Initial Evaluation and Follow Up for Patients with Hepatitis C

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Conflicts of Interest

• None
Objectives

• Discuss the initial laboratory testing for patients with Hepatitis C

• Describe the importance of and options for liver fibrosis staging

• Discuss monitoring during and post treatment
Hepatitis C Screening
Hepatitis C Screening

• ~ 3.5 million HCV-infected persons in the United States
  – 2.7 million in the general population
  – 800,000 incarcerated, institutionalized, or homeless persons
  – 50% of all infected people are unaware
Recommendations for One-time HCV Testing

• For all persons born between 1945 and 1965, without prior ascertainment of risk
  
  – 75% of people with hepatitis C born during these years

  – Increasing HCV associated morbidity and mortality

  – Testing based solely on elevated ALT is estimated to miss 50% of chronic infections

MMWR 2012; 61; 1-18
Recommendations for One-time HCV Testing

- Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed if present
  - Risk Behaviors
    - Injection Drug use
    - Intranasal illicit drug use
  - Risk exposures
    - Long term hemodialysis (ever)
    - Percutaneous/parenteral exposures to HCV infected blood
    - Children born to HCV infected women
    - Prior recipients of transfusions or organ transplants, including persons who
      - Received transfusion of blood products or underwent an organ transplant before July 1992
      - Received clotting factor concentrates produced before 1987
      - Were notified that they received blood from a donor who later tested positive for HCV
  - Incarceration
  - Other Considerations
    - HIV
    - Sexually active with persons about to start pre-exposure prophylaxis for HIV
    - Unexplained chronic liver disease and/or chronic hepatitis including elevated alanine aminotransferase levels
    - Solid organ donors
Recommendations for HCV Testing
Those with Ongoing Risk Factors

• Annual testing for...
  – Persons who inject drugs
  – HIV positive men who have unprotected sex with men

• Periodic testing for...
  – Other persons with ongoing risk factors for exposure to HCV
Hepatitis C Testing

- HCV Antibody
  - Nonreactive
    - No HCV Antibody Detected
      - Stop
  - Reactive
    - HCV RNA
      - Detected
        - Current HCV Infection
          - Link to Care
      - Not Detected
        - No Current HCV Infection
          - Additional Testing as Appropriate

www.hcvguidelines.org
Hepatitis C Testing

What about universal screening?
HCV Screening – UK HealthCare Emergency Department

- Opt out screening for all adult patients coming through the emergency department
- Project funded by Gilead FOCUS
  – PI James Moore, MD
HCV Screening – UK HealthCare
Emergency Department

<table>
<thead>
<tr>
<th>Days Reported</th>
<th>July 2018</th>
<th>August 2018</th>
<th>September 2018</th>
<th>October 2018</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16</td>
<td>31</td>
<td>30</td>
<td>7</td>
<td>84</td>
</tr>
<tr>
<td>Unique Patients Screened</td>
<td>2,012</td>
<td>3,893</td>
<td>3,814</td>
<td>888</td>
<td>9,708</td>
</tr>
<tr>
<td>Unique Continued Patients</td>
<td>1,242</td>
<td>2,582</td>
<td>2,513</td>
<td>575</td>
<td>6,516</td>
</tr>
<tr>
<td>Continue Rate</td>
<td>59.4%</td>
<td>62.9%</td>
<td>62.4%</td>
<td>63.5%</td>
<td>62.1%</td>
</tr>
<tr>
<td>HCV Ab Results Received</td>
<td>883</td>
<td>1,823</td>
<td>1,767</td>
<td>381</td>
<td>4,854</td>
</tr>
<tr>
<td>HCV Ab invalid/indeterminate/no result</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>HCV Ab+</td>
<td>101</td>
<td>203</td>
<td>217</td>
<td>44</td>
<td>565</td>
</tr>
<tr>
<td>HCV Ab+ Rate</td>
<td>11.5%</td>
<td>11.2%</td>
<td>12.3%</td>
<td>11.6%</td>
<td>11.7%</td>
</tr>
<tr>
<td>RNA Results Received</td>
<td>96</td>
<td>195</td>
<td>197</td>
<td>38</td>
<td>526</td>
</tr>
<tr>
<td>HCV RNA invalid/indeterminate/no result</td>
<td>23</td>
<td>28</td>
<td>22</td>
<td>2</td>
<td>75</td>
</tr>
<tr>
<td>HCV RNA+</td>
<td>51</td>
<td>107</td>
<td>105</td>
<td>19</td>
<td>282</td>
</tr>
<tr>
<td>HCV RNA+ Rate</td>
<td>53.1%</td>
<td>54.9%</td>
<td>53.3%</td>
<td>50.0%</td>
<td>53.6%</td>
</tr>
</tbody>
</table>

