2019 POST-AASLD WRAP-UP: AUTOIMMUNE HEPATITIS

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DIAGNOSIS

THE PRESENCE OF RADIOGRAPHIC HEPATIC STEATOSIS IS ASSOCIATED WITH PROLONGED TIME TO DIAGNOSIS OF AIH AND ADVANCED FIBROSIS AT TIME OF DIAGNOSIS

- Yang, et al.
- 54 adult AIH pts
- Multivariate analysis (adjust for age, Ab titer, ALT); eval NAFLD-associated pt characteristics with time to dx from ALT elevation and fibrosis stage at dx of AIH.

Table 1. Multivariate Analysis: Factors associated with time to AIH Diagnosis and advanced fibrosis stage at diagnosis.

	Effect on Days from Abnormal LFTs to Diagnosis	P value	Odds Ratio for Advanced Fibrosis at Diagnosis	P value
Steatosis on Imaging	547	0.030	8.32	0.025
Sex	83.6	0.73	2.14	0.413
High-Titer Autoantibody	0.798	0.998	5.02	0.221
Degree of ALT abnormality	-187	0.045	1.39	0.354

DIAGNOSIS OF PAEDIATRIC AIH BY USING THE COMBINATION OF MULTIPARAMETRIC MRI AND QUANTITATIVE MRCP ANALYSIS

- Cheng,etal.

- Prospectively-collected cohort, age 6-18, n=41; 20 age-matched controls.
- All had iron-corrected T1 multiparametric MRI (LiverMultiScan; LMS), and a novel quantitative MRCP (MRCP+).
- 25 variables evaluated using logistic regression to differentiate AIH from controls, then to select optimal combinations of variables for differentiation.
- AUROC were calculated.

- 2 LMS and 1 MRCP+ variables signif. greater in AIH
  - Median liver cT1
  - Liver cT1 IQR
  - Sum of relative dilation severity

- Using the 3 combined variables and optimal cutoff points:
  - AUROC 0.88 (95% CI 0.8-0.97)
  - Sensitivity 0.83
  - Specificit 0.80

DIAGNOSTIC PERFORMANCE OF FIBROTEST AND TRANSIENT ELASTOGRAPHY BY FIBROSCAN IN PATIENTS WITH AIH USING HISTOLOGICAL REFERENCE.

- Sandler, etal. (validation study)
- Prospectively accrued AIH cohort, n=45
  - 53.5% with AIH/PBC overlap features. N=31 had both FT/TE
- FT and TE performed w/in 3d of liver biopsy.
  - Avg LBx length 12mm
- AUROC to assess performance to determine F2-4, F3-4, F4.
- AUROC (FT): 0.79/0.77/0.91 (all signif)
- AUROC (TE): 0.73/-/0.90 (similar performance to FT)
- Performance improved in pts w/o severe activity (A3)

CO-PREVALENT AUTOIMMUNITY VARIES BETWEEN AUTOIMMUNE DISEASES: A PRIMARY CARE PRACTICE DATABASE STUDY

Table: Relative risk compared to controls for extra-hepatic autoimmunity across autoimmune liver diseases

