Cases in Liver Disease

Clare Hawkins, MD, MSc
Texas Chief Medical Officer
Main Street Health
Houston, Texas

Educational Objectives

By completing this educational activity, the participant should be better able to:

1. Describe the disease burden, natural history and management of nonalcoholic fatty liver disease.
2. Discuss screening strategies and new systemic therapies for liver cancer.
3. Describe end-stage liver disease complications and their management for primary care physicians.

Speaker Disclosure

Dr. Hawkins disclosed that he has no financial relationships with any ineligible organizations or commercial interests.

Cases in Liver Disease

TAFP Texas Family Medicine Symposium
La Cantera Hill Country Resort
Friday June 10th, 8-9 AM
Clare Hawkins, MD, FAAFP
CMO, Main Street Health Texas

1

1

Disclosure

- Dr. Hawkins disclosed that he has no financial relationships with any ineligible organizations or commercial interests.

2

2

Objectives

1. Describe the disease burden, natural history and management of **nonalcoholic fatty liver disease (NAFLD).**
2. Describe **end-stage liver disease complications** and their management for primary care physicians.
3. Discuss screening strategies and new systemic therapies for **liver cancer.**

3

3

Objectives

1. Describe the disease burden, natural history and management of nonalcoholic fatty liver disease.
2. Describe end-stage liver disease complications and their management for primary care physicians.
3. Discuss screening strategies and new systemic therapies for liver cancer.

4

4

Case 1 – Lorenzo

- 60 yo M who is alcohol abstinent but has gained weight over successive years to be 250 lbs. He is 5' 8" so his BMI is 38. He has always been alcohol abstinent.
- Because of some RUQ pain he had Gall Bladder imaging ordered for possible stones but found fatty liver.
- Transaminases were elevated but not Alk Phos.
- His physician ruled out toxic liver medications including acetaminophen.

5

Audience Polling Question #1

What is the next step?

1. Hepatology Referral
2. Liver Biopsy
3. Biochemical estimation of liver fibrosis (blood test)
4. MR elastography

6

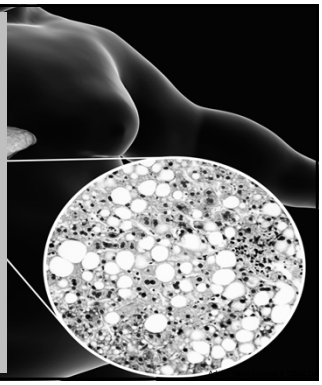
6

7

7

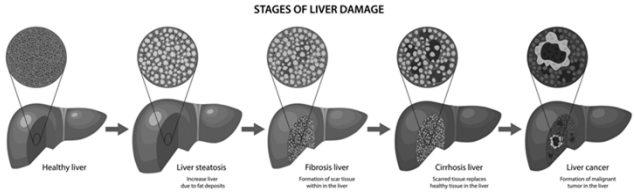
NAFLD

- **Most Common Liver Disease**: up to 30% of adults
- PROJECTION: **100 million people** in the United States will have nonalcoholic fatty liver disease by 2030
- PROJECTION: Direct medical costs of about **$103 billion annually**
- **Tripled since 2004** By 2030 leading cause of liver transplantation



8

- **Nonalcoholic fatty liver (NAFL):** 5% or greater hepatic steatosis without hepatocellular injury or fibrosis
- **Nonalcoholic steatohepatitis (NASH),** progresses to hepatocellular injury and inflammation, with or without fibrosis

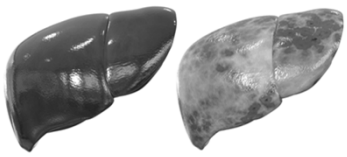


Adobe Stock License # 279207589

9

9

Risk Factors for NAFLD



- Obesity
- DMII
- Metabolic Syndrome
- Dyslipidemia
- Genetic variation of the *PNPLA3* gene
- HIV
- Hypothyroidism
- Obstructive sleep apnea
- Polycystic ovary syndrome

Adobe Stock license # 127487138

10

10

NAFLD: Screening or Testing?

- Screening not recommended
- Suspected in patients with;
  - Elevated liver enzymes
  - Hepatic steatosis on abdominal imaging
- Treatment for NAFLD is same as you wo recommend for people with the risk-factors

Adobe Stock license # 38855413

11

11

Investigation

- Ratio of AST / ALT
- Hepatitis B surface antigen
- Hepatitis C virus antibody
- Ferritin
- Iron
- Fasting Lipids
- Fasting glucose or A1C levels
- Abdominal ultrasonography
- (ANA Anti sm muscle AB)
- (Alpha 1-antitrypsin)
- (Ceruloplasmin)

12

12

How Do We Check For Fibrosis?

- Imaging: Ultrasound preferred but not very sensitive for steatosis < 20%
- **Elastography** tests (vibration controlled or MR elastography)
- Blood Testing with composite score
  - **NAFLD Fibrosis Score** (Age, AST, ALT, Platelets BMI, Albumin)
  - **Fibrosis-4 Score** (Age, AST, ALT, Platelets)
- Biopsy (0.01%- 0.3% mortality and 0.1% to 4.6% major bleeding)

NAFLD fibrosis score http://gihep.com/calculators/hepatology/nafld-fibrosis-Score Accessed 5/23/2022
Fibrosis 4 Score: *http://gihep.com/calculators/hepatology/fibrosis-4-score Accessed 5/23/2022*

13

13

Management of NAFLD (All Evidence Rating "C")

