Lenox Hill Hospital
Northwell Health

Academic Half Day – Liver & Biliary Disease

Agenda:
1:00-1:05 Rapid Review
1:05-2:25 Cases
2:25-2:30 Questions for the Expert

Objectives:

- Describe Clinical Presentation of those with Cirrhosis
- Categorize Etiologies of Cirrhosis
- Review Complications and their management of Cirrhosis
- Interpret LFTs and use them to compare and contrast liver/biliary diseases
- Review Biliary Diseases and management decisions related

Case 1

Jack Daniels is a 56-year-old male with essential hypertension, Diabetes type 2, chronic alcohol use with recently diagnosed cirrhosis. He presented to the Emergency Department with three days of generalized abdominal pain.

1. **What additional specific HPI/ROS questions will you ask about?**
   a. **Presence of weight gain:** Patient admits to 10 lbs of weight gain over the past few months
   b. **Abdominal Distention:** Patient has noticed increasing distention
   c. **Risk Factors?** Genetic Predisposition (alpha-1-antitrypsan, Wilson's, Hemochromatosis): FH of cirrhosis, IVUD/Sexual Practices: Hepatitis, Alcohol Abuse, Diabetes/Metabolic Syndrome
      Patient has a long standing history of alcohol use, daily drinks 4 glasses whiskey, decreasing amount lately 2/2 to decreased appetite
   d. **What constitutes decompensated cirrhosis?** Bleeding varices, ascites, hepatic encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome.
   e. **Signs of decompensation:** no episodes of GI Bleed, confusion, fever or chills
   f. **History of complications**: no History of SBP, GI bleeds, varices, encephalopathy, HCC screening, time of last EGD

The Rational Clinical Examination: Evidence-Based Clinical Diagnosis > Ascites

David L. Simel, Drummond Rennie+
Table 6-2Accuracy of the Clinical History[a]

Historical Item or Symptom	Sensitivity	Specificity	LR+	LR–
Increased girth	0.87	0.77	4.2	0.17
Recent weight gain	0.67	0.79	3.2	0.42
Hepatitis	0.27	0.92	3.2	0.80
Ankle swelling	0.93	0.66	2.8	0.10
Heart failure	0.47	0.73	2.0	0.73
Alcoholism	0.60	0.58	1.4	0.69
History of carcinoma	0.13	0.85	0.91	1.0

Abbreviations: LR+, positive likelihood ratio; LR–, negative likelihood ratio.

[a]Adapted from Simel et al.[9]

2. **What specific Physical Exam findings will you elicit?**

Ask group why you would find each finding (portal HTN vs Hyperestrogenism vs Insufficiency)

- Abdominal exam for ascites
- Palmar erythema
- Caput medusa
- Spider angiomas
- Gynecomastia
- Testicular atrophy
- Hepatosplenomegaly
- Jaundice
- Scleral Icterus
- Edema/Anasarca
- Asterixis

Abdominal Exam for ascites:
Fluid wave: Patient or colleague places hand down in center of abdomen. This will prevent vibrations from abdominal wall. You tap one flank and place your hand on other flank. If you feel vibrations this is from a fluid wave.

Shifting dullness: Percuss the abdomen. Areas of ascites will be dull, areas of air/intestine will be tympanic. Start from midline and work your way down the side. Mark where dullness starts. Ask the patient to roll on side and repeat, area of dullness should move.

The Rational Clinical Examination: Evidence-Based Clinical Diagnosis > Ascites

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Table 6-5Pooled Results of Physical Examination Studies

Physical Sign	LR+ (95% CI)	LR– (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Bulging flanks	2.0 (1.5-2.6)	0.3 (0.2-0.6)	0.81 (0.69-0.93)	0.59 (0.50-0.68)
Flank dullness	2.0 (1.5-2.9)	0.3 (0.1-0.7)	0.84 (0.68-1.00)	0.59 (0.47-0.71)
Shifting dullness	2.7 (1.9-3.9)	0.3 (0.2-0.6)	0.77 (0.64-0.90)	0.72 (0.63-0.81)
Fluid wave	6.0 (3.3-11)	0.4 (0.3-0.6)	0.62 (0.47-0.77)	0.90 (0.84-0.96)
	1.6 (0.8-3.4)	0.8 (0.5-1.2)	0.45 (0.20-0.70)	0.73 (0.61-0.85)

Abbreviations: CI, confidence interval; LR+ positive likelihood ratio; LR–, negative likelihood ratio.

