

## SURGICAL TREATMENT OF GASTRIC CANCER

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### Summary

Gastric cancer remains one of the commonest causes of cancer death worldwide. According to Croatian Cancer Registry, 1282 new patients with gastric cancer were reported in year 2003 in Croatia. Radical surgical resection is the only potentially curable method of treatment of these patients. Since lymph node metastases occur during the early stages of disease, regional lymphadenectomy is recommended as a part of radical gastrectomy but there is no worldwide consensus about the extent of the lymphadenectomy needed to achieve optimal results. Japanese surgeons first introduced radical D2 lymphadenectomy with distal splenopancreatectomy and achieved impressive long term survival results using this method. No western randomized trial showed better survival results after D2 lymphadenectomy compared to D1, but patients after D2 had significantly higher postoperative mortality and morbidity. European authors showed improved survival rates without increase in morbidity and mortality in patients treated by modified D2 operation – D2 extent lymphadenectomy without pancreaticosplenectomy. Our aim in this paper is to give a review of current surgical therapy of gastric cancer and to show postoperative results in patients operated for gastric cancer in our surgical department from year 2001 to 2005.

KEY WORDS: *gastric cancer, surgical treatment, lymphadenectomy*

### KIRURŠKO LIJEČENJE RAKA ŽELUCA

#### Sažetak

Rak želuca još uvijek je jedan od najčešćih uzroka smrti od raka u cijelome svijetu. Prema podacima Hrvatskog registra za rak u Hrvatskoj je u 2003. godini zabilježeno 1282 novih bolesnika s rakom želuca. Radikalna kirurška resekcija za te je bolesnike jedina metoda liječenja s mogućnošću izlječenja. Kako se metastaze limfnih čvorova pojavljuju u ranim stadijima bolesti, u sklopu radikalne gastrektomije preporučuje se regionalna limfadenektomija, ali nije postignut konsenzus u cijelome svijetu o opsegu limfadenektomije koju je potrebno provesti da se postignu optimalni rezultati. Japanski su kirurzi prvi uveli radikalnu D2 limfadenektomiju s distalnom splenopankreotomijom i primjenom te metode dugoročno postigli zavidne rezultate s obzirom na preživljenje. Nijedno randomizirano kliničko ispitivanje koje se provodilo na Zapadu nije pokazalo bolje rezultate preživljenja nakon provedene D2 limfadenektomije uspoređeno s D1, ali je nakon D2 u bolesnika zabilježena znatno veća stopa postoperacijske smrtnosti i obolijevanja. Europski autori su predložili bolju stopu preživljenja bez povećanog obolijevanja i smrtnosti u bolesnika liječenih modificiranim D2 zahvatom – D2 limfadenektomijom bez pankreatikosplenektomijom. U ovome radu nastojali smo dati pregled kirurških oblika liječenja raka želuca koji se danas primjenjuju te prikazati postoperativne rezultate u bolesnika koji su zbog raka želuca operirani na našem kirurškom odjelu od 2001. do 2005. godine.

KLJUČNE RIJEČI: *rak želuca, kirurško liječenje, limfadenektomija*

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## INTRODUCTION

Despite the steady and well-known decline in gastric cancer incidence in the Western countries, gastric cancer is still the second most common cancer worldwide, mostly due to high incidence in Far Eastern countries (Japan, China, Korea) and in many developing countries. In Western countries, gastric cancer remains one of the major cause of cancer death. With incidence of 36 cases per 100,000 men and 17 cases per 100,000 women, Central and Eastern European countries are in the middle, between Japan (78/100,000 men, 33/100,000 women) and USA (8.4/100,000 men, 4/100,000 woman). According to Croatian Cancer Registry, 1,282 new patients with gastric cancer were reported in Croatia in 2003. The decline in gastric cancer incidence is mostly due to decline in the intestinal type, localized in the distal portion of the stomach. On the other hand, the steady rise in incidence of diffuse type of cancer, located in the more proximal portions of the stomach or in the gastroesophageal junction, has been documented. Radical surgical resection remains the only treatment modality offering the possibility of cure for patients with gastric cancer. In order to achieve the best possible results in gastric cancer treatment, early diagnosis is of vital importance.

