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Ascites Is a Poor Prognostic Factor in Advanced Pancreatic Adenocarcinoma and May Be Undertreated: A Prospective Cohort Study

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INTRODUCTION: **Pancreatic ductal adenocarcinoma is associated with significant morbidity and mortality as most patients present with advanced disease. The development of ascites has been associated with poor outcomes and further characterization and contemporary management strategies are needed.**

METHODS: **A total of 437 patients enrolled in the Gastrointestinal Biobank at Cedars-Sinai Medical Center who had epithelial pancreatic malignancy were included in the prospective cohort group. Overall, 41.7% of patients included in this study developed ascites. Most patients with ascites (>80%) had high serum-ascites albumin gradient ascites. In both univariate and multivariate analysis, a history of ≥1 form of chemotherapy was significantly associated with ascites. Estimated median overall survival in patients with ascites was significantly lower than in patients without ascites, 473 days vs 573 days, and ascites had a hazard ratio of 1.37.**

RESULTS: **Patients with ascites who received diuretics and indwelling peritoneal catheter had an estimated median survival of 133 days from diagnosis of ascites, and those who received only the indwelling peritoneal catheter without diuretics had an estimated median survival of only 54 days. The estimated median survival from the diagnosis of ascites was 92 days, and the median time to puncture was 7 days. The median time from first tap to death was 45 days.**

DISCUSSION: **The use of diuretics is lower than would be expected for patients with pancreatic ductal adenocarcinoma with elevated serum-ascites albumin gradient. Other therapies such as beta blockers should be investigated in this subset of patients. The etiology of ascites in these patients is poorly understood, and further research is needed to establish treatment guidelines and improve outcomes.**

KEYWORDS: malignant ascites; pancreatic cancer; serum-ascites albumin gradient; supportive care; diuretic

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INTRODUCTION

Pancreatic cancer has historically had among the worst prognosis of all types of cancer, with dismal 5-year survival rates of 3% in the mid-1970s, rivalling the survival rates of liver/intrahepatic bile duct and esophageal cancer. Since then, the most up-to-date Surveillance, Epidemiology, and End Results data from 2012 to 2018 reflect a substantial improvement of esophageal and liver/intrahepatic bile duct 5-year survival rates to 21%, while pancreas cancer survival rates have improved only to 12% over the same time period, making it the deadliest type of cancer by site (1).

Pancreatic ductal adenocarcinoma (PDAC) is by far the most common subtype of pancreatic cancer, making up greater than 90% of all pancreatic cancer cases. Ascites involves the accumulation of fluid in the abdomen and can arise from both cancer-related and non-oncologic etiologies such as cirrhosis. Ascites in patients with gastrointestinal malignancy is relatively understudied compared with ascites in ovarian cancer, despite having a prevalence of up to 15% (2,3). Malignant ascites has been associated with poor prognosis in patients with cancer especially those with nonovarian cancer, although data on malignant ascites in patients with PDAC remain limited (2,4–10). Current standard of care focuses on the palliation of symptoms with (oftentimes serial) large volume paracentesis, indwelling catheter placement, shunts, intraperitoneal chemotherapy or systemic cancer therapy,

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Table 1. GI-Bank patient characteristics by ascites status

Characteristic	Total (N = 437)	No ascites (N = 255)	Ascites (N = 182)
Age at diagnosis, median (IQR)	67 (61–74)	68 (62.5–76.5)	66 (58.25–72)
Female, n (%)	208 (47.6)	120 (47.1)	89 (48.9)
Race, n (%)			
White	297 (68.0)	187 (73.3)	110 (60.4)
Black	31 (7.1)	16 (6.3)	15 (8.2)
Asian	55 (12.6)	30 (11.8)	25 (13.7)
Hispanic	45 (10.3)	20 (7.8)	25 (13.7)
Other	9 (2.06)	2 (0.8)	7 (3.8)

IQR, interquartile range.

and sometimes diuretics (2,6,8,11–14). Malignant ascites in pancreatic cancer is challenging to manage because there are no current guideline recommendations for ascites management in pancreatic cancer (13,15), but guidelines are desperately needed due to the high rate of complications associated with catheter placement and oftentimes poor outcomes in this group of patients despite current efforts in treatment (11,12).

