

Calculation of a clinical predictive factors identifying peritoneal disease on a staging laparoscopy in gastric cancers

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Abstract

Introduction: Staging laparoscopy (SL) is the current standard staging workup for loco-advanced gastric cancers (GCs). **Materials and Methods:** We analyzed the data of all patients with loco-regionally advanced, nonmetastatic GCs, who underwent SL for the evaluation of peritoneal carcinomatosis (PC). **Results:** Between December 2013 and October 2016, 363 patients underwent SL, of which 75 (20.7%) were found to have PC on SL. Age ≤ 40 years, CA 19-9 > upper limit of normal, and low serum albumin levels (≤ 3.5 g/dl) correlated significantly with the presence of PC on SL. There was a statistically significant difference in the median overall survival between patients with radiologically detected PC and SL detected PC (8.67 months vs. 15.3 months; $P < 0.0001$). **Conclusion:** SL upstaged disease status in 20.7% of patients. Clinical factors, identified in this study, need further validation in larger prospective cohorts before being used in clinical practice. Patients with radiologically detected PC have lower survival as compared to those with PC on SL.

Key words: Computed tomography scan, gastric cancers, peritoneal disease, predictive factors, staging laparoscopy

Introduction

Majority of the country- and region-specific guidelines on the diagnosis of peritoneal disease or peritoneal carcinomatosis (PC) in gastric cancer (GC) have included a staging laparoscopy (SL) as part of the diagnostic algorithm, although with slightly differing indications across the spectrum of GC.^[1-4] However, consensus regarding the optimal methods of diagnosing PC has not been achieved. SL has an overall predictive accuracy of 85%–98.9% in diagnosing metastatic intraperitoneal disease and a major role in thereby preventing additional unnecessary laparotomies (8.5%–43.8%).^[5] We assessed our patients who underwent SL and looked at predictive factors.

Materials and Methods

This study was conducted as part of the Institutional Review Board and Ethics Committee (EC) approved project (Institutional EC number IEC/0517/1868/001). The medical records of patients who were diagnosed with GC between December 2013 and October 2016 were retrieved from a prospective maintained database at the Tata Medical Hospital. Patients with clinical T3 or T4 (EUS performed if radiologically T1/T2) and/or N positive and M0 according to the American Joint Committee on Cancer (tumor-node-metastasis) classification (7th edition) based on preoperative computed tomography were selected. All patients were confirmed to have gastric adenocarcinoma before SL by preoperative endoscopy and biopsy. Patients without a baseline SL were excluded from the study. Peritoneal washing cytology is not part of the standard protocol in our institution, and it is not reported in this study.

The standard technique for SL was used with the insertion of two or three ports in the upper abdomen. Areas inspected on the procedure were stomach, liver, surfaces in the pelvis, and paracolic gutters, thereby entailing an evaluation of the entire coelomic cavity.

The factors evaluated as potentially predictive for the presence of PC were age ($<$ or ≥ 40 years), raised CA 19.9 versus CA 19.9 levels below the upper limit of normal (ULN) (institutional ULN-37 U/L), serum albumin levels at presentation (>3.5 g/dl or ≤ 3.5 g/dl), degree of differentiation (poorly differentiated vs. well differentiated/moderately differentiated/adenocarcinoma not otherwise specified), signet-ring morphology (presence vs. absence), and location (proximal vs. distal).

Statistical considerations

The incidence of SL-PC diagnosed on SL was calculated as a simple percentage. The Chi-squared test was used to analyze the variables associated with positive peritoneal metastases and to correlate demographic variables with histology. Those found to have a $P < 0.05$ were included in the multivariate logistic regression analysis.

The median overall survival (mOS) for patients with SL diagnosed PC (SL-PC) and radiologically diagnosed PC (R-PC) was estimated using Kaplan–Meier method. OS was calculated from the date of diagnosis till date of death, whatsoever the cause.

Results

Between December 2013 and October 2016, 363 consecutive patients were included in the analysis. Baseline demographic is shown in Table 1. A total of 75 patients (20.7%) were found to have overt PC.