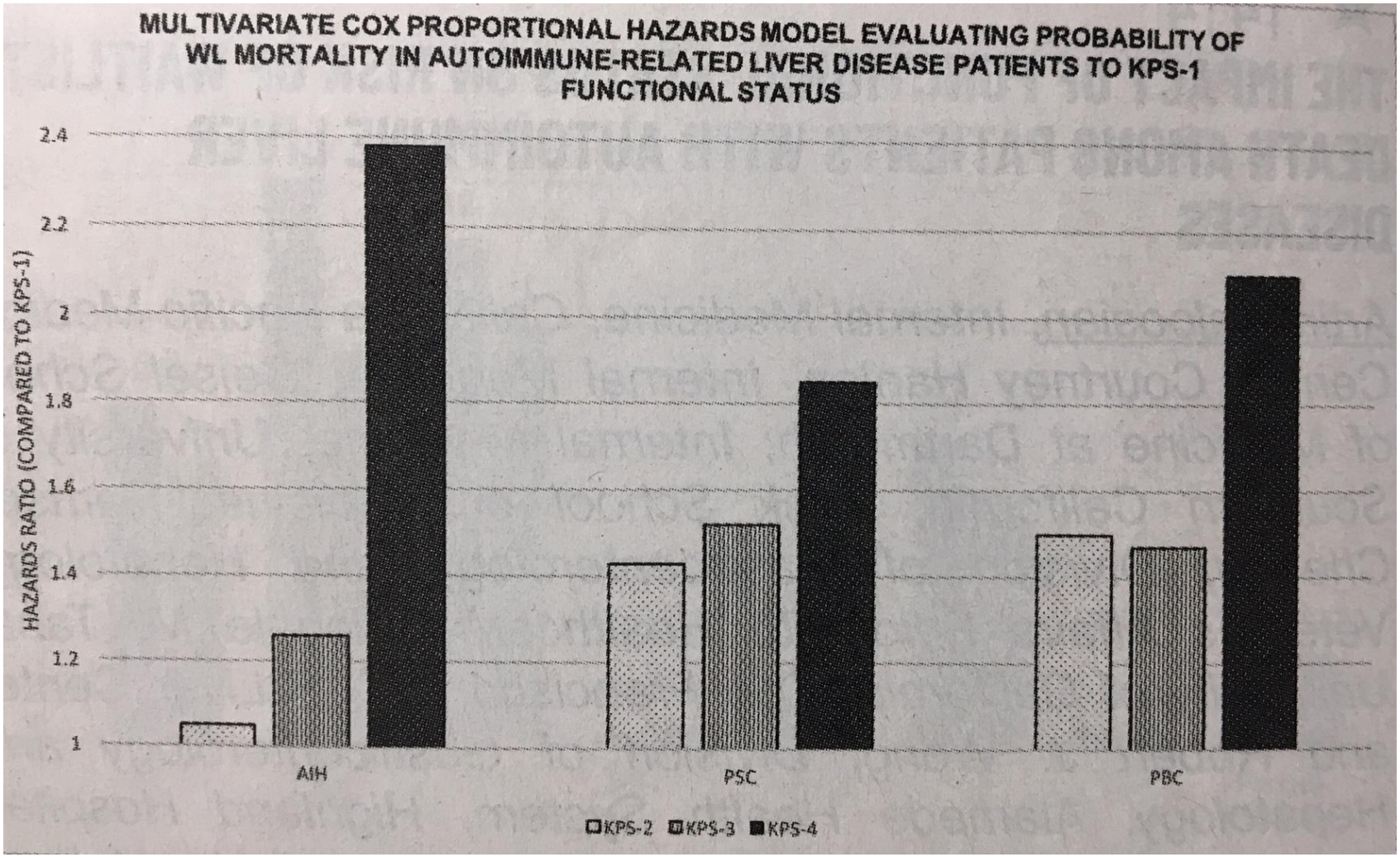
	AIH (n = 2043) RR vs controls (95%CI)	PBC (n = 2441) RR vs controls (95%CI)	PSC (n = 679) RR vs controls (95%CI)
Autoimmune thyroid disease	2.2 (2.0-2.4)	1.9 (1.7-2.0)	1.5 (1.2-1.9)
Coeliac disease	3.8 (2.7-5.2)	4.4 (3.4-5.5)	6.0 (3.5-9.3)
Crohn's disease	3.2 (2.2-4.5)	1.6 (1.0-2.5)	38.9 (34.5-43.3)
ITP	6.5 (4.0-9.9)	5.1 (3.2-7.7)	6.6 (2.5-13.3)
Multiple sclerosis	1.6 (0.9-2.7)	1.1 (0.6-1.8)	1.5 (0.3-3.9)
Pernicious anaemia	1.9 (1.3-2.6)	1.6 (1.2-2.2)	2.7 (1.4-4.5)
Psoriasis	1.2 (1.0-1.5)	1.7 (1.4-1.9)	1.8 (1.3-2.3)
Raynaud's syndrome	1.8 (1.3-2.3)	3.6 (3.1-4.2)	1.7 (0.9-2.8)
Rheumatoid arthritis	2.3 (1.8-2.8)	2.0 (1.7-2.4)	2.6 (1.7-3.7)
Scleroderma	1.9 (1.3-2.5)	3.3 (2.8-3.9)	1.9 (0.8-3.6)
Sjögren syndrome	8.4 (6.1-11.0)	17.1 (14.8-19.6)	9.3 (4.0-17.2)
Type 1 diabetes mellitus	2.8 (2.0-3.7)	2.2 (1.6-2.9)	5.0 (3.5-6.9)
Ulcerative colitis	5.4 (4.3-6.5)	1.8 (1.3-2.5)	73.9 (72.3-75.2)

