Hepatobiliary Quiz Answers – 18 (2016)

Answers to Multiple Choice Questions

1. Answers: A, C and E

Ectopic varices are dilated portosystemic collateral veins located at sites other than the gastroesophageal region. These constitute upto 5% of variceal bleeds in patients with intrahepatic portal hypertension, and 20% to 30% of those with extrahepatic portal hypertension.¹⁻³ Of all patients with ectopic varices, the frequency according to site are as follows- duodenal varices(32.9%), jejunum(4%), ileum (1.2%), colon(3.5%), rectal (44.5%) and peristomal (5.8%)⁴. Another study shows the prevalence of anorectal varices to be 77.7%, and that they are much more common in patients with noncirrhotic portal hypertension (89.3%).⁵

Management of bleeding ectopic varices involve volume resuscitation and use of vasopressors, followed by endoscopic management with band ligation or glue injection into the bleeding varices. If these options fail, Transjugular intrahepatic portosystemic shunt (TIPS), Balloon occluded retrograde transvenous obliteration and Percutaneous transhepatic obliteration are the rescue options. Almost all patients who undergo TIPS achieve initial hemostasis. The rate of rebleed is around 21%. Patients who do not respond to interventional radiologic procedures may require surgical intervention including shunt surgery.³

2. Answers: B, C and D

Hepatotoxicity due to antitubercular therapy (ATT) is seen in 5%–28% of people treated with these drugs, leading to discontinuation of drug in 11% of patients. The liver injury is idiosyncratic in nature. ATT hepatitis is usually due to metabolic idiosyncrasy due to the drug metabolites, not hypersensitive idiosyncrasy. Hypersensitive idiosyncrasy is associated with skin rashes, fever, eosinophilia and/or lymphadenopathy, which is usually seen with antiepileptics and sulfonamides.^{6,7}

ATT-hepatitis that warrants cessation of therapy involves elevation of transaminases over 5 times upper limit of normal (ULN), in the absence of hyperbilirubinemia or symptoms; or up to 3 times ULN in the presence of symptoms or hyperbilirubinemia (bilirubin $2 \times$ ULN).⁸ Thus, isolated hyperbilirubinemia does not warrant cessation by itself.

Concomitant viral hepatitis should be excluded, as it may be responsible for the deranged liver function in upto 15% cases.⁹ Upto 63% of individuals who developed ATT-hepatotoxicity, including acute liver failure were being treated empirically.¹⁰

Older age is a risk factor for development of ATT-hepatitis, with patients older than 35 years being at a 4 times higher risk. Although men are affected more frequently than women, probably as more men are under

treatment for tuberculosis, females are likely to have more severe liver disease including death.^{11,12}

3. Answers: B, C and D

Gram-negative bacilli (GNB) are the major cause of SBP, with *E. coli* being the commonest organism. Gram-positive cocci (GPC) are responsible for less than a quarter of cases. However, among patients on norfloxacin prophylaxis, GPCs were found in 57% of patients with SBP, of which Methicillin Resistant *Staphylococcus aureus* constituted 77%.¹³

Risk factors for recurrence of SBP include ascitic fluid protein <1 gm/dl, bilirubin >4 mg/dl and Prothrombin index $\leq 45\%$.¹⁴ Proton Pump Inhibitor (PPI) therapy has been associated with a 3-fold higher risk of SBP compared to those not receiving acid suppressive medication in both prospective and retrospective studies. It has also been reported to be associated with pneumonia. Though a causal relationship has not yet been established, it would be prudent to restrict its use in patients who do not have a clear indication for acid-suppressive therapy.^{15,16}

Renal involvement is seen in upto 40% patients with SBP and is the best biochemical predictor for mortality. Use of albumin has a renoprotective effect, but it is not indicated for all patients. Patients with serum creatinine > 1 mg/dL, bilirubin > 4 mg/dL, BUN > 30 mg/dL and those with chronic kidney disease show the most benefit.¹⁷

4. Answers: B and C

Cirrhosis is marked by a state of hyperdynamic circulation and decreased systemic vascular resistance, effectively leading to circulatory hypovolemia and splanchnic vasoconstriction. Thus, blood flow to the liver is reduced, especially in the presence of portal hypertension. Hemodynamic alterations during surgery are thus poorly tolerated by these patients, who are highly susceptible to fluid shifts due to volume loss and vasoactive drugs. This results in hypoxemic injury to the liver, and may precipitate hepatic decompensation. However, patients with chronic liver disease without cirrhosis are not susceptible to these hemodynamic alterations, and thus risk-stratified similarly to the general population.^{19,20}

