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Impact of Bone Metastases in Biliary Tract Cancer

Authors: Ramis Andaleeb[1], Karim El-Shakankery[1], Joanna Kefas[1], Paula Muehlschlegel[1], Prof. John Bridgewater[1,2]
[1]Department of Medical Oncology, University College London Hospital, 235 Euston Road, London, UK, NW1 2BU
[2]University College London Cancer Institute, Paul O'Gorman Building, 72 Huntley St, London, UK, WC1E 6DD

Corresponding Author: Dr. Karim El-Shakankery
karim.el-shakankery@nhs.net

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Introduction:

Biliary tract cancers (BTC) represent just 1% of all cancers.[1-3] BTC include cholangiocarcinoma, gallbladder cancers and ampullary cancers with pancreatobiliary differentiation.[3-4] Frequently diagnosed at advanced stages, BTC patients have poor prognoses and limited responses to systemic anti-cancer therapies (SACT).[2-3]

While BTC lymph node, lung and liver metastases are well-documented, bone metastases (BM) prevalence remains poorly understood and underreported.[5-6] Their impact on survival is also uncertain.

Using a real-world BTC cohort, this study aimed to estimate the true prevalence of Bone Metastases, evaluate survival outcomes with standard-of-care treatments, and explore the relationship between BM, prognosis and genomic alterations.

Methods:

Patients with histology-confirmed BTC, reviewed at a university cancer centre between January 2019 and August 2022, were assessed. Data extracted from records included BTC subtype, molecular profiling, systemic anti-cancer therapy (SACT) use, relapse and survival time points. Stratification by BTC subtype, metastasis sites and other variables occurred. Median overall survival (mOS) was defined as time from relapse or metastases to death. Survival analysis was conducted using the Cox Proportional Hazard model. Categorical variables were compared with the Chi-squared test. P<0.05 was considered significant.

Results:

Of 197 patients, 37.6% had intrahepatic and 34% had extrahepatic cholangiocarcinoma. Patients with relapsed disease (n=45) had an 18.3-month mOS compared to 13.7 months in *de novo* inoperable/metastatic disease (n=123).

For all incurable cases (inoperable, metastatic, relapsed), mOS was 15.1 months. 17.3% patients had BM during their disease course with 7.1% identified at initial diagnosis.

Category		Result
Age (Years)	Mean (Standard Deviation)	63.1 (49.6-76.6)
	Range	25-90
Gender	Male	83 (42.1%)
	Female	114 (57.9%)
Biliary Tract Cancer Subtype*	Intrahepatic Cholangiocarcinoma	74 (37.6%)
	Extrahepatic Cholangiocarcinoma	67 (34.0%)
*Not = 100% due to rounding	Cholangiocarcinoma NOS Not Otherwise Specified	1 (0.1%)
	Gallbladder	46 (23.4%)
	Ampulla	9 (4.6%)
	Total	197 (100%)
Status at Primary Diagnosis	Localised/Operable	74 (37.6%)
	Inoperable or Metastatic	123 (62.4%)
	Total	197 (100%)
Relapse post-curative treatment	Yes	45 (22.8%)
	No	16 (8.2%)
	Not Applicable	136 (69.0%)
	Total	197 (100%)
Bone Metastases At Any Time (All Stages at Diagnosis)	Yes	34 (17.3%)
	No	163 (82.7%)
Bone Metastases (Inoperable, Relapsed and de novo Metastatic cases only)	Yes	34 (20.2%)
	No	134 (79.8%)
	Total	168 (100%)
Liver Metastases At Any Time (All Stages at Primary Diagnosis)	Yes	102 (51.8%)
	No	95 (48.2%)
Liver Metastases (Inoperable, Relapsed and de novo Metastatic cases only)	Yes	102 (61.0%)
	No	66 (39.0%)

Table 1: Real-World Study Biliary Tract Cancer Population Demographics

Of 197 patients, 74 (37.6%) had intrahepatic and 67 (34%) had extrahepatic cholangiocarcinoma. Patients with relapsed disease (n=45) had an 18.3-month mOS (95%CI 13.8-37.2), compared to 13.7 months (95%CI 11.2-19.2) in *de novo* inoperable/metastatic disease (n=123). For all incurable cases (inoperable, metastatic, relapsed), mOS was 15.1 months (95%CI 12.5-19.5). 34 patients had BM during their disease (17.3%), with 14 identified at initial diagnosis.

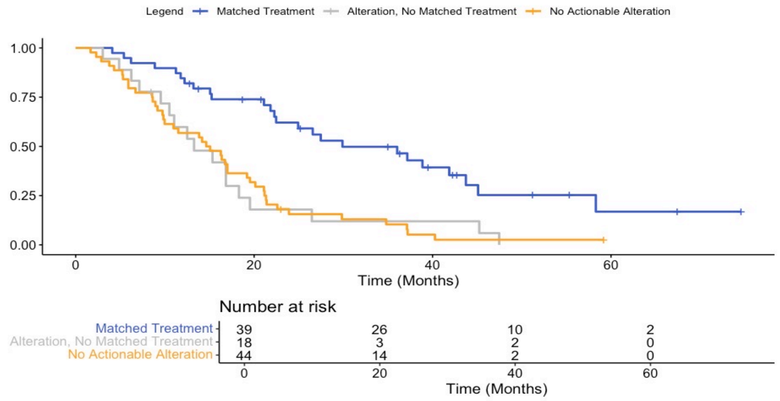

Figure 1: Kaplan Meier Overall Survival Curve – Actionable Alterations and Targeted Treatments

OS was not significantly influenced by bone (HR 1.15; 95%CI 0.78-1.70; P=0.48) or liver metastases (HR 1.09; 95%CI 0.78-1.53; P=0.6). Actionable alterations were equally likely in patients with (52.4%) and without BM (58.5%). Patients receiving matched, targeted SACT had a significantly longer mOS of 29.9 months, compared to 13.3 months in those with actionable alterations but no SACT matching (HR 0.35; 95%CI 0.19-0.66; P<0.005). Patients without actionable alterations had a mOS of 14.4 months.

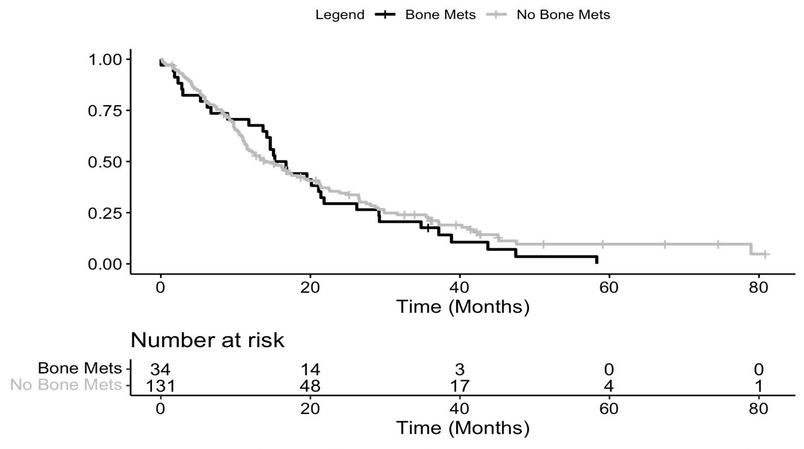

Figure 2: Kaplan Meier Overall Survival Curve – Presence vs Absence of Bone Metastases

Conclusions:

In advanced BTC, BM do not affect OS. Reported for the first time, actionable alterations are no more likely in this cohort. Over all cohorts, actionable alterations improved OS when treated with matched SACT.

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