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Factors Predicting Survival in Patients with Metastatic Pancreatic Cancer and Ascites

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ABSTRACT

Determining elements linked to post-ascites survival in individuals with metastatic pancreatic cancer (mPC) could inform therapeutic choices and aid in preserving quality of life for this group experiencing significant symptoms. Through retrospective review of medical records, we identified all individuals managed for mPC at the Medical University of Vienna from 2010 to 2019 who experienced ascites during their illness. We examined general risk elements, sites of metastasis, markers of systemic inflammation and hepatic function, along with post-ascites management approaches, for links to survival. The analysis encompassed 117 individuals with mPC and ascites. The median interval from mPC diagnosis to ascites detection was 8.9 months (range 0-99 months), with median overall survival (OS) post-ascites being 27.4 days (range 21.3-42.6 days). Factors at ascites detection independently linked to reduced OS included hepatic metastases [hazard ratio (HR): 2.07, 95% confidence interval (CI) 1.13-3.79, P = 0.018], peritoneal carcinomatosis (HR: 1.74, 95% CI 1.11-2.71, P = 0.015), and portal vein obstruction (HR: 2.52, 95% CI 1.29-4.90, P = 0.007). Relative to best supportive care alone, ongoing systemic treatment following ascites detection was independently linked to survival (HR: 0.35, 95% CI 0.20-0.61, P < 0.001), yielding median OS of 62 days (95% CI 51-129 days, P < 0.001) compared to 16 days (95% CI 11-24 days). Hepatic and peritoneal metastases, together with portal vein obstruction, emerged as predictors of outcome following ascites in mPC cases. Ongoing systemic treatment post-ascites was linked to extended OS, warranting assessment in larger trials incorporating quality-of-life measures.

Keywords: Ascites, Metastatic pancreatic cancer, Liver metastases, Peritoneal carcinomatosis, Systemic inflammation

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Introduction

Metastatic pancreatic cancer (mPC) continues to carry a poor outlook, with survival typically under 1 year [1, 2]. During this brief illness trajectory, individuals frequently endure substantial symptoms that profoundly impact quality of life (QoL) [3]. Accordingly, numerous cases exhibit compromised performance status not solely in advanced phases but often from the outset, restricting systemic treatment possibilities. Beyond standard chemotherapy, palliative interventions thus hold a central place in alleviating symptoms for this population [4].

Ascites ranks among the commonest complications, impacting roughly 20% of cases [5]. Recent reports highlight various contributors like hepatic and peritoneal metastases, hepatic function, portal vein obstruction (PVO), and inflammation as key elements raising ascites probability in mPC [5]. Ascites imposes notable symptomatic load, diminishing psychological and physical well-being, thereby further impairing QoL in a group already facing grim prospects [6-8]. Additionally, it poses treatment difficulties [7, 9]. Tumor-directed therapy is frequently hindered by performance limitations. Thus, palliative measures such as paracentesis and indwelling catheters constitute the primary interventions [10]. Given the short median survival of about 1 month from ascites onset in these cases, pinpointing prognostic indicators at this point appears essential for enhancing QoL [5, 6, 8].

We therefore performed a systematic evaluation of clinical elements and their relation to survival in an extensive real-world series of mPC cases with ascites. Particular emphasis was placed on possible advantages from sustaining chemotherapy beyond ascites onset in this subgroup.

Materials and Methods

Patients

We gathered clinical details encompassing demographics, medical history, and survival for mPC cases via retrospective medical record analysis. Only those experiencing ascites alongside or following metastatic disease confirmation were incorporated. Management aligned with prevailing guidelines and optimal clinical standards across their illness at our tertiary facility [11]. The Ethics Committee of the Medical University of Vienna approved this work (vote number 2026 of 2021), conducted per the Declaration of Helsinki and updates.

Study design and objectives

The chief goal was to evaluate various clinical elements at ascites onset affecting survival. Ascites was defined as evident intraperitoneal fluid buildup detected clinically via abdominal computed tomography (CT) or ultrasound. Cases with solely perihepatic fluid were omitted.

