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The Effects of Overlapping Autoimmune Liver Conditions on the Post-Liver Transplant Prognosis of Patients with Autoimmune Hepatitis

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Background and Aims

Among patients with autoimmune hepatitis (AIH), the presence of overlapping primary biliary cholangitis (PBC) or primary sclerosing cholangitis (PSC) can alter the disease progression and outcomes. Less is known about the effects of overlapping diagnoses on the post-liver transplant (LT) prognosis of patients with AIH.

Methods

2005-2019 UNOS registry was used to sample populations with AIH who underwent LT. For the purposes of this study, overlapping diagnoses were made when PBC or PSC was enlisted as LT registering diagnoses in the entry database. Using the co-presenting diagnoses, the sample was stratified into either PSC-AIH or PBC-AIH population and was compared to recipients without the overlapping diagnosis. Recipients under 18 years of age and those with multi-organ/living donor transplantation were excluded. For each comparison, Cox-regression analysis was performed (adjusting for MELD and covariates) to delineate the risks of death and the specific-causes of death following LT.

Results

From the database, there were 1927 without a diagnostic overlap, 52 with PSC-AIH overlap, and 69 with PBC-AIH overlap. The median follow-up time was 3.94 years. Compared to those without PSC-overlap, PSC-AIH recipients were likely to be male (55.8 vs 28.0% p<0.001) and likely to be White or Black (White 59.6 vs 58.4; Black 32.7 vs 19.6; Hispanic 3.85 vs 17.7; Asian 1.92 vs 2.49; other 1.92 vs 1.76% p=0.01). However, there was no difference in age (46.1 vs 49.5y p=0.06) or in MELD (25.30 vs. 24.70 p=0.54). With respect to outcomes, there was no difference in all-cause mortality (aHR 1.10 95%CI 0.61-1.97) and graft failure (aHR 2.04 95%CI 0.80-5.19). Compared to those without PBC-overlap, PBC-AIH recipients were older (53.1 vs 49.5y p<0.05), likely to be female (85.5 vs 72.0% p=0.02), and likely to be Hispanic or Asian (White 49.3 vs 58.4; Black 13.0 vs 19.6; Hispanic 27.5 vs 17.7; Asian 7.25 vs 2.49; other 2.90 vs 1.76% p=0.02). However, there was no difference in MELD (25.30 vs. 25.10 p=0.90). PBC-AIH had higher risk of graft failure (aHR 3.53 95% CI 1.73-7.24), as well as deaths due to general respiratory causes (aHR 3.55 95% CI 1.22-10.36), acute respiratory distress syndrome (aHR 18.07 95% CI 3.31-98.74), and recurrent disease (aHR 9.65 95% CI 1.82-51.15). The case-incidence rates also corroborated these findings (expressed in 1000 person-years; graft failure 28.87 vs 9.15; general respiratory causes 12.83 vs 3.87; acute respiratory distress syndrome 6.42 vs 0.43; recurrent disease 6.42 vs 1.18).

Conclusion

This study shows AIH recipients with a concurrent diagnosis of PBC may be at a higher risk of graft failure, and death due to respiratory causes and recurrent disease. PSC-AIH overlap patients are a higher risk for death due to graft infection. While further studies are needed to ascertain the histological variations of the overlap, clinical caution should be practiced when addressing the prognostic risks of PBC-AIH and PSC-AIH candidates prior to LT.

Univariate Analysis

Characteristics	Without Overlap Syndrome	Primary Sclerosing Cholangitis	P-value	Primary Biliary Cholangitis	P-value
Number of Patients	1927	52		69	
Recipient Demographics					
Age, mean ± SD, y	49.50 ± 13.80 year	46.10 ± 13.60 year	0.06	53.10 ± 11.60 year	0.05 *
Male sex, *n* (%)	540 (28.00) %	29 (55.80) %	< 0.001 ***	10 (14.50) %	0.02 *
Race, *n* (%)			0.01 † *		0.02 † *
White	1125 (58.40) %	31 (59.60) %		34 (49.30) %	
Black	378 (19.60) %	17 (32.70) %		9 (13.00) %	
Hispanic	342 (17.70) %	2 (3.85) %		19 (27.50) %	
Asian	48 (2.49) %	1 (1.92) %		5 (7.25) %	
Other	34 (1.76) %	1 (1.92) %		2 (2.90) %	
BMI, mean ± SD, kg/m²	29.10 ± 6.70 kg/m²	25.50 ± 4.69 kg/m²	< 0.001 ***	27.10 ± 5.28 kg/m²	0.04 *

