Utility of PET CT in prediction of response to neo-adjuvant therapy in patients with gastric carcinoma

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### Aims and objectives

Gastric carcinoma is the fourth most common cancer and the second most fatal carcinoma worldwide \(^1\). Approximately 95% of gastric carcinoma is adenocarcinoma \(^1\). According to Lauren's classification gastric carcinoma is classified in two pathological subtypes; intestinal and diffuse. It is observed that these two subtypes have different prognosis and biological behavior. Intestinal variety is more common in countries with higher incidence of gastric carcinoma like the far eastern countries and the South American countries. It is often seen in older age group, predominant in males and is associated with environmental risk factors. However, diffuse variety is relatively more common in countries with lower incidence of gastric carcinoma such as the USA and other western European countries, has a poorer prognosis and is more common in younger individuals, shows no sex preponderance and is not as strongly associated with environmental risk factors. The incidence of diffuse subtype is gradually increasing in all populations.

18 FDG PET has been evolved as cancer imaging modality depending on the fact that tumor cells show a high glycolysis and glucose uptake rate \(^2\). In tumor cells usually there is an overexpression of glucose transporter-1 (GLUT-1) which is responsible for 18 Fluoro-deoxyglucose uptake \(^2\). It has been reported that diffuse subtype has a lower density of Glut1 compared to intestinal therefore showing significantly decreased FDG activity compared to intestinal variety \(^3\). 18 F FDG PET CT has been found to be useful in management of patients with gastric carcinoma with sensitivity and specificity of 50% - 93%, 98% respectively in primary tumor detection, 34% - 41%, 88% - 100% respectively in lymph node metastasis detection, and 42.9% - 95.8 %, 59.7% - 100% respectively in detection of recurrence after curative surgery \(^4, 5, 6, 7, 8, 9, 10, 11\). However, the utility of PET CT in predicting response to neo-adjuvant therapy (NT) in these two different subtypes is not clearly known.

Our aim was to investigate the role of PET CT in assessment of response of the primary tumor to NT in patients with intestinal and diffuse varieties. We hypothesized that PET CT would be more predictive in the intestinal subtype than the diffuse one depending on the fact that diffuse subtype is less FDG avid than intestinal one.
Methods and materials

Subjects:

From January 2006 to October 2014, 128 consecutive patients presented to our institution with gastric carcinoma who had PET CT were included in the study. Out of these patients, only those with pre and post neo-adjuvant treatment (NT) PET CT followed by curative gastric resection with lymphadenectomy were included in the study. 17 patients remained in the study.

Neo-adjuvant therapy:

All study group received NT; 12 of them received chemo-radiation therapy and 5 received chemotherapy only.

PET CT:

Patients fasted for at least 6 hours before PET CT. Blood glucose was measured 1 hour before injection of FDG. If the blood glucose level exceeded 150 mg/dL (8.3 mmol/L), the examination was deferred. Approximately 1 hour before imaging, patients received an injection of radioactively labeled FDG (mean, 13 mCi; range, 8.1 - 19.6 mCi). All scans were obtained on an integrated PET/CT scanner.

Unenhanced CT from the base of the skull to the upper thigh was performed for attenuation correction and diagnosis (300 mA; tube rotation time, 0.5 second; 120 kVp; table speed, 13.5 mm/rotation; beam collimation, 8 × 1.25 mm). Axial CT images were reconstructed with a soft reconstruction kernel with a slice thickness of 3.75 mm and an interval of 3.27 mm to match the PET images.

Pathological assessment:

Pathological reports were retrospectively reviewed to classify patients according to the pathological subtype whether diffuse or intestinal, assess residual tumor mass reported in percentage, and correlate it with degree of change in SUV-max pre and post NT. According to the residual tumor mass patients were classified in three groups responders (viable cells < 10%), partial responders (viable cells from 10 to 80%), and non-responders (viable cells > 80%).

Statistical analysis:
The population was divided in two groups according to the pathological subtypes (Diffuse/ intestinal). Binary classification test was used to calculate sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of PET CT in each pathological subtype.
Images for this section:

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<table>
<thead>
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<tbody>
<tr>
<td>Male : Female</td>
<td>15:2</td>
</tr>
<tr>
<td>Mean age</td>
<td>62</td>
</tr>
<tr>
<td>Intestinal : Diffuse</td>
<td>11 : 6</td>
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Patients’ characteristics

Fig. 1

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Results

Out of the study population, 4 showed good response to therapy (<10% viable cells), 8 showed 30-80% residual disease and 5 had no response to treatment. The overall Sensitivity, Specificity, PPV, NPV was 70%, 75%, 87.5% and 50%.

Diffuse / Signet cell carcinoma:

3 (50%) tumors showed no uptake in the primary at baseline but showed significant residual disease. 2 showed significant residual disease despite complete metabolic response. 1 showed complete pathological and metabolic response.

Intestinal subtype:

2 of the 3 with complete pathological response showed associated complete metabolic responses but one patient showed only 40% reduction in SUV-max. 1 showed significant residual disease despite metabolic response. 7 with significant residual disease showed residual metabolic activity (37%-82% of baseline). Sensitivity, Specificity, PPV, NPV of 88%, 67%, 88% and 67% respectively.
Images for this section:

Fig. 2

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54 years old male patient having intestinal subtype who had complete pathological (viable cells <10%) and metabolic response.

Fig. 3

50 years old male patient with intestinal subtype showed complete metabolic response despite that there were >80 % viable cells on pathological assessment.
Fig. 4

82 years old male patient with diffuse subtype showed complete metabolic response with 60% residual viable cells on pathological assessment.
Conclusion

Discussion:

Gastric carcinoma is a heterogeneous group of malignancies with different histologic, genetic and molecular profile which dictates biologic behavior. There are significant differences in the two commonly reported subtypes - the intestinal variety and the diffuse variety which predominantly is signet cell carcinoma.

In our study we found that PET-CT is of little value in assessment of response to NT in diffuse subtype, and it may be useful in intestinal subtype. In diffuse subtype, there was nearly no correlation between the metabolic response and actual response to NT. As shown in the results only one patient out of 3 has complete metabolic and pathological response while the other two showed complete metabolic response but had significant residual tumor on pathological assessment of the surgically explanted specimen.

In our small cohort, we found a sensitivity and specificity of PET-CT is 88%, 67% for the intestinal subtype. There are not enough studies which have looked at the utility of PET CT in this scenario. Two studies (Hyun Woo Chung et al 2010 and Giganti 2014) conclude that PET CT had low predictive value in chemotherapy response assessment.

There are a few limitations to our study. As we decided to study only the primary tumor, our population size was small due to the tight selection criteria. Our study was retrospective in nature and this did not allow us to accurately confirm the subtype which was obtained from pathologic reports. But the results of our study demonstrate again the differing metabolic profiles of these two subtypes. Further studies which include and report proper classification of the subtypes may offer further clarification of this. This finding may have important implications in the appropriate use of PET CT based on histological subtype.

Conclusion:

PET CT should not be used in assessment of response to neo-adjuvant therapy in patients with diffuse subtype. It may be useful in predicting response in the intestinal subtype.
References


