

**Resectable Stomach Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. <i>CA Cancer J Clin.</i> 2013;63(1):11-30.	Review/Other-Tx	N/A	To provide the expected numbers of new cancer cases and deaths in 2013 nationally and by state, as well as an overview of current cancer statistics using data through 2009, including incidence, mortality, and survival rates and trends. The article also estimate the total number of deaths averted as a result of the decline in cancer death rates since the early 1990s, and provide the actual reported numbers of deaths in 2009 by age for the 10 leading causes of death and the 5 leading cancer types.	In 2009, Americans had a 20% lower risk of death from cancer than in 1991, when cancer death rates peaked. Despite this substantial progress, all demographic groups have not benefitted equally, particularly for cancers such as colorectal and breast, for which mortality declines have been attributed to earlier detection and improvements in treatment. Further progress can be accelerated by applying existing cancer control knowledge across all segments of the population, with an emphasis on those groups in the lowest socioeconomic bracket as well as other disadvantaged populations.	4
2. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. <i>CA Cancer J Clin.</i> 2011;61(2):69-90.	Review/Other-Tx	N/A	To provide an overview of the global cancer burden, including the estimated number of new cancer cases and deaths in 2008 and the incidence and mortality rates by region for selected cancer sites.	Based on the GLOBOCAN 2008 estimates, about 12.7 million cancer cases and 7.6 million cancer deaths are estimated to have occurred in 2008; of these, 56% of the cases and 64% of the deaths occurred in the economically developing world. Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females, accounting for 23% of the total cancer cases and 14% of the cancer deaths. Lung cancer is the leading cancer site in males, comprising 17% of the total new cancer cases and 23% of the total cancer deaths. Breast cancer is now also the leading cause of cancer death among females in economically developing countries, a shift from the previous decade during which the most common cause of cancer death was cervical cancer.	4
3. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations), National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2009_pop_s09/ , based on November 2011 SEER data submission, posted to the SEER web site, April 2012. Accessed June 12, 2013.	Review/Other-Tx	N/A	To provide SEER cancer statistics based on November 2011 SEER data submission.	No results stated in abstract.	4

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4. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. editors. AJCC cancer staging manual. 7th ed. New York, NY: Springer; 2010.	Review/Other-Tx	N/A	AJCC Cancer Staging Manual.	No results stated in abstract.	4
5. Rusch VW, Rice TW, Crowley J, Blackstone EH, Rami-Porta R, Goldstraw P. The seventh edition of the American Joint Committee on Cancer/International Union Against Cancer Staging Manuals: the new era of data-driven revisions. <i>J Thorac Cardiovasc Surg.</i> 2010;139(4):819-821.	Review/Other-Tx	N/A	Seventh edition of the American Joint Committee on Cancer/International Union Against Cancer Manual through intensive collaboration between the UICC and the AJCC and unprecedented efforts to develop and analyze large international databases leading to evidence-based revisions of the staging system.	No results stated in abstract.	4
6. Lauren P. The Two Histological Main Types of Gastric Carcinoma: Diffuse and So-Called Intestinal-Type Carcinoma. An Attempt at a Histo-Clinical Classification. <i>Acta Pathol Microbiol Scand.</i> 1965;64:31-49.	Review/Other-Tx	N/A	No abstract available.	No abstract available.	4
7. Marrelli D, Roviello F, de Manzoni G, et al. Different patterns of recurrence in gastric cancer depending on Lauren's histological type: longitudinal study. <i>World J Surg.</i> 2002;26(9):1160-1165.	Review/Other-Tx	412 patients	To evaluate the pattern of recurrence in patients submitted to potentially curative surgery for intestinal-type and diffuse-type gastric cancer.	Recurrence of disease was found in 41% of group A cases and 65% of group B cases (P<0.0001). The incidence of locoregional, hematogenous, and peritoneal recurrence was 20%, 19%, and 9% in group A, and 27%, 16%, and 34% in group B, respectively; the difference between the 2 groups was statistically significant for peritoneal recurrence (P<0.0001). Multivariate analysis identified as prognostic variables lymph node status, depth of invasion, extent of lymphadenectomy, advanced age, and male gender in group A; depth of invasion, extent of lymphadenectomy, tumor size, and lymph node status, in group B. Whereas, in group A the incidence of peritoneal recurrence was limited in all subgroups examined, in group B very high rates were observed in cases with infiltration of the serosa, involvement of second-level lymph nodes, or large tumor size.	4

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8. 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. <i>Cancer</i> . 2000;88(4):921-932.	Review/Other-Tx	50,169 gastric carcinoma cases	To provide an analysis of patients whose treatment included gastrectomy and to evaluate the "different disease" hypothesis as an explanation for superior Japanese results, outcomes for Japanese Americans were examined.	Stage-stratified 5-year and 10-year relative survival rates were as follows: Stage IA, 78%/65%; Stage IB, 58%/42%; Stage II, 34%/26%; Stage IIIA, 20%/14%; Stage IIIB, 8%/3%; and Stage IV, 7%/5%. Stage-stratified survival for Japanese Americans was higher. Males had a poorer prognosis than females, and the male-to-female ratio for Japanese Americans was lower. Proximal tumors were associated with a worse prognosis than distal tumors; the proportion of Japanese Americans with proximal disease was less than in the overall patient group. Japanese Americans underwent resection of adjacent organs less frequently. In this series, adjuvant therapy did not substantially affect survival. Overall, 20% were 10-year survivors; of these, 67% were lymph node negative and 98% had ≤8 involved lymph nodes. 5-year stage-stratified survival increased for cases with ≥15 lymph nodes analyzed. Stage migration was evident in cases with ≤15 nodes examined.	4
9. Janjigian YY, Kelsen DP. Genomic dysregulation in gastric tumors. <i>J Surg Oncol</i> . 2013;107(3):237-242.	Review/Other-Tx	N/A	To summarize the genetic and epigenetic changes thought to drive gastric cancer and the emerging paradigm of gastric cancer as 3 unique disease subtypes.	No results stated in abstract.	4
10. Hundahl SA, Menck HR, Mansour EG, Winchester DP. The National Cancer Data Base report on gastric carcinoma. <i>Cancer</i> . 1997;80(12):2333-2341.	Review/Other-Tx	57,407 gastric carcinoma cases	To summarize NCDB findings concerning gastric carcinoma in the US, focusing on the time period 1987-1993.	Stage-stratified 5-year relative survival for the 1987-1988 cohort was as follows: IA, 71%; IB, 56%; II, 37%; IIIA, 18%; IIIB, 11%; IV, 5%. Without noteworthy changes in stage distribution, demographics, or other factors, the proportion of patients treated by total gastrectomy is increasing slightly, but proximal gastrectomy for proximal cancers remains surprisingly popular. The proportion of cases receiving postoperative adjuvant treatment has declined slightly. Presumably because of advanced age and/or medical infirmity, a substantial proportion of U.S. patients with disease at every stage receive no treatment for cancer.	4

