ACG Practice Management Toolbox

Fat(ty Liver) is our Future: Setting Up a Disease Management Program in Your Practice

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INTRODUCTION

High quality disease management programs are an excellent way for medical practices to distinguish themselves within their respective markets. Common examples of such programs for gastroenterologists include esophageal disease, inflammatory bowel disease, and hepatitis. Fatty liver disease may also represent a very promising opportunity.

Some reasons why you should consider developing a fatty liver program in your practice:

- Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver condition in the United States and will soon replace hepatitis C as the #1 reason for liver transplantation.
- NAFLD is present in over 50% of adults with type II diabetes mellitus or the metabolic syndrome.
- The management and evaluation of these patients is rapidly evolving:
  - Multiple guidelines and/or guidance statements regarding the management of this condition have been released over the past 4 years.
  - Several drugs to treat advanced NASH are in Phase III trials in the therapeutic pipeline.
- This is a slowly evolving disease that requires
  - Disease detection
  - Risk stratification
  - Therapeutic intervention in high risk groups.

OVERVIEW

NAFLD is thought to be present in about one third of the US population. While most affected individuals have simple steatosis, which is not thought to progress to cirrhosis, a substantial portion (3-5%) have non-alcoholic steatohepatitis (NASH). This condition may progress to cirrhosis and even hepatocellular carcinoma in a small percentage of patients. As in most chronic liver conditions the rate of progression is rather prolonged, causing disease to be clinically apparent only after it is well advanced. Fortunately, this long phase of progression provides us with an opportunity for disease assessment and risk-reduction prior to development of end-stage liver disease.

IDENTIFYING CASES IN YOUR PRACTICE:

Identifying the patients with fatty liver requires examining multiple sources. With approximately 30% of Americans classified as obese, abnormal transaminases are often identified in these individuals on routine laboratory tests for employment physicals or annual primary care visits. Fatty liver may be found incidentally on an abdominal ultrasound, or cross-sectional imaging performed for other reasons. Thus, primary care, endocrinology, cardiology, and orthopedics often refer patients to gastroenterologists for unexplained elevations in transaminases. Patients with no other definite cause...
for abnormal transaminases often have occult fatty liver disease. Risk factors for fatty liver such as diabetes, obesity, insulin resistance and the metabolic syndrome will identify which patients are at high-risk for fatty liver. These should then be evaluated with abdominal ultrasound or other forms of screening.

RISK STRATIFICATION:
The following tests may be used to assess a patient’s risk for disease progression or the presence of advanced disease:

- **Simple serum markers (readily obtainable)**
  - APRI: AST and platelet count
  - NALFD score: AST, ALT, Albumin, platelet, age, BMI, DM
  - FIB-4 score: AST, ALT, platelet, age.

- **Serum Biomarkers (blood tests, costlier):**
  - ELF (Enhanced liver fibrosis) panel
  - FibroTest®
  - NASH-Fibrosure®.

- **Imaging techniques:**
  - Vibration controlled transient elastography (VCTE), available commercially as FibroScan®
  - Magnetic resonance elastography (MRE)
  - Shear wave elastography.

- **Histology:** The 'gold standard' for diagnosis has long been liver biopsy. It is not feasible to perform liver biopsies in the large numbers of at risk patients. Biopsy is usually reserved for patients with inconclusive or contradictory lab results. It is especially useful when patients have findings suggestive of other liver diseases that are treated differently.

MANAGEMENT
Currently, published clinical guidelines recommend diet and exercise to promote weight loss and delay disease progression. Although, none of the guidelines specifically address alternatives to manage obesity (pharmacologic, endoscopic, surgical). In the United States, there is no currently FDA approved therapy for NASH as a primary indication. However, published guidelines and guidance statements have suggested that vitamin E and/or piaglitazone be considered. Studies to date have not been uniform in determining what endpoints correlate with real-world clinical outcomes, such as improvement in transaminases, NASH scoring, fibrosis, prevention of cirrhosis or regression of advanced fibrosis. Given the unpredictable outcome of fatty liver in an individual patient, and the frequent comorbidities in this population, careful and close follow-up of these patients is necessary.

