

THE FEASIBILITY OF AN EXTENDED LYMPHADENECTOMY IN GASTRIC CANCER TREATMENT

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V.V. Slugarev, PhD, Head of the 2nd Oncological Department¹;

S.V. Gamayunov, PhD, Oncologist of the 2nd Oncological Department¹;

I.G. Terentiev, D.Med.Sc., Head of the Department of Oncology, the Faculty of Doctors' Advanced training, Vice-Rector on Scientific Work²;

A.A. Chernyavsky, D.Med.Sc., Professor, Head of the Department of Oncology, Radiotherapy and Radiodiagnosis²;

A.N. Denisenko, PhD, Chief Physician¹;

S.R. Pakhomov, PhD, Radiologist¹;

R.R. Kalugina, Oncologist of the 2nd Oncological Department¹

¹Nizhny Novgorod Regional Oncological Hospital, Rodionova St., 190, Block 5, Nizhny Novgorod, Russian Federation, 603126;

²Nizhny Novgorod State Medical Academy, Minin and Pozharsky Square, 10/1, Nizhny Novgorod, Russian Federation, 603005

The aim of the investigation is to evaluate the tolerance of patients with advanced gastric cancer to extended D2 lymphodissection and its effect on the postoperative period.

Materials and Methods. The background of the research is the clinical observation of 288 patients within the age of 33 to 77 with morphologically verified stomach cancer. The 1st group (n=141) underwent the surgical treatment with lymphodissection D1 or D1+7, and the 2nd group (n=147) — the surgical treatment with lymphodissection D2.

Conclusion. With relevant experience and appropriate accompanying therapy, extended lymphodissection is well tolerated and safe. Increase in time of surgical treatment, the amount of blood loss and lymphorrhea, a slight increase in the frequency of postoperative pancreatitis are not fatal and do not lead to an increase in severe complications, such as lack of anastomosis, intraabdominal abscess and peritonitis. D2 lymphodissection does not result in an increase of postoperative mortality. Such volumes of surgical treatment can be performed in a standard oncologic dispensary.

Key words: gastric cancer, stomach malignant tumors, extended lymphodissection.

Surgical treatment is the primary method of gastric cancer treatment. More than 76% of operable patients undergo surgery only [1–4]. There is great worldwide experience of extended (D2) and super extended (D3) lymphadenectomies in gastric malignancies. D3 operations in gastric malignant tumours, is more complicated, with many postoperative complications including specific conditions (hardly stopped diarrhea, prolonged chylorrhea) [5, 6], showed no improvements of the 5-year survival rate in comparison with D2, and thus was not recommended as a standard operation [7–12]. There is no clear opinion about the D2 lymph dissection. It can be explained by the fact that the results of European and American studies on the D2 efficiency are not always convincing, and essential faults have been revealed [7–12] in the organizations of research and technical training of surgeons (multicenter studies have found many centers to perform maximum 10–15 operations annually. In Japan, randomized researches on direct comparison of the results of D2 and D1 operations are not carried out for ethical reasons. However, most authors recommend D2 lymph dissection [10, 13–16]. The V International Congress of Stomach Cancer (2009) and the VII Congress of Russian Oncologists (2009) recognized extended lymph dissection as standard and recommended as a required procedure. The limiting factor of widespread introduction of extended lymph dissection as a standard is

the lack of large studies comparing directly the results of D1 and D2 lymphadenectomies, objective technical complexity of the operation, a small number of schools and training centers. One of the arguments of the opponents of the operation is a negative effect of the latter on postoperative period and the increase of intraoperative complications [5, 7, 9, 10]. Therefore, the study of the patients D2 lymphadenectomy tolerance still remains an urgent problem, namely, the surgeons awareness of possible complications, their prevention and demonstration of the safety of the technique in specialized departments.

The aim of the investigation is to evaluate the tolerance of patients with gastric cancer to extended D2 lymph dissection and its effect on the postoperative period.