We mainly assessed links to survival for these elements. Laboratory values were categorized as 'below normal', 'normal', or 'above normal' per laboratory standards, detailed below:

- General risk elements: age, sex, Eastern Cooperative Oncology Group performance status (ECOG PS)
- Metastatic sites: liver, peritoneum, lung, bone
- PVO: due to thrombosis or tumor, as noted on CT by radiologists
- Hepatic function markers: total protein (64-83 g/l), albumin (35-52 g/l), albumin-bilirubin (ALBI) score. The ALBI score served as a hepatic function indicator owing to its survival links in chronic liver conditions and hepatocellular carcinoma (HCC) [12]. Preset grades from favorable (grade 1) to unfavorable (grade 3) were derived from serum albumin and bilirubin.
- Systemic inflammation markers: c-reactive protein (CRP <0.5 mg/dl), platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), leukocyte-lymphocyte ratio (LLR)
- Management post-ascites: best supportive care (BSC), systemic chemotherapy (defined as delivery of at least one chemotherapy cycle following ascites detection)

Statistical methods

Data analysis was performed with R software (version 4.2.2). Categorical data were described by frequencies and proportions, while continuous data were reported as medians with ranges. Associations between these variables and post-ascites survival were evaluated through a risk regression approach. To account for possible confounding effects, the model was adjusted for the duration between metastatic disease diagnosis and ascites onset, along with the count of prior systemic therapy regimens. Variables deemed clinically important or showing a P value below 0.1 in univariate testing were included in multivariable modeling. Statistical significance was set at a two-sided $P < 0.05$, with results accompanied by 95% confidence intervals (CIs). The time to ascites onset was calculated from the date of metastatic pancreatic cancer (mPC) diagnosis to the detection of ascites. Overall survival (OS) from ascites was measured from the ascites diagnosis date to death or the most recent follow-up, and was estimated using the Kaplan-Meier method. Given the exploratory nature of this investigation, no corrections for multiplicity were performed [13].

Patient cohort and baseline features

From the pancreatic cancer registry at the Medical University of Vienna, 824 individuals with metastatic pancreatic cancer (mPC) who received treatment between 2010 and 2019 were screened for the occurrence of ascites. A total of 241 patients (noted as 241/822 in records, approximately 29.3%) were removed from consideration because of missing details on disease progression. This left 581 patients with adequate documentation, of whom 459 (79.0%) did not develop ascites, with 414 (90.2%) having documented survival outcomes. Of the initial 122 cases with ascites, 5 (4.1%) were excluded due to ascites appearing prior to cancer detection. Thus, the study cohort consisted of 117 patients who developed ascites either at the time of or following mPC diagnosis.

In this group of 117 patients, 70 (59.8%) were men and 47 (40.2%) were women. The median age at ascites detection was 63 years (range 36–82), and ascites appeared a median of 8.8 months (range 8.4–10.4) after metastatic disease was confirmed. Ascites was identified simultaneously with mPC in 4 patients (3.4%), and emerged subsequently in 103 patients (88.0%). At the time of ascites diagnosis, the median ECOG performance status was 2 (range 0–4), with metastatic involvement in the liver in 93 cases (79.5%), peritoneum in 75 (64.1%), lungs in 40 (34.2%), and bones in 9 (7.7%). Management at that point involved best supportive care (BSC) for 73 patients (62.4%) and ongoing systemic chemotherapy for 44 (37.6%), the latter being maintained post-ascites in 36 patients (30.8%). The median OS following ascites diagnosis was 27.4 days (range 21.3–42.6). Further details on patient features at the time of ascites are provided in **Table 1.**

Table 1. Patients' characteristics at diagnosis of ascites

Characteristic	At ascites diagnosis	Value
Patients		117
Sex	Female	47 (40.2%)
	Male	70 (59.8%)
Median age	years (range)	63 (36–82)
Median ECOG performance status	(range)	2 (0–4)
ECOG performance status	0–1	47 (40.2%)
	≥2	70 (59.8%)
Metastatic sites	Liver	93 (79.5%)
	Lung	40 (34.2%)
	Peritoneum	75 (64.1%)
	Bone	9 (7.7%)
Median number of metastatic sites	(range)	2 (0–4)
Timing of metastatic disease	Metachronous	47 (40.2%)
	Synchronous	70 (59.8%)
Previously applied treatment	Surgery of the primary tumor	21 (23.9%)
	Radiation of the primary tumor	17 (14.8%)
Median lines of systemic therapies	(range)	2 (1–6)
Timing of ascites occurrence	At diagnosis of metastatic disease	14 (11.9%)
	Later during course of disease	103 (88.0%)
Treatment at ascites diagnosis	Best supportive care	73 (62.4%)
	Systemic therapy	44 (37.6%)
Systemic therapy continued after ascites diagnosis		36 (30.8%)
Chemotherapy regimen applied after ascites diagnosis	Gemcitabine + nab-paclitaxel	16 (44.4%)
	5-FU + (liposomal) irinotecan	9 (25.0%)
	5-FU + oxaliplatin	4 (11.1%)
	FOLFIRINOX	3 (8.3%)
	Gemcitabine + others	3 (8.3%)
	Capecitabine alone	1 (2.8%)

5-FU, 5-fluorouracil; ECOG PS, Eastern Cooperative Oncology Group performance status.