Both CTP and MELD scores correlate well with 30-day post-operative mortality. Child class B is associated with a 30 day mortality of 30% to 31%, while the risk is as high as 76% to 82% for Child class C patients.^{21,22}

TIPS has been tried by some centers in order to reduce the portal pressure, given its impact on hemodynamics in cirrhotic patients, and has revealed a lower risk of perioperative mortality with prophylactic placement of TIPS. Thus, placement 4 to 6 weeks before a procedure may allow patients to undergo surgery that might otherwise be contraindicated.²³

Cirrhotic patients are susceptible to development of gallstones, and often need cholecystectomy. The risk for hepatic decompensation in the post operative period is lower for patients with MELD scores up to 13, Child class A, and Child class B cirrhosis without portal hypertension. The risk of decompensation is around 7.7% in laparoscopic and 18.1% in open cholecystectomy cases. Thus, laparoscopic approach is the preferred approach.²⁴

Umbilical hernias are common in patients with cirrhosis. These may be repaired even in Child C cirrhosis, however, patients with high MELD scores or hypoalbuminemia are at a higher risk of infections. Ascites must be controlled aggressively before the repair to prevent wound dehiscence and poor healing.¹⁹

5. Answers: A and D

Women constitute 27% of adults with cirrhosis. This lower prevalence in women seems to be related to the lower prevalence of viral hepatitis and alcohol abuse, as well as iron overload.²⁵

The natural history of HCV too differs between women and men. Spontaneous clearance of the virus occurs more frequently among women (37% vs 21%).²⁶ Female sex is also protective against progression of liver fibrosis, especially in premenopausal age group. Even among post menopausal patients, fibrosis was less advanced in those who received hormone replacement. This is believed to be due to the protective effect of estrogens.²⁷

Chronic hepatitis B too shows similar gender differences, with males having a 2.5 times higher risk of progression to cirrhosis.²⁸ They also have a higher incidence of HBV related HCC (3-6 times), and are more prone to develop disease flares and HBV reactivation after HBsAg seroconversion.^{29,30}

6. Answer: D

Premenopausal women with cirrhosis frequently have irregular menstruation and ovulation, secondary to hypothalamic-pituitary dysfunction and altered sex hormone metabolism. Almost 27% women have irregular menstruation, and 20% have amenorrhea. However, over half of the women (53%) had regular menstrual cycles.³¹⁻³³

Though there have been concerns regarding a potential association between oral contraceptive use and risk of Hepatocellular Carcinoma (HCC), a meta-analysis of existing evidence did not find sufficient correlation between the two. Women with compensated cirrhosis may use any hormonal contraceptive method, however, women with severe, decompensated cirrhosis, the risks usually outweigh the benefits.^{34,35}

Pregnancy in women with cirrhosis leads to worsening of portal hypertension, which starts around the sixth week and peak between the 30th and 34th week of gestation, and

lead to complications like variceal bleeding, ascites and encephalopathy. MELD score ≥ 10 predicts significant liver-related complications.³⁶⁻³⁸

Other complications include a higher risk of preeclampsia, preterm delivery, low birth weight, small for gestational age, and neonatal death.³⁹

The endoscopic management of variceal bleed during pregnancy is similar to nonpregnant patients. However, the concomitant use of octreotide in the acute phase is debatable. Even though its approved as USFDA category B drug, its similarity to vasopressin raises the concerns for splanchnic vasoconstriction, leading to placental insufficiency and risk of placental abruption.⁴⁰

7. Answers: D and E

Primary Biliary Cirrhosis (PBC) is a liver-specific autoimmune disease which predominantly affects women in their 5th and 6th decade. Over 90% of the cases are females, and first degree relatives are 10 times more likely to be affected than the general population.⁴¹

The exact pathophysiology is unknown, however, both genetic and environmental factors seem to be involved. Pathogenesis may include a combination of sex hormone abnormalities and X chromosome instabilities and defects.⁴²

