Fatty Liver Disease
Diagnostic Challenges and Updates

Ryan M. Gill, M.D., Ph.D.
Department of Pathology
University of California, San Francisco
Obesity in Antiquity

Obesity Treatment
Brisk walking
Wrestling
Definitions

- **NAFLD** – Fat (≥5%) in the liver (imaging or histology) in a patient without secondary fat accumulation.

- **NASH** - NAFLD with histologic evidence of liver injury in the form of ballooned hepatocytes and inflammation +/- fibrosis.

- **NAFL** – NAFLD without the above histologic findings associated with NASH.
Secondary Hepatic Fat

• Macrovesicular
  – Excess alcohol
  – HCV
  – Wilson Disease
  – Starvation/TPN
  – Medications (amiodarone, methotrexate, tamoxifen, corticosteroids)

• Microvesicular
Secondary Hepatic Fat

- Macrovesicular
- Microvesicular
  - Reye Syndrome
  - Acute Fatty Liver of pregnancy
  - Medications (e.g. antiretrovirals, valproate)
Natural History

- **NASH**: Can progress to cirrhosis and liver failure (and rarely hepatocellular carcinoma)

- **NAFL**: Risk of progression to cirrhosis and liver failure is considered *minimal* (with *increased risk associated with NAFL with inflammation*)
The Diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guidance From the American Association for the Study of Liver Diseases

Naga Chalasani, Zobair Younossi, Joel E. Lavine, Michael Charlton, Kenneth Cusi, Mary Rinella, Stephen A. Harrison, Elizabeth M. Brunt, and Arun J. Sanyal
<table>
<thead>
<tr>
<th>Common Conditions With Established Association</th>
<th>Other Conditions Associated With NAFLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>Hypothyroidism</td>
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<tr>
<td>T2DM</td>
<td>Obstructive sleep apnea</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>Hypopituitarism</td>
</tr>
<tr>
<td>MetS*</td>
<td>Hypogonadism</td>
</tr>
<tr>
<td>Polycystic ovary syndrome</td>
<td>Pancreatoduodenal resection</td>
</tr>
<tr>
<td></td>
<td>Psoriasis</td>
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</tbody>
</table>

*The Adult Treatment Panel III clinical definition of MetS requires the presence of three or more of the following features: (1) waist circumference greater than 102 cm in men or greater than 88 cm in women; (2) TG level 150 mg/dL or greater; (3) HDL cholesterol level less than 40 mg/dL in men and less than 50 mg/dL in women; (4) systolic blood pressure 130 mm Hg or greater or diastolic pressure 85 mm Hg or greater; and (5) fasting plasma glucose level 110 mg/dL or greater."
Genetic Factors

– *PNPLA3* – encodes adiponutrin. A SNP at position 148 is associated with hepatic steatosis, NASH, and increased fibrosis stage (as well as incidence of HCC)

– *TM6SF2* – a SNP at position 167 has similar associations as *PNPLA3* SNP
Scoring Systems

- **NAS** - Unweighted composite of steatosis, lobular inflammation, and ballooning scores. Useful to measure changes in biopsies in clinical trials. Fibrosis is scored separately.

- **SAF score** – Semiquantitative score consisting of steatosis amount, activity (lobular inflammation and ballooning) and fibrosis.
Conclusions

• With continued high rates of adult obesity and diabetes, in an aging population, NAFLD related liver disease and mortality will increase in the US.

• Strategies to slow growth of NAFLD and therapeutic options are necessary to mitigate disease burden.
Response to the Crisis

Number of Publications by Five Year Intervals, Keyword: "Non-alcoholic Steatohepatitis"
Outline

1. Essential histologic criteria for diagnosis of steatohepatitis
2. Centrizonal arteries
3. Aggressive NASH
4. Diagnostic pitfalls
5. Revisiting the NAS
Steatohepatitis: Essential Features

AASLD and NASH Clinical Research Network

- Steatosis (≥5%)
- Inflammation (lobular)
- Hepatocellular injury
  - Ballooned hepatocytes
- +/- Pericellular fibrosis
Steatohepatitis: Essential Features

AASLD and NASH Clinical Research Network

- Steatosis (>5%)
- Inflammation (lobular)
- Hepatocellular injury
  Ballooned hepatocytes

+/- Pericellular fibrosis
Large or Small Droplet Macrovesicular Steatosis

Estimation of Steatosis

Mild Steatosis (Grade 1, scale 0-3)