Predictors of survival following ascites onset

General clinical factors, metastatic involvement, and portal vein obstruction (PVO)

Univariate analysis identified several factors linked to reduced overall survival (OS): poorer Eastern Cooperative Oncology Group performance status (ECOG PS) [ECOG PS 2 (HR 2.59, 95 percent CI 1.20–5.58, P = 0.015); ECOG PS 3 (HR 3.37, 95 percent CI 1.48–7.67, P = 0.004); ECOG PS 4 (HR 7.63, 95 percent CI 1.56–37.24, P = 0.012)], presence of liver metastases (HR 1.78, 95 percent CI 1.10–2.87, P = 0.02), peritoneal carcinomatosis (HR 1.46, 95 percent CI 0.99–2.15, P = 0.055), and portal vein obstruction (PVO) (HR 3.63, 95 percent CI 2.06–6.40, P < 0.001). In multivariable modeling, liver metastases (HR 2.07, 95 percent CI 1.13–3.79, P = 0.018), peritoneal carcinomatosis (HR 1.74, 95 percent CI 1.11–2.71, P = 0.015), and PVO at the time of ascites detection (HR 2.52, 95 percent CI 1.29–4.90, P = 0.007) retained independent prognostic significance for OS.

Liver function parameters and markers of systemic inflammation

Low serum albumin levels (HR 1.22, 95 percent CI 1.12–3.63, P = 0.020) and an ALBI score of grade 3 (HR 2.83, 95 percent CI 1.09–7.33, P = 0.032) demonstrated significant associations with shorter OS in univariate testing. However, neither parameter maintained independent prognostic value in multivariable analysis. No assessed markers of systemic inflammation showed any significant relationship with survival in univariate evaluation.

Impact of treatment administered after ascites detection

Continuation or initiation of systemic chemotherapy following ascites diagnosis was strongly linked to improved OS in univariate analysis (HR 0.27, 95 percent CI 0.17–0.43, P < 0.001). This association persisted after adjustment for potential confounders in multivariable analysis (HR 0.35, 95 percent CI 0.20–0.61, P < 0.001), including ECOG PS (P > 0.05), liver metastases (HR 2.07, 95 percent CI 1.13–3.79, P = 0.018), peritoneal metastases (HR 1.74, 95 percent CI 1.11–2.71, P = 0.015), PVO (HR 2.52, 95 percent CI 1.29–4.90, P = 0.007), albumin levels (P > 0.05), and ALBI score (P > 0.05). Additional covariates entered into the model—the interval from metastatic pancreatic cancer diagnosis to ascites onset and the number of prior systemic therapy lines—did not reach significance (P > 0.1) and were therefore excluded from the final multivariable model. Patients with higher ECOG PS values were significantly less likely to receive systemic treatment (P < 0.001). Median OS was markedly longer in those treated with chemotherapy (62 days) compared to best supportive care alone (16 days; P < 0.001, log-rank test); **(Figure 1).** Furthermore, ascites resolution was observed more frequently in the chemotherapy group (three cases) than in the best supportive care group (none; P < 0.001).