FOLLOWING RESULTS
Success in any disease management program requires a process of data collection and review. We recommend this be kept as simple as possible while providing evidence that supports the program. This data will be essential when communicating with referring physicians, hospitals, involved colleagues and patients. Demonstrating effectiveness in this program will distinguish your practice when negotiating contracts and marketing your practice.

EXAMPLES OF DATA COLLECTED

- Demographic data
- Body Measurements (Ht, Wt, BMI)
- Related co-morbidities (diabetes, hepatitis C)
• Relevant Social factors (Alcohol intake)
• Lab values such as transaminases and HgA1C
• Measures of fibrosis
• Weight loss interventions
• Follow up
• Patient-measured outcomes

QUESTIONS

1) How should I provide patient and provider education regarding the potential significance of fatty liver?
2) Who and how will patients be risk stratified in your office?
3) To what extent are dietary and or lifestyle modifications going to be offered within your practice or outsourced?
4) How will you follow patients; who you will identify as low risk for progression?
5) How will you treat or manage patients who you identify as high risk for progression or those with advanced fibrosis or cirrhosis?
6) Is a fatty liver program financially viable?
   a. Risk assessment is through evaluation and testing that is not well reimbursed
   b. There are no current FDA approved therapies
   c. Diet and life style modification recommendations are not reimbursed.
7) Can a fatty liver program be used to identify patients who need other care from your practice?
   a. Those who need screening for HCV
   b. Those with occult advanced liver disease/cirrhosis, or hepatocellular carcinoma
   c. Those who need colorectal cancer risk assessment and screening.
8) How will the data be collected and maintained?

RECOMMENDATIONS FOR YOUR PRACTICE:

1) Identify an individual, such as an advance practice provider, to be your practice's champion in the evaluation and management of these patients.
2) Review the current guidelines and obtained some consensus as to how these patients will be identified, risk stratified, and treated by your practice. We suggest reviewing *World J Gastroenterol* 2018 August 14; 24(30): 3361-3373 which provides a recent summary of all the guidelines and guidance statements in the past 3-4 years.
3) Educate your patients and referring providers about fatty liver disease using widely available sources from guidelines or industry.
4) Use (or develop) a scripted intake protocol for historical risk assessment of these patients. See appendix A
5) Develop a protocol to risk assess these patients. AASLD guidance statements suggest NAFLD fibrosis score (NFS), FIB-4 score and Elastography (vibration (FibroScan) or magnetic resonance). See appendix B for calculator.
6) Develop a recall system to follow low risk individuals: Many guidelines/guidance statements are silent about this. See appendix C for an example.
7) Determine how your practice will provide dietary and lifestyle modification to all patients
   • For high risk patients: See appendix D
8) Set up a data base for this project.
9) Arrange monthly reports to involved colleagues.
10) Advertise the program to referral sources.
11) Provide periodic follow up to referring providers.
Appendix A: Intake history
Fatty Liver Screening/Surveillance Form
(This can be completed by patient with help of medical assistant)

<table>
<thead>
<tr>
<th>Question</th>
<th>Y</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any personal history of liver disease?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any family history of liver disease?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For females: Do you consume &gt; 14 drinks per week?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For males: Do you consume &gt; 21 drinks per week?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is your BMI (we will measure your height/weight to help answer this) &gt; 25?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is your BMI (we will measure your height/weight to help answer this) &gt; 30?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is your BMI (we will measure your height/weight to help answer this) &gt; 35?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you have Type II diabetes?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you have high blood lipids?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you have high blood pressure?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you have polycystic ovary syndrome?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you suffer from low functioning thyroid?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you have (or are thought to have) obstructive sleep apnea?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were you ever told that your liver lab tests were abnormal?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you had an abdominal ultrasound?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If you were born between 1945 and 1965, have you been tested for hepatitis C?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is there any family history in your brother, sister, mother, father of colon polyps?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is there any family history in your brother, sister, mother, father of colon cancer?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you had screening for colon cancer with stool tests or colonoscopy?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix B: FIB-4/Steatosis score calculator:

The medical assistant enters data once: Spreadsheet calculates both scores:

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Steatosis score calculation</td>
<td>FIB-4 calculation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patient Values</td>
<td>Calculated Values</td>
<td>FIB-4 calculation</td>
<td>Calculated Values</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patient Age (years)</td>
<td>0</td>
<td>-1.675</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BMI (kg/m²)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diabetes (1=Yes; 0=No)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>AST</td>
<td>#DIV/0!</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALT</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Platelet Count</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Albumin (g/Dl)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fibrosis score</td>
<td>#DIV/0!</td>
<td>FIB-4 score</td>
<td>#DIV/0!</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Interpretation

| <0.676 | Stage 3/4 fibrosis | > 2.67 | Stage 3/4 fibrosis |
|<1.4555 | Stage 0/2 fibrosis | <1.3 | Stage 0/2 fibrosis |

Examples of Currently Available Calculators

(Disadvantage: To obtain both scores, may need to enter same data twice!)

