Is Splenectomy Necessary or Beneficial in Curative Surgery of Gastric Cancer?

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Background: *Gastrectomy with D2 lymphadenectomy is a standard treatment of gastric cancer in Japan and Korea. Splenectomy in gastric cancer surgery has no clear benefits for removing lymph nodes unless it is removing the metastasis of the lymph nodes at the splenic hilum (Group 10).*
Objective: *Report the outcome of post gastrectomy with or without splenectomy, together with the effects on lymph node metastasis, including lymph nodes at the splenic hilum and examined lymph nodes.*
Material and Method: *A retrospective chart review was made of all patients who presented with gastric cancer after curative surgery resection between January 1, 2006 and December 31, 2016 at Ramathibodi Hospital, Bangkok, Thailand. Comparisons were made between the non-splenectomy group and the splenectomy group.*
Results: *Seventy patients were included in the non-splenectomy group and 35 patients were included in the splenectomy group. The data including age, gender, histologic type, location of cancer, and TMN staging showed no statistical difference between the groups. For the lymph node Group 10 metastasis, the number of lymph nodes dissected and lymph node metastasis showed no statistical significance in both groups (p-value = 0.524 and 0.160 respectively). The rate of lymph node Group 10 metastasis was 6.25%, which was found in the splenectomy group. The data showed that the patients in the splenectomy group had more dissected lymph nodes than the non-splenectomy group (p-value = 0.0004). Conversely, the lymph node metastasis in both groups showed no statistical difference (p-value = 0.925). The median follow-up time was 59.51 months. The recurrence rate, metastasis rate, and overall survival showed no statistical difference in both groups. The five years' survival in the non-splenectomy group was 44.88 months and the splenectomy group was 53.75 months (p-value = 0.9368).*
Conclusion: *In most cases, curative gastric resection with D2 lymphadenectomy is an adequate treatment for gastric cancer. Unnecessary splenectomy does not benefit overall survival.*

Keywords: *Splenectomy, Non-splenectomy, Curative resection, Total gastrectomy, Subtotal gastrectomy*

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The standard treatment of gastric adenocarcinoma is curative resection with adequate regional lymphadenectomy. Standard gastrectomy is the surgical procedure of choice for curative intent[1]. Total gastrectomy is necessary for cancer at the proximal part of stomach. Once the tumor invades adjacent organs such as the spleen, pancreas, the en-bloc resection is performed with curative intent. The risk of lymph node metastasis to the splenic hilum lymph nodes for tumors located at the proximal part of the stomach is 10 to 20%. In these cases, splenectomy is necessary to completely remove the splenic hilum lymph nodes[2].

In 2002, Csendes et al reported a prospective randomized study comparing D2 total gastrectomy versus D2 total gastrectomy plus splenectomy in 187 patients with gastric carcinoma. This report showed that the five years' overall survival in the splenectomy group and the splenic preservation group was 42% and 36% respectively, which is statistically not significantly different[3]. In 2006, Yu et al reported a randomized clinical trial of splenectomy versus splenic preservation in patients with proximal gastric cancer. The report showed that gastrectomy with splenectomy had benefits of removing lymph node metastasis at the splenic hilum and gave better survival rates. However,

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potential complications increased morbidity and mortality rates. The present study did not show statistically significant differences in both groups. They concluded that gastrectomy with splenectomy had no benefits for prophylaxis lymph node metastasis at the splenic hilum[4]. In 2017, Sano et al reported a randomized control trial to evaluate splenectomy in total gastrectomy for proximal gastric carcinoma. They enrolled 505 patients from multiple institutes. This report revealed that their splenectomy group showed high morbidity and 5-year survival was 75.1% and 76.4% in the splenectomy and the splenic-preserved groups respectively. They concluded that the splenectomy increased the likelihood of morbidity and did not improve survival in proximal gastric cancer[2].