TRANSPLANT ISSUES

THE IMPACT OF FUNCTIONAL STATUS ON RISK OF WAITLIST DEATH AMONG PATIENTS WITH AUTOIMMUNE LIVER DISEASES

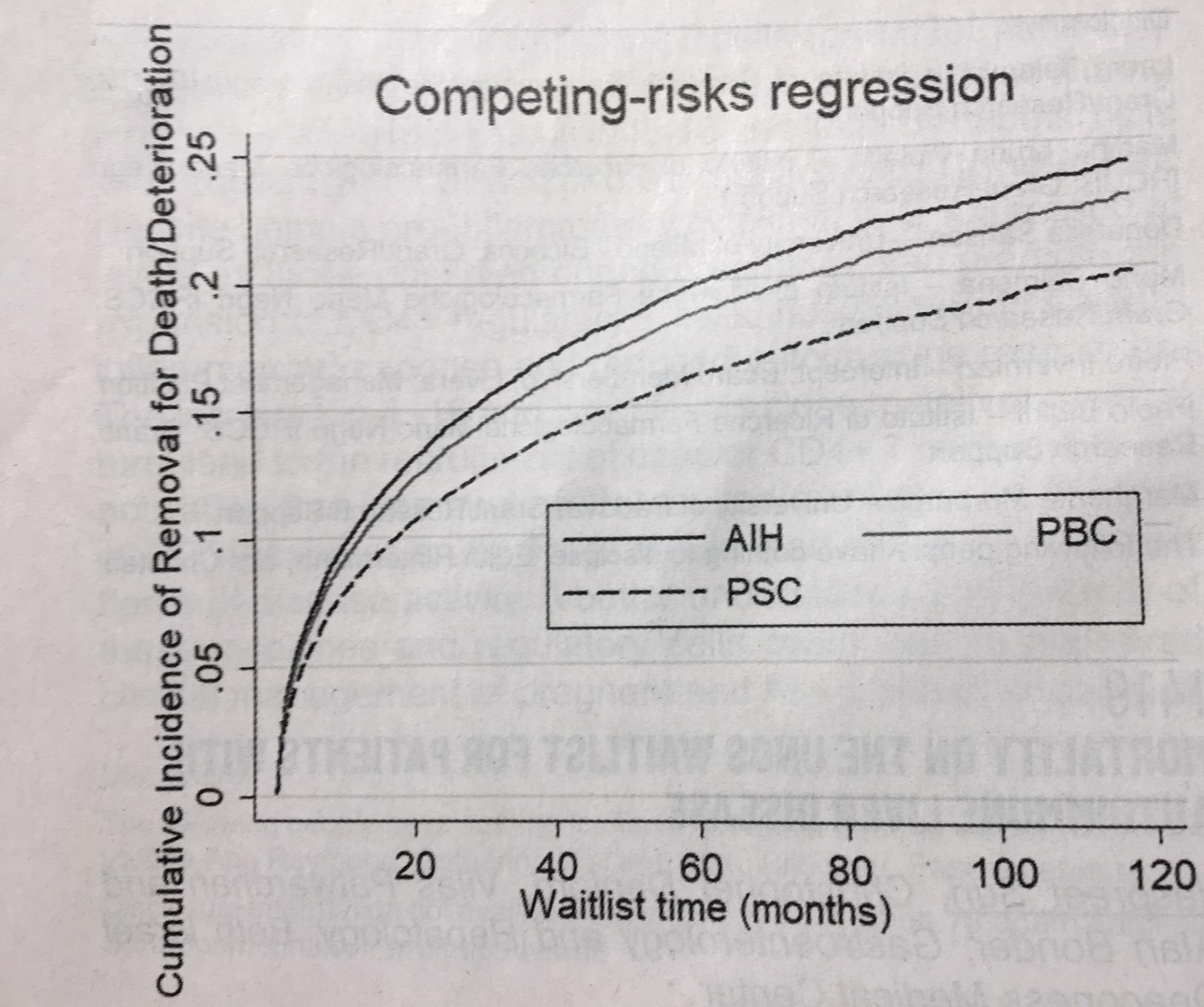
- Galoosian, etal
- Retrospective eval of UNOS database, 2004-17
- Functional status at time of listing assessed using Karnofsky Performance Status (KPS 1-4)
- WL survival stratified by KPS group, liver dz etiology
- Eval'd with Kaplan Meier methods and multivariate Cox proportional hazards models
- Corrected for age, MELD, sex, race, insurance status, co-morbidities