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013, adapted with permission from Elsevier.
Moderate Steatosis (Grade 2, scale 0-3)

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013), adapted with permission from Elsevier.
Severe Steatosis (Grade 3, scale 0-3)

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013), adapted with permission from Elsevier.
Steatohepatitis: Essential Features

AASLD and NASH Clinical Research Network

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- Inflammation (lobular)
- Hepatocellular injury
  - Ballooned hepatocytes
- +/- Pericellular fibrosis
Lobular Inflammation in NASH

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Portal Inflammation in NASH

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Ballooned Hepatocyte

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Multiple Ballooned Hepatocytes

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013), adapted with permission from Elsevier.
BH Mimic – Small Droplet Fat

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Steatohepatitis: Essential Features

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- Steatosis (>5%)
- Inflammation (lobular)
- Hepatocellular injury
  - Ballooned hepatocytes
  - +/- Pericellular fibrosis
<table>
<thead>
<tr>
<th>Stage 1A</th>
<th>Pericentral/sinusoidal Fibrosis – Delicate</th>
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<tbody>
<tr>
<td>Stage 1B</td>
<td>Pericentral/sinusoidal Fibrosis – Dense</td>
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<tr>
<td>Stage 1C</td>
<td>Periportal Fibrosis</td>
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<tr>
<td>Stage 2</td>
<td>Pericentral/sinusoidal and Periportal Fibrosis</td>
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<tr>
<td>Stage 3</td>
<td>Bridging Fibrosis</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Cirrhosis</td>
</tr>
</tbody>
</table>

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013), adapted with permission from Elsevier.
Stage 1

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013, adapted with permission from Elsevier.
Stage 2

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013), adapted with permission from Elsevier.
Stage 3

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Stage 3

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Stage 4

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013), adapted with permission from Elsevier.
Fibrosis Pitfall – Tangential

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Fibrosis Pitfall - Subcapsular

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013, adapted with permission from Elsevier.
Fibrosis Pitfall – Overstained

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013), adapted with permission from Elsevier.
Fibrosis Pitfall – Histiocyte Aggregate
Fibrosis Pitfall – Histiocyte Aggregate
Regression
Steatohepatitis: Non-essential Features

- Mallory hyaline in Zone 3
- Mild iron deposits in hepatocytes or sinusoidal cells
- Megamitochondria
- Glycogenated nuclei
- Lipogranulomas
- Acidophil bodies (occasional)
- Centrizonal arteries
Mallory Hyaline

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013), adapted with permission from Elsevier.
Histologic Variation

PATTERN 1: CLASSIC STEATOHEPATITIS

Steatosis with mild inflammation, hepatocellular ballooning, and pericellular fibrosis
Histologic Variation

PATTERN 2: STEATOSIS WITHOUT HEPATOCYTOLOGY INJURY

Steatosis without hepatocyte ballooning or pericellular fibrosis is insufficient for a diagnosis of steatohepatitis and represents NAFL.

Low rate of progression (~5%) to significant fibrosis.
Histologic Variation

PATTERN 3: STEATOSIS WITH SWOLLEN HEPATOCYTES/NON-CLASSIC BALLOONED HEPATOCYTES

Borderline for steatohepatitis; if clinical risk factors are present, it is best to manage the patient as appropriate for steatohepatitis
Histologic Variation

**PATTERN 4: BALLOONED HEPATOCYTES OR PERICELULAR FIBROSIS WITHOUT STEATOSIS**

Uncommon in patients with metabolic risk factors

<table>
<thead>
<tr>
<th>Ballooned Hepatocytes Only</th>
<th>Pericellular Fibrosis Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent cessation of Alcohol</td>
<td>Chronic venous outflow obstruction</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Remote CZ injury</td>
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</tbody>
</table>
Histologic Variation

PATTERN 5: STEATOSIS WITH PERICELLULAR FIBROSIS, BUT NO BALLOONED HEPATOCYTES

Borderline for steatohepatitis in the appropriate clinical context

Other considerations: chronic venous outflow obstruction, drug (e.g. oxaliplatin), remote parenchymal rejection (post-transplant)
Histologic Variation

PATTERN 6: CIRRHOSIS WITH STEATOSIS AND/OR BALLOONED HEPATOCYTES

Cirrhosis with histologic features of NAFLD is best considered NASH cirrhosis. Some cases may show residual pericellular fibrosis.
Original Article