Cox Iterations for Primary Endpoints

Primary Sclerosing Cholangitis

(A) All-cause Mortality

Incidence Rates per 1000 Person-Years		
With Primary Sclerosing Cholangitis	46.66	(24.34 - 80.08)
Without Primary Sclerosing Cholangitis	47.46	(43.23 - 51.98)

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.86	1.06	(0.59 - 1.88)
2	0.89	1.04	(0.58 - 1.86)
3	0.74	1.10	(0.62 - 1.97)
†FM	0.75	1.10	(0.61 - 1.97)

(B) Graft Failure

Incidence Rates per 1000 Person-Years		
With Primary Sclerosing Cholangitis	19.44	(6.34 - 44.78)
Without Primary Sclerosing Cholangitis	9.15	(7.31 - 11.30)

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.16	1.94	(0.77 - 4.88)
2	0.17	1.92	(0.76 - 4.84)
3	0.14	2.01	(0.79 - 5.09)
†FM	0.14	2.04	(0.80 - 5.19)

Primary Biliary Cholangitis

(A) All-cause Mortality

Incidence Rates per 1000 Person-Years		
With Primary Biliary Cholangitis	73.77	(47.34 - 108.64)
Without Primary Biliary Cholangitis	47.46	(43.23 - 51.98)

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.07	1.48	(0.97 - 2.26)
2	0.06	1.49	(0.98 - 2.28)
3	0.06	1.51	(0.99 - 2.31)
†FM	0.07	1.49	(0.97 - 2.28)

(B) Graft Failure

Incidence Rates per 1000 Person-Years		
With Primary Biliary Cholangitis	28.87	(13.28 - 54.09)
Without Primary Biliary Cholangitis	9.15	(7.31 - 11.30)

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	< 0.001 ***	3.39	(1.68 - 6.85)
2	< 0.001 ***	3.41	(1.68 - 6.91)
3	< 0.001 ***	3.53	(1.73 - 7.18)
†FM	< 0.001 ***	3.53	(1.73 - 7.24)

Cox Iterations for Specific Causes of Death

Primary Sclerosing Cholangitis

(A) Death due to Graft Infection

Incidence Rates per 1000 Person-Years		
With Primary Sclerosing Cholangitis	3.89	(0.10 - 21.47)
Without Primary Sclerosing Cholangitis	0.32	(0.07 - 0.94)

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.04 *	13.32	(1.20 - 148.00)
2	0.009 **	20.83	(2.17 - 200.33)
3	0.003 **	31.72	(3.30 - 305.18)
†FM	0.002 **	38.39	(3.98 - 370.49)

Primary Biliary Cholangitis

(B) Death due to General Respiratory Causes

Incidence Rates per 1000 Person-Years		
With Primary Biliary Cholangitis	12.83	(3.51 - 32.52)
Without Primary Biliary Cholangitis	3.87	(2.71 - 5.36)

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.04 *	2.91	(1.03 - 8.23)
2	0.03 *	3.19	(1.11 - 9.15)
3	0.03 *	3.34	(1.16 - 9.63)
†FM	0.02 *	3.55	(1.22 - 10.36)

(C) Death due to Acute Respiratory Distress Syndrome

Incidence Rates per 1000 Person-Years		
With Primary Biliary Cholangitis	6.42	(0.78 - 22.98)
Without Primary Biliary Cholangitis	0.43	(0.12 - 1.10)

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.003 **	13.85	(2.49 - 77.07)
2	< 0.001 ***	23.57	(4.31 - 129.00)
3	< 0.001 ***	19.26	(3.52 - 105.29)
†FM	< 0.001 ***	18.07	(3.31 - 98.74)

