crohn's colitis

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Name of Clinical Care Pathway

Approach to Abnormal Liver Tests in IBD

Objective

To provide guidance on the evaluation of abnormal liver enzymes in patients with inflammatory bowel disease (IBD).

Patient Population

Adult patients (≥18 years) with inflammatory bowel disease (IBD) who present with abnormal liver enzyme levels.

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These clinical decision support tools were developed by Canadian experts in PSC, based on their interpretation of current evidence and considerations specific to Canadian healthcare. International guidelines from Europe and the United States are available. However, these may reflect regional factors that might not directly be applicable in Canada.

PACE IBD National Clinical Care Pathways

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Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ALP	Alkaline phosphatase
GGT	Gamma-glutamyl transferase
ULN	Upper limit of normal
ANA	Antinuclear antibody
ASMA	Anti–smooth muscle antibody
AMA	Antimitochondrial antibody
IgG	Immunoglobulin G
tTG	Tissue transglutaminase antibody
EBV	Epstein–Barr virus
CMV	Cytomegalovirus
MRC	Magnetic resonance cholangiography
MRCP	Magnetic resonance cholangiopancreatography
PSC	Primary sclerosing cholangitis
US	Ultrasound
anti-TNF	Tumor necrosis factor inhibitor
DI-ALH	Drug-induced autoimmune-like hepatitis
6-MP	6-mercaptopurine
NRH	Nodular regenerative hyperplasia
HBc Ab	Hepatitis B core antibody
HBsAg	Hepatitis B surface antigen
HBsAb	Hepatitis B surface antibody
HCV Ab	Hepatitis C antibody
HAV IgM	Hepatitis A virus immunoglobulin M
HbA1c	Hemoglobin A1c
LFT	Liver function tests

Highlight Box

- Abnormal liver tests are common in people with inflammatory bowel disease (IBD), and most cases are self-limiting, with approximately 5% having clinically significant liver disease.

- The disorders more frequently associated with abnormal liver tests in IBD include primary sclerosing cholangitis (PSC), metabolic dysfunction-associated steatotic liver disease (MASLD) and drug-induced liver injury (DILI).

- A thorough clinical evaluation, serological tests, imaging studies, and in some cases, histological assessment can be used to help establish the causality of abnormal liver tests in people with IBD.

Introduction

Abnormal liver tests are common in people with inflammatory bowel disease (IBD). The prevalence of abnormal liver tests in IBD ranges from 20 to 40%, depending on the designation used for abnormal liver tests. For example, a normal alanine aminotransferase (ALT) level for males should be less than 35 U/L, and less than 25 U/L in females.

Abnormal liver tests can be the result of several conditions, with the most frequent in those with IBD being primary sclerosing cholangitis (PSC), metabolic dysfunction-associated steatotic liver disease (MASLD), and drug-induced liver injury (DILI).

While most liver test abnormalities are mild and might resolve spontaneously, a chronic elevation warrants a comprehensive investigation to identify the cause and appropriate management, which might include stopping or changing medication.

The use of immunomodulatory medications in patients with IBD has led to a rise in the frequency of abnormal liver tests in IBD. The majority of cases of abnormal liver tests resolved spontaneously, and clinically significant liver damage is infrequent. The use of azathioprine and anti-TNF (tumour necrosis factor) antibodies has the greatest risk of liver injury. A well-defined timeline of drug initiation or dose escalation is essential when interpreting abnormal liver tests to identify DILI. Signs of serious liver dysfunction should prompt immediate cessation of the drug. Otherwise, a patient-centred approach is required when deciding on drug alteration, including assessing therapeutic efficacy and the availability of alternative treatment options.

The severity of the elevation of liver enzymes and the pattern (hepatocellular, cholestatic or mixed) will mandate the algorithm to follow.

In addition, the cases of doubt about the type of pattern of elevation of liver enzymes, clinicians can use the R liver factor. The R liver factor formula is: R = (ALT value / ALT ULN) / (Alkaline Phosphatase value / ALP ULN), which is used to classify liver injury patterns.

An R Factor >5 suggests hepatocellular pattern of liver injury, and potential cases include acute viral hepatitis, autoimmune hepatitis, and DILI, which should be ruled out as causes.

Commonly used drugs that can cause this pattern of liver injury include nitrofurantoin, minocycline, statins and NSAIDs.

An R Factor <2 suggests a cholestatic pattern of liver injury. Causes include PSC and PBC, and commonly used drugs that can cause this pattern of liver injury include azathioprine, amoxicillin/clavulanate, and trimethoprim/sulfamethoxazole.