Diagnosis is made during workup for fatigue, pruritus, or incidentally detected elevation of alkaline phosphatase. Antimitochondrial antibody (AMA) is quite specific for PBC, being present in 95% of cases, while its incidence in general population is <1%.⁴³

Treatment with ursodeoxycholic acid (UDCA) improves transplant free survival, especially if started early in the course of disease. UDCA stimulates ductular secretions and protects against injury from toxic bile acids. It has also been shown to downregulate B cells and AMA production, thereby reducing inflammation.⁴⁴

Patients with PBC are more likely to have osteoporosis compared with age-matched controls, (Prevalence 20% -52%). The risk increases with histologic severity of liver disease, older age, and duration of cholestasis.⁴⁵⁻⁴⁷

8. Answers: A, C, D and E

Prophylactic antibiotics in cirrhotic patients with high risk of infections has led to a decreased incidence of bacterial infections. However, this is at the cost of altering microbial flora and promoting development of resistant organisms. Thus, judicious use of antibiotic prophylaxis is warranted.⁴⁸

Long-term prophylaxis with norfloxacin is indicated in patients who have had one episode of SBP. These patients have a 3 fold higher chance of recurrence of SBP if not on antibiotic prophylaxis as compared with those on norfloxacin at 1 year.⁴⁹

Use of prophylactic antibiotics to prevent the first episode of SBP is indicated in patients with low ascitic fluid

protein (<1.5 gm/dl), when atleast one of the following features associated with advanced cirrhosis or renal dysfunction are present- Child-Pugh score ≥ 9 points with serum bilirubin ≥ 3 mg/dL, serum creatinine ≥ 1.2 mg/dL, blood urea nitrogen ≥ 25 mg/dL, or serum sodium ≤ 130 mEq/L. In this subgroup of patients, primary prophylaxis of SBP with norfloxacin has been shown to reduce the probability of developing renal dysfunction as well as improved survival.⁵⁰

Variceal bleeding increases the risk of SBP and other infections within the first 5-7 days of the bleeding episode. The risk is higher in patients with advanced cirrhosis. Use of prophylactic antibiotics in these patients is associated with a reduced incidence of in-hospital infection, rebleeding within 7 days, and 28 day mortality.^{51,52}

Rifaximin is a nonabsorbable antibiotic with a broad spectrum of activity against gram-negative and gram-positive aerobes and anaerobes. Its use does not seem to significantly alter the stool microbiome or increase antibiotic resistance, and its use has been associated with lower incidence of development of SBP.⁵²⁻⁵⁴

9. Answers: B, C and E

Cholangiocarcinoma (CCA) is the second most common type of primary liver cancer, and forms ~3% of all gastrointestinal neoplasias. It is much more commonly seen in certain countries and regions, including Chile, Bolivia, South Korea and North Thailand. Based on location, CCAs can be classified into intrahepatic (iCCA), perihilar (pCCA) and distal CCA (dCCA). There has been a plateau in the incidence of iCCA incidence worldwide over the last decade. Conversely, the incidences of both pCCA and dCCA have been decreasing.⁵⁵

Most of pCCA and dCCA are mucinous adenocarcinomas. iCCAs, on the other hand, show two main histological subtypes- bile ductular type (mixed), and bile duct type (mucinous).⁵⁶

Chronic hepatitis B and hepatitis C infections are identified as a risk factors for CCA especially iCCA.⁵⁷ This type of CCA usually presents with mass-forming grown pattern (>90%) while infiltrative pattern is usually seen in pCCA and dCCA. Such mass forming lesions may often be confused with HCC. Contrast-enhanced MRI lacks characteristic features of HCC like arterial enhancement followed by delayed wash-out. However, Contrast Enhanced Computed Tomography shows these characteristics in larger nodules (>3 cm). Smaller nodules of CCA often have an enhancement and wash-out pattern similar to HCC.^{58,59}

10. Answers: A, B and C

Cirrhotic patients who are malnourished are more likely to have portal hypertension, portosystemic collaterals, and varices. They also have more severe portal hypertension and higher risk of variceal bleeding.⁶⁰

Most of our body proteins are located in the skeletal muscle, thus, adult protein malnutrition is primarily defined as skeletal muscle loss. Sarcopenia in cirrhosis worsens with advancing Child Pugh score and the development of portosystemic shunting.⁶¹