Screening

- Opt Out 31.6%
- Unable to Answer 6.1%
- Continue 62.1%

HCV Ab+

- N/A < 18
- 11.7%
- 88.3%

HCV RNA+

- 46.4%
- 53.6%

Preliminary Data
HCV Screening – UK HealthCare Emergency Department

Patient Age Distribution

Preliminary Data
HCV Screening – UK HealthCare Emergency Department

• ½ of patients are lost to follow up from diagnosis to initial visit
• Majority of HCV positive patients are outside of CDC recommended age cohort testing or targeted screening
• Overall HCV ab+ prevalence – 12%
  – Age 25-64 prevalence – 19%
HCV Screening – UK HealthCare
Emergency Department

The Future...

• Real time HCV RNA testing
• Real time initiation of treatment
• Paired with medication assisted therapy
HCV Linkage to Care

• HCV screening will have minimal impact without improvements in linkage to care

• Patient related barriers
  – Lack of acceptance of treatment
  – Lack of access to treatment

• Clinician related barriers
  – Lack of expertise
  – Resistance to treating persons using illicit drugs
  – Concern about the cost of HCV treatment
HCV Linkage to Care

• Strategies
  – HIV care models
    • Use of case manager and patient navigators
  – Collaborate with specialists (telemedicine and Project ECHO)
  – Co-localization (integrated care)
Initial Assessment
History and Physical

• When and how diagnosed
• Risk factors
  – Injection drug use
  – Nasal drug use
  – Tattoos
  – Blood transfusions
  – Tattoos and piercings
  – Sexual exposures
  – Family exposures
• Prior work up
• Prior treatment
• Comorbidities
  – EtOH use, hepatotoxic drugs
  – Psychiatric
• Family hx of liver disease
• Current Medications
Initial Labs

- CBC
- INR
- Hepatic Function Panel
- Calculated GFR
- HCV genotype with subtype
- Quantitative HCV RNA
- HIV
- Total anti-HAV
- HBsAg / Anti-Hbs /Anti-HBc
Optional Screening Considerations

• Alpha-1 antitrypsin deficiency
  – Alpha-1 antitrypsin level
  – Alpha-1 antitrypsin phenotype
• Wilson’s Disease
  – Ceruloplasmin
  – Urinary copper
• Autoimmune liver disease
  – ANA, anti-smooth muscle ab, antimitochondrial ab
• Genetic hemochromatosis
  – Ferritin, iron saturation
Transmission Reduction Counseling

Persons with Hepatitis C should...

• Avoid sharing razors/toothbrushes

• Be counseled to stop illicit drugs and enter substance abuse treatment

• Be advised not to donate blood and to discuss HCV status prior to donation of body organs, other tissue, or semen

• Be encouraged to use barrier precautions to prevent sexual transmission if they have HIV, multiple sexual partners, or sexually transmitted infections

• Clean and disinfect visible blood using a 1:10 household bleach dilution
Natural History of Hepatitis C

Ray, S et al. Ch 154 *Hepatitis C. Principles and Practice of Infectious Disease. 7th Ed.*
Pre-Treatment Assessment

• Other recommended assessments
  – Hepatic Fibrosis Staging
    • Liver biopsy, imaging, and/or noninvasive markers
  – Potential drug-drug interactions
    • Never too early to consider this
Hepatic Fibrosis Staging
Non-Invasive Fibrosis Staging

**Blood Test**
- FibroSure / FibroTest
- AST to Platelet Ratio (APRI)
- FIB-4

**Imaging**
- Transient Elastography
- MRI elastography
- MR Spectroscopy
- Diffuse weighted MRI
Non-Invasive Fibrosis Staging

AST to Platelet Ratio Index (APRI) Calculator

This is an AST to Platelet Ratio Index (APRI) calculator tool. Enter the required values to calculate the APRI value. The APRI Score will appear in the oval on the far right (highlighted in yellow). Most experts recommend using 40 IU/L as the value for the AST upper limit of normal when calculating an APRI value.

\[
\text{APRI} = \frac{\text{AST Level (IU/L)}}{\text{AST (Upper Limit of Normal) (IU/L)}} \times 100
\]

➤ 1 = sensitivity of 76% and specificity of 72% for predicting cirrhosis

➤ 0.7 = sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis

www.hepatitisc.uw.edu
Non-Invasive Fibrosis Staging

Fibrosis-4 (FIB-4) Calculator

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

\[
\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)} \times \sqrt{\text{Platelet Count (10^9/L)} \times \text{ALT (U/L)}}}{\text{Platelet Count (10^9/L)} \times \text{ALT (U/L)}}
\]

< 1.45 = negative predictive value of 90% for advanced fibrosis

> 3.25 = 97% specificity and positive predictive value of 65% for advanced fibrosis
Hepatic Fibrosis Staging