R Factor between 2 and 5 suggests a mixed pattern of liver injury.

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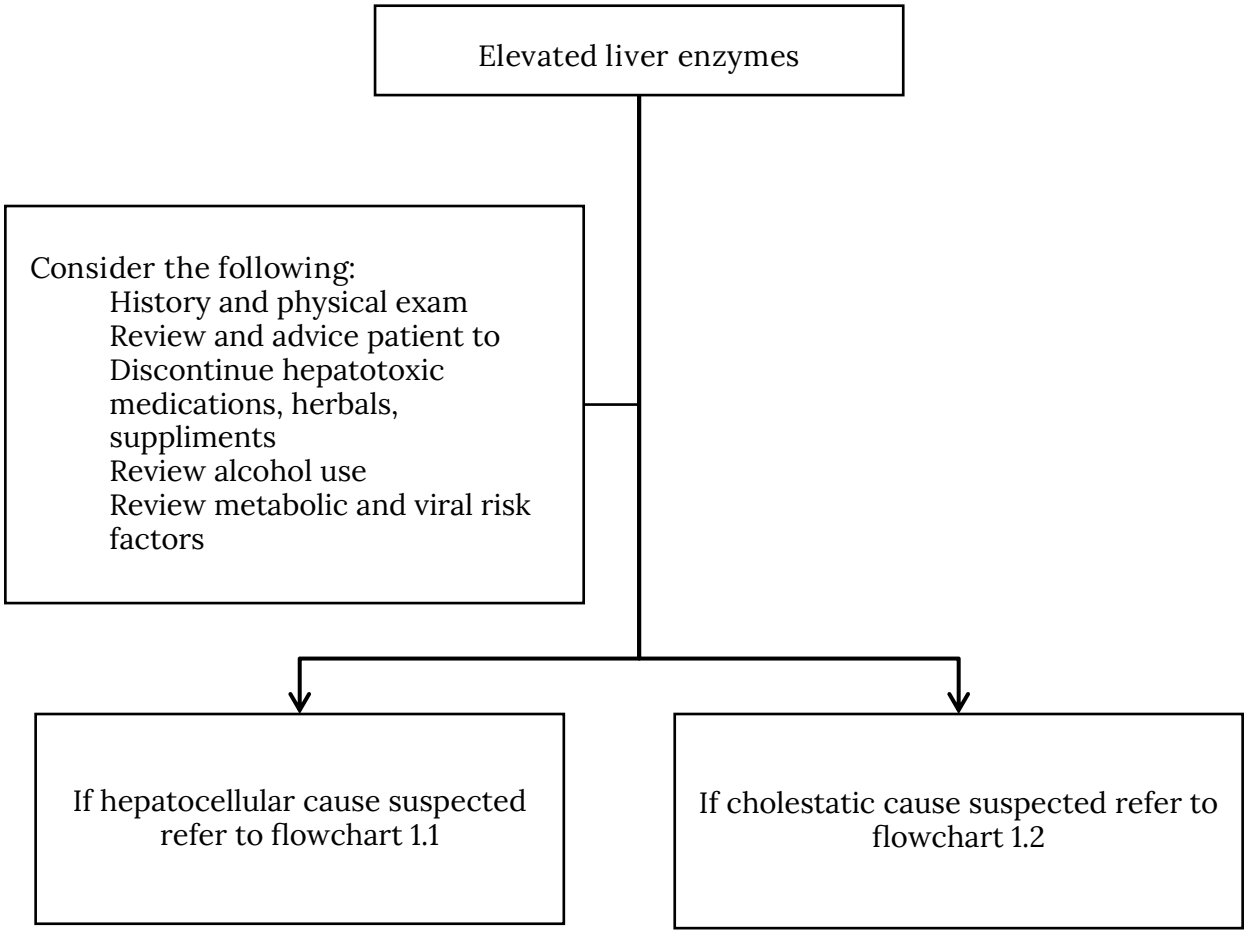
Diagnostic and imaging algorithms:

Flowchart 1.0: Algorithm for evaluating elevated liver enzymes that may lead to the PSC clinical pathway.