Bioelectrical Impedance analysis can determine the total body fat mass, and the remaining weight is considered lean body mass. 40% to 60% of lean body mass is contributed by skeletal muscle mass. Thus, estimation of lean body or fat-free mass may be considered a measure of whole body skeletal muscle mass.⁶²

Creatinine height index is an unreliable marker of malnutrition, as patients with cirrhosis often have associated renal dysfunction

Placement of TIPS has been shown to improve sarcopenia, even though it worsens shunting and hyperammonemia. It also reduces portal hypertension, potentially leading to improved gut motility and nutrient absorption, and increases appetite by reducing ascites.

Conflict of Interest

The authors have none to declare.

REFERENCES

1. Helmy A, Al Kahtani K, Al Fadda M. Updates in the pathogenesis, diagnosis and management of ectopic varices. *Hepatol Int*. 2008; 2:322-334.
2. Lebrec D, Benhamou JP. Ectopic varices in portal hypertension. *Clin Gastroenterol*. 1985;14:105-121.
3. Sarin SK, Kumar CKN. Ectopic Varices. *Clin Liv Dis*. 2012;1: 167-172.
4. Watanabe N, Toyonaga A, Kojima S, Takashimizu S, Oho K, Kokubu S, et al. Current status of ectopic varices in Japan: results of a survey by the Japan Society for Portal Hypertension. *Hepatol Res*. 2010;40:763-776.
5. Chawla Y, Dilawari JB. Anorectal varices-their frequency in cirrhotic and noncirrhotic portal hypertension. *Gut*. 1991;32:309-311.
6. Ramappa V, Aithal GP. Hepatotoxicity Related to Anti-tuberculosis Drugs: Mechanisms and Management. *J Clin Exp Hepatol*. 2013; 3:37-49.
7. Devarbhavi H. Antituberculous drug-induced liver injury: current perspective. *Tropical Gastroenterology*. 2011;32:167-174.
8. Saukkonen JJ, Cohn DL, Jasmer RM, Schenker S, Jereb JA, Nolan CM, et al. ATS (American Thoracic Society) Hepatotoxicity of Anti-tuberculosis Therapy Subcommittee. An official ATS statement: hepatotoxicity of antituberculosis therapy. *Am J Respir Crit Care Med*. 2006;174:935-952.
9. Sarda P, Sharma SK, Mohan A, Makharia G, Jayaswal A, Pandey RM, et al. Role of acute viral hepatitis as a confounding factor in antituberculosis treatment induced hepatotoxicity. *Indian J Med Res*. 2009;129:64-67.
10. Kumar R, Shalimar. Bhatia V, Khanal S, Sreenivas V, Gupta SD, et al. Antituberculosis therapy-induced acute liver failure: magnitude, profile, prognosis, and predictors of outcome. *Hepatology*. 2010; 51:1665-1674.
11. Devarbhavi H, Dierkhising R, Kremers WK. Antituberculosis therapy drug-induced liver injury and acute liver failure. *Hepatology*. 2010; 52:798-799.

