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Survival outcomes of billroth-I reconstruction following distal gastrectomy for gastric cancer patients in Vietnam: A 5-year follow-up

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ABSTRACT

This study aims to describe the long-term survivorship of Billroth I (or Pean's) reconstruction technique in patients with distal gastric cancer. A single-arm longitudinal observational study was conducted at Viet Duc University Hospital, Hanoi, Vietnam, from 2018 to 2021. A total of 103 patients who were diagnosed with primary carcinoma in the lower third of the stomach and underwent lower pole gastrectomy with Péan anastomosis were recruited. The Kaplan–Meier analysis was used to estimate the survival outcome. A multivariate Cox proportional hazard regression model was used to measure the factors associated with survivorship. Results showed that 8.7% died during the study period. The Restricted Mean Survival Time (RMST) was 61.9 (95%CI=59.4-64.4) months. RMST was significantly different across the stages of cancer, T and N. Specifically, patients with advanced stage (III) had a substantially lower RMST (49.2 months) compared to those with early-stage (I&II). Patients with T4 or N3 also had the lowest RMST compared to those with other characteristics (p<0.05). Female patients had a lower risk of dying than their male counterparts (HR=0.092, 95%CI=0.013-0.661). Patients with a higher level of Node (N) had a significantly higher risk of dying than those with a lower level (HR=5.103; 95%CI=1.716-15.178). Having comorbidities was associated with a lower risk of dying (HR=0.066; 95%CI=0.008-0.531) than not having comorbidity. To conclude, the findings indicate favourable long-term results for patients with distal gastric cancer undergoing the Billroth I (or Pean's) reconstruction technique. The practice above may be the established protocol for managing these particular patients.

Keywords: Survival outcome, Billroth-I Reconstruction, Pean anastomosis, Distal gastrectomy, Gastric cancer.

INTRODUCTION

Gastric cancer is one of the most common types of cancer worldwide. In 2018, it was estimated that there were 1,033,700 new cases of gastric cancer worldwide, resulting in over 782,600 deaths ^[1]. In Vietnam, according to Globocan 2018, gastric cancer ranks third in both genders after liver cancer and lung cancer, with an agestandardized incidence rate of 11—38 per 100,000 population ^[2]. Despite a declining incidence rate in recent decades, cancer remains the third leading cause of death worldwide ^[1]. Gastric cancer commonly occurs in the antrum of the stomach (constituting 60-70% of cases), followed by the lesser curvature of the stomach (18-30%), with other regions being less frequently affected, such as the greater curvature of the stomach (~3%), the gastric fundus (12%), and the

gastric cardia (9%). Adenocarcinoma is a prevalent malignant type, accounting for 90% of gastric cancers and has been extensively researched ^[3].

Péan (1879) was the first to perform a for a patient with gastric cancer. Since then, surgical treatment for gastric cancer has made significant advancements, playing a crucial role in the management of gastric cancer^[4]. The Japanese Gastric Cancer Association provided guidelines for the treatment of gastric cancer, recommending radical surgery by the standard, which involves resection of at least 2/3 of the stomach in combination with D2 lymph node dissection ^[5]. The concept of partial gastrectomy is a commonly used term in medical literature. Several scientists have concluded that early detection and radical surgery are two measures to prolong the survival time of patients with gastric cancer^[6]. Studies on the lymphatic system, metastatic characteristics of gastric cancer, the boundaries of gastric resection, lymph node dissection techniques, preand post-operative chemotherapy and radiotherapy, and targeted therapy have provided valuable insights into improving the quality of treatment and prognosis and extending the survival time of patients ^{[7-} 10]

In recent decades, there has been a growing trend in the early detection rate of early-stage gastric cancer, along with the global consensus on the principle of radical surgery, contributing to an improvement in the 5-year survival rate of patients ^[11]. Numerous authors have conducted research to improve the postoperative quality of life for patients and provided initial insights into the role of revascularisation methods following subtotal gastrectomy for the treatment of lower third gastric cancer. Two options were chosen, including the Billroth I and Roux-en-Y methods [6]. In Vietnam, there is significant research on the pathology of gastric cancer ^[12]; however, there is a paucity of studies explicitly focusing on postoperative circulation recovery following the Billroth I method and Péan type reconstruction after partial gastrectomy for lower-third gastric cancer. This study aims to describe the long-term survivorship of Billroth I (or Pean's) reconstruction technique in patients with distal gastric cancer. healthcare.

