Original Research Article

Comparison of D2 versus D1 gastrectomy in Kashmiri patients in a tertiary care cancer centre

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ABSTRACT

Background: The aim of this study was to compare the clinical outcomes, survival, morbidity and mortality of D1 and D2 gastrectomy in Kashmiri population in a high-volume tertiary care centre.
Methods: Data were collected retrospectively from the prospective database maintained by Department of Surgical Gastroenterology at SKIMS, Kashmir India. We did direct comparison of D1 and D2 gastrectomy in gastric cancer patients who underwent surgery between January 2016 to December 2021 and fulfilled the eligibility criteria. A total of 98 patients were included in the study of which 46 underwent a D1 gastrectomy and 52 underwent a D2 gastrectomy.
Results: Male-female ratio was 3:1 in both groups with a mean age of 61 years. There was no significant difference in terms of age or gender between D1 and D2 groups (p>0.05). The mean number of harvested lymph nodes (LN) was (7±1.9) in the D1 group compared to (27.6±10.1) the D2 group (p=0.001). Average hospital stay was comparable in both groups. The median survival was 26 months for the D2 and 19 months for the D1 group (p≤0.01). The survival in the D2 group was significantly higher than in the D1 group. There was no difference in postoperative complications between two groups in our study.
Conclusions: our study indicates that D2 gastrectomy should be the standard of treatment for advanced stage II /III disease as it improves the survival outcome in these patients without affecting overall hospital stay, morbidity and mortality.

Keywords: Gastric cancer, Kashmir, D1 and D2 gastrectomy, Survival

INTRODUCTION

Gastric cancer remains one of the most common and deadly cancers worldwide. Based on GLOBOCAN 2018 data, stomach cancer is the 5th most common neoplasm and the 3rd most deadly cancer, with an estimated 783,000 deaths in 2018.[1] The incidence of gastric cancer varies in different parts of the world and among various ethnic groups. Gastric cancer (GC) is common in the northeast and southern parts of India, although incidence in India is low compared with western countries and China.[2,3] Incidence of GC varies widely among the various regions within India due to diverse culture and related food habits. Kashmiri population a geographically and ethnically distinct population with special cultural and dietary habits. Kashmir has a high incidence of stomach cancers compared to rest of India.[4] It is the third most common cancer in Kashmir and has shown a gradual increase during the last 5 years.[5] Gastric cancer is an aggressive disease and a multidisciplinary approach has

been proven to improve the outcome for advanced-stage gastric cancer patients, but surgical resection offers the most effective therapy for those with curable disease. lymphadenectomy plays a key role in the surgical strategy of gastric cancer, mostly because nodal metastases could occur in early stages of disease.[6] However, the extent of lymph node resection for curative intent varies between surgeons and centres globally and within India. The lymph node status in gastric cancer is a key prognostic factor in patient survival.[7,8] There has been debate concerning the extent of lymph node dissection performed between western and eastern countries with eastern countries supporting D2 lymphadenectomy and western studies revealing arguable results.[9] The United Kingdom (UK) MRC-STO1 trial and the Dutch DGCT trial didn't report any statistically significant difference in survival, but a significantly higher mortality/ mortality in the D2 group compared to D1.[10,11] Nevertheless, a 15-year follow-up of the same Dutch trial demonstrated an improved local regional recurrence and lower gastric cancer-related deaths after a D2 resection.[12] The Italian gastric cancer study group (IGCSG) did not find a significant difference in overall 5-year survival between D1 and D2 patients; nevertheless, a subgroup investigation indicated a tendency towards enhanced survival for T2-T4 tumors and node-positive disease in D2 dissection.[13] In the light of good survival outcomes after D2 dissection in Japan, gastrectomy with D2 dissection is becoming increasingly acceptable in Western countries. The latest national comprehensive cancer network guidelines for gastric cancer stated that D2 dissection should be considered as a recommended but not a required procedure.[14] Lately, there is increasing consensus on a D2 lymphadenectomy with spleen and pancreas preservation and has become the standard of care, mostly in European centers. In Kashmir valley gastric cancer is a high incidence cancer but there is a paucity of data on gastrectomy outcomes of D1 and D2 lymphadenectomy. The objective of this study was to evaluate and compare the surgical outcome, postoperative morbidity, in-hospital mortality and survival between D2 gastrectomy with traditional D1 gastrectomy.

