

## RESEARCH ARTICLE

# Mortality and Morbidity and Disease Free Survival after D1 and D2 Gastrectomy for Stomach Adenocarcinomas

AH Talaiezhadeh<sup>1</sup>, M Asgari<sup>1</sup>, MA Zargar<sup>1\*</sup>

## Abstract

**Background:** A number of randomized trials addressing alternative operative and multimodality approaches to gastric cancer have characterized early postoperative morbidity and mortality rates. The aim of this study was to compare mortality and morbidity and disease free survival after D1 and D2 gastrectomy for adenocarcinomas of the stomach. **Materials and Methods:** From June 2006 to January 2012, patients were selected according to information of the cancer administrator center of Ahvaz Jundishapur Medical University. The inclusion criteria were age between 20-85 years and histologically proven adenocarcinoma of the stomach without evidence of distant metastasis. Patients were excluded if they had previous or coexisting cancer or disability disease. In this research, D1 was compared to D2 gastrectomy. **Results:** 131 patients were randomised, 49 allocated to D1 and 82 to D2 gastrectomy. The two groups were comparable for age, sex, site of tumors, and type of resection performed. The overall post-operative morbidity rate was 17.5%. Complications developed in 14.2% of patients after D1 and in 19.5% of patients after D2 gastrectomy (p=0.07). Postoperative mortality rate was 0.8% (one death); it was 2% after D1 and 0% after D2 gastrectomy. In this research disease free-survival after 3 years was 71.2% with 63.2% after D1 and 76.8% after D2 gasterctomy. **Conclusions:** This study indicates that D2 gastrectomy with pancreas preservation is not followed by significantly higher morbidity and mortality than D1 resection. Based on the results of present study, D2 resection should be recommended as the standard surgical approach for resectable gastric cancer.

**Keywords:** : Gastric cancer - D1 gastrectomy - D2 gastrectomy - morbidity - mortality

*Asian Pac J Cancer Prev*, 16 (13), 5253-5256

## Introduction

Approximately 1 million case of gastric cancer are diagnosed annually making it the fourth most common malignancy worldwide (Ferlay et al., 2012). Although less frequent in the United States, gastric cancer remains a highly lethal disease associated with a 5-year survival of 28% overall (Howlader et al., 2012).

Resection remains the mainstay of therapy for patients with localized disease, although the importance of multimodality therapy in limiting recurrence is now well established. A number of randomized trials addressing alternative operative and multimodality approaches to gastric cancer have characterized early postoperative morbidity and mortality rates. Reported operative complication rates range widely from 9-46%, with Western series reporting morbidity in at least 25% of patients after gastrectomy. In these same studies, short-term postoperative mortality rates vary from 0.8 to 13%, with greater rates in Western studies (Cuschieri et al., 1996; Hartgrink et al., 2004; Yu et al., 2006; Cunningham et al., 2006; Sasako et al., 2008).

In Western Europe and the USA, optimum local control and survival seemed to be reached with surgery as a single-modality treatment, based mainly on two large European trials, the Dutch Gastric Cancer Trial (DGCT) (Hartgrink et al., 2004) and the UK Medical Research Council (MRC) randomized trial (Cuschieri et al., 1999). In both trials, standardized extended (D2) lymphadenectomy did not improve survival, and was associated with significantly higher morbidity and mortality compared with standardized limited (D1) lymphadenectomy. The unfavorable outcomes were mostly associated with pancreatico-splenectomy, which was an integral part of the D2 resection in both trials. In 2004, results from a study by Degiuli and colleagues (Degiuli et al., 2004) suggested a survival benefit after pancreas-preserving D2 resections, and in 2006, a Taiwanese single-institution trial (Wu et al., 2006) found that extended lymph-node dissection (D2) led to better results (no postoperative mortality) than D1 lymphadenectomy. In 2010, result from Songun and colleagues D2 lymphadenectomy is associated with lower loco regional recurrence and gastric-cancer-related death rates than D1 surgery (Songun et al., 2010).

<sup>1</sup>Department of Surgery, Cancer Research Center, Imam Khomeini Hospital, School of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran \*For correspondence: zargaramin@yahoo.com

The D2 procedure was also associated with significantly higher postoperative mortality, morbidity, and reoperation rates. Because a safer, spleen-preserving D2 resection technique is currently available in high-volume centers, D2 lymphadenectomy is the recommended surgical approach for patients with curable gastric cancer (Songun et al., 2010).

The current article report mortality and morbidity and free dieses survival after D1 and D2 gastrectomy for adenocarcinoma of gastric cancer of Ahvaz hospital from 2006-2012.