Materials and Methods. This study is based on clinical observation of 288 patients aged from 33 to 77 years with morphologically verified diagnosis of gastric cancer who were treated in the 2nd Oncological Department of Nizhny Novgorod Regional Oncology Center from 2003 to 2009. Taking into account the dependence of the operations results on the surgeons' experience, the study included the patients operated only by specialists who had perform more than 30 radical operations within a year.

In accordance with the tasks, all patients included in the study were divided into two comparable groups. Group 1 (n=141) consisted of the patients who underwent

For contacts: Gamayunov Sergey Victorovich, tel. +7 905-667-41-76; e-mail: Gamajnovs@mail.ru

surgical treatment with D1 or D2+7 lymph dissection, the 2nd (n=147) — the patients with surgery and D2 lymph dissection. No special selection of patients for extended lymphadenectomy was carried out.

A pooled analysis of clinical data revealed the studied groups to be comparable in sex, age, the nature of associated pathology, location and type of tumour, tumour stage, volume of resection of the stomach, and the extent of radical surgery according to the classification of the Japanese Gastric Cancer Association (JGCA, 1998) [17].

Taking into consideration the existing opinion about the difference of specifications of performing lymph node dissection, depending on a patient's body weight, the groups were compared by body mass index (BMI). Underweight (BMI<20) was found in 24% of patients in group 1 and 26% in group 2. Overweight (II–III degree obesity, BMI >35) was diagnosed in 18 and 20%, respectively. More than a half of the patients had a normal BMI (58 and 54%, respectively). Thus, the groups were comparable according to BMI as well.

In group 1 with D1 lymphadenectomy, the number of dissected lymph nodes was statistically significantly lower than that in the 2nd group that enables to study the postoperative period and oncological results due to the volume of lymph node dissection.

The staging of tumour process was carried out in accordance with the rules of the International Classification of tumours (TNM UICC, 6th ed., 2002) recommended by the Federal Agency of Health and Social Development of the Russian Federation, and finally verified according to the results of routine histological examination of a dissected organ.

The distribution of patients according to the disease stage and number of examined lymph nodes is given in Table 1 and 2.

Table 1
Distribution of patients by disease stage

| Stage of cancer (UICC, 1997) | Number of patients, absolute number/% | | Total (n = 288) |
|------------------------------|---------------------------------------|---------------------------------|-----------------|
| | 1 st group (n = 141) | 2 nd group (n = 147) | |
| IA | 4/3 | 3/2 | 7/2 |
| IB | 4/3 | 3/2 | 7/2 |
| II | 24/17 | 28/19 | 52/18 |
| T3N0M0 | 8/6 | 10/7 | 18/7 |
| T2N1+T1N2M0 | 16/11 | 18/12 | 34/11 |
| IIIA | 47/33 | 50/34 | 97/34 |
| T4N0M0 | 10/7 | 12/8 | 22/7 |
| T3N1M0 | 24/17 | 22/15 | 46/14 |
| T2N2M0 | 13/9 | 16/11 | 29/9 |
| IIIB | 10/7 | 7/5 | 17/6 |
| IV | 52/37 | 56/38 | 108/30 |
| T4N+M0 | 28/20 | 34/23 | 62/24 |
| M1 | 24/17 | 22/15 | 46/18 |
| $\chi^2 = 1.8; p > 0.1^*$ | | | |

* χ^2 criterion is calculated by converting the contingency table: IV stage vs II+IIIA+IIIB.

Table 2

The distribution by the number of lymph nodes examined

| Description | Number of nodes examined, items | |
|--|---------------------------------|-----------------------|
| | 1 st group | 2 nd group |
| Min | 7 | 22 |
| Max | 24 | 48 |
| Me (25%; 75%) | 16 (12; 19) | 32 (27; 42) |
| U — Mann-Whitney test: 1.5; Z = -5.37; p < 0.005 | | |

For statistical processing of the data in Microsoft Excel 2003 there was formed a database to store all the information about the patients included into the study. The data processing was performed using licensed software packages Statistica 6.0 and Microsoft XLSTAT 2009. After checking the compliance with the standard distribution of the parameters, parametric criteria of analysis were used. The differences in the groups were considered reliable in p>0.05

Results and Discussion.

