The Role of Ultrasound in Fatty Liver

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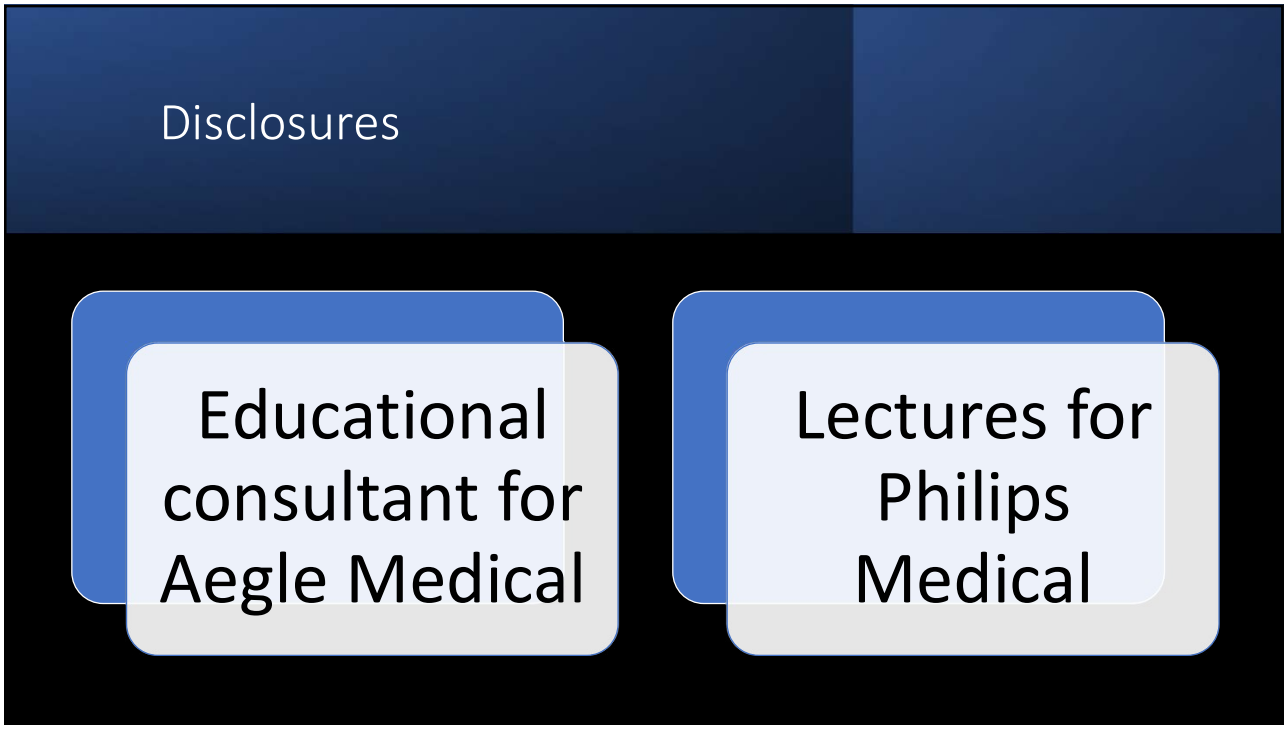

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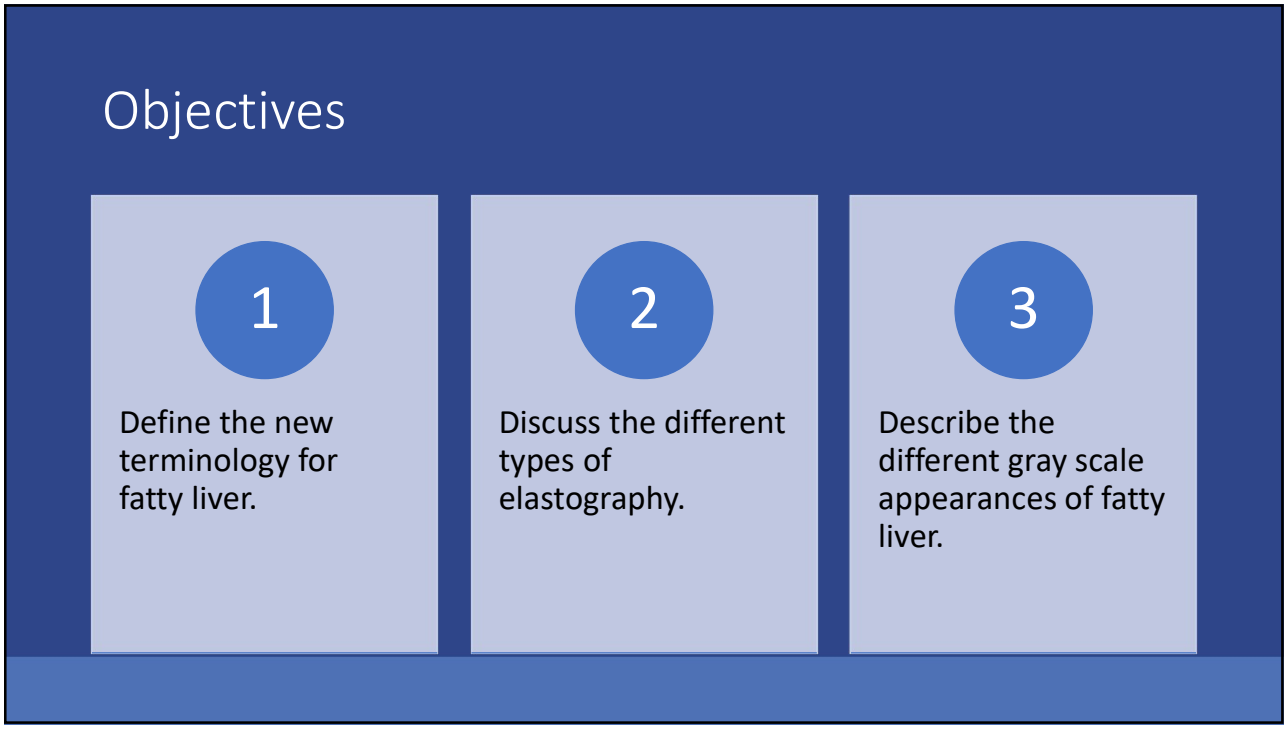

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What is Steatosis (Fatty) Liver Disease?

When >5 – 10% of liver weight is fat

Two main types of Steatotic Liver Disease (SLD)

- Alcoholic fatty liver disease (ALD)
- Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Usually no symptoms or serious liver problems

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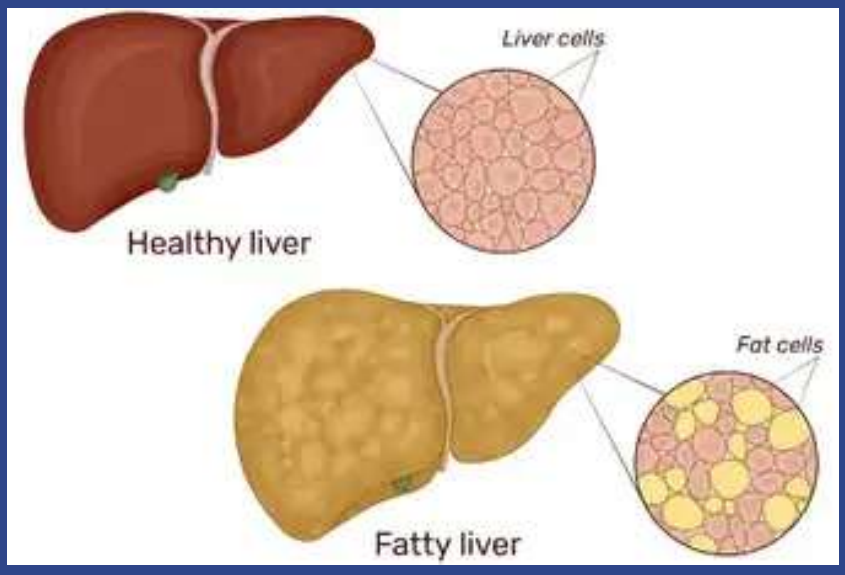

Pathak N. A Guide to Metabolic Dysfunction-Associated Steatohepatitis (MASH). Published April 02, 2024. Accessed July 31, 2024. https://www.webmd.com/digestive-disorders/ss/slideshow-guide-to-mash

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Normal vs Fatty Liver

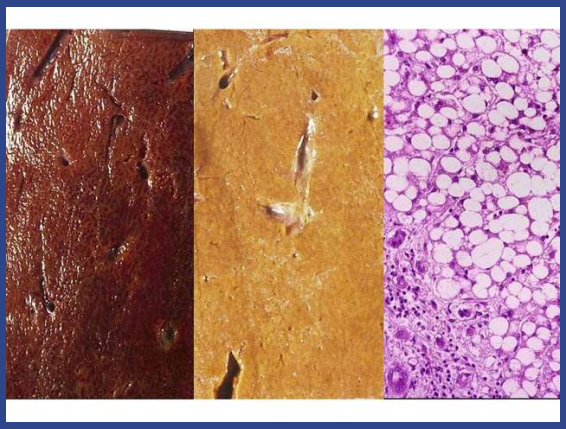
Normal dark brown color..

Fatty liver yellow-brown

- This color change is due to the accumulation of lipid in the liver

High power view shows marked accumulation of lipid droplets within hepatocytes.

