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Periampullary Regional Tumors, Pylorus Preserving Whipple Procedure and More Than 10-Year Survival

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ABSTRACT

Introduction: This study analyzed factors affecting postoperative survival in patients with periampullary region tumors who underwent Whipple procedure and assessed survival of such patients more than 10 years.

Method: Patients with periampullary pancreatic tumors who underwent Whipple procedure in the last 3 years were retrospectively analyzed. Survival rates were statistically analyzed using the Kaplan-Meier method, and compared by the log-rank test. Multivariate survival was analyzed using a Cox proportional hazards model.

Results: Twenty-eight patients, 20 men and 8 women underwent surgery for periampullary tumor. There was no early mortality. Two patients had major and five had minor complications. One patient had chronic pancreatitis, one had duodenal gastrointestinal stromal tumor, and another had pancreatic neuroendocrine tumor while 25 of the patients had pancreatic, ampullary or choledochal adenocarcinoma. Postoperative survival was significantly longer in patients with ampullary than pancreatic cancer ($p<0.001$). Median survival rates of patients with stages I–IV tumors were 69.75, 33.80, 21.90 and 6.00 months, respectively ($p<0.001$). Overall survival was significantly longer in patients who received R0 resection ($p<0.001$) and in patients with node negative tumors ($p=0.003$). Survival rate was 13 folds lower in patients with portal vein resection ($p=0.022$).

Conclusion: Despite improvements in diagnosis, surgery and adjuvant treatments, patients with periampullary tumors have a very low survival rate≥10 years, if they are histopathologically diagnosed with adenocarcinoma. Early diagnosis, extended resection and optimal adjuvant treatment are needed to extend patient survival.

Keywords: Periampullary tumors, ampullary tumors, duodenum tumors, choledochal tumors, whipple procedure

ÖZ

Periampuller bölge tümörlerinde uygulanan pilor koruyucu whipple ameliyatı ve 10 yıllık sağkalım

Giriş: Bu çalışmada periampuller bölge tümörü olan ve Whipple prosedürü uygulanan hastalarda postoperatif sağkalımı etkileyen faktörler analiz edildi ve bu hastaların 10 yıldan fazla hayatta kalma olasılıkları değerlendirdi.

Yöntem: Son 3 yılda periampuller pankreas tümörü nedeniyle Whipple prosedürü uygulanan hastalar retrospektif olarak incelendi. Hayatta kalma oranları, Kaplan-Meier yöntemi kullanılarak istatistiksel olarak analiz edildi ve log rank testiyle karşılaştırıldı. Çok değişkenli sağ kalım, bir Cox orantılı risk modeli kullanılarak analiz edildi.

Bulgular: Periampuller bölgenin tümörü olan yirmi sekiz hasta (E/K:20/8) ameliyat edildi. Erken dönem mortalite gözlenmedi. İki hastada major, beşinde minör komplikasyonlar görüldü. Bir hastada kronik pankreatit, bir hastada duodenal gastrointestinal stromal tümör, bir hastada pankreatik nöroendokrin tümör, 25 hastada ise pankreatik, ampuller veya koledok adenokarsinomu vardı. Ampuller tümörü olan hastalarda postoperatif sağkalım pankreatik kansere göre anlamlı olarak daha uzun bulundu ($p<0.001$). Evre I-IV tümörlü hastaların medyan sağkalım oranları sırasıyla 69.75, 33.80, 21.90 ve 6.00 ay olarak saptandı ($p<0.001$). Genel sağkalım R0 rezeksiyon yapılan hastalarda ve lenf nodu negatif olan hastalarda anlamlı derecede daha uzun bulundu ($p=0.003$). Portal ven rezeksiyonu yapılan hastalarda sağkalım oranı 13 kat daha düşüktü ($p=0.022$).

Sonuç: Tanı, cerrahi ve adjuvan tedavilerdeki gelişmelere rağmen, periampullar bölge tümörleri olan hastalar, histopatolojik olarak adenokarsinoma tanısı alırsa, 10 yıl üzerinde hayatta kalma oranları çok düşüktür. Hastanın yaşam süresini uzatmak için erken tanı, genişletilmiş rezeksiyon ve optimal adjuvan tedaviye ihtiyaç vardır.