The serum-ascites albumin gradient (SAAG) is of particular importance in the diagnosis of ascites in PDAC (6) because it may inform whether the etiology of the ascites is likely due to peritoneal carcinomatosis (low SAAG) or portal hypertension (high SAAG) which can determine prognosis and treatment strategies (16,17). Little is known about the relationship between portal hypertension and ascites in PDAC; potential causes of portal hypertension in this population include either those that are liver related (existing cirrhosis and Budd-Chiari syndrome) or non-liver related (lymphatic obstruction or portal vessel invasion by tumor, heart failure, or portal fibrosis) (6,7,16). Recent studies have reported evidence of portal hypertension–related ascites despite a lack of liver metastases or disease in a significant subset of patients with PDAC (2,16). A previous study of ascites in PDAC reported that 82% of the cohort had high SAAG ascites, while only 18% had low SAAG, although only a small fraction of the total patients had their ascitic fluid analyzed in this study (2). In this group, diuretics have been observed to be inconsistently used at proper doses despite reports of clinical efficacy and being a first-line treatment consideration (16,18). To the best of our knowledge, there are no clinical studies of diuretics in pancreatic cancer–associated ascites, and practicing oncologists rely on empirical therapy or guidelines for ascites due to cirrhosis (6,16,19).

We performed a comprehensive analysis of clinical and biological data in our institutional biobank to describe the incidence, associated clinical factors, and outcomes of ascites in pancreatic cancer, the relationship between portal hypertension and malignant ascites, and the outcomes of supportive treatments chosen for ascites in PDAC.

Table 2. Ascitic fluid characteristics

Characteristic	
Ascites patients (N = 182)	
Received paracentesis, n (%)	141 (77.5)
Time to puncture, median days	7
First tap to death, median days	45
SAAG score present, n (%)	104 (57.1)
SAAG score unable to be obtained, n (%)	37 (20.3)
Patients with SAAG score (N = 104)	
High SAAG >1.1, n (%)	88 (84.6)
Low SAAG ≤1.1, n (%)	16 (15.4)
Patients with high SAAG (N = 88)	
(+) cytology, n (%)	17 (19.3)
(−) or inconclusive cytology, n (%)	54 (61.4)
Cytology not performed, n (%)	17 (19.3)
Patients with low SAAG (N = 16)	
(+) cytology, n (%)	7 (43.8)
(−) or inconclusive cytology, n (%)	7 (43.8)
Cytology not performed, n (%)	2 (12.5)

SAAG, serum-ascites albumin gradient.

METHODS

The Gastrointestinal Biobank ("GI-Bank") at Cedars-Sinai Medical Center collects patient specimens, associated clinical data, and self-reported questionnaires, without explicit inclusion or exclusion criteria. A total of 777 patients were prospectively and consecutively enrolled by practicing GI-oncologists in the GI-Bank by the time of analysis. Of these, 445 patients with complete data (meaning that all relevant demographics, clinical data, and outcomes had been entered into data consolidation software, without missing or unknown values) were included. All these patients had a pancreatic malignancy. Patients with pancreatic neuroendocrine tumors (n = 8) were excluded. Other histological subtypes, including adenosquamous (n = 7), acinar cell carcinoma (n = 1), and PDA with mucinous differentiation (n = 3), were considered sufficiently similar to PDAC (n = 426) to include in the analysis. Patients were not excluded based on any comorbidities i.e., a history of cirrhosis or congestive heart failure. Data were consolidated using a standard web application. All statistical analysis, except for univariate and multivariate Cox regression and logistic regression modeling, was conducted using Excel and using Datatab.net software tools. Univariate and