- **Limit alcohol** content, With Liver fibrosis consider abstinence
- Excessive is
  - <21 standard drinks per week for men
  - <14 standard drinks per week for women
- **Vaccinate** for Hep A and B
- **Weight Loss**:
  - 3% to 5% to improve steatosis
  - 7% to 10% fibrosis with NAFLD
- **Mediterranean Diet** reduced liver fat independent of weight loss
- Repeat liver enzyme tests and ultrasonography in **6 to 12 months**
- **If low risk for fibrosis, Follow up 12 to 24 months** with a complete blood count; measurement of liver enzyme, lipid, and fasting glucose or A1C levels; and calculation of fibrosis risk scores (NAFLD Fibrosis Score or Fibrosis-4 Score)

14

14

Management of NAFLD (All Evidence Rating "C")

- Potential Benefit
  - Bariatric surgery
  - Vitamin E (AASLD recommended for non-DMII)
  - Pharmacologic therapy
    - Thiazolidinediones suggested but cause weight gain
    - Glucagon-like peptide-1 analogues (GLP1)
- NASH (can progress)
  - Monitor for progression
  - Higher risk for;
    - CVD, Cancer and ESLD

Patient Ed. https://familydoctor.org/condition/nonalcoholic-fatty-liver-disease/

15

15

Drugs Which Can Cause NAFLD

- Amiodarone
- Aspirin
- Chemotherapy drugs;
  - Fluorouracil
  - Tamoxifen
  - Irinotecan [Camptosar]
  - Cisplatin
  - Asparaginase [Erwinaze]
- Cocaine
- Glucocorticoids
- Methotrexate
- NSAID
- Tetracyclines
- Valproic acid

16

16

Objectives

1. Describe the disease burden, natural history and management of nonalcoholic fatty liver disease.
2. Describe end-stage liver disease complications and their management for primary care physicians.
3. Discuss screening strategies and new systemic therapies for liver cancer.

17

17

Case 2 – Gerald

- A 58 yo M with longstanding intake of alcohol > 6 drinks per day. (but frequently under-represented)
- ED with Abdominal distension and pain.
- Ascites on exam, and with u/s guided paracentesis Liver found to have cirrhosis.
- No jaundice, but persistently elevated transaminases with AST/ALT = 4

Acute-on-Chronic Liver Failure Clinical Guidelines Bajaj, Jasmohan S.; O'Leary, Jacqueline G.; Lai, Jennifer C.; More The American Journal of Gastroenterology. 117(2):225-252, February 2022. https://journals.lww.com/ajg/Fulltext/2022/02000/Acute_on_Chronic_Liver_Failure_Clinical_Guidelines.15.aspx?context=FeaturedArticles&collectionId=2 Accessed 5_4_2022

18

18

Case 2 – Gerald, Cont.

- Careful questioning revealed mild intermittent encephalopathy
- EGD revealed mild varices grade 1 without bleeding.
- He was advised to avoid alcohol and this was reinforced at physician visits and transplant evaluation.

19

Audience Polling Question #2

Alcoholic Cirrhosis is

1. A moral failing
2. A hopeless situation
3. Is easy to treat
4. Is often found late in the course of illness

20

20

Cirrhosis

- 8th leading cause of death in the United States
- Mortality having increased by 45.6% from 1990 to 2013
- $12 billion and $23 billion dollars in health care expenses annually
- 630,000 Americans have cirrhosis, yet less than one in three knows it
- Racial Disparities: prevalence highest among non-Hispanic blacks, Mexican Americans, and those living below the poverty level

21

21

Treatment Costs

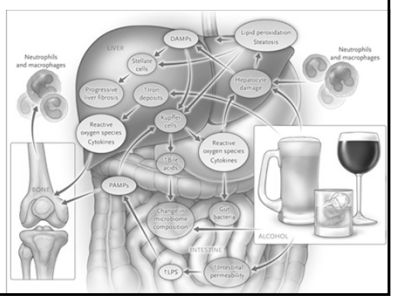
- $2,400 diuretic-sensitive ascites,
- $24,800 diuretic-refractory ascites,
- $25,600 variceal hemorrhage
- $16,400 hepatic encephalopathy
- $44,200 hepatocellular carcinoma
- $163,000 Liver transplant
- Recurring admissions

22

22

- Oxidative stress
- Lipid peroxidation
- Steatosis
- Increased iron deposits
- Hepatocyte damage
- Progressive fibrosis
- Change in microbiome
- Increased intestinal permeability
- Increased Lipopolysaccharides (LPS)
- Translocation of bacterial products
  - Endotoxin
  - PAMP
- (Pathogen associated molecular patterns)

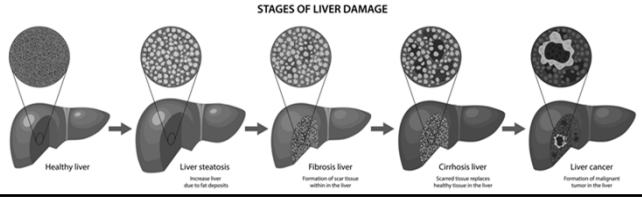
Pathophysiology



23

Pathophysiology of Cirrhosis

- Hepatocyte inflammation then fibrosis, Formation of fibrous septae and nodules
- Collapse of liver structures
- Distortion of hepatic parenchyma and vascular architecture



24

24

Alcoholic Liver Disease

- Alcohol use accounts for 6.8% of age-standardized deaths in men and 2.2% in women, with a disproportionate effect on young people
- Except for tobacco, alcohol accounts for a **higher burden of disease than any other drug**

