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Modern strategy of surgical treatment of gastric cancer

The article reviews the epidemiology and modern strategy of surgical treatment of gastric cancer by using extended lymph node dissection techniques. The authors present the results of surgical treatment of 348 patients with gastric cancer by extended lymph node dissection.

Keywords: gastric cancer, surgical treatment, lymph node dissection.

Introduction. By the early 20th century, the incidence of gastric cancer (GC) has declined in nearly all the mature countries; this trend remains even in the regions with a high risk of GC. The reason for this might be the change in the diet, the conditions of food storage and cooking [1, 2]. Still, GC remains one of the main causes of death from malignant neoplasms nearly worldwide.

The incidence of GC is quite disputable both in the world and within the countries. Thus, Japan, Korea and China have the highest incidence of GC, while in the US this disease is extremely rare. In Russia, the average incidence is 38.9 per 100,000, with more than 160 per 100,000 in the High North.

In the Republic of Kazakhstan, GC for many years ranks second among all malignant tumours after lung cancer, with the incidence rate of 20.4 per 100,000. Qostanay Region, North Kazakhstan, Kyzylorda Region, East Kazakhstan, and Atyrau Region have incidence rates above the average [3].

Epidemiology of GC. The comparative analysis of regions with high and low incidence allows suggesting some possible etiological factors of GC.

The reliable association of GC with genetic factors is currently disputed [2] while environmental factors have a more significant impact. The analysis has shown a reduction in the risk of GC when moving from regions with a high incidence to the areas with lower incidence, with a more notable reduction in the next generation [4, 5].

The most powerful exogenic factor is the diet. High-calorie food including meat, smoked products, a high concentration of salt is associated with a high risk of GC. In contrast, the consumption of fresh fruits, fiber and vitamins is a protective factor against GC (especially, the intestinal type of cancer) [6].

The association of *Helicobacter pylori* (HP) with GC has been recently proven. The infectious carcinogenesis is associated with the ability of the microorganism to induce a pronounced infiltrative gastritis with intensive cell proliferation. A long period of inflammation causes atrophy and intestinal metaplasia which should be interpreted as precancerous changes of intestinal type. HP is also associated with a 100% of cases of diffuse-type GC [6].

Surgical treatment policy. Despite of some successes in combined treatment, the synthesis of new

chemotherapeutic agents, surgery remains the only method promising a recovery or long-term remission for GC. The radical nature of any cancer surgery was always assessed not only by adequate resection of the organ, but also by monoblock removal of regional lymphocytes as pathways for lymphogenous metastasis. The term of «lymphadenectomy» meaning the removal of a region of possible metastasis is known for more than a century. Recently more and more scientists are inclined to the concept of «lymph node dissection» as it is more capacious than lymphadenectomy and involves the removal of the entire lymphatic apparatus with surrounding cellular tissue.

Many studies have demonstrated a high degree of lymphogenous metastasis of GC as one of the most aggressive GIT tumours. Therefore the need to perform lymph node dissection as one of the main stages of GC surgery is no doubt, both in therapeutic and preventive purposes.

The extended lymph node dissection is pre-conditioned by:

- the improvement of local control in order to reduce the risk of loco-regional recurrence;
- the ability to determine the real prevalence of tumour process and the formation of strategy for post-surgery treatment and prognosis.

Modern literature describes only a few randomized studies of extended lymph node dissection in surgical treatment of GC. Most of the researchers are guided only by their own long-term experience and the results of the leading world clinics dealing with this issue. Japanese researchers are the world leaders in studying this problem. The best treatment results were achieved in Japan since the adoption of the National Program for the Study of Gastric Cancer in the early 1960s. The Japanese Scientific Society for the Study of Gastric Cancer (JRS GC) and, later, the Japan Gastric Cancer Association (JGCA, 1998) have defined and described in details 16 groups of regional lymph nodes that form 3 consecutive stages of lymphatic metastasis of GC from various sections of the organ – N1-N3.

