A Prospective Study of Early Postoperative Course and Pathological Outcome of Modified D2 Gastrectomy-A Single Institute Experience

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Abstract: Survival after curative surgery in advanced carcinoma is not so promising. Even after use of chemotherapy, radiation therapy the goals are not met. So it is the tumour biology which is important and the future would be probably biological therapy. Considering western data on stomach cancer molecular profile Her2neu would be promising marker for target therapy to be considered. But the fact has not been adequately tested in Indian scenario and the present study does not support routine testing of Her2neu in cases of stomach cancer considering financial aspect of Indian patient population as well as rate of its positivity in various samples of gastric cancer tissue. However, practice of individualized medicine allows it can be done in metastatic set up. As Her2neu positivity signals aggressive disease it is likely that rate of its positivity should be more in metastatic group rather than the operable gastric cancer group. Hence more studies regarding its positivity and other markers should be done in metastatic gastric cancer in Indian population particularly.

Key Words: early postoperative course, pathological outcome, modified D2 Gastrectomy

I. Introduction

Stomach cancer is one of the important leading causes of cancer related death in worldwide. According to epidemiological study, it ranks fourth after lung, breast and colorectal cancer. Annually, it was diagnosed with 9,89,600 new cases and 7,38,000 deaths (10% of all cancer death) in worldwide. But, in India, it was diagnosed with 35,675 new cases irrespective of gender. The overall prognosis is not very favorable. However, surgery in the form of gastrectomy is the only treatment modality for a chance of long term survival as well as hope for cure. Thus, prospective study with gastrectomy is necessary for optimum extent of surgery. Surgery in the form of gastric resection was first carried out by Theodre Billroth in Vienna in 1881. Till now, gastric resections remain standard treatment for carcinoma stomach in the world. The overall survival rate of stomach cancer patients using gastrectomy in Japan (50-60%) was higher compared with rest of the world (10-30%). This was mainly due to two factors, one active screening leading to early diagnosis and the other one extensive lymphadenectomy along with gastric resection. As per the Japanese study, if lymph node is not dissected then 5yr overall survival of the patients is about 20.3%. Survival of patients with D1 dissection is 41% and with D2 dissection is 50-62%. Thus, Japanese literature suggested D2 lymphadenectomy for stomach cancer. However, D2 lymphadenectomy for stomach cancer did not produce the same result in Europe. It is suggested that high postoperative morbidity and mortality and associated with extensive lymph nodal dissection. In addition, Dutch trial after 15yr follow up confirmed that D2 gastrectomy has got survival advantages with low cancer specific death rate and low loco regional recurrence compared to D1 gastrectomy. But the question is also remained about high post operative morbidity and mortality. The subgroup analysis showed that the excess mortality was due to resection of pancreatic tail and splenectomy associated with D2 gastrectomy. On the other hand, the British study confirmed that modified D2 gastrectomy preserving spleen and pancreas is feasible and it carries much lower mortality. D2 gastrectomy is also considered to be choice of procedure so far as pathological staging of the disease is concerned. This staging data is very important for planning of adjuvant treatment as cancer management has become multimodal nowadays. The average node retrieval is 15 in D1 gastrectomy, 27 in D2 gastrectomy and 43 in D3 gastrectomy (wegner et al.) from autopsy findings. So NCCN...
2010 has laid down the principle of examining at least 16 lymph nodes for proper pathological staging of stomach cancer. Thus, lighting on modified D2 gastrectomy is necessary for improvement of better survival of gastric patients.

In spite of standardization of surgical method, multimodal management stage wise 5 year survival for advanced gastric cancer is very poor. However, mass endoscopy for early diagnosis is not possible in all community. Apart from this mass endoscopy, TOGA trial Her2-neu positivity were used as marker for cancer in esophagus and cancer in GEJ. Thus, analysis of molecular profile of gastric cancer leads to early diagnosis and management of advanced gastric cancer as well as in metastatic setup.

II. Material and Methods

Demography of patients:
As per the inclusion and exclusion criteria a total 40 number of gastric cancer patients who were underwent gastrectomy were considered in this study. The study was conducted at Chittaranjan National Cancer Institute (CNCI) Kolkata, India from 1st May 2014 – 30th April 2016. Among these cases, biopsy proven and operable cases of adenocarcinoma of stomach enrolled in our institute in the aforementioned period are considered for the study.

Inclusion criteria- All cases of histologically proven Gastric Adenocarcinoma which were operable as per CT scan abdomen findings.

Exclusion criteria-
1. Patients with metastatic disease, poor surgical candidates and locally advanced gastric cancer patients requiring neoadjuvant therapy.
2. Patients with peritoneal metastasis on laparoscopic staging.

