SCIE DOI: 10.14744/scie.2022.95815
South. Clin. Ist. Euras. 2022;33(3):326-330

Original Article

Comparison of Resected Ampullary and Pancreatic Head Carcinomas: A Single-Center Experience

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Submitted: 24.07.2022
Accepted: 08.08.2022

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Keywords: Adenocarcinoma; ampulla; jaundice; survival.

ABSTRACT

Objective: The aim of this study was to investigate the differences between ampullary carcinomas and pancreatic head carcinomas and to contribute significantly to this issue, which has not been sufficiently addressed in the literature.

Methods: The study was a retrospective descriptive study. The data of 125 patients with resected periampullary adenocarcinoma were retrospectively reviewed between July 2011 and July 2020. The patients were divided into two groups, ampullary and nonampullary carcinomas, and were compared in terms of clinical, demographic, and pathological aspects.

Results: A total of 109 patients were included in the study with nonampullary carcinoma predominance (59.6% had nonampullary and 40.4% had ampullary). The most common admission complaint was jaundice. The median follow-up was 24 months (range: 1.4–80.4 months). Both median overall survival (OS) and median disease-free survival (DFS) were statistically significant longer in ampullary carcinomas compared with nonampullary carcinomas (OS: 74.5 months vs 16.9 months, 95% CI: 12.6–21.2, p<0.001; DFS: 21.6 months vs 8 months, 95% CI: 10.7–32.6, p<0.001).

Conclusion: Ampulla carcinomas are rare tumors with a better prognosis and longer survival than pancreatic head carcinomas. If it is evaluated in a different category from pancreatic tumors, it may be possible to receive less aggressive treatment and avoid unnecessary toxicity for selected patients. Further studies are needed.

INTRODUCTION

Ampullary carcinomas are rare tumors with an increased incidence in recent years.[1] They account for only 0.2% of all gastrointestinal cancers and 7% of periampullary cancers.[2] Ampullary carcinomas have a better prognosis with a longer survival than other periampullary carcinomas. Five-year survival rates are around 30%–50%.[3,4]

The most common presentation of ampullary carcinomas is jaundice, and abdominal pain, nausea, vomiting, and dyspepsia are other common complaints.[5]

It is difficult to differentiate ampullary carcinomas and pancreatic carcinomas histologically. The most common histological subtypes of ampullary carcinomas are intestinal (47%) and pancreatobiliary (24%).[5] Pancreatobiliary type has a poor prognosis with significantly shorter survival.[6]

A multidisciplinary approach is important in the treatment of ampullary carcinomas. As in pancreatic carcinomas, an operation is the only curative approach. While curative surgical resection is possible in 50% of ampulla cancers, this rate is below 10% for pancreatic cancers.[7] Although oncological treatment is not yet clear, pancreatic cancer treatment guidelines are considered.

MATERIALS AND METHODS

The data of 125 patients diagnosed with ampullary and pancreatic head adenocarcinoma who were operated on and followed up in our oncology clinic between July 2011 and July 2020 were retrospectively analyzed. A total of 16 patients with incomplete follow-up data and without adenocarcinoma histology were excluded from the study. The demographic data, clinical follow-up parameters, treatment responses, and survival information were recorded.

American Joint Committee on Cancer (version 8) was used for staging of tumors. Patients with ampullary and nonampullary tumors were examined and analyzed in two groups.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethical approval was taken from our University Ethics Committee with number 05.03.2021/09.2020.1109.

Statistical analysis

Descriptive statistics were given as numbers and percentages for categorical variables and averages, standard deviations, minimums, and maximums for numeric variables. Two independent group comparisons of numerical variables were performed using the Mann–Whitney U test when normal distribution conditions were not achieved. More than two independent group comparisons were performed with the Kruskal–Wallis test. The confidence interval (CI) was selected as 95%, and a two-sided p-value less than 0.05 was accepted as statistically significant.