Stage 1: perigastric lymph nodes of the ligamentous apparatus of the stomach (Nos. 1-6);

Stage 2: lymph nodes along the branches of the celiac trunk (celiac trunk, left gastric artery, common hepatic artery, spleen gates and along the spleen artery, Nos. 7-11);

Stage 3: retroperitoneal lymph nodes of the hepatoduodenal ligament (No.12), the retropancreatoduodenal zone (No.13), along the upper mesenteric artery (No. 14), along the middle colonic artery (No. 15) and para-aortic lymph nodes (No. 16).

It should be noted that the lymph nodes can relate to different stages of metastasis depending on the localizations of the gastric tumour.

The involvement of N1-N2 reservoirs in the tumour process is considered as regional metastasis, whereas N3 serves for distant metastasis.

Table 1 - Different strategies of lymph node dissection

Type of intervention	Volume of lymph node dissection		
	N1	N2	N3
Standard gastrectomy D1	+	-	-
Standard radical gastrectomy D2	+	+	-
Extended radical gastrectomy D3	+	+	+

It should be immediately noted that this classification of radical operations is applicable only to some leading clinics of the world since in many cases D2-lymph node dissection is regarded as an extended one.

The first retrospective comparative analysis of the results of extended lymph node dissection was made by Mine et al. (1970). The authors showed some improvement in the results, especially in the detection of metastases in the lymph nodes; 5-year survival D0-1 and D2-3 totalled to 49%, 10% and 53%, 21%, respectively, in the presence and absence of metastases in the lymph nodes.

Kodama (1981) showed in a similar study an increase in 5-year survival from 33% to 58% when performing D0-1 and D2-3 lymph node dissection.

By 1990s, Japan has completed the methodology of extended lymph node dissection. According to prof. K. Maruyama (1995), one of the founders of the methodology, the expansion of surgery has increased the resectability of the process up to 95%, with a stably low mortality of 0.4%.

The analysis of treatment of more than 61,000 patients with GC in 98 institutions of Japan has shown that:

- at stage I without metastases in the lymph nodes, D2-3 lymph node dissection increases the survival rate up to 92.4% vs. 74% at D1-lymph node dissection;

- at stage II, standard and extended gastrectomy deliver a significant improvement in survival rate – up to 76.8% and 52.5%, respectively;

- at stage III, extended surgery provides a two-fold increase in survival vs. standard surgery – 45.7% and 24.6%, respectively.

D2-lymph node dissection is a standard procedure in Japan based on the accumulated experience of the leading clinics in terms of significant improvement in the long-term outcome with satisfactory rates of complications and mortality.

Despite the successes of Japanese researchers, European and American surgeons were only testing the technique of enlarged lymph dissection by the early 1990s. However, the sequence in the actions of Japanese researchers, the lack of reliable improvement in the results of various combined therapies have incentivized the study of efficiency of extended lymph node dissection in the surgical treatment of GC.

The German group for the study of gastric cancer is one of the leading schools in Europe. According to their classification,

the lymph node dissection D1 is a limited resection, while D2 is a complete or radical resection. More than 1.500 cases were analysed. The resection of more than 25 lymph nodes is the criterion for radical surgery. The German researchers consider the extended lymph node dissection to be most efficient at GC stages II and IIIa. With the prolapse of the tumour through all the layers of the stomach wall and massive lymphogenous metastasis, lymph node dissection does not improve the distant outcome.

At the II International Congress on Gastric Cancer (Munich, 1997), the Dutch group on the study of gastric cancer has presented the results of a randomized study of 711 cases of surgical treatment of GC (380 - standard surgery, and 331 - extended surgery). The authors came to a conclusion that the extended lymph node dissection did not provide a significant improvement in the long-term outcome of treatment (the 5-year survival rate of 60% and 55%, respectively) while the postoperative complications and mortality have doubled (25% and 43%, 4% and 10%, respectively).