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11. Japanese Gastric Cancer A. Japanese Classification of Gastric Carcinoma - 2nd English Edition. <i>Gastric Cancer</i> . 1998;1(1):10-24.	Review/Other-Tx	N/A	To provide a common language for the clinical and pathological description of gastric cancer and thereby contribute to continued research and improvements in treatment and diagnosis.	No results stated in abstract.	4
12. Hartgrink HH, van de Velde CJ, Putter H, et al. Extended lymph node dissection for gastric cancer: who may benefit? Final results of the randomized Dutch gastric cancer group trial. <i>J Clin Oncol</i> . 2004;22(11):2069-2077.	Experimental-Tx	711 patients	To conduct a randomized trial to compare the results of a limited (D1) and extended (D2) lymph node dissection in terms of morbidity, mortality, long-term survival and cumulative risk of relapse.	A total of 711 patients (380 in the D1 group and 331 in the D2 group) were treated with curative intent. Morbidity (25% vs 43%; P<001) and mortality (4% vs 10%; P=.004) were significantly higher in the D2 dissection group. After 11 years there is no overall difference in survival (30% vs 35%; P=.53). Of all subgroups analyzed, only patients with N2 disease may benefit of a D2 dissection. The relative RR for morbidity and mortality is significantly higher than 1 for D2 dissections, splenectomy, pancreatectomy, and age >70 years.	1
13. McCulloch P, Nita ME, Kazi H, Gama-Rodrigues J. Extended versus limited lymph nodes dissection technique for adenocarcinoma of the stomach. <i>Cochrane Database Syst Rev</i> . 2004(4):CD001964.	Review/Other-Tx	N/A	To evaluate survival and peri-operative mortality after limited or extended lymph node removal during gastrectomy for cancer.	2 randomized and 2 nonrandomized comparisons of limited (D1) vs extended (D2) node dissection and 11 cohort studies of either D1 or D2 resection were analyzed. Meta-analysis of randomized trials did not reveal any survival benefit for extended lymph node dissection (RR = 0.95, 95% CI, 0.83 - 1.09), but showed increased postoperative mortality (RR 2.23, 95% CI, 1.45 - 3.45). Pre-specified subgroup analysis suggested a possible benefit in stage T3+ tumors (RR = 0.68, 95% CI, 0.42-1.10). Nonrandomized comparisons showed no significant survival benefit for extended dissection (RR 0.92, 95% CI, 0.83 - 1.02), but decreased mortality (RR 0.65, 95% CI, 0.45-0.93). Subgroup analysis showed apparent benefit in UICC stage II and IIIa. Observational studies of D2 resection reported much better mortality and survival than those of D1 surgery, but the settings were strikingly different.	4

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14. Songun I, Putter H, Kranenbarg EM, Sasako M, van de Velde CJ. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. <i>Lancet Oncol.</i> 2010;11(5):439-449.	Experimental-Tx	996 patients	To assess the effect of D2 compared with D1 surgery on disease recurrence and survival in patients treated with curative intent.	A total of 1,078 patients were entered in the study, of whom 996 were eligible. 711 patients underwent the randomly assigned treatment with curative intent (380 in the D1 group and 331 in the D2 group) and 285 had palliative treatment. Data were collected prospectively and all patients were followed up for a median time of 15.2 years (range 6.9-17.9 years). Analyses were done for the 711 patients treated with curative intent and were according to the allocated treatment group. Of the 711 patients, 174 (25%) were alive, all but 1 without recurrence. Overall 15-year survival was 21% (82 patients) for the D1 group and 29% (92 patients) for the D2 group (P=0.34). Gastric-cancer-related death rate was significantly higher in the D1 group (48%, 182 patients) compared with the D2 group (37%, 123 patients), whereas death due to other diseases was similar in both groups. Local recurrence was 22% (82 patients) in the D1 group vs 12% (40 patients) in D2, and regional recurrence was 19% (73 patients) in D1 vs 13% (43 patients) in D2. Patients who had the D2 procedure had a significantly higher operative mortality rate than those who had D1 (n=32 [10%] vs n=15 [4%]; 95% CI for the difference 2-9; P=0.004), higher complication rate (n=142 [43%] vs n=94 [25%]; 11-25; P<0.0001), and higher reoperation rate (n=59 [18%] vs n=30 [8%]; 5-15; P=0.00016).	1
15. Dikken JL, van de Velde CJ, Coit DG, Shah MA, Verheij M, Cats A. Treatment of resectable gastric cancer. <i>Therap Adv Gastroenterol.</i> 2012;5(1):49-69.	Review/Other-Tx	N/A	To investigate several preoperative and postoperative treatment strategies of resectable gastric cancer.	No results stated in abstract.	4