Anahtar kelimeler: Periampuller tümörler, ampulla tümörleri, duodenum tümörleri, koledok tümörleri, whipple ameliyatı

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INTRODUCTION

Surgical resection using the Whipple procedure is the only curative treatment for patients with periampullary pancreatic tumors (1,2). Over the last 20 years, mortality rate of patients undergoing the Whipple procedure has declined markedly to less than 5%, although morbidity rates have remained high (30%-50%) (3-5). Despite significant improvements in surgical techniques, perioperative care and adjuvant chemo-radiotherapy options, 5-year survival rate has improved only from 3% to 5% over the last 20 years (6). In the United States, 5-year survival rates for patients with local, locally advanced, and metastatic disease are 20%, 8% and 2%, respectively. Among these patients, only 7% present with potentially curable disease that is truly localized (2,6).

Most follow-up studies do not exceed 5 years due to the low survival rates. Therefore, correlates of long-term survival after resection have not been determined. Very few studies have described patients who survive more than 10 years. Increased life expectancy following the Whipple procedure in patients with periampullary pancreatic tumors depends on many factors, including negative nodal status, negative resection margins, small tumor diameter and a diagnosis of well-differentiated carcinoma.

This study retrospectively analyzed patients, who underwent surgery for periampullary pancreatic tumors between January 2004 and January 2007 and were followed-up for at least 10 years. Results of these patients were compared with those in the literature to assess factors associated with increased overall survival, including factors associated with survival for more than 10 years after the Whipple procedure.

MATERIAL AND METHOD

Our study retrospectively evaluated patients with periampullary pancreatic tumor, who underwent the Whipple procedure between January 2004 and January 2007 at Istanbul Training and Research Hospital. Factors evaluated included patient gender, age, preoperative radiologic findings, preoperative application of stent or endoscopic retrograde cholangiopancreatography (ERCP), operation duration, peri-operative blood loss, portal vein resection, pathological findings (resection type, tumor diameter, pathological diagnosis, number of lymph nodes and existence and phasing of invaded lymph nodes), postoperative early complications and date of death.

All patients were consulted with the oncology department. None received neoadjuvant chemoradiotherapy. Patients diagnosed with adenocarcinoma received postoperative adjuvant chemotherapy for 28–50 days (median, 35 days), as warranted. Chemotherapy was a standard 5-FU based regimen. Patients who were node positive and/or underwent R1 resection received 40 Gy radiotherapy along with chemotherapy.

Survival rates were statistically analyzed by Kaplan-Meier method and compared by the log-rank test. Multivariate survival was analyzed using a Cox proportional hazards model ($p<0.05$).

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional ethics committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

RESULTS

During the study period, 28 patients (20 men, 8 women with mean ages 68 and 65 years, respectively) underwent surgery for periampullary tumors, with all operations performed by the same surgical team. The procedure was pylorus preserving Whipple procedure in every patient. Ten underwent extended lymphatic dissection, and one underwent simultaneous metastectomy of the liver left lobe lateral segment because of a metastatic tumor of diameter 6–7 mm.

Six patients underwent pre-operative biliary drainage, including four who underwent ERCP and internal stent, and two who underwent percutaneous transhepatic cholangiography (PTC) and external drainage.

Median duration of surgery was 315 minutes (range, 280–360 minutes), with median intraoperative blood loss of 400 ml (range, 350–1000 ml). One patient had a 2/3 circular portal vein invasion, requiring total excision of the portal vein and its replacement by a graft. Three patients had less than 1/3 portal vein tumor invasion, resulting in portal vein wedge resection with primary anastomosis.

None of patients died within the first 30 days following surgery. Two patients had major complications, including one with post-operative bleeding and one with a pancreatic fistula; and five had minor complications, including two with delayed gastric emptying and three with wound infection, making the cumulative complication rate 25%.

Pathologic analyses showed that there were chronic pancreatitis, duodenal gastrointestinal stromal tumor (GIST), and a pancreatic neuroendocrine tumor in one patient for each, whereas 25 patients had pancreatic, ampullary, or choledochal adenocarcinomas (Table 1).

Table 1: Pathologic analysis of the 28 patients who underwent the Whipple procedure

Pathology	Female	Male
Average tumor size		
Adenocarcinoma	3	10
Endocrine tumor	1	0
Ampullary cancer	0	4
Duodenal cancer		
Adenocarcinoma	1	3
Stromal tumor	1	0
Bile duct cancer	1	3
Chronic pancreatitis	1	0

The patient with chronic pancreatitis was excluded from this study.