Disease-free survival (DFS) time was defined as the time interval (in months) between the time of surgery and first clinical and/or radiologic progression or in the absence of progression, death, or last visit if the patient was still alive. Overall survival (OS) time was defined as the time interval (in months) between the diagnosis of disease and death or last visit if the patient was still alive. Median DFS and

Table 1. Descriptive features

Descriptive	n (%)	Ampullary, n (%)	Nonampullary, n (%)	p
Gender				
Female	49 (45)	21 (47.7)	28 (43.1)	0.38
Male	60 (55)	23 (52.3)	37 (56.9)	
Performance status				
ECOG 0-1	99 (90.8)	39 (88.6)	60 (92.3)	0.51
ECOG 2-3	10 (9.2)	5 (11.4)	5 (7.7)	
Diagnostic age				
<60 years	46 (42.2)	22 (50)	24 (36.9)	0.12
≥60 years	63 (57.8)	22 (50)	41 (63.1)	
Presentation				
Jaundice	45 (41.3)	25 (56.8)	20 (30.8)	0.001
Abdominal pain	23 (21.1)	9 (20.5)	14 (21.5)	
Nausea/vomiting	22 (20.2)	10 (22.7)	12 (18.5)	
Other	19 (17.4)	0 (0)	19 (29.2)	
Histological grade				
Grade 1	28 (25.7)	24 (54.5)	4 (6.2)	<0.001
Grade 2	38 (34.9)	18 (40.9)	20 (30.8)	
Grade 3	43 (39.4)	12 (4.5)	41 (63.1)	
Lymph node involvement				
Positive	84 (77.1)	33 (75)	51 (78.5)	0.42
Negative	25 (22.9)	11 (25)	14 (21.5)	
TNM stage				
Stage 1	39 (35.8)	36 (81.8)	3 (4.6)	<0.001
Stage 2	19 (17.4)	8 (18.2)	11 (16.9)	
Stage 3	51 (46.8)	0 (0)	51 (78.5)	
PNI/LVI				
Yes	92 (84.4)	27 (61.4)	65 (100)	<0.001
No	17 (15.6)	17 (38.6)	0 (0)	
Surgical margin				
Positive	49 (45)	8 (18.2)	41 (63.1)	<0.001
Negative	60 (55)	36 (81.8)	24 (36.9)	
Adjuvant treatment				
Gemcitabine	79 (72.5)	29 (65.9)	50 (76.9)	0.17
Gemcitabin + capecitabine	10 (9.2)	3 (6.8)	7 (10.8)	
Capecitabine	6 (5.5)	3 (6.8)	3 (4.6)	
Folfirinox	1 (0.9)	0 (0)	1 (1.5)	
None	13 (11.9)	9 (20.5)	4 (6.2)	

ECOG: Eastern Cooperative Oncology Group; TNM: Tumor necrosis metastasis; PNI: Perineural invasion; LVI: Lymphovascular invasion.

OS were estimated with the Kaplan–Meier method and log-rank test. All statistical analyses were performed using SPSS version 22.0 (SPSS, Inc., Chicago, IL, USA).

RESULTS

A total of 109 patients with resected periampullary carcinomas consisting of 40.4% ampullary and 59.6% nonampullary tumors were included in the study. The most common presentation was jaundice (45%). All tumors have adenocarcinoma histology. While 63.6% of the ampullary carcinomas were of intestinal subtype, the others were pancreatobiliary subtypes. The median age at diagnosis was 62 years (range: 36–78). Although the two groups were similar in terms of demographic characteristics, clinical and pathological features were different. Descriptive features are presented in Table 1.

Our study determined that 88.1% of all patients received adjuvant chemotherapy, and 11.9% could not receive adjuvant chemotherapy for various reasons such as poor performance and delayed wound healing. The most commonly used chemotherapy regimens were single-agent gemcitabine (72.5%), gemcitabine–capecitabine combination (9.2%), and single-agent capecitabine (5.5%).

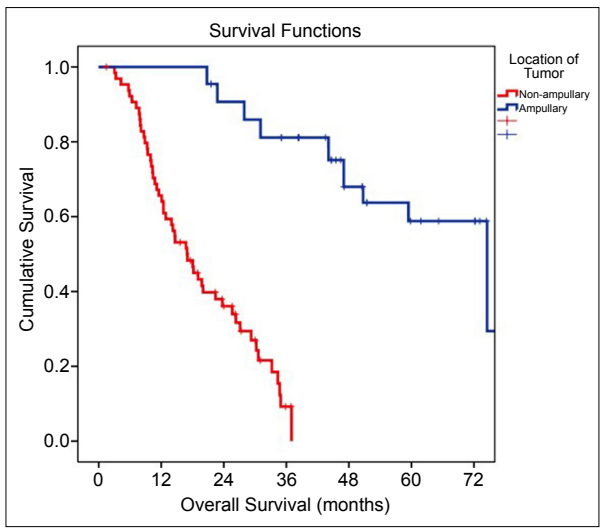

Figure 1. Kaplan–Meier curves for overall survival of ampullary and nonampullary tumors.