Mr. Daniel's states that his abdomen has been getting more swollen over the past 2 months. Lately he has had no appetite. In addition he has been lethargic over the past few days. He denies any hematemesis, melena, hematochezia. He was admitted once previously for hepatic encephalopathy over a year ago. He has never had a GI bleed or history of SBP. His last EGD performed 6 months ago showed no evidence of variceal disease. Last HCC screening was done last year. Patient takes lactulose, amlodipine, and glyburide.

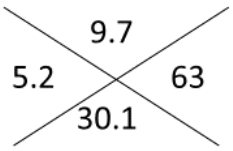
His vital signs are T 99.2, HR 94, BP 96/64 96% on Room air. He is lethargic, arousable to voice, AAOx3. Cardiac, pulmonary, and neurologic exams are within normal variants. Patient does not have asterixis. Abdominal exam reveals distension, with tense abdomen, +fluid wave. Rectal Exam is without signs of bleeding. Skin exam reveals jaundice. Hair pattern is normal without signs of gynecomastia.

3. **What is the problem representation for this patient? *read update to history**

56-year-old male with history of alcohol induced cirrhosis, current alcohol use who presents with progressive weight gain, decreased appetite, abdominal distention and acute onset abdominal pain who was found to have anasarca and fluid wave on exam.

4. **What are the next steps in Management for this patient?**
    a. Labs: CBC – Thrombocytopenia? Leukopenia?; Coagulation Panel – INR/Liver Synthesis, CMP – Kidney function (Hepatorenal?), Sodium level, LFTs
    b. Diagnostic Paracentesis – rule out SBP: Cell count, gram stain and culture
        i. recommended for patients with new onset ascites whether inpatient or outpatient (American Association for the study of Liver Diseases Class I, Level C)
        ii. Mortality reduced by 24% when paracentesis was performed
        iii. Greater reduction in those done <1 day into admission
    c. New decompensation – evaluate for etiologies
        i. Alcohol Use, Bleeding, Dehydration, Constipation, Medications
        ii. U/S with doppler – no new portal vein thrombosis or HCC
        iii. Infection – Blood Cultures, patients are at increased risk of infection
    d. Ammonia level?

5. **What are your interpretation of the Labs?**
    a. Thrombocytopenia + Macrocytic Anemia
    b. AKI
    c. Hepatic Synthetic Dysfunction (Coagulopathy, Hypoalbuminemia)
    d. Hyperbilirubinemia



MCV: 108
Neutrophil: 68%
Lymphocytes: 25%
Basophils 0.3%
Eosinophils: 2%
Monocytes: 3.7%

135	107	26	127
3.9	25	1.8	

Alk Phos: 152 IU (normal 46-139)
AST: 28 IU (normal 7-46)
ALT: 32 IU (normal 11-35)
Total Protein 6.8
Albumin 2.9 gm% (normal 3.5-5)
Total Bilirubin 2.2 mg/dl (normal 0.2-1.0)
Indirect Bilirubin 0.7 mg/dl

INR 1.8 (normal 0.9-1.1)
PT 19 (normal 11.6-14)
PTT 28 (normal 25-35)

6. **Should FFP/Vitamin K/Kcentra be administered prior to paracentesis?**

Ascites fluid: 50cc, translucent, yellow fluid
Fluid Cell count:
RBC 12
WBC 450 with 80% segs, 15% leukocytes, and 5% monocytes
Albumin: 1.7 g/dL
Protein: <2 g/dL
Gram stain & culture: processing

A prospective study of 1100 large-volume paracenteses documented no bleeding complications with no pre- or post-procedure transfusions required despite INRs as high as 8.7 and platelet counts as low 19,000/mL [7].

In another report (in which occasional patients received prophylactic fresh frozen plasma, platelets, or desmopressin [DDAVP]), severe bleeding was observed in only 9 of 4729 paracenteses (0.19 percent) [8]. The mortality rate attributable to the procedure was 0.016 percent. Eight of the nine patients who bled had renal failure, suggesting that the qualitative platelet dysfunction associated with renal failure contributed to the bleeding risk. Thus, it may be reasonable to use DDAVP before performing paracentesis in patients with cirrhosis and renal failure, although no studies have formally established a benefit.