Lymph node metastasis determined the prognosis of gastric adenocarcinoma. Several studies reported lymph node metastasis and examined lymph nodes, which is useful to predict the prognosis of gastric cancer. In this study, the outcome of post gastrectomy with or without splenectomy was reported together with effects on lymph node metastasis, including lymph nodes at the splenic hilum (Group 10)[5] and examined lymph nodes.

Material and Method

A retrospective chart review was made of all patients who presented with gastric cancer after curative surgery resection between January 1, 2006 and December 31, 2016 Ramathibodi Hospital, Bangkok, Thailand. All patients were aged 18-years-old or older at the time of surgery. The diagnosis was performed by esophagogastroduodenoscopy (EGD) or imaging, including ultrasonography, Computer Tomography (CT) or Magnetic Resonance Imaging (MRI). All tissues were confirmed by Pathology. All patients had not previously received neoadjuvant therapy and showed no distant metastasis. The patients who presented with distant metastasis during surgery were excluded. The surgery was performed for curative intent. After each operation, the patients received adjuvant therapy following the standard regimen. The data of patients included age, gender, underlying diseases, chief complaints, types of surgery resection, pathological reports, regional lymph node metastasis and removal, adjuvant treatment, and time of recurrence or metastasis. The staging of tumors was according to the seventh edition of AJCC classification 2010[6].

Statistical analysis

The data was analyzed by STATA version 14.0 Chi-square and t-test were used to compare the patients and tumors in both groups. The Kaplan-Meier curve estimates overall survival (Log-rank test). The *p*-value lower than 0.05 is statistically significant.

Results

Between January 1, 2006 and December 31, 2016, 105 patients with gastric cancer were included in the present study. These patients underwent curative surgery with lymphadenectomy. The patients were divided in to two groups, which were with and without splenectomy (non-splenectomy group and splenectomy group). Seventy patients were included in the non-splenectomy group and 35 patients were included in the splenectomy group. The clinical data and pathological staging is shown in Table 1. This data shows the statistical significance in patients who underwent total gastrectomy with splenectomy and subtotal gastrectomy with splenic preservation group.

The staging of patients was according to TNM staging seventh edition of AJCC classification 2010. All of the data is shown in Table 2. The patients were grouped according to their staging after complete surgical resection and data is shown the pathological (p) staging.

The incidence of dissected lymph nodes and lymph node metastasis is shown in Table 3. The data shows that the patients in the splenectomy group had a higher number of lymph nodes dissected or retrieved than the non-splenectomy group and the statistics are significant (*p*-value = 0.0004). Conversely, the lymph node metastasis in both groups did not show a significant statistical difference (*p*-value = 0.925). The rate of lymph node metastasis was 21.05% (4.34 to 35.71) in the non-splenectomy group and 6.66% (0 to 33.33) in the splenectomy group, but the difference is not statistically significant (*p*-value = 0.263). Finally, rate of lymph node metastasis was 12.63% (1.96 to 35.71). For the lymph node Group 10 metastasis, the number of lymph nodes dissected and lymph node metastasis showed no statistical significance in both groups by *p*-value, 0.524 and 0.160 respectively. The rate of lymph node Group 10 metastasis was 0% in the non-splenectomy group and 6.25% (0 to 41.66) in the splenectomy group (*p*-value = 0.129). Due to the small number of patients who underwent lymph node Group 10 dissection, the total rate of lymph node group 10 metastasis was 0% (0 to 16.66).