Centrizonal Arteries and Microvessels in Nonalcoholic Steatohepatitis

Ryan M. Gill, MD, PhD,* Patricia Belt, BS,† Laura Wilson, ScM,† Nathan M. Bass, MD, PhD,‡ and Linda D. Ferrell, MD*

### TABLE 1. NASH Fibrosis Stage Versus Prevalence of Centrizonal Arteries (Grade)*

<table>
<thead>
<tr>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1b/1c</td>
<td>17</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stage 2</td>
<td>25</td>
<td>7</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Stage 3</td>
<td>15</td>
<td>8</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Stage 4</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>18</td>
<td>13</td>
<td>9</td>
</tr>
</tbody>
</table>

Artery grades: 0, no central zones with artery; 1, 1 to 2 central zones with artery/biopsy; 2, > 2 and < 50% of central zones with artery; 3, ≥50% of central zones with artery. Definitions of stages: 1b = centrizonal fibrosis only, without the use of trichrome stain (ie, readily discernible on H&E stain), 1c = periportal fibrosis only, 2 = centrizonal and periportal fibrosis, 3 = bridging fibrosis, 4 = cirrhosis.

*P < 0.001 using univariate ordinal logistic regression.
Aggressive non-alcoholic steatohepatitis following rapid weight loss and/or malnutrition

Jia-Huei Tsai¹,², Linda D Ferrell³, Vivian Tan⁴, Matthew M Yeh⁵, Monika Sarkar⁶ and Ryan M Gill³
Aggressive NASH

• NASH presenting as ALF
• We described 6 patients who developed ALF following rapid loss or malnutrition
• 4 patients either died or required urgent liver transplant
• Pathologic findings similar to advanced alcoholic steatohepatitis
Pathologic Features

- Extensive/circumferential centrizonal pericellular fibrosis
- Central scar with perivenular sclerosis/veno-occlusion with superimposed hepatocellular dropout
- Abundant/prominent hepatocellular balloons, and numerous Mallory-Denk bodies
- Centrizonal arteries often prominent
Severe Centrizonal Scarring

Prominent BH and Centrizonal Arteries

Ductular Reaction, Cholestasis, and Central Vein Occlusion

Diagnostic Challenges

1. Alcoholic steatohepatitis
2. Burnt out NASH cirrhosis
3. Drug induced steatohepatitis
4. Hereditary hemochromatosis
5. Metabolic disorders
6. Microvesicular steatosis
7. More than mild portal inflammation
Alcoholic Steatohepatitis

• Alcoholic steatohepatitis can not be definitively distinguished from NASH by histology

<table>
<thead>
<tr>
<th></th>
<th>NASH</th>
<th>ASH</th>
</tr>
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<tbody>
<tr>
<td>Steatosis</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Ballooned hepatocytes</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Lobular inflammation</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Mallory hyaline</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Neutrophil infiltrate</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Cholestasis</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Obliterated CV</td>
<td>+/-</td>
<td>+</td>
</tr>
</tbody>
</table>
Burnt-out NASH Cirrhosis

• Typical steatohepatitis features regress with progression of fibrosis and may be lost with cirrhosis
• Many cases labeled as cryptogenic cirrhosis; since this population has a high incidence of type 2 DM, NASH is considered to be the most likely etiology
• Rule out other etiologies and correlate with NASH risk factors
Drug Induced Steatohepatitis

- Histologic changes identical to NASH have been identified in patients without NASH risk factors exposed to certain drugs.

<table>
<thead>
<tr>
<th>Definite Association</th>
<th>Possible Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>Tamoxifen</td>
</tr>
<tr>
<td>Irinotecan</td>
<td>Steroids</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Estrogen</td>
</tr>
<tr>
<td>Perhexiline Maleate/Diethylaminoethoxyhexesterol</td>
<td>Diethylstilbestrol</td>
</tr>
</tbody>
</table>
Amiodarone Toxicity

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Methotrexate

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Methotrexate with Portal Fibrosis

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Hereditary Hemochromatosis

- A mild to moderate hepatocyte siderosis (generally nonzonal) and/or Kupffer cell siderosis is seen in ~20% of NAFLD patients.
- Serum ferritin is an acute phase reactant that is commonly increased in NAFLD patients.
- Increased iron saturation would more strongly suggest hereditary hemochromatosis.
- C282Y HFE mutation in an established NASH patient may warrant biopsy to evaluate iron overload.
Periportal Siderosis in HH

