Preoperative evaluation of computed tomography (CT) in patients with peritoneal carcinomatosis (PC) with the recognised peritoneal cancer index (PCI)

Poster No.: C-0498
Congress: ECR 2012
Type: Scientific Paper
Authors: C. Duhr, W. Kenn, R. Kickuth, J. Pelz, D. Hahn; Wuerzburg/DE
Keywords: Abdomen, CT, Staging
DOI: 10.1594/ecr2012/C-0498

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Purpose

PCI has been recognized as an independent prognostic indicator and as a utility of preoperative CT in assessing Sugarbaker's PCI. This study aimed at evaluating whether CT is an effective procedure for preoperative staging of patients with PC.
Methods and Materials

Three individual readers of two radiologists and one surgeon evaluated pre-operative contrast enhanced abdominal CT scans for a population of 37 patients. Patients in the population underwent explorative laparotomy and were suspected to have PC from primary solid tumors.

Tumor spread, localization and size were described and documented applying Sugarbaker's PCI and lesion size schemes in both, radiological as well as surgical investigations. Radiological observations were retrospectively compared to surgical observations, whereby surgical findings were regarded as the Gold Standard. Radiological findings were then statistically analyzed using correlation analyses including inter-observer as well as intra-observer reliability analyses.

CT protocol

All patients underwent CT scans according to a standardized CT acquisition protocol. Contrast enhancements were used including an oral contrast agent and the rectal filling Gastrolux (Sanochemia Diagnostics, Germany). All patients received intravenous injections of 110mL Iomeprol (Imeron 300, Bracco Imaging, Germany) with a flow rate of 3mL/s. A multi-slice CT scan (Siemens Somatotom Sensation 64, Germany) was used and all scans were conducted at 120kV with 220mAs as well as applying a care dose. Subsequent CT scans were started with a delay of 70 seconds. The collimation was 0.6mm and the slice thickness was 5mm, including coronal and sagittal reformations.

Patient population

In this study a sample of 37 patients was investigated. Within this population 23 female and 14 male patients were between 24 and 78 years with an average age of 66 years at the time of the CT scan. All patients have shown solid primary tumors and underwent primary tumor surgery shortly after the CT scan (no more than 4 weeks).

In this population 32 patients had PC and 5 no PC; no patients were excluded from the study. The median time between CT scan and surgery was 10 days. Out of the 37 patients, 7 had colon cancer, 6 had gastric cancer, 5 had pseudomyxoma peritonei, 5 had ovarian cancer, 4 had pancreatic cancer, 3 had cancer of unknown primary, 2 had appendiceal cancer, and one patient each had adenocarcinoma of the abdominal wall, malignant mesenterial mesothelioma, gastrointestinal stomal tumor, mammary carcinoma, and pleural mesothelioma.

System of tumor determination and description of PCI and LS score
The PCI is an accepted score for the quantification of tumor spread and localization. It serves as an indicator for therapy planning and prognosis. The entire abdominal and intestinal region is divided into 13 regions (Fig. 1 on page 6).

In each of the 13 regions the maximum visible lesion size is measured and assigned to a lesion size score between LS=0 and LS=3. LS=0 means no tumor visible, LS=1 means a tumor lesion size below 0.5cm, LS=2 means a tumor lesion size between 0.5cm and 5cm, and LS=3 means a tumor lesion size larger than 5 cm or describes a confluent tumor.

LS scores in the individual regions are summed up to the PCI score which can assume a minimum score of 0 and a maximum score of 39.

The PCI is a semi-quantitative indicator for the determination of the extent of spread of peritoneal tumor. The success of complete cytoreductive surgery and prognosis of the patient correlates with the PCI. Patients with PC of colorectal origin with a reported PCI score of less than or equal to 10 have a 5 year survival rate of 50%; and lower survival rates of 20% and 0% for PCI scores between 11 and 20, and over 20, respectively.

**Radiological analyses**

CT scans were conducted before explorative laparotomy with CT results being compared to intra-operative findings. In total, all CT scans were evaluated three times independently with some time-lag between each evaluation reading. Two radiological senior physicians with 20 years of experience evaluated the PCI scores independently from each other to achieve inter-observer reliability. Radiologist 1 reviewed scans twice to achieve intra-observer reliability, whereas Radiologist 2 only reviewed once. In order to obtain unbiased results evaluating radiologists were neither informed about the status of primary tumor nor the PC. In addition, a control group of 5 patients was added to the study that did not show PC in the explorative laparotomy.

**Fig. 2** on page 6 shows a CT scan of a patient's abdominopelvic region with a diagnosed PCI of 25.

**Surgical analyses**

The explorative laparotomy and intra-operative data evaluations were conducted by a surgical team of one surgeon following a standard procedure and protocol. All patients underwent surgery in the same institution. Surgical and pathological findings were evaluated prospectively and documented.