Complications after surgery in both groups are shown in Table 4. The data found only one case each of anastomosis leakage, surgical wound infection,

Table 1. Patient and tumor characteristics

Factor	Non-splenectomy group n = 70 (%)	Splenectomy group n = 35 (%)	*p*-value
Age (mean ± SD)	59.85 (1.57)	58.00 (2.18)	0.490
Sex			0.268
Male	40 (57.14)	16 (45.71)	
Female	30 (42.86)	19 (54.29)	
Surgical resection			
Total gastrectomy	17 (24.29)	29 (82.86)	0.000
Subtotal gastrectomy	44 (62.86)	4 (11.43)	0.000
Partial gastrectomy	3 (4.29)	1 (2.86)	0.718
Proximal gastrectomy	1 (1.43)	0	0.477
Lymphadenectomy			0.05
D1	8 (11.43)	0	
D2	62 (88.57)	35 (100)	
Histology type			
Well differentiate	1 (1.43)	2 (5.71)	0.214
Moderate differentiate	17 (24.29)	7 (20.00)	0.622
Poor differentiate	30 (42.86)	20 (57.14)	0.167
Undifferentiated	0	1 (2.86)	0.155
Signet ring cell	12 (17.14)	11 (31.43)	0.095
Location			
Proximal stomach	4 (5.71)	3 (8.57)	0.684
Middle stomach	14 (20.00)	12 (34.29)	0.150
Distal stomach	23 (32.86)	7 (20.00)	0.252

D1 and D2 lymphadenectomy according to Japanese gastric cancer treatment guidelines 2010 (ver. 3)[7]

pancreatic leakage, and intra-abdominal collection with post-operative pneumonia. In the non-splenectomy group, the post-operative complication was surgical wound infection in one case. All data of each complications shows no statistical significance in both groups. The patients' complications show statistical significance in both groups (*p*-value = 0.023).

The median follow-up time was 59.51 months. The rate of patients' follow-up was 91.42%. At the follow-up time, the recurrence was 12.86% in the non-splenectomy group and 8.57% in splenectomy group (*p*-value = 0.515). The metastasis occurrence was 24.29% in the non-splenectomy group and 20.00% in splenectomy group (*p*-value = 0.622).

At the follow up time, the five years' overall survival in the non-splenectomy group was 44.88 months and the splenectomy group was 53.75 months (*p*-value = 0.9368) (Fig. 1).

Discussion

In the present study, the data was compared between the non-splenectomy group and the splenectomy group in patients with gastric cancer who underwent curative resection with radical lymphadenectomy. In general, the data including age, gender, histologic type, location of cancer, and TMN staging showed no significant difference in both groups. Most patients in the non-splenectomy group underwent subtotal gastrectomy and those in the splenectomy group total gastrectomy. Subtotal gastrectomy with splenic preservation was correlated with the tumor location mostly located at the distal stomach area (32.86%). Conversely, total gastrectomy with splenectomy was correlated with the tumor located at middle of the stomach (34.29%).

In several studies, the number of lymph nodes removed was similar between the splenic preserved and splenectomy groups. For example, 40 versus 40[4] or 31.7 versus 28.9[8]. In our study, the difference between the non-splenectomy group and the splenectomy group was greater. The number of removed lymph nodes in the non-splenectomy group was 22 and in the splenectomy group was 43 (*p*-value = 0.0004). This is because most of splenectomy group was

Table 2. TNM staging of tumor

TNM staging	Non-splenectomy group n = 70 (%)	Splenectomy group n = 35 (%)	*p*-value
pT1	3 (4.92)	4 (12.12)	0.160
pT2	12 (19.67)	2 (6.06)	
pT3	29 (47.54)	14 (42.42)	
pT4	17 (27.87)	13 (39.39)	
pN0	14 (22.95)	9 (26.47)	0.934
pN1	18 (29.51)	8 (23.53)	
pN2	14 (22.95)	8 (23.53)	
pN3	15 (24.59)	9 (26.47)	
pM0	60 (98.36)	33 (100)	0.720
pM1	1 (1.63)	0	
Stage 1A	2 (3.28)	3 (9.09)	0.332
Stage 1B	4 (6.56)	0	
Stage 2A	8 (13.11)	4 (12.12)	
Stage 2B	16 (26.23)	6 (18.18)	
Stage 3A	14 (22.95)	5 (15.15)	
Stage 3B	11 (18.03)	9 (27.27)	
Stage 3C	5 (8.02)	6 (18.18)	
Stage 4	1 (1.64)	0	