Singal A et al. ACG Clinical Guideline: Alcoholic Liver Disease. *American Journal of Gastroenterology*. 113(2):175-194, February 2018.
https://journals.lww.com/ajg/Fulltext/2018/02000/ACG_Clinical_Guideline__Alcoholic_Liver_Disease.9.aspx?context=FeaturedArticles&collectionId=2 Accessed 5_4_2022
Fuster D, Samet JH. Alcohol Use in Patients with Chronic Liver Disease *N Engl J Med* 2018; 379:1251-1261

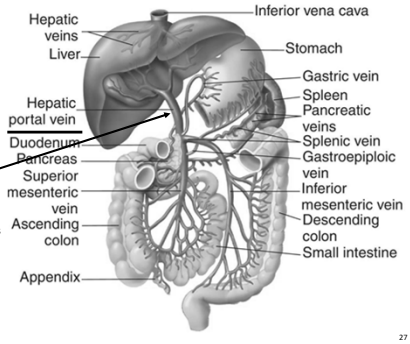
25

Encephalopathy Pathophysiology

- When the liver cannot clear toxins including ammonia, then patient can develop higher levels
- Ammonia level not a direct correlation and not used to track
- Behavioral inventories available to track early cognitive change
- Practically patients with confusion
- Loose stools prevent absorption of toxins and hence, **Lactulose**
- **Rifaximin** prevents bacterial fermentation causing toxins

26

"Plumbing" & Ascites



When blood can't travel through
The liver because of scarring, these vessels
End up with more pressure, and complications
-splenomegaly
-varices
-caput medusae
-ascites

27

Compensated or Uncompensated

- Compensated:
  - Liver Fibrosis but not yet or not active complications
  - 10–15-year life expectancy (4.7 x likelihood of death than the general population)
- Uncompensated:
  - Liver Fibrosis with Ascites, Encephalopathy or Portal Hypertension
  - 2-year life expectancy (Less than 6 m if still drinking alcohol) 9.7 x likelihood of death than the general population

28

Causes of Liver Disease in US

- Alcohol
- Hepatic Steatosis
- NAFLD
- Hepatitis B & C
- Hemochromatosis
- Wilson's Disease
- Primary Biliary Cirrhosis
- Sclerosing Cholangitis
- "Cardiac Cirrhosis"

29

Diagnosis:

- History:
  - Alcohol
  - FHX
  - Medication Review
  - CHF
- Physical Exam
  - Liver enlargement
  - Jaundice
  - Ascites
  - Other Liver Stigmata
    - Liver flap
    - Palmar erythema

30

Wilson's Disease

- COPPER
- Rare autosomal recessive genetic disorder related to ineffective copper metabolism.
- One in 30,000 persons
- Eastern Europeans
- Presents before 40 years of age
- Kayser-Fleischer rings (i.e., copper deposition around the cornea) Brown
- Neuropsychiatric symptoms
- Serum ceruloplasmin

31

31

Autoimmune Hepatitis

- 11 to 17 per 100,000 persons
- More often in women
- Commonly associated with other autoimmune disorders
- Hypergammaglobulinemia is common, and the total gamma globulin or immunoglobulin G levels are generally 1.2 to 3.0 times normal
- Serum protein electrophoresis testing has high sensitivity for autoimmune hepatitis
- ANA has lower sensitivity and specificity
- Could include smooth muscle antibody and liver/kidney microsomal antibody type 1 testing

32

32

Primary Biliary Cholangitis

- Formerly Primary Biliary Cirrhosis
- Mostly affects women, FHx, all races but predominantly Northern European
- Chronic inflammation causes bile duct damage then scarring

33

33

Abnormal Liver Chemistries (Expert Consensus ACG 2017)

- **Hepatocellular injury** is defined as disproportionate elevation of AST and ALT levels compared with alkaline phosphatase levels
- **Cholestatic injury** is defined as disproportionate elevation of alkaline phosphatase level as compared with AST and ALT levels
- If Abnormal Liver Tests, repeat the serum chemistry, or order a clarifying test, **GGT** if serum alkaline phosphate is elevated
- **GGT** should not be used as a screening test without other Liver tests since it is non-specific

ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries
Kwo, Paul Y; Cohen, Stanley M; Lim, Joseph K, *American Journal of Gastroenterology*. 112(1):18-35, January 2017.
https://journals.lww.com/ajg/Fulltext/2017/01000/ACG_Clinical_Guideline__Evaluation_of_Abnormal.13.aspx?context=FeaturedArticles&collectionId=2 Accessed 5_4_2022

34

34

Abnormal Liver Chemistries (Expert Consensus ACG 2017)

- Elevated ALT has been associated with increased liver-related mortality
- AST>ALT should be considered at risk for alcoholic liver disease
- <5X ULN: **A**lcohol, **C**eruloplasmin, Alpha 1 antitrypsin
- 5–15X ULN, evaluation should also assess for acute hepatitis A, B, and C
- ALT and/or AST levels >15X ULN, acetaminophen toxicity or shock liver

ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries
Kwo, Paul Y; Cohen, Stanley M; Lim, Joseph K, *American Journal of Gastroenterology*. 112(1):18-35, January 2017.
https://journals.lww.com/ajg/Fulltext/2017/01000/ACG_Clinical_Guideline__Evaluation_of_Abnormal.13.aspx?context=FeaturedArticles&collectionId=2 Accessed 5_4_2022