Table 2: Tumor specifications

Median (range) tumor diameter, cm	2.9 (1–6)
Patient characteristics, n	
R0 resection	16
Extended lymphatic dissection	10
Stage I	6
Stage II	10
Stage III	10
Stage IV	1
High grade differentiated	3
Moderately differentiated	17
Poorly differentiated	7
Chronic inflammation	1
Median (range) number of lymph nodes	12 (8–26)
Median (range) number of positive lymph nodes	3 (0–7)

Table 2 shows tumor diameters, number of patients with underwent R0 resection, results of lymphatic dissection, tumor staging and other tumor characteristics.

Two patients who underwent surgery in May and June 2004, and who did not have adenocarcinoma pathology remained alive in 2016. These two patients are summarized below:

Patient 1 was a 26-year-old woman who presented with anemia. Radiological examination revealed a tumor of the pancreas uncinate process. Surgery was performed, consisting of the pylorus preserving Whipple procedure and extended lymphatic dissection. Pathological results showed a high-risk gastrointestinal stromal tumor, measuring 4 x 2.5 x 3 cm, originating from the posterior duodenum wall. The tumor was positive for pancreatic invasion, an expansive infiltration pattern, and necrosis. The tumor showed 40/50 BBS mitosis, with tumor cells positive for vimentin and over 50% positive for CD 117. The tumor was immunohistochemically negative for smooth muscle actin, desmin, CD34 and S-100. Invasion was not observed within surgical margins. A total of 18 lymph nodes were dissected, with all being tumor negative. Following resection, she did not receive adjuvant therapy. The patient was followed-up periodically. A CT examination in 2012 detected a suspect metastatic image and the patient was started on imatinib.

Patient 2 was a 27-year-old female woman who had presented with icterus. Radiological scans revealed intra- and extra-hepatic biliary tree dilatation, with narrowing of the last 2 cm of the distal choledocus and an external mass image. Surgery was performed, involving the pylorus preserving Whipple procedure and extended lymphatic dissection. Pathological results indicated a pancreatic tumor, measuring 1.5 x 1.2 x 1 cm and diagnosed as a well-differentiated endocrine tumor. The surgical margins were negative. A total of 26 lymph nodes were dissected, with none showing evidence of tumor invasion. The mitotic rate was <2 per 10 high power fields. Immunohistochemical staining showed that tumor cells were positive for NSE and synaptophysin and weakly positive for chromogranin. The patient did not receive adjuvant chemo-radiotherapy. During regular follow-ups, the patient has not shown any clinical, radiological or laboratory abnormalities.

After excluding these two patients, along with the patient with chronic pancreatitis, the remaining 25 patients with adenocarcinoma could be divided in four groups based on the site of the primary tumor: the pancreas, ampulla of Vater, distal choledochus and duodenum. Comparison of

Table 3: Overall survival of patients with pancreatic, ampullary, distal choledocus, andduodenal cancer

Primary tumor site	Mean(a)				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
Pancreas	20.231	2.013	16.285	24.177	21.000	3.595	13.954	28.046
Ampulla	69.750	2.689	64.480	75.020	68.000	5.000	58.200	77.800
Choledochus	32.500	1.893	28.790	36.210	30.000	.	.	.
Duodenum	42.500	2.500	37.600	47.400	42.000	4.000	34.160	49.840
Overall	33.680	3.810	26.212	41.148	30.000	1.470	27.119	32.881

Table 4: Overall survival of patients with pancreatic and other types of peri-ampullary cancer

Pancreas	Mean(a)				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
1.00	20.231	2.013	16.285	24.177	21.000	3.595	13.954	28.046
9.00	48.250	4.907	38.632	57.868	42.000	5.196	31.816	52.184
Overall	33.680	3.810	26.212	41.148	30.000	1.470	27.119	32.881

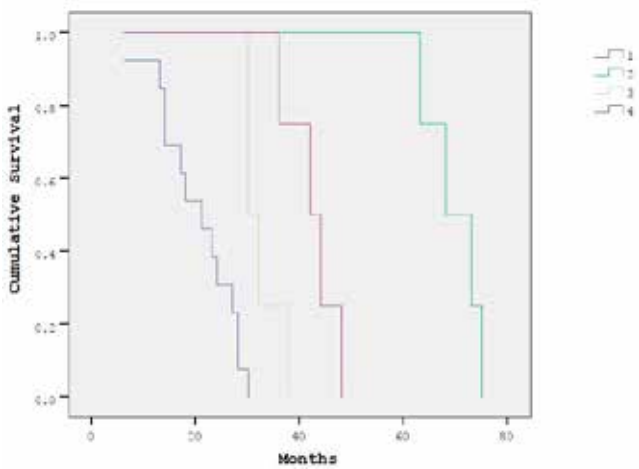

Figure 1: Kaplan-Meier analysis of overall survival duration of patients with pancreatic (Group 1), ampullary(Group 2), distal choledocus (Group 3), andduodenal (Group 4) cancers

