The Diagnosis and Management of NASH

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Hepatology & Gastroenterology
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McGill
Accreditation

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### Financial Interest Disclosure

<table>
<thead>
<tr>
<th>Commercial Interest</th>
<th>Relationship*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astellas</td>
<td>Speaker</td>
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<tr>
<td>BMS</td>
<td>Consultant, speaker</td>
</tr>
<tr>
<td>Gilead</td>
<td>Consultant, speaker</td>
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<td>Janssen</td>
<td>Consultant</td>
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<tr>
<td>Merck</td>
<td>Consultant, speaker, investigator</td>
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<tr>
<td>Novartis</td>
<td>Speaker, investigator</td>
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<tr>
<td>Roche</td>
<td>Consultant, speaker, investigator</td>
</tr>
<tr>
<td>Vertex</td>
<td>Investigator</td>
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</table>

Products made by these companies will not be discussed in this presentation.
<table>
<thead>
<tr>
<th>Role</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical Expert</strong></td>
<td>(as Medical Experts, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional attitudes in their provision of patient-centered care. Medical Expert is the central physician Role in the CanMEDS framework.)</td>
</tr>
<tr>
<td><strong>Communicator</strong></td>
<td>(as Communicators, physicians effectively facilitate the doctor-patient relationship and the dynamic exchanges that occur before, during, and after the medical encounter.)</td>
</tr>
<tr>
<td><strong>Collaborator</strong></td>
<td>(as Collaborators, physicians effectively work within a healthcare team to achieve optimal patient care.)</td>
</tr>
<tr>
<td><strong>Manager</strong></td>
<td>(as Managers, physicians are integral participants in healthcare organizations, organizing sustainable practices, making decisions about allocating resources, and contributing to the effectiveness of the healthcare system.)</td>
</tr>
<tr>
<td><strong>Health Advocate</strong></td>
<td>(as Health Advocates, physicians responsibly use their expertise and influence to advance the health and well-being of individual patients, communities, and populations.)</td>
</tr>
<tr>
<td><strong>Scholar</strong></td>
<td>(as Scholars, physicians demonstrate a lifelong commitment to reflective learning, as well as the creation, dissemination, application and translation of medical knowledge.)</td>
</tr>
<tr>
<td><strong>Professional</strong></td>
<td>(as Professionals, physicians are committed to the health and well-being of individuals and society through ethical practice, profession-led regulation, and high personal standards of behaviour.)</td>
</tr>
</tbody>
</table>
“At the end of this program participants should know”:

- **OBJECTIVES**

  1. the factors playing a role in the pathogenesis of NAFLD
  2. how to diagnose and stage NAFLD
  3. how to provide specific advices regarding diet and exercise
  4. what and when to use supplements and drugs
Non-Alcoholic Fatty Liver Disease (NAFLD)

- Steatosis by imaging or histology in the absence of secondary causes (alcohol, other drugs, etc)
- Histologic spectrum of liver damage
- At the cirrhotic stage often “burnt out” or “cryptogenic”
NASH: CLINICAL IMPACT

- Nonalcoholic Fatty Liver Disease (NAFLD) is the most common liver disease in Western countries

- **NAFLD** vs. **NASH**
  - 25-46% (general) vs 3%
  - 70% (diabetics) vs 22%
  - 90% (obese) vs 14-37%

Ratziu et al, J Hepatol 2010
## RISK FACTORS ASSOCIATED WITH NAFLD

<table>
<thead>
<tr>
<th>Conditions with established association</th>
<th>Conditions with emerging association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>Polycystic ovary syndrome</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>Obstructive sleep apnea</td>
</tr>
<tr>
<td><strong>Metabolic syndrome</strong></td>
<td>Hypopituitarism</td>
</tr>
<tr>
<td></td>
<td>Hypogonadism</td>
</tr>
<tr>
<td></td>
<td>Pancreateo-duodenal resection</td>
</tr>
</tbody>
</table>
Definitions: Clinical Syndrome

- Metabolic syndrome\(^1\)
  - Obesity
  - Diabetes
  - Hypertension
  - Hyperlipidemia

- No alcohol: 20 grams vs 40 grams (20-210)\(^2\)

- Absence of other cause of liver disease

Increasing Rate Of Obesity and Metabolic Syndrome

Signs Of Modern Times

From Pre-historic to the Modern Time
NAFLD is common and commonly asymptomatic

- Dallas heart study (n=2200)
- Liver fat assessed by MR spectroscopy

Liver fat

- normal (< 5.5%)
- > 5.5% (31%)