Table 1. Comparison of FIB-4 Index and Liver Biopsy Results

<table>
<thead>
<tr>
<th>FIB4 Index</th>
<th>F0-F1-F2</th>
<th>F3-F4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.45</td>
<td>94.7% (n = 521)</td>
<td>5.3% (n = 29)</td>
<td>550</td>
</tr>
<tr>
<td>1.45-3.25</td>
<td>73.0% (n = 168)</td>
<td>27.0% (n = 62)</td>
<td>230</td>
</tr>
<tr>
<td>&gt;3.25</td>
<td>17.9% (n = 12)</td>
<td>82.1% (n = 55)</td>
<td>67</td>
</tr>
<tr>
<td>Total</td>
<td>82.8% (n = 701)</td>
<td>17.2% (n = 146)</td>
<td>847</td>
</tr>
</tbody>
</table>

Hepatology, Vol. 46, No. 1, 2007
## Hepatic Fibrosis Staging

**Table 2. Comparison of FIB-4 Index and FibroTest Results**

<table>
<thead>
<tr>
<th>FIB4 Index</th>
<th>F0-F1-F2</th>
<th>F3-F4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.45</td>
<td>92.1% (n = 409)</td>
<td>7.9% (n = 35)</td>
<td>444</td>
</tr>
<tr>
<td>1.45-3.25</td>
<td>62.2% (n = 178)</td>
<td>37.8% (n = 108)</td>
<td>286</td>
</tr>
<tr>
<td>&gt;3.25</td>
<td>24.0% (n = 12)</td>
<td>76.0% (n = 38)</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>76.8% (n = 599)</td>
<td>23.2% (n = 181)</td>
<td>780</td>
</tr>
</tbody>
</table>

Hepatology, Vol. 46, No. 1, 2007
Hepatic Fibrosis Staging

Elastography: Fibroscan

- Absent or mild fibrosis (Metavir F0-F1)
- Significant fibrosis (F2)
- Severe fibrosis (F3)
- Cirrhosis (F4)

Affected by weight, access of probe (2 cm), steatosis
Transient Elastography

Sensitivity 84%

Specificity 90%

Monitoring
Monitoring During Therapy

• Clinic visits or telephone contact as indicated to ensure
  – Medication adherence
  – Monitoring for adverse events
  – Assess for potential drug-drug interactions

• At Treatment Week 4
  – Creatinine level, calculated GFR, and a hepatic function panel
  – Quantitative HCV viral load
Monitoring During Therapy

• At End of Treatment (EOT)
  – Consider quantitative HCV viral load testing

• At 12 weeks post treatment
  – Quantitative HCV viral load testing

• At 24 weeks post treatment
  – Consider quantitative HCV viral load testing
Monitoring During Therapy

• Hepatitis B Surface Ag positive with HBV DNA level that does not meet AASLD criteria for treatment
  – Initiate prophylactic antiviral therapy until 12 weeks after completion of therapy

OR

– Monitor HBV DNA levels during and immediately after therapy
  • Start tx for HBV if DNA rises to >10 fold above baseline or > 1000 IU/mL if previously undetectable or unquantifiable
Monitoring During Therapy

- Discontinuation of Treatment Because of Lack of Efficacy
  - If HCV RNA detectable at week 4:
    - Repeat after 2 additional weeks
      - If HCV viral load has increased by > 10 fold, discontinue therapy
      - If lower but still positive, no recommendation to stop or extend is provided by the guidelines
Monitoring After Therapy

• Post treatment monitoring for patients in whom treatment failed to achieve SVR
  – Evaluate and consider for retreatment
  – Assess disease progression every 6 to 12 months with hepatic function panel, CBC, and INR
  – Screen for hepatocellular carcinoma and esophageal varices as indicated
Monitoring After Therapy

• Post treatment monitoring for patients who achieved a Sustained Virologic Response (SVR)
  – For patients without advanced fibrosis (F0-2), follow up is same as if they were never infected
  – Assess for recurrence if ongoing risk
  – For patients with advanced fibrosis (F3-4), assess for HCC with ultrasounds every 6 months
  – Baseline assessment for esophageal varices if cirrhosis is present
Summary

• Current recommendations include screening patients at risk for HCV based on risk factors and age
  – Consider additional screening if local rates of HCV infection are high
• Linkage to care is critical
• All patients need baseline hepatic fibrosis assessment
• Monitoring during therapy can vary but all patients should at least get labs at 4 weeks of treatment and at 12 weeks post treatment
• Hepatocellular carcinoma risk continues for patients with cirrhosis even after Sustained Virologic Response has been achieved
  – Screen with ultrasounds every 6 months