12. Devarbhavi H, Dierkhising R, Kremers WK, Sandeep MS, Karanth D, Adarsh CK. Single-center experience with drug-induced liver injury from India: causes, outcome, prognosis, and predictors of mortality. *Am J Gastroenterol*. 2010;105:2396–2404.
13. Campillo B, Richardet JP, Kheo T, et al. Nosocomial spontaneous bacterial peritonitis and bacteremia in cirrhotic patients: impact of isolate type on prognosis and characteristics of infection. *Clin Infect Dis*. 2002;35:1–10.
14. Llach J, Rimola A, Navasa M, et al. Incidence and predictive factors of first episode of spontaneous bacterial peritonitis in cirrhosis with ascites: relevance of ascitic fluid protein concentration. *Hepatol*. 1992;16:724.
15. Dever JB, Sheikh MY. Review article: spontaneous bacterial peritonitis – bacteriology, diagnosis, treatment, risk factors and prevention. *Aliment Pharmacol Ther*. 2015;41:1116–1131.
16. Yu T, Tang Y, Jiang L, Zheng Y, Xiong W, Lin L. Proton pump inhibitor therapy and its association with spontaneous bacterial peritonitis incidence and mortality: A meta-analysis. *Dig Liver Dis*. 2016;48:353–359.
17. Follo A, Llovet JM, Navasa M, et al. Renal impairment after spontaneous bacterial peritonitis in cirrhosis: incidence, clinical course, predictive factors and prognosis. *Hepatology*. 1994;20:1495–1501.
19. Prenner S, Ganger D. Risk stratification and preoperative evaluation of the patient with known or suspected liver disease. *Clin Liv Dis*. 2016;7:101–105.
20. Runyon BA. Surgical procedures are well tolerated by patients with asymptomatic chronic hepatitis. *J Clin Gastroenterol*. 1986;8:542–544.
21. Garrison RN, Cryer HM, Howard DA, Polk Jr HC. Clarification of risk factors for abdominal operations in patients with hepatic cirrhosis. *Ann Surg*. 1984;199:648–655.
22. Mansour A, Watson W, Shayani V, Pickleman J. Abdominal operations in patients with cirrhosis: still a major surgical challenge. *Surgery*. 1997;122:730–735. discussion 735–736.
23. Kim JJ, Dasika NL, Yu E, Fontana RJ. Cirrhotic patients with a transjugular intrahepatic portosystemic shunt undergoing major extrahepatic surgery. *J Clin Gastroenterol*. 2009;43:574–579.
24. Laurence JM, Tran PD, Richardson AJ, Pleass HC, Lam VW. Laparoscopic or open cholecystectomy in cirrhosis: a systematic review of outcomes and meta-analysis of randomized trials. *HPB (Oxford)*. 2012;14:153–161.
25. Giard GM, Terrault NA. Women with Cirrhosis: Prevalence, Natural History, and Management. *Gastroenterol Clin N Am*. 2016;45:345–358.
26. Grebely J, Page K, Sacks-Davis R, et al. The effects of female sex, viral genotype, and IL28B genotype on spontaneous clearance of acute hepatitis C virus infection. *Hepatology*. 2014;59:109–120.
27. Di Martino V, Lebray P, Myers RP, et al. Progression of liver fibrosis in women infected with hepatitis C: long-term benefit of estrogen exposure. *Hepatology*. 2004;40:1426–1433.
28. Fattovich G. Natural history and prognosis of hepatitis B. *Semin Liver Dis*. 2003;23:47–58.
29. Lok AS, Lai CL. Acute exacerbations in Chinese patients with chronic hepatitis B virus (HBV) infection, Incidence, predisposing factors and etiology. *J Hepatol*. 1990;10:29–34.
30. Chu CM, Liaw YF. Predictive factors for reactivation of hepatitis B following hepatitis B e antigen seroconversion in chronic hepatitis B. *Gastroenterology*. 2007;133:1458–1465.
31. Cundy TF, Butler J, Pope RM, et al. Amenorrhoea in women with non-alcoholic chronic liver disease. *Gut*. 1991;32:202–206.
32. Burra P, De Martin E, Gitto S, et al. Influence of age and gender before and after liver transplantation. *Liver Transpl*. 2013;19:122–134.
33. Mass K, Quint EH, Punch MR, et al. Gynecological and reproductive function after liver transplantation. *Transplantation*. 1996;62:476–479.
34. Maheshwari S, Sarraj A, Kramer J, et al. Oral contraception and the risk of hepatocellular carcinoma. *J Hepatol*. 2007;47:506–513.
35. Kapp N. WHO provider brief on hormonal contraception and liver disease. *Contraception*. 2009;80:325–326.