Diagnosis and surgical procedure
All the cases of biopsy proven adenocarcinoma of stomach will undergo detailed clinical examination, Chest x-ray, contrast enhanced CT scan of abdomen and pelvis. Only operable and fit patient were planned for surgery. Before surgery diagnostic laparoscopies was carried out and proceed in those cases where there was no gross peritoneal disease. The surgery was carried out as per standard guideline. The modifications done were as follows:

1. Modification of extent of lymph node dissection was as per given below:
   - For distal gastrectomy-1,3, 4s, 4d, 5, 6, 7, 8a, 9, 12a irrespective of T stage
   - For total gastrectomy-1, 7, 8a, 9, 11p, 12a (avoiding 11d & 10 group of lymph node)

As recommended by Japanese cancer association
2. Resection of pancreatic tail and spleen were avoided until unless they are directly involved by tumors.
3. Lymph node dissections at 10 and 11d were done in proximal cancer if they were visibly enlarged
4. Post-operative period:
   - Patients were kept in High Dependency Unit (HDU) for at least 24 hrs with routine monitoring.
   - Feeding jejunostomy was started after 48 hrs.
   - Encouraged early mobilization and removal of drain when 24 hr collection below 100ml
   - Suture removed on 10th to 12th post operative day,
   - Feeding jejunostomy (FJ) removed after 3 to 4 weeks.

Surgical findings were as follows:-
1. Intra-operative parameters were as follows:-
   a) Operative time, b) Intra-operative bloodloss, c) Inadvertent splenectomy, d) Bowel and pancreatic tail injury, e) Major vascular injury, f) Peri-operative blood transfusion, g) Duration of surgery
2. Post-operative parameters were as follows:-
   a) Post-operative ICU stay, b) Post-operative bleeding, c) Post-operative leaks, d) Post-operative infection, e) Duration of hospital stay, f) Drain output
3. Pathological outcome:
   a) Histopathological variety of the tumour, b) Numbers of lymph node isolated by standard grossing method, c) Levels of tumour infiltration (i.e. T stage of tumour), d) Number of positive lymph nodes, e) Her-2 neu positivity of the tumour, f) Grade of the tumour.

Statistical analysis
Statistical Analysis was performed with help of Epi Info (TM) 7.2.2.2. EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC).
Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations (s.d.). Test of proportion was used to find the Standard Normal Deviate (Z) to compare the difference proportions and chi-square ($\chi^2$) test was performed to find the associations. Corrected chi-square ($\chi^2$) test was used where any one of the cell frequencies was less than zero. t-test was used to compare the means. Pearson correlation co-efficient (r) was calculated to find the correlation between two variables. Odds Ratio (OR) with 95% confidence interval (CI) had been calculated to find the risk factors. Fisher Exact test was used where one of cell frequency was 0. p<0.05 was taken to be statistically significant.

### Table 1: Demographic parameters of patients.

<table>
<thead>
<tr>
<th>Demographic parameters</th>
<th>Number</th>
<th>%</th>
<th>Test Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age Group (in years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-34</td>
<td>2</td>
<td>50.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-44</td>
<td>7</td>
<td>17.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-54</td>
<td>20</td>
<td>50.0</td>
<td>Z=3.26</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>≥55</td>
<td>11</td>
<td>27.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gender (Male: Female = 3:1)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>30</td>
<td>75.0</td>
<td>Z=7.07</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>25.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23.0-24.9 (Normal weight)</td>
<td>10</td>
<td>25.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25.0-29.9 (Over weight)</td>
<td>22</td>
<td>55.0</td>
<td>Z=7.07</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>≥30.0 (Obese)</td>
<td>8</td>
<td>20.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Presenting symptoms of the patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOO</td>
<td>11</td>
<td>40.0</td>
<td>Z=1.86</td>
<td>0.0629 NS</td>
</tr>
<tr>
<td>Malaena</td>
<td>4</td>
<td>27.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>4</td>
<td>10.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysphagia</td>
<td>3</td>
<td>10.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>1</td>
<td>7.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>1</td>
<td>2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Addiction of the patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>11</td>
<td>27.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drinking of Alcohol</td>
<td>5</td>
<td>12.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chewing tobacco</td>
<td>3</td>
<td>7.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>21</td>
<td>52.5</td>
<td>Z=3.60</td>
<td>&lt;0.001*</td>
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<tr>
<td><strong>Co-morbidities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>4</td>
<td>10.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>4</td>
<td>10.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes with Hypertension</td>
<td>2</td>
<td>5.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>1</td>
<td>2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>29</td>
<td>72.5</td>
<td>Z=6.36</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

The mean age (mean ± s.d.) of the patients was 49.10±8.32 years with range 28-66 years and the median age was 48.5 years. Test of proportion showed that the proportion of the patients in the age group 45-54 years (50.0%) were significantly higher than other age group (Z= 3.26; p<0.001). Only 5.0% were with age between 25-34 years and 27.5% of the patients were with age ≥55 years. Thus in this study the patients with age between were in higher risk of having gastric cancer.

Proportion of males (75.0%) was significantly higher than that of females (25.0%) (Z=7.07; p<0.0001). The sex ratio was found as Male: Female = 3:1. Thus in this study males were in higher risk of having gastric cancer than females. Chi-square ($\chi^2$) test showed that there was no significant association between age groups and gender of the patients (p=0.34). The mean age (mean± s.d.) of males was 50.33±8.36 years with range 28-66 years and the median age was 50.5 years. The mean age (mean± s.d.) of females was 45.40±7.41 years with range 32-60 years and the median age was 45.0 years. Though the mean age of males was higher than that of females, t-test showed that there was no significant difference in mean ages of males and females (t38=1.65;p=0.91). Thus in this study females were in higher risk of having gastric cancer at a younger age than males.