35

35

36

Alcohol & Cirrhosis

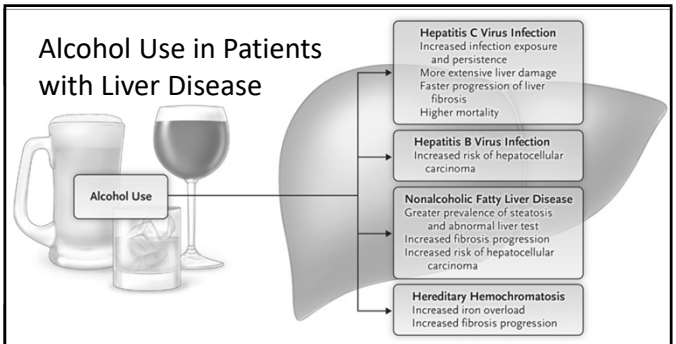
- 30% of the U.S. population is affected by alcohol misuse
  - Most of these persons engage in risky use
  - >85,000 deaths/ y attributable to alcohol misuse
  - 3rd leading cause of preventable deaths in the US and increasing
  - ~8-10% of Physicians have Alcohol Use Disorder

Adobe Stock license #138899977

37

37

Alcohol Use in Patients with Liver Disease



Fuster D, Samet JH Alcohol Use in Patients with Chronic Liver Disease *N Engl J Med* 2018; 379:1251-1261

38

38

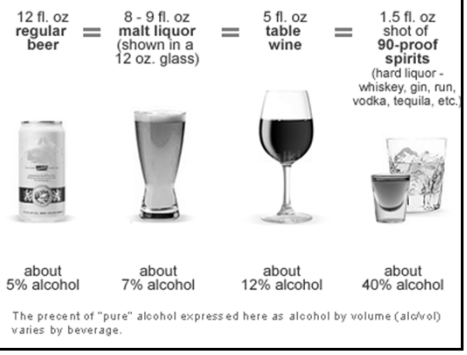
Early Identification & Prevention Alcohol

- **AUDIT** screen for risky use of alcohol has best benefit of sensitivity, specificity
- **AUDIT-C** (three questions)
- **Single Question**: "*How many times in the past year have you had 5 [for men] or 4 [for women and all adults older than 65 years] or more drinks in a day?*"
- CAGE (Cut-down, annoyed, Guilty, Eye-Opener)

39

39

Alcohol Equivalents



40

40

First Audit-C Question

How often do you have a drink containing alcohol?

0. Never
1. Monthly or less
2. 2-4 times a month
3. 2-3 times a week
4. 4 or more times a week

41

41

Second Audit Question

How many standard drinks containing alcohol do you have on a typical day when drinking?

0. 1 or 2
1. 3 or 4
2. 5 or 6
3. 7 to 9
4. 10 or more

42

42

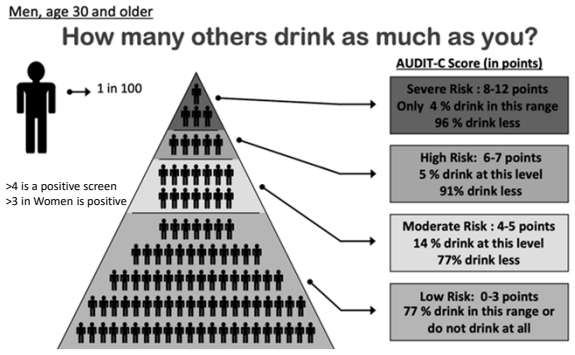
Third Audit Question

How often do you have six or more drinks on one occasion?

0. Never
1. Less than monthly
2. Monthly
3. Weekly
4. Daily or almost daily

43

43



44

Harmful Use of Alcohol ICD-10

- A pattern of drinking that causes damage to physical or mental health
- F10.9 Alcohol use, unspecified
- F10.92 Alcohol use, unspecified with intoxication
- F10.920 Uncomplicated
- F10.921 Delirium
- F10.929 Unspecified
- F10.94 With alcohol-induced mood disorder
- F10.28 Alcohol dependence with other alcohol-induced disorders

45

45

Alcohol Use Disorder 2 of;

1. Alcohol is often taken in larger amounts or over a longer period than was intended
2. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use
3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects
4. Craving, or a strong desire or urge to use alcohol
5. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home
6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol

DSM V 2013

46

46

Alcohol Use Disorder 2 of;

7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use
8. Recurrent alcohol use in situations in which it is **physically hazardous**
9. **Alcohol use is continued despite knowledge of having a persistent or recurrent physical** or psychological problem that is likely to have been caused or exacerbated by alcohol
10. Tolerance, as defined by either of the following:
    7. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect
    8. A markedly diminished effect with continued use of the same amount of alcohol
11. Withdrawal, as manifested by either of the following:
    7. The characteristic withdrawal syndrome for alcohol
    8. Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms

DSM V 2013

47

47

Alcohol and Cirrhosis Prognosis

- 65% of the patients who abstain from drinking alcohol are alive at 3 years
- 0% are alive at 3 years who continue drinking alcohol

Adobe Stock license # 51740483

48

48

Prognosis in Advanced Liver Disease

- **Surprise Question**: "Would you be surprised if this patient passed away in the next year?"
- **Functional Parameters**: (Palliative Performance Score)
- **Behavioral Parameters**: If not abstinent prognosis drops precipitously
- **Complications**: Every upper GI bleed from varices lowers prognosis
- **Hypotension**: Mean BP of 82 (from lack of clearance of nitric oxide)
- **Scoring Systems**: Child-Pugh, MELD and ACLF