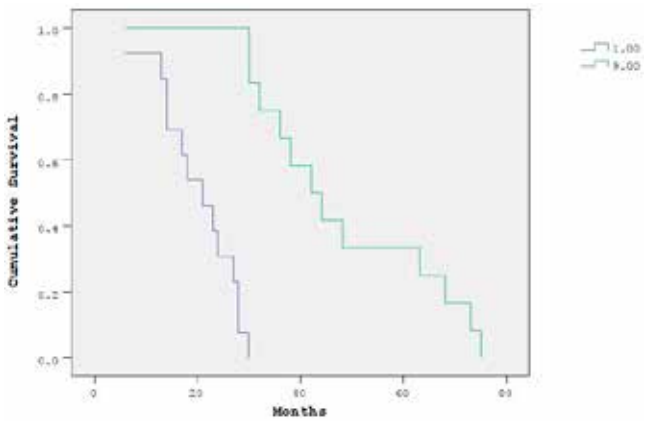

Figure 2: Kaplan-Meier analysis of overall survival duration of patients with pancreatic cancer (Group 1), and other types of peri-ampullary cancers (Groups 2–4)

their post-operative survival rates showed that overall survival was shortest in patients with pancreatic cancer and longest in patients with ampullary cancer (Log-rank test p<0.001, Chi-Square=30.500) (Table 3, Figure 1).

A comparison of patients with pancreatic and other peri-ampullary tumors showed a significant difference in post-operative overall survival, with survival duration being shorter in patients with pancreatic adenocarcinoma (median, 21 months; mean, 20.23 months) than in the other three groups (median, 42 months; mean, 48.25 months) (Log-Rank test p<0.001, Chi-Square=24.840) (Table 4, Figure 2).

Similarly, a comparison of patients with ampullary tumors and those with other types of periampullary tumors showed a significant difference in postoperative overall survival. Survival duration was significantly longer in patients with ampullary adenocarcinomas (median, 68 months; mean, 69.75 months) than in the other three groups (median, 28 months; mean, 26.81 months) (Log-Rank test p<0.001, Chi-Square=12.158) (Table 5, Figure 3).

Kaplan-Meier analysis of the 25 patients with periampullary adenocarcinoma divided by tumor stage showed statistically significant differences in overall postoperative survival. Median survival in patients with stages I–IV tumors were 69.75, 33.80, 21.9 and 6.00 months, respectively (Log-Rank

Table 5: Overall survival of patients with ampullary and other types of peri-ampullary cancers

Ampullary	Mean(a)				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
1.00	69.750	2.689	64.480	75.020	68.000	5.000	58.200	77.800
9.00	26.810	2.404	22.098	31.521	28.000	3.024	22.074	33.926
Overall	33.680	3.810	26.212	41.148	30.000	1.470	27.119	32.881

Table 6: Overall survival duration of patients with stages I–IV peri-ampullary cancers

Stage	Mean(a)				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
1	69.750	2.689	64.480	75.020	68.000	5.000	58.200	77.800
2	33.800	3.190	27.548	40.052	32.000	4.743	22.703	41.297
3	21.900	1.969	18.041	25.759	21.000	3.953	13.252	28.748
4	6.000	.000	6.000	6.000	6.000	.	.	.
Overall	33.680	3.810	26.212	41.148	30.000	1.470	27.119	32.881

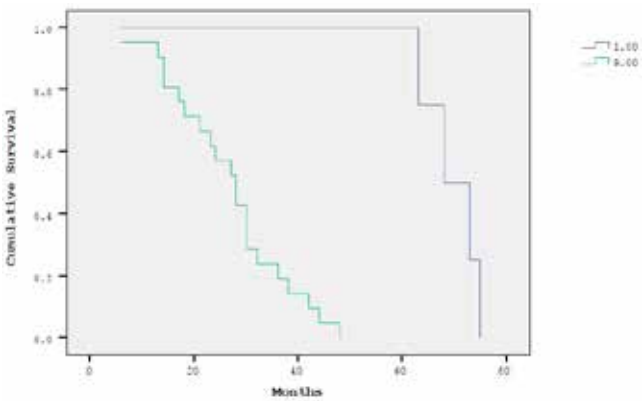

Figure 3: Kaplan-Meier analysis of overall survival duration of patients with tumors of the ampulla of Vater (Group 2), and other types of peri-ampullary cancers (Groups 1, 3, 4)