On evaluation of predictive factors, raised CA 19.9 levels ($P = 0.002$), age < 40 years ($P < 0.001$), serum albumin levels ≤ 3.5 g/dl ($P = 0.028$), and the presence of signet-ring histology ($P = 0.048$) predicted for greater incidence of PC using univariate analysis. These factors retained statistical significance on multivariate regression analysis excepting signet-ring histology. Baseline characteristics, shown in Supplementary Table 1 of patients with R-PC and of PC-SL,

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Table 1: Baseline characteristics

| Characteristic | PC cohort (%) | Non-PC cohort (%) | P |
|-----------------------------------|---------------|-------------------|-------|
| <i>n</i> | 75 (100) | 288 (100) | - |
| Gender | | | |
| Males | 47 (63) | 204 (71) | 0.206 |
| Female | 28 (37) | 84 (29) | |
| Median age (years) | | | |
| <40 | 22 (29) | 33 (12) | 0.001 |
| ≥40 | 53 (71) | 255 (88) | |
| Differentiation | | | |
| PDAC | 35 (44) | 177 (56) | 0.638 |
| WDAC/MDAC/adenocarcinoma NOS | 12 (56) | 51 (44) | |
| Presence of signet-ring histology | 40 (51) | 117 (33) | 0.048 |
| Raised CA 19.9 (> ULN) levels | 31 (41) | 75 (28) | 0.002 |
| Tumor location | | | |
| Proximal (including body) | 31 (41) | 105 (36) | 0.437 |
| Distal | 44 (59) | 183 (64) | |
| Albumin levels (g%) | | | |
| ≤3.5 | 12 (16) | 82 (28) | 0.028 |
| >3.5 | 63 (84) | 206 (72) | |

PC=Peritoneal carcinomatosis, PDAC=Poorly differentiated adenocarcinoma, WDAC=Well-differentiated adenocarcinoma, MDAC=Moderately differentiated adenocarcinoma, NOS=Not otherwise specified, ULN=Upper limit of normal

were comparable (no statistical difference). On comparing mOS between the two groups using Kaplan–Meier method, patients with SL-PC had a superior mOS (15.1 months, 95% confidence interval [CI]: 13.18–17.10) as compared to patients with R-PC (8.67 months, 95% CI: 6.70–10.63), and this was statistically significant ($P < 0.001$).

Discussion

The ability of SL to detect occult metastasis in our study was 20.7%, which is similar to previously published studies.^[6] It is also representative of incidence of PC on SL in a region where the distal-to-proximal migration of GC has yet to take place.^[7]

Factors that have been associated with an increased incidence of PC include tumor morphology, signet-ring morphology, gastro-esophageal junction location of primary, nodal burden, raised CA 19.9 levels, and peripheral blood neutrophil/lymphocyte ratio.^[8-11] Our study identified two previously identified factors – signet-ring morphology and raised CA 19.9 levels – along with two new factors – age <40 years and low serum albumin levels (≤3.5 g/dl) – as predictive for PC on SL.

While there is some evidence for signet-ring morphology and raised CA 19.9 levels as predictive for metastasis and PC *per se*, a younger age (<40 years) and low serum albumin levels (≤3.5 g/dl) as being predictive for PC is a potentially new concept.^[11-15] The age cutoff of 40 years was selected based on the results of a large Japanese study comprising 3818 patients, which indicated a worse prognosis for patients below the age of 40 years and not undergoing surgery.^[16]

The difference in mOS between the R-PC and SL-PC was statistically significant (15.10 months, vs. 8.67 months, $P < 0.001$). While there is no immediate intervention that may contribute to improving outcomes for patients with R-PC

viz-a-viz SL-PC, it bears keeping in mind when explaining prognosis to patients in the clinic.

Conclusion

SL is an important component of the staging workup of patients with GC and upstages patients in 20.7% in our series. Clinical factors, such as those identified in this study, need further validation in larger prospective cohorts. Patients with R-PC have lower survival as compared to those with SL-PC.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Baseline comparison between peritoneal carcinomatosis diagnosed on staging laparoscopy and peritoneal carcinomatosis diagnosed radiologically

| Characteristic | PC (diagnosed on SL) | PC diagnosed radiologically | P |
|--|-----------------------------|------------------------------------|----------|
| Number of patients | 75 | 56 | |
| Gender | | | |
| Male | 47 | 34 | 0.950 |
| Female | 28 | 22 | |
| Age (≤ 40 years) | 22 | 15 | 0.845 |
| Presence of signet-ring morphology | 38 | 26 | 0.724 |
| Raised CA 19.9 ($> \text{ULN}$) levels | 33 | 33 | 0.942 |
| Absence of PDAC | 30 | 15 | 0.189 |

PDAC=Poorly differentiated adenocarcinoma, ULN=Upper limit of normal, PC=Peritoneal carcinomatosis, SL=Staging laparoscopy