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Metabolic Disorders

- **Glycogenic hepatopathy**
  - Type 1 DM with poor glycemic control
  - Glycogenosis, minimal fat, and abundant megamitochondria

- **Diabetic hepatosclerosis**
  - Non-zonal perisinusoidal fibrosis and BM deposition in patients with long standing insulin dependent DM, minimal steatosis, no ballooning

- **Wilson disease**
  - Steatosis (non-zonal), glycogenated nuclei, Mallory hyaline, swollen hepatocytes, portal inflammation and fibrosis
Glycogenic Hepatopathy

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Glycogenic Hepatopathy

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Diabetic Hepatosclerosis

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Steatosis and Portal Inflammation in Wilson Disease

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Periportal Fibrosis in Wilson Disease

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Wilson Disease with Swollen Hepatocytes

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Wilson Disease with Pericellular Fibrosis

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Microvesicular Steatosis

• Pure microvesicular steatosis does not occur in NASH and indicates severe mitochondrial injury
• Reye syndrome, acute fatty liver of pregnancy, alcoholic foamy liver degeneration, drug (cocaine, tetracycline, valproic acid, zidovudine), and rare genetic disorders.
• Many NAFLD cases will have a minor component of microvesicular fat
Diffuse Microvesicular Steatosis

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More than Mild Portal Inflammation

• NASH portal inflammation is typically mild
• Prominent portal inflammation raises consideration of other causes (HBV, HCV, AIH, PBC, Wilson disease)
• If other etiologies are excluded, this can be considered NASH with prominent portal inflammation
• May be associated with a higher degree of fibrosis
More than Mild Portal Inflammation

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Pediatric NASH

- NASH cirrhosis seen as young as 8 years of age
- AST/ALT screening has been considered for obese children starting at age 10
- Type 1 pediatric NASH: Identical to adult type NASH
- Type 2 pediatric NASH: Severe panacinar steatosis, no ballooned hepatocytes, early portal based fibrosis (stage 1C)
- Children younger than age 2 with fatty liver should be evaluated for rare genetic disorders
Severe Pan-acinar Steatosis

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013), adapted with permission from Elsevier.
NASH CLINICAL RESEARCH NETWORK (CRN)
NIDDK Workshop on Fatty Liver Disease 1998

• No good estimates of disease prevalence or severity (but suspected that this was a big problem)
• Little information on the natural history
• No non-invasive diagnostic tests
• No standard methods for evaluating liver biopsy
• No approved therapies

Courtesy of Dr. David Kleiner, NIH
NASH Clinical Research Network

- Sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases
- 18 Participating Academic Clinical Centers (8 Adult, 10 Pediatric), 1 Data Coordination Center, and the NIDDK Project Scientists
- Established to focus on the etiology, contributing factors, natural history, complications, and therapy of nonalcoholic steatohepatitis

Courtesy of Dr. David Kleiner, NIH
NASH CRN Studies

- Background development
- RFA writing
  - Jay Hoofnagle, M.D.
  - Patricia Robuck, Ph.D., M.P.H.

Funding, 1st mtg

RFA release

- '00
- '01
- '02
- '03
- '04
- '05
- '06
- '07
- '08
- '09
- '10
- '11
- '12
- '13
- '14

Foundation for trials:
- Pathology standardization → NAFLD Activity Score ("NAS")
- Utility of laboratory ALT reference ranges
- Impact of TZDs on mitochondrial ultrastructure

Primary Goal of the Pathology Committee

Create a scoring system for evaluating liver biopsies that could be used for clinical trials and natural history studies

Courtesy of Dr. David Kleiner, NIH
Design and Validation of a Histological Scoring System for Nonalcoholic Fatty Liver Disease

David E. Kleiner,1 Elizabeth M. Brunt,2 Mark Van Natta,3 Cynthia Behling,4 Melissa J. Contos,5 Oscar W. Cummings,6 Linda D. Ferrell,7 Yao-Chang Liu,8 Michael S. Torbenson,9 Aynur Unalp-Arida,3 Matthew Yeh,10 Arthur J. McCullough,11 and Arun J. Sanyal12 for the Nonalcoholic Steatohepatitis Clinical Research Network13

• H&E and Trichrome only
• 9 pathologists, 2 independent reads
• Scoring system included features for grading/staging plus other findings
• Defined an “Activity Score” for use in clinical trials to objectively measure composite histologic change
• Score based on results of multivariable analysis
• Excluded fibrosis to avoid mixing “stage” with “grade”