49

49

Child-Turcotte-Pugh Classification

Clinical Criteria	1	2	3
Encephalopathy	None	Mild-moderate	Severe (gr 3-4)
Ascites	None	Mild - moderate	Large or refractory to diuretics
Bilirubin (mg/dl)	<2	2-3	>3
Albumin (g/dl)	> 3.5	2.8-3.5	<2.8
PT: seconds	< 4	4-6	>6
INR	<1.7	1.7-2.3	> 2.3

THREE GROUPS: A (5-6 points), B (7-9 points) or C (10-15 points)

50

50

MELD (Model for End Stage Liver Disease)

- Primarily used to stratify patients ≥12 years old on liver transplant waiting lists.
- Predicts mortality in the following scenarios:
  - (a) After transjugular intrahepatic portosystemic shunt (**TIPS**)
  - (b) Patients with Cirrhosis having **non-transplantation surgical** procedures
  - (c) acute **alcoholic hepatitis**
  - d) acute **variceal** hemorrhage.
- In February 2002, MELD was accepted by the United Network for Organ Sharing (UNOS) for prioritization of patients waiting for liver transplantation in the United States, **replacing the Child-Pugh Score**
- It has been widely studied and validated.
- The MELD was updated in January 2016 and **now includes serum sodium** level.

51

51

Risk Scoring: MELD: Example Values

- INR 2.0
- Total Bili 3
- Serum Cr 1.5
- Serum Na 130
- Dialysis > = 2 x week: No
  - MELD 22, Mortality 19.6%

- 40= 71.3% mortality
- 30-39 = 52.6 mortality
- 20-29 = 19.6% mortality
- 10-19 = 6.0 % mortality
- < 9 = 1.9% mortality

Kamath PS. *Hepatology*. 2001 Feb 33(2): 464-70, Kim WR. *NEJM* 2008 Sep 4;359(10): 1018-26

52

52

ACLF (Acute on Chronic Liver Failure) Grade

0. No organs failing (except brain) Cr < 1.5
1. One organ failing (kidney, liver or brain with high Cr)
2. Two organs failing
3. Three organ failing

53

53

Mortality of Patients with Cirrhosis Based on Three Scoring Systems

	28 day	90 day	365 day
Child-Pugh			
A			5
B			20
C			55
MELD Score			
10-19		6	
20-29		20	
30-39		53	
ACLF Grade			
ACLF 1	22	41	
ACLF 2	32	52	
ACLF 3	77	79	

- Child Pugh
- MELD Score used for Transplant Consideration
- Meld-Na score slightly better
- ACLF is able to better predict short term prognosis
- ACLF is dynamic and may be best calculated on day 5-7 of a hospital stay

54

54

Cirrhosis Complications & Management

Complication	Treatment	Prevention
Ascites	Diuretics & Na restriction Spironolactone/ Furosemide 4:1 Therapeutic paracentesis Consider Transjugular intrahepatic portosystemic shunt for refractory ascites	Not fluid restriction Universal Hep C screening (USPSTF) Birth Hep B vaccination
Hepatic Encephalopathy	Lactulose Rifaximin	Avoid sedatives Protein restriction not beneficial
Pain Management	Acetaminophen max 2g/d Opioids (fentanyl, morphine and buprenorphine) lower starting dose and longer interval	Avoid NSAID due to risk of mucosal bleeding and renal impairment, precipitating hepatorenal syndrome
Malnutrition	Late evening snack before bedtime (210 Kcal)	No role for protein restriction
Depression	SSRI no alteration in starting dose but maximum dose reduced by 1/2	Avoid TCA due to sedative and anticholinergic
HTN	Often necessary to d/c antihypertensives (even propranolol for variceal prevention	Avoid ACE inhibitors

55

Encephalopathy

- When the liver cannot clear toxins including ammonia, then patient can develop higher levels
- Ammonia level **not** a direct correlation and not used to track
- Behavioral inventories available to track early cognitive change
- Loose stools prevent absorption of toxins and hence, **lactulose**
- Rifaximin prevents bacterial fermentation causing toxins (Good Rx = $500/m)
- Assign a family member / support person to supervise medications

56

56

Encephalopathy

- Apathy, irritability, attention, working memory, psychomotor speed, visuospatial ability, disinhibition
  - Often reported by relative
- Progressive disorientation to time and space
- Inappropriate behavior
- Acute confusional state
- 21% with decompensated liver failure, 10-50% of TIPS,
- Overall, 30-40% of those with cirrhosis at some time in their clinical course, usually repeatedly
- Risk is 5-25% within 5 yrs of cirrhosis dx
- Risk is 40% of recurrence after initial episode

57

57

Varices

- Vigilance for coffee ground emesis or melena
- Grades:
  - Grade 1 – Small, straight esophageal varices
  - Grade 2 – Enlarged, tortuous esophageal varices occupying less than one third of the lumen
  - Grade 3 – Large, coil-shaped esophageal varices occupying more than one third of the lumen
- Present in 30% of patients with Cirrhosis but increase to 90% at 10 yrs
- 7% year
- 1 year rate of bleed is 12%
- Rebleed rate is 60%
- 6-week mortality from each episode is 20%

58

58

Varices: Hospital Treatment

- Vasopressin, somatostatin, and analogues octreotide and vapreotide parenterally in ICU.
- TIPS as salvage therapy for 10-20% of patients whom medical therapy fails
- 6-12 Endoscopy surveillance and sclerosis as indicated, (goal is variceal obliteration)
- Antibiotic prophylaxis ceftriaxone, norfloxacin or cipro