The mean BMI (mean ± s.d.) of the patients was 27.10±2.88 kg/m² with range 22.0- 34.0 kg/m² and the median was 27.0 kg/m². Most of the patients were overweight and obese (75.0%) followed by normal weight (25.0%) (Z=7.07;p<0.001). 20.0% of the patients were obese. Most of the patients were having dyspepsia (40.0%) which was not significantly higher (Z=1.86;p=0.0629) followed by GOO (27.5%). Only 2.5% had bleeding and another 2.5% had loss of appetite. 52.5% of the patients had no addiction which was higher than addiction (47.5%) but it was not significant (Z=0.71;p=0.47). Out of the all addictions smoking (27.5%) was more prevalent than drinking of alcohol (12.5%) and chewing tobacco (7.5%). Thus tobacco and alcohol had
positive affect on gastric cancer. Most of the patients had no co-morbidity (72.5%) which was significantly higher than having co-morbidity (27.5%) (Z=6.36; p<0.0001). Out of the all co-morbidities diabetes and hypertension (10.0%) were more prevalent. Only 5.0% and 2.5% had diabetes with hypertension and hypothyroidism (2.5%) respectively. None of the patients had previous history of hospitalization.

The mean intra-operative blood loss (mean ± s.d.) of the patients was 280.25±119.91 ml with range 120-620 ml and the median was 227.50 ml. The mean duration of surgery (mean ± s.d.) of the patients was 207.07±41.09 minutes with range 145-300 minutes and the median was 195 minutes. The mean post operative ileus (mean ± s.d.) of the patients was 5.10±1.19 days with range 3-8 days and the median was 5 days. 35.0% of the patients had post operative ileus > 5 days. 55.0% of the patients had duration of drainage > 5 days (Z=1.41; p =0.15). Only 10.0% of the patients had bile leak out of which 7.5% had bile leak and 2.5% had mild bile leak. 35.0% of the patients had post-operative infection. The mean duration of ICU stay (mean ± s.d.) of the patients was 3.70±2.58 days with range 2-15 days and the median was 3 days. Only 2(5.0%) of the patients were having Her2neu positivity. There was no post-operative mortality.

There were 2 Her2-neu positive cases and all the positive cases were in Proximal. Test of proportion showed that proportion of Her2 neu positive cases were significantly higher in Proximal (40.0%) than that of Distal (0.0%) (Z=7.07 p<0.0001).

### Table 2: Distribution of different post operative finding parameters

<table>
<thead>
<tr>
<th>Demographic parameters</th>
<th>Number</th>
<th>%</th>
<th>Test Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-operative ileus (in days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5</td>
<td>14</td>
<td>35.0%</td>
<td>Z=4.24</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>≤5</td>
<td>26</td>
<td>65.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of drainage (in days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5</td>
<td>22</td>
<td>55.0%</td>
<td>Z=1.41</td>
<td>0.15</td>
</tr>
<tr>
<td>≤5</td>
<td>18</td>
<td>45.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile leak and its nature</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile leak</td>
<td>3</td>
<td>7.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild bile leak</td>
<td>1</td>
<td>2.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>36</td>
<td>90.0%</td>
<td>Z=11.59</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Post-operative Infection</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14</td>
<td>35.0%</td>
<td>Z=4.24</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>No</td>
<td>26</td>
<td>65.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest infection</td>
<td>4</td>
<td>10.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>2</td>
<td>5.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild chest infection</td>
<td>2</td>
<td>5.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>1</td>
<td>2.5%</td>
<td></td>
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<tr>
<td>Thrombophlebitis</td>
<td>4</td>
<td>10.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>27</td>
<td>67.5%</td>
<td>Z=8.40</td>
<td>&lt;0.001*</td>
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</table>

### Table 3: Distribution of different histological parameters after surgery

<table>
<thead>
<tr>
<th>Histological parameters</th>
<th>Number</th>
<th>%</th>
<th>Test Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of tumour</td>
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<td></td>
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<tr>
<td>Distal</td>
<td>35</td>
<td>87.5%</td>
<td>Z=10.60</td>
<td>&lt;0.001*</td>
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<tr>
<td>Proximal</td>
<td>5</td>
<td>12.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Adenocarcinoma</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>8</td>
<td>20.0%</td>
<td>Z=8.48</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Intestinal</td>
<td>32</td>
<td>80.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade of Tumour</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>11</td>
<td>27.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>28</td>
<td>70.0%</td>
<td>Z=5.65</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Low</td>
<td>1</td>
<td>2.5%</td>
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<td></td>
</tr>
<tr>
<td>Pathological stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA</td>
<td>1</td>
<td>2.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IB</td>
<td>3</td>
<td>7.5%</td>
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A Prospective Study of Early Postoperative Course and Pathological Outcome of Modified D2...