NAFLD Activity Score (NAS) = Steatosis (0-3) + Lob. Inf. (0-3) + Ballooning (0-2)

Hepatology 41: 1313; 2005

Courtesy of Dr. David Kleiner, NIH
Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis

Effect of Vitamin E or Metformin for Treatment of Nonalcoholic Fatty Liver Disease in Children and Adolescents
The TONIC Randomized Controlled Trial

Farnesoid X nuclear receptor ligand obeticholic acid for non-cirrhotic, non-alcoholic steatohepatitis (FLINT): a multicentre, randomised, placebo-controlled trial

www.thelancet.com Published online November 7, 2014 http://dx.doi.org/10.1016/S0140-6736(14)61933-4

Courtesy of Dr. David Kleiner, NIH
Ballooning is Associated with Long Term Survival, Whereas Steatosis is Not

Angulo et al., Gastroenterology 149: 389; 2015

Steatosis

P = 0.607

Ballooning

P < 0.001

Courtesy of Dr. David Kleiner, NIH
Problem
Steatosis accounts for more weight in the NAS than Ballooning

Possible Solutions
- Drop Steatosis from the score
- Extend the Ballooning Scale

Courtesy of Dr. David Kleiner, NIH
Pathology committee discussions on better characterization of ballooning

Defined two new concepts for prospective evaluation:

- Classical vs Non-Classical Ballooning
- Severe vs Not Severe Ballooning

New definitions implemented with the first case in DB2

Funding, 1st mtg

RFA release

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<thead>
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<th>Year</th>
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</tbody>
</table>

* Courtesy of Dr. David Kleiner, NIH
Classical vs Non-Classical

- **Classical ballooning**
  - Enlarged (>1.5x normal)
  - Cytoplasmic clearing
  - Cytoplasmic clumping
  - May have Mallory-Denk bodies

- **Non-Classical ballooning**
  - Typically in zone 3, perivenular
  - Smaller
  - Same cytoplasmic alterations
  - Lack Mallory-Denk bodies
Non-Classic Ballooned Hepatocyte

Gill R. M. and Kakar S. Non-alcoholic steatohepatitis, an update on diagnostic challenges, Surgical Pathology Clinics, Volume 6, Issue 2, Pages 227-257, June 2013), adapted with permission from Elsevier.
Classical vs. Non-Classical HB

Substantial agreement (weight kappa 0.76 (95% CI=0.64, 0.88))
Severe Hepatocyte Balloons

- Several foci of classic hepatocyte balloons immediately apparent at low magnification (4x)

Courtesy of Dr. David Kleiner, NIH
Extending the Ballooning Score Beyond 2: A Proposal for a New Balloon Score

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- 1226 biopsies
- Demographic, anthropometric, laboratory data within 6 months of biopsy extracted
## Proposed Modified Hepatocyte Balloon Score

<table>
<thead>
<tr>
<th>Old Ballooning Score</th>
<th>Classical?</th>
<th>Severe?</th>
<th>New Ballooning Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - None</td>
<td>No</td>
<td>No</td>
<td>0</td>
<td>No ballooning</td>
</tr>
<tr>
<td>1 - Few or 2 - Many</td>
<td>No</td>
<td>No</td>
<td>1</td>
<td>Only Non-classical</td>
</tr>
<tr>
<td>1 - Few</td>
<td>Yes</td>
<td>No</td>
<td>2</td>
<td>Few Classical</td>
</tr>
<tr>
<td>2 - Many</td>
<td>Yes</td>
<td>No</td>
<td>3</td>
<td>Many Classical</td>
</tr>
<tr>
<td>2 - Many</td>
<td>Yes</td>
<td>Yes</td>
<td>4</td>
<td>Severe, Many Classical</td>
</tr>
</tbody>
</table>

- Reduces effect of many “non-classical” hepatocyte balloons when no classical ballooning seen
- Gives more weight to ballooning
- Better correlation with diagnosis
Highlights presented at AASLD

1. Diagnosis
2. Fibrosis
3. Age and gender associations
4. Diabetes and metabolic syndrome
5. Liver enzymes
Summary and Conclusions

• We have proposed a new ballooning score based on careful morphological characterization of the range of ballooned hepatocytes
• The new balloon score doubles the dynamic range of the current balloon score
• The score shows excellent correlation with clinical disease features, as well as with patient demographics
Acknowledgments

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