Review Article

Gastric cancer treatment: similarity and difference between China and Korea

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Abstract: Chinese populations have many demographic similarities to Korean populations. However, the long-term survival rates of gastric cancer patients in China are still not satisfactory when compared with Korea, especially for the advanced cases. In this article, we discuss about the similarity and difference of gastric cancer treatment in terms of screening, surgical approach, stomach resection, digestive tract reconstruction, lymphadenectomy, harvested lymph nodes, operative morbidity and mortality, postoperative chemotherapy as well as follow-up between China and Korea. Given that a variety of factors ranging from tumor characteristics to different treatment strategies are seen between the two countries, the reasons accounting for the differences in survival should be focused and the corresponding strategy should be considered and finally promote to improve the prognosis of gastric cancer.

Keywords: Gastric cancer; treatment; similarity; difference; China; Korea

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Introduction

Although the incidence has decreased globally in recent years, gastric cancer still has high incidence and mortality in both China and Korea (1). The treatment model of gastric cancer is surgery-based comprehensive treatments. And D2 lymphadenectomy is accepted as the standard surgery in East Asia. As the neighbouring countries, Chinese populations have many demographic similarities to Korean populations, including the environment, genetic susceptibility, as well as the treatment strategy of gastric cancer. However, the long-term survival rates of gastric cancer patients in China are still not satisfactory when compared with Korea, especially for the advanced cases (2,3), which may indicate us that there would be some differences of gastric cancer treatments between Korea and China. In this article, we discuss about the similarity and difference of gastric cancer treatment between China and Korea.

Screening

The national population-based gastric cancer screening program has been launched from 1999 in Korea (4). Since then, the detection rate of early gastric cancer has gradually been increasing (5). In the contrast, nationwide cancer screening program is absent in China. For the tumor characteristics of Chinese patients, therefore, the tumor is larger, depth of invasion is greater, the rate of lymph node involvement is higher, the proportion of early cancers is much lower and advanced stage is more frequent, compared to Korean patients. And the patients with R1/R2 resection or distant metastasis are more in China (3). Jeong *et al*. analyzed the Korean data of gastric cancer treatment in 2009 and found that early cancers accounted

for 57.6% of all cases (6). Our previous study reported that the percentage of early cancer in Yonsei Cancer Center was 54.47% during 2006–2010. In the contrast, the diagnosis of early gastric cancer in China was only around 20% (3). This supported the judgment that higher proportion of patients with advanced stages of cancer as the main reason contributed to the poorer survival of Chinese patients to Japan and Korea. Consequently, establishment of a nationwide screening program for gastric cancer should be advocated to promote early detection and improve the survival of gastric cancer in China.

Surgical approach

Laparoscopic or robotic gastrectomy in the treatment of early gastric cancer has been widely accepted in the world due to the advantages when compared with open surgery, including reduced intraoperative blood loss, reduced postoperative pain, and accelerated recovery without compromising the survival (7-11). In the 2009 Korean Nationwide Survey on Surgically Treated Gastric Cancer Patients, 25.8% of patients underwent the laparoscopic surgery (6). And the number of laparoscopic surgeries dramatically increased to 50.1% in 2014 (12), whereas the percentage of minimal invasive surgery in one high-volume Chinese hospital was only around 15% during 2006–2010 (3). Although laparoscopic gastric surgery has spread rapidly and developed in mainland China during recent years (13), the number of minimal invasive gastrectomy was still limited since the application of minimal invasive gastrectomy for advanced gastric cancer remains controversial and should be limited in clinical studies as proposed by the Japanese gastric cancer treatment guideline (14). The high proportion of advanced gastric cancer in China would be attributed to the differences of treatment patterns to some extent. Furthermore, the operative difficulties and learning curve of minimal invasive gastrectomy may be a hurdle in its development in the initial period (15,16).