In short, there is no indication to correct coagulopathy prior to paracentesis.

7. **Interpret Ascites fluid, what would be your next steps?**
    a. Calculate SAAG (Serum Albumin Ascites Gradient): 1.2
        i. If SAAG >1.1 g/d = Portal Hypertension
        ii. If SAAG <1.1g/d = non-portal HTN related
    b. Diagnose SBP: PMN>250., in this case 80% of 450 WBC = PMNs of 360
        i. Occurs from translocation of gut flora across bowel wall
        ii. Monobacterial infection: E coli, Klebsiella, enteric Gran negs, S. pneumo
        iii. Polymicrobial infection: think secondary bacterial peritonitis (>90% mortality when treated with antibiotics alone)
    c. Treatment of SBP: 3rd generation cephalosporin, Ceftriaxone 2g q24h x 5 days
        i. If no improvement after 5 days should consider repeat Paracentesis
    d. Renal Failure with SBP: Treat with albumin: 1.5g/kg within 6 hours of diagnosis of SBP, followed by 1.0 g/kg on day 3
        i. Decreased mortality from 29% to 10%
        ii. Albumin should be given if any of the following are true: Serum Cr >1.0, BUN>30, Total Bilirubin >4.0
    e. When else would you consider giving albumin following paracentesis?
        i. Large Volume therapeutic tap: >5.0L, must replace albumin 6-8g/L removed
8. **How would your diagnosis and management change if the Ascites Protein was 3.0 g/dl?**
    a. Diagnosis of cardiac ascites, work up right sided heart failure

9. **How do you assess the severity of illness?**
    a. MELD/MELDa: Model for End-Stage Liver Disease. 3-month mortality risk and marker for severity, used in determination of organ allocation
        i. Originally developed to risk stratify how patients would do following TIPS procedure
            1. MELD > 18 have 40% 3-month survival after TIPS
            2. MELD < 19 have at 90% 3-month survival after TIPS
        ii. Calculated using age, creatinine, bilirubin, INR, and now sodium
            1. Hyponatremia is an independent risk factor for death in cirrhotics and adding sodium as a a determinant in the MELD improved its ability to predict death, particularly in patients with low MELD scores
        iii. MELD exceptions: HCC, Hepatopulmonary syndrome, and portopulmonary syndrome give a score of 22 with increased points as time goes on.

iv. MELD for our patient: 23 can enter values

b. Child-Pugh. Initially developed as a predictive mortality score for non-shunt procedures/abdominal surgeries in patients with cirrhosis, now utilized as a severity predictor.
   i. Includes albumin, bilirubin, ascites, encephalopathy, and PT
   ii. Abdominal Surgery Mortality: Class A – 10% mortality, Class B – 30% mortality, Class C – 82% mortality
   iii. Non-surgery related survival (1-year survival rates): A – 100%, B – 80%, C – 45%
   iv. Our patient: Child Class C

10. In preparation of his discharge what medications will you expect to see him discharged on? What lifestyle modifications would you include on the paperwork?

a. Lifestyle: Quit drinking (referral to AA?), sodium restriction in diet (<2g/day)
b. SBP prophylaxis: Bactrim DS one tab Qd or Ciprofloxacin 500mg Qd
c. Ascites Management: Furosemide + Spironolactone 40:100 ratio (40mg Lasix to 100mg Spironolactone), usually fluid restriction not needed until Na<125
d. HCC Screening: Abdominal US q6 months
e. Esophageal Varices: EGD screening every 2-3y until EV present
f. Avoid: NSAID use to avoid Renal toxicity in HRS
   i. NSAIDs reduce prostaglandins in renal vasculature. In HRS, patients have diminished PGE2 synthesis and increased TXA2 synthesis. NSAID's exacerbate this picture by further reducing renal blood flow, GFR, and sodium excretion (leading to increased sodium retention and free water retention)
g. Prognosis: Based on a systematic review, patients with decompensated cirrhosis and a Child-Pugh score >/=12 or MELD >/= 21 have a median survival of </= 6 months. Patients with decompensated cirrhosis who have been hospitalized for an acute liver related illness (SBP, variceal bleed) and have a MELD >/=18 or Child-Pugh >/= 12 have a mean survival of <6 months. Consider referral for liver transplant.
h. Stop: Patient remained hypotensive during admission -> Stop Amlodipine