## Materials and Methods

The patient was selected according to information of Cancer research center of Ahvaz Jundishapur Medical University. Oral informed consent was obtained according to helsinki Convention. Hospitals of Ahvaz (center of Khuzestan province, southwest of Iran) were corporate in this research. The inclusion criteria was the age between 20-85 years old had histologically proven adenocarcinoma of the stomach without evidence of distance metastasis

**Table 1. Patient Characteristics**

	D1	D2	TOTAL
No. of patients	49	82	131
Age			
>60	22	57	79
<60	27	25	52
Sex			
Male	23	58	83
Female	26	24	52
Location of tumor			
Proximal	18	26	44
Medium	7	4	11
Distal	24	50	74
Diffuse	0	2	2
Type of resection			
Total gastrectomy	22	38	60
Distal gastrectomy	27	44	71
Neoadjuvant chemotherapy	10	18	28
Nemoadjuvant chemoradiotherapy	39	64	103

**Table 2. Post-operative Complication and Mortality**

	D1(49)	D2(82)	TOTAL(131)
Non-surgical complications	3(6.1%) Cardiac3	5(6.1%) Pulmonary3 Cardiac2	8(6.1%)
Surgical complications	4(8.1%) Duodenal leakage1 Jaundice1 Dehiscence fascia2	8(9.7%) Duodenalleakage1 Pancreatic leakage2 Abdominal abcess2 Dehiscence fascia3	12(9.1%)
Non-surgical andsurgical complications	0(0.0%)	3(4.8%) Pulmonary and Dehiscence fascia1 Cardiac and wound infection3	3(2.2%)
Total morbidity	7(14.2%)	16(19.5%)	23(17.5%)
Mortality	1(2%) Myocardial infarction	0	1(0.8%)

and were in adequate physical condition for D1 or D2 lymphadenectomy. Patients were excluded if they had previous or coexisting cancer or disability disease. The Questionnaire was consisted of information about the patient and the surgery procedures and free disease survival after three years. All the information of questionnaire is based on discharge sleeps and cases admitted in hospital.

The operative details of the two procedures respected the general rules for gastric cancer study, as described by the Japanese Research Society for Gastric Cancer in 1981. D1 resection entailed removal of the nodes usually defined as perigastric nodes ‘en bloc’ with the specimen, according to the JGCA. In the D2 arm, during total gastrectomy, the pancreas was removed only when it was suspected to be involved by the tumor (Maruyama et al., 1995).

The SPSS program (version 16) and R version 2.9.1 were used for statistical analysis. A two sided p value of 0-05 was considered statistically significant. Logistic regression was used to assess the influence of prognostic factors on postoperative mortality. The  $\chi^2$  test was applied to assess differences in proportions, and the log-rank test was used to assess the difference in survival and recurrence rates between groups, although the assumption of proportional hazards was not always satisfied.

## Results

From June 2006 to January 2012, 131patients that had our criteria were registered from Ahvaz hospital which participated in our research.49 patient (37.4%) underwent D1 gasrectomy and 82 patient (62.6%) underwent D2gasrectomy. The two groups were comparable with respect to median age, sex and location of the tumor and type of resection, as reported in Table 1.

Medium of pack red blood cell (PRBCs) given to patient in D1 and D2 gastrectomy during surgery. Average PRBCs that given during surgery in D1gastrectomy 2.14 units and in D2 gastrectomy 2.93 units (p<0.05).

The data on hospital stay excluded the early death, and consequently were based upon 131 patients. The median time of hospital stay was 8.71 days for D1 groups and 9.32 days for D2 group (p<0.05).

Table 2 gives data on post-operative course. Overall,

**Table 3. Randomized trial Comparing the extended lymphadenectomy**

	Mortality	Morbidity	NUMBER	Mortality	Morbidity	NUMBER
Cuschieri et al., (1999)	200D1	28	5	200D2	46	13
Bonenkenet al., (1999)	380D1	25	4	331D2	43	10
Hertginken et al., (2004)	380D1	25	4	331D2	43	10
Deguili et al., (2004)	76D1	10.5	1.3	86D2	16.3	0
Wu et al., (2006)	110D1	7.3	0	111D2	17.1	0
Sasako et al., (2008)	263D2	20.9	0.8	260D2+PAND	28	0.8

\*D1=standardized limited lymphadenectomy. D2 = standardized extended lymphadenectomy. PAND= Para-aortic nodal dissection.

the post-operative hospital morbidity was 17.5%. The rate was higher in the D2 group (19.5%) than in D1 group (14.2%), but this difference was not statistically significant ( $p=0.07$ ).

In both groups there were more complications after distal than after total gastrectomy, but again this difference was not significant. In both groups there were more complications after neoadjuvant chemoradiotherapy than after neoadjuvant chemotherapy, but again this difference was not significant ( $p=0.09$ ).

The overall hospital mortality was 0.7%. This death occurred after a D1 gastrectomy and was due to myocardial infarction; obviously no significant difference could be observed between D1 and D2 group as concerns mortality.

In this research disease free-survival after 3 years was overall 71.2 % that for D1 gastrectomy was 63.2% and for D2 gastrectomy 76.8%.