Stomach resection

Majority of tumors were in the lower portions of the stomach in both of the countries (12,17-19). And there were similar proportions of total gastrectomy and distal gastrectomy between two countries (3,18). In the past 20 years, the proportions of proximal gastric cancer have gradually increased in both of countries (20,21). Our previous study showed that the proportion of proximal gastric cancer in the Korean patients was 13.67% compared with 25.57% in Chinese patients (3), which is in keeping with the report that the incidence of proximal gastric cancer has gradually increased from 11.2% to 16.0% over the last two decades in Korea (22). Interestingly, the percentage of proximal gastrectomy in Korea was only 1% *vs.* 17% in China (3,12). Even now, the best surgical approach for tumors of the proximal stomach is a matter of debate although proximal gastrectomy has been defined for only early proximal tumors by Japanese guideline proposed in 2010 (14), before which proximal gastrectomy could be performed for proximal cancers. Since the possibilities of No.5 and No.6 lymph nodes metastases are very low for proximal tumors, it remains unclear whether patients could benefit from total gastrectomy even if safety margins are ensured with preserving the distal stomach as a reservoir. It has been reported that total gastrectomy and proximal gastrectomy had similar overall survival outcome for proximal gastric cancers (23-25). Furthermore, proximal gastrectomy appears to be valuable in terms of long-term quality of life for proximal gastric cancer (26,27). Hence, some surgeons would still choose proximal gastrectomy for selected patients (24,27,28). Nevertheless, it is promising that total gastrectomy trend to be superior to proximal gastrectomy, through decreasing the recurrence rate and contributing to the postoperative life quality by diminishing reflux esophagitis and anastomotic stenosis (23), which may be the reason why Korean doctors prefer total gastrectomy. Actually, the proportion of proximal gastrectomy has declined and total gastrectomy has gradually increased for proximal tumors in Chinese hospital (20). In addition, pylorus preserving gastrectomy or wedge resection sometimes was chosen in Korea because of the high percentage of early cancers, whereas they are very rare in China (12).

Digestive tract reconstruction

Regarding the reconstruction, Roux-en-Y esophagojejunostomy was the most popular method after total gastrectomy in either country (3,12). The proportions of patients with Roux-en-Y anastomosis were similar between the two countries, which matched to the proportions of total gastrectomy (3). Other reconstructions after total gastrectomy, such as jejunal interposition or pouch esophagojejunostomy, were seldom (12). Billroth-I and Billroth-II were most frequently performed after

distal gastrectomy (3,12,18). Roux-en-Y gastrojejunostomy and uncut Roux-en-Y gastrojejunostomy only account for a small percentage in both of countries (12,18). However, Billroth-I reconstruction may be the preference in Korea due to the advantages of technical simplicity and the physiological intestinal continuity (3,12). The concern of tension on the anastomosis after Billroth-I reconstruction is attenuated because it is likely to achieve a minimum resection margin (2 cm) for the high proportion of early cancers in Korea (14). Considering to the dominated portion of advanced cancers in China, Billroth-II reconstruction is a safe, simple and economic procedure compared with Roux-en-Y and can still be accepted as alternative option for patients although the disadvantage of reflux is emphasized. Nowadays, Roux-en-Y reconstructions are increasing in both Korea and China after distal gastrectomy (6,12). For proximal gastrectomy, the double-tract anastomosis in Korea and esophagogastrostomy in China were most frequently performed (3,12,18).

Lymphadenectomy

Controversy over the extent of lymph node dissection for gastric cancer has persisted for several decades. In the past, the D2 procedure was believed to increase the postoperative morbidity and mortality, rather than the survival benefit (29-31). Therefore, the D1 lymphadenectomy was popular in Western countries. However, D2 lymphadenectomy has been the standard procedure for resectable tumors since 1980 in Japan and Korea (32). Compared to the West, the survival outcome of gastric cancer was better in Eastern countries (33-35). Although different tumor characteristics and ethnic-related differences may be responsible for the different survival outcomes from East to West (33,36,37), the major reason was because in Western countries with low incidence of gastric cancer, the performance of more extensive lymphadenectomies is generally limited to few specialized centers and very limited lymphadenectomy are performed to treat majority of patients (38). Until recently, the 15-year follow-up results of Dutch trial has supported the advantage of D2 lymphadenectomy to decrease the local recurrence and gastric cancer related death, compared with D1 (39). Meanwhile, the benefit of additional para-aortic nodal dissection has been abolished by JCOG 9501 trial (40). Therefore, the effect of the standard D2 lymph node dissection on overall survival of gastric cancer should not be controversial. As indicated by Cuschieri (41), the principle investigator of the MRC trial, the expired results of this trial are no longer a sustainable argument against D2 gastrectomy in modern surgery for invasive gastric cancer. Training standards necessary for D2 gastrectomy and the quality of performance are new challenges needed to be addressed (41).

In the Chinese hospitals, standard D2 lymphadenectomy was selectively performed for medically fit patients with advanced stages since 2000 and may be insufficient sometimes (17). Only D1 or D1+ lymphadenectomy was performed for some patients with less advanced gastric cancer in the earlier decades (17). Through making efforts on the training and spread of D2 lymphadenectomy in China, the gastric cancer surgery has become more standardized in recent years. Our data demonstrated the increased proportion of D2 lymphadenectomy was found to be accompanied by increasing in the surgical duration, the number of harvested lymph nodes and overall survival from 2000–2005 period to 2006–2010 period in West China hospital (17), which also justified the survival benefit brought by D2 lymphadenectomy. Even, some Chinese institutes have reported that D2 lymphadenectomy was performed in more than 80% of cases (18,19). Nevertheless, the percentage of real D2 lymphadenectomy in some Chinese hospitals still do not correspond to the proportions of advanced gastric cancer cases and the extent of so-called D2 lymphadenectomy is less than the standard D2 lymphadenectomy in many areas. It has been reported that less than 50% of Chinese patients with stage II and III gastric cancers have undergone D2 lymphadenectomy, whereas more than 80% of Korean patients with the same stage underwent this surgery (3). Therefore, training and spread of D2 lymphadenectomy are urgently advocated in China.