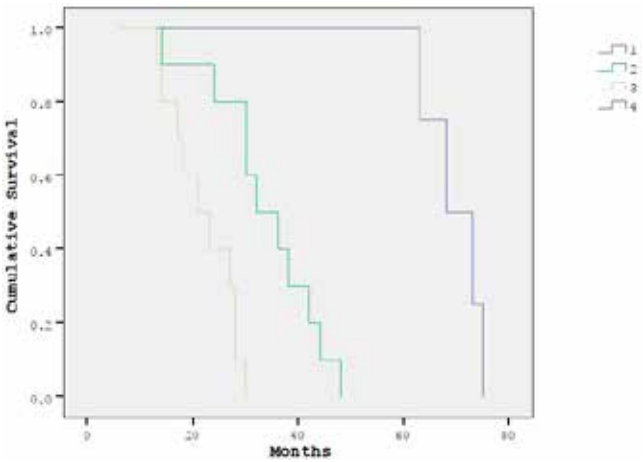

Figure 4: Kaplan-Meier analysis of overall survival of patients with stages I–IV peri-ampullary cancers

Table 7: Overall survival duration of patients who underwent R0 and R1 resection of peri-ampullary cancers

Resection type	Mean(a)				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
R0	43.143	5.354	32.648	53.637	38.000	5.612	27.000	49.000
R1	21.636	2.417	16.899	26.373	23.000	4.954	13.289	32.711
Overall	33.680	3.810	26.212	41.148	30.000	1.470	27.119	32.881

test p<0.001, Chi-Square=45.455) (Table 6, Figure 4).

Overall survival was also compared in patients who underwent R0 and R1 resection. Kaplan-Meier analysis showed that overall survival was significantly longer in patients who underwent R0 than R1 resection (Log-Rank test p<0.001, Chi-Square=13.193) (Table 7, Figure 5).

Overall survival was also compared in node negative and node positive patients. Kaplan-Meier analysis showed that overall survival was significantly longer in node positive (mean, 36.85 months; median, 30 months) than in node negative (mean, 17 months; median, 13 months) patients (log-rank test p=0.003, Chi-square=9.061) (Table 8, Figure 6).

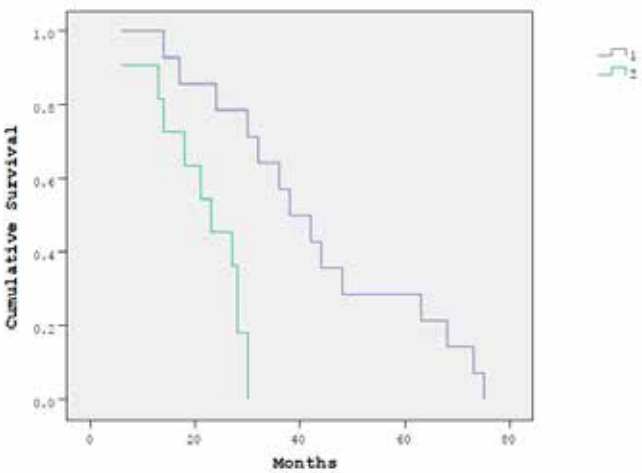

Figure 5: Kaplan-Meier analysis of overall survival of patients who underwent R0 and R1 resection for peri-ampullary cancers

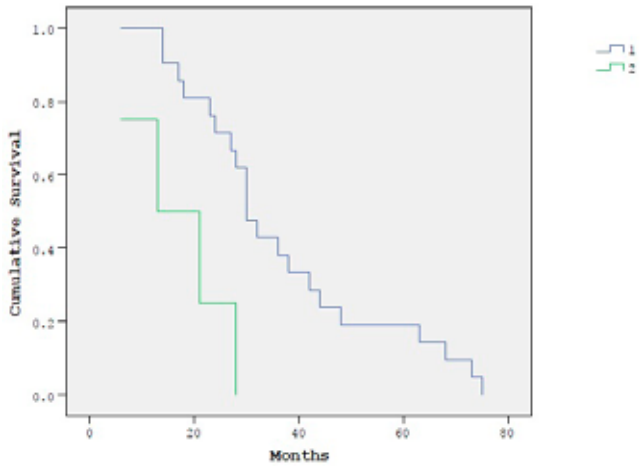

Figure 6: Kaplan-Meier analysis of overall survival of patients with node negative (1) and node positive (2) tumors

