Efficiency of Multi Detector Computed Tomography in Staging of Gastric Carcinoma and Detection of Distant Metastatic Disease

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ABSTRACT

Introduction: A proper preoperative evaluation is essential to plan the surgery to attain the aim of a R0 resection. This study was aimed at comparing the efficiency of preoperative staging of gastric cancer using Contrast Enhanced Computed Tomography (CECT) scan by assessing tumor location, depth of invasion, lymph node involvement and adjacent organ involvement as compared to post-operative histopathological staging.

Material and Methods: All patients with histopathologically confirmed gastric malignancy by endoscopy underwent CECT for preoperative staging. The finding was compared with post-operative histopathologic findings. The findings were analysed for sensitivity, specificity, positive predictive value and negative predictive value of CECT for T staging, detecting nodal status and adjacent organ involvement.

Results: The mean age of the patients were 58.9 years with 61% patients being males. All patients included had serosal involvement at the time of presentation and all of them were picked up by CECT. The ability of CECT to detect sub layer involvement could not be assessed. For N staging, CECT was less sensitive while for N1 disease, maximum specificity of 94.44%. For N2 disease, it showed maximum sensitivity of 55.55%. On evaluating the adjacent organ involvement CECT showed least sensitivity for bowel involvement (16.66%) and maximum sensitivity for pancreatic involvement (71.43%).

Conclusion: CECT remains poor at identifying lymph node metastases and in determining depth of tumour invasion (T1–T3). But it was highly specific which meant that a positive spiral CT result could be relied upon. It was also effective in identifying the invasion of pancreas and in some cases of distant metastatic disease.

Keywords: Contrast Enhanced Computed Tomography, Gastric Cancer, Preoperative Evaluation, Sensitivity, Specificity.

INTRODUCTION

Gastric cancer describes a broad mix of malignant neoplasms derived from the different histological components that make up the stomach. These include adenocarcinoma, lymphoma, carcinoid tumours and sarcoma. Among these, gastric adenocarcinoma accounts for over 90% of all cases of gastric cancers globally. According to 2014 cancer statistics, gastric cancer is the second most common cause of gastrointestinal malignancy, in both, newly detected case and cancer related deaths in U.S.1 The worldwide incidence of gastric cancer has declined rapidly over the recent few decades. Despite its declining incidence, it is the third most common cause of cancer-related mortality globally.1 The decline may be partially due to the recognition of certain risk factors such as H. pylori and other dietary and environmental risks.2 The gastric cancer prevalence in India is 5.14 for both sexes (male: 5.14, females: 3.34). The mortality rates according to GLOBOCAN registry is 5.65 for both sexes (male:8 and female: 3.4).3 Weight loss has been considered among the potential prognostic factors for gastric cancer by at least 13 studies so far, and in 10 of these it significantly and independently related to the fatal outcome.4,5 Delay in diagnosis was longer for patients without alarm symptoms compared to that of patients with alarm symptoms.4,6 Neoadjuvant treatment is recommended for any gastric cancer patient without metastatic disease who is either node positive or staged as T2 or greater in the preoperative setting. It is of great importance for the operating surgeon to know the adjacent organ involvement to obtain an R0 resection. Despite increased referral for consideration of surgical treatment, 15–30% of patients have unresectable disease and undergoes no procedure other than open biopsy. Traditionally, staging has been performed at the time of surgery, although a sensitive and reliable staging tool which
could identify patients with unresectable disease would be of great benefit in saving patients from unnecessary laparotomy. Contrast Enhanced Computed Tomography (CECT) scan of abdomen and pelvis is the most commonly used investigation for pre-operative staging. But its value remains controversial. So this study was aimed at comparing the CECT staging with post operative histopathological staging in carcinoma stomach.