METHODS

Patient selection

The study involved retrospective analysis of prospectively maintained data of operated gastric cancer patients who underwent surgery between January 2016 to December 2021 and fulfilled the eligibility criteria. The study was conducted in the Department of Surgical Gastroenterology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar Kashmir, a tertiary care referral hospital with regional cancer centre. A total of 98 patients were enrolled in the study. Eligibility criteria were a histologically proven adenocarcinoma of the stomach without evidence of distance metastasis, age younger than 85 years, and in this study operated cases of carcinoma

stomach patients were classified into two groups on the basis the of type of lymphadenectomy performed: D2 lymphadenectomy (n=52) and D1 lymphadenectomy (n=46). A standardized D1 or D2 lymphadenectomy with spleen/pancreas preservation was performed according to surgeon preference. D1 or D2 was performed by specialists trained in upper gastrointestinal surgery. The patients in the two groups were matched for age, gender and stage. Sample size calculations were created on a previous literature survey which indicated that the 5-year survival rate of D1 resection was likely to be 20%, and is found to improves to approximately to 60% with D2 gastrectomy. The statistical power was calculated using the 'nQuery Advisor' statistics package (Statistical solutions, Stonehill corporate Center, USA).

Operative procedure

According to the Japanese gastric cancer treatment guidelines 2014 (version 4), the Japanese gastric cancer association (JGCA) defined the extent of lymphadenectomy according to the type of gastrectomy.[15] In case of total gastrectomy, lymph nodes dissected in D1 include nodes in stations 1 to 7; D2 includes nodes in D1 stations plus 8a, 9, 10, 11p, 11d, and 12a. lymph node dissection in Station 10 may be avoided.[16] While for subtotal gastrectomy, distal gastrectomy includes lymph node dissection in D1 including nodes in stations 1, 3, 4sb, 4d, 5, 6 and 7; D2 includes dissection of nodes in D1 stations plus 8a, 9, 11p, and 12a.

Chemotherapy was given to all patients postoperatively after surgery. Chemo protocol consists of 8 cycles of capecitabine with oxaloplatin.

Data collection

Preoperative demographic data included age, gender. Pathological data included tumor location, depth of tumor (T), nodal status (N), tumor differentiation type (well, moderate, poor) and tumor stage (TNM). Staging was done according to the American Joint Committee on Cancer (AJCC) 7th edition staging system.[17] Operative data comprised of gastrectomy type (total, partial, subtotal) location (proximal, distal), lymphadenectomy type (D1, D2), blood loss during surgery, and lymph node yield.[18] Postoperative data included postoperative complications graded according to the Clavien-Dindo classification, hospital stay, in hospital death, median survival.[19] Hospital mortality was defined as postoperative death of any cause within 30 days, death within same hospital stay.

Follow up

Patients were followed up every 3 months after surgery for 2 years and every 6 months beyond two years. Baseline investigations, CA19-9, CEA levels were done. CECT abdomen was done yearly for first three years. The two groups were compared with respect to postoperative

complications, morbidity, mortality as well as the survival etc.

Statistical analysis

The association between two categorical variables was assessed using either the chi-square test or Fisher's exact test. To compare quantitative (continuous) variables between two groups, the two-sample t-test was applied. Survival rates were estimated using Kaplan-Meier analysis. All statistical tests applied were two-tailed, and a p≤0.05 was considered statistically significant. Statistical analyses were performed using the Statistical Product and Service Solutions (SPSS), version 20.0, for Windows (SPSS Inc., Chicago, IL).

RESULTS

Demographic and clinicopathological characteristics of patients are presented in Table 1. The two groups were well balanced as there was no significant difference in baseline data. The age and gender distribution of the patients was matched in both groups. A total of ninety-eight patients were recruited in this study (Table 1). D1 group consisted 35 male and 11 female patients, while the D2 group consisted of 39 male and13 female patients. Mean age of male patients in D2 group was (61.05±11.26) Range (40-80) and mean age of females in D2 group was 59.76±12.37 (Range 40-80). Mean age of male patients in D1 group was 60.10±10.14 and mean age of females in D1 group was (58.74±11.20). In both groups majority of patients were elderly males with mean age of 61 years. Male female ratio was 3:1 in both the

groups. There was no significant difference in terms of age or gender between D1 and D2 groups (p>0.05) (Table 1). Of the 98 patients, 46 underwent a D1 lymphadenectomy and 52 underwent D2 lymphadenectomy. Most common tumour location was antropyloric, 60% in D2 and 65% in D1group. In our study 90% of patients were having (T3, T4) tumors in both groups. In D2 group 75% have (N2, N3) nodal involvement. Partial/subtotal gastrectomy was commonly done operation in both groups 67% in D2 and 71% in D1. The mean number of harvested lymph nodes (LN) was (7±1.9) in the D1 group compared to (27.6±10.1) the D2 group. These figures were statistically significant (p=0.001). Average blood loss during operation was (390.23±37.51 ml) in D2 group vs (377.20±35.36 ml) in D1 group. Mean operative time was (190±28.1 min) in D2 group vs (130±20.4 min) in D1 group (Table 2). Average hospital stay was (9±1.39 days) in D2 group vs (8.6±1.13 days) in D1 group (Table 2).