In particular, the PCI score assignment was conducted by a surgical senior physician with 11 years experience in PC surgery. Intra-operative results regarding PC existence, lesion size, and localization served as Gold Standard.
Corresponding to the CT scan with a diagnosed PCI of 25 (Fig. 2 on page 6), the surgical intraoperative PCI evaluation diagnosed a PCI of 26 (Fig. 3 on page 7).

**Statistical analyses**

Radiological and surgical PCI scores were compared to each other applying the Spearman correlation coefficient to measure inter-rater reliability. Inter-observer reliability between two radiological readings was also analyzed using the Spearman correlation coefficient. Intra-observer reliability between the two readings of the same radiologist was measured using the intra-class correlation coefficient ("ICC"). All correlations were tested for statistical significance using the p-value. Different PCI scores were also evaluated for statistical difference applying the Wilcoxon rank test. In addition to correlation coefficients, both, sensitivities and specificities were calculated for the individual abdominal regions as well as lesion size. Statistical analyses were performed using Excel software with Analyse-IT statistical package.
Peritoneal Cancer Index

<table>
<thead>
<tr>
<th>Regions</th>
<th>Lesion Size</th>
<th>Lesion Size Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Central</td>
<td>-----</td>
<td>LS 0 No tumor seen</td>
</tr>
<tr>
<td>1 Right Upper</td>
<td>-----</td>
<td>LS 1 Tumor up to 0.5 cm</td>
</tr>
<tr>
<td>2 Epigastrium</td>
<td>-----</td>
<td>LS 2 Tumor up to 5.0 cm</td>
</tr>
<tr>
<td>3 Left Upper</td>
<td>-----</td>
<td>LS 3 Tumor &gt; 5.0 cm or confluence</td>
</tr>
<tr>
<td>4 Left Flank</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>5 Left Lower</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>6 Pelvis</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>7 Right Lower</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>8 Right Flank</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>9 Upper Jejunum</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>10 Lower Jejunum</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>11 Upper Ileum</td>
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<td></td>
</tr>
<tr>
<td>12 Lower Ileum</td>
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</tbody>
</table>

PCI

Fig. 1: Sugarbaker's Peritoneal Cancer Index (PCI)

Fig. 2: CT scan of abdominopelvic region with PCI 25 (corresponding to shown surgical intraoperative picture)

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Fig. 3: Surgical intraoperative picture with PCI 26 (corresponding to shown CT scan)

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Results

Differences in PCI results for intra-operative and radiological diagnosis

PCI observations of 37 intra-operative procedures conducted by a single surgeon are compared with independent PCI observations of two radiologists. Key findings are high levels of correlation between the intra-operative and radiological observations showing correlation coefficients of around 0.9. In particular, compared to intra-operative findings, Radiologist 1 shows correlations of 0.930 and 0.888 for his first and second reading, respectively. Radiologist 2 shows a correlation of 0.887.

All correlation coefficients in Fig. 4 on page 11 are statistically significant at p-values below 0.001. In order to assess the reliability of findings, the intra and inter-rater reliabilities of observations by Radiologist 1 and Radiologist 2 were examined. Results for intra-rater reliability of Radiologist 1 first and second reading show high levels of reliability indicated by an intra-class correlation coefficient ("ICC") of 0.909 (p-value < 0.001). Correlation coefficients of 0.913 and 0.953 between readings of Radiologist 1 and Radiologist 2 demonstrate high inter-rater reliability. Fig. 5 on page 11 compares PCI findings between the surgeon and Radiologist 1.

Sensitivity and specificity between Radiologist 1 (first reading) and the Gold Standard are 94% and 80%, respectively (Fig. 6 on page 11). Specificities are consistent for the other two radiological readings at 80% as both radiologists correctly detected 4 patients without PC (i.e., without an intra-operative PC finding) but observed 1 false positive for the same patient without PC. However, for this fifth patient without PC, PCI scores are PCI=2 with 2 regions of LS=1 for the first reading of Radiologist 1, PCI=10 with 8 regions of LS=1 and 1 region of LS=2 for the second reading of Radiologist 1, as well as PCI=7 with 7 regions of LS=1 for the first reading of Radiologist 2. This demonstrates that the false positives were assigned small lesion sizes. The sensitivity for the second reading of Radiologist 1 is 94% corresponding to his first reading although true positives and/or false negatives are different by one patient. Radiologist 2 shows a sensitivity of 97% (Fig. 6 on page 11).

For most relations the Wilcoxon rank test, used to analyze differences among the intra-operative observations and radiologist observations, indicates statistically insignificant differences at p-values > 0.05 (Fig. 7 on page 12).

In light of high levels of correlation between intra-operative and radiological observations the insignificantly different recorded findings suggest that both radiologists evaluated the magnitude of PCI insignificantly differently than the surgeon (i.e. Gold Standard).