<table>
<thead>
<tr>
<th>Status of LVI/PNI</th>
<th>Duration of drainage&gt;5 days (n=22)</th>
<th>Duration of drainage≤5 days (n=18)</th>
<th>Test statistic</th>
<th>p-value</th>
<th>Odds Ratio with 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVI and PNI+</td>
<td>3.18±0.58</td>
<td>3.70±0.60</td>
<td>t=2.77</td>
<td>0.0086*</td>
<td>NA</td>
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<tr>
<td>LVI+</td>
<td>10.50±1.92</td>
<td>12.00±2.53</td>
<td>t=2.13</td>
<td>0.0397*</td>
<td>NA</td>
</tr>
<tr>
<td>PNI+</td>
<td>26.68±3.46</td>
<td>27.61±1.94</td>
<td>t=1.01</td>
<td>0.31</td>
<td>NA</td>
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<tr>
<td>Negative</td>
<td>48.36±1.67</td>
<td>50.00±6.48</td>
<td>t=0.61</td>
<td>0.54</td>
<td>NA</td>
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</table>

### Smoking

<table>
<thead>
<tr>
<th>Smoking</th>
<th>Duration of drainage&gt;5 days (n=22)</th>
<th>Duration of drainage≤5 days (n=18)</th>
<th>Test statistic</th>
<th>p-value</th>
<th>Odds Ratio with 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>5(22.7%)</td>
<td>6 (33.3%)</td>
<td>χ²=0.55</td>
<td>0.45</td>
<td>[OR-0.58(0.14,2.38)]</td>
</tr>
<tr>
<td>No</td>
<td>17(77.3%)</td>
<td>12(66.7%)</td>
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</table>

### Stage of the disease

<table>
<thead>
<tr>
<th>Stage of the disease</th>
<th>Duration of drainage&gt;5 days (n=22)</th>
<th>Duration of drainage≤5 days (n=18)</th>
<th>Test statistic</th>
<th>p-value</th>
<th>Odds Ratio with 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>0(0.0%)</td>
<td>1(5.6%)</td>
<td>χ²=16.12</td>
<td>0.013*</td>
<td>NA</td>
</tr>
<tr>
<td>IB</td>
<td>1(4.5%)</td>
<td>2(11.1%)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>IIA</td>
<td>1(4.5%)</td>
<td>5(27.8%)</td>
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<tr>
<td>IIB</td>
<td>5(22.7%)</td>
<td>8(44.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIIA</td>
<td>4(18.2%)</td>
<td>2(11.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIIB</td>
<td>6(27.3%)</td>
<td>0(0.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIIC</td>
<td>5(22.7%)</td>
<td>0(0.0%)</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

### Presence of diabetes

<table>
<thead>
<tr>
<th>Presence of diabetes</th>
<th>Duration of drainage&gt;5 days (n=22)</th>
<th>Duration of drainage≤5 days (n=18)</th>
<th>Test statistic</th>
<th>p-value</th>
<th>Odds Ratio with 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>4(18.2%)</td>
<td>2(11.1%)</td>
<td>χ²=0.38</td>
<td>0.53</td>
<td>[OR-1.77(0.28, 11.03)]</td>
</tr>
<tr>
<td>No</td>
<td>18(81.8%)</td>
<td>16(88.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Site of the disease

<table>
<thead>
<tr>
<th>Site of the disease</th>
<th>Duration of drainage&gt;5 days (n=22)</th>
<th>Duration of drainage≤5 days (n=18)</th>
<th>Test statistic</th>
<th>p-value</th>
<th>Odds Ratio with 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal</td>
<td>17(77.3%)</td>
<td>18(100.0%)</td>
<td>Fisher Exact Test</td>
<td>0.04*</td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>5(22.7%)</td>
<td>0(0.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Duration of ileus:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Duration of ileus&gt;5 days (n=14)</th>
<th>Duration of ileus≤5 days (n=26)</th>
<th>Test statistic</th>
<th>p-value</th>
<th>Odds Ratio with 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum albumin</td>
<td>3.10±0.59</td>
<td>3.38±0.60</td>
<td>t=1.30</td>
<td>0.20</td>
<td>NA</td>
</tr>
<tr>
<td>Level of Pre-op Hb</td>
<td>10.07±1.71</td>
<td>5.81±2.41</td>
<td>t=5.85</td>
<td>&lt;0.0001*</td>
<td>NA</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.71±3.53</td>
<td>27.30±2.52</td>
<td>t=0.61</td>
<td>0.54</td>
<td>NA</td>
</tr>
<tr>
<td>Age (years)</td>
<td>50.00±10.42</td>
<td>48.61±7.14</td>
<td>t=0.49</td>
<td>0.62</td>
<td>NA</td>
</tr>
<tr>
<td>Smoking</td>
<td>2(14.3%)</td>
<td>9(34.6%)</td>
<td></td>
<td>0.16</td>
<td>[OR-0.31(0.05, 1.72)]</td>
</tr>
</tbody>
</table>

**Post-operative morbidities:**

**Duration of drainage:**

**Table-4:** Comparison of duration of drainage with different parameters

**Table-5:** Comparison of duration of ileus with different parameters
A Prospective Study of Early Postoperative Course and Pathological Outcome of Modified D2....