Prevalence of Fatty liver

45% Hispanics
33% Whites
24% Blacks

79% with steatosis nl enzymes

Met synd > in hispanics than whites
Met Synd also common in blacks

NAFLD is common and commonly asymptomatic

- National Health and Nutrition Examination Survey (NHANES) III
  - Prevalence of elevated liver enzymes = 8%
  - Unexplained in 5.5%
  - Many of these had metabolic syndrome

Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

### Obesity (BMI ≥30 kg/m²)

<table>
<thead>
<tr>
<th>Year</th>
<th>No Data</th>
<th>&lt;14.0%</th>
<th>14.0-17.9%</th>
<th>18.0-21.9%</th>
<th>22.0-25.9%</th>
<th>&gt;26.0%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
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<td>2000</td>
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<tr>
<td>2008</td>
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</table>

### Diabetes

<table>
<thead>
<tr>
<th>Year</th>
<th>No Data</th>
<th>&lt;4.5%</th>
<th>4.5-5.9%</th>
<th>6.0-7.4%</th>
<th>7.5-8.9%</th>
<th>≥9.0%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
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<td>2008</td>
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</tr>
</tbody>
</table>

Obesity map by total population

Figure 1

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>15-19%</td>
</tr>
<tr>
<td>2003</td>
<td>20-24%</td>
</tr>
<tr>
<td>2005</td>
<td>25-29%</td>
</tr>
<tr>
<td>2007</td>
<td>30-34%</td>
</tr>
<tr>
<td>2008</td>
<td>≥35%</td>
</tr>
<tr>
<td>2009</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td></td>
</tr>
</tbody>
</table>
Obesity map by female population

Figure 2

Gotay, C. Can J Public Health 2013
Obesity map by male population

Figure 3

- 15-19%
- 20-24%
- 25-29%
- 30-34%
- ≥35%

2000

2003

2005

2007

2008

2009

2010

2011

Gotay, C. Can J Public Health 2013
# Associated Conditions for NAFLD

## Nutritional/Metabolic
- obesity
- diabetes
- hyperlipidemia
- accelerated weight loss
- acute starvation
- TPN

## Drugs
- amiodarone
- synthetic estrogens
- tamoxifen
- nifedipine
- steroids

## Gastrointestinal
- JI bypass
- extensive SB resection
- gastroplexy
- biliopancreatic division

## Miscellaneous
- Limb lipodystrophy
- Weber-Christian disease
- Abetalipoproteinemia
- Idiopathic
- Small bowel diverticulosis
NAFLD in High-Risk Populations

Bariatric surgery candidates

- Systematic reviews
- High variability in NASH rates
  NAFL: 91%
  NASH: 37% (24-98%)
- Mild fibrosis: 40%
- Advanced fibrosis: 10% (cirrhosis 1.4%)
- Main association for advanced fibrosis: diabetes

Machado et al. J Hepatol 2006;45(4):600-606
Vernon et al. Alim Pharm Ther 2011; 34:274-85
NAFLD in High-Risk Populations Type 2 Diabetes Mellitus

- Ambulatory (n=180):
  - prevalence of steatosis by US was 69%
    [Trig > 2.8 mmol/L, ALT > 39, Waist > 102 cm/88 cm]
- NASH unusually common (n=204,148)
  - NAFL, no NASH: 12 - 28%
  - NASH: 62-87%
- Fibrosis or cirrhosis documented in 20%
- Severity of liver disease does not parallel DM control or other complications of diabetes

Leite et al. Liver Int 2009:29-113-9
Prashanth et al. J Assoc Phys India 2009;57:205-10
NAFLD kills

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adams 2005</td>
<td>13.5%</td>
<td>1.34 [1.01, 1.79]</td>
</tr>
<tr>
<td>Ekstedt 2006</td>
<td>11.7%</td>
<td>1.46 [0.96, 2.21]</td>
</tr>
<tr>
<td>Haring 2009 (females)</td>
<td>8.8%</td>
<td>1.62 [0.85, 3.07]</td>
</tr>
<tr>
<td>Haring 2009 (males)</td>
<td>11.6%</td>
<td>1.57 [1.03, 2.41]</td>
</tr>
<tr>
<td>Jepsen 2003</td>
<td>15.2%</td>
<td>2.60 [2.35, 2.87]</td>
</tr>
<tr>
<td>Matteoni 1999</td>
<td>12.6%</td>
<td>1.16 [0.81, 1.65]</td>
</tr>
<tr>
<td>Ong 2008</td>
<td>14.1%</td>
<td>1.37 [1.09, 1.73]</td>
</tr>
<tr>
<td>Soderberg 2009</td>
<td>12.4%</td>
<td>1.69 [1.17, 2.44]</td>
</tr>
</tbody>
</table>