MATERIALS AND METHODS

Study Design and Patients

A single-arm longitudinal observational study was conducted at Viet Duc Friendship Hospital, Hanoi, Vietnam, from 2018 to 2021. The selection criterion is that all patients diagnosed with primary carcinoma in the lower third of the stomach underwent lower pole gastrectomy with Péan anastomosis and consented to participate in the study at the hospital. The exclusion criteria include patients with advanced gastric primary adenocarcinoma with distant metastasis, peritoneal metastasis, or patients with primary adenocarcinoma in the lower third of the stomach, with metastases invading the duodenum, or those for whom surgery is not indicated due to systemic illness. A total of 103 patients were recruited for the study. The research has been approved by the Ethics Council of Hanoi Medical University: Code: 497/ GCN-HĐĐĐNCYSH-DHYHN.

Study Procedures and Data Collection

The patients who were admitted to the hospital and underwent surgery for the resection of 1/3 of the stomach with the Billroth I (or Pean's) reconstruction technique for the treatment of primary adenocarcinoma were screened according to selection criteria and excluded as appropriate. Patients who met the criteria were invited to participate in the study and asked to provide their informed consent to participate in the research. During the course of patient treatment at the hospital, patient information was gathered through standard medical records, including demographic characteristics (age, gender, living location, occupation), comorbidities, Tumor (T), Node (N), staging of cancer according to TNM classification ^[13], histological type of cancer, and tumour location.

After discharge, patients were scheduled for follow-up appointments every month for the first six months post-discharge and then every three months from month 6 to month 12 after surgery (in the first year) to detect complications of the anastomosis such as reflux syndrome, dumping, ulceration, anastomotic stenosis, and adverse effects of postoperative chemical therapy. Subsequently, a yearly follow-up examination was conducted to evaluate the recurrence of the condition and the extent of local and distant metastasis in conjunction with the time of detection. The survivorship was also recorded. The overall survival time was calculated from the time of surgery to the time of confirmed death or the patient still alive at the study's end (30/6/2023).

Statistical Analysis

The data were examined using Stata version 16.0. The study variables were summarised using percentage, frequency, average, and standard deviation. The Kaplan–Meier analysis was used to estimate the survival outcome. Due to this study's low occurrence of events, the Restricted Mean Survival Time (RMST) was calculated to assess the mean overall survival time ^[14]. The Log-rank test was employed to evaluate variations in survival rates among different characteristics. The study utilised a Multivariate Cox Proportional Hazard Regression Model to examine factors that could predict survival outcomes. A p-value equal to or less than 0.05 was deemed statistically significant.

RESULTS

Of 103 patients, Table 1 shows that 41.8% were female. The mean age was 60.6 (SD=12.5) years old. Most of the patients lived in urban areas (57.3%) and were retired (37.9%)

Table 2 shows that 34.9% had any comorbidities. Regarding TNM classification, most of the patients had T1 (44.7%) and T3 (26.2%), N0 (50.5%) and N1 (19.4%). The majority of patients were

At stage IA (32.0%), followed by IIA (15.5%), IIIA (13.6%) and IIIB&C (13.6%). Adenocarcinoma was the most common histological type (74.8%), followed by signet ring cell carcinoma and others (25.2%). The majority of patients had tumours at lesser curvature position (50.5%), posterior wall (17.5%) and pyloric (13.6%).

Table 1: Demographic characteristics of patients					
Characteristics	Value				
Gender, Female, n (%)	43 (41.8%)				
Age, years, Mean (SD)	60.6 (12.5)				
Living location, Urban, n (%)	59 (57.3%)				
Occupation, n (%)					
Self-employed	17 (16.5%)				
Farmers	23 (22.3%)				
Retirement	39 (37.9%)				
Others	24 (23.3%)				

Overall, 8.7% died during the study period. The mean RMST was 61.9 (95%CI=59.4-64.4) months. Table 3 and Figure 2 show that RMST was significantly different across the stages of cancer, T and N. Specifically, patients with advanced stage (III) had a substantially lower RMST (49.2 months) compared to those with early-stage (I&II). Patients with T4 or N3 also had the lowest RMST compared to those with other characteristics (p < 0.05)

Table 4 shows the results of the Multivariate Cox Proportional Hazard model. Female patients had a lower risk of dying than their male counterparts (HR=0.092, 95%CI=0.013-0.661). Patients with a higher level of Node (N) had a significantly higher risk of dying than those with a lower level (HR=5.103; 95%CI=1.716-

15.178). Having comorbidities was associated with a lower risk of dying (HR=0.066; 95% CI=0.008-0.531) than not having comorbidity.