<table>
<thead>
<tr>
<th>NAFLD-Score</th>
<th>FIB-4 Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="https://www.mdapp.co/hepatic-steatosis-index-hsi-calculator-357/">https://www.mdapp.co/hepatic-steatosis-index-hsi-calculator-357/</a></td>
<td><a href="https://www.mdapp.co/fibrosis-4-fib-4-score-calculator-107/">https://www.mdapp.co/fibrosis-4-fib-4-score-calculator-107/</a></td>
</tr>
</tbody>
</table>
Appendix C: Low risk

This is an example: You may choose different protocol/pathway

<table>
<thead>
<tr>
<th>Steatosis Score</th>
<th>FIB-4 score</th>
<th>Liver elastography</th>
<th>F/u</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;-1.455</td>
<td>&lt; 1.3</td>
<td>F0-F1</td>
<td>Liver Elastography in 5 years</td>
</tr>
<tr>
<td>&gt;-1.455</td>
<td>&lt; 1.3</td>
<td>F0-F1</td>
<td>Liver Elastography in 3 years/Labs</td>
</tr>
<tr>
<td>&lt;-1.455</td>
<td>&gt; 1.3</td>
<td>F0-F1</td>
<td>Liver Elastography in 3 years/Labs</td>
</tr>
<tr>
<td>&gt;-1.455</td>
<td>&gt; 1.3</td>
<td>F0-F1</td>
<td>Liver Elastography in 2 years/Labs</td>
</tr>
<tr>
<td>Any value</td>
<td>Any value</td>
<td>F2</td>
<td>Liver elastography in 2 years/Labs</td>
</tr>
</tbody>
</table>
Appendix D: Low risk

This is an example: You may choose different protocol/pathway

If patient has F3 by liver elastography or is suspected by other testing of fibrosis to possibly have advanced fibrosis:

Option #1: Follow clinically with periodic labs, markers of fibrosis and liver elastography (every 6-12 months)

Option #2: Perform liver biopsy to confirm disease type (NASH vs simple steatosis vs other liver disease) AND to assess level of FIBROSIS)

If patient has confirmed NASH with advanced fibrosis histologically:

Option #1: Follow clinically with periodic labs and liver elastography (every 6-12 months)

Option #2: Therapeutic option: Off label use of Vitamin E or pioglitazone (as per guidelines/guidance statements)

Option #3: Refer to research center for phase III trials

If patient has F4 (Cirrhosis) by liver elastography or cirrhosis is highly suspected:

Option #1: Consider confirmation by other imaging and/or liver biopsy

Option #2: Enroll in compensated cirrhosis follow-up program to include:

1) Labs every 3-6 months for AFP and MELD score calculation

2) Abdominal ultrasound every six months for hepatocellular carcinoma surveillance

3) Vaccinations against HAV and HBV if not immune

4) Periodic clinic visits if there is a change in patient status.

5) Periodic endoscopy to screen/survey for esophageal varices (if platelet <150 or kPa > 19.5)

6) Consideration for referral to transplant center if decompensation or rising MELD score > 14.
References

Guidelines and Guidance Statements:


European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD) and European Association for the Study of Obesity (EASO). EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol 2016; 64: 1388–1402

NICE guideline. Non-alcoholic fatty liver disease (NAFLD): assessment and management. nice.org.uk/guidance/ng49


Educational Resources for Patient/Provider:

https://gi.org/topics/fatty-liver-disease-nafld
https://www.the-nash-education-program.com
https://www.niddk.nih.gov/health-information/liver-disease/nafld-nash
https://liverfoundation.org/for-patients/resources/brochures Scroll to Diseases then NASH-NAFLD for several .pdf resources

Scholarly Articles about NAFLD