<table>
<thead>
<tr>
<th>No</th>
<th>12(85.7%)</th>
<th>17(65.4%)</th>
</tr>
</thead>
</table>

### Table 6: Comparison of Wound Infection with different parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Wound Infection (n=26)</th>
<th>No Wound Infection (n=14)</th>
<th>Test-statistic</th>
<th>p-value</th>
<th>Odds Ratio with 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum albumin (Mean±s.d.)</td>
<td>3.25±0.54</td>
<td>3.50±0.68</td>
<td>t=1.27</td>
<td>0.21</td>
<td>NA</td>
</tr>
<tr>
<td>Level of Pre-op Hb (Mean±s.d.)</td>
<td>10.28±2.44</td>
<td>11.65±2.13</td>
<td>t=1.76</td>
<td>0.0865</td>
<td>NA</td>
</tr>
<tr>
<td>BMI (kg/m²) (Mean±s.d.)</td>
<td>27.57±3.58</td>
<td>26.48±2.47</td>
<td>t=1.01</td>
<td>0.31</td>
<td>NA</td>
</tr>
<tr>
<td>Age (years) (Mean±s.d.)</td>
<td>49.42±8.89</td>
<td>48.92±8.18</td>
<td>t=0.17</td>
<td>0.86</td>
<td>NA</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5(35.7%)</td>
<td>6(42.9%)</td>
<td>$\chi^2 =0.72$</td>
<td>0.39</td>
<td>[OR=1.85(0.44, 7.69)]</td>
</tr>
<tr>
<td>No</td>
<td>9(64.3%)</td>
<td>20(57.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Wound Infection:

### Table 7: Comparison of Chest Infection with different parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Chest Infection (n=6)</th>
<th>No Chest Infection (n=34)</th>
<th>Test-statistic</th>
<th>p-value</th>
<th>Odds Ratio with 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum albumin (Mean±s.d.)</td>
<td>3.18±0.41</td>
<td>3.54±0.66</td>
<td>t=1.28</td>
<td>0.20</td>
<td>NA</td>
</tr>
<tr>
<td>Level of Pre-op Hb (Mean±s.d.)</td>
<td>11.21±1.63</td>
<td>11.16±2.43</td>
<td>t=0.05</td>
<td>0.96</td>
<td>NA</td>
</tr>
<tr>
<td>BMI (kg/m²) (Mean±s.d.)</td>
<td>26.33±3.14</td>
<td>27.23±2.87</td>
<td>t=0.69</td>
<td>0.49</td>
<td>NA</td>
</tr>
<tr>
<td>Age (years) (Mean±s.d.)</td>
<td>51.00±13.71</td>
<td>48.76±7.26</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3(50.0%)</td>
<td>8(23.5%)</td>
<td>$\chi^2 =1.79$</td>
<td>0.18</td>
<td>[OR=3.25(0.54, 19.38)]</td>
</tr>
<tr>
<td>No</td>
<td>3(50.0%)</td>
<td>26(76.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Chest Infection:
A Prospective Study of Early Postoperative Course and Pathological Outcome of Modified D2....

<table>
<thead>
<tr>
<th>Stage of the disease</th>
<th>Lymphnodes retrieved</th>
<th>Test Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage-I (n=4)</td>
<td>15.75±2.50</td>
<td>t=6.38</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Stage-II (n=19)</td>
<td>19.73±2.82</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage-III (n=17)</td>
<td>29.58±6.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site of the disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal (n=35)</td>
<td>22.00±5.79</td>
<td>t=4.48</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Proximal (n=5)</td>
<td>34.20±4.76</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### IV. Discussion

While the incidence of gastric cancer has declined all over the world including India it remains the second leading cause of cancer mortality worldwide.\(^8\) In India the stomach cancer was estimated to be fifth leading cancer site in males and seventh in females.\(^9\) Gastric cancer is an aggressive disease. While loco regional disease has better prognosis the overall five year survival for resectable gastric cancer is usually 20-30%\(^10\), \(^11\). Still then radical surgery is the cornerstone of treatment and offers only chance of cure. But the opinion regarding the optimum resection for patients with gastric cancer remains divided. The impressive outcomes after D2 gastrectomy as per Japanese literature have not been reproduced in randomized control trials in Europe. But with the results of 15 yr follow up of Dutch trial which showed that D2 gastrectomy has survival advantages. Some authors have proposed that D2 gastrectomy improves survival even in node negative early gastric cancer probably due to resection of micro metastatic nodes.\(^16\) Despite these favorable statements D2 gastrectomy is criticized for its significant postoperative morbidity and mortality. As per Cuschieri et al. majority of complications arise due to resections of pancreas and spleen. Hence it was thought that modified D2 gastrectomy sparing spleen and pancreas would be a better option to avoid the excessive postop morbidity and mortality.

The first outcomes after modified D2 gastrectomy for gastric cancer were originally published in Britain by Sue-Ling etal1993 and subsequently by Griffith et al. in 1995. Qin et al. in 2001 mentioned in Chinese literature mentioned that a pancreas, spleen preserving gastrectomy is feasible. It improves postoperative complications compared to gastrectomy where they are resected. The 5 yr survival, 10 yr survival rates are significantly higher with PSP then classic D2 gastrectomy. Maruyama et al. in 1995 has explained the technique of pancreas preserving total gastrectomy. According to him the 5yr overall survival rate for those with stageII was 70.5% and for stage III it is 54.1% which was significantly higher than the pancreas resection group.\(^15\) Galizia et al. in 2015 compared standard D2 gastrectomy with modified D2 gastrectomy. He found that modified D2 has less postop death and morbidity. The 5 yr disease free survival or the site of tumour relapse was not different. The incidence of involvement of nodal station 10,11d and 12 a was 5% and the 5 yr disease free survival was zero when they are involved. So the benefit of removing them when they are involved is almost nil excepting surgical staging. Hence he proposed a form of modified D2 gastrectomy which explains surgery without dissection of 11d,10 nodal stations which we have done here excepting where they are grossly involved or there is direct spread of tumour to spleen or pancreatic tail.