Table 3. Incidence of lymph node metastasis and number of dissected lymph nodes (LN) and lymph nodes at splenic hilum (Group 10) metastasis

Lymph nodes (LN)	Non-splenectomy (n = 70)	Splenectomy (n = 35)	*p*-value
Number of LN (total)			
LN dissected, median (range)	22 (14 to 37)	43 (26 to 64)	0.0004*
LN metastasis, median (range)	3 (1 to 9)	3 (0 to 7)	0.925
Rate of LN metastasis, (%) median (range)	21.05 (4.34 to 35.71)	6.66 (0 to 33.33)	0.263
Number of LN (Group 10)			
LN dissected, median (range)	5 (2 to 6)	5 (2 to 10)	0.524
LN metastasis, median (range)	0 (0 to 0)	1 (0 to 1)	0.160
Rate of LN group 10 metastasis, (%) median (range)	0 (0 to 0)	6.25 (0 to 41.66)	0.129

* Significant level <0.05

performed by total gastrectomy. However, the number of lymph node metastasis was similar in both groups (3 versus 3). According to previous studies, the rate of lymph node metastasis could be predicted by the prognosis of patients and represents overall survival[9,10]. In the present study, the metastasis lymph node was similar in both groups, but the number of removed lymph nodes was different, therefore, the lymph node metastasis rate was different. However, the different lymph node metastasis rate shows no significant statistical difference (*p*-value = 0.263) and does not affect the overall survival in both groups. For lymph node group 10, the number of removed lymph nodes and lymph node metastasis shows no significant difference in both groups. The number of removed lymph nodes was similar (5 lymph nodes in both groups, *p*-value = 0.524). The lymph node Group 10 metastasis was one lymph node in the splenectomy group and no

Table 4. Post-operative complications

Complications	Non-splenectomy group n = 70 (%)	Splenectomy group n = 35 (%)	*p*-value
Anastomosis leakage	0	1 (2.86)	0.155
Surgical wound infection	1 (1.43)	1 (2.86)	0.614
Intra-abdominal collection	0	1 (2.86)	0.155
Pancreatic leakage	0	1 (2.86)	0.155
Pneumonia	0	1 (2.86)	0.155
Total patients	1 (1.43)	4 (11.43)	0.023

Table 5. Patients who had recurrence and metastasis at follow-up

Event	Non-splenectomy group n (%)	Splenectomy group n (%)	*p*-value
Recurrence	9 (12.86)	3 (8.57)	0.515
Metastasis	17 (24.29)	7 (20.00)	0.622

metastasis in the non-splenectomy group (*p*-value = 0.160). The rate of lymph node Group 10 metastasis was 6.25% found in the splenectomy group. The total rate of lymph node group 10 metastasis was 0% (0 to 16.66) because of the small number of patients who underwent lymph node group 10 dissection. Like several studies, the splenectomy in gastric cancer shows limited or no benefits for patients who undergo gastric resection with splenectomy and some reports show high mortality rate for splenectomy group[2-4,11].

In the splenectomy group, there is a higher incidence of complication than in the non-splenectomy group including anastomosis leakage, surgical wound infection, intra-abdominal collection, pancreatic leakage, and post-operative pneumonia but not statistically significant although the total patients' complication shows statistical significance (*p*-value = 0.023).

The splenectomy in previous studies shows no benefit or affects to the overall survival between splenic preserved and splenectomy group. In this study, the median follow-up time was 59.51 months. At the follow-up time, the recurrence rate and metastasis rate showed no significant difference in both groups. Five years' survival in the non-splenectomy group was 44.88 months and in the splenectomy group 53.75 months. This difference did not show a statistical significance.