Features of surgical component and extended lymphadenectomy. Based on the inclusion criteria, all the patients underwent extended resection of the stomach (gastrectomy or distal subtotal resection) with D1 or D1+7 lymph nodes dissection in group 1 and D2 lymph dissection in group 2. Distal subtotal resection was performed if there was of antral exophytic tumour, up to 3 cm in its greatest dimension, without serosa invasion, and having the structure of moderate- or high-grade differentiated adenocarcinoma. Due to the limited indications of organ preservation surgeries, gastric resection rate was 17% (49 out 288 cases) and did not differ in the studied groups. Gastrectomy with D2 lymph dissection was followed by splenectomy. When performing the distal subtotal gastrectomy, the spleen was preserved, and lymphadenectomy was performed in NS, and the removal of cellular tissue and lymph nodes along the proximal splenic artery up to the level of divergence of posterior gastric artery.

The resection of adjacent organs was performed only in the case of direct tumour extension to these organs or the detection of solitary resectable metastasis. There were no preventive removals or resections in order to increase the efficiency of the operation (except for splenectomy when performing extended lymph node dissection). There were performed most frequently the pancreas resections (16%), omental sac peritonectomy (5%), hepatectomy (4%), the resection of lower third of the esophagus above the diaphragm segment (3.5%), left adrenal gland resection, mesocolon, transverse colon, diaphragm (by 3%). Totally, combined surgeries with multiple resections (≥2) were performed in 12% of patients in Group 1 and 11% of the patients of the 2nd group.

When performing the reconstruction stage of the operation in order to prevent the regurgitation of intestinal contents to the gastric stump and esophagus, there were used anti-reflux anastomoses to cut off Roux loop of the small intestine. In gastrectomy there was formed a dip rocker esophageal intestinal anastomosis developed in N. Blokhin Russian Cancer Center [18] that enabled

to prevent esophageal-intestinal reflux and reduce significantly the failure frequency. The technique of forming of gastroenteroanastomosis proposed by Ya. D. Vitebsky was used in distal subtotal gastrectomy [19].

Improving lymphadenectomy technique in gastric cancer, we sought to introduce an easy and safe procedure meeting the principles of oncological radicalism. In the method of D2 lymphadenectomy we developed, there is performed monoblock removal of tissue with the lymph nodes of regional collectors, along with the stomach, lesser and greater omentum.

The volume of D2 lymph dissection with lymph collectors included stage I and II of lymphatic metastasis (NI–NII) in accordance with the recommendations of generally accepted Classification of regional gastric lymph nodes (JGCA, 1998) [17, 20]. The classification reflects the phasing of lymphatic metastasis of the tumour due to its localization (Table 3).

To our opinion, the following principles are fundamental when performing lymphadenectomy:

1. Wide access to the operating field for adequate review and manipulation in the surgical wound that is achieved by cutting an abdominal wall with the resection of the xiphoid process and installation of Sigal retractors. In addition to the technical possibility of performing an adequate lymphadenectomy, such an access provides security while working with major vascular structures and reduces the risk of intraoperative complications.

2. Monoblock removal of organs with the lymph nodes and fiber within the fascial structures in the direction “from periphery to center”, celiac trunk acting as the center.

3. The wide use of electrosurgical tissue dissection method helps prevent lymphorrhoea of postoperative wound due to the coagulation of lymphatic vessels. In the last two years we also made good use of an ultrasonic dissector.

4. Adequate drainage of postoperative field.

5. Intensive pre-, intra- and postoperative therapy aimed at prevention of postoperative pancreatitis and inflammatory complications. Early activation of patients with a complex of medical and physical training and breathing exercises, as well as the use of modern drugs for prophylaxis contribute to

significant reduction of bronchopulmonary complication rate including hypostatic and ventilator-associated pneumonias. All patients in the pre- and postoperative period received prophylaxis of postoperative pancreatitis (Octreotide 100 mcg subcutaneously before surgery and then three times a day, infusion therapy, diet, nutritional support with modern nutrient mixtures, cold on the epigastric area).