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16. Kim HH, Hyung WJ, Cho GS, et al. Morbidity and mortality of laparoscopic gastrectomy versus open gastrectomy for gastric cancer: an interim report--a phase III multicenter, prospective, randomized Trial (KLASS Trial). <i>Ann Surg.</i> 2010;251(3):417-420.	Experimental-Tx	342 patients	An interim report of an ongoing trial to evaluate the safety of this trial with respect to morbidity and mortality.	A total of 342 patients were randomized (LADG, 179 patients; ODG, 161 patients) between January 1, 2006 and July 19, 2007. There were no significant differences between the 2 groups in age, gender, and comorbidities. The postoperative complication rates of the LADG and ODG groups were 10.5% (17/179) and 14.7% (24/163), respectively (P=0.137). Reoperations were required in 3 cases each group. The postoperative mortality was 1.1% (2/179) and 0% (0/163) in the LADG and ODG groups (P=0.497), respectively.	1
17. Karpeh MS, Leon L, Klimstra D, Brennan MF. Lymph node staging in gastric cancer: is location more important than Number? An analysis of 1,038 patients. <i>Ann Surg.</i> 2000;232(3):362-371.	Observational-Tx	1,038 patients	To compare the impact of staging systems on the survival of 1,038 patients with gastric cancer undergoing resection for cure in a North American center.	The location of positive nodes did not significantly affect median survival when analyzed by the number of positive nodes. In contrast, the number of positive lymph nodes had a profound influence on survival. The new N categories served as a better discriminator of median survival when 15 or more nodes were examined. Survival estimates for stages II, IIIA, and IIIB were significantly influenced by examining 15 or more nodes.	1
18. Zhang BY, Yuan J, Cui ZS, Li ZW, Li XH, Lu YY. Evaluation of the prognostic value of the metastatic lymph node ratio for gastric cancer. <i>Am J Surg.</i> 2014;207(4):555-565.	Observational-Tx	399 patients	To investigate the prognostic value of metastatic LNR compared with pathologic node category.	LNR and pathologic node were correlated with OS. For the node-positive group with ≥ 15 LNs retrieved, pathologic node and LNR were independent prognostic factors, with the HR higher for LNR; neither was correlated with the number of retrieved lymph nodes. For the group with < 15 lymph nodes retrieved, LNR but not pathologic node was an independent prognostic factor, with LNR uncorrelated with the number of lymph nodes retrieved. For the node-negative group, the number of lymph nodes retrieved retained an independent prognostic factor.	1

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19. Bang YJ, Kim YW, Yang HK, et al. Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): a phase 3 open-label, randomised controlled trial. <i>Lancet</i> . 2012;379(9813):315-321.	Experimental-Tx	1,035 patients	To investigate the effect on DFS of adjuvant chemotherapy with capecitabine plus oxaliplatin after D2 gastrectomy compared with D2 gastrectomy only in patients with stage II-IIIb gastric cancer.	1,035 patients were randomized (520 to receive chemotherapy and surgery, 515 surgery only). Median follow-up was 34.2 months (25.4-41.7) in the chemotherapy and surgery group and 34.3 months (25.6-41.9) in the surgery only group. 3 year DFS was 74% (95% CI, 69-79) in the chemotherapy and surgery group and 59% (53-64) in the surgery only group (HR 0.56, 95% CI, 0.44-0.72; P<0.0001). Grade 3 or 4 adverse events were reported in 279/496 patients (56%) in the chemotherapy and surgery group and in 30/478 patients (6%) in the surgery only group. The most common adverse events in the intervention group were nausea (n=326), neutropenia (n=300), and decreased appetite (n=294).	1
20. Sakuramoto S, Sasako M, Yamaguchi T, et al. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. <i>N Engl J Med</i> . 2007;357(18):1810-1820.	Experimental-Tx	529 patients to the S-1 group and 530 patients to the surgery-only group	To test S-1 as adjuvant chemotherapy in patients with curatively resected gastric cancer.	The trial was stopped on the recommendation of the independent data and safety monitoring committee, because the first interim analysis, performed 1 year after enrollment was completed, showed that the S-1 group had a higher rate of OS than the surgery-only group (P=0.002). Analysis of follow-up data showed that the 3-year OS rate was 80.1% in the S-1 group and 70.1% in the surgery-only group. The HR for death in the S-1 group, as compared with the surgery-only group, was 0.68 (95% CI, 0.52-0.87; P=0.003). Adverse events of grade 3 or grade 4 (defined according to the Common Toxicity Criteria of the National Cancer Institute) that were relatively common in the S-1 group were anorexia (6.0%), nausea (3.7%), and diarrhea (3.1%).	1