- Appear as clear, well-demarcated vacuoles in the cytoplasm



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Fatty/Steatotic Liver Terminology

OLD	NEW
NAFLD/MAFLD	MASLD
NASH	MASH
MetALD	New Term
ALD	No Change

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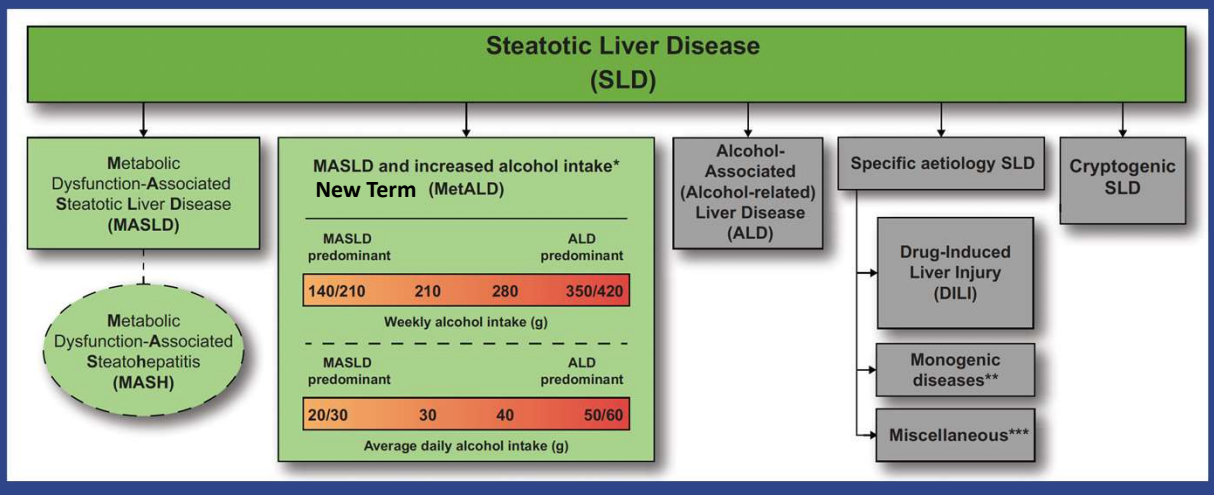

Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. *Ann Hepatol*. 2024;29(1):101133. doi:10.1016/j.aohep.2023.101133

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NAFLD vs MASLD

- **Nonalcoholic Fatty Liver Disease**
  - NAFLD is often associated with obesity, type 2 diabetes, insulin resistance, high cholesterol, and high triglycerides.
- **Metabolic dysfunction-associated steatotic liver disease**
  - Emphasizes the role of metabolic dysfunction, such as obesity and insulin resistance, in the development of fatty liver disease
- NAFLD focused on what the disease wasn't (non-alcoholic), while MASLD focuses on what the disease is (metabolic dysfunction)

https://www.aasld.org/new-masld-nomenclature

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MASLD

About **100 million** people (about 25%) in the United States are estimated to have MASLD

MASLD is the **most ordinary form of liver disease in children** and has more than doubled over the past 20 years

Rise in MASLD is linked to the increasing rates of obesity and type 2 diabetes

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MASLD – Worldwide problem

Leading cause of liver disease worldwide

Estimated to affect 38% of the global population

- 47 cases per 1,000 population
- Higher among males
- Has increased over time, from 26% in 2005 or earlier to 38% from 2016

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MASLD

Multisystem disease associated with metabolic syndrome

- No hepatocellular injury, inflammation or fibrosis

Progressive accumulation of fat (triglycerides) in liver cells

- Not caused by alcohol

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MASLD

Risk Factors

- Diabetes or Pre-Diabetes
- Obesity
  - Obesity thought to be most common cause
- Hypertension
- High cholesterol
- Genetics

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Metabolic Syndrome: 3 or More of Following

BMI (Body mass index) ≥ 30
- Particularly those with abdominal obesity

Insulin resistance and diabetes
- Have a greater risk for MASH

Low HDL cholesterol (good cholesterol)

High triglycerides

High cholesterol

High blood pressure

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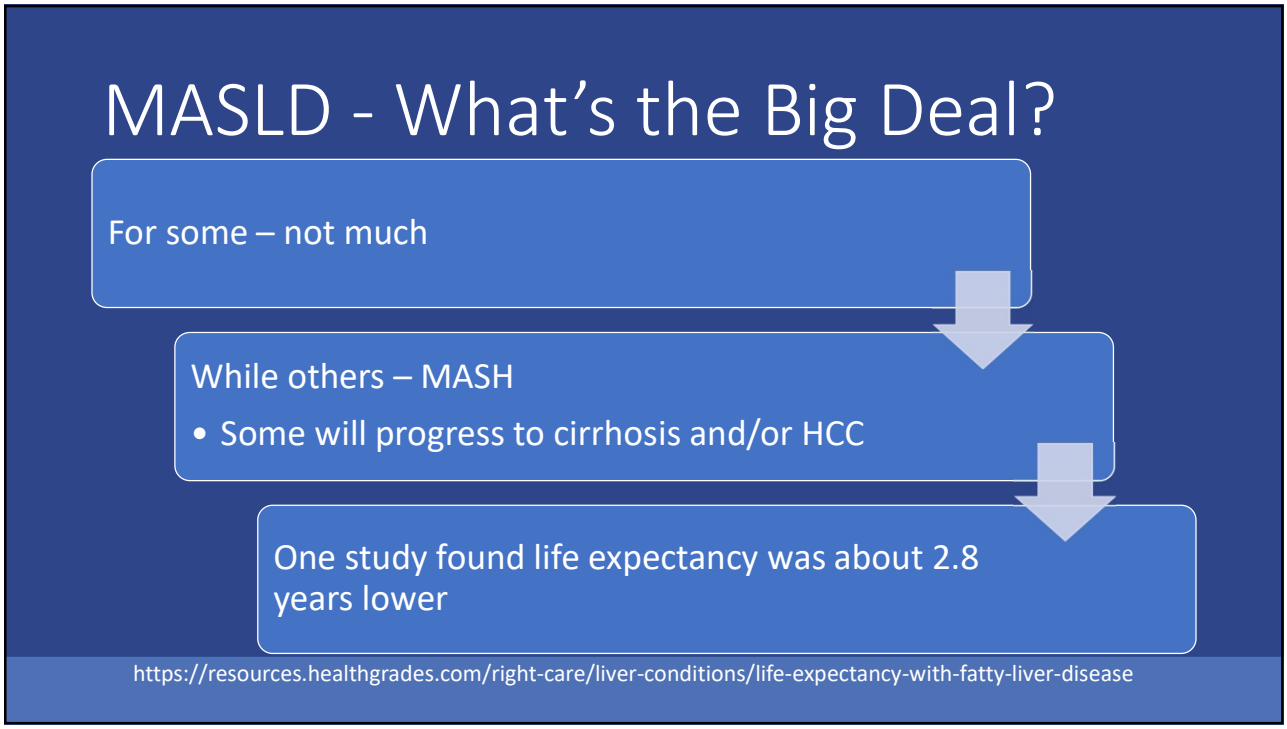

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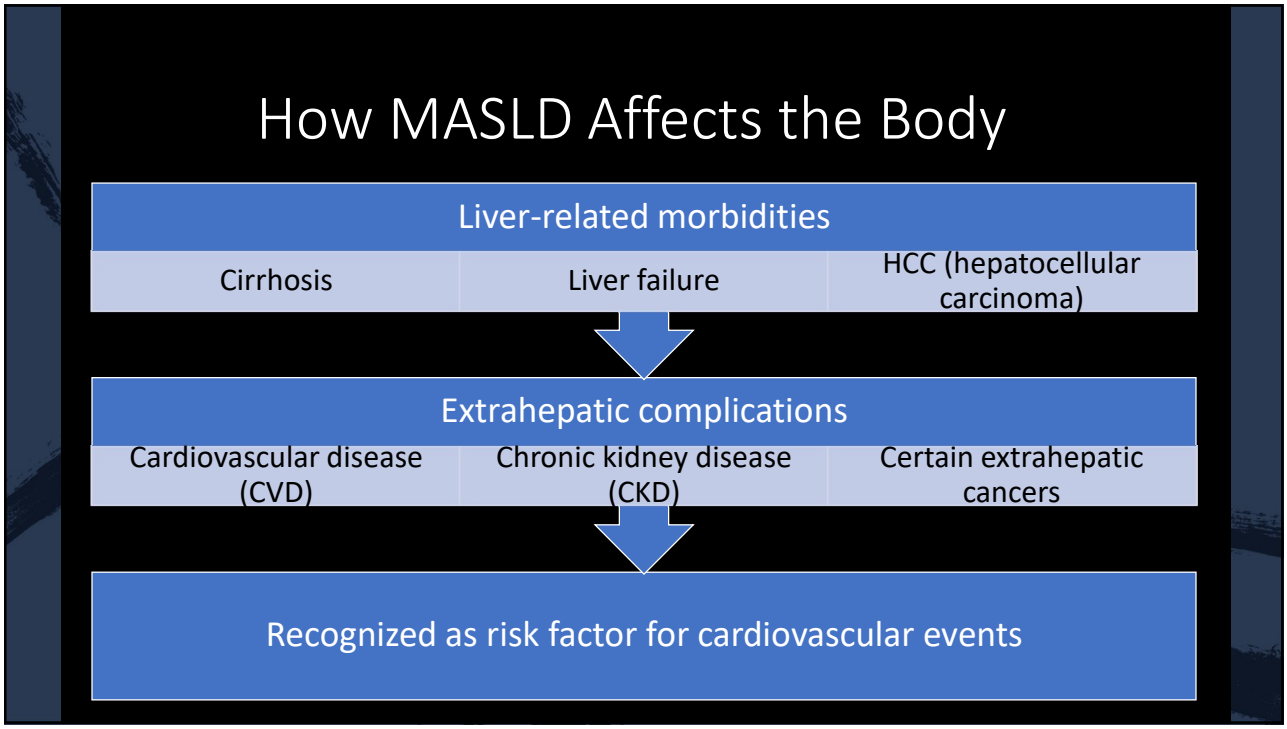

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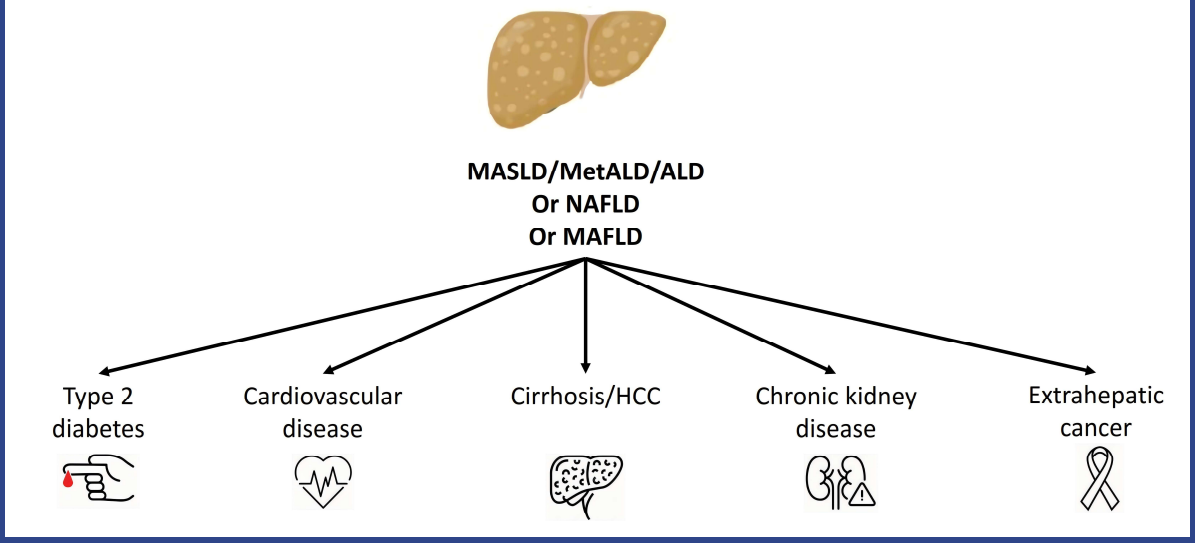