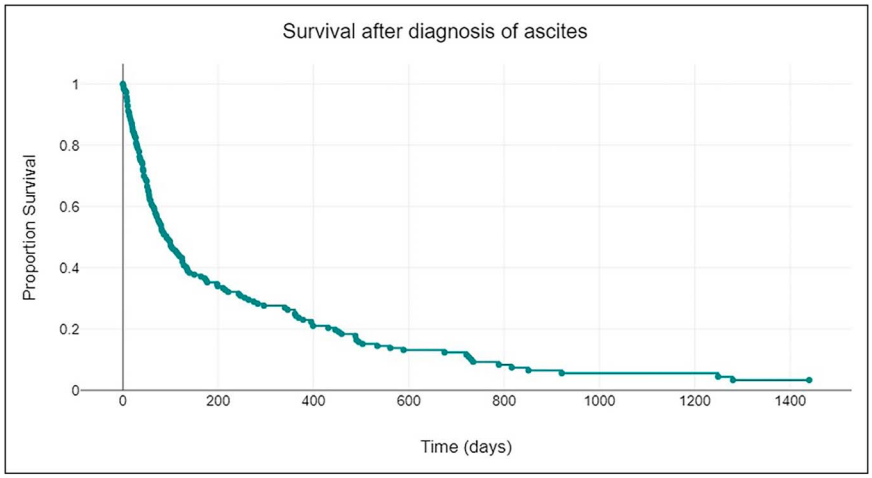

Figure 1. Survival after diagnosis of ascites. Kaplan-Meier estimates of survival in patients with pancreatic ductal adenocarcinoma after diagnosis of ascites. Estimated median survival 92 days (95% confidence interval 71–124).

multivariate Cox regression and logistic regression models were performed using R (version 4.1.2; R Core Team 2021).

RESULTS

Of the 437 patients with PDAC, 182 (41.7%) developed ascites (Table 1). Ascitic fluid data were obtained in 104 patients; 88 (84.6%) had SAAG >1.1. Of patients with a low SAAG score <1.1 (n = 16, 15.4%), 7 (43.8%) had positive cytology whereas in patients with high SAAG >1.1 only 17 (19.3%) had positive cytology (Table 2). The estimated median survival from the diagnosis of ascites was 92 days (71–124) (Figure 1), and the median time to puncture was 7 days. The median time from first tap to death was 45 days (Table 2).

To elucidate the association between potential risk factors in the patient history and development of ascites, logistic regression was performed. In univariate analysis, both the presence of metastasis to the peritoneum (defined by the presence of initial peritoneal metastases or recurrence to the peritoneum) and a history of ≥1 form of chemotherapy were significantly associated with ascites (Table 3), and this relationship remained significant in multivariate analysis ($P = 0.011$ for peritoneal metastases, $P < 0.001$ for a history of ≥1 form of chemotherapy) (Table 4). Metastasis to the liver, tumor resectability status, history of radiation or surgery, and SMAD4 mutation status were all not significantly associated with development of ascites (Table 3).

Patients were treated with either diuretics only (n = 69, 38.1%), PleurX catheter only (n = 20, 11.1%), both (n = 21, 11.6%), or neither (n = 71, 39.2%). Estimated median survival from the date of ascites diagnosis was highest in the group of patients who received both diuretics and PleurX (133 days [81–340]), followed by diuretics only (110 days [70–164]). Patients who received PleurX only had the lowest survival (54 days [42–264]) (Figure 2a–d).

Overall survival (OS) between ascites and nonascites groups were significantly different by log-rank test ($P = 0.001$), and the estimated median OS was 473 days (95% confidence interval [CI] 407–537) in patients with ascites vs 573 days (95% CI 473–681) in nonascites patients (Figure 3). In multivariate Cox regression analysis, positive ascites status, presence of liver metastases, an Eastern Cooperative Oncology Group of 3 or higher, and borderline or nonresectable primary tumor status were significantly associated with decreased survival. Ascites status carried a hazard ratio (HR) of 1.35 (1.04–1.76). Liver metastases (defined by the presence of initial liver metastases or recurrence to the liver) carried a HR of 1.56 (1.17–2.07). Compared with fully resectable primary tumors, borderline resectable status carried a HR of 1.87 (1.22–2.87), locally advanced HR 3.23 (2.21–4.73), and metastatic HR 2.94 (1.99–4.34). Compared with patients with an Eastern Cooperative Oncology Group of 0, scores of 1 and 2 were not significantly associated with decreased survival but higher scores of 3 and 4 were (HR 3.38 and HR 5.35, respectively) (Table 5). The presence of peritoneal metastases was not associated with significantly decreased survival in univariate analysis (Table 6).