## STAGING AND DIAGNOSIS

Accurate and uniform staging is essential to make operative treatment strategy, to assess response to the treatment and to predict prognosis. Unfortunately, the staging system for gastric cancer has changed many times and is not identical in the USA, Europe and Asia. The most widely used staging system is the 5<sup>th</sup> edition of TNM cancer classification published in 1997 by AJCC (American Joint Committee on Cancer)/UICC (Union Internationale Contra la Cancrum)(1). The T status is divided in 4 levels depending on depth of invasion with recent subdivision of the T2 level into T2a (invasion of muscularis propria) and T2b (invasion of subserosa). According to the 5<sup>th</sup> ed. TNM classification, the N status reflects the number of lymph nodes involved with the requirement that at least 15 lymph nodes be removed for the patient to be properly staged

(N0 – no lymph node metastasis, N1 – metastasis in 1 to 6 lymph nodes, N2 – metastasis in 7 to 15 lymph nodes, N3- metastasis in more than 15 lymph nodes). This is a shift from the 4<sup>th</sup> ed. TNM classification (1988) where the anatomical location of the positive nodes and not their number was crucial; N1 and N2 node metastases were defined as within 3 cm or more than 3 cm of the primary tumor. The Japanese staging system defines nodal status by anatomic location of the tumor, and the proximity of the positive nodes to the tumor. There are also several important prognostic factors incorporated in Japanese staging system. The location of primary tumor is determined by dividing the stomach in three anatomic regions: the upper third (fundus and cardia), the middle third (corpus) and the lower third (antrum). The location of tumor determines the extent of gastric resection and influences the classification of nodal involvement. The T status in Japanese classification is determined not only by the depth of invasion through the gastric wall, but also according to the pattern of subserosal and serosal involvement and other pathological features of the tumor. After TNM classification patients are grouped in 4 different stages of disease, where stages I to III represent locoregional resectable disease, and the stage IV represents metastatic systemic disease. In order to implement surgical therapeutic efforts in staging and prognostic purposes, residual tumor (R) classification is being used to complement the TNM staging system (R0 – no residual tumor after resection, R1 – microscopic residual tumor, R2 - macroscopic residual tumor). The TNM classification has proved to have good prognostic value and is simpler to use than Japanese classification.(2)

Careful diagnostic preoperative regimen is necessary and consists of esophagogastroduodenoscopy and biopsy of the suspect lesion (position and the size of the tumor, histological type of the tumor), abdominal ultrasound, CT scan of the abdomen and pelvis (primary tumor, metastasis, ascites, lymph nodes), chest x-ray and complete laboratory studies. Endoscopic ultrasound (EUS) can be helpful in determining the depth of gastric wall invasion and lymph node assessment. In case of proximal tumors, chest CT scan can be helpful in determining the esophageal involve-

ment. Because of limitations of abdominal CT scan (inability to differentiate hepatic or peritoneal metastasis smaller than 5 mm, inaccurate lymph node assessment) diagnostic laparoscopy with cytological analysis of peritoneal fluid is valuable method for selecting patients for potentially curative resection or palliation if indicated.

## SURGICAL TREATMENT

In the absence of disseminated disease, aggressive surgical resection remains the mainstay of curative therapy. Surgical resection of gastric cancer involves a wide enough resection to achieve negative margins as well as en block resection of lymph nodes and any adherent organ. A gross margin of 5 to 6 cm is usually needed to ensure adequate negative margins by final histological analysis. The specific type of resection will depend on the location, stage and pattern of spread of particular tumor. In proximal gastric cancers (Siewert Classification type II and III) total gastrectomy and Roux-en-Y reconstruction is the operation of choice, as in the midstomach (corpus) tumors. For the cancers in the antral (distal) region, which comprise about 35% gastric cancers, prospective randomized trials have revealed no survival advantage to performing total gastrectomy as opposed to a distal subtotal gastrectomy. In addition, in most series, the quality of life after a subtotal gastrectomy is superior to that after a total gastrectomy and therefore subtotal gastrectomy should be performed when an adequate resection margin can be obtained (5 to 6 cm).

The extent of lymph node dissection remains the most controversial issue in surgical management of gastric cancer. The Japanese surgeons practice radical lymph node dissection, including removal of paraaortic lymph nodes in some cases(6). Retrospective studies from Japan suggest that extended lymphadenectomy can improve survival, particularly in patients with stage II or III disease, with overall reported 5-year survival rates of over 60%, compared with 20% in most European studies. By looking at these results, one must take into account high proportion early gastric cancer or stage I patients in Japanese cohorts (over 50%), due to extensive gastric cancer screening policies in Japan (8). The

majority of Western surgeons believe that the lymph node metastases represent a marker of systemic disease, and that such a radical lymphadenectomy will rarely improve the overall survival but may instead increase morbidity and mortality associated with the surgical procedure.