11. What if patient was admitted with hematemesis, what would you do?

a. Two large bore IVs, T&S, Transfuse Hgb<7
b. Octreotide as soon as possible
c. Consult GI for urgent EGD/Consult ICU
d. SBP Prophylaxis: Ceftriaxone 1g q24 x 7d, improved mortality 9% in meta-analysis

Indications for Spontaneous Bacterial Peritonitis (SBP) Prophylaxis	
Indicator	**Comments**
Prior episode(s) of SBP	Indefinite duration unless ascites resolves
Patients with cirrhosis and ascites who have ascitic fluid total protein less than 1.5 g/dL and at least one of the following: - Serum creatinine ≥1.2 mg/dL, - Blood urea nitrogen ≥ 25 mg/dL, - Serum sodium ≤ 130 mEq/L, or - Child-Pugh Score ≥ 9 + bilirubin ≥ 3 mg/dL	Indefinite duration unless ascites resolves
Acute gastrointestinal bleeding	Duration limited to 7 days

12. **EGD showed esophageal varices with stigmata of recent bleeding. What additional medication would you prescribe at time of discharge?**
    a. Non-selective Beta blocker. If patient cannot tolerate, esophageal variceal ligation maybe used alone.

Cirrhotic patient should undergo EGD q2-3 years until diagnosed with +Varices. Then start propranolol/nadolol (Nonselective BB) with goal titration HR 55-60 bpm.Non-selective betablockers are indicated for primary and secondary prevention of variceal bleeding but should be discontinued in the following settings: sepsis, HRS (hepatorenal syndrome), decompensated cirrhosis, refractory ascites, hypotension.

    b. Primary ppx:
        i. Not needed in small varices that have not bled and Childs-Pugh A
        ii. Needed in Class B or C regardless of size of varices
        iii. Needed in large varices regardless of class

13. **After discharge Mr. Daniels continues to have episodes of GI bleeding, what additional procedures can be performed.**
    a. Referral for TIPS (transjugular intrahepatic portosystemic shunt).
        i. A channel between the portal vein and hepatic vein to decrease the resistance through the liver and decrease portal HTN.
        ii. TIPS Side Effects:
            1. Hepatic encephalopathy- direct access of ammonia to systemic system.
        iii. Indications for TIPS (1) refractory GIB, (2) refractory ascites.

14. **Following TIPS Mr. Daniels comes to the ED with acute AMS and asterixis on exam. How do you evaluate HE? How to you treat?**
    a. Determine cause of HE: HEPATICS pneumonic: **H**emorrhage; **E**lectrolyte abnormalities; **P**rotein consumption; **A**lcohol; **T**rauma; **I**nfection; **C**onstipation; **S**urgery/ **S**hunt (TIPS)/ **S**edatives
    b. Hepatic encephalopathy is due to numerous factors: hyperammonemia occurs in

cirrhosis because of shunting of portal blood away from a fibrosed/architecturally distorted liver to the venous system and thus ammonia is not cleared by the liver. Ammonia is also increased in patients with muscle wasting as striated muscle clears ammonia – less muscle = more ammonia. Ammonia can cause direct neurotoxicity by directly damaging and inducing swelling to brain astrocytes.

c. According to AASLD, "overt hepatic encephalopathy is diagnosed by clinical criteria and can be graded according the West Haven Criteria and the GCS (GRADE II-2, B, 1)." ***Please refer to figure 5 of the appendix.***
According to Leise et al., grades 3 and 4 HE require ICU level of care as these patients are at high risk for airway compromise due to decreased consciousness and may soon require intubation with mechanical ventilation

d. Treatment: lactulose, lactulose, lactulose. If unable to take PO can use NG or enemas. May also start rifaximin if able to take PO/NG tube.
Lactulose Inhibits intestinal ammonia production (stimulates colonic metabolism of lactulose to lactic acid and results in acidification of gut lumen, also converts ammonium to ammonia and passage of ammonia from tissues into gut lumen.) Gut acidification itself inhibits "ammoniagenic" bacteria and increases nonammoniagenic lactobacilli. Also works as a cathartic, reducing colonic bacterial load overall

e. When mental status improves, titrate and discharge on lactulose with goal of 2-3 BM daily.
f. No need to restrict protein intake, may actually recommend a high protein diet (1-1.5 g/kg body weight daily)

Case 2:
Mr. Sir Ross Is is a 24 yo male with a history of anxiety and depression. He takes no medications but he admits to IVDU and etoh use. He works at a Popeye's restaurant in Kentucky and mainly keeps to himself aside from his family, though they note he used to be more social when he was younger. They attribute this change to his substance abuse. Mr. I presents with a 3 day history of fatigue, nausea, vague abdominal pain and jaundice.