Note:
Review IBD medications – cross-reference LiverTox

- Anti-TNF therapy (can have transient ALT elevation, DI-ALH, hepatitis B reactivation, cholestatic liver injury)
- Thiopurines, 6-MP (NRH or obliterative portal venopathy)
- Methotrexate (chronic hepatitis, steatohepatitis, NRH)
- Mesalamine (idiosyncratic cholestatic or hepatocellular)
- JAK inhibitors (transient ALT elevation)
- Vedolizumab (ALT elevation)
- Risankizumab (ALT elevation)
- Ustekinumab (hepatitis B reactivation)

Urgent consultation with the transplant centre if signs of acute liver failure

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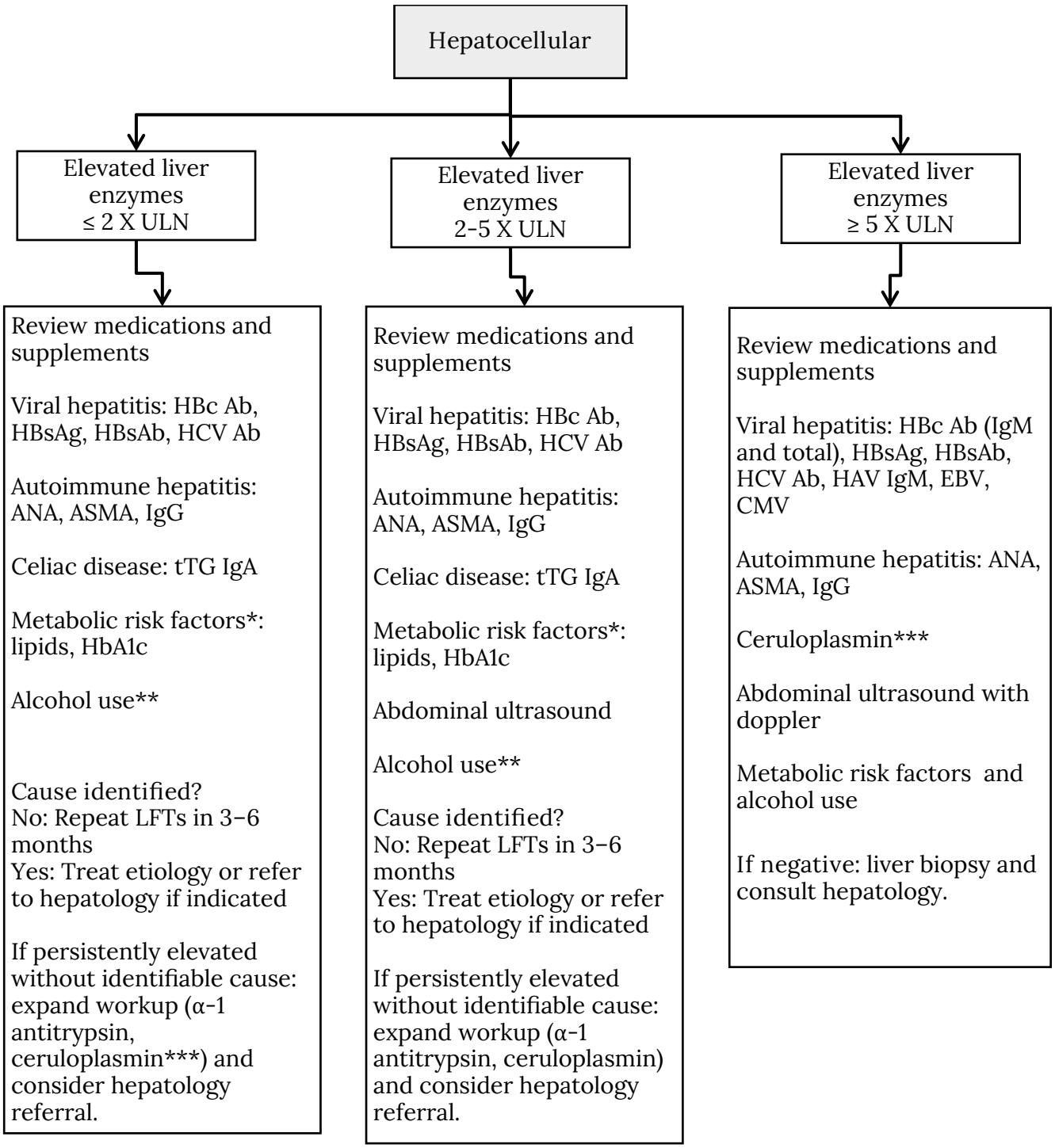
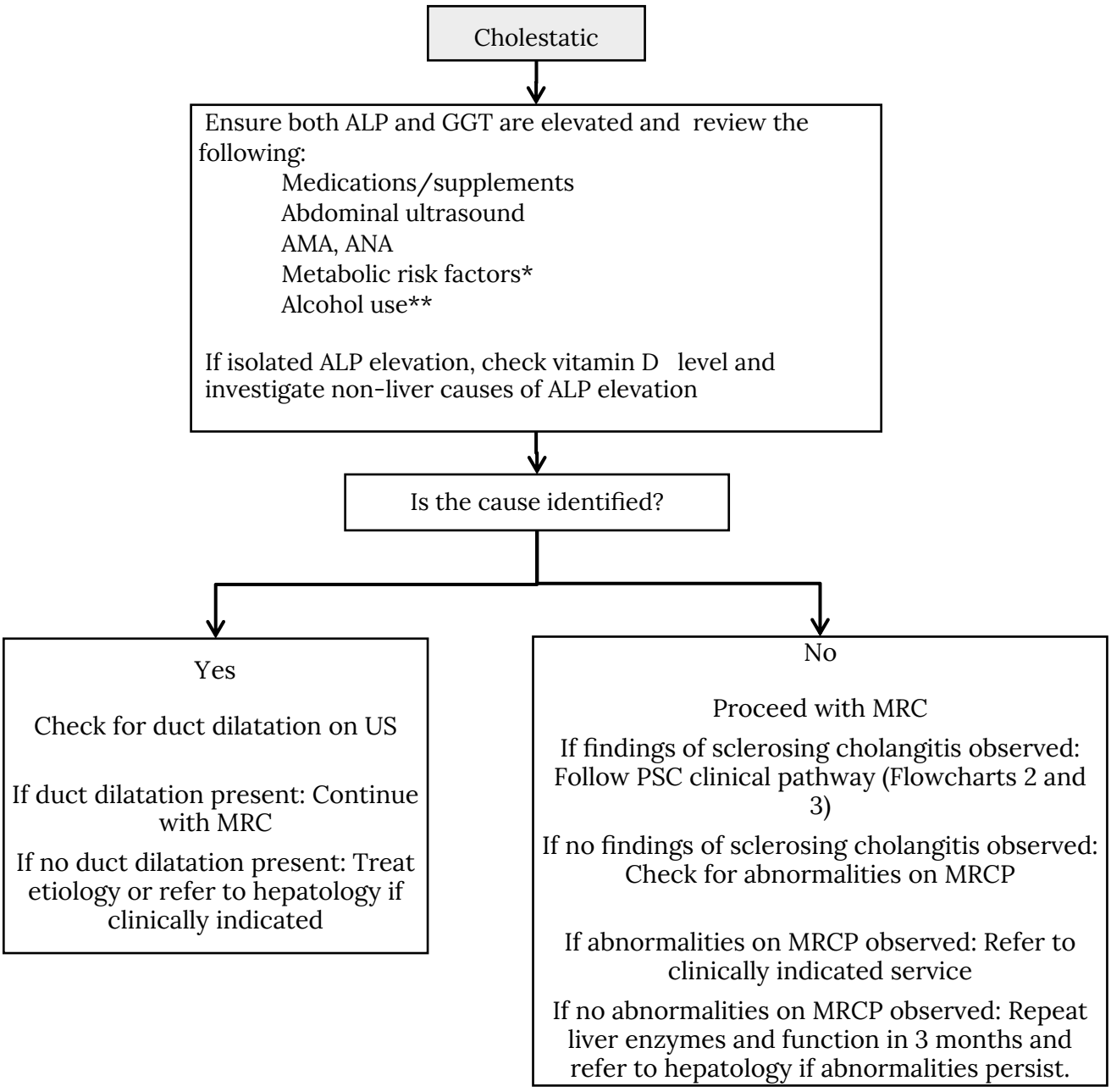
Flowchart 1.1: Assessment of hepatocellular causes of elevated liver enzymes



Flowchart 1.2: Assessment of cholestatic causes of elevated liver enzymes



*Check BMI, blood pressure, lipid profile, and hemoglobin A1c. Work with the family physician on screening for and managing metabolic risk factors.
**AUDIT-C can be used to screen for alcohol use. Offer local addictions, treatment resources and pharmacotherapy.
***Check ceruloplasmin if age <50 years old or if otherwise clinically indicated.

Note: Metabolic and/or alcohol will not cause ALT >400 on its own; other causes must be explored.

Resources for Providers

- LiverTox - NCBI Bookshelf – NIH. National Institutes of Health (.gov) https://www.ncbi.nlm.nih.gov › books › NBK547852
- Guidelines on the management of abnormal liver blood tests https://doi.org/10.1136/gutjnl-2017-314924
- ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries https://pubmed.ncbi.nlm.nih.gov/27995906/

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