Table 2. Clinical ak

Table 2: Clinical characteristics of patients				
Characteristics	Value			
Having cormobidity, n (%)				
No	67 (65.1%)			
Yes	36 (34.9%)			
Stage of cancer, n (%)				
IA	33 (32.0%)			
IB	13 (12.6%)			
IIA	16 (15.5%)			
IIB	13 (12.6%)			
IIIA	14 (13.6%)			
IIIB	9 (8.7%)			
IIIC	5(4.9%)			
Tumour (T), n (%)				
T1	46 (44.7%)			
T2	10 (9.7%)			
T3	27 (26.2%)			
T4	20 (19.4%)			
Node (N), n (%)				
N0	52 (50.5%)			
N1	20 (19.4%)			
N2	17 (16.5%)			
N3	14 (13.6%)			
Histological type of cancer				
Adenocarcinoma	77 (74.8%)			
Signet ring cell carcinoma and others	26 (25.2%)			
Tumor position				
Anterior	3 (2.9%)			
Posterior	18 (17.5%)			
Pyloric	14 (13.6%)			
Greater curvature	13 (12.6%)			
Lesser curvature	52 (50.5%)			
Antrum	3 (2.9%)			

Table 3: Survival time among patients							
Characteristics		Survival rate	Restricted Mean Survival Time (months)	Log-rank test			
		N (%)	Mean (95%CI)				
Total		94 (91.3%)	61.9 (59.4-64.4)				
Gender	Male	54 (90.0%)	57.6 (54.3-61.0)	0.51			
	Female	40 (93.0%)	62.9 (59.8-66.1)				
Age (years)	< 60	38 (95.0%)	63.0 (59.3-66.7)	0.28			
	≥ 60	56 (88.9%)	60.7 (57.2-64.3)				
Occupation	Self-employed	15 (88.2%)	56.8 (50.4-63.3)	0.37			
	Retirement	34 (87.2%)	56.9 (52.6-61.1)				
	Others	45 (95.7%)	63.9 (61.1-66.6)				
Stage of cancer	Early stage (I&II)	75 (100.0%)	65.8 (65.8-65.8)	< 0.01			
	Advanced stage (III)	19 (67.9)	49.2 (42.2-56.1)				
Histological type of cancer	Adenocarcinoma	68 (88.3%)	60.5 (57.2-63.8)	0.07			
	Squamous cell carcinoma and others	26 (100.0%)	65.8 (65.8-65.8)				
Tumor (T)	T1	46 (100.0%)	65.8 (65.8-65.8)	< 0.01			
	T2	10 (100.0%)	60.0 (60.0-60.0)				
	Т3	22 (81.5%)	54.6 (48.8-60.4)				
	T4	16 (80.0%)	53.7 (46.4-61.0)				
Node (N)	N0	52 (100.0%)	65.8 (65.8-65.8)	< 0.01			
	N1	20 (100.0%)	65.8 (65.8-65.8)				
	N2	13 (76.5%)	52.1 (44.1-60.1)				
	N3	9 (64.3%)	42.9 (33.4-52.3)				
Comorhidity	No	60 (89.6%)	60.9 (57.5-64.4)	0.40			
Comorbidity	Yes	34 (94.4%)	63.3 (60.0-66.7)				

Table 4: Factors associated with survivorship of gastric cancer patients

Factors	Hazard Ratio	p-value	95%CI	
Age	1.068	0.119	0.983	1.159
Gender (Male vs Female)	0.092	0.018	0.013	0.661
Occupation (vs Self-employed)				
Retirement	0.375	0.381	0.042	3.362
Others	0.092	0.059	0.008	1.099
Tumor (T)	1.539	0.381	0.586	4.037
Node (N)	5.103	0.003	1.716	15.178
Having comorbidity (No vs. Yes)	0.066	0.011	0.008	0.531

Figure 1: Kaplan-Meier survival curve according to different clinical characteristics



DISCUSSION

This study partly contributed to the body of literature about the long-term outcomes of Billroth I (or Pean's) reconstruction technique following distal gastrectomy for gastric cancer patients in Vietnam. We found a high rate of overall survival after five years of follow-up. Moreover, several factors such as gender, comorbidities and cancer characteristics were found to be associated with a higher risk of dying.

The Billroth I method of connecting the stomach to the duodenum involves two techniques: the Péan style, which consists of sewing the remaining stomach to reduce narrowing before connecting to the duodenal apex, and the Von Habeer style, which leaves the remaining gastric apex intact to communicate to the duodenum apex. This approach aligns with the body's natural physiological processes as it allows the food to be digested in the stomach, pass through the duodenum, and be absorbed with bile and pancreatic juice. Breaking down food and taking in essential nutrients are very similar. The consistent action of digestive enzymes leads to fewer cases of diarrhoea and dumping syndrome and lower rates of ulcer and anastomotic cancer recurrence ^[15]. This method can be performed quickly, with only one anastomosis and without the need to close the

duodenal apex, which helps prevent complications. Due to the creation of only a single connection and avoiding opening the jejunum, the surgery is more hygienic and less prone to infection. This method has limitations, as it is challenging to suture because of the broad, thick gastric process, the narrow duodenal process, and the thin wall that may lead to anastomotic leaks. Additionally, it can be challenging to perform in cases of duodenal inflammation with sclerosis.