Post-operative morbidity and mortality

There was no difference in postoperative complications between two groups in our study depicted in Table 3. 1 patient each group had duodenal stump leaks, which was managed conservatively, anastomotic leaks1 in each group were managed conservatively and 2 patients in each groups had collections, managed by percutaneous drainage. None of the patients required re exploration. There was no in hospital mortality or within 30 days of discharge from hospital in both groups. 90% of patients were followed up to death or 3 years.

Table 1: Demographic and clinicopathological characteristics of patients undergoing gastrectomy with D1 or D2 gastrectomy.

Parameters	Group	D2 (%)	D1	P value
Age (years)	<50	11 (21.1)	9 (19.56)	0.84
	≥50	41 (78.8)	37 (80.43)	
Mean age (years)	Male	61.05±11.26	60.10±10.14	0.95
	Female	59.76±12.37	58.74±11.20	0.94
Gender	Male	39 (75)	35 (76.08)	0.9
	Female	13 (25)	11 (23.91)	
Smoking status	Yes	30 (57.69)	28 (60.86)	0.74
	No	22 (42.30)	18 (39.13)	
Tumor location	Antropyloric	31 (59.61)	30 (65)	0.83
	Body	06 (11.53)	4 (8.6)	
	GE-Junction	15 (28.84)	12 (26.08)	
Type of gastrectomy	Distal-partial	18 (34.61)	25 (54.34)	0.21
	Sub-total	17 (32.69)	8 (17.39)	
	Total	08 (15.38)	6 (13.04)	
	Proximal	07 (13.46)	7 (13.46)	
	Iverlewis	01 (1.92)	-	
	Orringer	01 (1.92)	-	
Staging	I/II	04 (7.69)	5 (10.86)	0.73
	III	48 (92.30)	41 (89.13)	
No. of nodes retrieved	<20	15 (28.84)	44 (95.65)	0.001
	≥20	37 (71.15)	2 (4.34)	

Continued.

Parameters	Group	D2 (%)	D1	P value
T level	T1	03 (5.76)	2 (4.34)	0.91
	T2	06 (11.53)	4 (8.69)	
	T3	17 (32.69)	14 (30.43)	
	T4	26 (50.0)	26 (56.52)	
N category	N0	05 (9.61)		--
	N1	8 (15.38)		
	N2	14 (26.92)		
	N3	25 (48.07)		
Differentiation	Well diff.	18 (34.6)	15 (32.60)	0.85
	Moderate diff.	28 (53.8)	27 (51.9)	
	Poor diff.	6 (11.53)	4 (8.69)	

Table 2: Operative parameters of D2 and D1 gastrectomy patients.

Operative parameters	D2	D1	P value
Mean blood loss (ml)	390.23±37.51	377.20±35.36	0.081
Mean operative time (min)	190±28.1	130±20.4	0.001
Average no of nodes retrieved	27.6±10.1	7±1.9	0.001
Mean hospital stay (days)	9±1.39	8.6±1.13	0.12

Table 3: Complications of D2 vs D1 gastrectomy.

Post-operative complications	D2, n=52 (%)	D1, n=46 (%)	P value
Atelectasis	10 (19.2)	8 (17.39)	0.84
Consolidation	3 (5.76)	2 (4.34)	0.76
Surgical site infection (SSI)	8 (15.38)	6 (13.04)	0.77
Duodenal leak	1 (1.92)	1 (2.17)	0.93
Intraabdominal collections	2 (3.57)	2 (4.34)	0.91
Anasomotic leaks	2 (3.57)	1 (2.17)	0.64
Bleeding	1 (1.92)	1 (2.17)	0.93
DVT	3 (5.76)	2 (4.34)	0.76
In hospital death	Nil	Nil	

Survival analysis

In D2 group the mean follow-up was 21.81±10.51 months and in D1 group it was 16.6±0.4.9 mo. The median survival was 26 months for the D2 and 19 months for the D1 group (p≤0.01). The length of survival in D2 group was significantly higher than in D1 group (Figure 1). Twenty-eight patients (53%) in the D2 and 15 patients (32%) in the D1 group were alive at last follow-up.
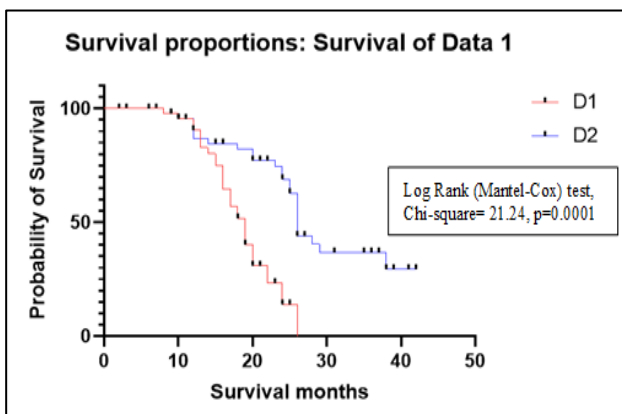

Figure 1: Kaplan-Meier survival curve.