- N= 11,733 (32.7% AIH, 32.8% PSC, 34.5% PBC)
- 90-d WL survival worse w/ worse KPS for all dz's
- Functional status at registration worse for AIH pts
  - %KPS-4: 47.7% AIH, 29.4% PSC, 22.9% PBC, $p<0.001$
- On multivariate analysis, detrimental impact of worse KPS (1 vs 4) was greatest in AIH
  - (HR 2.38, 95%CI 1.58-3.60)


MULTIVARIATE COX PROPORTIONAL HAZARDS MODEL EVALUATING PROBABILITY OF WL MORTALITY IN AUTOIMMUNE-RELATED LIVER DISEASE PATIENTS TO KPS-1 FUNCTIONAL STATUS
HAZARDS RATIO (COMPARED TO KPS-1)
2.4
2.2
2
1.8
1.6
1.4
1.2
1
AIH
PSC
PBC
KPS-2
KPS-3
KPS-4

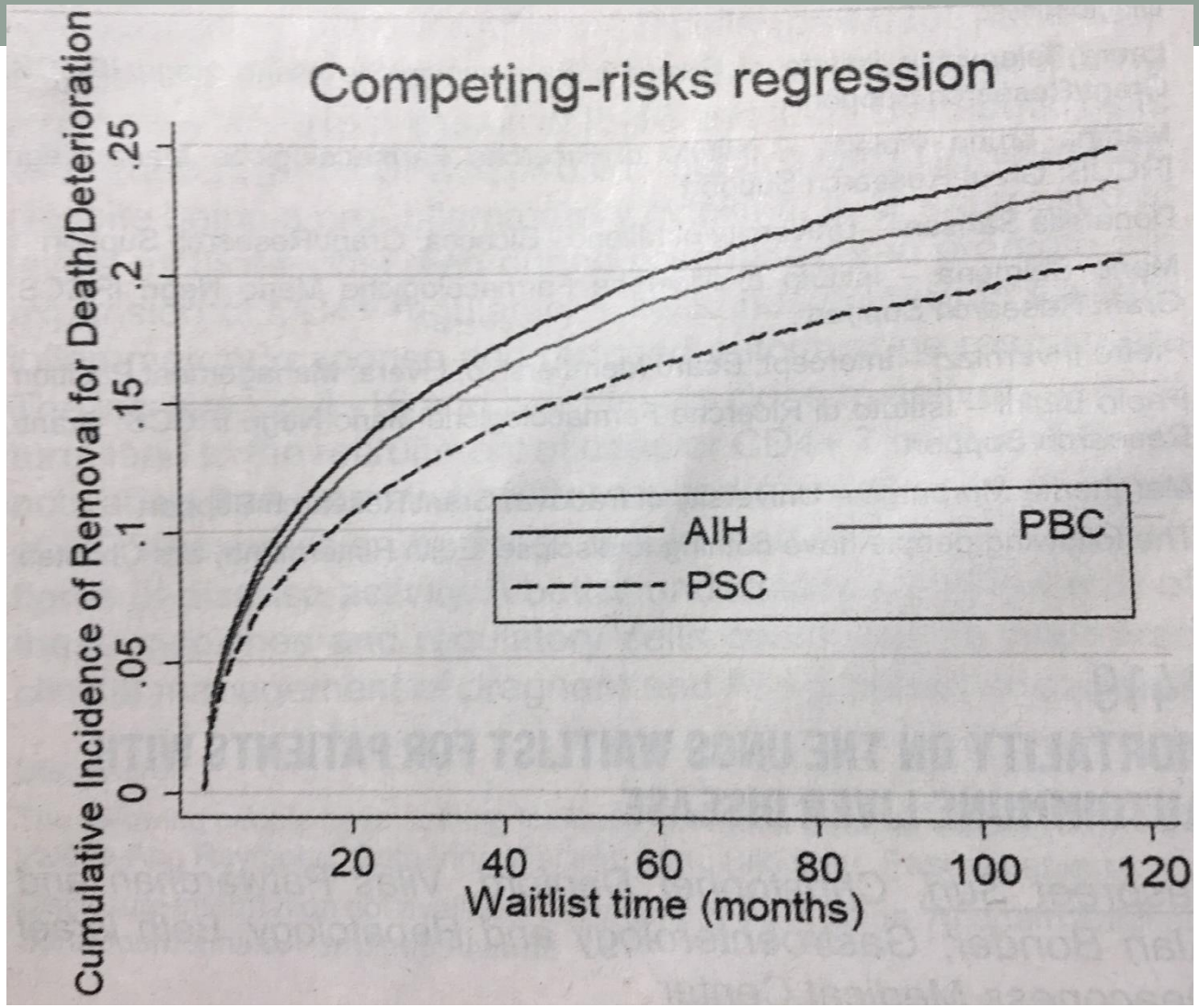
MORTALITY ON THE UNOS WAITLIST FOR PATIENTS WITH AUTOIMMUNE LIVER DISEASE

- Suri, etal
- Included pts with AIH/PBC/PSC listed for OLT in UNOS database 1987-2016.
- Compared waitlist survival using competing risk analysis.
- N= 26,432 (7412 AIH, 8119 PBC, 10,901 PSC)
- AIH pts younger (44.6/54.9/45.6, $p<0.001$), with higher MELD (18.9/17.1/16.4, $p<0.001$)
- WL removal for death/deterioration greater for AIH/PBC than PSC (17.5/15/10.2)
  - (controlled for age, sex, blood type, region, listing MELD)


Competing-risks regression
Cumulative Incidence of Removal for Death/Deterioration
0
.05
.1
.15
.2
.25
20
40
60
80
100
120
Waitlist time (months)
AIH