So we conducted a study in our institute on patients admitted,investigated and operated at our institute. Most of them are of advanced stage so D1 gastrectomy is not an option for them. Hence in the study we went for modified D2 gastrectomy during the aforementioned period and prepared the above mentioned database. Total no. of 40 patients randomly collected who met the inclusion and exclusion criteria and are operable candidates. The mean age group was 49.10, with lowest one is 28 and highest one is 66. The most common age group affected was 45-54. This was quite different from observation made by Degiuli et al., 2014 and H Danielson et al.
who have majority of patients in the age group of more than 60 yrs. The proportion of females is considerably low in comparison to males. Themale: female ratio is 3:1 which is very much same as that by W.G Lewis et al. and P.Edwards et al. 2004. The mean age in the female group was 45.40 and male was 50.33 explaining slightly higher age incidence in male group. But the age difference was not significant. But a trend can be seen that in early ages females suffer more from gastric cancer and latter stages usually after 54 males suffer more from the disease. It is not clear whether male hormone is protective or female hormone is the causative agent for that. Interestingly we have found that high grade variety of the cancer is mostly found in these lower age group females and whether female hormone has got something to do with it is to be seen. So far BMI is concerned hardly any patient is underweight. Majority have a BMI above 25. This indicates significant weight loss in ca stomach is an accompaniment of advanced or inoperable disease rather than socioeconomic status as majority of the patients are of low socioeconomic status. That means significant weight loss is probably an indirect sign of inoperability. Among the symptoms the most common are in the order of frequency are dyspepsia, GOO, malaena or bleeding, pain abdomen, anorexia. It is same as the observation made by Wanabe H J et al. 1993. However because of its vague presentation early diagnosis is of concern. Secondly we have found that significant pain indicates advanced stage of disease probably due to involvement of nerve fibers around celiac plexus involved by malignant lymph nodes. Majority of the patients do not have any addiction. Among those have addiction smoking is the commonest. So probably substance uses have little to do with gastric cancer. But as the sample size is too limited it is difficult to comment on correlation between addiction and gastric cancer. So far co morbidities are concerned majority 70.5% don’t have any co morbidities. The most common co morbidity in the scenario is hypertension which is usual in the age group we have shown. Next order of co morbidity is diabetes. So the patient population is medically healthy. None of the patients have any surgical procedure or any major hospitalization. In fact we have excluded those patients having previous abdominal surgery so that the outcome is not to be affected by other factors.

The most common site of the tumour was distal about in 87.5% of the cases. This was almost like that of Huang et al. (80%) in 2011. The rest were in proximal stomach. Distal gastrectomy was done for distal tumour and rest others are approached by total gastrectomy. We have excluded tumours involving GEJ or lower esophagus. Hence the controversy regarding the extent of resection whether total gastrectomy or esophagogastrectomy is negated altogether. None of the patients has undergone proximal gastrectomy considering the intractable complication they carry. We didn’t have a single case of duodenal infiltration or disease involving grossly the spleen or pancreatic tail. So none of the cases needed pancreatico splenectomy as per the study. Cases of distal gastrectomy were reconstructed by Billroth-II gastrojejunosotomy and side to side JJ for bile reflux and those with total gastrectomy reconstruction is done by Roux-en Y esophagojejunostomy. Feeding jejunostomy was done in all cases for the sake of postoperative nutrition. This procedure is followed by P Edwards et al. in 2004.

The post-op ileus lasted for a range of 3-8 days considering the cases where there is some complications like bile leak. The mean was 5.1 days. We have considered post-op ileus significant only if it is more than 5 days of duration. The standard is usually 3 days following abdominal surgery. But considering Indian scenario and open surgery we have arbitrarily raised it to 5 days and it is judged by the day patient appreciates passage of flatus and there is bowel sound all together. So only in 35% of cases the ileus was longer than 5 days. In majority cases the bowel activity returned well in time. The drainage is more than 5 days in 55% cases. Bile leak the most major complication found in only 10% of cases. Usually all bile leak cases were stage IIIb or IIIC cases. So it is implied that the complication rate increases with increase in stage of disease. The complication in the form of wound infection was present in 35% of cases. This is probably higher in comparison to any standard data. A Nafae et al. presented in his paper 13% of wound infection D1 and 3.7% wound infection in D2 group. The increased rate of wound infection is a sign of poor maintenance of infection control protocol perioperatively as well as some inferior quality of drugs being prescribed to patients. Mean ICU stay was 3.7+2.8 days. This is unacceptable as there is no major complications. But it is because of increased wound infection and protectiveness from our point of view that the average ICU stay is more in comparison to other studies. The average hospital stay was 11.45 days. In our case hospital stay we considered the days after the date of surgery. So more accurately it could be mentioned as postoperative stay. So if a patient stays 2-4 days preoperatively the real hospital stay would be 14 to 16 days. The result are same as that of JJ Bonenkamp and H. Danielson. The majority of patients have low or intermediate grade tumour and majority of intestinal variety. Tumours in our study were differentiated carcinomas. This finding was contradictory to Chang Ming Huang et al., 2011 (differentiated growths = 22.1% and undifferentiated = 77.9%) and Asada Methasate et al., 2010 (differentiated = 40% and undifferentiated = 60%).