MATERIAL AND METHODS

Descriptive cross sectional study was conducted among patients who attended the General Surgery and Surgical Oncology departments of Amala Institute of Medical Sciences, Thrissur, Kerala from January, 2015 to July, 2016. Histopathology reports and CT scan reports were collected from Pathology and Radiology departments respectively. Both males and females of age between 35 and 75 years who were provisionally diagnosed as gastric carcinoma (using endoscopic biopsy) were included in the study. Patients who had undergone neo-adjuvant treatment or presented with an acute abdomen or recurrences and patients aged less than 35yrs and more than 75 yrs were excluded from the study. Sample size-61 was calculated based on the previous study where 48% sensitivity for CT scan in the preoperative staging of gastric cancer was reported and also based on the prevalence of the disease assumed to be 6.3%.

Procedure of the study

All patients with inclusion criteria during the study period were taken up for study. An informed consent was obtained from the patient. Pre operative staging was done using CECT of abdomen and pelvis. All necessary pre operative investigations were done in patients selected for surgery. Post operative histopathological specimen which included gastrectomy specimen along with relevant lymph node stations; and biopsy/cytology specimen from suspicious lesion in adjacent organs like peritoneum, omentum, liver, serosal surface of bowel and pelvic deposits were obtained. Histopathological data included size, location, depth of invasion, lymph node status and biopsy proven distant metastasis.

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS-23 software. Sensitivity, specificity, positive predictive value and negative predictive value of preoperative Multi Detector CECT was estimated individually for location, depth of invasion, lymph node status and adjacent organ spread. Analysis was done using Chi square test. P<0.05 was considered as significant.

RESULTS

Distribution of age of the patients is depicted in table 1. Among the total cases, 28 (45.6%) cases were in the age group of 61-70 years. The mean age of the study group was 58.9 ±10.3 years. Males patients were 37 (60.7%) and females were 24 (39.3%) with a ratio of 1.54:1. All of the 61 cases had T4 disease. Pre-operative CECT evaluation showed 4.9% with N1 disease, 50.8% with N2 disease, 24.6% with N3 disease and 19.7% with N4 disease (Table 2).

CECT identified involvement of N1 lymph nodes in 0/7 patients, giving a sensitivity of 0. However, CT correctly identified 51/54 patients who did not have nodal involvement (specificity 94.44%). Operative assessment of N1 nodal status was superior to that of CECT, correctly identifying 1 of the 7 cases (sensitivity 14.29%), but with a specificity of 100% (54/54) identifying all 54 patients without N1 disease status.

Table-1: Distribution of age

| Age     | Frequency | Percent |
|---------|-----------|---------|
| ≤40     | 3         | 4.9     |
| 41-50   | 10        | 16.4    |
| 51-60   | 16        | 26.2    |
| 61-70   | 28        | 45.9    |
| ≥71     | 4         | 6.6     |
| Total   | 61        | 100.0   |

Table-2: CECT N staging

| N       | Present | Absent | Total |
|---------|---------|--------|-------|
| N1-2    | 1       | 0      | 1     |
| N3-6    | 10      | 61     | 71    |
| N15     | 15      | 46     | 61    |

Fisher’s Exact Test p value=0.386; Sensitivity=0, Specificity=94.44 +ve predictive value=0, -ve predictive value=87.93

Table-3: Contingency table for CT vs histopathology findings of N1 disease (1= present, 0= absent)

| N       | Present | Absent | Total |
|---------|---------|--------|-------|
| N1-2    | 1       | 0      | 1     |
| N3-6    | 10      | 61     | 71    |
| N15     | 15      | 46     | 61    |

Pearson Chi-Square p value=0.510 Sensitivity=55.55 Specificity=52.94 +ve predictive value=48.38, -ve predictive value=60

Table-4: Contingency table for CT vs histopathology findings of N2 disease (1= present, 0= absent)

| N       | Present | Absent | Total |
|---------|---------|--------|-------|
| N1-7    | 1       | 0      | 1     |
| N15     | 15      | 46     | 61    |

Pearson Chi-Square p value=0.383 Sensitivity=18.18 Specificity=94.44 +ve predictive value=26.66, -ve predictive value=60.86

Table-5: Contingency table for CT vs histopathology findings of N3 disease (1= present, 0= absent)
In other series, a smaller size was used than the 10 mm used in previous reports. This lower sensitivity and specificity may be due in part to the larger size of the lesions detected. The reason that sensitivity is lower in the current study compared to previous reports is likely due to the more aggressive nature of the lesions. CECT was reasonably specific, however, in the detection of N1 lymph nodes, with a sensitivity of 0% and a specificity of 99.16%. Similar to detection of pelvic deposits, intraoperative findings were superior to spiral CT, with a sensitivity of 94% and a specificity of 95%.