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21. Paoletti X, Oba K, Burzykowski T, et al. Benefit of adjuvant chemotherapy for resectable gastric cancer: a meta-analysis. <i>JAMA</i> . 2010;303(17):1729-1737.	Review/Other-Tx	31 eligible trials (6,390 patients)	To perform an individual patient-level meta-analysis of all randomized control trials to quantify the potential benefit of chemotherapy after complete resection over surgery alone in terms of OS and DFS, and to further study the role of regimens, including monochemotherapy; combined chemotherapy with fluorouracil derivatives, mitomycin C, and other therapies but no anthracyclines; combined chemotherapy with fluorouracil derivatives, mitomycin C, and anthracyclines; and other treatments.	There were 1,000 deaths among 1,924 patients assigned to chemotherapy groups and 1,067 deaths among 1,857 patients assigned to surgery-only groups. Adjuvant chemotherapy was associated with a statistically significant benefit in terms of OS (HR, 0.82; 95% CI, 0.76-0.90; P<.001) and DFS (HR, 0.82; 95% CI, 0.75–0.90; P<.001). There was no significant heterogeneity for OS across randomized control trials (P=.52) or the 4 regimen groups (P=.13). 5-year OS rate increased from 49.6% to 55.3% with chemotherapy.	4
22. Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. <i>N Engl J Med</i> . 2006;355(1):11-20.	Experimental-Tx	250 patients with perioperative chemotherapy; 253 patients with surgery alone	To assess whether the addition of a perioperative regimen of infused fluorouracil to surgery improves outcomes among patients with potentially curable gastric cancer.	Infused fluorouracil-related adverse effects were similar to those previously reported among patients with advanced gastric cancer. Rates of postoperative complications were similar in the perioperative-chemotherapy group and the surgery group (46% and 45%, respectively), as were the numbers of deaths within 30 days after surgery. The resected tumors were significantly smaller and less advanced in the perioperative-chemotherapy group. With a median follow-up of 4 years, 149 patients in the perioperative-chemotherapy group and 170 in the surgery group had died. As compared with the surgery group, the perioperative-chemotherapy group had a higher likelihood of OS (HR for death, 0.75; 95% CI, 0.60–0.93; P=0.009; 5-year survival rate, 36% vs 23%) and of progression-free survival (HR for progression, 0.66; 95% CI, 0.53–0.81; P<0.001).	1

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23. Ychou M, Boige V, Pignon JP, et al. Perioperative chemotherapy compared with surgery alone for resectable gastroesophageal adenocarcinoma: an FNCLCC and FFCD multicenter phase III trial. <i>J Clin Oncol.</i> 2011;29(13):1715-1721.	Experimental-Tx	224 patients	A phase III trial to evaluate the benefit in OS of perioperative fluorouracil plus cisplatin in resectable gastroesophageal adenocarcinoma.	Compared with the S group, the CS group had a better OS (5-year rate 38% vs 24%; HR for death: 0.69; 95% CI, 0.50 to 0.95; P=.02); and a better DFS (5-year rate: 34% vs 19%; HR, 0.65; 95% CI, 0.48 to 0.89; P=.003). In the multivariable analysis, the favorable prognostic factors for survival were perioperative chemotherapy (P=.01) and stomach tumor localization (P<.01). Perioperative chemotherapy significantly improved the curative resection rate (84% vs 73%; P=.04). Grade 3 to 4 toxicity occurred in 38% of CS patients (mainly neutropenia) but postoperative morbidity was similar in the 2 groups.	1
24. Schuhmacher C, Gretschel S, Lordick F, et al. Neoadjuvant chemotherapy compared with surgery alone for locally advanced cancer of the stomach and cardia: European Organisation for Research and Treatment of Cancer randomized trial 40954. <i>J Clin Oncol.</i> 2010;28(35):5210-5218.	Experimental-Tx	144 patients	To examine the value of purely preoperative chemotherapy in a phase III trial with strict preoperative staging and surgical resection guidelines.	This trial was stopped for poor accrual after 144 patients were randomly assigned (72:72); 52.8% patients had tumors located in the proximal third of the stomach, including locally advanced adenocarcinoma of the stomach or esophagogastric junction type II and III. The International Union Against Cancer R0 resection rate was 81.9% after neoadjuvant chemotherapy as compared with 66.7% with surgery alone (P=.036). The surgery-only group had more lymph node metastases than the neoadjuvant group (76.5% vs 61.4%; P=.018). Postoperative complications were more frequent in the neoadjuvant arm (27.1% vs 16.2%; P=.09). After a median follow-up of 4.4 years and 67 deaths, a survival benefit could not be shown (HR, 0.84; 95% CI, 0.52–1.35; P=.466).	1

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25. Hallissey MT, Dunn JA, Ward LC, Allum WH. The second British Stomach Cancer Group trial of adjuvant radiotherapy or chemotherapy in resectable gastric cancer: five-year follow-up. <i>Lancet</i> . 1994;343(8909):1309-1312.	Experimental-Tx	436 patients	A prospective, randomized, controlled trial comparing survival following adjuvant mitomycin, doxorubicin, and fluorouracil; or RT to that of a control group undergoing surgery alone.	436 patients entered a prospective, randomized, controlled trial of adjuvant RT or cytotoxic chemotherapy with mitomycin, doxorubicin, and fluorouracil after gastrectomy for adenocarcinoma. After at least 5 years, there have been 372 deaths of which 7 were due to surgical complications and 327 from recurrent cancer. Following stratified randomization, 145 patients were allocated to surgery alone, 153 to receive adjuvant RT, and 138 to adjuvant combination chemotherapy. The overall 2-year and 5-year survival were 33% (95% CI, 31%–35%) and 17% (13%–21%). No survival advantage has been shown for those patients receiving either adjuvant therapy compared to those undergoing surgery alone. The 5-year survival for surgery alone was 20%, for surgery plus RT 12%, and for surgery plus chemotherapy 19%.	1
26. Zhang ZX, Gu XZ, Yin WB, Huang GJ, Zhang DW, Zhang RG. Randomized clinical trial on the combination of preoperative irradiation and surgery in the treatment of adenocarcinoma of gastric cardia (AGC)--report on 370 patients. <i>Int J Radiat Oncol Biol Phys</i> . 1998;42(5):929-934.	Experimental-Tx	370 patients	To define the role of RT before operation for adenocarcinoma of gastric cardia.	The 5- and 10-year survival rates of the R+S Group and the S Alone Group were 30.10% and 19.75%, 20.26% and 13.30%, respectively. The survival curves of these 2 groups diverged right from the beginning after the operation over the ninth year. Statistics by Kaplan-Meier log rank test proves that the difference is significant ($\chi^2 = 6.74$, $P=0.0094$). The immediate results were: resection rate 89.5% and 79.4% ($P<0.01$); pathologic stage after resection T2 12.9% and 4.5% ($P<0.01$), T4 40.3% and 51.3% ($P<0.05$), lymph node metastasis rates 64.3% and 84.9% ($P<0.001$); operative mortality rates 0.6% and 2.5%; intrathoracic leak rates 1.8% and 4.0%, respectively. The causes of failure were: local uncontrol and recurrence 38.6% vs 51.7% ($P<0.025$), regional lymph node metastasis 38.6% vs 54.6% ($P<0.005$), distant metastasis 24.3% vs 24.7%.	1

