Mini-Review

Evaluation of skeletonization of the hepatoduodenal ligament for the lower third advanced gastric cancer

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Abstract: The application of skeletonization of the hepatoduodenal ligament (SHDL) in the treatment of gastric cancer is rare. In this study, we reviewed the literature concerning the role of the No.12 lymph node dissection for gastric cancer, in order to evaluate the significance of SHDL in radical gastrectomy. We found that the application of SHDL with dissection of the No.12a, No.12b, and No.12p lymph nodes could improve the prognosis of patients with lymph node metastasis. The incidence of complications would not increase when the surgery was performed by experienced surgeons.

Keywords: Skeletonization; gastric cancer; lymph node dissection

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The application of skeletonization of the hepatoduodenal ligament (SHDL) in the treatment of hilar cholangiocarcinoma has been widely reported (1). However, its application in gastric cancer is not nearly as well known. In previous years at our center, SHDL has been applied in advanced gastric cancer. In 2010, Professor Cai's multivariate analysis showed that the No.12 lymph node metastasis was an independent prognostic factor, and it was recommended that the No.12 lymph node should be resected for lower third gastric cancer (2). In 2013, we first reported the value of SHDL in lower third advanced gastric cancer and suggested that dissection of the No.12a, No.12b, and No.12p lymph nodes could increase the survival rate for gastric cancer patients with lymph node metastases (3). In the present study, we reviewed the literature which discussed the role of the No.12 lymph node dissection for gastric cancer, in order to evaluate the significance of SHDL in radical gastrectomy.

The evolution of No.12 lymph nodes classification in The Japanese Classification of Gastric Carcinoma

For gastric cancer, the lymph nodes are classified according to their location. In 1990, The 13th edition of *The Japanese Classification of Gastric Carcinoma* revised the sub-classification of regional lymph nodes and lymph node dissection for gastric cancer. The regional lymph nodes were divided into 3 stations (N1 to N3) while N4 was removed. The lymph nodes beyond the region were classified as distant metastasis (M1). In addition, the corresponding surgical procedures were divided into D0 to D3. In the 12th edition of *The Japanese Classification of Gastric Carcinoma*, the D2 lymph node dissection included the No.1, 3, 4d, 5, 6, 7, 8a, and 9 lymph nodes for lower third advanced gastric cancer. In the newer 13th and 14th editions, in addition to the above lymph nodes, the No11p,

12a and 14V lymph nodes were added for D2 lymph node dissection for lower third advanced gastric cancer. Retrieval of the 12p/12b lymph node was defined as D3 dissection.

The rate of lymph node metastasis

In 1989, Maruyama reported that No.12 lymph node metastasis was found in 145 cases (9%) of 1931 cases of gastric cancer. Among the patients with lymph node metastasis, lower gastric cancer accounted for 59% (4). In 2007, Di Leo *et al.* reported 545 cases of gastric cancer. The number of pT1 and pT2 gastric cancers with No.12 lymph node metastasis accounted for 2% and 4% respectively, with all of them being lower gastric cancer. Moreover, pT3–4 gastric cancers with lymph node metastasis accounted for 7% (5). In 2011, de Manzoni *et al.* reported that 6% of the 294 patients with pT2–4 gastric cancer had No.12p metastasis, while 5% had No.12a metastasis (6).