Harvested lymph nodes

The number of retrieved lymph nodes is an important factor for an accurate staging, and to impact the prognosis of patients (42-44). Also, stationing the harvested lymph nodes is very important for the researches as well as predicting the survival of patients, and it could be applied to assess the quality of lymph nodes dissection. However, except some specialized institutions in the field of gastric cancer, most of the Chinese hospitals do not complete the stationing and picking of lymph nodes. In the Korea, the surgeons only do the stationing work and the lymph nodes are picked out by the pathologists. The number of harvested LNs could

be influenced by several factors, including age, gender, race, tumor characteristics, and the surgical skills of the surgeons and involvement of pathologists (43). The mean number of retrieved lymph nodes was no time differences in Korea in the past 20 years (21); while it had significantly increased in China (17). Although satisfied the minimum requirement of at least 15 lymph nodes recommended by National Comprehensive Care Network (NCCN) (45), the mean number was still less in Chinese patients compared to Korean patients, even in a D2 lymphadenectomy (3). Efforts should be made on the dissection and picking of lymph nodes.

Morbidity and mortality

With respect to safety, gastric cancer surgery is routinely performed with low morbidity and mortality by experienced surgeons in East Asian countries, even by western surgeons after adequate training and the preliminary stage of learning curve (38,46,47). The morbidity has been reported to be 12–15% (3,48,49). And the 30-day mortality rates are usually less than 1% in both of countries (3,18,19). The previous studies failed to show significant differences in morbidity or mortality between the two countries (3,18). Most of the postoperative surgical related complications and non-surgical related complications are would problems and pulmonary infections respectively. According to the Clavien-Dindo Classification of complications (50), there was also no significant difference between the two countries (3). However, it was somewhat different on the spectrum of complications between the two countries. Differences in comorbidities, diverse habits of operation, varied operative procedures, and different proportions of reconstruction, resection type or minimal invasive surgery were considered to be associated with the discrepancies (51-55).

Postoperative chemotherapy

Adjuvant chemotherapy is applied to reduce postoperative recurrence and improve the overall survival, and its efficacy has been proved by several studies (56-59). In our previous study, we have also found that postoperative chemotherapy can improve the survival of patients with advanced gastric cancer, even partly compensating for the absence of D2 lymphadenectomy in patients with stage II gastric cancer (3). It has been reported the percentage of patients receiving adjuvant chemotherapy were around 60% in China and 35% in Korea (3,18,19). It seems that Chinese patients received more postoperative chemotherapy compared with their Korean counterparts. However, we should notice that most of the gastric cancer patients in China are advanced cases (more than 80%) who may be most likely to benefit from the addition of chemotherapy, whereas more than 60% of Korean patients are early cancer (3,12). Therefore, the proportion of advanced patients receiving adjuvant therapy was considerably smaller in China than in Korea. Furthermore, the situations that patients who were administered chemotherapy were diverse in different regions of China (3,18,19). The proportion of patients receiving chemotherapy was only 40% in the western part of China versus 60% in eastern part (3,18,19). Economic factor, culture background and low compliance of patients from the two countries contribute to this phenomenon. Future attention should be paid in China to the spread and education about chemotherapy, the invention of new drugs or regimens with lower toxicity, and the appropriate application of chemotherapy (3).

Follow-up

Regular postoperative follow-up is very important, including management of side effects of surgery, oncological recurrence surveillance, psychological support, and data collection for research (60). In China, because of the low compliance of patients and availability of doctors, the important role of follow-up after the operation is somewhat ignored. Therefore, the postoperative follow-up is usually symptom-driven surveillance or even absence. Accordingly, the complete survival data of patients in most of the Chinese hospitals was lacked. When the patients come to the doctors, the tumor might recur in a very advanced stage and the prognosis is poor although there is no randomized controlled trial to support the scheduled follow-up for recurrent disease (60). In the contrast, Korean patients are usually followed-up regularly and survival status at the last follow-up could be found from the data registered with the Korean National Cancer Center (3).

Conclusions

This article briefly outlined the similarity and difference of gastric cancer treatment between China and Korea. Although Chinese populations have many similarities to Korea in terms of gastric cancer treatment, the long-term survival rates of gastric cancer patients in China are still inferior to Korea. Given that a variety of factors ranging

from tumor characteristics to different treatment strategies are seen between the two countries, the reasons accounting for the differences in survival should be focused and the corresponding strategy should be considered and finally promote to improve the prognosis of gastric cancer.

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Footnote

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