Preoperative knowledge of adjacent organ invasion and distant metastases is important in planning the operative procedure, allowing the surgeon to decide whether surgery is likely to be potentially curative or palliative in nature and also whether additional organs may need to be resected. Compared with previous reports of conventional CT, CECT scanning seems to be less sensitive but a more specific method for demonstrating invasion of both the small bowel and mesentery. CECT correctly identified only 2 of the 12 cases with liver metastases (sensitivity 62.5%). These metastases were identified at operation and confirmed histologically. However, there are other reports of CT correctly demonstrating 5/8 cases of liver metastases, which turned out to be inflammatory changes in 7 patients and 1 patient with a granulomatous lesion. CECT showed a sensitivity of 60% detecting only 3/5 mesenteric deposits, and an equal low specificity of 78.57% excluding as many as 44 patients without disease. Fifty percent of patients with splenic lesion were identified by CECT (sensitivity 50%) and excluded 53/57 patients without splenic invasion (specificity 92.97%). Of the total 11 patients who had omental involvement on histological examination, CECT detected only 3 cases (sensitivity 27.27%), but could exclude 44/50 patients without omental disease (specificity 88%). Surgical findings were superior to CT in detecting 7/11 patients with omental deposits (sensitivity 63.63%) and excluding all 50 patients without omental disease (specificity 100%). Similar to detection of pelvic deposits, intraoperative assessment for peritoneal deposits had 100% sensitivity and specificity, where as CECT had only 33.33% sensitivity but with a comparable specificity of 96.15%.

**DISCUSSION**

CECT is an inaccurate method of identifying lymph node metastases from gastric carcinoma. Our findings are consistent with those of other authors who have reported sensitivities ranging from 0 to 61%.10-12 Detection of involved N1 lymph nodes was particularly poor, with a sensitivity of 0%. CECT was reasonably specific, however, in the detection of uninvolved N1 nodes (specificity 94.44%). When paraaortic nodes were examined, the results were consistent with that of Andaker et al. with a sensitivity of 26% and specificity of 99%.13 The reason that sensitivity is so low and specificity so high is probably in part due to large cut-off size (10 mm) used to define “involved” nodes. In other series, a smaller size was used than the 10 mm used in our series and any lowering of the size criterion will obviously permit identification of a greater proportion of malignant nodes, thus increasing sensitivity but at a cost of lowered specificity. The ability of spiral CT to identify involvement of N2 lymph nodes was better than for N1 nodes, the sensitivity being 55.55% and specificity of 52.94%. Sendler et al have reported that CT is better at demonstrating involved N2 lymph nodes than involved N1 nodes for a number of reasons.14 Differentiation between involved nodes near the tumour and the primary tumour itself can be difficult. Nodes of normal size may contain metastatic deposits and enlarged N2 lymph nodes are more clearly distinguished from adjacent, highly enhancing vessels using the early phase of dynamic scanning.15

Preoperative knowledge of adjacent organ invasion and distant metastases is important in planning the operative procedure, allowing the surgeon to decide whether surgery is likely to be potentially curative or palliative in nature and also whether additional organs may need to be resected. Compared with previous reports of conventional CT, CECT scanning seems to be less sensitive but a more specific method for demonstrating invasion of both the small bowel and mesentery. CECT correctly identified only 2 of the 12 cases with liver metastases (sensitivity 62.66%) with invasion of the bowel and 3 of 5 cases (sensitivity 60%) with mesentry involvement. The findings were in agreement with, Andaker et al13, who found conventional CT was insensitive in evaluating the invasion to colon and mesocolon, demonstrating this in only three of 12 cases with histological evidence of invasion (sensitivity 25%). Operative assessment was superior to spiral CT, with a sensitivity of 94% and specificity of 95%.