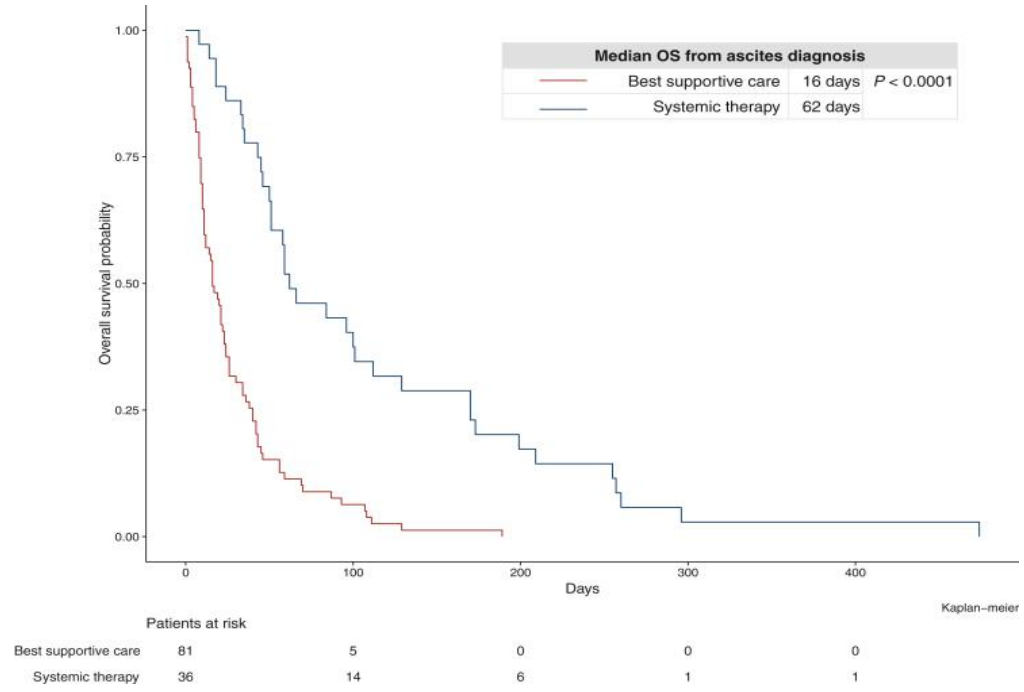

Figure 1.

Kaplan–Meier estimates of overall survival following the diagnosis of ascites, stratified by receipt of systemic chemotherapy versus best supportive care alone. OS denotes overall survival.

Information regarding the findings from the risk assessment is provided in **Table 2**, while the outcomes of the multivariable analysis are presented in **Figure 2**.

Table 2. Variables influencing overall survival following the onset of ascites. Results from univariate and multivariable Cox proportional hazards regression models.

Variable	Univariate Analysis HR (95% CI)	P-value	Multivariable Analysis HR (95% CI)	P-value
Age at metastatic pancreatic cancer diagnosis (per 10-year increase)	1.00 (0.99–1.03)	0.466	—	—

Sex Female (reference)	1	—	—	—
Male	1.32 (0.90–1.93)	0.156	1.37 (0.88–2.14)	0.159
ECOG performance status 0 (reference)	1	—	1	—
1	1.28 (0.59–2.78)	0.526	0.97 (0.36–2.63)	0.948
2	2.59 (1.20–5.58)	**0.015**	1.35 (0.49–3.76)	0.564
3	3.37 (1.48–7.67)	**0.004**	1.17 (0.39–3.50)	0.777
4	7.63 (1.56–37.24)	**0.012**	5.42 (0.92–32.1)	0.062
Sites of metastasis				
Lung	0.78 (0.53–1.16)	0.216	0.77 (0.49–1.23)	0.283
Bone	1.41 (0.68–2.92)	0.360	0.60 (0.25–1.43)	0.253
Liver	1.78 (1.10–2.87)	**0.019**	2.07 (1.13–3.79)	**0.018**
Peritoneum	1.46 (0.99–2.15)	0.055	1.74 (1.11–2.71)	**0.015**
Portal vein thrombosis Absent (reference)	1	—	—	—
Present	3.64 (2.06–6.43)	**<0.001**	2.52 (1.29–4.90)	**0.007**
Serum total protein Normal (reference)	1	—	—	—
Low	1.29 (0.78–2.14)	0.316	—	—
Serum albumin Normal (reference)	1	—	1	—
Low	1.22 (1.12–3.63)	**0.020**	2.19 (0.97–4.92)	0.059
ALBI grade Grade 1 (reference)	1	—	1	—
Grade 2	1.67 (0.65–4.25)	0.285	0.86 (0.24–3.01)	0.810
Grade 3	2.83 (1.09–7.33)	**0.032**	0.90 (0.24–3.38)	0.872
Serum CRP Normal (reference)	1	—	—	—
Elevated	1.49 (0.21–10.70)	0.694	—	—
Neutrophil-lymphocyte ratio (NLR) (per unit increase)	1.01 (0.98–1.05)	0.388	—	—
Leukocyte-lymphocyte ratio (LLR) (per unit increase)	1.00 (0.99–1.00)	0.676	—	—
Monocyte-lymphocyte ratio (MLR) (per unit increase)	1.10 (0.92–1.32)	0.285	—	—
Platelet-lymphocyte ratio (PLR) (per 100-unit increase)	1.00 (1.00–1.00)	0.498	—	—
Management after ascites development Best supportive care (reference)	1	—	—	—
Systemic chemotherapy	0.27 (0.17–0.43)	**<0.001**	0.35 (0.20–0.61)	**<0.001**
Time from diagnosis of metastases to ascites (per day)	1.00 (1.00–1.00)	0.5	—	—
Number of prior lines of systemic therapy (per additional line)	1.01 (0.87–1.18)	0.890	—	—

Statistically significant results ($P < 0.05$) are shown in **bold**.