The lymph node retrieval was 23.52 and avg no. of positive nodes are 3.42. The lymph node retrieval by Cushchieri et al. was 17, with JJ Bonenkamp it is 30 and Digiuli et al. it is 37. So our lymph node retrieval was more than that of cushchieri but less than others. Majority of patients are in stage IIA near about 32.5%. Very few cases are in stage Ia. Which indicates that most patients are in advanced stage of disease. Almost similar findings were
obtained by P. Edwards et al., 2004 (stage I- 20%, stage II- 28%, stage IIIA- 23%, and stage IIIB- 29%) . Cushieri et al., 1999 has shown most of their patients had stage III disease in both the groups, while as in our study most of the patients had stage IIIB disease . M. Degiuli et al., 2014 have shown that 41% in modified D2 had stage I disease. While as in our study only 10% patients had stage I disease and 2.5% have stage I A disease.

So far early post-op course is concerned we have considered bile leak, increased drainage for more than 5 days, prolonged ileus, wound infection as more specific complications related to surgery itself. Whereas other nonspecific complications as chest infection, fever, bedsores, thrombophlebitis incidence was 32.5% of cases. The above complications lead to enhanced (slightly) hospital stay and ICU stay. But non contributed to mortality. This is in sharp contrast to the earlier studies which have reported mortality in D2 gastrectomy. Mortality rates associated with radical resection of stomach cancer have improved greatly owing to more rigorous patient selection and development in the surgical techniques and postoperative care. As for example bile leak most lethal complication was managed by draining the collections image guided when require, escalating the antibiotic regimen and most importantly maintaining a very good nutrition post operatively through FJ feeding tube. Nutrition has been maintained usually by giving polymeric diet as milk, protein powder. But in case of leak we have provided 25- 50% of that with semi elemental diet keeping adequate calorie and protein intake. In case there is GI intolerance in the form of abdominal distension, diarrhea we have supplemented with parental nutrition with regular insulin. But in our study majority are managed by enteral nutrition itself. The criteria to start with enteral nutrition was not bowel sound or passing flatus. We started the enteral feed if abdomen is not distended and there is no frank features of peritonitis or vomiting, pain associated with FJ feeding. A systematic review and meta-analysis of randomized controlled trials which compared any type of enteral feeding started <24 hours after elective gastrointestinal surgery versus nil by mouth management concluded that early feeding reduced infective risks by approximately 30% and mean length of hospital stay by nearly one day. Second most important aspect is the age group of the study is significantly lower compared to other study. The BMI as well as serum albumin level was maintained in the patient population significantly. Last but not the least non of the patient has undergone pancreaticosplenectomy as a part of the surgical procedure except one. Together with these proper patient selections, use of modern gadgets, proper technique has made it a safe procedure with almost zero morbitality. Now what happens to these patients in long term, during adjuvant treatment is a matter to be seen which is not beyond the scope of disease. As per Alfar Nafae at al. in there study didn’t find any death which is directly related to the procedure itself except one where hemorrhage is the cause which could have managed by meticulous surgery. So zero mortality is possible in modified D2 gastrectomy.

The major co morbidities are analyzed. Increased drainage that is more than 5 days is related to low albumin (<3.2) and increased stage of the disease. Similarly ileus is correlated with preop Hb% level. It is an unknown factor for post op ileus. The statistical significance of it is unknown. Given the small sample size in this study larger study needs to be done regarding the impact of low hemoglobin and postop paralytic ileus. Regarding other minor complications which are not related to surgical procedure itself there is no significant correlation with hemoglobin, Sr albumin, BMI, stage of the disease, age, smoking and the preop complications. This is because improved perioperative management. Only one parameter that is wound infection is significantly higher in our study. This is explained by quality control over the supplied antibiotics and presence of iatrogenic resistant species of organism. So this entails more rigorous microbial monitoring of our centre.