(D) Death due to Recurrent Nonhepatitis

Incidence Rates per 1000 Person-Years		
With Primary Biliary Cholangitis	6.42	(0.78 - 22.98)
Without Primary Biliary Cholangitis	1.18	(0.59 - 2.12)

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.006 **	9.64	(1.93 - 48.22)
2	0.005 **	10.15	(2.00 - 51.57)
3	0.008 **	9.21	(1.79 - 47.26)
†FM	0.008 **	9.65	(1.82 - 51.15)

Prognostic Curves for Clinical Endpoints

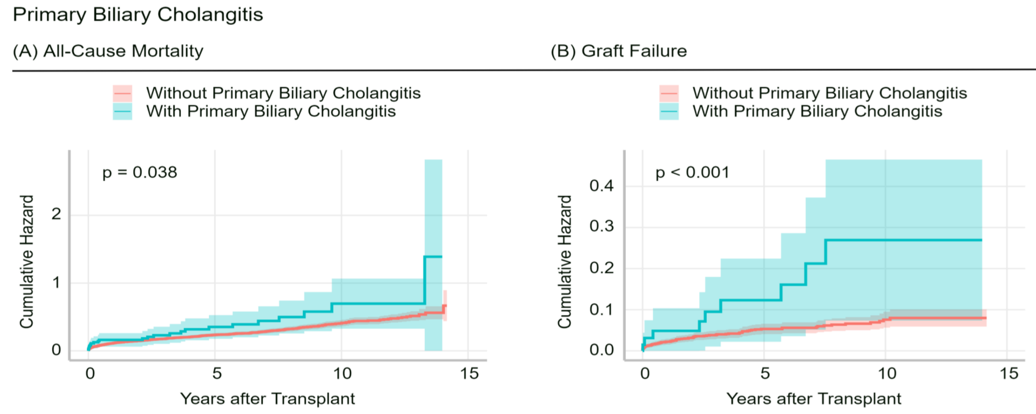
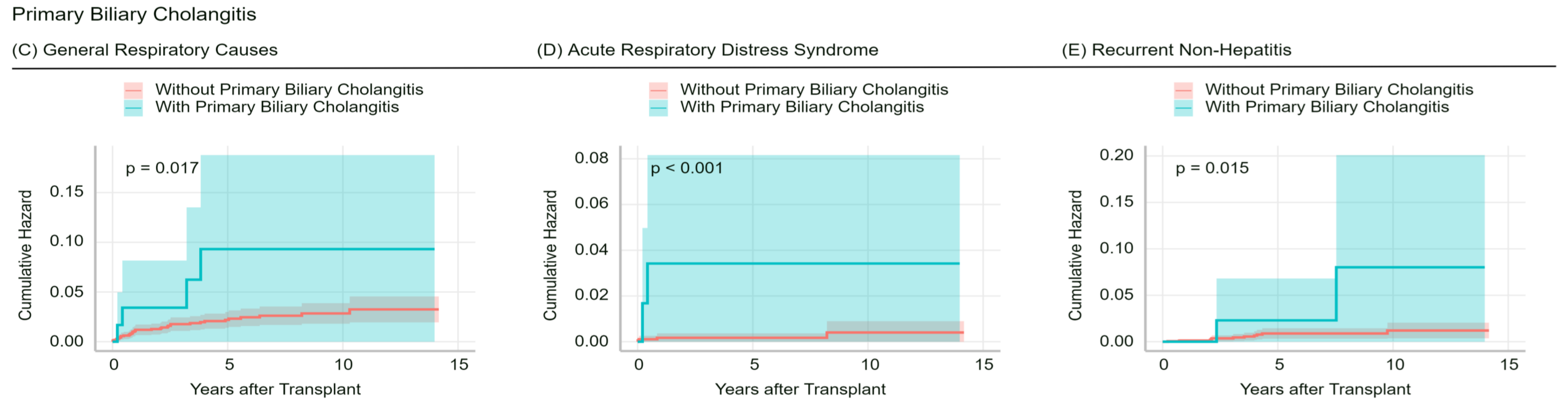


Figure 1B: Prognostic Differences in the Cumulative Hazards of Specific-Causes of Death



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