59

59

Esophageal Varices Treatment

- Beta-blockers for primary and secondary prevention
- **Non-selective B Blockers** (i.e., propranolol)
- EGD Only if moderate-to-large esophageal Varix with or without variceal bleeding
- Prognosis much worse with each bleeding episode
- EGD performed for ablation of bleeding varices
- Octreotide rx for initial episode
- Bleeding risk increases with coagulopathy
- "Window Closes"
  - no longer effective when refractory ascites, hypotension, the hepatorenal syndrome, spontaneous bacterial peritonitis, sepsis, or severe alcoholic hepatitis develops

Patient Resources: Cirrhosis and Portal HTN
https://familydoctor.org/condition/cirrhosis-and-portal-hypertension/

60

60

Caput Medusae

- Palm Tree sign
- Distended, engorged superficial epigastric veins
- Radiating from umbilicus across abdomen

61

61

Physical Exam Ascites

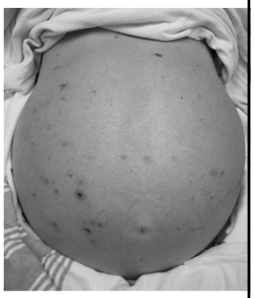
- Full, bulging abdomen should prompt percussion of flanks
- Tympany-dullness interface 1,500 ml
- Shifting dullness 83% sensitive and 56% specific
- Fluid Wave and Puddle Sign cumbersome and less sensitive

62

62

Ascites

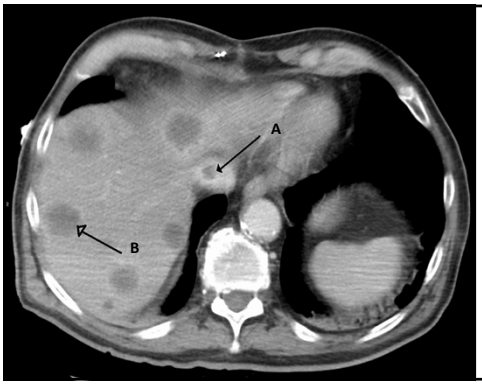
- 85% due to Cirrhosis
  - Ask about lifetime BMI, and DM II (NASH risk) & alcohol intake
- 15% nonhepatic cause of fluid retention
  - Peritoneal carcinomatosis (does not respond to diuretic therapy)
  - Cancer with massive liver metastasis
  - Pancreatitis
  - Heart failure, renal, (nephrotic) thyroid disease, (myxedema) TB
  - Post-op lymphatic leak
  - Budd-Chiari



Wikipedia image CC BY-SA 3.0 citation James Heilman. https://en.wikipedia.org/wiki/Ascites#/media/File:Hepaticfailure.jpg Accessed 8_12_17

63

63



Budd Chiari

A. IVC Clot
B. Metastases to Liver

64

64

Ascites Treatment

- High Volume Paracentesis
- Infuse Albumin if high-volume
- Spontaneous Bacterial Peritonitis (SBP)
- Spironolactone if Cr > 30 and no hyperkalemia at ratio 4 x furosemide
- Sodium restriction, not fluid restriction
- TIPS Transjugular Intrahepatic Portosystemic Shunt

65

65

Spontaneous Bacterial Peritonitis (SBP)

1. Bacterial translocation from the gut to mesenteric lymph nodes
2. Depressed activity of the reticuloendothelial phagocytic system
3. Decreased antimicrobial capacity of ascitic fluid

- 12% at time of hospital admission for paracentesis, therefore, conduct paracentesis (I,B)
- PMN count > 250 without an obvious cause
- "Clinical" diagnosis without paracentesis not adequate
- Empiric treatment does not permit appropriate narrow antibiotic spectrum: Third generation cephalosporin

66

66

SBP Prevention

- **Prophylactic** oral **Norfloxacin** for people with cirrhosis and ascites with an ascitic protein of 15 g/liter or less, until the ascites has resolved.
- PPI increases rate of SBP so restrict use
- Variceal hemorrhage: Norfloxacin 400 bid 7 d or ceftriaxone 1g/d x 7 d (I,A)
- Prior SBP, low protein ascites 69% recurrence,
  - Norfloxacin (or tmp/smx) continuously to patients after first episode (I,A)
  - Intermittent dosing inferior (IIb, C)

67

67

Hepatic Hydrothorax

- In 5% of those with ascites
- Ascites passes to chest through diaphragmatic defect
- Avoid chest tubes
  - Thoracentesis
  - Medical therapy preferred (same regimen as cirrhosis)
  - Consider spontaneous Bacterial Empyema

68

TIPS Procedure

- Catheter in hepatic vein
- Guidewire into a portal vein branch
- Dilatation with balloon & contrast
- Self-expandable metallic stent yet to be placed over the wire
- Better ascites control +/- survival advantage
- Higher cost, and more encephalopathy?
- Cardiac EF > 60%, and no parenchymal renal disease

69

69

Umbilical Hernia

- 20% of patients with ascites
- Frequently can become strangulated during paracentesis
- Train patients in reducing manually, and wearing abdominal binder
- Avoid surgery, if possible, (73% if ascites present during surgery)
- Surgeon with familiarity

70

70

Ascites: Diagnostic Paracentesis (IIa, C)

- Ultrasound guided
- SAAG, Ascitic total fluid protein, Cell Count, Culture (in Aerobic and Anaerobic Bottles)
- **Cytology only if high index of suspicion**, hand-carry to lab, three samples 83%, 93%, 97%
  - Breast, colon, gastric, pancreas
- Could use NAAT or mycobacterial culture if high suspicion $$ (Immunosuppressed or endemic area)
- **No need for CA 125**: will be elevated when mesothelial cells under pressure from fluid (therefore very nonspecific)

71

71

Serum-Ascites Albumin Gradient (SAAG)