**Total (95% CI)**

**100.0%**

**1.57 [1.18, 2.10]**

**Total events**

Heterogeneity: \( \tau^2 = 0.14; \) \( \chi^2 = 57.31, \) df = 7 (\( P < 0.00001 \)); \( I^2 = 88\% \)

Test for overall effect: \( Z = 3.05 (P = 0.002) \)

Forest plot of comparison: outcome: overall mortality rate.
Major risk factors for advanced liver disease

- Independent Risk Factors for fibrosis
  - Older age (>45)
  - Obesity (BMI > 30)
  - Long-standing diabetes (> 15 yrs)
  - Triglycerides > 5.65 (2.8?) mmol/L
  - AST > ALT
  - ALT > 2 x ULN and/or AST > normal

2. P Sorrentino et al. J Hepatol 2004;41:751
Major Causes Of Death Are Not Liver

- **Cause of Death:**
  - Malignancy: 28%
  - Cardiovascular: 25%
  - Liver: 13%

- For 45 – 54 yr old group CV causes most significant
  - Standardized mortality ratio all causes: 4.4 (1.2 - 13.2)
  - SMR for CV disease: 8.15 (2 – 33.2)
NAFLD is also a risk factor for Diabetes and other CV disease

- Incident type 2 Diabetes based on:
  - ALT: 1.95 (1.6 – 2.3)
  - GGT: 2.71 (2.3 – 3.2)
  - US: 3.51 (2.3 – 5.4)

- Incident Carotid plaques:
  - Based on 7 studies: 3.13 (1.8 – 5.6)
Is NAFLD progressive?
PATHOGENESIS: “TWO HITS” OR “DISTINCT HITS”?

Traditional view of NAFLD pathogenesis

Simple steatosis
- First hit
  - Insulin resistance
  - Deposition of lipids in the hepatic parenchyma
- Second hit
  - Oxidative stress
  - Adipokines

NASH
- Increased susceptibility to multiple injuries
  - Progressive fibrosis
  - Liver failure, hepatocellular carcinoma

"Distinct-hit" hypothesis of NAFLD
Simple steatosis and NASH are two distinct entities with different pathogenetic pathways

- Insulin resistance
- Steatosis
- NASH
- Progression?

Ylmaz et al, APT 2012
Environment and genetics play a role in the pathogenesis

- Diet: high saturated fat, soft drinks and meat as well as low in anti-oxidants and omega-3 => NASH
- Polymorphisms in genes encoding microsomal triglyceride transfer protein, phosphatidylethanolamine transferase, superoxide dismutase 2, TNF, TGF and angiotensinogen all implicated
Pathogenesis 1: Is Fatty Liver Hereditary?

- In part, yes, but the heritability is low to moderate (0.27)
- There are clear ethnic differences
  - Hispanic >> Whites
- Familial clustering is found
- Most important genetic contributor thus far is the PNPLA3 gene (encodes adiponutrin)

Hormones vs. Cytokines: Adiponectin and TNF

- **Adiponectin (decr.)**
  - Anti-inflammatory
  - Decreases fatty acid uptake
  - Stimulates fatty acid oxidation / lipid export
  - Enhances insulin sensitivity

- **TNF alpha (incr.)**
  - Pro-inflammatory
  - Pro-apoptotic
  - Recruits WBCs
  - Promotes insulin resistance
Overview of 2 hit hypothesis of NASH

- Insulin Resistance
- Increased lipolysis
- Increased delivery FFA to liver
- Hepatic lipogenesis
- Oxidative stress
- Steatosis
- Steatohepatitis
- Fibrosis

Factors:
- Adiponectin
- TNF α
- Leptin / Angiotensin
- Noradrenaline
- PPAR α / γ
Be careful when working up “a diagnosis of exclusion”

- Elevated serum autoantibodies are common in patients with NAFLD and are generally considered to be an epiphenomenon.
  