PBC
PSC

FACTORS ASSOCIATED WITH RECURRENCE OF AIH AFTER OLT AND EFFECTS ON GRAFT AND PATIENT SURVIVAL

- Montano-Loza,etal.
- N=480 (AIH pts who underwent OLT 1987-2019, 17 centers)
- Cox regression analysis assessed factors for recurrence
- Association of recurrence with graft loss/overall survival analyzed.
- Recurrence incidence: 24% at 5 yrs, 41% at 10 yrs.
- Risk higher if age <40 at (HR 1.74, p=0.4), ALT >1.5xNl at 1y p-OLT (HR 3.55, p<.001); risk lower if prednisone used p-OLT (HR 0.48, p=.01)
- Recurrence associated signif with graft loss and lower survival



- 5/10/15yr graft survival:
  - w/ recurrence = 77/62/55%
  - w/o recurrence = 89/84/84%

JUST CAUSE IT'S NEAT…

NANOPARTICLE DEPENDENT ADMINISTRATION OF DEXAMETHASONE PREVENTS ITS SYSTEMIC SPREAD AND REDUCES INFLAMMATORY MARKERS IN A MURINE MODEL OF AIH

- Used a pH sensitive linker to load dexamethasone to a nanoformulation (released at pH<6).
- Mice dosed intraperitoneally with free or linked dxm.
- Fluorescently labelled nanosteroids localized by microscopy in liver and whole body.
- HPLC measured free drug in liver and plasma.
- With nanosteroid, free drug detected only in liver; resulted in decreased markers of inflammation, fibrosis deposition, and levels of circulating autoantibodies.