In our center's home country, China, the rate of No.12 lymph node metastasis was reported to be 10–26%. In 2005, Wei *et al.* reported that the metastatic rates of No.12a, No.12b and No.12p were 26.1%, 13.1% and 2.2% respectively (7). In 2007, Gu *et al.* from Shanghai Jiao Tong University reported that, by using reverse transcription polymerase chain reaction (RT-PCR) technology and (CK20) mRNA as the marker gene, 23 No.12 lymph nodes metastasis was detected in 86 lymph nodes of 45 patients with advanced gastric antrum cancer (8). Cai *et al.* reported on 251 consecutive patients who underwent No.12 lymph node dissection in radical gastrectomy for gastric cancer, and routine hematoxylin and eosin (H&E) staining showed that the No.12 lymph nodes were positive in 41 cases (16.33%), and negative in 210 cases (83.67%). In patients with No.12 negative lymph nodes, lymph nodes were detected by serial section for HE staining. Ten samples were found to be micrometastasis by HE staining and 12 samples were found to be micrometastasis by immunohistochemistry (IHC). Ten samples were identified as positive both for HE and IHC. No.12 lymph nodes were detected positive in 53 patients (53/251, 21.12%). The rates of No.12a, 12b and 12p lymph node metastasis were 17.93% (45/251), 11.16% (28/251), and 1.20% (3/251) respectively. In addition, there were significant differences in No.12 lymph node metastasis between different tumor invasion depth, clinical stage, tumor diameter and lymph node metastasis (2).

Data from gastrointestinal surgery center, the First Affiliated Hospital, Sun Yat-sen University showed that 29 patients (11.7%) of the 248 patients for gastric cancer with radical gastrectomy and D2 lymph node dissection, were found to have No.12 lymph node metastasis. Of these patients, 20 patients (18.2%) were found with No.12 lymph node metastasis in 110 patients with SHDL, while 9 patients (6.5%) were with found No.12 lymph node metastases in 138 patients without SHDL. Of the 110 patients who underwent SHDL, 20 (18.2%) had No.12a metastasis, 9 (8.2%) had No.12b metastasis, and 12 (10.9%) had No.12p metastasis.

No.12 lymph nodes and prognosis of gastric cancer

No.12 lymph node dissection has been confirmed that it could improve the prognosis of gastric cancer (4,9).

Wu reported that D2/D3 lymph node dissection could increase the 5-year survival rate of patients with gastric cancer when compared with D1 lymph node dissection (59.5% *vs.* 53.6%, P<0.05) (10). Gu *et al.* reported 22 patients (21.6%) of the 102 patients with gastric cancer were found to have No.12 lymph node metastasis. It was safe and feasible to conduct standardized regional lymphadenectomy for the No.12 lymph nodes in patients with advanced distal gastric cancer (11).

Professor Cai *et al.*'s multivariate analysis in 2010 showed that No.12 lymph node metastasis was an independent prognostic factor, and it was recommended that the No.12 lymph node should be resected for lower third gastric cancer (2). In 2013, data from gastrointestinal surgery center, the First Affiliated Hospital, Sun Yat-sen University showed that SHDL could significantly increase the five-year survival rate (58.8% *vs.* 38.6%, P=0.037) for patients with lower gastric cancer with lymph node metastasis, and reduce the risk of lymph node recurrence (4.3% *vs.* 0%, P=0.035) (3). In conclusion, the application of SHDL with dissection of the No.12a, No.12b, and No.12p lymph nodes could improve the prognosis of patients with lymph node metastasis.

Surgical techniques and complications of No.12 lymph node dissection

There are inherent hepatic arteries, common bile ducts and portal veins in the hepatoduodenal ligament. Surgeons should pay attention not to damage these 3 important organs when resecting the No.12 lymph nodes. The steps of No.12 lymph node dissection are as follows:

(I) Exposure of the hepatoduodenal ligament. The assistant gently pulls the liver belly upward and

pulls the duodenum duodenal bulb and the gastric antrum to the bottom so as to fully expose the hepatoduodenal ligament.

(II) Surgical approach. First, remove the visceral peritoneum on the surface of the hepatoduodenal ligament, then cut the retroperitoneum from the right side of the common bile duct upward until the cystic duct. Finally, the liver and duodenum retroperitoneum are cut horizontally, and then stripped down.