  Vuppalanchi. Hepatology 2009

- NASH Clinical Research Network
  - +ANA > 1:160 or SMA > 1:40 in 21% of NAFLD patients without more advanced histologic features

  Vuppalanchi R. Hepatol Int. 2011
  Chalasani Am J Gastro 2012 Guidelines NAFLD
Which is the best test?

- Liver enzymes: can be normal in NAFLD and NASH (sensitivity may be poor)
- Liver US is potentially more sensitive but $$ and not easily done
- Histology may be best
- Look for NASH-related fibrosis when elevated liver enzymes, presence of insulin resistance (IR) as well as histological ballooning of hepatocytes

Chalasani Am J Gastro 2012 Guidelines NAFLD
Lee. J Hepatol 2007
Williams CD. Gastroenterology 2011
Browning JD. Hepatology 2004
Baranova A. BMC Gastroenterol 2011
Younossi Aliment Pharmacol Ther. 2014
EVALUATION OF FIBROSIS: HOW?

- Liver biopsy (gold standard)
  - Advantages: direct information on fibrosis, inflammation, steatosis, comorbidities
  - Limits: semiquantitative, invasive, costly, prone to sampling errors

- Blood tests (biomarkers)
- Fibroscan (transient elastography)
SERUM NON-INVASIVE MARKERS for LIVER FIBROSIS

DIRECT MARKERS
Matrix Components and Enzymes regulating Fibrogenesis / Fibrolysis

INDIRECT MARKERS
Markers of Liver Inflammation / Function

Combination of Direct / Indirect Tests

Procollagen III, Type IV collagen, Hyaluronic acid, YKL-40, Metalloproteinases and their Inhibitors

AST, ALT, γGT, Platelets, Bilirubin, Albumin, Cholesterol, ApoA1, a2-Macroglobulin, Haptoglobin
# Indirect Biomarkers

<table>
<thead>
<tr>
<th></th>
<th>AUC for $\geq$F2</th>
<th>AUC for F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>APRI</td>
<td>0.73-0.87</td>
<td>0.84</td>
</tr>
<tr>
<td>Forns’ index</td>
<td>0.60-0.86</td>
<td>NA</td>
</tr>
<tr>
<td>Fib-4</td>
<td>0.70-0.85</td>
<td>NA</td>
</tr>
<tr>
<td>ALT/AST</td>
<td>NA</td>
<td>0.74</td>
</tr>
<tr>
<td>BARD score</td>
<td>0.70-0.81</td>
<td>NA</td>
</tr>
</tbody>
</table>

APRI = AST, platelets
Forns’ index = $\gamma$GT, cholesterol, platelets, age
Fib-4 = platelets, AST, ALT, age
BARD = BMI, AST/ALT and presence of diabetes

Wai et al, Hepatology 2003; Forns et al, Hepatology 2002; Sebastiani et al, CCLM 2011; Sebastiani et al, APT 2011
AST/ALT Ratio
53% sensitive, 100% specific

- >1 high = likelihood of cirrhosis
- Highly predictive of cirrhosis if ratio > 1, 100% specificity and positive predictive value in distinguishing cirrhotic from noncirrhotic patients, with a 53.2% sensitivity and 80.7% negative predictive value in HCV patients

Baranova BMC Gastroenterol. 2011 Aug 17;11:91
APRI (AST/Platelet ratio) 89% sensitive, 75% specific

- Most validated in viral hepatitis vs. Other diseases

\[
\frac{\text{AST}_{\text{patient}}}{\text{AST}_{\text{ULN lab}}} \times 100
\]

Platelet count of patient

- ≤ 0.5 is normal, no fibrosis
- ≥ 1.5 indicates likely cirrhosis
- 0.5 – 1.5 is the grey zone

SIMPLE BIOMARKERS BASED ON CUT-OFF VALUES: APRI

\[ \text{APRI} = \frac{[\text{AST} / \text{ULN} \times 100]}{\text{Platelet} \times 10^9 / \text{L}} \]

Absence of significant fibrosis

50% of Pts

Presence of significant fibrosis

Wai et al, Hepatology 2003
NAFLD Fibrosis Score

go to gihep.com – formula containing Age, AST, ALT, Platelet Count, BMI, Albumin, Impaired Fasting Glucose/Diabetes

If the NAFLD Score is:
- $<-1.455 = F_0-F_2$ (NPV 88-93% and 88% PPV)
- $>0.675 = F_3-F_4$ (PPV 82-90%)
- $-1.455 - 0.675 =$ indeterminate score

- a liver biopsy would have been avoided in 75% of the 733 patients, with 90% accuracy.