Evaluation of tolerance to extended D2 lymphadenectomy and its effect on postoperative period. One of the arguments of opponents of extended lymph dissection is the negative effect of the technique on the postoperative period, and an increased risk of postoperative complications. Therefore, we have studied the characteristics of “tolerance” to extended D2 lymph dissection and obtained the following results:

1. D2 lymph dissection does not lead to the increase of number of intraoperative complications. In proven technology the number of wounds of great vessels is reduced to singular occasional events.

2. D2 lymphadenectomy statistically significantly increases the operation time (192±12 min in D1 vs. 248±16 min in D2, p<0.005) and blood loss volume (459±43 ml in D1 vs. 583 ± 45 ml in D2, p<0.05) that has no apparent negative effect on the course of the operation and early postoperative period.

3. D2 lymph dissection causes the increase of the number of specific complications in the postoperative period, such as postoperative pancreatitis (5% in D1 vs. 19% for D2, p<0.05) and lymphorrhoea (498 ± 35 ml/5 days in D1 vs. 836 ± 56 ml/ 5 days in D2, p<0.005). Competent prevention and correction of arising complications contribute to a favorable postoperative course with minimal repeated surgical interventions and fatal cases.

4. Extended lymphadenectomy does not result in an increase of severe postoperative complications such as anastomotic insufficiency (2.1% in D1 vs. 1.4% for D2, p>0.5), peritonitis and intraabdominal abscess (5% in D1 vs. 7% in D2, p>0.5), and is not accompanied by an increase in postoperative mortality (2.8% in D1 vs. 2% for D2, p>0.5).

5. D2 lymph dissection when performed by experienced specialists can be routine and safe procedure in any standard oncologic dispensary.

Table 3

Lymphatic collectors removed in different volumes of lymph dissection according to JGCA classification (1998)

| Localization of tumour | Lymph dissection | | |
|---|--------------------------------|----------------------------------|--|
| | D1 | D2 | D3 |
| Total | 1, 2, 3, 4sa + sb + d, 5, 6 | 7, 8a, 9, 10, 11p+d, 12a, 14v | 8p, 12b+p, 13, 16a2+b1, 19, 20 |
| Proximal 2/3 | 1, 2, 3, 4sa + sb + d, 5, 6 | 7, 8a, 9, 10, 11p+d, 12a | 8p, 12b+p, 16a2+b1, 19, 20 |
| Proximal 1/3 | 1, 2, 3, 4sa + sb | 4d, 7, 8a, 9, 10, 11p+d | 5, 6, 8p, 12a, 12b+p, 16a2+b1, 19, 20 |
| Average 1/3 | 1, 3, | 7, 8a, 9, | 2, 4sa, 8p, 10, |
| Distal 2/3 | 4sb + d, 5, 6 | 11p, 12a | 11d, 12b+p, 13, 14v, 16a2+b1 |
| Distal 2/3 | 3, 4d, 5, 6 | 1, 7, 8a, 9, 11p, 12a, 14v | 4sb, 8p, 12b+p, 13, 16a2+b1 |
| Further removals in tumour involvement of the esophagus | 20 | 19 | 110, 111, 112 |

Thus, the analysis shows acceptable tolerability of extended lymphadenectomy, the possibility of routine performing of the specified operation volume in a standard oncology dispensary.

Conclusion. In the presence of relevant experience and appropriate accompanying therapy, extended lymph dissection will be tolerable and safe. The increase of surgical treatment time, volume of blood loss and lymphorrhea, a slight increase of postoperative pancreatitis prevalence are not fatal and do not lead to growth of severe complications, such as anastomotic insufficiency, intra-abdominal abscess and peritonitis. D2 lymph node dissection is not accompanied by rising postoperative death rates, and such volumes of surgical treatment are possible in a standard oncology hospital.

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