The pancreas is an organ that has been notoriously difficult to assess both at laparotomy and on preoperative imaging. Previous reports have described sensitivities for assessment of pancreatic invasion varying from 27 to 95%.11 In our hands, CECT scored a superior result at demonstrating invasion of the pancreas. Of the 7 patients with pancreatic invasion, 5 were correctly identified on CECT, whereas surgical assessment correctly identified all 7 patients. Both CECT and surgical assessment were highly specific, but operative assessment was better. CT visualization of the pancreas can be difficult in patients with gastric cancer as they are frequently malnourished and visceral fat between the organs is depleted.14 Although a clear fat plane between stomach and pancreas can reliably be taken to indicate non-invasion, the absence of a fat plane between these organs does not necessarily imply invasion. In similar fashion, irregularity of the interface does not necessarily represent invasion.15 Differentiation between inflammatory adhesion, oedema and true invasion, both on CECT and at operation, can be extremely difficult.11 In this study, both false-positive operative assessments were found to represent inflammatory reaction on subsequent histological examination. CECT has the potential to demonstrate both liver and peritoneal metastases because it can be used to examine the entire abdominal cavity, unlike EUS.16 CECT correctly demonstrated 5/8 cases with liver metastases (sensitivity 62.5%). These metastases were identified at operation and confirmed histologically. It is important to remember that for assessment of hepatic metastases, the CT findings were compared against the operative findings confirmed histologically. However, there

**Table-6: Contingency table for CT vs histopathology findings of N3b disease (1= present, 0= absent)**

| hi n &gt;15nos | Total |
|---------------|-------|
| Ct n &gt;15nos | 1     | 0     |
| 1.0           | 3     | 9     | 12 |
| 0             | 2     | 47    | 49 |
| Total         | 5     | 56    | 61 |

Fisher’s Exact Test p value=0.036  Sensitivity=60, Specificity=83.93, +ve predictive value=25, -ve predictive value=95.91
may have been other small intrahepatic metastases which were not identified at operative assessment. This indicates that there could have been a number of false negative cases that were not identified. Ideally intra-operative ultrasound has been used as a gold standard for detecting hepatic metastases. It has been reported previously that CT is limited in the demonstration of peritoneal metastases, being able to identify peritoneal disease only in the presence of ascites. Whilst CT can identify obvious gross peritoneal disease, with large omental cake-like deposits, it is poor at visualizing small individual peritoneal nodules due to its limits of resolution. In our study, CECT correctly demonstrated 3 of the 9 cases only (sensitivity 33.33%) in which peritoneal metastases were found at sites separate from the main tumour. It comes as no surprise that CT is poor at predicting the T stage of disease in patients with gastric cancer. Although CT was able to demonstrate the stomach wall as a three layer structure corresponding to the mucosal, submucosal and muscular layers, the outer musculo-serosal layer (thin in places) cannot always be visualized.

 Destruction of this layered structure together with gastric wall thickening may be seen on scanning, although correct assignment to a T stage (T1–T3) may be extremely difficult or even impossible. In our study, all of our patients presented late with lesions already in T4 stage. This, together with limited ability of CT to identify lymph node metastases, means that this modality is of limited value as a predictor of overall stage of gastric cancer. From this study, however, it is clear that due to high specificity, when CT demonstrates an “uninvolved” node, it is very likely not to contain tumour on histological examination. Of most concern from recent reports is the suggestion that CT can over-stage patients, by falsely predicting the presence of irresectable disease which was not confirmed at subsequent laparotomy. In this series, CECT was found to be highly specific, which meant that there was a low incidence of false positive findings.

 For surgeons who practise radical “D2” resections, the most important information required is whether distant metastatic (M1) disease is present, which implies that a potentially curative resection cannot be performed.

**CONCLUSION**

CECT remains poor at identifying lymph node metastases and in determining depth of tumour invasion (T1–T3), but was highly specific which meant that a positive spiral CT result could be relied upon. It was also of value in identifying invasion of adjacent organs and some cases with distant metastatic (M1) disease. At present, we perform CECT routinely on all patients and adopt a selective staging laparoscopy/ mini laprotyomy policy in those patients in whom the status of the peritoneal cavity and liver remains in doubt.

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