Abbreviations: ALBI, albumin-bilirubin; CI, confidence interval; CRP, C-reactive protein; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; LLR, leukocyte-to-lymphocyte ratio; mPC, metastatic pancreatic cancer; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

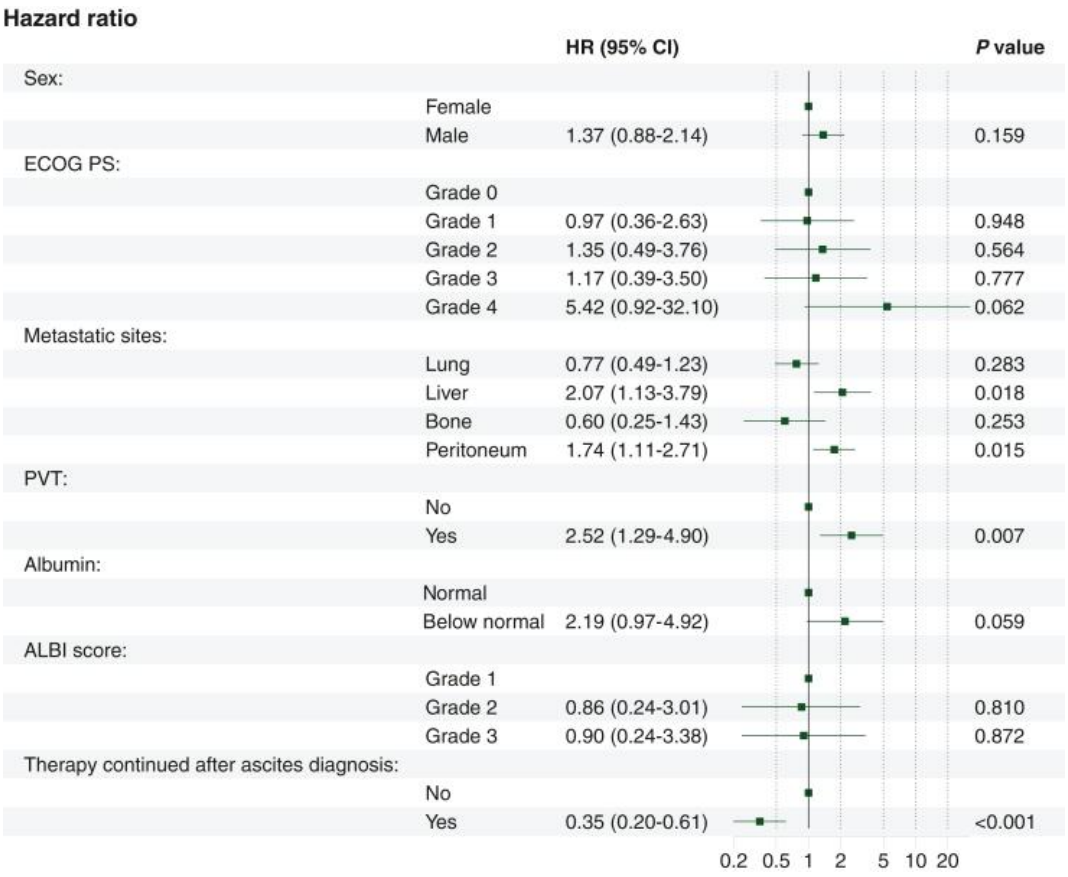

Figure 2.

Forest plot of factors associated with survival after ascites diagnosis as stratified by Cox proportional hazard models

ALBI score, albumin-bilirubin score; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; PVT, portal vein thrombosis.

Ascites leads to substantial patient discomfort, adversely affecting physical and psychological health, and is associated with a poor prognosis. Building on our previous comprehensive evaluation of risk factors for ascites development in patients with metastatic pancreatic cancer (mPC) [5], the current analysis aimed to identify prognostic factors in this population, with particular focus on whether to continue systemic chemotherapy following ascites diagnosis. Recognizing patients at high risk of poor outcomes after ascites onset is essential for tailoring individualized treatment strategies, especially given that ascites marks a late-stage event in pancreatic cancer, with a median overall survival (OS) of 27.4 days.

