TD, Glenn D, Morris DL. Evaluation of preoperative computed tomography in estimating peritoneal cancer index in colorectal peritoneal carcinomatosis. Ann Surg Oncol 2009;16:327–33. https://doi.org/10.1245/s10434-008-0234-2.
[3] Iversen LH, Rasmussen PC, Laurberg S. Value of laparoscopy before cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis. Br J Surg 2013;100:285–92. https://doi.org/10.1002/bjs.8908.
[4] Jacquet P, Sugarbaker PH. Clinical research methodologies in diagnosis and staging of patients with peritoneal carcinomatosis. Canc Treat Res 1996;82:359–74. https://doi.org/10.1007/978-1-4613-1247-5_23.
[5] Sugarbaker PH. Successful management of microscopic residual disease in large bowel cancer. Canc Chemother Pharmacol 1999;43:S15–25. https://doi.org/10.1007/s002800051093.
[6] 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. https://doi.org/10.1155/2016/2495131.
[7] Jimenez W, Sardi A, Nieroda C, Sittig M, Milovanov V, Nunez M, et al. Predictive and prognostic survival factors in peritoneal carcinomatosis from appendiceal cancer after cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. Ann Surg Oncol 2014. https://doi.org/10.1245/s10434-014-3869-1.
[8] Brandl A, Weiss S, von Winterfeld M, Krannich A, Feist M, Pratschke J, et al. Predictive value of peritoneal cancer index for survival in patients with mucinous peritoneal malignancies treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: a single centre experience. Int J Hyperther 2018. https://doi.org/10.1080/02656736.2017.1351627.
[9] de Bree E, Koops W, Kröger R, van Ruth S, Witkamp AJ, Zoetmulder FAN. Peritoneal carcinomatosis from colorectal or appendiceal origin: correlation of preoperative CT with intraoperative findings and evaluation of interobserver agreement. J Surg Oncol 2004;86:64–73. https://doi.org/10.1002/jso.20049.
[10] Sugarbaker PH, Sardi A, Brown G, Dromain C, Rousset P, Jelinek JS. Concerning CT features used to select patients for treatment of peritoneal metastases, a pictoral essay. Int J Hyperther 2017;33:497–504. https://doi.org/10.1080/02656736.2017.1317368.
[11] Sugarbaker PH. Laparoscopy in the diagnosis and treatment of peritoneal metastases. Ann Laparosc Endosc Surg 2019;4:42. https://doi.org/10.21037/ales.2019.04.04.
[12] 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;36:1922–9. https://doi.org/10.1200/JCO.2018.77.8613.
[13] Esquivel J, Averbach A, Chua TC. Laparoscopic cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in patients with limited peritoneal surface malignancies. Ann Surg 2011;253:764–8. https://doi.org/10.1097/SLA.0b013e31820784df.
[14] Canbay E, Mizumoto A, Ichinose M, Ishibashi H, Sako S, Hirano M, et al. Outcome data of patients with peritoneal carcinomatosis from gastric origin treated by a strategy of bidirectional chemotherapy prior to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in a single specialized center in Japan. Ann Surg Oncol 2014;21:1147–52. https://doi.org/10.1245/s10434-013-3443-2.
[15] Leimkühler M, de Haas RJ, Pol VEH, Hemmer PHJ, Been LB, van Ginkel RJ, et al. Adding diagnostic laparoscopy to computed tomography for the evaluation of peritoneal metastases in patients with colorectal cancer: a retrospective cohort study. Surg Oncol 2020;33:135–40. https://doi.org/10.1016/j.suronc.2020.02.010.
[16] Agha R, Abdall-Razak A, Crossley E, Dowlut N, Iosifidis C, Mathew G, et al. STROCSS 2019 Guideline: strengthening the reporting of cohort studies in surgery. Int J Surg 2019;72:156–65. https://doi.org/10.1016/j.ijsu.2019.11.002.
[17] Villeneuve L, Thivolet A, Bakrin N, Mohamed F, Isaac S, Valette PJ, et al. A new internet tool to report peritoneal malignancy extent. PeRitOneal MalIgnancy

Stage Evaluation (PROMISE) application. Eur J Surg Oncol 2016;42:877–82. https://doi.org/10.1016/j.ejso.2016.03.015.
[18] Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159. https://doi.org/10.2307/2529310.
[19] Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med 2016;15:155–63. https://doi.org/10.1016/j.jcm.2016.02.012.
[20] Glehen O, Gilly FN, Arvieux C, Cotte E, Boutitie F, Mansvelt B, 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;17:2370–7. https://doi.org/10.1245/s10434-010-1039-7.
[21] Elias D, Quenet F, Goéré D. Current status and future directions in the treatment of peritoneal dissemination from colorectal carcinoma. Surg Oncol Clin 2012;21:611–23. https://doi.org/10.1016/j.soc.2012.07.014.
[22] Pomel C, Appleyard TL, Gouy S, Rouzier R, Elias D. The role of laparoscopy to evaluate candidates for complete cytoreduction of peritoneal carcinomatosis and hyperthermic intraperitoneal chemotherapy. Eur J Surg Oncol 2005;31:540–3. https://doi.org/10.1016/j.ejso.2005.01.009.
[23] Garofalo A, Valle M. Laparoscopy in the management of peritoneal carcinomatosis. Canc J 2009;15:190–5. https://doi.org/10.1097/PPO.0b013e3181a58e93.
[24] Valle M, Garofalo A. Laparoscopic staging of peritoneal surface malignancies. Eur J Surg Oncol 2006;32:625–7. https://doi.org/10.1016/j.ejso.2006.03.015.
[25] Esquivel J, Chua TC, Stojadinovic A, Melero JT, Levine EA, Gutman M, et al. Accuracy and clinical relevance of computed tomography scan interpretation of peritoneal cancer index in colorectal cancer peritoneal carcinomatosis: a multi-institutional study. J Surg Oncol 2010;102:565–70. https://doi.org/10.1002/jso.21601.
[26] Ahmed S, Abou-Taleb H, Ali N, Badary DM. Accuracy of radiologic- laparoscopic peritoneal carcinomatosis categorization in the prediction of surgical outcome. Br J Radiol 2019;92(1100):20190163. https://doi.org/10.1259/bjr.20190163.
[27] Torkzad MR, Bergman A, Ahlström H, Mahteme H. Comparison between MRI and CT in prediction of peritoneal carcinomatosis index (PCI) in patients undergoing cytoreductive surgery in relation to the experience of the radiologist. J Surg Oncol 2015;111(6):746–51. https://doi.org/10.1002/jso.23878.
[28] Duhr CD, Kenn W, Kickuth R, Kerscher AG, Germer C-T, Hahn D, et al. Optimizing of preoperative computed tomography for diagnosis in patients with peritoneal carcinomatosis. World J Surg Oncol 2011;9:171. https://doi.org/10.1186/1477-7819-9-171.
[29] Courcoutsakis N, Tentes AA, Astrinakis E, Zezos P, Prassopoulos P. CT-Enteroclysis in the preoperative assessment of the small-bowel involvement in patients with peritoneal carcinomatosis, candidates for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Abdom Imag 2013;38:56–63. https://doi.org/10.1007/s00261-012-9869-3.
[30] Kim H, Kim B-H, Lee D, Shin E. Genomic alterations in signet ring and mucinous patterned colorectal carcinoma. Pathol Res Pract 2019;215:152566. https://doi.org/10.1016/j.prp.2019.152566.
[31] 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. https://doi.org/10.1016/j.amjsurg.2016.03.008.