DISCUSSION

Lymph node involvement is one of the strongest predictors of survival in gastric cancer. Studies have demonstrated the importance of both the numerical and anatomic extent of lymph node assessment in its impact on proper identification of nodal metastases as well as an important factor in achieving an R0 resection.[20] A number of studies including clinical trials have clearly demonstrated that within the same TNM-stage, the greater the number of lymph node assessed the better the prognosis.[21,22] There is now an increasing global consensus on performing a D2 lymphadenectomy for gastric cancer due to long-term results of large Western studies in conjunction with Eastern data.[12,23,24] Radical gastrectomy with D2 lymphadenectomy, first presented by Japanese surgeons, provides survival advantage and is the current standard of care for nonmetastatic, respectable T3/T4 GC.[12,25,26] However there is scarcity of data from Kashmir valley-a high incidence area of gastric cancer regarding the outcome of D2 gastrectomy.[5] In this study we did a direct comparison between D1 and D2 gastrectomy to analyze the clinical outcome and survival of D2 vs D1 gastrectomy. Our study revealed an improved survival of patients undergoing D2 dissection

compared to D1 gastrectomy (median survival 26 months for D2 group vs 19 months for the D1 group (p≤0.01). In a recent retrospective study conducted on 533 gastric cancer patients, the median survival by stages IIIB and IIIC were 28.0 and 14.8 months and D2-Lymph node dissection appeared as the major prognostic indicator of survival.[27] These findings are consistent with our results since most of our patients (90%) presented with the pathological stage III. several other studies have also reported potential survival benefits from D2 dissection.[12,28-30] The DGCT and MRC trials and few other studies failed to show any benefit for a D2 dissection after 5 years. This might be explained by scantiness of pretrial surgical training and the subsequent increased morbidity and mortality. Numerous studies have described a close association between the number of cases treated in a hospital and outcome in the surgical treatment of cancer.[31] An Italian trial with adequately trained surgeons showed that a D2 dissection can be performed safely in Western countries.[32] In Europe only the long-term follow-up of the DGCT showed a decrease in cancer-related deaths after D2 dissection.[12] Over 2/3 of patients in our series were male patients with mean age of 61 years. Male female ratio was 3:1 in both groups, which are comparable with other studies.[33-36] There was no significant difference in terms of age or gender between D1 and D2 groups (p>0.05) (Table 1). The male preponderance is in line with data from the American cancer surveillance database, surveillance, epidemiology, and end results (SEER).[37] In our study the most common tumour location in both groups was antropyloric (59.61% in D2 and 65% in D1) in both groups in contrast to earlier study conducted in year 2000 from Kashmir in which the commonest site of cancer was the body of stomach 40.7%, followed by the antrum (35.5%) suggesting a possible changing trend in the location of gastric tumor in this region.[38] Other reports from India also suggest distal/antral tumours as more common than proximal tumors.[39] In keeping with other reports from India, the most of the patients in our series presented at higher disease stage/stage III (92% in D2 and 86% in D1).[40] A similar trend was seen in other regions where population-based cancer screening is not done such as America, Europe, and China.[41-43] In D2 group lymph node yield was significantly higher than in the D1 group (p<0.001).We didn't find any significant difference in the mean blood loss during surgery in the two groups. Moreover, mean operative time was comparable in both groups. The average hospital stay was also similar in both groups. These findings were consistent with results of Shirkhande et al.[26] There was no difference in postoperative complications between two groups in our study.

Limitation

The limitation of this study is that the study involved experience of a single tertiary care referral center and is subject to referral bias. Further study period was short and thus short follow-up of the patients.

CONCLUSION

Our study indicates that D2 gastrectomy for advanced stage II /III gastric cancer improves the survival outcome in these patients without affecting overall hospital stay, morbidity and mortality as compared to D1 gastrectomy. D2gastrectomy should be the standard of treatment for operable gastric cancer. However further studies with larger sample size and longer follow up needs to be carried out to substantiate our findings. Surgery for GCs in high-volume centers might result in improved perioperative outcomes.

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