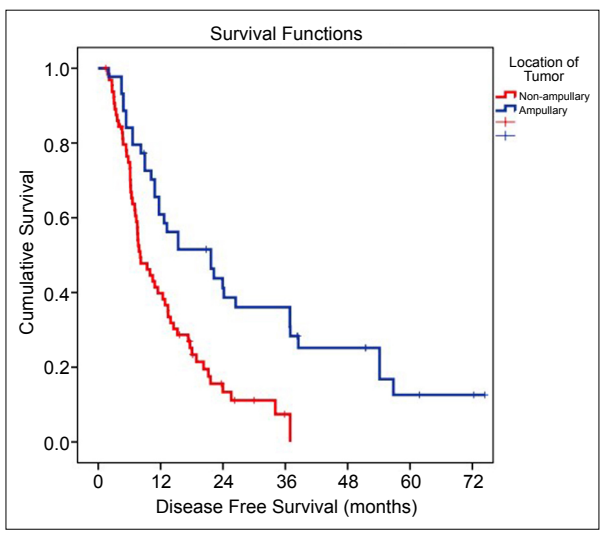

Figure 2. Kaplan–Meier curves for disease-free survival of ampullary and nonampullary tumors.

The median follow-up period was 24 months (range: 1.4–80.4 months). The median OS was 30.6 months, and the median DFS was 11.6 months. Both OS and DFS were statistically significantly longer in ampullary tumors compared with nonampullary tumors (OS: 74.5 months vs 16.9 months, 95% CI: 12.6–21.2, p<0.001; DFS: 21.6 months vs 8 months, 95% CI: 10.7–32.6, p<0.001). The Kaplan–Meier curves are given in Figures 1 and 2. When the ampullary tumors were evaluated according to their histological subtypes, the survival of patients with the intestinal subtype was longer compared with the pancreatobiliary subtype (74.5 months vs 47 months, 95% CI: 59.2–89.8, p=0.02).

DISCUSSION

This study aimed to investigate the clinical, pathological, and survival differences between primary ampullary carcinomas and pancreatic head carcinomas and to share our real-life experience on this subject.

It is well known that patients with ampullary carcinomas had higher survival than other periampullary carcinomas.[4,8,9] In our study, patients with ampullary carcinomas had a statistically significant higher survival rate than pancreatic carcinomas, consistent with the literature. Many factors contribute to prolonged survival. Previous studies reported that ampullary carcinomas were diagnosed at an early stage as they often cause obstruction due to their location.[10] Patients with symptomatic tumors were admitted to clinics earlier and diagnosed at an early stage. Similarly, in our study, ampulla carcinomas were diagnosed at an early stage with statistical significance.

Another factor contributing to prolonged survival is the higher R0 (no microscopic tumor in resection margin after surgery) resection rate in ampullary carcinomas. It has been reported in previous studies that surgical margin positivity is a poor prognostic factor for all periampullary tumors.[11–13] While margin positivity has been reported at 37% in pancreatic carcinomas in the literature, this rate is around 6% for ampullary carcinomas.[14] The reason for a higher R0 resection rate in ampullary carcinomas is that the operation is technically easier due to its anatomical location and early diagnosis (while being less invasive). Thus, patients with ampullary carcinomas have a higher chance of curative treatment and a higher survival rate than pancreatic head carcinomas.

Although both ampullary and pancreatic head carcinomas are located similarly, it is very difficult to differentiate them histologically. Identification of primary ampullary carcinomas and the invasion of the pancreatic head carcinomas into the ampulla requires careful evaluation by senior experienced pathologists. In addition, the pathological fea-

tures of ampulla carcinomas also differ from pancreatic head carcinomas. In previous studies, it has been shown that ampullary carcinomas had good prognostic features such as less nodal involvement,[15–17] low grade,[18] and less perineural invasion (PNI) pathologically compared with other periampullary tumors.[10] Brown et al.[19] determined that 5-year survival decreased from 78% to 25% in ampullary tumors having lymph node invasion. Moreover, PNI has also been provided as a route for metastatic spread,[20] and patients with tumors that have PNI live shorter. Consistent with the literature, our study detected low grade, less nodal involvement, and less PNI in ampullary carcinomas. These pathological features are also good prognostic factors and contribute to longer survival.