Fib-4

Score = \frac{\text{age} \times \text{AST (IU/l)}}{\text{platelets (x10^9/L)}} \times \sqrt{\text{ALT (IU/l)}}

- <1.45: \text{NPV F3-F4 (94.7%)}
- 3.25: \text{PPV F3-F4 (82%)}
- >10: \text{PPV F4 excellent}

Fib-4
70% sensitive, 74% specific

For HCV with or without HIV:
- Fib4 score < 1.45 = F0-F1
- Fib4 score > 3.25 = F3-F4

For NASH:
- Fib4 score < 1.30 = F0-F1
- Fib4 score > 2.67 = F3-F4

Baranova BMC Gastroenterol. 2011 Aug 17;11:91
Sterling RK et al. HEPATOLOGY 2006; 43: 1317-1325.
## Direct Biomarkers and Combination Panels

<table>
<thead>
<tr>
<th>Method</th>
<th>Parameters</th>
<th>AUC for ≥F2</th>
<th>AUC for F4</th>
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</thead>
<tbody>
<tr>
<td>Fibrotest®</td>
<td>γGT, bilirubin, haptoglobin, ApoA1, α2M</td>
<td>0.75-0.86</td>
<td>0.75</td>
</tr>
<tr>
<td>Hyaluronan</td>
<td>Hyaluronan, TIMP1, α2M</td>
<td>0.73-0.97</td>
<td>0.92</td>
</tr>
<tr>
<td>ELF®</td>
<td>Hyaluronan, PIIINP, TIMP1</td>
<td>0.82-0.98</td>
<td>0.90-0.99</td>
</tr>
<tr>
<td>Fibrometer®</td>
<td>Platelets, PT, AST, α2M, hyaluronan, BUN</td>
<td>0.94</td>
<td>0.92</td>
</tr>
</tbody>
</table>

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FibroScan

Painless

Rapid (5 min)

Bedside/Outpatient

Immediate results
(3 - 75 kPa)
Successful Fibroscan

Stiffness (kPa)
Median value of 10 shots
3.9 Kilo Pascals

IQR * (kPa)
Interval around median
Contains 50% of valid shots
\leq 25\% of median value

At least 10 shots
Success Rate: \geq 60\%
Different cut-off values exist for different diseases.

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>F2</th>
<th>AUROC</th>
<th>F3</th>
<th>AUROC</th>
<th>F=4</th>
<th>AUROC</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV(^7)</td>
<td>7.2</td>
<td>0.81</td>
<td>8.1</td>
<td>0.93</td>
<td>11.0</td>
<td>0.93</td>
<td>6</td>
</tr>
<tr>
<td>HCV(^30)</td>
<td>7.1</td>
<td>0.83</td>
<td>9.5</td>
<td>0.90</td>
<td>12.5</td>
<td>0.95</td>
<td></td>
</tr>
<tr>
<td>HCV(^6)</td>
<td>8.8</td>
<td>0.79</td>
<td>9.6</td>
<td>0.91</td>
<td>14.6</td>
<td>0.97</td>
<td>5</td>
</tr>
<tr>
<td>HCV/HIV(^8)</td>
<td>4.5</td>
<td>0.72</td>
<td>-</td>
<td>-</td>
<td>11.8</td>
<td>0.97</td>
<td>7</td>
</tr>
<tr>
<td>PBC or PSC(^10)</td>
<td>7.3</td>
<td>0.92</td>
<td>9.8</td>
<td>0.95</td>
<td>17.3</td>
<td>0.96</td>
<td>9</td>
</tr>
<tr>
<td>NAFLD(^9)</td>
<td>6.6</td>
<td>0.87</td>
<td>9.8</td>
<td>0.90</td>
<td>17.5</td>
<td>0.99</td>
<td>8</td>
</tr>
</tbody>
</table>
Using a cut-off range instead of a single value for each disease is simpler.
Fibroscan algorithm

Perform LSM

- ≤ 6 kPa: No significant fibrosis → F0
- Intermediate values: Grey area → F2
- ≥ 12 kPa: Advanced fibrosis → F3 or F4

- F0: No biopsy
- F1: No biopsy
- F2: Biopsy if results influence management
- F3 and F4: No biopsy

FIBROSCAN FAILURE
n=2114

Failure : 4.5 %
BMI > 28

Wong et al: 25.5% if BMI > 30,
2.6% if BMI < 30

Reliable results with the XL probe were obtained in 61% of patients in whom the M probe was unreliable.