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27. Valentini V, Cellini F, Minsky BD, et al. Survival after radiotherapy in gastric cancer: systematic review and meta-analysis. <i>Radiother Oncol.</i> 2009;92(2):176-183.	Review/Other-Tx	N/A	A systematic review and meta-analysis was performed to assess the impact of RT on both 3- and 5-year survival in patients with resectable gastric cancer.	RT had a significant impact on 5-year survival. Using an intent to treat and a Per Protocol analysis, the overall 5-year RR was 1.26 (95% CI, 1.08-1.48; NNT=17) and 1.31 (95% CI, 1.04-1.66; NNT=13), respectively. Although the quality of the studies was variable, the data were consistent and no clear publication bias was found.	4
28. Goodman KA, Khalid N, Kachnic LA, et al. Quality Research in Radiation Oncology analysis of clinical performance measures in the management of gastric cancer. <i>Int J Radiat Oncol Biol Phys.</i> 2013;85(2):355-362.	Review/Other-Tx	250 patients	To determine national patterns of RT practice in patients treated for stage IB-IV (nonmetastatic) gastric cancer.	Clinical performance measures were computed for 250 eligible patients at 45 institutions (median age, 62 years; 66% male; 60% Caucasian). Using 2000 American Joint Committee on Cancer criteria, 13% of patients were stage I, 29% were stage II, 32% were stage IIIA, 10% were stage IIIB, and 12% were stage IV. Most patients (43%) were treated at academic centers, 32% were treated at large nonacademic centers, and 25% were treated at small to medium sized facilities. Almost all patients (99.5%) underwent computed tomography-based planning, and 75% had dose-volume histograms to evaluate normal tissue doses to the kidneys and liver. 70% of patients completed RT within the prescribed time frame. IMRT and image-guided RT were used in 22% and 17% of patients, respectively. Image-guided RT techniques included positron emission tomography (n=20), magnetic resonance imaging (n=1), respiratory gating and 4-dimensional CT (n=22), and on-board imaging (n=10). 19% of patients received preoperative RT.	4

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29. Moertel CG, Childs DS, Jr., Reitemeier RJ, Colby MY, Jr., Holbrook MA. Combined 5-fluorouracil and supervoltage radiation therapy of locally unresectable gastrointestinal cancer. <i>Lancet</i> . 1969;2(7626):865-867.	Experimental-Tx	187 patients	To determine the dosage of 5-fluorouracil that would produce definite but clinically tolerable toxicity when used in combination with RT applied to the abdomen or pelvis.	A prospective, controlled double-blind study involving a substantial number of patients suggests that 5-fluorouracil significantly augments the effectiveness of RT for locally unresectable carcinoma of the stomach, pancreas, and large bowel. It is also possible that rarely this therapy may be curative. This approach should not be advocated as routine treatment since the vast majority of these patients still die of their cancer; and, if the present results are not spurious, the method offers only a few extra months of life. These results should, however, serve as stimulus and foundation for continued study of augmented RT.	1
30. A comparison of combination chemotherapy and combined modality therapy for locally advanced gastric carcinoma. Gastrointestinal Tumor Study Group. <i>Cancer</i> . 1982;49(9):1771-1777.	Experimental-Tx	90 total patients	To compare the therapeutic effectiveness of combined RT and chemotherapy, with combination chemotherapy alone for patients with the locally advanced stage of gastric cancer.	The minimum period of follow-up is 4 years. During the initial 12 months, combined modality therapy was associated with an increased number of early deaths attributable to progression of tumor within the radiation field, or nutritional and hematologic complications. During the second to fourth years of follow-up, patients treated with combined RT have shown a significantly lower death rate compared to those treated with chemotherapy alone, with 8/45 patients alive and disease-free. Patients who received only chemotherapy, in contrast, have demonstrated a continued probability for tumor relapse and death, with 3/45 patients alive at 4 years.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
31. Ajani JA, Winter K, Okawara GS, et al. Phase II trial of preoperative chemoradiation in patients with localized gastric adenocarcinoma (RTOG 9904): quality of combined modality therapy and pathologic response. <i>J Clin Oncol.</i> 2006;24(24):3953-3958.	Observational-Tx	43 patients	To report on the strategy of preoperative chemoradiotherapy conducted at 20 Radiation Therapy Oncology Group (RTOG) institutions.	20 institutions participated. 49 patients were entered and 43 were assessable (12% stage IB; 37% stage II; and 52% stage III). The pathCR and R0 resection rates were 26% and 77%, respectively. At 1 year, more patients with pathCR (82%) are living than those with less than pathCR (69%). Grade 4 toxicity occurred in 21% of patients. Chemotherapy, RT, and surgery per protocol (including acceptable variations) occurred in 98%, 44%, and 63% of patients, respectively. A D2 dissection was performed in 50% of patients. Of 18 major RT variations, 17 were due to the lack of inclusion of the L3-4 vertebral interphase as prespecified.	1
32. Walsh TN, Noonan N, Hollywood D, Kelly A, Keeling N, Hennessy TP. A comparison of multimodal therapy and surgery for esophageal adenocarcinoma. <i>N Engl J Med.</i> 1996;335(7):462-467.	Experimental-Tx	58 patients assigned to multimodal therapy; 55 assigned to surgery	To conduct a prospective, randomized trial comparing surgery alone with combined chemotherapy, RT, and surgery.	Of the 58 patients assigned to multimodal therapy and the 55 assigned to surgery, 10 and 1, respectively, were withdrawn for protocol violations. At the time of surgery, 23/55 patients (42%) treated with preoperative multimodal therapy who could be evaluated had positive nodes or metastases, as compared with 45/55 patients (82%) who underwent surgery alone (P<0.001). 13/52 patients (25%) who underwent surgery after multimodal therapy had complete responses as determined pathologically. The median survival of patients assigned to multimodal therapy was 16 months, as compared with 11 months for those assigned to surgery alone (P=0.01). At 1-, 2-, and 3-years, 52%, 37%, and 32%, respectively, of patients assigned to multimodal therapy were alive, as compared with 44%, 26%, and 6% of those assigned to surgery, with the survival advantage favoring multimodal therapy reaching significance at 3 years (P=0.01).	1