DISCUSSION

This prospective cohort analysis is the largest to date of patients with PDAC with respect to ascites. Ascites was a poor prognostic factor in our patients with PDAC, with median survival of 92 days after diagnosis of ascites. This translated into a decrease in median OS of 100 days between patients with and without ascites. In Cox multivariate analysis, having ascites was associated with a HR of 1.37 and carried a statistically significant increased likelihood of death. The incidence of portal hypertension–associated ascites was nearly 80%, significantly higher than previously reported by some studies (16) and consistent with a recent analysis performed at Memorial Sloan Kettering Cancer Center (2).

Despite ascites being an important prognostic factor for patients with PDAC, little is known about its etiology in pancreas cancer. We attempted to address the question of why ascites develops in some patients with PDAC but not others. In multivariate logistic regression analysis, metastasis to the peritoneum was significantly associated with ascites, which likely represents the subset of patients with peritoneal carcinomatosis and ascites, a well-known cause of malignant ascites. However, this subset only represented a minor subset of our study population, in which nearly 80% of patients had a high SAAG score (indicating portal hypertension as the primary cause of ascites) and low rates (<25%) of positive cytology. In patients with PDAC in this data set, portal hypertension, rather than peritoneal carcinomatosis, was the leading cause of ascites, although the exact mechanism leading to it remains unclear.

Table 3. Univariate logistic regression of the outcome ascites

Characteristic	N	OR	95% CI	*P* value
Initial CA 19-9 level	384	1.00	1.00–1.00	0.75
Resectability	436			0.17
Resectable		—	—	
Borderline resectable		2.09	1.08–4.08	
Locally advanced		1.37	0.79–2.39	
Metastatic		1.46	0.88–2.45	
Initial metastasis site liver	437			0.54
No initial liver mets		—	—	
Initial liver mets		0.88	0.57–1.33	
Initial metastasis site peritoneum	437			0.057
No initial peritoneal mets		—	—	
Initial peritoneal mets		2.28	0.98–5.58	
Radiation history	437			0.69
No radiation		—	—	
At least 1 form of radiation		0.92	0.60–1.39	
Chemotherapy history	437			**<0.001**
No chemotherapy		—	—	
At least 1 form of chemotherapy		5.82	2.44–17.2	
Surgical history	437			0.37
Tumor not resected		—	—	
Tumor resected		0.83	0.55–1.25	
smad4 genotype	437			0.15
WT		—	—	
SMAD4 mutation		0.51	0.18–1.27	
Site of recurrence liver	437			0.84
No recurrence to liver		—	—	
Liver recurrence		1.04	0.69–1.57	
Site of recurrence peritoneum	437			0.056
No peritoneal recurrence		—	—	
Peritoneal recurrence		2.38	0.98–6.12	
Liver metastasis	437			0.78
No		—	—	
Yes		1.06	0.72–1.55	
Peritonealmetastasis	437			**0.005**
No		—	—	
Yes		2.49	1.31–4.88	

The bold entries are variables that were found to be independently associated with the outcome ascites.
CI, confidence interval; OR, odds ratio; WT, wild-type.