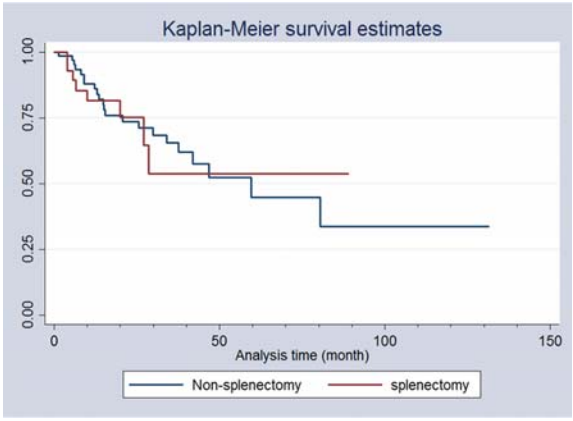

Fig. 1 The Kaplan-Meier Curve estimates overall survival of patients who had gastrectomy with and without splenectomy (*p*-value = 0.9368) (Log-rank test).

The limitation of this study was that it was a retrospective analysis. In Thailand, there is a low incidence of recorded cases of gastric cancer. Further studies are necessary to support our findings. The data in some patients was not complete and the small sample size in some analysis limited our study. Although this study had a small number of patients and is a retrospective review, some data shows the result not to be different from previous studies.

Conclusion

In the present data, the lymph node group 10 metastasis was low, and splenectomy provided limited or no benefits for removing lymph node group 10. In addition, for overall survival rates, there is no significant difference between performing splenectomy and splenic preservation. Patients who underwent splenectomy were presented with post-operative complications, although not significantly different between groups. Thus, gastric resection with lymphadenectomy is the preferred option for patients with gastric cancer. Splenectomy is an optional treatment for gastric cancer, however, in most cases it has no benefits and does not affect overall survival.

What is already know on this topic?

Gastrectomy with D2 lymphadenectomy is a standard treatment of gastric cancer in Japan and Korea. Splenectomy in gastric cancer surgery has no clear benefits for removing lymph nodes unless removing metastasis of lymph nodes at splenic hilum (Group 10).

What this study adds?

The lymph node group 10 metastasis was low, and splenectomy provided limited or no benefits for removing lymph node group 10. In addition, there was no significant difference between performing splenectomy and splenic preservation in the overall survival. Patients who underwent splenectomy were presented with post-operative complications, although not significantly different between groups. Splenectomy is an optional treatment for gastric cancer, however, in most cases it has no benefits and does not affect overall survival.

Potential conflicts of interest

None.

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ประโยชน์ของการตัดม้ามในการผ่าตัดรักษาโรคมะเร็งกระเพาะอาหาร

ไชยรัตน์ ทรัพย์สมุทรชัย, ธีรวุฒิ รักชอบ, ปิติโชติ หิรัญเทพ, ชุลีพร เจียรพินิจนันท์, ณัฐพงศ์ งามไพบูลย์, ปัตตาเวีย ช้อยเครือ

ภูมิหลัง: *การผ่าตัดกระเพาะอาหารร่วมกับการผ่าตัดต่อมน้ำเหลืองบริเวณรอบกระเพาะอาหารยังคงเป็นวิธีมาตรฐานในการรักษามะเร็งกระเพาะอาหาร โดยเฉพาะที่ประเทศญี่ปุ่นและประเทศเกาหลีใต้ แต่ประโยชน์จากการผ่าตัดม้ามออกเพื่อให้ได้ต่อมน้ำเหลืองโดยเฉพาะอย่างยิ่งบริเวณขั้วม้าม (Group 10) นั้นยังไม่ชัดเจน*

วัตถุประสงค์: *เพื่อศึกษาถึงผลลัพธ์ของการผ่าตัดมะเร็งกระเพาะอาหารร่วมกับการตัดม้ามเปรียบเทียบกับการไม่ตัดม้ามออกในการเลาะต่อมน้ำเหลืองบริเวณกระเพาะอาหารรวมถึงโอกาสในการที่มะเร็งกระจายไปที่ต่อมน้ำเหลืองรอบกระเพาะอาหารและบริเวณขั้วม้าม*