**Resectable Stomach Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Ajani JA, Mansfield PF, Crane CH, et al. Paclitaxel-based chemoradiotherapy in localized gastric carcinoma: degree of pathologic response and not clinical parameters dictated patient outcome. <i>J Clin Oncol.</i> 2005;23(6):1237-1244.	Observational-Tx	41 patients	To evaluate paclitaxel-based induction chemotherapy and chemoradiotherapy in patients with localized gastric or gastroesophageal adenocarcinoma to determine its feasibility, impact on the R0 resection rate, type of pathologic response, OS, and DFS.	41 patients were enrolled. Most carcinomas were proximal (83%) and pretreatment stage EUST3 (85%). 40 patients (98%) underwent surgery, and 78% had an R0 resection. We observed a pathCR rate of 20% and a pathologic partial response rate of 15% (<10% residual cancer cells in the resected specimen). No pretreatment parameter (sex, cancer location, baseline T stage, or baseline N stage) predicted the type of postsurgery pathologic response, OS, or DFS. However, pathCR (P=.02), pathCR + pathologic partial response (P=.006), R0 resection (P<.001), and postsurgery T and N stages (P=.01 and P<.001, respectively) were associated with OS. Same parameters were significantly correlated with DFS. Toxicity was manageable.	1
34. Balandraud P, Moutardier V, Giovannini M, et al. Locally advanced adenocarcinomas of the gastric cardia: results of pre-operative chemoradiotherapy. <i>Gastroenterol Clin Biol.</i> 2004;28(8-9):651-657.	Observational-Tx	42 patients	To examine the effects of preoperative chemoradiotherapy in locally advanced adenocarcinomas of the gastro-esophageal junction.	38 patients underwent subsequent surgery and complete resection was achieved in 34. Operative mortality was 13.2% (5/38). A histological complete response was observed in 6 patients. Median survival was 23 months (range: 15-31) and median DFS was 19 months (range: 15-23). At 1- and 2-years, 70.7% and 45.6% of the patients were alive, respectively. The pTNM status, node involvement and tumor size were predictors of survival.	2

**Resectable Stomach Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Hazard L, O'Connor J, Scaife C. Role of radiation therapy in gastric adenocarcinoma. <i>World J Gastroenterol.</i> 2006;12(10):1511-1520.	Review/Other-Tx	N/A	To review the role of RT in the treatment of resectable and unresectable gastric carcinoma, focusing on current recommendations in the United States.	Outcomes in patients with gastric cancer in the United States remain disappointing, with a 5-year OS rate of approximately 23%. Given high rates of local-regional control following surgery, a strong rationale exists for the use of adjuvant RT. Randomized trials have shown superior local control with adjuvant RT and improved OS with adjuvant chemoradiation. The benefit of adjuvant chemoradiation in patients who have undergone D2 lymph node dissection by an experienced surgeon is not known, and the benefit of adjuvant RT in addition to adjuvant chemotherapy continues to be defined. In unresectable disease, chemoradiation allows long-term survival in a small number of patients and provides effective palliation. Most trials show a benefit to combined modality therapy compared to chemotherapy or RT alone. The use of preoperative, intra-operative, 3D-CRT and IMRT in gastric cancer is promising but requires further study.	4

**Resectable Stomach Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
36. Moertel CG, Childs DS, O'Fallon JR, Holbrook MA, Schutt AJ, Reitemeier RJ. Combined 5-fluorouracil and radiation therapy as a surgical adjuvant for poor prognosis gastric carcinoma. <i>J Clin Oncol</i> . 1984;2(11):1249-1254.	Experimental-Tx	62 patients	This study does not establish 5-fluorouracil plus radiation as effective surgical adjuvant therapy for gastric cancer but suggests this approach as a possible fruitful area for continued research. This study also illustrates the potential problems that may be encountered in interpreting results when patients are randomized to a study before consent is obtained.	62 patients with resectable but poor-prognosis gastric carcinoma were randomized to either no surgical adjuvant therapy or treatment with 5-fluorouracil (15 mg/kg by rapid intravenous injection X 3) plus radiation (3,750 rad in 24 fractions) initiated 3 1/2 to 6 weeks postoperatively. Informed consent was obtained after randomization and only from the 39 randomized to treatment. 10 patients refused their treatment assignment. The 5-year survival rate for patients randomized to treatment was 23%, and for those randomized to no treatment, 4% (P<.05). Both the survival distributions and the alive-without-recurrence distributions were significantly different for the 2 groups (P=.024) and favored treatment assignment. When the treatment assignment group was broken down to those patients actually receiving treatment and those refusing, 5-year survival rates were: treated, 20%; treatment refusal, 30%; controls, 4%; the 3 survival distributions were not significantly different. 39% of patients actually treated had a local-regional component of first clinical recurrence compared with 54% of those who received no treatment.	1
37. Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. <i>N Engl J Med</i> . 2001;345(10):725-730.	Observational-Tx	556 patients	To investigate the effect of surgery plus postoperative (adjuvant) chemoradiotherapy on the survival of patients with resectable adenocarcinoma of the stomach or gastroesophageal junction.	The median OS in the surgery-only group was 27 months, as compared with 36 months in the chemoradiotherapy group; the HR for death was 1.35 (95% CI, 1.09-1.66; P=0.005). The HR for relapse was 1.52 (95% CI, 1.23-1.86; P<0.001). 3 patients (1%) died from toxic effects of the chemoradiotherapy; grade 3 toxic effects occurred in 41% of the patients in the chemoradiotherapy group, and grade 4 toxic effects occurred in 32%.	1