Liver metastases have been reported to both correlate with poor OS and development of malignant ascites in patients with PDAC (4,7,16,20). The presence of liver metastases, particularly massive liver metastases (21), has been believed to be the mechanism of high-SAAG, portal hypertension–related malignant ascites in patients with PDAC (7,21). Interestingly, our data do not suggest that clinically detectable liver metastases are associated with ascites but do suggest such liver metastases are associated with decreased OS. Peritoneal metastases were predictably associated with ascites, but this is well-known to be a cause of low-SAAG ascites (2,6,21,22) and does not account for the high-SAAG ascites observed in roughly 80% of the peritoneal fluid analyzed in the GI-Bank. Portal hypertension in these patients may be largely driven by microscopic, clinically

Table 4. Multivariate logistic regression of the outcome ascites

Characteristic	Event N	OR	95% CI	*P* value
Resectability				
Resectable	35	—	—	
Borderline resectable	29	1.97	1.00–3.91	0.050
Locally advanced	48	1.53	0.87–2.71	0.14
Metastatic	69	1.42	0.84–2.43	0.2
Chemotherapy history				
No chemotherapy	5	—	—	
At least one form of chemotherapy	176	5.96	2.47–17.8	<0.001
smad4 genotype				
WT	175	—	—	
SMAD4 mutation	6	0.40	0.14–1.01	0.065
Peritoneal metastasis				
No	156	—	—	
Yes	25	2.46	1.24–5.05	0.011

CI, confidence interval; OR, odds ratio; WT, wild-type.

undetectable hepatic sinusoidal metastases. SMAD4 mutation, which has been associated with portal vein invasion, metastatic disease, and poor survival in PDAC (23–26), was not associated with development of ascites in our data; however, it is possible that in these patients splanchnic vessel invasion may be occurring independently of SMAD4, and SMAD4 status has failed to predict locoregional recurrence after excision (27,28).

It is also possible that portal hypertension in many of these cases are not related to metastatic disease at all. Receipt of 1 or more forms of chemotherapy was the only factor other than peritoneal metastases in our multivariate analysis significantly correlated with ascites. Two mechanisms by which chemotherapy may cause portal hypertension–related ascites are sinusoidal obstruction syndrome (SOS) and nodular regenerative hyperplasia. Chemotherapy may

