ONE-PAGER ON ADVANCED FIBROSIS (aka CIRRHOSIS) WITH OR WITHOUT PORTAL HYPERTENSION GUIDANCE FOR PRIMARY CARE PROVIDERS IN AMBULATORY CARE

Introduction

Advanced fibrosis, often called cirrhosis, represents the severe stage of chronic liver disease, characterized by extensive scarring and the formation of regenerative nodules. This disrupts the normal architecture and function of the liver. Advanced fibrosis can occur with or without portal hypertension, which is increased pressure in the portal vein due to hampered blood flow through the liver. While there are over 35 conditions that can lead to advanced fibrosis including steatotic liver disease, viral hepatitis, genetic conditions and immune-mediated disorders, routine testing typically screens for about 10 of these, with effective treatments available for 7 conditions.

Patients with compensated advanced fibrosis—those who have no or mild symptoms—have a five-year survival rate of over 95%. However, once advanced fibrosis progresses to decompensation, marked by symptoms like worsening jaundice, poorly controlled ascites, or severe grade 3-4 hepatic encephalopathy, the median survival drops to less than two years. For these patients, liver transplantation can be a life-saving option, though availability is limited due to the scarcity of donors. In Atlantic Canada, fewer than 30 liver transplants occur annually due to donor limitations.

Early identification, regular monitoring, and proactive management of patients with advanced fibrosis are essential to improve outcomes and prevent serious complications. Primary care providers play a crucial role in this process by ensuring early referral to hepatology specialists when necessary and managing comorbid conditions that can exacerbate liver disease.

Risks for Progression

Patients with advanced fibrosis are at a high risk for:

- **Decompensation:** Manifestations include (a) accumulation of large volume ascites requiring paracentesis, (b) development of spontaneous bacterial peritonitis (SBP), (c) grade 3 or 4 hepatic encephalopathy requiring repeated hospitalizations, or (d) recurrent portal hypertensive gastrointestinal (GI) bleeding.
- **Acute on Chronic Liver Failure:** This is precipitated acutely by infections, alcohol consumption, GI bleeding, and hepatotoxic drugs and toxins with multi-organ failure, high morbidity and mortality.
- **Hepatocellular Carcinoma (HCC):** Increased risk requires consistent surveillance.
- **Accelerating Factors:** Ongoing alcohol consumption, poorly controlled diabetes, high BMI, chronic hepatitis B and C, and genetic liver disorders (e.g., hemochromatosis, Wilson's disease).
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Non-Invasive Assessment

- **FIB-4 Score:** This tool uses age, ALT, AST, and platelet count to estimate fibrosis risk:
    - < 1.5 (ages 36-65) or < 2.0 (ages 65+): Low likelihood of advanced fibrosis.
    - 1.5-3.25: Intermediate risk; consider additional non-invasive tests or imaging.
    - 3.25: High likelihood of advanced fibrosis; referral to hepatology is recommended especially if the patient does not have absolute contraindications such as active substance abuse, untreated malignancy, severe cardiopulmonary disease, or non-compliance with medical care. Relative contraindications include frailty, significant mental health issues, poor psychosocial support, high BMI > 40.

- **Fibroscan (Transient Elastography):** A preferred method to measure liver stiffness, correlating with fibrosis severity. It maybe be used regularly for monitoring of progression or regression of fibrosis, although reliability decreases in patients with high BMI more than 39 or acute liver inflammation, congestion or injury from alcohol and hepatotoxic drugs.