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People with cardiovascular disease(CVD) and/or type 2 diabetes(T2D) are more likely to have MASLD and MASH

Conversely, people with MASLD or MASH are more likely to have CVD and/or T2D

CVD leading cause of mortality in people who have MASH

- Twice as likely to die from CVD than general population

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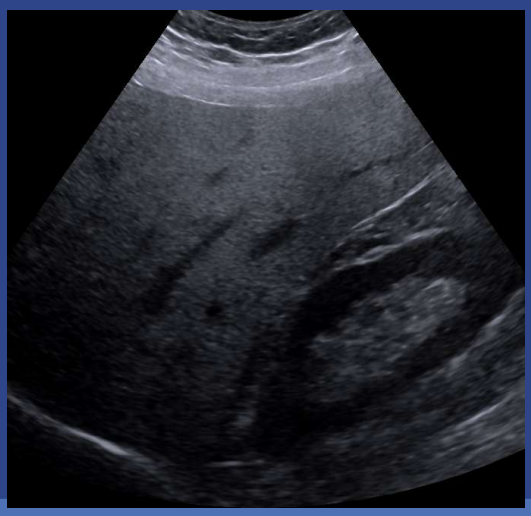
MASLD Symptoms

Usually none

- Fatigue
- RUQ pain/discomfort
- Hepatomegaly

LFTs may be normal

Typically discovered on imaging



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MASLD (Metabolic Dysfunction-associated Steatotic Liver Disease)
vs
MAFLD (Metabolic Dysfunction-associated Fatty Liver Disease)

Terms used to describe fatty liver disease linked to metabolic dysfunction

Differ in their diagnostic criteria.

- MASLD requires hepatic steatosis plus at least one cardiometabolic risk factor
- MAFLD requires hepatic steatosis plus either overweight/obesity, type 2 diabetes, or at least two metabolic risk abnormalities.

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MAFLD (Metabolic Dysfunction-associated Fatty Liver Disease)

- Created in 2020 to replace NAFLD
- Requires presence of hepatic steatosis and at least one of following: overweight/obesity, type 2 diabetes, or evidence of metabolic dysfunction
- Emphasizes metabolic component by requiring specific metabolic abnormalities for diagnosis
- Some studies suggest that MAFLD better identifies individuals at higher risk of liver fibrosis and disease progression

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MASLD (Metabolic Dysfunction-associated Steatotic Liver Disease)

- Requires presence of hepatic steatosis and one or more cardiometabolic risk factors, with exclusion of excessive alcohol consumption.
- Definition potentially captures a larger population with fatty liver disease, including those with less severe metabolic issues
- Some studies suggest MASLD might be better at predicting cardiovascular outcomes.
- Introduces a new term, MetALD to designate subgroup with both MASLD and significant alcohol consumption.
- MAFLD was a step in right direction, but MASLD is current and preferred term

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MASLD Statistics

MASLD would increase from 33.7% in 2020 to 41.4% in 2050

- Approximately 122 million US adults will have MASLD in 2050.
- After 30 years, prevalent cases of decompensated cirrhosis would more than triple
- Incident cases of liver cancer would almost double
- Liver transplant would almost quadruple.

Cause of 138,000 deaths in 2021

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What is MASH?

- Severe form of MASLD
- Defined as 5% or greater hepatic steatosis **plus** hepatocellular injury and inflammation, with or without fibrosis
- About 20% of people with MASLD have MASH
- Affects 2-5% of population
  - 6.5-16.3 million people
- Expected by 2030 MASH will be most frequent reason for liver transplants

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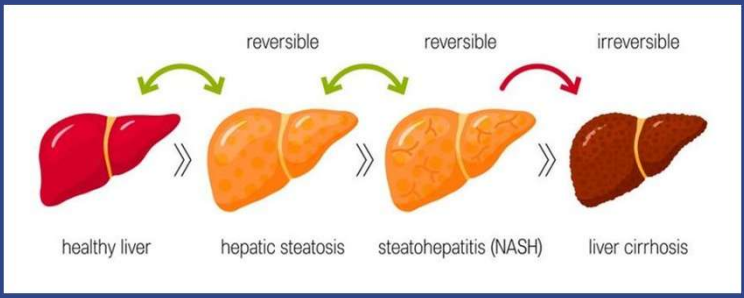
Liver Fibrosis

- Inflammation affects liver cells
  - Liver cells cannot repair themselves
  - Scar tissue cannot function
- Scars continue to build and replace healthy tissue
  - Scars grow together "bridging"
- Fibrosis restricts blood flow
  - Eventually results in portal hypertension



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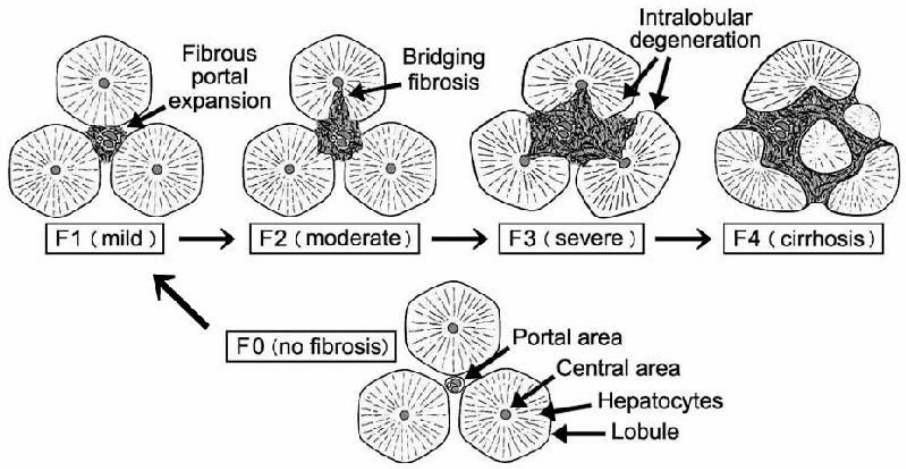
Metavir Score



Shimizu I, Shimamoto N, Saiki K, Furujo M, Osaw K. Lipid Peroxidation in Hepatic Fibrosis [Internet]. Lipid Peroxidation. InTech; 2012. Available from: http://dx.doi.org/10.5772/46180

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MASH Symptoms

No noticeable symptoms in early stages	Jaundice/itchy skin
RUQ discomfort	Bleed or bruise easily
Decreased appetite	Portal Hypertension
Nausea	Splenomegaly

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MASH Complications

- About 20% -30% of people with MASH will develop cirrhosis
- 5% risk for HCC (hepatocellular carcinoma)
- May increase risk of progression to end-stage liver disease
  - Terminal condition
- CDC states chronic liver disease and cirrhosis 12th leading cause of death
  - 4th leading cause of death in 45-65 years old

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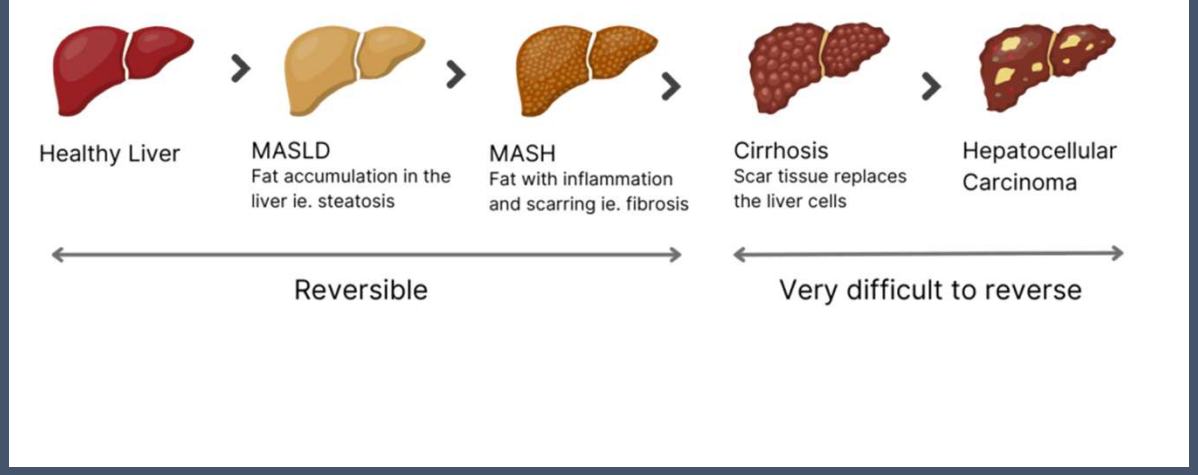

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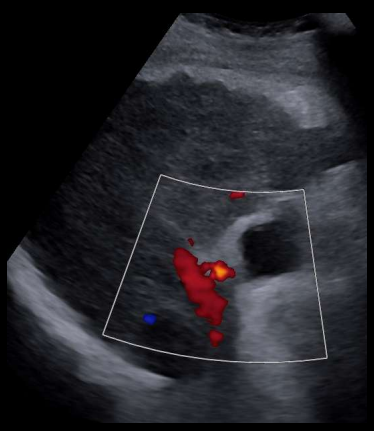
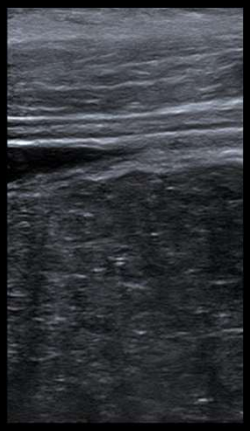
Cirrhosis





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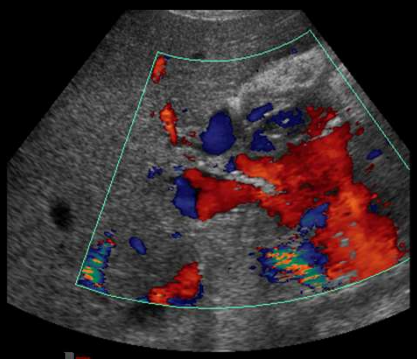
Portal Hypertension

Portal hypertension has significant morbidity and mortality rates

Gastroesophageal variceal hemorrhage most serious and lethal complication

- 30 - 60% mortality rate with each episode
- 70% chance of bleeding again
  - 30% chance of death