CT analysis by abdominopelvic regions
Correlation analyses by abdominopelvic region were conducted between the intraoperative findings (Gold Standard) and the first reading of Radiologist 1. Results by region show varying correlation coefficients ranging from 0.418 to 0.881 at statistically significant levels (p-value < 0.05) (Fig. 8 on page 12).

The analysis of results shows relatively higher correlations in the upper and middle abdominopelvic regions compared to the lower region and the smaller bowel. However, the upper and middle abdominopelvic regions show lower sensitivity and specificity at 86% and 73%, respectively, compared to the lower abdominopelvic region. This result suggests a relatively high CT performance. CT performance in the smaller bowel is inferior with lower levels of correlation and levels of sensitivity below 0.6 and 70%, respectively (Fig. 9 on page 12).

CT performance is high in the middle abdominopelvic regions which have more evenly distributed lesions sizes of 1, 2, and 3 compared to the upper region with a concentration around lesion size 1.

Differences in results by abdominopelvic region appear to be due to different lesion sizes (excepted for small bowel evaluation) and not because of anatomic or pathologic differences.

**Analysis by lesion size**

Analysis of findings by lesion size show that results depend on lesion size and that sensitivities are improved with increasing lesion sizes but matching observations (defined as the number of correct radiological tumor size observations divided through the number of total observations) show a declining rate (Fig. 10 on page 13).

While sensitivities increase from 74% for LS=1 to 90% for LS=3 with a peak at LS=2 of 97%, the proportion of actually matching observations between the Gold Standard and Radiologist 1 declines from 84% for LS=0 to 34% for LS=3.
Images for this section:

<table>
<thead>
<tr>
<th>Intra-operative</th>
<th>Radiologist 1</th>
<th>Radiologist 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st Reading</td>
<td>2nd Reading</td>
</tr>
<tr>
<td>Intra-rater Reliability</td>
<td>1st Reading Radiologist 1</td>
<td>0.909</td>
</tr>
<tr>
<td>Inter-rater Reliability</td>
<td>1st Reading Radiologist 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2nd Reading Radiologist 1</td>
<td></td>
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</tbody>
</table>

**Fig. 4:** Overview of correlation coefficients

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**Fig. 5:** Correlation between radiological PCI and surgical PCI

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Fig. 6: Overview of sensitivities and specificities of Radiologist 1 and Radiologist 2

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Significance of difference in results

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Fig. 7: Significance of difference in results demonstrated with the Wilcoxon rank test

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Fig. 8: Results by abdominopelvic region including correlation coefficient, p-value, sensitivity, specificity, under-estimation, and over-estimation

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Fig. 9: PCI analysis by abdominopelvic region

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Fig. 10: Analysis of findings by lesion size

\[
\begin{array}{|c|c|c|c|}
\hline
\text{Tumor size} & \text{LS=0} & \text{LS=1} & \text{LS=2} \\
\hline
< 0.5 \text{cm} & 199 & 159 & 73 & 50 \\
0.5 - 5 \text{cm} & 74\% & 97\% & 90\% \\
> 5 \text{cm} & 84\% & 53\% & 48\% & 34\% \\
\hline
\text{True positives} & \text{n.a.} & 118 & 71 & 45 \\
\text{False negatives} & \text{n.a.} & 41 & 2 & 5 \\
\text{Sensitivity} & \text{n.a.} & 74\% & 97\% & 90\% \\
\text{Specificity} & 84\% & \text{n.a.} & \text{n.a.} & \text{n.a.} \\
\text{Accuracy} & 84\% & 53\% & 48\% & 34\% \\
\text{Under estimate} & \text{n.a.} & 26\% & 34\% & 66\% \\
\text{Over estimate} & 16\% & 21\% & 18\% & \text{n.a.} \\
\hline
\end{array}
\]

\[n = 481 \ (37 \text{ patients} \times 13 \text{ abdominopelvic regions})\]
\[\text{n.a.} = \text{not available}\]
Conclusion

In line with previous research, this study underpins that CT is an effective imaging modality for the pre- and post-operative staging of patients. A standardized CT acquisition protocol in a certified PC center and readings performed by highly experienced radiologists could result in sufficiently high correlation coefficients, sensitivity and specificity rates for an effective patient selection process. Relatively high sensitivities and specificities results could be achieved by abdominopelvic region as well as by lesion size. However, results by abdominopelvic region showed lower correlation, therefore suggest lower efficacy. These results are supported by analyses of sensitivity and accuracy by lesion size. The appropriateness of CT for the evaluation of the small bowel region is still insufficient and needs to be further investigated.

The findings of this study suggest that Computed Tomography is an effective procedure for pre-operative staging but is less suitable for determining a tumor’s accurate extent.
References


Personal Information

Carolin D. Duhr

University Hospital Wuerzburg, Department of Radiology, Wuerzburg, Germany

Email: carolin.duhr@gmx.de