The extent of lymph node dissection is designated by "D". A D1 dissection includes removal of the perigastric lymph nodes, greater and the lesser omentum. A classis D2 dissection also includes lymph nodes along the hepatic, left gastric, celiac and splenic arteries, lymph nodes in the splenic hilum, as well as the bursa omentalis and the front leave of the transverse mesocolon. D3 dissection includes nodes in porta hepatic, retropancreatic and periaortic regions. For a curative resection, it is recommended that the level of dissection is one level greater than the highest echelon of involved lymph nodes (4). Today, Japanese centers and many specialized centers for surgical oncology in Western countries recommend standard D2 resection, with the best centers reporting perioperative mortality rates of less than 2%(8).

There are two European prospective randomized trials examining the extent of lymphadenectomy for gastric cancer, namely, comparing D1 and D2 dissection. In the Dutch trial (5) of 711 patients undergoing R0 resection, overall morbidity and mortality were significantly higher in the D2 group with no advantage in survival. Problem of this study was also the failure to remove the required number of lymph nodes that was present in 36% of patients in D1 group and 51% in patients undergoing D2 resection. It was also noted in the Dutch trial that the majority of morbidity and mortality of the D2 resection was secondary to removal of the distal pancreas and spleen. Further analysis of this trial, however, revealed that patients having undergone a D2 resection had a decreased local recurrence rate and patients with stage II and III have a survival advantage when undergoing a D2 resection. The MRC (United Kingdom) (3) trial randomized total of 400 patients to D1 or D2 resection and also found an increase in morbidity and mortality following a D2 resection, due to removal of the distal pancreas and spleen. Study showed no survival benefit for patients who underwent D2 resection. In 2004, the Italian Gastric Cancer Study

Group published results of their cohort of 191 consecutive patients with resectable gastric cancer who underwent pancreas-preserving D2 dissection, and they report postoperative mortality of 3.1% and 5-year overall survival of 55%. Authors argue that these good results are due to experienced high volume centers and well-trained experienced surgeons who participated in this multicentric trial (9). Japanese surgeons conducted trial examining even more aggressive resections – D3 versus D2. Over 500 patients have been enrolled and postoperative mortality has been less than 1% (6). Survival results are still to be published. Our belief is that there is benefit for patients in D2 resection, but this complex surgical procedure should be performed in experienced high volume centers which demonstrate low postoperative morbidity and mortality, due to well-trained and experienced surgical team, and which have the pathology team dedicated to careful evaluation of lymph node specimen.

The main reason to do distal pancreatectomy and splenectomy in D2 dissection was not to compromise an adequate dissection of lymph nodes in splenic hilum. But metastases in these lymph nodes are associated with poor prognosis and removal of these nodes is not associated with significant survival benefit, but carries significant rise in postoperative morbidity and mortality. Therefore, pancreas and spleen sparing procedures have now become standard in Japan as well as in many Western countries (7). Resection of the pancreas and spleen are recommended only in case of direct growth of the tumor in these organs.

Concerning the quality of life after surgery for gastric cancer, essential is avoidance of malnutrition, reflux esophagitis and Dumping syndrome. The surgeon can to a certain level prevent these problems by careful reconstruction after gastrectomy. Options for reconstruction after subtotal gastrectomy include gastroduodenostomy (Billroth I), gastrojejunostomy (Billroth II) or a Roux-en-Y gastrojejunostomy. A Roux-en-Y reconstruction has the advantage of being simple to construct with greater likelihood for tension-free anastomosis than Billroth I, as well as avoiding a problem of bile reflux associated with Billroth II reconstruction, particularly if the length of Roux limb is 45 cm or greater. After a

total gastrectomy, preferred method of reconstruction is Roux-en-Y esophagojejunostomy. The esophagojejunostomy is created using circular stapler (25 to 29 mm). This anastomosis, which was traditionally a critical point, nowadays after introducing stapler technique, is safe, with dehiscence rate of 1% to 3%. The other methods of reconstruction after total gastrectomy are jejunal interposition or construction of a pouch, which are more difficult to construct with equivalent functional outcome.

Due to the high number of patients with advanced disease appropriate use of palliative techniques is important. Palliative surgical procedure is indicated in patients who have distant metastases or peritoneal carcinosis and have symptoms of tumor bleeding or obstruction. Resection, even a total gastrectomy is indicated in some cases (proximal obstruction), if it can be conducted with acceptable morbidity. Results of a surgical bypass, which is also one method of surgical palliation, are usually poor, therefore in selected patients resection is preferred method. Surgical palliation is generally used in combination with endoscopic, percutaneous and radiotherapeutic interventions.