Gastric Varices

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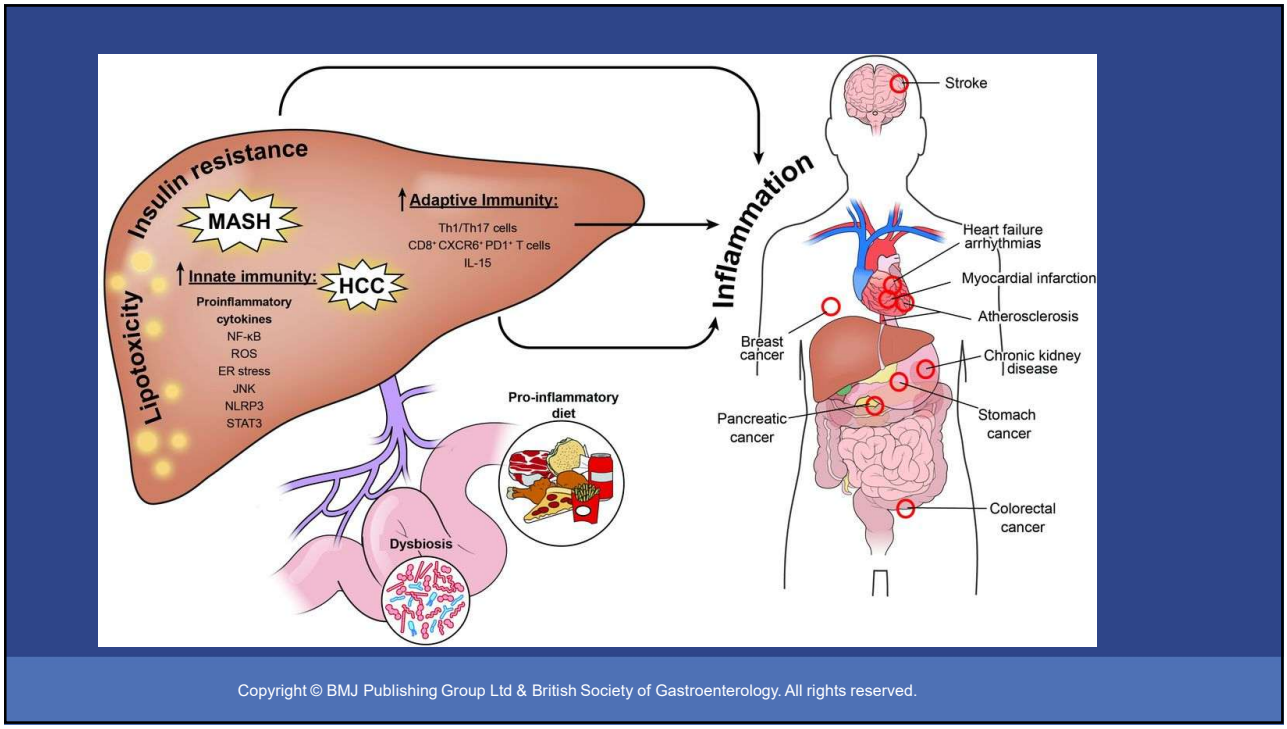

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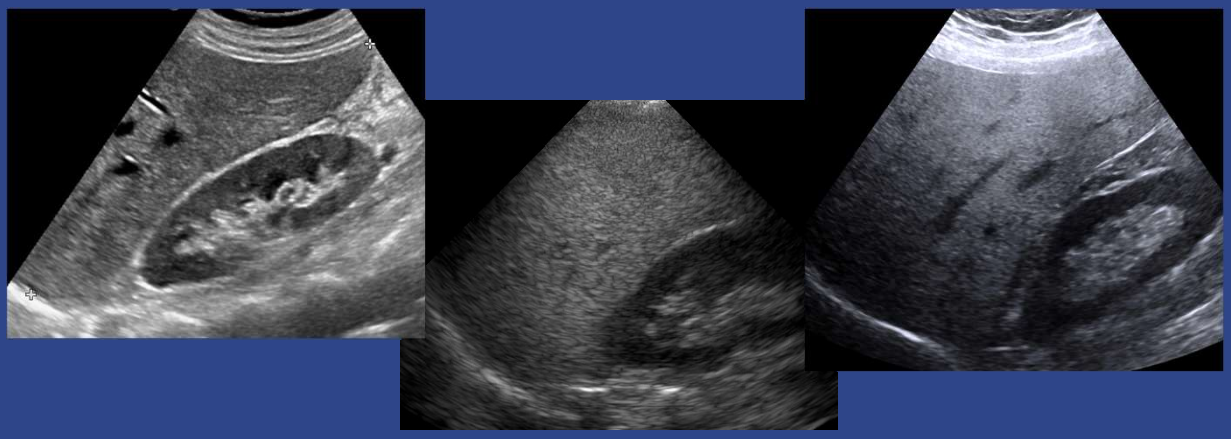
Ultrasound and Fatty Liver



Normal

Mild

Moderate

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Role of Ultrasound: Usually first ordered imaging test

Gray Scale

- Liver/Right Kidney
  - Difference in echogenicity
- Attenuation
  - Far Field/Diaphragm
  - Bright is diaphragm
- Evaluate Vessels

Elastography

- Use to quantify amount of fat and fibrosis
- Follow-up to assess progression or regression
- Monitor patients on drug therapy

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Ultrasound and Fatty Liver

Grading of hepatic steatosis	Histological findings	Ultrasonographic findings
Grade 0 steatosis	Less than 5% of hepatocytes contain fat	
Grade 1 steatosis	6–33% of hepatocytes contain fat	Hepatic echogenicity is more than the renal cortex.
Grade 2 steatosis	34–66% of hepatocytes contain fat	Liver echogenicity obscures echogenic wall of portal venous branches.
Grade 3 steatosis	> 66% of hepatocytes contain fat	Diaphragmatic wall and portal venous walls are not visible due increased hepatic echogenicity.

Paul, J. Recent advances in non-invasive diagnosis and medical management of non-alcoholic fatty liver disease in adult. Egypt Liver Journa. 2020;10 (1): 1 – 18. doi:org/10.1186/s43066-020-00043-x

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Fatty Liver S1

Liver texture is not uniform

Kidney less echogenic

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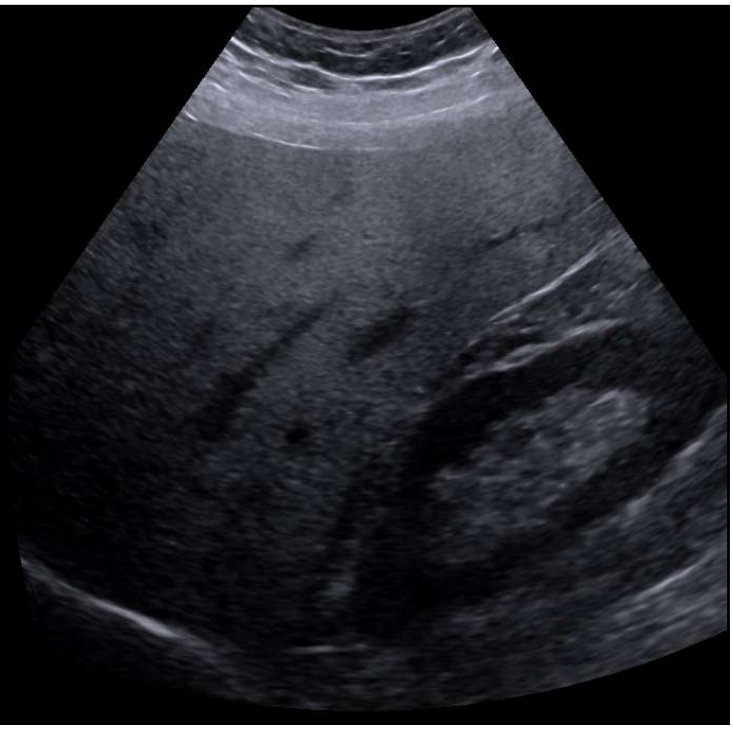
Fatty Liver S2

- Liver texture is not uniform
- No vessel walls are seen
- Far field is dark
- Diaphragm not bright white



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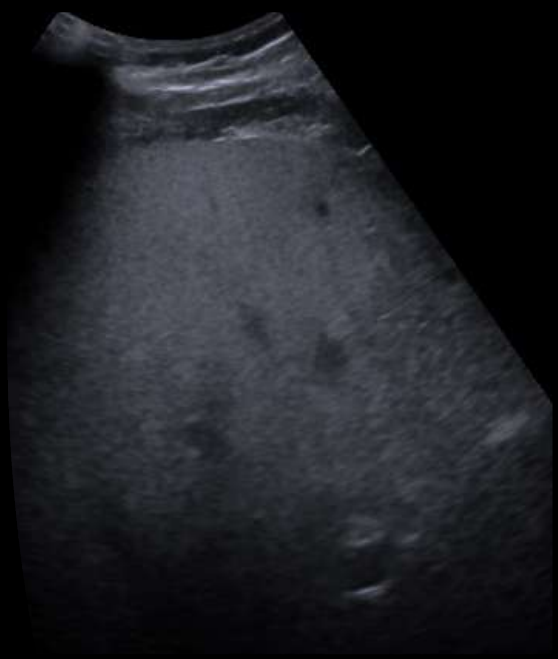
Fatty Liver S3

- No far field echoes
- Can’t see diaphragm



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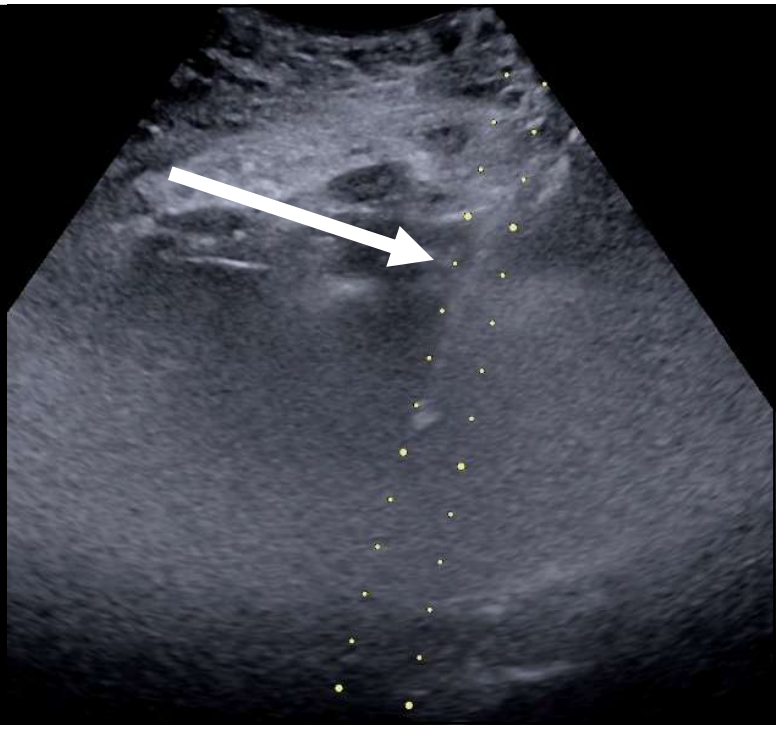
Fatty Liver S3 Where's the Needle?