Finally, there is no consensus in the literature about the oncological treatment of primary ampullary carcinomas. Currently, the treatment is applied according to pancreatic cancer guidelines.[21,22] It is well documented in the literature that the histological subtypes of ampullary carcinomas have different survival rates, with pancreatobiliary subtype having a similar survival rate to pancreatic carcinomas. In our study, patients with intestinal subtypes had a statistically significantly longer survival compared with pancreatobiliary subtypes. Therefore, we believe that it is not a good practice to treat patients with tumors of different histological subtypes in the same way as pancreatic cancer. It is still unclear what adjuvant treatment after curative resection of ampullary carcinoma is optimal according to subtypes. Available data are conflicting in the literature.[6,23–26] Prospective and large sample-sized studies are needed on this subject.

CONCLUSION

Primary ampullary carcinomas differ from pancreatic head carcinomas in their anatomical features, biological behavior, clinical presentation, and pathological features. We believe that further studies on ampullary carcinomas are needed. If histological, molecular, and genetic differences in ampullar carcinomas can be revealed, a specific treatment guide can be prepared for these tumors, different from pancreatic carcinomas. Thus, some patients may avoid unnecessary treatment toxicity.

Limitations of our study were retrospective design, shorter follow-up period, and small sample size. The sample size did not allow us to compare chemotherapy options and contribute to the literature in this regard.

Ethics Committee Approval

This study approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee (Date: 05.03.2021, Decision No: 09.2021.319).

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: T.B.; Design: T.B.; Supervision: F.D., P.F.Y.; Materials: T.B., P.F.Y.; Data: T.B., N.C.D., R.A., T.A.T., S.I., A.Y., A.Ç., Ö.E.; Analysis: T.B., Ö.E.; Literature search: N.C.D., R.A.; Writing: T.B.; Critical revision: P.F.Y.

Conflict of Interest

None declared.

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Rezeke Edilmiş Ampuller ve Pankreas Başı Karsinomlarının Karşılaştırılması: Tek Merkez Deneyimi

Amaç: Bu çalışmada, ampulla karsinomları ile pankreas başı karsinomları arasındaki farkları araştırdık. Literatürde henüz yeterince ele alınmamış olan bu konuya katkıda bulunabileceğimize inanıyoruz.

Gereç ve Yöntem: Temmuz 2011 ile Temmuz 2020 arasında rezeke edilmiş periampuller adenokarsinomlu 125 hastanın verileri geriye dönük olarak incelendi. Hastalar ampuller ve ampüller olmayan karsinomlar olarak iki gruba ayrıldı ve klinik, demografik ve patolojik açıdan karşılaştırıldı.

Bulgular: Ampulla dışı kanserlerin çoğunlukta olduğu 109 hasta çalışmaya dahil edildi (%59.6'sı ampulla dışı ve %40.4'ü ampulla). En sık başvuru şikayeti sarılıktı. Ortanca takip süresi 24 aydı (aralık: 1.4 ay–80.4 ay). Ortanca genel sağkalım (GS) 30.6 aydı (%95 güven aralığı (GA): 24–37.1). Ortanca hastalıksız sağkalım (HS) 11.6 aydı (%95 GA: 8.9–14.4). Hem GS hem de HS ampulla tümörlerinde ampulla dışı tümörlere kıyasla istatistiksel olarak anlamlı şekilde uzundu (p=<0.001).

Sonuç: Ampulla karsinomları, pankreas başı karsinomlarına göre daha iyi prognozlu ve daha uzun sağkalıma sahip nadir tümörlerdir. Pankreas tümörlerinden farklı bir kategoride değerlendirilirse seçilmiş hastalarda daha az agresif tedavi almak ve gereksiz toksisiteden kaçınmak mümkün olabilir. Bu konuda daha ileri çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: Adenokanser; ampulla; sağkalım; sarılık.