(III) Lifting of the inherent artery of the liver, the common bile duct and the portal vein. Open the hepatic artery sheath, separate the hepatic artery up and down in the outer membrane, and pull it to the left with a rubber belt. During the course of dissociation, the right hepatic artery can be found from the left hepatic artery . Clamp, cut and lash it. If the ectopic gallbladder artery arises from the hepatic artery, pay attention not to damage it; otherwise, the gallbladder will be necrotic. Free the common bile duct and use the rubber belt to lift the choledochus tube and pull it to the right. Then, separate the loose tissue from the common bile duct and hepatic artery to the outer membrane of the portal vein. Dissect the loose tissue between the common bile duct and the hepatic artery until the outer membrane of the portal vein. Exfoliate the loose tissue before the portal vein and remove it. Next, carefully separate the portal vein from the posterior surface of the hepatoduodenal ligament. After separating the portal vein completely, lift it and pull it.

(IV) Lymph node dissection. Separate the common bile duct, hepatic artery and portal vein in the hepatoduodenal ligament. Then, carefully remove the lymph nodes and loose tissues of the hepatoduodenal ligament and the pylorus.

In this way, SHDL was completed. The lower end of skeletonization was to the upper edge of the duodenum where the junction of the proper hepatic artery, the gastroduodenal artery and the common hepatic artery was exposed. At the junction of the proper hepatic artery, the gastroduodenal artery and the common hepatic artery, the anterior common capsule of the common hepatic artery was opened to the outer membrane of the artery. To facilitate separation to the proximal end, a small segment of the common hepatic artery can be separate d at the distal end, and the artery is lifted with a rubber band. On the left side of the portal vein, the inferior border of the liver and the superior border of the pancreas, the peripheral lymph nodes and loose tissues of the common hepatic artery were separated and resected with the general specimen. When dissecting tissue around the junctions of the three arteries, the gastric coronary vein that converges into the portal vein can be seen. A total of 70–80% of the gastric coronary vein passes through the common hepatic artery to the portal vein, and the rest runs into the splenic vein at the root of the common hepatic artery. If the surgeon is not very familiar with the anatomical structure, it will still cause bleeding when removing the surrounding tissue of the hepatic artery. Some small veins near the duodenum bleed easily and therefore careful attention should be paid when ligating them. In the rear of the common bile duct, there is often a large lymph node shaped like a broad bean. The lymph node is soft and the pathological examination is often negative. However, in order to ensure that there is no omission, it should be removed simultaneously. Lymph node dissection posterior of hepatoduodenal ligament can be accomplished by adjusting the 3 vessels. SHDL not only can resect the No.12 lymph node completely, but also helps to ligate the right artery of the stomach in the root, so the duodenum can be removed easily.

SHDL procedures can involve a few complications. One complication is bleeding, including intraoperative and postoperative bleeding. Intraoperative bleeding is often caused by injury of the portal vein, the gastroduodenal artery and its branches, the right stomach artery, the trunk of the portal vein, and the variant blood vessels. Postoperative bleeding is often related to incomplete hemostasis and loss of ligature. Postoperative bleeding in some patients is due to postoperative biliary fistula, pancreatic fistula, duodenal stump fistula and other corrosive vessels which corroded blood vessel. Another issue in SHDL can be choledochal fistula which occurs if the common bile duct is injured and not discovered in time. Gallbladder necrosis is another complication and is related to the intraoperative injury or ligature of the cystic artery . Finally, liver injury, such as excessive traction, can occur during the procedure, and lead to liver laceration. Although several complications are likely to occur during SHDL, the complications can be avoided when the surgeon is sufficiently familiar with the anatomical structure of the region.

Conclusions

For patients with lower third advanced gastric cancer,

it is recommended that SHDL should be carried out to thoroughly clean the No.12a, nNo.12b, and No.12p lymph nodes, which can decrease the recurrence rate and increase the survival rate. However, the current evidence does not support the notion that D3 dissection (retrieval of 12p/12b node) has better survival than D2 dissection for gastric cancer. Therefore, more randomized clinical trial is needed to support our viewpoint.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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