วัสดุและวิธีการ: *ศึกษาโดยวิธีการเก็บข้อมูลผู้ป่วยย้อนหลัง (Retrospective chart review) ในผู้ป่วยทุกรายที่ได้รับการวินิจฉัยโรคมะเร็งกระเพาะอาหารและได้รับการรักษาโดยวิธีการผ่าตัดเพื่อให้หายขาดจากโรคในช่วงเวลาระหว่างวันที่ 1 มกราคม พ.ศ. 2549 ถึง วันที่ 31 ธันวาคม พ.ศ. 2559 ในโรงพยาบาลรามาธิบดี โดยเปรียบเทียบผู้ป่วยในกลุ่มที่ผ่าตัดกระเพาะอาหารและเก็บรักษาม้ามกับกลุ่มที่ผ่าตัดกระเพาะอาหารร่วมกับการผ่าตัดนำม้ามออก*

ผลการศึกษา: *จากการเก็บข้อมูลพบผู้ป่วย 70 คน ในกลุ่มเก็บรักษาม้ามและ 35 คน ในกลุ่มผ่าตัดนำม้ามออก ข้อมูลโดยทั่วไป เช่น อายุ เพศ ชนิดของชิ้นเนื้อ ตำแหน่งรอยโรค และระยะของตัวโรคไม่พบว่ามีความแตกต่างกันทางสถิติ สำหรับการเลาะต่อมน้ำเหลือง Group 10 พบว่าของผู้ป่วยทั้งสองกลุ่มไม่มีความแตกต่างกันทั้งในด้านจำนวนต่อมน้ำเหลืองที่เลาะได้และจำนวนต่อมน้ำเหลืองที่มะเร็งกระจายไป (p-value = 0.524 และ 0.16 ตามลำดับ) อัตราการกระจายของมะเร็งไปที่ต่อมน้ำเหลือง Group 10 คิดเป็นร้อยละ 6.25 ซึ่งพบในกลุ่มที่ตัดม้ามออก ส่วนจำนวนต่อมน้ำเหลืองที่เลาะออกได้ทั้งหมดรวมกับต่อมน้ำเหลือง group 10 แล้วนั้นพบว่าจำนวนต่อมน้ำเหลืองที่เลาะได้พบมากในกลุ่มที่ตัดม้ามออกด้วย (p-value = 0.0004) แต่อย่างไรก็ตามอัตราการกระจายไปต่อมน้ำเหลืองของมะเร็งนั้นไม่มีความแตกต่างกันทางสถิติ (p-value = 0.925) ติดตามการรักษาผู้ป่วยไปเป็นระยะเวลาประมาณ 59.51 เดือน ไม่พบความแตกต่างกันในเรื่องของการกลับเป็นซ้ำ การกระจายไปบริเวณอื่นๆ รวมถึงอัตราการมีชีวิตรอด โดยที่อัตราการรอดชีวิตในกลุ่มที่เก็บรักษาม้ามคิดเป็นร้อยละ 44.88 และกลุ่มที่ผ่าตัดนำม้ามออกคิดเป็นร้อยละ 53.75 (p-value = 0.9368)*

สรุป: *การผ่าตัดกระเพาะอาหารร่วมกับการผ่าตัดต่อมน้ำเหลืองบริเวณรอบกระเพาะอาหาร โดยไม่มีความจำเป็นต้องตัดม้ามออกด้วยนั้น เพียงพอต่อการรักษามะเร็งกระเพาะอาหาร และการผ่าตัดม้ามออกโดยไม่จำเป็นนั้นไม่มีผลต่ออัตราการรอดชีวิตของผู้ป่วย*