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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*

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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%) washigher compared with rest of the world (10-30%)[1,2].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 patientsis about 20.3%.Survival of patients with D1 dissection is 41% and with D2 dissection is 50-62%.Thus, Japanese literature suggested D2 lymhadenectomy for stomach cancer. However, D2 lymhadenectomy for stomach cancer did not produced the same result in Europe [3,4].It is suggested that high postoperative morbidity and mortality associated with extensive lymph nodedissection. 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[5,6].On the other hand, the British study confirmed that modified D2 gastrectomy preserving spleen and pancreas is feasible and it carries much lower mortality[7,8]. 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 5year 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 leadsto 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 candidatesand 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, 4sb,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.Lymphnode dissections at 10 and 11d were done in proximal cancer if they were visibly enlarged

Post-operative period:

1. Patientswere kept in High Dependency Unit(HDU) for at least 24 hrs with routine monitoring.
2. Feeding jejunostomy was started after 48 hrs.
3. Encouraged early mobilization and removal of drain when 24 hr collection below 100ml.
4. Suture removed on 10th to 12th post operative day,
5. Feeding jejunostomy(FJ) removed after 3 to 4 weeks.

Surgical findings were as follows:-

1.Intra-operative parameters were as follows:-

a) Operative timeb)intra-operative bloodloss, c)inadvertent splenectomy, d)bowel and pancreatic tail injurye)major vascular injury, f)peri-operative blood transfusion, g)duration of surgery

2. Post-operative parameterswere as follows:-

a) Post-operative ICU stayb) Post-operative bleeding, c) Post-operative leaks, d) Post-operative infectione) Post-operative ileusf) Duration of hospital stayg) Drain output

3.Pathological outcome-

a) Histopathological variety of the tumourb) Numbers of lymphnode isolated by standard grossing methodc) Levels of tumour infiltration (i.e.T stage of tumour)d) Number of positive lymphnodes e)Her-2neu positivity of the tumourf) 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 (χ^2) test was performed to find the associations. Corrected chi-square (χ^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.

III. Results

Table-1: Demographic parameters of patients.

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

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 (χ^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 (t_{38}=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/m^2 with range 22.0- 34.0 kg/m^2 and the median was 27.0 kg/m^2.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 mlwith 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.27(67.5%) of the patients did not have any other complications. Out of the 13(32.5%) cases of other complications 6(15.0%) had chest infection.The mean duration of hospital stay (mean ± s.d.) of the patients was 11.45±3.89 days with range 7-22 days and the median was 10 days. Most of the site of tumor was distal (87.5%) which was significantly higher than proximal (12.5%) (Z=10.60;p<0.0001). Most of the adenocarcinoma was intestinal (80.0%) which was significantly higher than diffuse (20.0%) (;p<0.0001).Most of the grade of tumor was intermediate (70.0%) which was significantly higher than others (Z=5.65 ;p<0.0001). The mean number of lymph node retrieved (mean ± s.d.) of the patients was 23.52±6.95 with range 13-41 and the median was 22.The mean number of positive lymph node (mean ± s.d.) of the patients was 3.42±2.80 with range 0-12 and the median was 3.All the margin statuses were negative. Only 2(5.0%) of the cases were having Her-2neu 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

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

Table-3: Distribution of different histological parameters after surgery

Histological parameters	Number	%	Test Statistic	p-value
Site of tumour				
Distal	35	87.5	Z=10.60	<0.001*
Proximal	5	12.5		
Type of Adenocarcinoma				
Diffuse	8	20.0%	Z=8.48	<0.001*
Intestinal	32	80.0%		
Grade of Tumour				
High	11	27.5%		
Intermediate	28	70.0%	Z=5.65	<0.001*
Low	1	2.5%		
Pathological stage				
IA	1	2.5%		
IB	3	7.5%		

IIA	6	15.0%		
IIB	13	32.5%	Z=2.98	0.0028
IIIA	6	15.0%		
IIIB	6	15.0%		
IIIC	5	12.5%		
Status of LVI/PNI				
LVI and PNI+	8	20.0%	Z=9.19	<0.001*
LVI+	24	60.0%		
PNI+	1	2.5%		
Negative	7	17.5%		
Her-2neu Status				
Negative	38	95.0%	Z=12.72	<0.001*
Positive	2	5.0%		

Post-operative morbidities:
Duration of drainage:

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

Parameters	**Duration of drainage>5 days (n=22)**	**Duration of drainage≤5 days (n=18)**	**Test-statistic**	**p-value**	**Odds Ratio with 95% Confidence Interval**
Serum albumin (Mean±s.d.)	3.18±0.58	3.70±0.60	t_{38}=2.77	0.0086*	NA
Level of Pre-op Hb (Mean±s.d.)	10.50±1.92	12.00±2.53	t_{38}=2.13	0.0397*	NA
BMI (kg/m^2) (Mean±s.d.)	26.68±3.46	27.61±1.94	t_{38}=1.01	0.31	NA
Age (years) (Mean±s.d.)	48.36±9.67	50.00±6.48	t_{38}=0.61	0.54	NA
Smoking					
Yes	5(22.7%)	6 (33.3%)	χ^2 =0.55	0.45	[OR-0.58(0.14,2.38]
No	17(77.3%)	12 (66.7%)			
Stage of the disease					
IA	0(0.0%)	1(5.6%)	χ^2 =16.12	0.013*	NA
IB	1(4.5%)	2(11.1%)			
IIA	1(4.5%)	5(27.8%)			
IIB	5(22.7%)	8(44.4%)			
IIIA	4(18.2%)	2(11.1%)			
IIIB	6(27.3%)	0(0.0%)			
IIIC	5(22.7%)	0(0.0%)			
Presence of diabetes					
Yes	4(18.2%)	2(11.1%)	χ^2 =0.38	0.53	[OR-1.77(0.28, 11.03]
No	18(81.8%)	16(88.9%)			
Site of the disease					
Distal	17(77.3%)	18(100.0%)	Fisher Exact Test	0.04*	
Proximal	5(22.7%)	0(0.0%)			

Duration of Ileus:

Table-5: Comparison of duration of Ileus with different parameters

Parameters	**Duration of Ileus >5 days (n=14)**	**Duration of Ileus≤5 days (n=26)**	**Test-statistic**	**p-value**	**Odds Ratio with 95% Confidence Interval**
Serum albumin (Mean±s.d.)	3.10±0.59	3.58±0.60	t_{38}=1.30	0.20	**NA**
Level of Pre-op Hb (Mean±s.d.)	10.07±1.71	5.81±2.41	t_{38}=5.85	<0.00018*	**NA**
BMI (kg/m^2) (Mean±s.d.)	26.71±3.53	27.30±2.52	t_{38}=0.61	0.54	**NA**
Age (years) (Mean±s.d.)	50.00±10.42	48.61±7.14	t_{38}=0.49	0.62	**NA**
Smoking					
Yes	2(14.3%)	9(34.6%)	χ^2	0.16	[OR-0.31(0.05, 1.72]

No	12(85.7%)	17(65.4%)			
Stage of the disease					
IA	0(0.0%)	1(3.8%)	χ^2 =12.86	0.045*	**NA**
IB	0(0.0%)	3(11.5%)			
IIA	0(0.0%)	6(23.1%)			
IIB	3(21.4%)	10(38.5%)			
IIIA	4(28.6%)	2(7.7%)			
IIIB	4(28.6%)	2(7.7%)			
IIIC	3(21.4%	2(7.7%)			
Presence of diabetes					
Yes	2(14.3%)	4(15.4%)	χ^2 =0.13	0.71	[OR-0.91(0.14, 5.75]
No	12(85.7%)	22(84.6%)			
Site of the disease					
Distal	12(85.7%)	23(88.5%)	χ^2 =0.06	0.80	[OR-0.78(0.11, 5.34]
Proximal	2(14.3%)	3(11.5%)			

Wound Infection:

Table-6: Comparison of Wound Infection with different parameters

Parameters	**Wound Infection (n=26)**	**No Wound Infection (n=14)**	**Test-statistic**	**p-value**	**Odds Ratio with 95% Confidence Interval**
Serum albumin (Mean±s.d.)	3.25±0.54	3.50±0.68	t_{38}=1.27	0.21	NA
Level of Pre-op Hb (Mean±s.d.)	10.28±2.44	11.65±2.13	t_{38}=1.76	0.0865	NA
BMI (kg/m^2) (Mean±s.d.)	27.57±3.58	26.48±2.47	t_{38}=1.01	0.31	NA
Age (years) (Mean±s.d.)	49.42±8.89	48.92±8.18	t_{38}=0.17	0.86	NA
Smoking					
Yes	5(35.7%)	6(23.1%)	χ^2 =0.72	0.39	[OR-1.851(0.44, 7.69]
No	9(64.3%)	20(76.9%)			
Stage of the disease					
IA	0(0.0%)	1(3.8%)	χ^2 =7.33	0.29	NA
IB	0(0.0%)	3(11.5%)			
IIA	1(7.1%)	5(11.5%)			
IIB	7(50.0%)	6(23.1%)			
IIIA	1(7.1%)	5(19.2%)			
IIIB	2(14.3%)	4(15.4%)			
IIIC	3(21.4%)	2(7.7%)			
Presence of diabetes					
Yes	3(21.4%)	3(11.5%)	χ^2 =0.69	0.40	[OR-2.09(0.36, 12.08]
No	11(78.6%)	23(88.5%)			
Site of the disease					
Distal	11(78.6%)	24(92.3%)	χ^2 =1.56	0.21	[OR-0.30(0.44, 2.09]
Proximal	3(21.4%)	2(7.7%)			