1. What further history do you want to obtain?
-New drugs/Medications: He was prescribed Bactrim for an upper extremity abscess about 2 weeks ago. No other medications or OTC supplements
-Did he take Tylenol: No, he was using ibuprofen for pain prescribed in the ER.
-Has anyone else been sick with similar symptoms?: No other family members have been ill
-If there a family history of liver disease or mental illness?: An uncle had cirrhosis and died at a young age and is descried as "odd". But otherwise no.
-any recent travel?: No

His exam is notable for: T 101 BP 100/78 HR 90 RR 14 99% on RA.
Appears fatigued, notable jaundice, alert and oriented. HR regular, no murmurs, Lungs clear, Abdomen moderately tender in the RUQ, notable hepatomegaly, no signs of chronic liver disease, no fluid wave. No asterixis.

LABS:
Renal panel: WNL

CBC: wbc 7 hb 14 hct 42 plt 370
Hepatic Panel: AST 4000 ALT 3297 AlK phos 60 Bili 8 (direct 5.8) INR 1.3 albumin 2.5

Does Mr. I have acute liver failure?

No. Acute liver failure is defined as abnormal INR and HE within 26 weeks of jaundice. But he does have markedly elevated LFTs.

What is your differential diagnosis? How do you approach abnormal LFTs.

Discuss what hx points towards each:

--**Dili**: Bactrim, **Acute hepatitis**: A/B/C: IVDU, popeye's exposure, **Acute alcoholic hepatitis**: etoh use, **Tylenol overdose**: Maybe depressed and suicidal, **Wilson's disease**: change in personality, family hx, low alk phos (usually a ratio <2 alk phos: bili suggests wilson's), young age of onset

--Cholestatic vs aminotransferase liver enzyme elevation. Specifically, aminotransferases >1000 is rare and cased by few specific etiologies: Pneumonic = O, DIVA: **O**ther (Wilson's disease, Budd-Chiari), **D**rugs (Tylenol, GNC supplements including designer steroids), **I**schemia (pathophysiology would include Budd-Chiari), **V**iral hepatitis, **A**utoimmune hepatitis.

--Searchable Liver toxin database by NIH: https://livertox.nih.gov/

What additional labs do you want?

a. Viral hepatitis panel: HAV IgM AB; HBVsAG; HBVcAB
b. Tylenol level
c. Lactate
d. EBV / CMV serology and PCR
e. HSV Viral PCR
f. ANA, Anti-Smooth Muscle Ab
g. Ceruloplasmin
h. US with doppler

Tylenol level is wnl, EBV/CMV negative, HSV negative, ANA/ASMA negative, Ceruloplasmin normal, US wnl. Hep A IgM Positive, Hep B surface Ag IgG Positive, Hep B Surface IgM negative, Hep B core IgG positive, Hep C Ab negative. US normal

What's your diagnosis?

Acute hepatitis A.

What's his hepatitis B status: Cleared natural infection.

What if the patient admitted to ingesting of ≥8gm Tylenol this morning? What would you do & how would you treat the condition?

a. Tylenol (APAP) overdose. Call poison control. Check serum Tylenol, serum salicylate level, fingerstick glucose and EKG. Secure ABC's.
b. If presented within 4 hours of known/suspected ingestion, then treatment with activated charcoal, 1 g/kg (maximum dose 50 g) by mouth. Otherwise…
c. Treat with N-acetylcysteine (NAC) based on modified Rumack-Matthew nomogram (pharmacy consult to assist with dosing!) and 20 vs 72-hr treatment protocol. IV NAC favored by patients. IV NAC required for patients with evidence of hepatic failure.