Table 8: Overall survival duration of patients with node positive and node-negative peri-ampullary tumors

Nodal status	Mean(a)				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
Negative	36.857	4.115	28.793	44.922	30.000	2.289	25.514	34.486
Positive	17.000	4.778	7.634	26.366	13.000	7.500	.000	27.700
Overall	33.680	3.810	26.212	41.148	30.000	1.470	27.119	32.881

Table 9: Overall survival duration in patients who did and did not undergo portal vein resection

Portal vein resection	Mean(a)				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
No	22.778	2.454	17.968	27.587	24.000	1.491	21.078	26.922
Yes	14.500	.866	12.803	16.197	14.000	.433	13.151	14.849
Overall	20.231	2.013	16.285	24.177	21.000	3.595	13.954	28.046

Kaplan-Meier analysis of overall survival of patients who had and did not have portal vein resection showed that survival was 13 folds lower in patients who did than did not undergo portal vein resection (p=0.022). Among the 13 patients with pancreatic adenocarcinoma, overall survival was significantly lower in patients who did (mean, 14.50 months; median, 24 months) than did not (mean, 22.77 months; median, 14 months) receive portal vein resection (Log-rank test p=0.004, Chi-square=8.196) (Table 9, Figure 7).

In contrast to those other factors, we found that age (p=0.599), ERCP (p=0.920), PTK (p=0.726) and tumor dimension did not correlate with overall survival. Gender showed a weak association (p=0.088) with survival rate, with rates higher in men than in women.

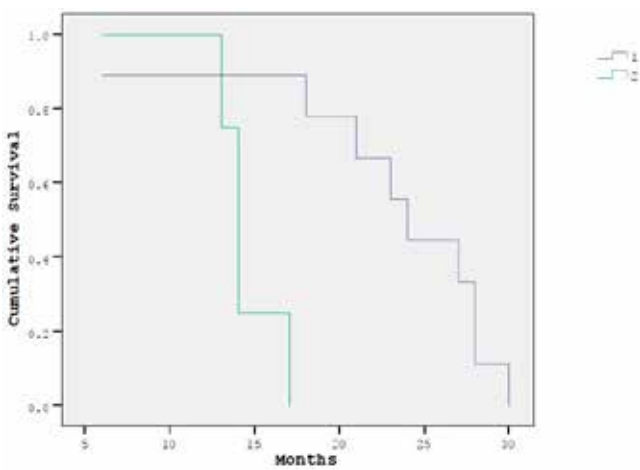

Figure 7: Kaplan-Meier analysis of overall survival of patients who did not (1) and did (2) undergo portal vein resection

DISCUSSION

Although the number of patients in this study was limited, we monitored them closely and regularly, starting from the preoperative stage, recording their radiologic, clinical and laboratory results. None of the patients with periampullary regional tumors diagnosed pathologically with adenocarcinoma survived 10 years after surgery. In contrast, two patients who were not diagnosed with adenocarcinoma survived for at least 12 years each. Previous studies have reported that negative margins, node negativity and tumor stage were significantly associated with survival. In contrast to earlier findings, we did not observe a significant association between tumor diameter and survival rate (p=0.088). Our results indicate that among patients diagnosed with periampullary region adenocarcinoma, those with ampulla of Vater tumors had the highest survival rate, followed by patients with duodenal and distal choledohcus tumors, with the lowest survival rates shown by patients with adenocarcinomas of the pancreas (p<0.001).

We also observed a significant negative correlation between portal vein resection and survival rate (p=0.022). This was an expected outcome, as portal vein invasion indicates that these tumors are locally advanced and therefore cannot undergo R0 resection. Interestingly, however, we found that survival rate tended to be higher in men than in women (p=0.088).

Factors not associated with postoperative survival included tumor diameter and well-differentiated carcinoma. Because pathologic type strongly affected survival, these factors were likely not strong enough to further influence survival. Moreover, the number of patients was likely too low to affect survival outcomes.

Over 95% of patients with periampullary tumors are diagnosed pathologically with adenocarcinoma. Despite advances in preoperative diagnostic methods, reduced perioperative mortality/morbidity rates and improvements in adjuvant therapies, patients with periampullary adenocarcinomas continue to show dismal long-term survival outcomes (6,7). In contrast, patients with colon and breast cancers may survive 20 years or longer after surgery. The much shorter postoperative overall survival of patients with periampullary tumors has been associated with a lack of effective methods for early diagnosis (6-8).

