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.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Effect on Days from Abnormal LFTs to Diagnosis</th>
<th>P value</th>
<th>Odds Ratio for Advanced Fibrosis at Diagnosis</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steatosis on Imaging</td>
<td>547</td>
<td>0.030</td>
<td>8.32</td>
<td>0.025</td>
</tr>
<tr>
<td>Sex</td>
<td>83.6</td>
<td>0.73</td>
<td>2.14</td>
<td>0.413</td>
</tr>
<tr>
<td>High-Titer Autoantibody</td>
<td>0.798</td>
<td>0.998</td>
<td>5.02</td>
<td>0.221</td>
</tr>
<tr>
<td>Degree of ALT abnormality</td>
<td>-187</td>
<td>0.045</td>
<td>1.39</td>
<td>0.354</td>
</tr>
</tbody>
</table>
DIAGNOSIS OF PAEDIATRIC AIH BY USING THE COMBINATION OF MULTIPARAMETRIC MRI AND QUANTITATIVE MRCP ANALYSIS

• Cheng, et al.

• 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
  • Specificity 0.80
Sandler, et al. (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)
## Table: Relative risk compared to controls for extra-hepatic autoimmunity across autoimmune liver diseases

<table>
<thead>
<tr>
<th>Condition</th>
<th>AIH (n = 2043) RR vs controls (95%CI)</th>
<th>PBC (n = 2441) RR vs controls (95%CI)</th>
<th>PSC (n = 679) RR vs controls (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune thyroid disease</td>
<td>2.2 (2.0-2.4)</td>
<td>1.9 (1.7-2.0)</td>
<td>1.5 (1.2-1.9)</td>
</tr>
<tr>
<td>Coeliac disease</td>
<td>3.8 (2.7-5.2)</td>
<td>4.4 (3.4-5.5)</td>
<td>6.0 (3.5-9.3)</td>
</tr>
<tr>
<td>Crohn's disease</td>
<td>3.2 (2.2-4.5)</td>
<td>1.6 (1.0-2.5)</td>
<td>38.9 (34.5-43.3)</td>
</tr>
<tr>
<td>ITP</td>
<td>6.5 (4.0-9.9)</td>
<td>5.1 (3.2-7.7)</td>
<td>6.6 (2.5-13.3)</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>1.6 (0.9-2.7)</td>
<td>1.1 (0.6-1.8)</td>
<td>1.5 (0.3-3.9)</td>
</tr>
<tr>
<td>Pernicious anaemia</td>
<td>1.9 (1.3-2.6)</td>
<td>1.6 (1.2-2.2)</td>
<td>2.7 (1.4-4.5)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>1.2 (1.0-1.5)</td>
<td>1.7 (1.4-1.9)</td>
<td>1.8 (1.3-2.3)</td>
</tr>
<tr>
<td>Raynaud's syndrome</td>
<td>1.8 (1.3-2.3)</td>
<td>3.6 (3.1-4.2)</td>
<td>1.7 (0.9-2.8)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>2.3 (1.8-2.8)</td>
<td>2.0 (1.7-2.4)</td>
<td>2.6 (1.7-3.7)</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>1.9 (1.3-2.5)</td>
<td>3.3 (2.8-3.9)</td>
<td>1.9 (0.8-3.6)</td>
</tr>
<tr>
<td>Sjögren syndrome</td>
<td>8.4 (6.1-11.0)</td>
<td>17.1 (14.8-19.6)</td>
<td>9.3 (4.0-17.2)</td>
</tr>
<tr>
<td>Type 1 diabetes mellitus</td>
<td>2.8 (2.0-3.7)</td>
<td>2.2 (1.6-2.9)</td>
<td>5.0 (3.5-6.9)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>5.4 (4.3-6.5)</td>
<td>1.8 (1.3-2.5)</td>
<td>73.9 (72.3-75.2)</td>
</tr>
</tbody>
</table>
TRANSPLANT ISSUES
THE IMPACT OF FUNCTIONAL STATUS ON RISK OF WAITLIST DEATH AMONG PATIENTS WITH AUTOIMMUNE LIVER DISEASES

- Galoosian, et al
- 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

Hazard Ratio (Compared to KPS-1)

- AIH
- PSC
- PBC

KPS-2 □ KPS-3 □ KPS-4
MORTALITY ON THE UNOS WAITLIST FOR PATIENTS WITH AUTOIMMUNE LIVER DISEASE

- Suri, et al
- 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

Waitlist time (months)

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

- Montano-Loza, et al.
- 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.