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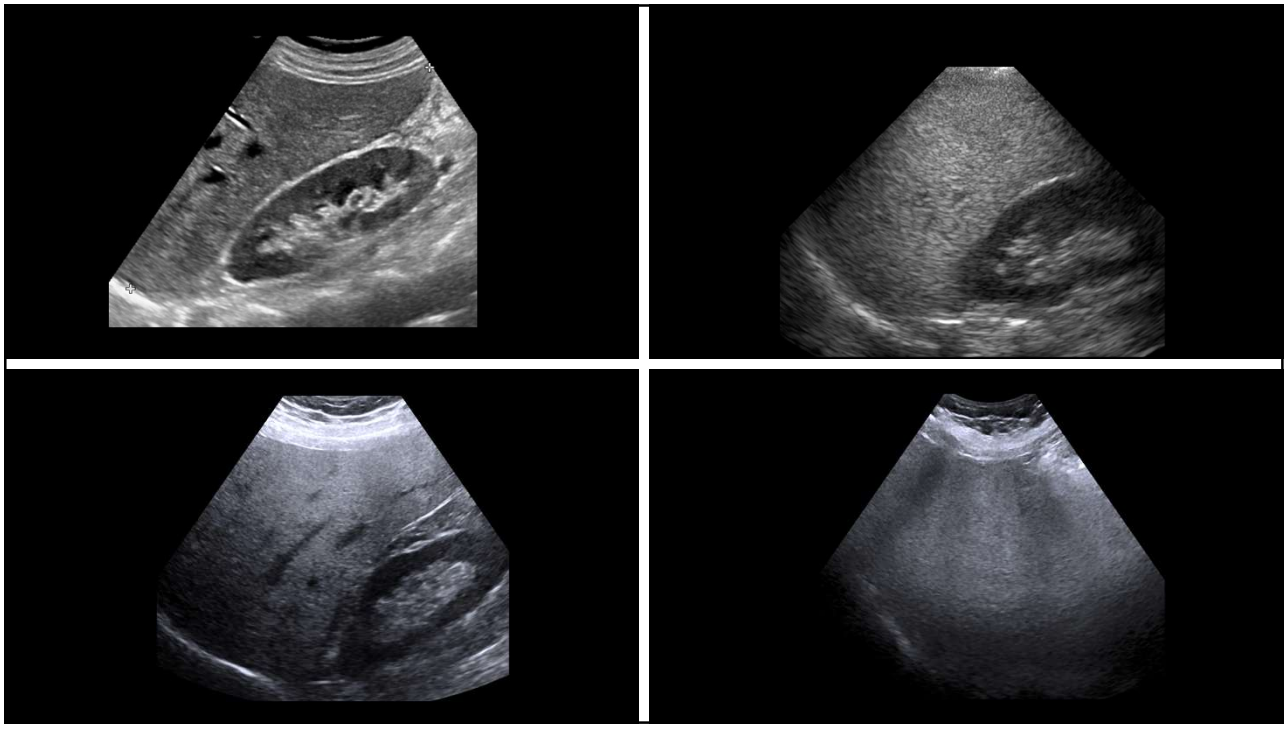

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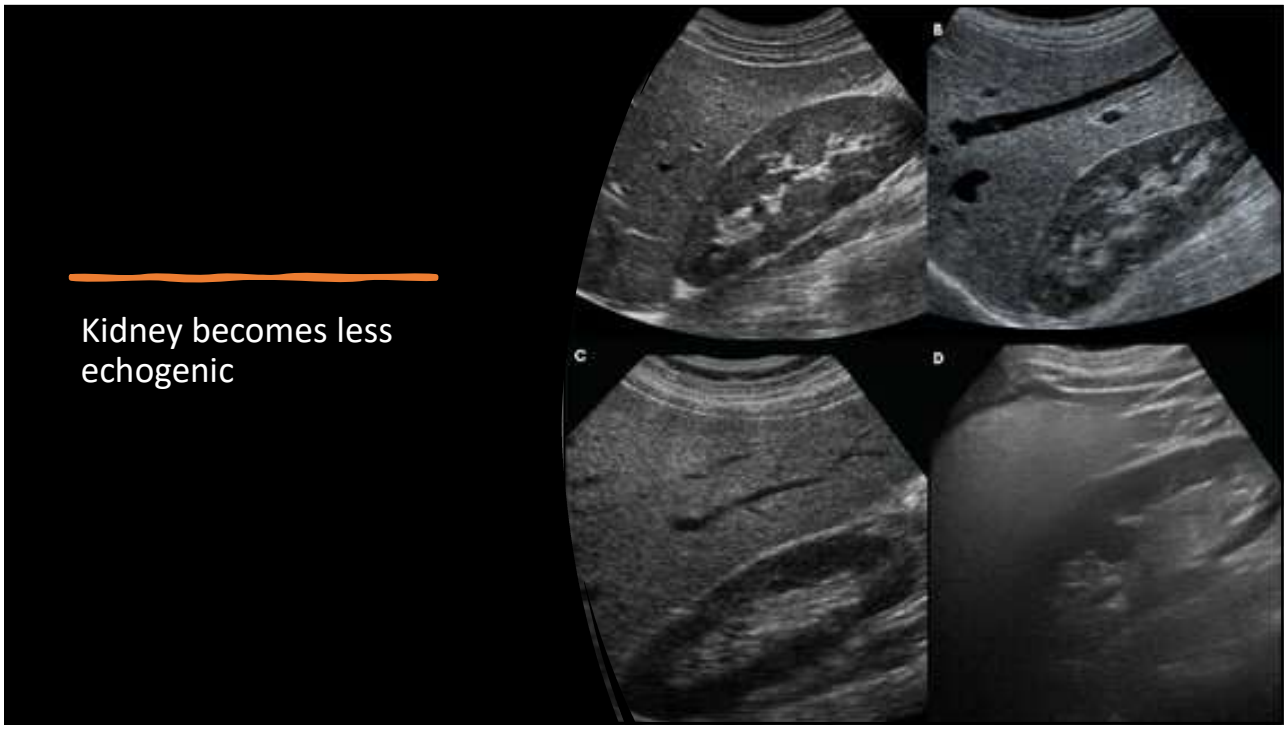

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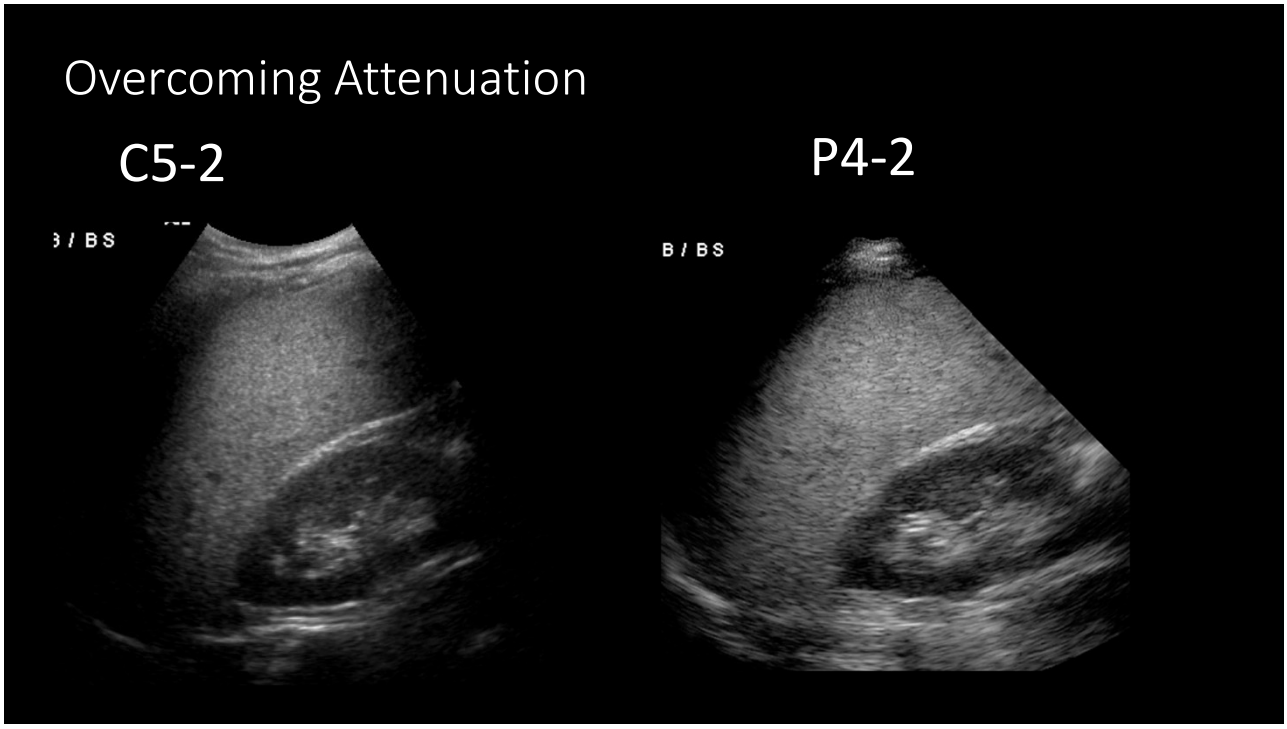