**Resectable Stomach Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Smalley SR, Benedetti JK, Haller DG, et al. Updated analysis of SWOG-directed intergroup study 0116: a phase III trial of adjuvant radiochemotherapy versus observation after curative gastric cancer resection. <i>J Clin Oncol.</i> 2012;30(19):2327-2333.	Experimental-Tx	559 patients	To perform a randomized phase III trial of postoperative radiochemotherapy in those at moderate risk of locoregional failure following surgery.	OS and relapse-free survival data demonstrate continued strong benefit from postoperative radiochemotherapy. The HR for OS is 1.32 (95% CI, 1.10-1.60; P=.0046). The HR for relapse-free survival is 1.51 (95% CI, 1.25-1.83; P<.001). Adjuvant radiochemotherapy produced substantial reduction in both overall relapse and locoregional relapse. Second malignancies were observed in 21 patients with RT vs 8 with observation (P=.21). Subset analyses show robust treatment benefit in most subsets, with the exception of patients with diffuse histology who exhibited minimal nonsignificant treatment effect.	1
39. Chakravarthy AB, Catalano PJ, Mondschein JK, et al. Phase II Trial of Paclitaxel/Cisplatin Followed by Surgery and Adjuvant Radiation Therapy and 5-Fluorouracil/Leucovorin for Gastric Cancer (ECOG E7296). <i>Gastrointest Cancer Res.</i> 2012;5(6):191-197.	Experimental-Tx	38 patients	Evaluate the tolerability and toxicity profile of neoadjuvant paclitaxel and cisplatin and postoperative chemoradiation therapy with 5-fluorouracil/leucovorin in high-risk gastric patients. Determine the pathologic response rate of gastric tumors to neoadjuvant paclitaxel and cisplatin chemotherapy, and estimate progression-free survival and OS.	From 1999 to 2002, 38 eligible patients were enrolled; 35 completed induction chemotherapy, and 29 went on to surgery. 16 patients did not develop metastatic progression, 10 developed metastatic disease, and 12 were unevaluable. There were no PathCR s after induction therapy. 25/38 patients suffered grade 3-4 toxicities during induction paclitaxel/cisplatin. 6/7 patients who received postoperative therapy suffered grade 3-4 toxicities. Only 3/38 (7.9%) eligible patients completed all assigned treatment. The median OS was 1.6 years, and the 2-year survival was 40%.	1

**Resectable Stomach Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
40. Dikken JL, Jansen EP, Cats A, et al. Impact of the extent of surgery and postoperative chemoradiotherapy on recurrence patterns in gastric cancer. <i>J Clin Oncol.</i> 2010;28(14):2430-2436.	Review/Other-Tx	91 patients	To retrospectively compare survival and recurrence patterns in 2 phase I/II studies evaluating more intensified postoperative chemoradiotherapy with those from the Dutch Gastric Cancer Group Trial (DGCT) that randomly assigned patients between D1 and D2 lymphadenectomy.	With a median follow-up of 19 months in the chemoradiotherapy group, local recurrence rate after 2 years was significantly higher in the surgery only (DGCT) group (17% vs 5%; P=.0015). Separate analysis of chemoradiotherapy patients who underwent a D1 dissection (n = 39) vs DGCT-D1 (n = 369) showed fewer local recurrences after chemoradiotherapy (2% vs 8%; P=.001), whereas comparison of chemoradiotherapy-D2 (n = 25) vs DGCT-D2 (n = 325) demonstrated no significant difference. Chemoradiotherapy significantly improved survival after a microscopically irradical (R1) resection. The Maruyama Index of Unresected Disease was found to be a strong independent predictor of survival.	4
41. Kim S, Lim DH, Lee J, et al. An observational study suggesting clinical benefit for adjuvant postoperative chemoradiation in a population of over 500 cases after gastric resection with D2 nodal dissection for adenocarcinoma of the stomach. <i>Int J Radiat Oncol Biol Phys.</i> 2005;63(5):1279-1285.	Observational-Tx	544 patients received postoperative chemoradiation; 446 patients received surgery	To investigate the effect of postoperative chemoradiotherapy on the relapse rate and survival rate of patients with D2-resected gastric cancer.	The median duration of OS was significantly longer in the chemoradiation group than in the comparison group (95.3 months vs 62.6 months), which corresponds to a HR for death of 0.80 (P=0.0200) or a reduction of 20% in the risk of death in the chemoradiation group. The 5-year survival rates were consistently longer in the chemoradiation group at Stages II, IIIA, IIIB, and IV than those in the comparison group. The chemoradiation was associated with increases in the median duration of relapse-free survival (75.6 months vs 52.7 months; HR for relapse, 0.80, P=0.0160).	1

