Clinical characterization of HCC/CCC mixed cancers in a population-based cohort

Andreas Teufel[1,2], Isaac Rodriguez[1], Irina Surovtsova[3], Claudia Winzler[3], Daria Kokh[3], Matthias Ebert[2,4], Philipp Morakis[3]

1 Division of Hepatology, Division of Clinical Bioinformatics, Department of Medicine II, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany
2 Clinical Cooperation Unit Healthy Metabolism, Center for Preventive Medicine and Digital Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany
3 Clinical State Registration Office (KLR) of the Baden-Württemberg Cancer Registry at the Baden-Württemberg Hospital Society e.V., Stuttgart, Germany
4 Department of Medicine II, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany

e-mail: andreas.teufel@medma.uni-heidelberg.de

Background:

Hepatocellular carcinoma (HCC) ranks among of the most common tumors worldwide. As diagnosis requirements have developed in favor of imaging modalities, biopsy is now performed in only a minority of these patients. Thus, tumors displaying partially characteristics of cholangiocarcinoma (CCA) and therefore being characterized as mixed HCC/CCA tumors may not be identified. However, these tumors may benefit from (currently emerging) alternative treatment strategies. The aim of our study therefore was to characterize the clinical course of mixed HCC/CCA cancers in order to evaluate the need of distinct treatment options.

Method:

The present population-based cohort study investigated a total of 8221 patients diagnosed in the state of Baden-Wuerttemberg (population ~ 11 millions) between 2009 and 2019. 5973 patients suffered from HCC, 2092 from CCA and 156 from mixed HCC/CCA. Explicit details regarding sex, age, tumor location, histologic type, UICC stage, grade, surgery, and perioperative therapy were registered, as well as survival and recurrences. Information on vital status was regularly updated by official authorities.

Baden-Württemberg Center for Preventive and Digital Medicine (BW-ZDFP)

Variable	cHCC-CCA (*N*=156)	HCC (*N*=5973)	iCCA (*N*=2092)
Gender			
women	51(33.1)	1052(17.8)	881(42.3)
men	103(66.9)	4876(82.2)	1203(57.7)
unspecified	2	45	8
Age (years), *n*(%)			
18-50	14(9)	300(5)	214(10.2)
51-65	44(28.2)	1865(31.2)	746(35.7)
≥66	98(62.8)	3808(63.7)	1132(54)
Median (years)	70	70	67
Mean (years)	67.6	68.5	65.7
Residence, *n*(%)			
Out of BW	36(23)	1020(17.1)	579(27.7)
Mid north	37(23.7)	1197(20)	289(13.6)
Northwest	26(16.7)	1007(16.9)	345(16.5)
Southwest	14(9)	1076(18)	298(14.2)
Middle south	24(15.4)	880(14.7)	297(14.2)
East	19(12.2)	793(13.3)	284(13.6)
Stage, *n*(%)			
I	18(24.3)	632(24.9)	144(11.1)
II	10(13.5)	568(22.4)	139(10.8)
III	6(8.1)	489(19.3)	124(9.6)
IV	40(54)	846(33.3)	886(68.5)
No data	82	3438	799
Grade, *n*(%)			
1	5(4.9)	793(21.1)	66(4.4)
2	38(37.3)	2290(60.9)	833(55)
3	58(56.9)	664(17.7)	612(40.4)
4	1(1)	14(0.4)	5(0.3)
No data	54	2212	576

Table 1: Patients characteristics

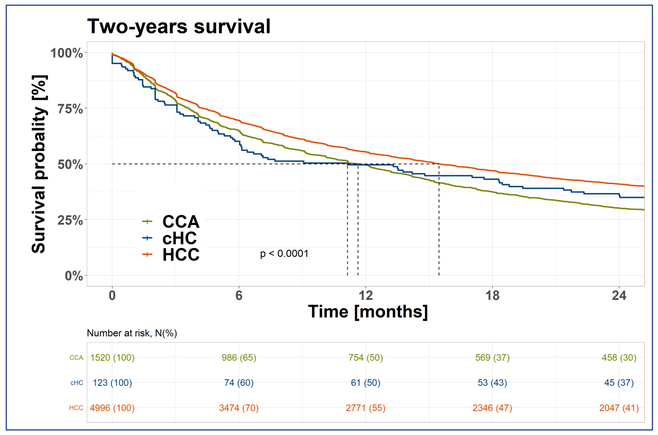

Figure 1: Survival analysis (Kaplan-Meier estimate)

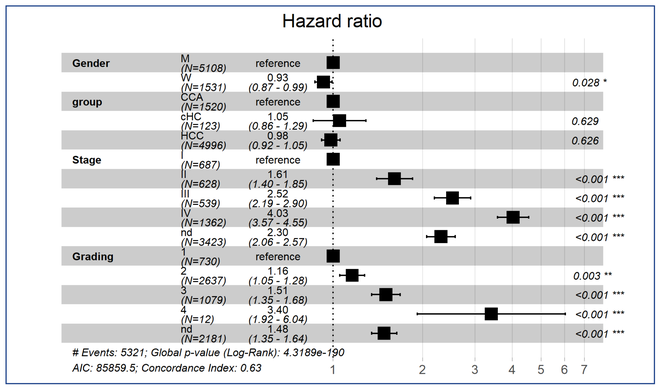

Figure 2: Multivariate analysis (Cox regression analysis)

Conclusion:

Data from our large retrospective population-based study demonstrate that mixed HCC/CCA tumors appear to have a distinct clinical course with worse overall survival compared to HCC. Therefore, diagnosis of these cancers by histology is important in order to provide them with accurate treatment options.

Results:

Investigating primary liver cancers in a large German cancer registry, 1.9% (156/8221) of patients were diagnosed with HCC/CCA mixed cancers. 62.8% of those mixed HCC/CCA cancer patients were older than 65 years (98/156). This was comparable to HCC (63.7%) but more than among CCA patients (54%). 54% of mixed HCC/CCA patients were diagnosed as stage IV cancers, which is more than for HCC (33.3%) but less compared to CCA (68.5%). As for grading, most patients were diagnosed with grade 3 HCC/CCA (56.9%).

Most importantly, overall median survival of HCC/CCA patients is worse compared to HCC (9-13 months vs. 15.5 months, p<0.001) and rather comparable to CCA (11.3 months).

This is in very good agreement with the previous study of Ref (1) that reported the median survival for HCC/CCA patients of 9 months (95% CI 7-11).

The further significant parameters (gender, stage, grading) were examined by a multivariate Cox proportional hazards regression analysis among patients with complete data sets. The present subgroup analyses did not demonstrate any gender differences, but showed strong correlation of survival with stage and grading

References:

(1) Wang J, Li E, Yang H, et al. Combined hepatocellular-cholangiocarcinoma: a population level analysis of incidence and mortality trends. World J Surg Oncol. 2019;17(1):43