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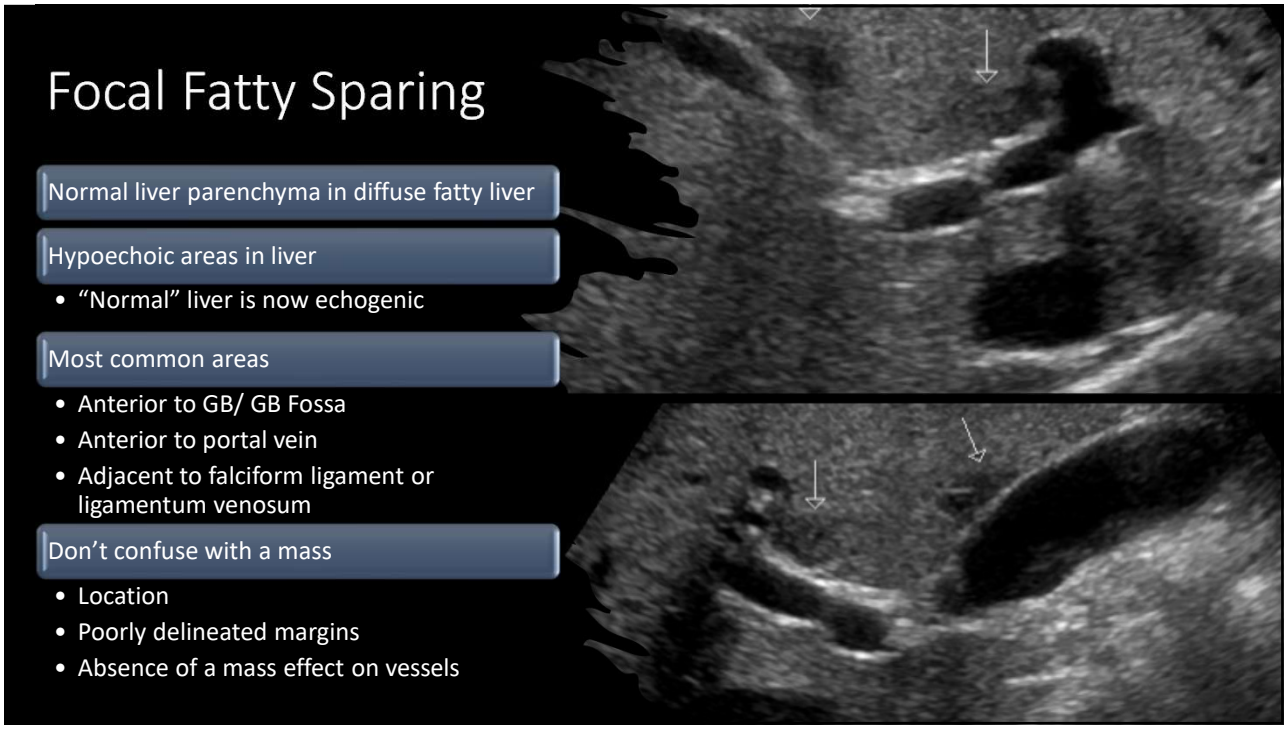

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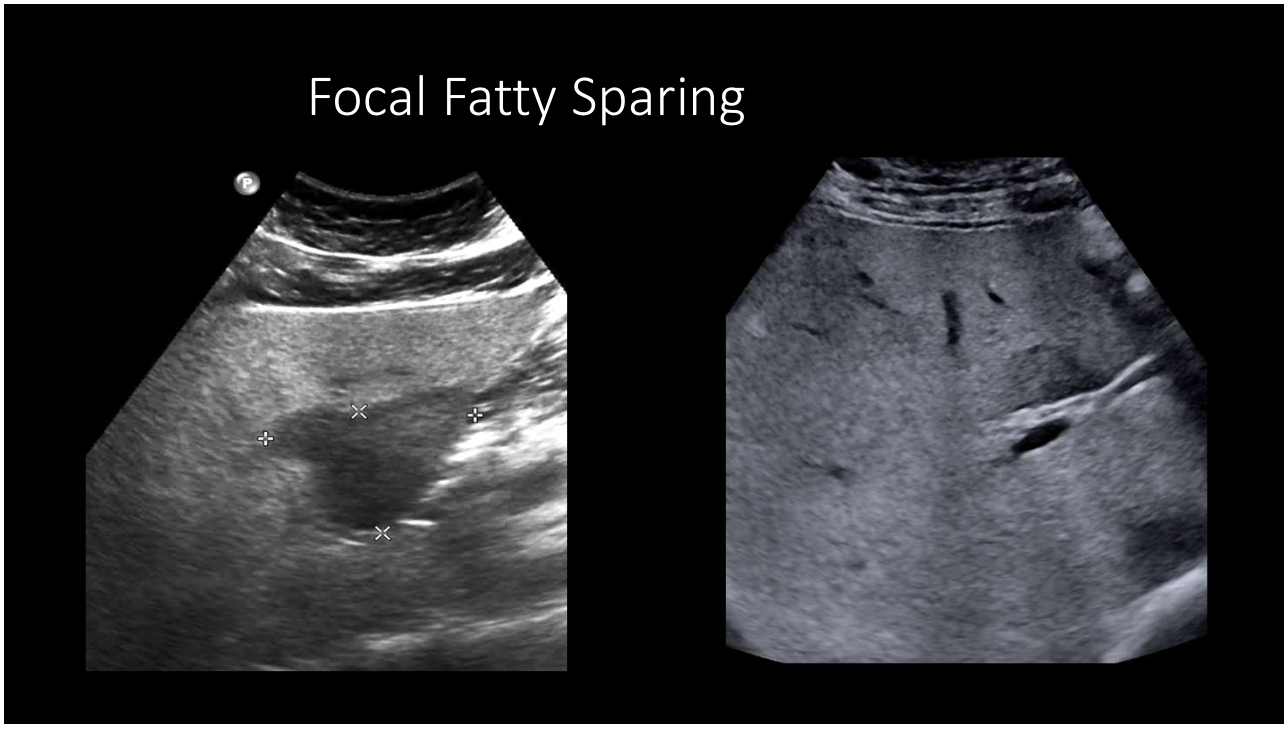

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Focal Fatty Infiltration

Echogenic areas in liver

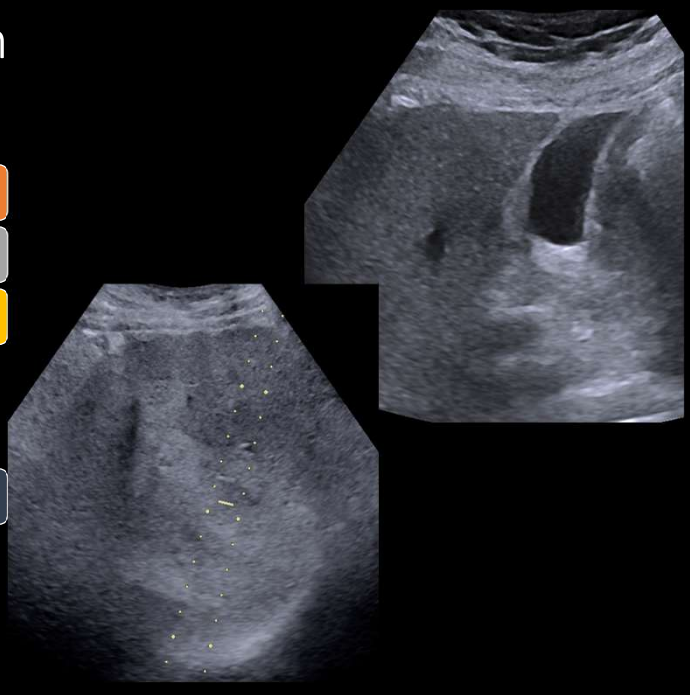
Normal vascular structures course through

Common locations

- Medial segment of left lobe
- Anterior to porta hepatis
- GB fossa
- Porta hepatitis

Differential diagnosis

- Hemangioma
- Neoplasm
- Abscess



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How Does Elastography Help?

Stage degree of liver steatosis

- Goal to prevent liver fibrosis

Stage the amount of liver fibrosis

- Goal to prevent the liver advancing to cirrhosis

Decrease biopsies

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Clinical Importance of Liver Elastography

Stage of liver fibrosis is needed to determine prognosis and treatment

Goal is to prevent fibrotic changes

Monitor progression or regression of MASLD during treatment

- Madrigal
  - Rezdiffra tablets
  - FDA Approved
- Other drugs in trials

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Shear Wave Elastography (SWE)

Types

- Transient Elastography (TE)
- 2D SWE

Assess velocity of shear waves

Propagation velocity of induced shear wave in tissue is measured

- Measured in m/sec
- Converted by Young modulus to kilopascals
- Stiff tissue exhibits a higher shear-wave velocity than does normal tissue.

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SWE

Eating causes increase in liver stiffness that may last for up to 3 hours

- Therefore, fasting for 4-6 hours is recommended

Other conditions can cause an increase in liver stiffness

- Liver congestion, inflammation, acute hepatitis, extra hepatic cholestasis, and infiltrative diseases
- Can't perform with active hepatitis

Stiffness value should be interpreted in context of patient's history, clinical conditions, and laboratory tests

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US Shear Wave Elastography (SWE)

VCTE - **V**ibration-**C**ontrolled **T**ransient **E**lastography or TE - **T**ransient **E**lastography

- Shear waves are generated by a body-surface-controlled vibration
- Measured in kPa
- Most validated and most used in the clinical practice
- 2003

ARFI – **A**coustic **R**adiation **F**orce **I**mpulse

- Shear waves are generated by the push-pulse of US beam
- Point SWE (pSWE) that measures the stiffness in a small and fixed area
- 2D-SWE measures stiffness over a larger area in which a color-coded map of the stiffness is displayed
- Measured in m/s
- 2014

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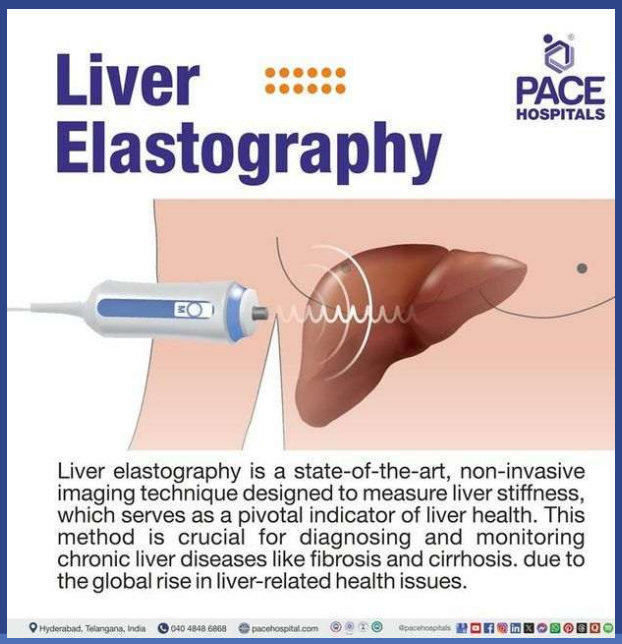
TE