Composite blood tests may correlate with NASH and degree of fibrosis

- Steatotest (AUROC = 0.8): total bilirubin, GGT, α2-macroglobulin, apolipoprotein A1, haptoglobin, AST, serum glucose, triglycerides and cholesterol

- NASH-Test (AUROC = 0.8): total bilirubin, GGT, α2-macroglobulin, apolipoprotein A1, haptoglobin, weight, height, AST, serum glucose, triglycerides, cholesterol

- Fibrotest (AUROC = 0.86-0.9): total bilirubin, GGT, α2-macroglobulin, apolipoprotein A1, haptoglobin

Poynard et al. BMC Gastroenterology 2006;6:6 and 34
Poynard et al. Comp Hepatol 2005;4:10
Circulating levels of cytokeratin-18 (CK18) fragments may be a useful biomarker for NAFLD

- Increased in NASH vs. simple steatosis or normal biopsies ($P < 0.001$)
- OR = 1.95 for NASH for every 50 U/l increase
- Reproduced in other studies
- Meta-analysis: estimated sensitivity of 78%, specificity of 87%, and an AUROC of 0.82 (95% CI: 0.78 – 0.88) for steatohepatitis in patients with NAFLD
How do you assess Steatosis?

- Normal liver enzymes do not exclude NASH
- No imaging modality distinguishes NAFLD from NASH or fibrosis

<table>
<thead>
<tr>
<th>Modality</th>
<th>AUROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound</td>
<td>0.87</td>
</tr>
<tr>
<td>Xenon133</td>
<td>0.87</td>
</tr>
<tr>
<td>CT</td>
<td>0.91</td>
</tr>
<tr>
<td>MRI-PDFF*</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Protein Density Fat Fraction

Mathiesen et al. Dig Liver dis. 2002;516-22
Albusafi et al. Can J Gastroenterol 2012;155-9
Noureddin AASLD 2013, Abstract
Xenon-133 scanning may be more accurate than Ultrasound

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>93.75%</td>
<td>100%</td>
<td>100%</td>
<td>50%</td>
</tr>
</tbody>
</table>

Al-busafi et al. Gastroenterology 2008;783
Controlled Attenuation Parameter - CAP

• A module developed to quantify hepatic steatosis with Fibroscan machine
• Result is expressed in decibel/m (dB/m) and interpreted according to cut-off values

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Sasso et al, 2010
Fig. 5. ROC curves and AUC for the detection of steatosis grades $S_G \geq S_1$, $S_G \geq S_2$ and $S_G = 3$. CAP has high accuracy for fat.
When should I do a liver biopsy?

- **AASLD 2012**
  - Consider in NAFLD patients at increased risk to have steatohepatitis and advanced fibrosis: presence of metabolic syndrome and high NAFLD Fibrosis Score.
  - Suspected NAFLD with competing aetiologies for steatosis.
When Should I do a Non-invasive assessment of fibrosis?

AASLD 2012

- NAFLD Fibrosis Score is useful for identifying NAFLD patients with higher likelihood of having bridging fibrosis and/or cirrhosis.
- Although CK18 is a promising biomarker for identifying steatohepatitis, it is premature to recommend in routine clinical practice.
Should we be screening everybody? (No)

EASL 2009 and AASLD 2012

→ Screening for NAFLD in adults attending primary care clinics or high-risk groups attending diabetes or obesity clinics is not advised at this time due to:
  - uncertainties surrounding diagnostic tests and treatment options
  - lack of knowledge related to the long-term benefits and cost-effectiveness of screening.
Liver biopsy remains an important tool to diagnose NASH and to stage liver fibrosis.

The presence of metabolic syndrome is the strongest predictor of NASH.

NAFLD fibrosis score or combination of Fibroscan and a serum test (Fibrotest) can be used to select patients at high risk of advanced fibrosis.

Reliable non-invasive methods to diagnose NASH are highly warranted.

Screening of general population not recommended; but at risk groups?
Any Questions?

Thank you for your attention

Thank you to Dr. Peter Ghali and Dr. Giada Sebastiani for slides and their expertise
Evaluation and Certificate of Attendance

Please visit the CAG website at http://www.cag-acg.org/ to complete the session evaluation and to print your certificate of attendance.

Thank you!