Prof. Sasako (1999) has analysed the materials of the Dutch group randomized study and mentioned a good organization and a detailed statistical analysis of the material but emphasized that:

- The study included a large number of surgeons (multicentre study) with insufficient experience in performing such operations;

- The surgeons were not trained individually to perform extended lymph node dissection. Prof. Sasako believes that it could have increased the postoperative complications and mortality. One of the examples was the hardware suturing because the surgeon was not experienced enough to do manual suturing;

- Limited radicality of surgery for the same reason. According to the results, in the Dutch protocol the number of dissected lymph nodes was equal 13 at N1, and 11 at N2, while in the Japanese study, the figures were 35 and 25, respectively. Insufficient number of dissected lymph nodes increased the likelihood of early relapse and the retention of metastatic lymph nodes;

- Lack of standardization in surgery: splenectomy was not always conducted in similar cases what is a violation of the Japanese methodology of extended surgery;

In the future, at the III and IV International Cancer Congresses for gastric cancer the Dutch authors have confirmed the reliability of the analysis by Prof. Sasako. They noted the improvement of remote treatment results in the D2-lymph node dissection group and the presence of metastases at the stage N1, i.e. at the stages II and IIIa.

At the close of the IV Consensus Conference (New York, 2001) prof. M.F. Brennan noted that during the development of methodology of extended lymph node dissection in specialized centres the immediate results of surgical interventions were comparable, and the remote results were approaching the figures provided by JGCA. In view of the accumulated experience, D2-lymph node dissection is considered to be a sufficiently safe procedure and shall become an integral element of GC surgical treatment.

Experience of KazIOR in extended lymph node dissection. The thoracic centre of the Kazakh Institute of Oncology and Radiology (KazIOR) has analysed the direct outcome of surgical treatment of 348 patients (men – 208, and women – 140) with GC in 2011-2015. 268 (77.1%) patients had tumour process stage III. All the patients received extended gastrectomy: 292 – gastrointestinal gastrectomy, and 56 – gastrectomy through combined laparotomic access. 79.1% cases involved combined surgery as in most cases the spleen was removed in a single block with the stomach according to the developed methodology. The rationale for that was the need for monoblock removal of lymphatic reservoirs without separation of the ligament apparatus. In some cases, the caudal, or corpora-caudal, resection of the pancreas was made in order to preserve the elasticity and achieve the radicality of surgery.

The incidence of lymphogenous metastasis was 45.9% (152 cases). One of the most important results of lymph node dissection was a reliable staging of the tumour process which allowed assessing the efficiency of surgery. About 10% of patients migrate to a more advanced stage due to the metastases in the lymph nodes. The average number of removed lymph nodes was 24.3.

Postoperative complications were noted in 86 patients (24.2%), lethality - 15 patients (4.3%). The main reason for complications and mortality was the respiratory and heart failure.

The peculiarity of extended surgery is the development of such key aspects of surgical intervention as: monoblock removal of lymphatic reservoirs, safe treatment of pancreas stump during its resection, the formation of a reliable esophago-intestinal anastomosis and adequate drainage of the abdominal cavity. For example, the use of invagination bowl esophageal-small intestinal anastomosis of Gilyarovich in the modification of M.I. Davydov allowed reducing the probability of such a previously formidable and often fatal complication as an inconsistency of sutures of the oesophageal-intestinal anastomosis. On the other hand, the adequate drainage of

abdominal cavity with rubber-glove discharging drainages installed in the prognostically dangerous places (lien spleen, pancreas stump, etc.) also significantly reduced the number of ulcers of the abdominal cavity presented during the development of methodology.

Conclusions. The experience of extended surgery leads us to the following conclusions:

- GC is characterized by early lymphogenous metastasis;
- the reliable staging of tumour process is possible only during extended lymph node dissection on the basis of the staging of lymphogenous metastasis;
- Optimization of postoperative period allows reducing the number of complications and mortality in patients undergoing extended operations;
- lymph node dissection can reliably improve the long-term treatment outcomes and reduce the number of early loco-regional relapses.

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