Shear waves are generated in same direction as sound waves



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Vibration Controlled Transient Elastography (VCTE)
Transient Elastography (TE)

Ultrasound transducer mounted on the axis of vibrator

- Controlled vibrating external "punch" on body surface generates shear waves
  - Vibration of a mild amplitude and low frequency (50 Hz)
  - Creates shear wave that propagates through liver

Image of liver is not available on all TE units

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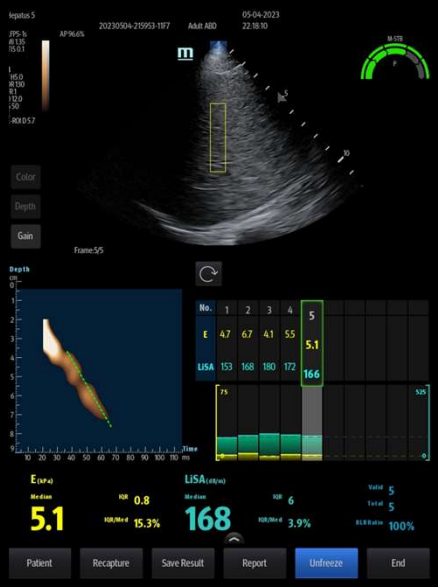
Transient Elastography

- Hepatologists and GI docs have units in office or clinic
- Quick to perform
- Train office personnel (not sonographers)
- Instant results
  - Discuss results and treatment plan if needed on same office visit



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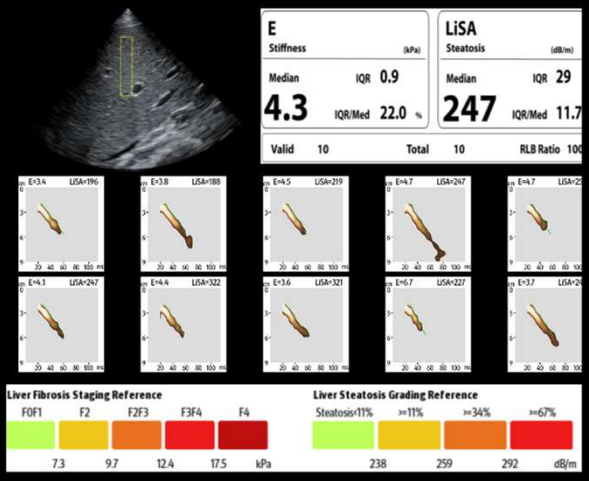
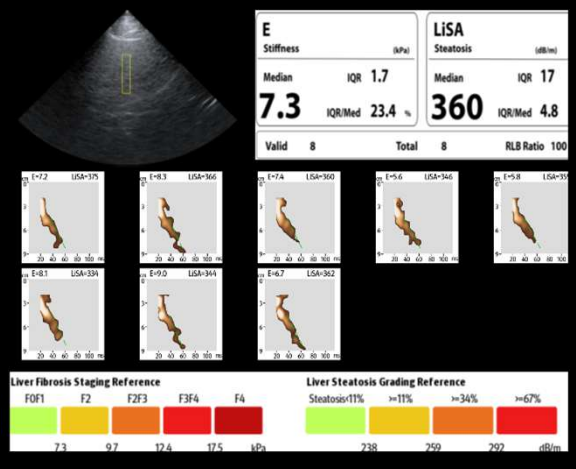
TE WITH IMAGING Abnormal



Mild Steatotic Liver, No fibrosis



F2 fibrosis, Severe Steatotic Liver
Probably MASH

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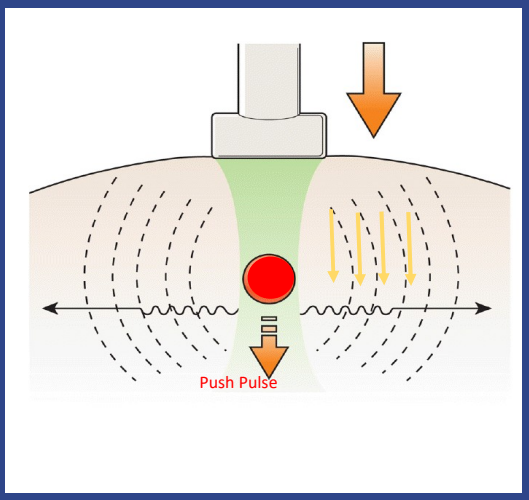
Acoustic Radiation Force Impulse (ARFI)

ARFI is used to generate shear waves

- Deforms tissue and generates shear wave
- Shear waves are generated perpendicular to push pulse

Your hand is "push pulse" slapping puddle of water

- Ripples are shear waves



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ARFI: How Does it Work?

Courtesy of Philips Ultrasound

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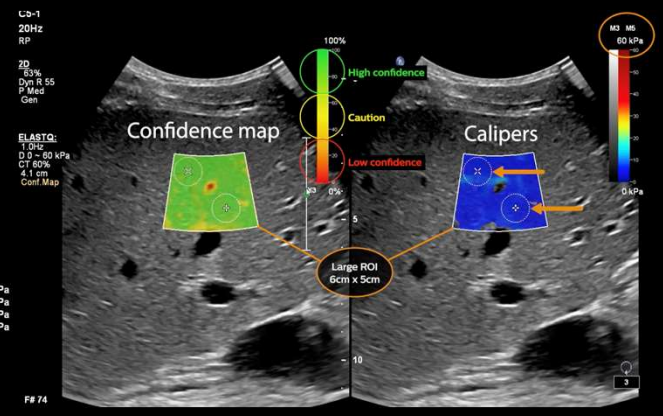
2D Shear Wave

- 2D-SWE evaluates a larger area around 20 cc of tissue
- Allows for multiple measurements inside the ROI
- Each value is an average of several measurements
  - 5 measurements are good when using a confidence map aka a quality assessment map



Courtesy of Philips Ultrasound

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IQR/Median Values

TE	ARFI
• Elastogram - < 30% • Steatosis - < 40%	• kPa- < 30% • m/s - < 15%

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SRU Updated Chart Summary

Below cut-off value there is high probability of no or mild fibrosis	• < 5 kPa or 1.3 m/s
In absence of other known clinical signs rules out cALCD. If there are known clinical signs may need further tests	• < 9 kPa or 1.7m/s
Suggestive of cALCD but needs further evaluation	• 9 – 13 kPa / 1.7 – 2.1 m/sec
Rules in cALCD	• > 13 kPa or 2.1 m/s
Suggestive of CSPH	• > 17 kPa or 2.4 m/s

cALCD=Compensated Advanced Chronic Liver Disease

CSPH – Clinically Significant Portal Hypertension

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- **Compensated Liver Disease:**
- Characterized by liver damage and scarring but without significant impairment of liver function or noticeable symptoms Liver is still able to perform most essential functions, and patients may not be aware they have a problem
- **Compensated Advanced Chronic Liver Disease (cACLD):**
- Specifically describes the stage where liver is still compensating for the damage but has progressed to advanced fibrosis or cirrhosis. It's a stage where patients are at high risk for decompensation
- **Decompensated Liver Disease:**
- Occurs when liver's ability to function is severely compromised leading to jaundice, fluid buildup in the abdomen (ascites), and gastrointestinal bleeding.

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Clinically significant portal hypertension (CSPH)

- Refers to condition where pressure in portal vein is significantly elevated
  - 10 mm Hg or greater, as measured by hepatic venous pressure gradient (HVPG)
- Elevated pressure is hallmark of advanced liver disease
  - Associated with increased risks of complications like variceal bleeding

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Alcoholic Liver Disease

Liver processes excessive alcohol intake

- Overwhelms it leading to fat accumulation

Can impair liver function

Progress to more serious liver diseases

- Alcoholic hepatitis
- Fibrosis
- Cirrhosis

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Alcoholic Liver Disease

Occurs when people drink excessively for several years

Moderate amounts are 14 grams of alcohol

12 fluid ounces of beer	5 fluid ounces of wine	1 shot of distilled spirits (e.g., gin, whiskey, vodka).

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Alcohol Limits

Hard liquor has a higher alcohol content than beer or wine	Serving size of alcohol are:	As of 2023, the National Institutes of Health defines heavy alcohol use as:
• It is false to think that beer or wine are safer alternatives • Any kind of alcohol consumed in higher than moderate amounts can cause severe liver damage	• Beer: 12 ounces • Wine: 5 ounces • Hard liquor: 1 to 1-1/2 ounces	• For men, consuming 5 or more drinks on any day or 15 or more drinks per week • For women, consuming 4 or more drinks on any day or 8 or more drinks per week

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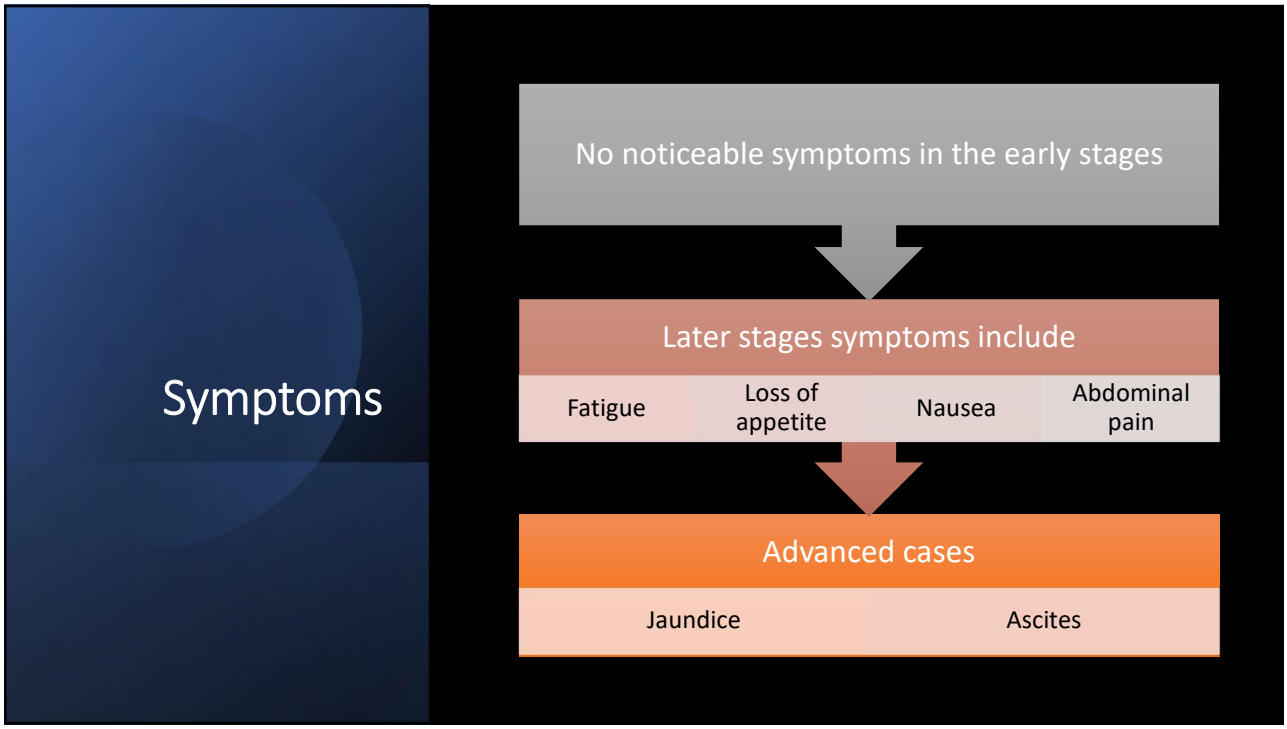