In this cohort, liver metastases and peritoneal metastases emerged as independent predictors of reduced survival post-ascites diagnosis. As previously reported, these metastatic sites are frequent in ascites patients and contribute to ascites formation through mechanisms such as lymphatic obstruction, enhanced vascular permeability, portal hypertension, and diminished hepatic functional reserve [5, 14–17]. Notably, liver metastases exerted a stronger negative prognostic impact (HR 2.07) than peritoneal carcinomatosis (HR 1.74) after ascites development, whereas peritoneal involvement appears more critical in ascites initiation. This aligns with prior studies across various malignancies associating liver metastases with particularly unfavorable outcomes relative to other extrahepatic sites [18, 19]. In colorectal cancer, for example, where liver metastases occur in up to 60% of cases, hepatic involvement is among the most potent predictors of survival, influenced only modestly by additional metastatic sites [20]. Potential explanations include compromised liver function precipitating complications like hemorrhage, cholestasis, encephalopathy, renal failure, hypotension, and hypoglycemia, alongside restrictions on systemic chemotherapy administration [21]. In contrast, peritoneal metastases primarily impair quality of life (QoL) through symptoms such as abdominal pain and dyspnea, with secondary effects on organ function via elevated intra-abdominal pressure [22, 23].

Portal vein obstruction (PVO) was an independent and potent adverse factor (HR 2.52) for survival following ascites diagnosis. PVO may arise from thrombosis, tumoral invasion, or external compression, promoting ascites, portal hypertension, and impaired liver function [5, 24, 25]. Similar associations between PVO and OS have been noted in hepatocellular carcinoma [26]. Guidelines for anticoagulation currently apply mainly to non-malignant cirrhosis [27]. Given PVO's substantial prognostic influence, prospective trials are needed to establish evidence-based management.

Previously reported independent links between systemic inflammation and survival were not confirmed in this mPC cohort with ascites [1, 28, 29]. This is noteworthy, as markers like C-reactive protein (CRP) and neutrophil-lymphocyte ratio (NLR) have been extensively linked to worse outcomes in other cancers [30]. Likewise, no independent prognostic role was found for liver function parameters, despite univariate associations with low albumin and ALBI grade 3. Hypoalbuminemia has been tied to inferior survival and incorporated into scores like the Glasgow Prognostic Score for inflammation and the validated ALBI for liver function [31, 32], with ALBI also prognostic in hepatocellular carcinoma [33]. The lack of independent associations here for inflammation or liver function markers may reflect masking by the extremely brief post-ascites survival in mPC.

A key observation was that continuing systemic chemotherapy (versus best supportive care alone) independently predicted better survival (HR 0.34), extending median OS by 46 days—and the sole favorable prognostic factor identified. This benefit persisted regardless of prior treatment lines or interval from mPC diagnosis to ascites, despite most patients having received ≥2 lines and developing ascites late (median 8.9 months). Even impaired performance status did not alter this finding. Thus, selected patients may derive benefit from ongoing chemotherapy, though careful patient selection is vital due to QoL implications. We noted three instances of complete ascites resolution with chemotherapy, albeit in a limited subgroup. With prior exhaustive use of optimal agents, regimen selection poses challenges, compounded by potential tolerability issues in advanced disease [11] and altered pharmacokinetics from peritoneal fluid accumulation, which may hinder drug penetration to peritoneal metastases [34, 35]. No prospective data guide optimal regimens, leaving decisions to clinical judgment. Where viable options and adequate performance status exist, chemotherapy may be warranted per guidelines [21]. Prospective studies incorporating QoL endpoints are essential to better define beneficiaries, while early palliative care integration remains fundamental for enhancing QoL and potentially outcomes [36–38].

Key limitations include the retrospective nature, precluding standardized ascites assessment or treatment randomization post-ascites. Pre-existing liver conditions and their prognostic effects could not be evaluated, nor chemotherapy's QoL impact. Comparisons of specific regimens were infeasible due to small subgroups and variable timing. Nonetheless, this represents the largest systematic analysis to date of prognostic factors post-ascites in mPC and the first structured evaluation of chemotherapy continuation in this context, hopefully spurring additional research.

Conclusion

In summary, multiple clinical factors were linked to worse survival after ascites in mPC. Continuing systemic therapy was the only identified favorable predictor.

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