Screening and Risk Assessment

- **Hepatocellular Carcinoma (HCC) Surveillance:**
  - Ultrasound with or without Alpha-Fetoprotein (AFP): Every 6 months. For lesions < 1 cm, conduct follow-up ultrasounds every 3 months for at least a year. Lesions > 1 cm or those showing size increase should be further evaluated using multiphasic CT or MRI.
  - Referral to Liver Mass Clinic: If imaging suggests HCC, refer to one of the four hepatobiliary surgeons at the QEII Victoria General site in Halifax (fax: 902-473-5297).
- **Esophageal Variceal Screening:**
  - Upper GI Endoscopy: For patients with advanced fibrosis, repeat endoscopy every 3 years if no varices are present, every 2 years if small varices are found, and annually in patients with decompensated liver disease and small varices.
  - Initiate Non-selective Beta-Blockers: Start with carvedilol (preferred), beginning at 3.125 mg BID and titrate up to a maximum of 6.25 mg BID if tolerated. For patients already on antihypertensive drugs or selective beta-blockers, consider transitioning to carvedilol. Note that this is a balancing act due to the risk of side effects, including worsening ascites due to further systemic vasodilation. Alternatives include nadolol or propranolol, aiming to maintain a target heart rate of 55-60 bpm. Beta-blockers should ideally be given once a day at bedtime to optimize adherence and minimize daytime side effects. This approach may reduce the need for frequent endoscopic screening, unless contraindications arise.

Management of Cirrhosis

- **Routine Bloodwork:** Every 6 months, including liver function tests (INR, albumin, total and direct bilirubin), AST, ALT, ALP, creatinine, CBC, and AFP.
- **Medication and Toxin Exposure:**
  - **Alcohol:** Complete abstinence is recommended to prevent further liver damage.
  - **Acetaminophen:** Safe up to 2 grams per day.
  - **NSAIDs and COX-2 inhibitors:** Contraindicated due to the increased risk of renal impairment and gastrointestinal bleeding.
  - **Sedatives and Hypnotics:** Avoid benzodiazepines, opioids, and narcotics to reduce the risk of hepatic encephalopathy.
- **Vaccinations:**
  - **Hepatitis A and B:** Verify immunity; vaccinate if non-immune.
  - **Pneumococcal Vaccines:** PCV13 followed by PPSV23.
  - **Influenza:** Annually.
  - **COVID-19:** As per public health recommendations.
  - **Herpes Zoster and Tdap:** For patients aged 65 or older, or 19-64 with chronic liver disease.
- **Bone Health:**
  - **Vitamin D:** 1,000 IU daily.
  - **Bone Mineral Density (BMD) Testing:** Baseline and every 2 years.

- **Nutrition and Exercise:**
    - **Diet:** A Mediterranean diet is recommended, focusing on high protein (1.2-1.5 g/kg/day) and low sodium (< 2,000 mg/day). Late-night high-protein, high-calorie snacks can help maintain nitrogen balance.
    - **Exercise:** Regular physical activity, including aerobic and strength training, is encouraged. Consider referrals to dietitians and physiotherapists.

Symptom Management

Common symptoms include muscle cramps, sleep disturbances, pruritis, depression, and anxiety. For sleep disturbances linked to hepatic encephalopathy, use lactulose to maintain 2-3 semi-formed bowel movements daily. Refer to resources such as the University of Alberta's Cirrhosis Care website for additional management strategies.

Timing of Referral for Hepatology and Future Liver Transplantation

Referral to a liver transplant program is recommended under the following conditions:

- **Decompensated Cirrhosis:** Persistent ascites unresponsive to diuretics and sodium restriction, INR > 1.7, or bilirubin > 50 µmol/L for over a month.
- **Treatable Liver Diseases:** Conditions such as chronic hepatitis B or C, hereditary hemochromatosis, Wilson's disease, or autoimmune liver diseases (e.g., autoimmune hepatitis, primary biliary cholangitis).

Contraindications:

- **Absolute:** Active substance abuse, untreated malignancy, severe cardiopulmonary disease, non-compliance with medical care.
- **Relative:** Advanced age with frailty, significant mental health issues, poor psychosocial support, morbid obesity (BMI > 40).

Resources

- **American Family Physician Article on Cirrhosis Management:** A valuable resource for further reading.
- **Virtual Hallway:** Consider virtual consultations for specific hepatology questions (http://www.VirtualHallway.ca).
- **CirrhosisCare.ca website:** Up to date and evidence-based resources for managing cirrhosis (https://cirrhosiscare.ca/practitioner-pathway/).