## Discussion

Gastric cancer is still a common lethal disease in western countries. For apparently resectable cancers, surgery offers the best loco regional control; but unfortunately, average 5-year survival rates for treated patients remain low in the western world, ranging from 15 to 30%. (Wanebo et al., 1993; Parikh et al., 1996) Over the years, Japanese surgeons have performed radical procedures involving extended lymphadenectomy, and have reported impressive survival figures with extremely low morbidity and mortality (Ferlay et al., 2012).

These preliminary data seem to confirm our reports. Overall morbidity is around 17.5%; although this figure is a slight underestimate due to the fact that the majority of centers have registered in their database major and minor nonsurgical but only major surgical complications, it is very low, and comparable to the best results shown in table 3. The overall morbidity is higher in D2 gastrectomy, but the difference between the two groups of patients is not statistically significant. Moreover, the rate of complications after D2 gastrectomy (19.5%) is considerably better than the rates of both arms (D1 and D2) in the English and Dutch trials (Cuschieri et al., 1999).

The importance of fascia dehiscence complications after extended gastric surgery, was confirmed by our data. Six out of the eleven complications registered after a D2 procedure were related to the fascia and wound infection.

Although the pancreas was not removed routinely during D2 total gastrectomies, two out of the eleven complications registered after a D2 procedure were related

to the pancreas.

Overall mortality was very low, at 0.8%. This rate is comparable to Deguili et al., (2004), and is different from the rates of reported in Cuschieri et al., (1999), Bonenken et al., (1999) and Hertginken et al., (2004).

The main outcomes of the surgical trials discussed in this paper are summarized in Table 3.

The result of this article show disease-free 3 years survival in D2 gasterctomy significantly more than D1 gastrectomy that similar to Songnn et al., (2010).

Our results suggest that a D2 resection provides better loco regional control and significantly better cancer specific survival compared with limited D1 surgery.

We believe D2 resection should be recommended as the standard surgical approach to resectable gastric cancer.

## Acknowledgements

This study was supported by Jundishapur university of Medical Science, Ahvaz, Iran.

## References

- Cunningham D, Allum WH, Stenning SP, et al (2006). Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med*, **355**, 11-20.
- Cuschieri A, Fayers P, Fielding J, et al (1996). Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomized controlled surgical trial. *Lancet*, **347**, 995-9.
- Cuschieri A, Weeden S, Fielding J, et al (1999). Patient survival after D1 and D2 resections for gastric cancer: long-term results of the MRC randomized surgical trial. *Br J Cancer*, **79**, 1522-30.
- Deguili M, Sasako M, Ponti A, et al (2004). Survival results of a multicentre phase II study to evaluate D2 gastrectomy for gastric cancer. *Br J Cancer*, **90**, 1727-32.
- Ferlay J, Soerjomataram I, Ervik M, et al (2012). Cancer incidence and mortality worldwide: IARC cancerbase No. 11 [Internet]. Lyon, France: international agency for research on cancer; 2013. Available from: <http://globocan.iarc.fr>. Accessed April 7, 2014.
- Hartgrink HH, van de Velde CJ, Putter H, et al (2004). Extended lymph node dissection for gastric cancer: who may benefit? Final results of the randomized Dutch gastric cancer group trial. *J Clin Oncol*, **22**, 2069-77.
- Howlader NA, Krapcho M, Neyman N, et al (2012). Cancer statistics review, 1975-m2010 (Vintage 2010 Populations). Bethesda, MD: national cancer institute. Available from: [http://seer.cancer.gov/csr/1975\\_2010\\_pops09/](http://seer.cancer.gov/csr/1975_2010_pops09/).
- Maruyama K, Sasako M, Kinoshita T, et al (1995). Pancreas-preserving total gastrectomy for proximal gastric cancer.

- Parikh D, Chagla L, Johnson M, et al (1996). D2 gastrectomy: lessons from a prospective audit of the learning curve. *Br J Surg*, **83**, 1595-9.
- Sasako M, Sano T, Yamamoto S, et al (2008). D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. *N Engl J Med*, **359**, 453-62.
- Songun I, Putter H, Kranenbarg EM, Sasako M, van de Velde CJ (2010). surgical treatment of gastric cancer: 15 Year follow-up result of the randomised nationwide Dutch D1D2 trial. *Lancet Oncol*, **11**, 439-49.
- Wanebo HJ, Kennedy BJ, Chmiel J, et al (1993). Cancer of the stomach. a patient care study by the American college of surgeons. *Am J Surg*, **218**, 583-92.
- Wu CW, Hsiung CA, Lo SS, et al (2006). Nodal dissection for patients with gastric cancer: a randomised controlled trial. *Lancet Oncol*, **7**, 309-15.
- Yu W, Choi GS, Chung HY (2006). Randomized clinical trial of splenectomy versus splenic preservation in patients with proximal gastric cancer. *Br J Surg*, **93**, 559-63.