**Resectable Stomach Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Lee J, Lim do H, Kim S, et al. Phase III trial comparing capecitabine plus cisplatin versus capecitabine plus cisplatin with concurrent capecitabine radiotherapy in completely resected gastric cancer with D2 lymph node dissection: the ARTIST trial. <i>J Clin Oncol</i> . 2012;30(3):268-273.	Experimental-Tx	458 patients	To investigate the role of postoperative chemoradiotherapy therapy in patients with curatively resected gastric cancer with D2 lymph node dissection.	Of 458 patients, 228 were randomly assigned to the capecitabine plus cisplatin arm and 230 to the capecitabine plus cisplatin/RT with capecitabine arm. Treatment was completed as planned by 75.4% of patients (172/228) in the capecitabine plus cisplatin arm and 81.7% (188/230) in the capecitabine plus cisplatin/RT with capecitabine arm. Overall, the addition of RT to capecitabine plus cisplatin chemotherapy did not significantly prolong DFS (P=.0862). However, in the subgroup of patients with pathologic lymph node metastasis at the time of surgery (n=396), patients randomly assigned to the capecitabine plus cisplatin/RT with capecitabine arm experienced superior DFS when compared with those who received capecitabine plus cisplatin alone (P=.0365), and the statistical significance was retained at multivariate analysis (estimated HR, 0.6865; 95% CI, 0.4735 to 0.9952; P=.0471).	1
43. NCCN Clinical Practice Guidelines in Oncology. Gastric Cancer. Version 2.2013. 2013; Available at: http://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf . Accessed June 12, 2013.	Review/Other-Tx	N/A	To provide NCCN Clinical Practice Guidelines in Oncology on Gastric Cancer.	No results stated in abstract.	4

**Resectable Stomach Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Ringash J, Perkins G, Brierley J, et al. IMRT for adjuvant radiation in gastric cancer: a preferred plan? <i>Int J Radiat Oncol Biol Phys.</i> 2005;63(3):732-738.	Review/Other-Tx	20 patients	To assess the potential advantage of IMRT over conformal planning for postoperative adjuvant RT in patients with gastric carcinoma.	In 18 (90%) of 20 cases, both oncologists chose the same plan. Cases with disagreement were given to a third “blinded” reviewer. A “preferred plan” could be determined in 19 (95%) of 20 cases. IMRT was preferred in 17 (89%) of 19 cases. In 4 (20%) of 20 IMRT plans at least 1 radiation oncologist had safety concerns because of the spinal cord dose (3 cases) or small bowel dose (2 cases). Of 42 ratings, IMRT was thought to provide better planning target volume coverage in 36 (86%) and better sparing of the spinal cord in 31 (74%) of 42, kidneys in 29 (69%), liver in 30 (71%), and heart in 29 (69%) of 42 ratings. The median underdose volume (1.7 vs 4.1 cm ³), maximal dose to the spinal cord (36.85 vs 45.65 Gy), and dose to 50% of the liver (17.29 vs 27.97), heart (12.89 vs 15.50 Gy), and left kidney (15.50 vs 16.06 Gy) were lower with IMRT than with the conformal plans.	4
45. Minn AY, Hsu A, La T, et al. Comparison of intensity-modulated radiotherapy and 3-dimensional conformal radiotherapy as adjuvant therapy for gastric cancer. <i>Cancer.</i> 2010;116(16):3943-3952.	Observational-Tx	57 patients	To compare the clinical outcomes and toxicity in patients treated with postoperative chemoradiotherapy for gastric cancer using IMRT vs 3D-CRT.	The 2-year OS rates for 3D-CRT vs IMRT were 51% and 65%, respectively (P=.5). Four locoregional failures occurred each in the 3D-CRT (15%) and the IMRT (13%) patients. Grade ≥2 acute gastrointestinal toxicity was found to be similar between the 3D-CRT and IMRT patients (61.5% vs 61.2%, respectively) but more treatment breaks were needed (3 vs 0, respectively). The median serum creatinine from before RT to most recent creatinine was unchanged in the IMRT group (0.80 mg/dL) but increased in the 3D-CRT group from 0.80 mg/dL to 1.0 mg/dL (P=.02). The median kidney mean dose was higher in the IMRT vs the 3D-CRT group (13.9 Gy vs 11.1 Gy; P=.05). The median kidney V20 was lower for the IMRT vs the 3D-CRT group (17.5% vs 22%; P=.17). The median liver mean dose for IMRT and 3D-CRT was 13.6 Gy and 18.6 Gy, respectively (P=.19). The median liver V30 was 16.1% and 28%, respectively (P<.001).	2

**Resectable Stomach Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Chakravarty T, Crane CH, Ajani JA, et al. Intensity-modulated radiation therapy with concurrent chemotherapy as preoperative treatment for localized gastric adenocarcinoma. <i>Int J Radiat Oncol Biol Phys.</i> 2012;83(2):581-586.	Observational-Tx	25 patients	To evaluate dosimetric parameters, acute toxicity, pathologic response, and local control in patients treated with preoperative IMRT and concurrent chemotherapy for localized gastric adenocarcinoma.	Target coverage, expressed as the ratio of the minimum dose received by 99% of the planning target volume to the prescribed dose, was a median of 0.97 (range, 0.92-1.01). The median V(30) (percentage of volume receiving at least 30 Gy) for the liver was 26%; the median V(20) (percentage of volume receiving at least 20 Gy) for the right and left kidneys was 14% and 24%, respectively; and the median V(40) (percentage of volume receiving at least 40 Gy) for the heart was 18%. Grade 3 acute toxicity developed in 14 patients (56%), including dehydration in 10, nausea in 8, and anorexia in 5. Grade 4 acute toxicity did not develop in any patient. There were no significant differences in the rates of acute toxicity, hospitalization, or feeding tube use in comparison to those in a group of 50 patients treated with preoperative 3D-CRT with concurrent chemotherapy. R0 resection was obtained in 20 patients (80%), and pathCR occurred in 5 (20%).	2

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
 - a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
 - b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
 - c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

3D-CRT = 3-D conformal radiotherapy

CI = Confidence interval

DFS = Disease-free survival

HR = Hazard ratio

IMRT = Intensity-modulated radiotherapy

LADG = Laparoscopic-assisted distal gastrectomy

LNR = Lymph node ratio

ODG = Open gastrectomy

OS = Overall survival

PathCR = Pathologic complete response

RR = Risk ratio

RT = Radiation therapy