- To diagnose cause of ascites
- With portal hypertension, fluid is pushed into the ascites
- Serum protein is more concentrated
- Albumin is a large molecule and does not easily move across the membrane

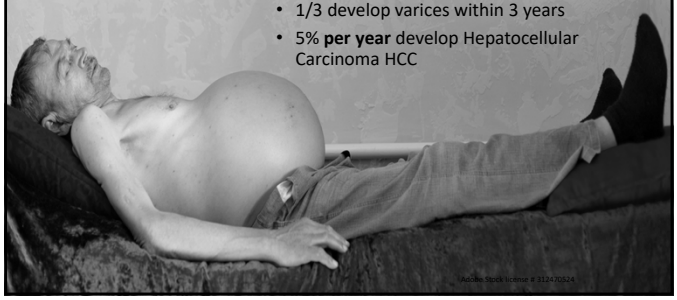
- Test albumin in serum and ascitic fluid on same day
- Subtract ascitic value from serum
- >=1.1 the patient has portal hypertension 97% accuracy
- Retains accuracy despite fluid infusion and diuretic use

72

72

Ascites Prognosis

- 15% die within a year
- 45% die within 5 years
- 1/3 develop varices within 3 years
- 5% **per year** develop Hepatocellular Carcinoma HCC



Adobe Stock license # 312470524

73

Malnutrition and Reduction of Liver Protein Synthesis

- 20-40% of patients with cirrhosis
- 1.0-1.5 gm/kg (of dry body weight), of protein per day in diet
- Lack of synthetic function of liver
  - All proteins
  - Coagulation factors
- Muscle Wasting (Sarcopenia)
- 2021 AASLD guideline

https://www.aasld.org/sites/default/files/2021-07/Malnutrition%2C%20Frailty%20Sarcopenia%20In%20Patient%20w%20Cirrhosis%202021%20hep.32049.pdf. Accessed 5_4_2022

74

74

Thrombocytopenia

- Sometimes the first indication of Cirrhosis
- Low Platelets (from sequestration in a swollen spleen from portal hypertension)
- High INR from reduced synthesis of Vitamin-K dependent clotting factors
- Stop Aspirin and other anticoagulants
- Not needing transfusion until < 25

75

75

Blood Pressure & Prognosis

- Patients with cirrhosis and Hypertension often become normotensive then hypotensive
- Nitric Oxide accumulation
- Mean arterial pressure (MAP) of 82 mm Hg or less is most strongly correlated with reduced **survival**
  - 20% at 24 months
  - 0% at 48 months
- MAP > 82
  - **70%** at 24 months **survival**
  - **50%** at 48 months **survival**
- Hepatorenal (not the same as concurrent CKD)
  - Poor renal perfusion with reduced BP
- Stop Antihypertensives and propranolol

76

76

Transplant Criteria

- The status of the person's liver disease
- Other diseases and conditions the person has
- The likelihood the person will survive the transplant operation
- The person's ability to follow instructions and the complex medical regimen required after a transplant
- The person's mental and emotional health
- The person's support system
- Organ Supply
- The national waiting list is maintained by the United Network for Organ Sharing (UNOS), which administers the U.S. Organ Procurement and Transplantation Network (OPTN) under contract with the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services.
- Long Term Anti-rejection meds
- 80-85% of livers are functioning at one-year

https://www.niddk.nih.gov/health-information/liver-disease/liver-transplant 12/25/2016

77

77

Objectives

1. Describe the disease burden, natural history and management of nonalcoholic fatty liver disease.
2. Describe end-stage liver disease complications and their management for primary care physicians.
3. Discuss screening strategies and new systemic therapies for liver cancer.

78

78

Case 3 – Rhonda

- 62 yo F with remote history of injection drug use and more recently **Alcohol Use Disorder.**
- After intervention from family and AA x 2, she has been abstinent for 15 months
- Completed antiviral treatment for Hep C 2 years ago and his Hep C RNA PCR is not detectible
- Last week she developed jaundice and RUQ discomfort
- Imaging revealed multiple liver nodules > 1cm which were biopsy proven to be Hepatocellular Carcinoma (HCC)

79

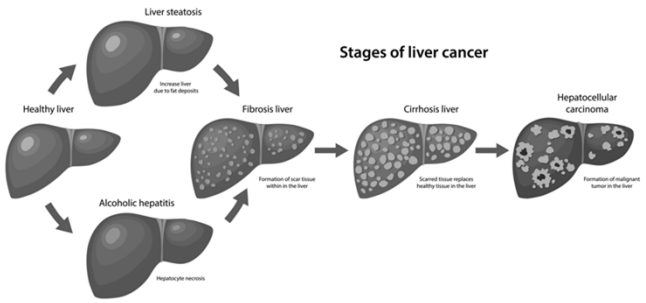
Audience Polling Question #3

Rhonda has tumors in three separate areas of the liver, each 1.5 cm. At this point she is potentially eligible for:

1. Surgical resection
2. Brachytherapy (focal radiation)
3. External Beam radiation
4. Chemotherapy
5. All of the above

80

80



Adobe Stock license # 279207546

81

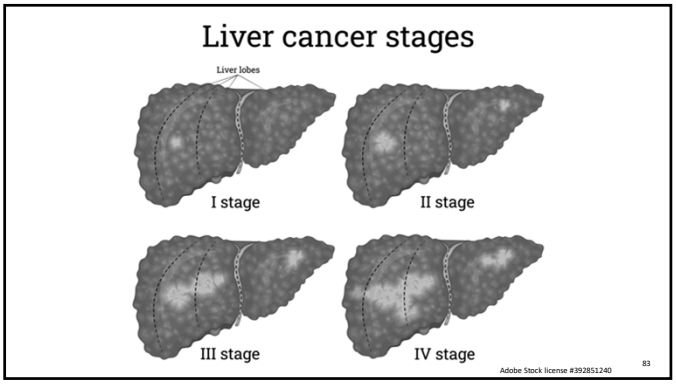
81

Hepatocellular Carcinoma HCC

- Liver Cancers are usually metastatic
- However, with cirrhosis comes a progressive risk for primary liver cancer
- 5 % of patients with cirrhosis (regardless of cause) **per year** develop liver cancer
  - (hence screening recommendations)
- It is a tumor of the Hepatic Cell, hence HCC

82

82

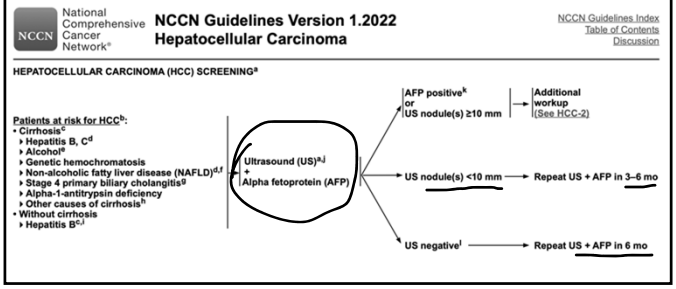


Adobe Stock license #392851240

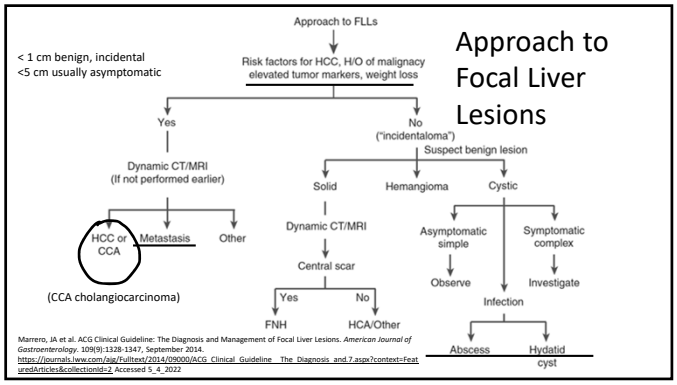
83

83

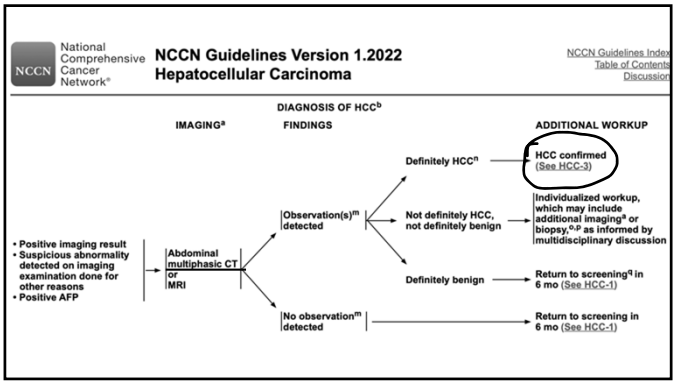
Screening for HCC in Patients with Ascites



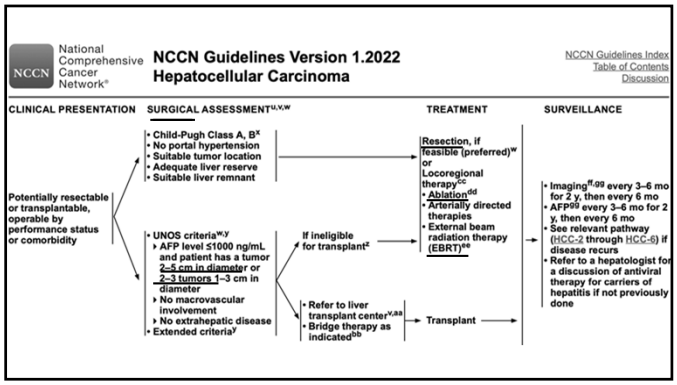
84



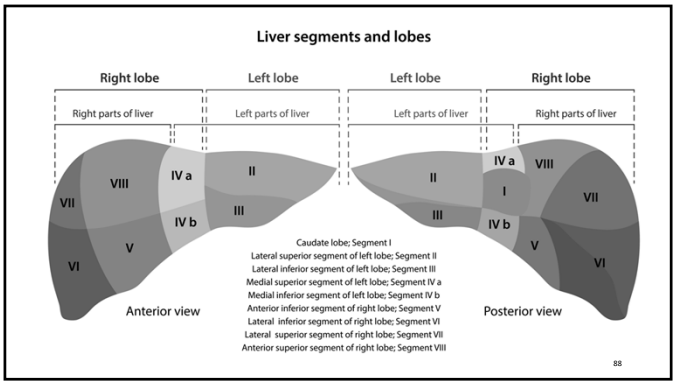
85



86



87



88

Summary

- NAFLD:
  - Common, no screen, lifestyle +
- Cirrhosis:
  - Encephalopathy, Ascites, Thrombocytopenia, Coagulopathy, Varices
  - Regardless of cause avoid alcohol and vaccinate
- Liver Tumor:
  - Regular screening for high-risk patients (cirrhosis)
  - Avoid pursuing "incidentalomas"
  - Monitor according to size and characteristics

89

89

Notes