#### **POSTOPERATIVE RESULTS IN PATIENTS OPERATED FOR GASTRIC CANCER IN OUR SURGICAL DEPARTMENT FROM 2001 TO 2005**

During these 5 years we operated 159 patients with gastric cancer, 100 of them male and 59 female. We performed 66 total gastrectomies and 70 subtotal gastrectomies, and in 23 patients locoregional disease was unresectable, so one of the palliative procedures was performed. Our aim was to achieve radical R0 resection with D2 lymphadenectomy and to avoid splenopancreatectomy to reduce postoperative morbidity and mortality.

Out of 126 gastrectomies, there were 79 D2 lymphadenectomies, and in 12 of these patients splenectomy was performed. We performed 3 simultaneous liver resections due to direct cancer ingrowth or metastasis, as well as 2 hysterectomies and adnexectomies and 2 transversal colon resections, also due to direct tumor ingrowth. There were 47 D1 lymphadenectomies. The me-

dian number of lymphnodes in resected specimen after D2 and D1 lymphadenectomy was 22 and 7, respectively. There were 11 early gastric cancers, and out of 126 resected patients 24 patients had negative lymphnodes.

Intraoperative red blood cell transfusion was needed in 37 patients (500 to 3500 ml packed red blood cells), and in 18 patients postoperative in ICU (500 to 700 ml).

There were 3 postoperative in-hospital deaths. This makes our overall postoperative in-hospital mortality 1.8%. Deaths were due to abdominal sepsis after esophagojejunal anastomosis dehiscence (2 patients) and duodenal stump dehiscence (1 patient), and the rate of morbidity was 22% with 6 patients reoperated. Larger complications included esophagojejunal anastomosis dehiscence (2 patients), duodenal stump dehiscence (5 patients), intraabdominal abscess (4 patients), acute postoperative pancreatitis (3 patients). Mean ICU stay was 1.5 days (1 to 11 days) and mean hospital stay was 10.4 days (8 to 28 days).

The follow-up of our patient cohort will enable us to review and publish the results of 5-year survival data in 4 years.

## CONCLUSION

Although gastric cancer is overall decreasing worldwide, patterns have shifted toward more aggressive variants of the disease. Adoption of radical lymph node dissection (D2 lymphadenectomy) combined with splenic and pancreatic preservation when possible has led to an increase in 5-year survival which has risen over 50%, and to decrease in postoperative morbidity and mortality, even in cohorts of patients operated in European centers of excellence. One of the clues to this improvement is an aggressive diagnostic approach with more patients in early stages of disease. Especially important is surgical experience and expertise in radical gastric cancer

surgery, surgeon and center volume and dedication of the pathologist. Results from our surgical department show the possibility to reduce the postoperative mortality rate below 2%, with acceptable rate of morbidity.

## REFERENCES

1. American Joint Committee on Cancer. AJCC Cancer Staging Manual. Philadelphia:Lipincott-Raven,1997
2. Cameron J L. Current Surgical Therapy 8/E. Philadelphia: Elsevier Mosby, 2004.
3. Cuschieri A, Weeden S, Fielding J . et al. Patient survival after D1 and D2 resections for gastric cancer: long-term results of the MRC randomized surgical trial.Br J Cancer 1999;79:1522-30.
4. Lewis W G, Edwards P, Barry J D. et al. D 2 or not D 2? The gastrectomy question. Gastric Cancer 2002;5: 29-34.
5. Hartgrink H H, Van de Velde C J H, Putter H . et al. Extended Lymph Node Dissection for Gastric Cancer:Who May benefit? Final Results of the Randomized Dutch Gastric Group Trial. J Clin Oncol 2004; 22:2069-2077.
6. Sano T, Sasako M, Yamamoto S. et al. Gastric cancer surgery:morbidity and mortality reusults from a prospective randomized controlled trial comparing D2 and extended para-aortic lymphadenectomy-Japan Clinical Oncology Group Study 9501. J Clin Oncol 2004;22: 2767-2773.
7. Hartgrink HH, van de Velde CJH. Status of extended lymph node dissection: locoregional control is the only way to survive gastric cancer. J Surg Oncol 2005; 90: 153-165.
8. McCulloch P, Eidi Nitta M, Kazi H et al. Gastrectomy with extended lymphadenectomy for primary treatment of gastric cancer. Br J Surg 2005;92:5-13.
9. Degiuli M, Sasako M, Ponti A et al. Survival results of multicentre phase II study to evaluate gastrectomy for gastric cancer. Br J Cancer 2004;90,1727-1732.

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