Most patients with periampullary region tumors have pancreatic ductal adenocarcinomas, and most such patients are not candidates for surgery at initial diagnosis. For example, a study of 16492 patients with pancreatic ductal adenocarcinomas in the United States found that the resectability rate was 13.3% and the 5-year overall survival rate was 4% (7,9). The ultimate goal in patients eligible for surgery is total cure, with one of the most important steps being margin free (R0) resection (6,7,10,11). Other important prognostic factors include lymph node positivity, number of positive lymph nodes, tumor diameter, well-differentiated carcinoma and intraoperative bleeding <750 ml (6,12,13). Factors not associated with long-term survival include extended lymphadenectomy, extended pancreatic resection, pylorus preservation, portal vein and/or superior mesenteric vein resection, tumor grade, and vascular and perineural invasion (6). A study of 890 patients who underwent pancreatoduodenectomy for various periampullary malignancies, including 564 with pancreatic malignancies, reported 5- and 10-year survival rates of 23% and 15%, respectively. Factors associated with long-term survival included negative nodal status, negative resection margins, tumor diameter, and well-differentiated carcinoma. Long-term survival was considerably worse for the 564 patients with pancreatic malignancies, with 5- and 10-year survival rates of 17% and 9%, respectively. Other studies have reported similar results, identifying tumor size, lymph node status, resection margin, grade of tumor differentiation, postoperative complications, adjuvant therapy, operation in teaching hospitals, and socioeconomic status as independent predictors of long-term survival (6,14).

Despite margin positivity being the only surgery-related factor associated with survival in patients with pancreatic ductal adenocarcinomas, margin positivity in studies range widely, from 10–84%. Although several studies have reported a significant difference in overall survival between groups of patients with negative and positive resection margins, other studies, including a meta-analysis of several randomized controlled trials, found no difference in overall survival between the two groups (11,15,16).

Pathologic stage has beewas reported prognostic of survival in several studies (17,18), with some showing that pathological T status and others showing that pathological N status are independent prognostic factors. Node positivity

and number of positive nodes were also found to be significantly prognostic of patient survival (17,19,20).

Pancreaticoduodenectomy was associated with potential cure in 80% of patients with node-negative ampullary cancers and in 20% of patients with node-positive ampullary carcinomas. One study demonstrated that the number, not the location, of positive regional lymph nodes independently affects survival after resection in patients with ampullary carcinoma. Thus, the number of positive nodes may be a useful indicator of nodal status as it affects the prognosis of patients with ampullary carcinoma (17).

Meta-analyses comparing pylorus preserving Whipple procedure (PPWP) with classical pancreaticoduodenectomy indicated that PPWP was associated with a lower mortality rate and longer postoperative survival (21). The lower rates of early postoperative complications and mortality were likely due to the less invasive nature of PPWP. Moreover, the longer overall survival might be due to the use of PPWP in patients with smaller tumors (21).

Our two patients that survived more than 12 years (are still alive) showed that surgical procedure of periampullary regional tumors at desired level could provide long survival rates of more than 10 years. This indicated that the key element was early diagnosis of adenocarcinoma tumors in this region. The identification of tumor may enable earlier diagnosis of periampullary region cancer. Earlier diagnosis, along with extended resection and adjuvant treatments may enhance overall survival rates among these patients. For future work, larger number of patients should be studied to confirm obtained results.

Ethics Committee Approval: Ethics committee approval was received for this study from the local ethics committee.

Informed Consent: Informed consent was obtained.

Author contributions: Development of study - X.X.; Methodological design of the study - X.X.; Data acquisition and process - X.X.; Data analysis and interpretation - X.X.; Literature review - X.X.; Manuscript writing - X.X.; Manuscript review and revision - X.X.

Conflict of Interest: Authors declared no conflict of interest.