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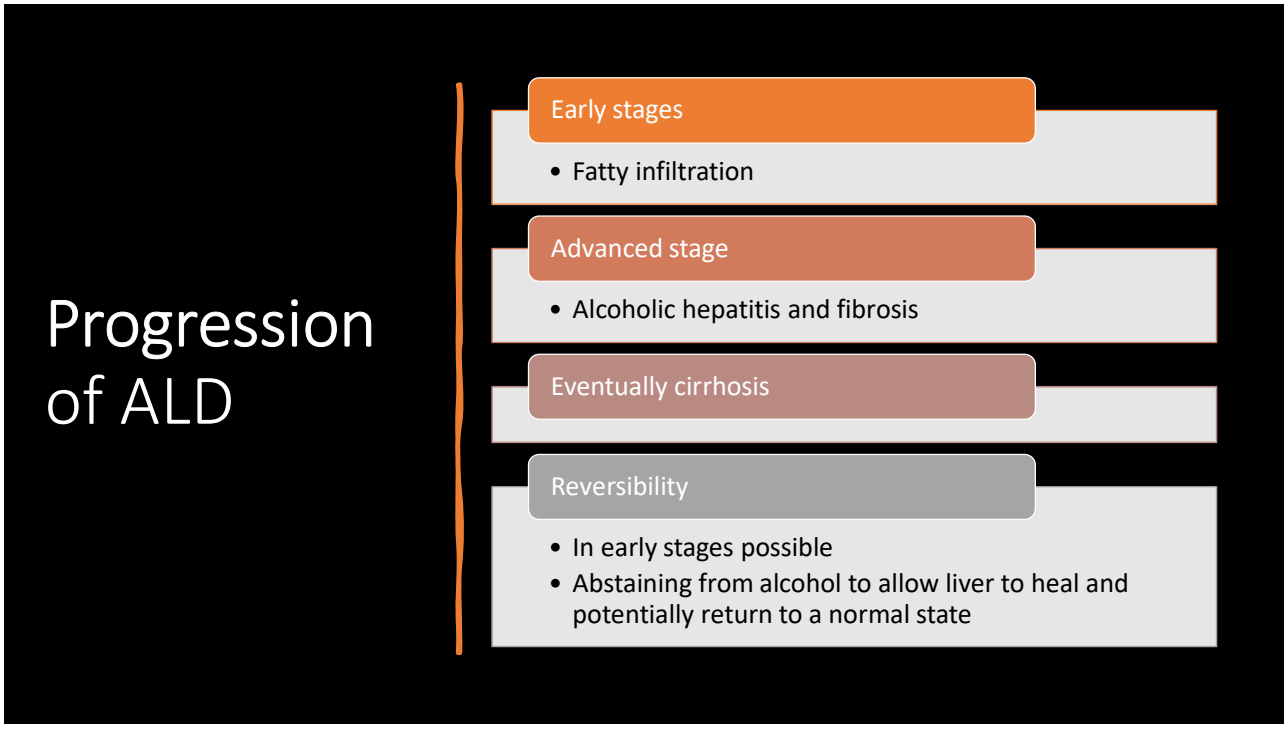

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Treatment

Primary treatment is complete abstinence from alcohol

Managing related complications

- Ascites
- Portal Hypertension

Severe cases

- Liver transplant

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ALD Patients

Increased risk of having hepatitis B or C virus

Patients with alcohol-associated acute hepatitis or cirrhosis can develop

Kidney problems	Gastrointestinal bleeding	Ascites	Liver cancer	Severe infections	Encephalopathy

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Non-Alcoholic Stages to Cirrhosis

Stage 1: Metabolic Dysfunction-Associated Steatotic Liver Disease (Simple fatty liver) (MASLD) Largely harmless build-up of fat in liver cells but not to an extent to cause symptoms

Stage 2: Metabolic Dysfunction-Associated Steatohepatitis (MASH) is a more serious form of MASLD and occurs if liver becomes damaged causing it to become inflamed. MASH is more likely to occur in people who are overweight or obese, or who have diabetes.

Stage 3: Fibrosis occurs when persistent inflammation causes scar tissue, but the liver is still able to function normally.

Stage 4: Cirrhosis, the most severe stage, happens when normal liver tissues are replaced by fibrosis to the extent that the structure and function of the liver is affected and can lead to liver failure and liver cancer.

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Alcoholic Stages to Cirrhosis

Stage 1: Steatosis (Fatty liver) is characterized by an excessive accumulation of fat inside the liver cells. Heavy drinkers usually get to the fatty liver stage in their early years of alcohol abuse.

Stage 2: Alcoholic Hepatitis is characterized by the inflammation of the liver leading to the degeneration of liver cells. Jaundice is the most common symptom in this stage.

Stage 3: Liver Cirrhosis is the last and final stage of Alcoholic Liver Disease where permanent scarring of healthy liver tissue occurs. It is a severe condition and an irreversible one. Ascites and Portal Hypertension can be seen.

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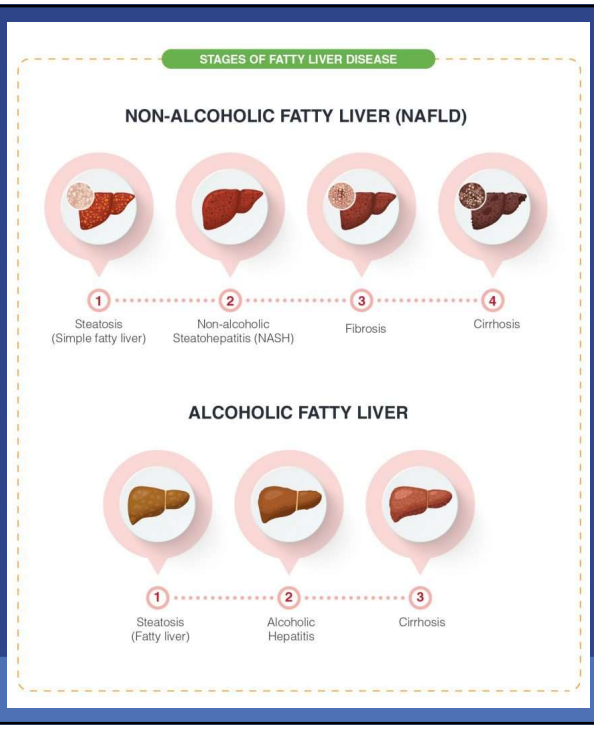

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Conclusion

- US can be helpful in diagnosing fatty liver
- With elastography can monitor changes
- Be careful using harmonics

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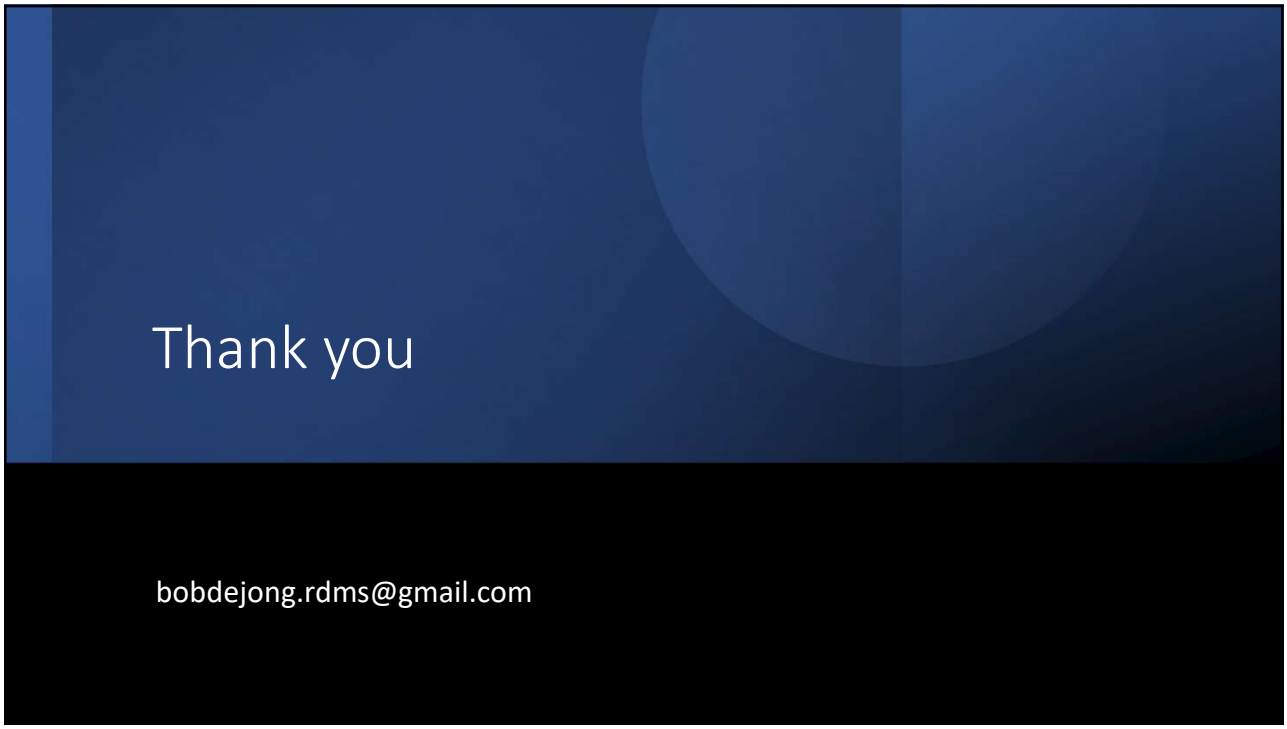

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