We utilised the Péan technique on patients with cancer located in the lower third of the stomach that has not spread to the duodenum. The findings indicated that there were no ulcers in the duodenum, the anastomosis was free from tension and ensured oncological safety, the distance between the upper and lower incision sites was promptly biopsied, and no cancerous tissue was left behind. To execute this technique, we conducted the Kocher procedure, repositioned the duodenum to prevent stretching of the anastomotic mouth during the anastomosis, and promptly biopsied the lymph node group 13, 16. We narrowed the stomach opening by sewing it after cutting; then, we opened nearly half of the circumference of the duodenum on the back. We used Vicryl 3/0 suture to sew the first layer of the stomach and duodenal muscle wall and then performed a second layer of total extraction using Vicryl 3/0 suture. Following that, we removed the rest of the duodenum in a curved shape, inserted a gastric tube through the connection to the D3-4 duodenum, and stitched the entire first layer with Vicryl 3/0 suture. Then, we used separate 3/0 Vicryl thread to suture the second layer of the gastric and duodenal muscles. Ultimately, we stitched the top and bottom edges of the connection together.

The findings of our study indicate that this approach yields favourable outcomes. The survival rate of our patients was 91.3%, and the RMST was 61.9 months. A recent study conducted in Japan revealed that approximately 60% of gastric cancer patients undergoing gastrectomy surgery were in the early stages of the disease. Furthermore, the 5-year survival rate for these patients exceeded 90% ^[16]. A study conducted in Korea found that patients who underwent partial gastrectomy for cancer and received Billroth I reconstruction had significantly shorter surgical durations, earlier removal of nasogastric tubes, and faster recovery of bowel function compared to their counterparts who did not undergo this specific reconstruction technique. The study found that there were no complications of fistula, bleeding, or death in either the Billroth II reconstruction or the gastrectomy group ^[17]. In European and North American countries, the Roux-en-Y method is frequently utilised for recovery as it has been shown to decrease reflux and minimise anastomotic inflammation. The Roux-en-Y method is recommended over alternative approaches for achieving these desired outcomes. The Roux-en-Y method is performed infrequently in Asian countries, mainly due to its intricate

technical demands and prolonged surgery duration compared to the Billroth I method ^[19]. Nevertheless, no significant disparity in the long-term outcomes was observed across the various techniques ^[16,17].

Our research indicates that male patients, patients with higher Node levels, and patients without comorbidity are at higher risk of mortality compared to other patient groups. In gastric cancer patients, the likelihood of mortality is higher in men compared to women due to differences associated with androgen receptors in the modulation of cell proliferation and tumour growth ^[18]. Therefore, despite the high success rate of the approach, the risk of mortality from gastric cancer in male patients remains higher than in female patients. Similarly, research has shown that patients with higher Node levels have a higher mortality risk, a finding consistent with earlier studies ^[19,20]. It is noteworthy that we observed a lower mortality risk among patients without comorbidities compared to those with comorbid conditions such as diabetes or hypertension. This phenomenon can be attributed to patients with comorbidities exhibiting better postoperative dietary and self-care practices due to their heightened awareness of their health condition. Meanwhile, in patients without comorbidities, their ability to manage their disease may be at a lower level [21].

It is important to note that this study has limitations. First, we could not evaluate all patients because of death, loss of follow-up, or lack of informed consent for the amended protocol. Most patients who participated in this study were followed in their respective hospitals, but it is possible that their interest in the prosecution diminished five years after surgery. Second, laparoscopic surgery is currently the standard surgical procedure for distal gastrectomy for gastric cancer. Further studies should be performed to measure the differences between laparoscopic surgery and the technique used in our study. Despite these limitations, our study should aid surgeons in deciding between the two procedures.

The current study had some significant limitations. First, we cannot guarantee that our database includes all potential factors that could create confusion. It is possible that overlooked factors, which are difficult to measure or unknown, may be necessary due to a bias in selection. Secondly, while evaluating surgical procedures is a widespread issue in research, the methods used vary among different institutions or surgeons. One example is the anastomotic methods that could impact the result, such as hand stitching or mechanical anastomosis. Furthermore, we have to consider the latest developments in surgical techniques and equipment. To predict the future results of this study, the patients who had gastrectomy surgery from 2018 to 2021 were evaluated. However, advancements in stapling devices, surgeons' skills, optical systems, and robot-assisted surgery have rapidly evolved during this decade. Hence, our findings may not

directly translate to current real-world applications. Thirdly, our research was conducted in a single hospital with limited participants, which hindered our ability to apply our findings to other groups. More extensive research involving more participants and conducted across multiple locations is necessary.

CONCLUSIONS

The findings indicate favourable long-term results for patients with distal gastric cancer undergoing the Billroth I (or Pean's) reconstruction technique. The practice above may be viewed as the established protocol for managing these patients.

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