Chest Infection:

Table-7: Comparison of Chest Infection with different parameters

Parameters	**Chest Infection (n=6)**	**No Chest Infection (n=34)**	**Test-statistic**	**p-value**	**Odds Ratio with 95% Confidence Interval**
Serum albumin (Mean±s.d.)	3.18±0.41	3.54±0.66	t_{38}=1.28	0.20	NA
Level of Pre-op Hb (Mean±s.d.)	11.21±1.63	11.16±2.43	t_{38}=0.05	0.96	NA
BMI (kg/m^2) (Mean±s.d.)	26.33±3.14	27.23±2.87	t_{38}=0.69	0.49	NA
Age (years) (Mean±s.d.)	51.00±13.71	48.76±7.26			NA
Smoking					
Yes	3(50.0%)	8(23.5%)	χ^2 =1.79	0.18	[OR-3.25(0.54, 19.38]
No	3(50.0%)	26(76.5%)			
Stage of the disease					
IA	0(0.0%)	1(2.9%)	χ^2 =6.35	0.38	NA
IB	0(0.0%)	3(8.8%)			

IIA	0(0.0%)	6(17.6%)			
IIB	1(16.7%)	12(35.3%)			
IIIA	1(16.7%)	5(14.7%)			
IIIB	2(33.3%)	4(11.8%)			
IIIC	2(33.3%)	3(8.8%)			
Presence of diabetes					
Yes	2(33.3%)	4(11.8%)	χ^2 =1.86	0.17	[OR-3.75(0.51, 27.49]
No	4(66.7%)	30(88.2%)			
Site of the disease					
Distal	4(66.7%)	31(91.2%)	χ^2 =2.80	0.09	[OR-0.19(0.02, 1.53]
Proximal	2(33.3%)	3(8.8%)			

Lymphnodes retrieved by surgery:

Table-8: Comparison of Lymphnodes retrieved by surgery

Parameters	**Correlation (r)**	**Test Statistic**	**p-value**
Correlation with age	r= -0.29		**0.0695**
Correlation with BMI	r= -0.42		**0.0070***
Correlation with Stage of disease	r= 0.75		**<0.0001***
Stage of the disease	**Lymphnodes retrieved**	**t-test**	
Stage-I (n=4)	15.75±2.50	t_{38}=6.38	**<0.0001***
Stage-II (n=19)	19.73±2.82		
Stage-III (n=17)	29.58±6.03		
Site of the disease			
Distal (n=35)	22.00±5.79	t_{38}=4.48	**<0.0001***
Proximal (n=5)	34.20±4.76		

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 [9, 10, 11].In India the stomach cancer was estimated to be fifth leading cancer site in males and seventh in females[12].Gastric cancer is an aggressive disease. Whileloco regional disease has better prognosis the overall five year survival for resectable gastric cancer is usually 20-30%[13, 14, 15].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 withPSP 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[17].Galizia et al. in 2015 in 2015 compared standard D2 gastrectomy with modified D2 gastrectomy.He found that modified D2 has less postop death andmorbidity. The 5 yr disease free survival or the site of tumour relapse was notdifferent. 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 D1gastrectomy 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 was45-54.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 [17,18].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 [19, 20]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[21].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 most common was smoking. 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[22].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 patient 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 gastrojejunostomy 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 than5 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.[23]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 controlprotocol 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.Tumoursin our study were differentiated carcinomas.This finding was contradictory to Chang Ming Huang et al., 2011 (differentiated growths = 22.1% and undifferentiated= 77.9%) [24] and Asada Methasate et al., 2010 (differentiated = 40% and undifferentiated = 60%)[25]

The lymph node retrieval was 23.52 and avg no. of positive nodes are 3.42.The lymphnode retrieval by Cushchieri et al. was 17,with J.J Bonenkamp it is 30 and Digiuli etal it is 37.So our lymphnode retrieval was more that of cuschieri but less than others.Majority of patients are in stageIIa 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 IIB 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 IA 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 [26, 27].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 is maintained usually by giving polymeric diet as milk ,protein powder. But in case of leak we have provided25- 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 withthese proper patient selections, use of modern gadgets, proper technique has made it a relative safe procedure with almost zeromortality. Now what happens to these patients in long term, during adjuvant treatment is a matter to be seen which at present is beyond the scope of disease, As per Alfar Nafae et 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.