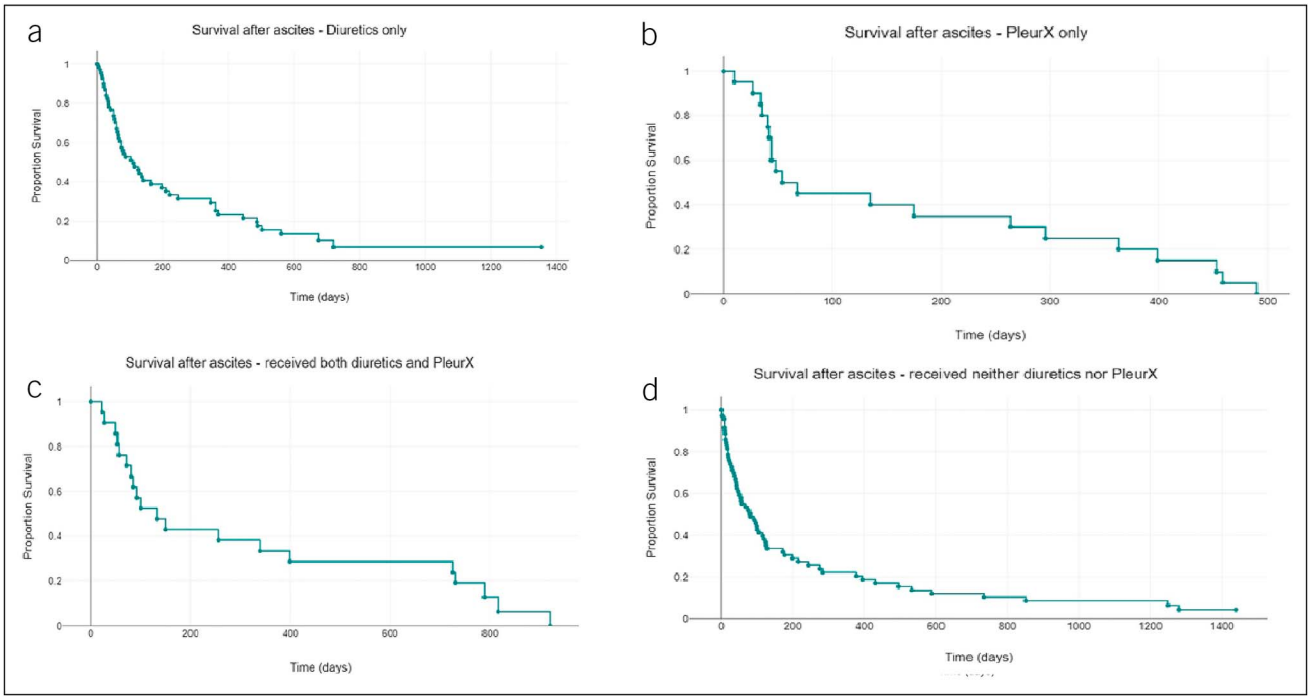

Figure 2. Survival by treatment received. (**a**) Treated with diuretics, N = 69, censored N = 15 (21.7%). Estimated median survival 110 days (95% CI 70–164). (**b**) Treated with PleurX, N = 21, censored N = 0 (0%). Estimated median survival 54 days (95% CI 42–264). (**c**) Treated with both diuretics and PleurX, N = 21, censored N = 1 (4.8%). Estimated median survival 133 days (95% CI 81–340). (**d**) Treated with neither diuretics nor PleurX, N = 71, Censored N = 9 (12.7%). Estimated median survival 82 days (95% CI 48–116). CI, confidence interval.

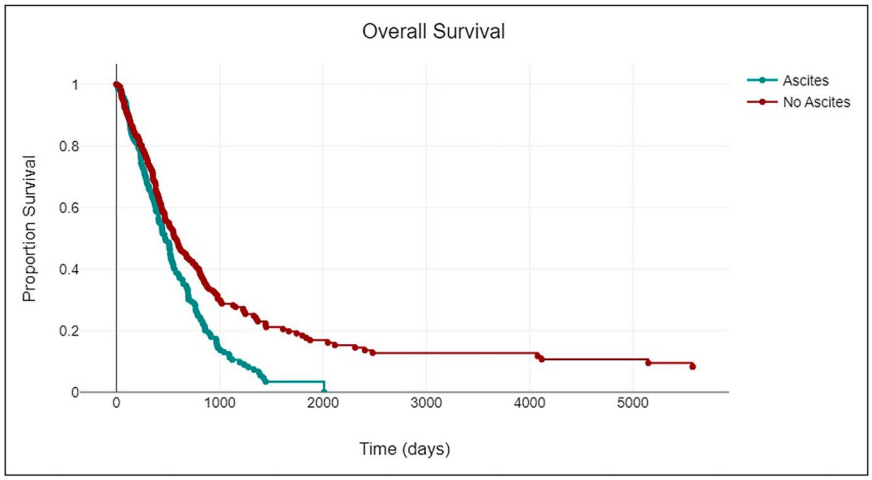

Figure 3. Overall survival by ascites status. Kaplan-Meier estimates of survival in patients with PDAC with and without ascites. The estimated median overall survival for the ascites group was 473 days (95% CI 407–537). The estimated median overall survival for the nonascites group was 573 days (95% CI 473–681). CI, confidence interval; PDAC, pancreatic ductal adenocarcinoma.

cause SOS, although the mainstays of treatment in our data set involved FOLFIRINOX or gemcitabine and paclitaxel which are not typically associated with SOS (29). Nodular regenerative hyperplasia is a sequela of multiple chemotherapeutic agents and may be underdiagnosed in patients with PDAC receiving many lines of chemotherapy because diagnosis is subtle and may require liver biopsy (29). Although there was an association within our data, it remains undetermined whether this relationship was causal, or the result of clinicians choosing chemotherapy for palliative or therapeutic reasons in patients with PDAC patients with ascites, which is performed often with modest results (8,30).