What if he had moderate ascites on exam and labs were as follows:

Laboratory tests:
CBC: 14.8 > 11.9 / 37.4 < 118
BMP: 132 / 4.2 / 98 / 24 / 18 / 1.2 < 144
Total bilirubin: 13.3 mg/dL (normal 0.2 - 1.0) Direct bilirubin: 10.0
ALT: 90 IU (normal 7 - 46) AST: 280 IU (normal 11 - 35)
Alk phos: 210 IU (normal 46 – 139) Albumin: 3.1 gm% (3.5 - 5.0)
PT: 24.2 (lab normal is 11.6-14.4) INR: 2.2 (0.9 - 1.1).

What is your DDx:

a. Labs are notable for leukocytosis and evidence of mixed liver injury with a conjugated hyperbilirubinemia, mild aminotransferase elevation with AST:ALT ratio of >2:1, and impaired liver synthetic function.
b. Differential includes but not limited to alcoholic hepatitis, acute liver failure, acute viral hepatitis, hepatic encephalopathy, drug-induced liver injury (DILI), sepsis with multi-organ failure

What additional labs/tests do you want to order?

a. Paracentesis with cell count and culture of ascitic fluid
b. UA (rule out infection for causes for confusion)
c. CXR (given exam findings and white count)
d. Blood cultures
e. Tylenol level
f. Viral hepatitis serologies
g. Ammonia level

Case continued: He undergoes paracentesis and Lab results as follows

Ascites fluid: 50cc, hazy, yellow fluid
Cell count:
RBC 2
WBC 108 with 45% neutrophils, 15% lymphocytes, and 5% monocytes
Albumin: 1.7 g/dL
Protein: <2 g/dL
Gram stain & culture: processing
UA: Negative LE, negative nitrite, 2 WBC, 2 RBCs.
Chest X-ray: no acute abnormalities
Ammonia: 98 Tylenol: negative
HCV Ab: negative HCV PCR: negative
HBsAg: negative Anti-HBs IgG: negative Anti-HBc IgM: negative
Anti-Hep A IgM: negative
Blood cultures pending

Interpret the above labs. What clinical diagnoses can be made at this time?

Paracentesis is negative for SBP. Culture pending. UA negative. No acute HAV infection, no HCV infection, no acute HBV infection and he is *not* immune (anti-HBs IgG is negative).
Most likely Diagnoses include: Acute alcoholic hepatitis

What disease severity tools are available to guide therapy?

Alcoholic hepatitis – At least 2 scoring systems: Maddrey's discriminant function and the Glasgow alcoholic hepatitis score. ***Refer learners to figures 6 & 7 in the appendix.***

i. Maddrey's discriminant function ≥ 32 threshold for treatment

ii. Glasgow Alcoholic Hepatitis Score ≥ 9 threshold for treatment

What medications/therapies would you start? Detail dosing and duration of therapy.

c. Alcoholic hepatitis: Prednisolone vs. Pentoxifylline
   i. Prednisolone 40 mg qd x28 days, followed by 14-d taper.
   ii. Pentoxifylline 400 mg tid x 28 days. It's a PDE inhibitor and TNF-alpha inhibitor

Brief EBM update:
2008 Cochran review showed a trend towards benefit with glucocorticoid treatment. This was supported in a 2011 meta-analysis of the five largest studies, which showed a mortality benefit with prednisolone treatment.

Published in 2015 by NEJM, the STOPAH trial randomized 1,092 patients with alcoholic hepatitis at 65 UK centers to a combination of prednisolone, pentoxifylline, and placebo in a double-blinded, 2x2 factorial design. Neither therapy showed significant reduction in mortality at 28 days and there were no significant differences between the mortality or liver transplantation rates at 90 days or at 1 year. However, prednisolone was associated with a mortality benefit trend of OR 0.72 with P=0.06. A logistic regression suggested that prednisolone may provide a mortality benefit at 28 days, though not at 90 or 365 days. Prednisolone was associated with an increase in incident infections.

You started treatment for alcoholic hepatitis. After 1 week repeat labs show an unchanged BMP, total bilirubin of 8, INR 1.5. What clinical tool do you use to adjust duration of therapy?

d. Lille's Score is calculated after 7 days of treatment to identify patient's non-responsive to steroids. Mr. B would score <0.45 which predicts a 6-month survival of 85%. Therapy should continue for full duration. However, is Lille score >0.45 then that predicts poor outcome (6-month survival of 25%). Patient may be non-responder to steroids. Consider alternative treatments, including transplant referral. ***Refer to figure 8 in the appendix.***