So 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 preopHb% 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 co morbidities.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 [28]. 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. Baiocchi et al.[29] and Chenet al.[30] 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

examination, about 17%–32% had LN micro metastases[37, 38]. The patients with micro metastases often have an especially high risk for recurrence[39].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 lymhnodes and distant sites,[40, 41, 42].This has led to establishment of many effective neoadjuvant,adjuvant protocol as a part of multimodality management of gastric cancer[43, 44, 45].Among these newer therapy immunotherapy ,target therapy has 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 [46]. 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 [47]. 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 [48]. 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 [49]. 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%) [50]. There was also a high concordance rate noted between IHC and FISH HER2 results from primary and metastatic sites [51].Very interestingly we have found that in around 40% of proximal cases the Her2neu 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 Indianscenario. As per TOGA trial chemotherapy 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.

Reference

[1]. Dikshit RP, Mathur G, Mhatre S, Yeole BB. Epidemiological review of gastric cancer in India. Indian J Med Paediatr Oncol. 2011;32(1):3-11.
[2]. Maruyama K, Okabayashi K, Kinoshita T. Progress in gastric cancer surgery in Japan and its limits of radicality. World J Surg. 1987;11:418–425.
[3]. Soga J, Kobayahsi K, Saito J, Fukimaki M, Muto T. The role of lymphadenectomy in curative surgery for gastric cancer. World J Surg. 1979;3:701–708.
[4]. Bonenkamp JJ, Hermans J, Sasako M, Van de Velde CJH. Extended lymph-node dissection for gastric cancer. N Engl J Med. 1999;340:908–914.
[5]. Cuschieri A, Fayers P, Fielding J, Craven J, Bancewicz J, Joypaul V, Cook P. Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomised controlled surgical trial. Lancet. 1996;347:995–999.
[6]. Bonenkamp JJ, Songun I, Herman J, Sasako M, Welvaart K, Plukker JT, van Elk P, Obertop H, Gouma DJ, Taat CW. Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. Lancet. 1995;345:745–748.
[7]. Cuschieri A, Weeden S, Fielding J, Bancewicz J, Craven J, Joypaul V, Sydes M, Fayers P. Patient survival after D1 and D2 resections for gastric cancer: long-term results of the MRC randomised surgical trial. Br J Cancer. 1999;79:1522–1530.
[8]. Griffith JP, Sue-Ling HM, Martin I, Dixon MF, McMahon MJ, Axon ATR, Johnston D. Preservation of the spleen improves survival after radical surgery for gastric cancer. Gut. 1995;36:684–690.
[9]. Wang Y,Huang CM,Zhang CH,Li P,Xi e JW et al.(20130 Classification of anatomic variation in the left gastric vein during laparoscopic gastrectomy.Anat Physiol 3:127.doi:10.4172?2161-0940.1000127
[10]. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, et al. Cancer statistics, 2006. CA Cancer J Clin 2006;56:106-30.
[11]. Rastogi T, Devesa S, Mangtani P, Mathew A, Cooper N, Kao R, et al. Cancer incidence rates among South Asians in four geographic regions: India, Singapore, UK and US. Int J Epidemiol 2008;37:147-60.
[12]. Kelley JR, Duggan JM. Gastric cancer epidemiology and risk factors. J Clin Epidemiol 2003;56:1-9.
[13]. Rao DN, Ganesh B. Estimate of cancer incidence in India in 1991. Indian J Cancer 1998;35:10-8.
[14]. Siewert JR, Böttcher K, Roder JD, Busch R, Hermanek P, Meyer HJ. Prognostic relevance of systematic lymph node dissection in gastric carcinoma. German Gastric Carcinoma Study Group. Br J Surg 1993;80:1015-8.
[15]. Breaux JR, Bringaze W, Chappuis C, Cohn I Jr. Adenocarcinoma of the stomach: a review of 35 years and 1,710 cases. World J Surg 1990;14:580-6.
[16]. Dicken BJ, Bigam DL, Cass C, Mackey JR, Joy AA, Hamilton SM. Gastric adenocarcinoma: review and considerations for future directions. Ann Surg 2005;241:27-39.
[17]. Park SS,Ryce Js,MinBW,KimWB,Kim SJ,Kim CS,Mok YJ.Importance of skip metastases in gastric cancer.ANZ J Surg 2005;75:645-649