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REFERENCES

1. Kausch W. Die Resektiun des mittieren duodenums: eine typische operation. Vorlaufige Mitteilung. Zentralblatt fur Chirurgie 1909;39:1350.
2. Hoem D, Viste A. Improving survival following surgery for pancreatic ductal adenocarcinoma-A ten-year experience. Eur J Surg Oncol 2012;38:245-51. [CrossRef]
3. Yang YM, Tian XD, Zhuang Y, Wang WM, Wan YL, Huang YT. Risk factors of pancreatic leakage after pancreaticoduodenectomy. World J Gastroenterol 2005;11:2456-61. [CrossRef]
4. Fujino Y, Suzuki Y, Ajiki T, Tanioka Y, Ku Y, Kuroda Y. Risk factors influencing pancreatic leakage and the mortality after pancreaticoduodenectomy in a medium-volume hospital. Hepatogastroenterology 2002;49:1124-9.
5. Sari YS, Koç O, Tunali V, Tomaoğlu K. Choice of the optimal pancreaticojejunal anastomosis technique: how can we improve patient safety in pancreatic surgery? J Hepatobiliary Pancreat Surg 2008;15:479-82. [CrossRef]
6. Schnelldorfer T, Ware AL, Sarr MG, Smyrk TC, Zhang L, Qin R, et al. Long-term survival after pancreatoduodenectomy for pancreatic adenocarcinoma: is cure possible? Ann Surg 2008;247:456-62. [CrossRef]
7. Smeenk HG, Tran TC, Erdmann J, van Eijck CH, Jeekel J. Survival after surgical management of pancreatic adenocarcinoma: does curative and radical surgery truly exist? Langenbecks Arch Surg 2005;390:94-103. [CrossRef]
8. Duffy JP, Hines OJ, Liu JH, Ko CY, Cortina G, Isacoff WH, et al. Improved survival for adenocarcinoma of the ampulla of Vater: fifty-five consecutive resections. Arch Surg 2003;138:941-50. [CrossRef]
9. Janes RH Jr, Niederhuber JE, Chmiel JS, Winchester DP, Ocwieja KC, Karnell JH, et al. National patterns of care for pancreatic cancer. Results of a survey by the Commission on Cancer. Ann Surg 1996;223:261-72. [CrossRef]
10. Verbeke CS. Resection margins in pancreatic cancer. Surg Clin North Am 2013;93(3):647-62. [CrossRef]
11. Ethun CG, Kooby DA. The importance of surgical margins in pancreatic cancer. J Surg Oncol 2016;113:283-8. [CrossRef]
12. Schmidt CM, Powell ES, Yiannoutsos CT, Howard TJ, Wiebke EA, Wiesenauer CA, et al. Pancreaticoduodenectomy: a 20-year experience in 516 patients. Arch Surg 2004;139:718-27. [CrossRef]
13. Lim JE, Chien MW, Earle CC. Prognostic factors following curative resection for pancreatic adenocarcinoma: a population-based, linked database analysis of 396 patients. Ann Surg 2003;237:74-85. [CrossRef]
14. Riall TS, Cameron JL, Lillemoe KD, Winter JM, Campbell KA, Hruban RH, et al. Resected periampullary adenocarcinoma: 5-year survivors and their 6- to 10-year follow-up. Surgery 2006;140:764-72. [CrossRef]
15. Chang DK, Johns AL, Merrett ND, Gill AJ, Colvin EK, Scarlett CJ, et al. Margin clearance and outcome in resected pancreatic cancer. J Clin Oncol 2009;27:2855-62. [CrossRef]

16. Raut CP, Tseng JF, Sun CC, Wang H, Wolff RA, Crane CH, et al. Impact of resection status on pattern of failure and survival after pancreaticoduodenectomy for pancreatic adenocarcinoma. Ann Surg 2007;246:52-60. [CrossRef]

17. Sunil BJ, Seshadri RA, Gouthaman S, Ranganathan R. Long-Term Outcomes and Prognostic Factors in Periampullary Carcinoma. J Gastrointest Cancer 2017;48:13-9. [CrossRef]

18. Feng J, Zhou X, Mao W. Prognostic analysis of carcinoma of the ampulla of Vater: pancreaticoduodenectomy versus local resection. Hippokratia 2012;16:23-8.

19. Bettschart V, Rahman MQ, Engelken FJ, Madhavan KK, Parks RW, Garden OJ. Presentation, treatment and outcome in patients with ampullary tumours. Br J Surg 2004;91:1600-7. [CrossRef]

20. Sakata J, Shirai Y, Wakai T, Yokoyama N, Sakata E, Akazawa K, et al. Number of positive lymph nodes independently affects long-term survival after resection in patients with ampullary carcinoma. Eur J Surg Oncol 2007;33:346-51. [CrossRef]

21. Iqbal N, Lovegrove RE, Tilney HS, Abraham AT, Bhattacharya S, Tekkis PP, et al. A comparison of pancreaticoduodenectomy with pylorus preserving pancreaticoduodenectomy: a meta-analysis of 2822 patients. Eur J Surg Oncol 2008;34:1237-45. [CrossRef]