Other possible explanations for portal hypertension and ascites in our patients with PDAC population were not supported by the analysis. Chemoradiation therapy historically has not demonstrated an OS benefit over chemotherapy alone in patients with PDAC (31,32). Our data do not support the hypothesis that this lack of benefit is driven by iatrogenic radiation–induced liver injury leading to ascites because a history of radiation was not associated with ascites, and radiation-induced liver injury is not known to be a common outcome of radiation therapy in pancreatic cancer. Any amount of ascites has been previously identified as a poor prognostic marker in patients with PDAC receiving chemoradiation therapy most likely because this finding indicates peritoneal carcinomatosis (10). Lymphatic obstruction by metastatic tumor has been proposed as a potential cause of malignant ascites (6,7,14,18) and bears further investigation in patients with PDAC as an explanation for portal hypertension.

A limitation of the GI-Bank data is that it contained only limited data on other medical comorbidities that can cause ascites such as cirrhosis and congestive heart failure (CHF). Data on patients' cirrhosis history were limited only to the subpopulation of patients with known ascites. Of the 182 patients who developed ascites, only 24 had a history of cirrhosis, making this an uncommon comorbidity (13.2%). Cirrhosis alone cannot fully explain the higher than expected prevalence of high SAAG ascites in this cohort, and confounding is unlikely although cannot be excluded given that data on the prevalence of cirrhosis in the nonascites subset were not present for analysis. Data on CHF history were also unfortunately not present in the current biobank. However, one benefit to prospective enrollment to the GI-Bank without explicit inclusion or exclusion criteria based on comorbidities is that the conclusions derived from this analysis are more applicable and generalizable to a real-world population which will contain patients with these comorbidities. Nonetheless, owing to the limitations listed above, the possibility that confounding occurred due to history of CHF or cirrhosis cannot be excluded. Further research with more extensive data collection on related comorbidities to ascites is required to address this limitation.

Although there exist no currently published guidelines on the management of PDAC ascites patients, patients in this cohort received treatment with PleurX catheter and diuretics, which are typical supportive care options chosen in this setting. Receipt of diuretics was correlated with increased survival compared with no treatment, but despite this, diuretic usage overall in our group was lower than would be expected for a population consisting of largely high SAAG ascites, representing a treatment gap that has been observed in other studies (2,14,16,18). Receipt of PleurX catheter was associated with worse survival than no treatment, perhaps due to an increase in complications associated with catheter placement. Patients with recurrent large volume ascites who require serial paracentesis often elect to have permanent catheters placed for convenience and symptom palliation, regardless of impact on survival (2). Interestingly, while intravascular volume depletion is a concern with both diuretics and indwelling catheters, patients who received both had the longest median survival, indicating that in a select group of patients, there may be a synergistic benefit of these treatments that outweighs the side effects.

Outside of oncology, a paradigm shift is occurring regarding the usage of beta blockers in patients with cirrhosis and clinically significant portal hypertension. The PREDESCI trial demonstrated that treatment of patients with compensated cirrhosis and clinically significant portal hypertension using propranolol or carvedilol based on prespecified protocols decreased decompensation events, which included ascites, variceal bleeding, or overt encephalopathy, compared with placebo (33). Although the previous paradigm focused on the use of beta blockers only in patients with endoscopically proven varices to prevent hemorrhage, PREDESCI demonstrated a significant reduction in development of ascites, the most frequent first decompensating

Table 5. Cox regression model: Multivariate analysis

Characteristic	HR	95% CI	*P* value
Age	1.02	1.00–1.03	0.006
Race			
White	—	—	
Other	2.38	1.01–5.56	0.046
African American	0.71	0.43–1.19	0.2
Asian	1.03	0.72–1.49	0.9
Hispanic	0.94	0.62–1.41	0.8
ECOG			
0	—	—	
1	0.98	0.67–1.44	>0.9
2	1.53	0.88–2.66	0.13
3	3.38	1.78–6.42	<0.001
4	5.35	1.54–18.6	0.008
Resectability			
Resectable	—	—	
Borderline resectable	1.87	1.22–2.87	0.004
Locally advanced	3.23	2.21–4.73	<0.001
Metastatic	2.94	1.99–4.34	<0.001
Ascites			
No ascites	—	—	
Ascites	1.35	1.04–1.76	0.023
Liver metastasis			
No	—	—	
Yes	1.56	1.17–2.07	0.002

CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio.
Risk factors with $P > 0.2$ (sex and tumor location) were excluded from the multivariate model. Model without perit_mets and rad_hx (both had *P* values >0.2).