[18]. Degiuli, M., Sasasko, M., Ponti, A., et al. (2014) Morbidity and Mortality in Italian Gastric Cancer Study Group Randomized Clinical Trial of D1 versus Modified D2 Resection for Gastric Cancer. British Journal of Surgery, 101, 23-31
[19]. Danielson, H., Kokkola, A., Kiviluoto, T., Siren, J., et al. (2007) Clinical Outcome after D1 versus D2-3 Gastrectomy for Treatment of Gastric Cancer. Scandinavian Journal of Surgery, 96, 35-40.
[20]. Lewis, W.G., Edwards, P., et al. (2002) D2 or Not D2? The Gastrectomy Question. Gastric Cancer, 5, 29-34.
[21]. Edwards, P., Blackshaw, G.R.J.C., Lewis, W.G., Barry, J.D., Allison, M.C. and Jones, D.R.B. (2004) Prospective Comparison of D1 vs. Modified D2 Gastrectomy for Carcinoma. British Journal of Cancer, 90, 1888-1892.
[22]. Wanebo, H.J., Kennedy, B.J., Chmiel, J., Steele, G., Winchester, D. and Osteen, R. (1993) Cancer of Stomach. A Patient Care Study by American College of Surgeons. Annals of Surgery, 218, 583-592.
[23]. Huang, C.-M., Lin, J.-X., Zheng, C.-H., Li, P., Xie, J.-W. and Wang, J.-B. (2011) Impact of the Number of Dissected Lymph Nodes on Survival for Gastric Cancer after Distal Subtotal Gastrectomy. Gastroenterology Research and Practice, 2011, Article ID: 476014.
[24]. Alfar Nafae*, Raiees Ahmad, Amber Aliya, Yawar Nisar, Pervaze Salam,Imtiyaz Ahmad Surgical Science, 2016, 7, 13-26
[25]. Huang, C.-M., Lin, J.-X., Zheng, C.-H., Li, P., Xie, J.-W. and Wang, J.-B. (2011) Impact of the Number of Dissected Lymph Nodes on Survival for Gastric Cancer after Distal Subtotal Gastrectomy. Gastroenterology Research and Practice, 2011, Article ID: 476014.
[26]. Methasate, A., Trakarnsanga, A., Akaraviputh, T., Chinsawangwathanakol, V. and Lohsiriwat, D. (2010) Lymph Node Metastasis in Gastric Cancer: Result of Modified D2 Dissection. Journal of the Medical Association of Thailand, 93,310-317.
[27]. Sano, T., Sasako, M., Yamamoto, S., Nashimoto, A., Kurita, A., Hiratsuka, M., et al. (2004) Gastric Cancer Surgery:Morbidity and Mortality Results from a Prospective Randomized Controlled Trial Comparing Modified D2 and Extended Para-Aortic Lymphadenectomy—Japan Clinical Oncology Group Study 9501. Journal of Clinical Oncology, 22,2767-2773.
[28]. Kinoshita, T., Maruyama, K., Sasako, M. and Okajima, K. (1993) Treatment Results of Gastric Cancer Patients: Japanese Experience. In: Nishi, M., Ichikawa, H., Nakajima, T., Maruyama, K. and Tahara, E., Eds., Gastric Cancer,Springer, Tokyo, 319-330.
[29]. Smith DD, Schwarz RR, Schwarz RE. Impact of total lymph node count on staging and survival after gastrectomy for gastric cancer: data from a large US-population database. J Clin Oncol. 2005;23:7114–7124.
[30]. Baiocchi GL, Tiberio GA, Minicozzi AM, Morgagni P, Marrelli D, Bruno L, et al. A multicentric Western analysis of prognostic factors in advanced, node-negative gastric cancer patients. Ann Surg. 2010;252:70–73.
[31]. Chen XZ, Yang K, Zhang B, Hu JK, Zhou C. Is retrieval of >25 lymph nodes a superior criterion for locally advanced gastric cancer surgery? Ann Surg. 2011;254:834–835.
[32]. Smith DD, Schwarz RR, Schwarz RE. Impact of total lymph node count on staging and survival after gastrectomy for gastric cancer: data from a large US-population database. J Clin Oncol. 2005;23:7114–7124.
[33]. 33. Bouvier AM, Haas O, Piard F, Roignot P, Bonithon-Kopp C, Faivre J. How many nodes must be examined to accurately stage gastric carcinomas? Results from a population based study. Cancer. 2002;94:2862–2866.
[34]. NCCN clinical practice guidelines in oncology (NCCN Guidelines): gastric cancer. V.2.2013 [Internet] Fort Wathing ton: National Comprehensive Cancer Network; c2012. [cited 2013 Dec 10].
[35]. Greenstein AJ, Litle VR, Swanson SJ, Divino CM, Packer S. Effect of the number of lymph nodes sampled on postoperative survival of lymph node-negative esophageal cancer. Cancer. 2008;112:1239–1246.
[36]. Feinstein AR, Sosin DM, Wells CK. The Will Rogers phenomenon. Stage migration and new diagnostic techniques as a source of misleading statistics for survival in cancer. N Engl J Med. 1985;312:1604–8.
[37]. Wu ZY, Li JH, Zhan WH, He YL, Wan J. Effect of lymph node micrometastases on prognosis of gastric carcinoma. World J Gastroenterol. 2007;13:4122–4125.