LN involvement is one of the strongest prognostic parameters after gastrectomy for survival and recurrence. Precise evaluation of the extent of LN metastasis offers the ability to more accurately predict oncologic outcomes for the individual patient. However, the appropriate degree of curative LN dissection differs between Western and Eastern countries. In a Japanese classification, the extent of LN dissection was represented by D0-D3 using the LN station system. The system is complicated and is hard to use due to variations in each category. Instead, the number of the examined LNs has been used as a simpler indicator of the extent of LN dissection. However, the absence of a fixed cutoff number of retrieved LNs for standard treatment in gastric carcinoma is a complication. The optimal extent of regional LNs during surgery for gastric adenocarcinoma continues to be debated. Baiozchi et al. 30 and Chenet et al. 31 proposed that the trend towards superior survival outcome could be followed after the retrieval of more than 25 LNs. Smith et al. 31 presented that the stage subgroup-specific survival depends strongly on the total number of LNs examined and culminates in the highest survival at counts of 40 LNs. Bouvier et al. 32 suggested that staging is not reliable when fewer than 10 LNs are examined. Although a universally accepted minimum number of LNs necessary for accurate staging of gastric cancer has not been recognized, retrieval of at least 15 LNs is recommended to avoid stage migration in NCCN guidelines version 2. 2013 33. As the number of LNs examined increases, the probability of missing a positive LN decreases and so does the proportion of patients with higher-stage disease who are misclassified as lower-stage. A low LNs examined results in an underestimation of stage, which is known as the Will Rogers phenomenon 34, 35. Second, the contribution of negative node number to the prognosis of patients is partly due to considerably high rate LN micro metastases 36. In node-negative patients identified by routine histological
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examination, about 17%–32% had LN micro metastases. The patients with micro metastases often have an especially high risk for recurrence. But the lymph noderetrieval is theoretically dependent on the extent of the lymphadenectomy as well as by proper and meticulous histopathological technique. Here we have found that the no. of lymph noderetrieval is positively correlated with stage of disease and is more in case of total gastrectomy. The last fact is obvious because more nodal stations are being dissected. But it is negatively correlated with BMI and the age of the patients. The last two facts are probably difficult to explain in the present state of information we have. Certainly patients having high BMI pose a challenge for D2 gastrectomy. As incomplete clearance is a possibility in case of difficult surgery this may be partly the explanation for the negative correlation. But looking at the study chart one can be well sure that in all stage II–III cases getting lymph node more than 15 is possible.

The majority of the patients even after adequate resection develop recurrences in stomach bed, the anastomotic site, regional lymphnodes and distant sites. This has led to establishment of many effective neoadjuvant, adjuvant protocol as a part of multimodality management of gastric cancer. Among these newer therapy immunotherapy, target therapy have come to picture in case of gastric cancer.

Gastric carcinomas show somatic KRAS mutations in <5–10% and BRAF in ~2.2% of gastric cancers. Mammano and colleagues evaluated EGFR protein expression and gene mutations in exons 18, 19 and 21 in 49 gastric adenocarcinomas. The EGFR gene mutation was not identified, but EGFR protein expression was seen in 6% of the cases. HER2 is over expressed in 10–25% of gastric cancer. Yano and colleagues showed HER2 was over expressed in 23% of cases in gastric cancer patients by IHC. Fluorescence in situ hybridization (FISH) assay showed 99.5% concordance. HER2 over expression was evaluated by both IHC and FISH in advanced gastric carcinoma by Song and colleagues and was shown to have a worse prognosis. In HER2-amplified patients the median survival was 5.5 months compared with 12.6 months in nonamplified patients. HER2 over expression was more commonly seen in the intestinal-type than diffuse-type cancers (32% versus 6%) There was also a high concordance rate noted between IHC and FISH HER2 results from primary and metastatic sites. Very interestingly we have found that in around 40% of proximal cases the HER2 is positive and mostly in diffuse variety of the tumours. This is almost contrary to the data presented. The explanation may be the Indian scenario where it is different than the western data. But considering the sample size more larger trial should be conducted in Indian scenario. As per TOGA trial chemotheraphy plus trastuzumab improves median survival by 2.5 months against chemotherapy only. So as a generalized guideline doing Her2neu testing in all cases of cancer stomach cannot be recommended in Indian scenario. But as a part of individualized medicine it should be done in metastatic gastric cancer considering financial and physiological status of the patients.

V. Conclusion

Surgery for gastric cancer is the only hope for cure or long term survival in the arena of multimodal management of cancers. It provides quick symptom relief by loco regional control, adds to survival of the individual, cure in case of early gastric cancer and proper staging for planning of subsequent adjuvant treatment. However controversy regarding the extent of surgery still remains today after so much advance in the field of cancer. From randomized control trial the limit for extent of gastrectomy is certainly D2 dissection as D3, D4 dissections do not provide any advantages in term of loco regional control, overall survival and most important safety of the procedures. The outstanding outcomes of D2 gastrectomy as per Japanese literature cannot be reproduced elsewhere in the world, even after some land mark trials as Dutch trial have shown definite survival advantage. This was mostly due to advanced stage of disease and excessive postoperative mortality in the western setup. The discrepancy in early stage disease was considered due to stage migration (Will Rogers phenomenon) as well as skip metastases, micrometastases where limited dissection was done. So though D2 gastrectomy has been considered by many as the recommended procedure for gastric cancer the excessive morbidity and mortality associated with it led to modified gastrectomy. Some authors have proved the oncological equivalency of D2 dissection avoiding 11d, 10 group of nodes thereby avoiding pancreaticosplenectomy altogether. This modification improves postoperative outcome significantly. With proper patient selection, proper postop care and improvement in surgical techniques the mortality (procedure specific) can be zero almost. Modified D2 gastrectomy provides adequate no. of lymph nodes to be examined fulfilling the criteria led down by NCCN guideline too. Though it is a safe procedure, yielding adequate lymph nodes for proper staging more trials are required for testing its survival advantage vis-à-vis D2 gastrectomy on long term follow up.
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Reference