Table 6. Cox regression model: Univariate analysis

Characteristic	N	HR	95% CI	*P* value
Age	437	1.01	1.00–1.02	0.16
Sex	437			
Male		—	—	
Female		0.96	0.78–1.18	0.69
Race	437			
White		—	—	
Other		1.67	0.82–3.39	0.16
African American		1.12	0.71–1.75	0.63
Asian		1.25	0.91–1.72	0.18
Hispanic		1.00	0.70–1.43	0.98
ECOG	343			
0		—	—	
1		1.20	0.83–1.73	0.33
2		1.21	0.72–2.05	0.47
3		3.57	1.96–6.48	<0.001
4		2.19	0.67–7.16	0.19
Tumor location	418			
Head/neck/uncinate		—	—	
Body/tail		1.04	0.81–1.33	0.77
Mixed		1.18	0.82–1.72	0.37
Initial CA 19-9 level	384	1.00	1.00–1.00	0.26
Resectability	436			
Resectable		—	—	
Borderline resectable		1.92	1.32–2.79	<0.001
Locally advanced		2.89	2.11–3.95	<0.001
Metastatic		3.51	2.60–4.73	<0.001
History of radiation	437			
No radiation		—	—	
At least one form of radiation		0.68	0.54–0.86	0.001
Ascites	437			
No ascites		—	—	
Ascites		1.45	1.17–1.81	<0.001
Liver metastasis	437			
No		—	—	
Yes		1.76	1.42–2.19	<0.001
Peritoneal metastatis	437			
No		—	—	
Yes		1.27	0.90–1.78	0.17

CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio.

event in cirrhosis (34). Within oncology, despite the high incidence of portal hypertension–related ascites in patients with end-stage PDAC, we are currently unaware of any studies to investigate the potential effectiveness of beta blockers in preventing the development of ascites in this population.

Since the results of the PREDESCI trial, beta blockers have been gaining popularity in delaying the development of ascites within cirrhosis patients with portal hypertension. Although the etiology of ascites in patients with PDAC remains uncertain, this study confirmed that most patients with PDAC experience portal hypertension–related ascites. As portal hypertension is common to both patients with cirrhotic and PDAC, beta blockers may have a role in preventing development of ascites in patients with PDAC as well, leading to both improved symptom-free survival and OS. Further well-controlled randomized clinical trials of beta blockers in patients with PDAC could be a promising future direction for investigation of the potential benefits and risks of this relatively cost-efficient intervention.

Ascites was much more prevalent than expected in our GI Bank population (41%), substantially higher than 15%, a previously reported rate of ascites in GI cancers (3). Because there are significant symptomatic and prognostic implications for ascites in patients with PDAC, future studies and clinical trials stand to benefit from collecting data on patients' ascites status about both associated risk factors and treatment effects.

CONFLICTS OF INTEREST

Guarantor of the article: Andrew Hendifar, MD.

Specific author contributions: All authors contributed to study conception and design, data collection, and manuscript preparation. The following authors provided analysis and interpretation of results, study conception and design, data collection, and manuscript preparation: J.W., Y.C., and A.H.

Financial support: None to report.

Potential competing interests: None to report.

Study Highlights

WHAT IS KNOWN

- ✓ Ascites is a late complication of pancreatic cancer.
- ✓ No formal guidelines exist to inform clinicians about management of ascites in this setting.

WHAT IS NEW HERE

- ✓ Ascites is a common complication in pancreatic ductal adenocarcinoma that is associated with poor survival after diagnosis.
- ✓ The serum-ascites albumin gradient is often elevated, which may differ from other types of malignant ascites.
- ✓ High serum-ascites albumin gradient ascites may respond to diuretics, which are inconsistently or under-used by oncologists in this setting.
- ✓ In the absence of formal guidelines, empiric therapy or cirrhosis guidelines may be used.

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