[38]. Kim JH, Park JM, Jung CW, Park SS, Kim SJ. The significances of lymph node micrometastasis and its correlation with E-cadherin expression in pT1–T3N0 gastric adenocarcinoma. J Surg Oncol. 2008;97:125–130.
[39]. Yasuda K, Adachi Y, Shiraishi N, Inomata M, Takeuchi H. Prognostic effect of lymph node micrometastasis in patients with histologically node-negative gastric cancer. Ann Surg Oncol. 2002;9:771–774.
[40]. Baiocchi GL, Tiberio GA, Minicozzi AM, Morgagni P, Marrelli D. A multicentric Western analysis of prognostic factors in advanced, node-negative gastric cancer patients. Ann Surg. 2010;252:70–73.
[41]. Dicken BJ, Bigam DL, Cass C, Mackey JR, Joy AA, Hamilton SM. Gastric adenocarcinoma: review and considerations for future directions. Ann Surg 2005;241:27-39.
[42]. Landry J, Tepper JE, Wood WC, Moulton EO, Koerner F, Sullinger J. Patterns of failure following curative resection of gastric carcinoma. Int J Radiat Oncol Biol Phys 1990;19:1357-62.
[43]. Hundahl SA, Phillips JL, Menck HR. The National Cancer Data Base Report on poor survival of U.S. gastric carcinoma patients treated with gastrectomy: Fifth Edition American Joint Committee on Cancer staging, proximal disease, and the "different disease" hypothesis. Cancer 2000;88:921-32.
[44]. Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, et al. MAGIC Trial Participants. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355:11-20.
[45]. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001;345:725-30.
[46]. Sakuramoto S, Sasako M, Yamaguchi T, Kinoshita T, Fujii M, Nashimoto A, et al. ACTS-GC Group. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. N Engl J Med 2007;357:1810-20.
[47]. stomach Lee S., Lee J., Soung Y., Kim H., Park W., Kim S., et al. (2003) BRAF and KRAS mutations in cancer. Oncogene 22: 6942–6945
[48]. Mammano E., Belluco C., Sciro M., Mencarelli R., Agostini M., Michelotto M., et al. (2006) Epidermal growth factor receptor (EGFR): mutational and protein expression analysis in gastric cancer. Anticancer Res 26(5A): 3547–3550
[49]. Yano T., Doi T., Ohtsu A., Boku N., Hashizume K., Nakanishi M., et al. (2006) Comparison of HER2 gene amplification assessed by fluorescence in situ hybridization and HER2 protein expression assessed by immunohistochemistry in gastric cancer. Oncol Rep 15: 65–71
[50]. Song Y., Huang J., Wang J. (2010) [Relationship between HER2/neu gene amplification and protein expression and prognosis in patients with advanced gastric carcinoma]. Chin J Cancer 29: 76–81
[51]. Bang Y., Chung H., Xu J., Lordick F., Sawaki A., Lipatov O., Al-Sakaff N., et al. (2009) Pathological features of advanced gastric cancer (GC): Relationship to human epidermal growth factor receptor 2 (HER2) positivity in the global screening programme of the ToGA trial. J Clin Oncol 27(215 Suppl.): abstract 4556.

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