36. Pritchard JA. Changes in the blood volume during pregnancy and delivery. *Anesthesiology*. 1965;26:393–399.
37. Sandhu BS, Sanyal AJ. Pregnancy and liver disease. *Gastroenterol Clin North Am*. 2003;32:407–436. ix.
38. Westbrook RH, Yeoman AD, O'Grady JG, et al. Model for end-stage liver disease score predicts outcome in cirrhotic patients during pregnancy. *Clin Gastroenterol Hepatol*. 2011;9:694–699.
39. Puljic A, Salati J, Doss A, et al. Outcomes of pregnancies complicated by liver cirrhosis, portal hypertension, or esophageal varices. *J Matern Fetal Neonatal Med*. 2016;29:506–509.
40. Allen AM, Hay JE. Review article: the management of cirrhosis in women. *Aliment Pharmacol Ther*. 2014;40:1146–1154.
41. Carey EJ, Ali AH, Lindor KD. Primary biliary cirrhosis. *Lancet*. 2015;386(10003):1565–1575.
42. Invernizzi P, Miozzo M, Selmi C, et al. X chromosome monosomy: a common mechanism for autoimmune diseases. *J Immunol*. 2005;175:575–578.
43. Miyakawa H, Tanaka A, Kikuchi K, et al. Detection of antimitochondrial autoantibodies in immunofluorescent AMA-negative patients with primary biliary cirrhosis using recombinant autoantigens. *Hepatology*. 2001;34:243.
44. Poupon R. Ursodeoxycholic acid and bile-acid mimetics as therapeutic agents for cholestatic liver diseases: an overview of their mechanisms of action. *Clin Res Hepatol Gastroenterol*. 2012;36 (Suppl 1):S3–S12.
45. Glass LM, Su GLC. Metabolic Bone Disease in Primary Biliary Cirrhosis. *Gastroenterol Clin N Am*. 2016;45:333–343.
46. Guanabens N, Pares A, Ros I, et al. Severity of cholestasis and advanced histological stage but not menopausal status are the major risk factors for osteoporosis in primary biliary cirrhosis. *J Hepatol*. 2005;42:573–577.
47. Solaymani-Dodaran M, Card TR, Aithal GP, et al. Fracture risk in people with primary biliary cirrhosis: a population-based cohort study. *Gastroenterology*. 2006;131:1752–1757.
48. Fernández J, Tandon P, Mensa J, Garcia-Tsao G. Antibiotic Prophylaxis in Cirrhosis: Good and Bad. *Hepatology*. 2016;63:2019–2031.
49. Gines P, Rimola A, Planas R, et al. Norfloxacin prevents spontaneous bacterial peritonitis recurrence in cirrhosis: results of a double-blind, placebo-controlled trial. *Hepatology*. 1990;12:716–724.
50. Fernandez J, Navasa N, Planas R, et al. Primary prophylaxis of spontaneous bacterial peritonitis delays hepatorectal syndrome and improves survival in cirrhosis. *Gastroenterology*. 2007;133:818–824.
51. Jalan R, Fernandez J, Wiest R, et al. Bacterial infections in cirrhosis: a position statement based on the EASL Special Conference 2013. *J Hepatol*. 2014;60:1310–1324.
52. Tandon P, Delisle A, Topal JE, Garcia-Tsao G. High prevalence of antibiotic-resistant bacterial infections among patients with cirrhosis at a US liver center. *Clin Gastroenterol Hepatol*. 2012;10:1291–1298.
53. Bajaj JS, Heuman DM, Sanyal AJ, Hylemon PB, Sterling RK, Stravitz RT, et al. Modulation of the metabiome by rifaximin in patients with cirrhosis and minimal hepatic encephalopathy. *PLoS One*. 2013;8:e60042.
54. Hanouneh MA, Hanouneh IA, Hashash JG, Law R, Esfeh JM, Lopez R, et al. The role of rifaximin in the primary prophylaxis of

spontaneous bacterial peritonitis in patients with liver cirrhosis. *J Clin Gastroenterol*. 2012;46:709–715.

55. Global Burden of Disease Cancer Collaboration 2013. The global burden of cancer. *JAMA Oncol*. 2015;1:505–527.
56. Banales JM, Cardinale V, Carpino G, et al. Cholangiocarcinoma: current knowledge and future perspectives consensus statement from the European Network for the Study of Cholangiocarcinoma (ENS-CCA). *Nat Rev Gastroenterol Hepatol*. 2016;13:261–280.
57. Shin HR, Lee CU, Park HJ, et al. Hepatitis B and C virus, *Clonorchis sinensis* for the risk of liver cancer: a case-control study in Pusan. *Korea Int J Epidemiol*. 1996;25:933–940.
58. Rimola J, Forner A, Reig M, et al. Cholangiocarcinoma in cirrhosis: absence of contrast washout in delayed phases by magnetic resonance imaging avoids misdiagnosis of hepatocellular carcinoma. *Hepatology*. 2009;50:791–798.
59. Iavarone M, Piscaglia F, Vavassori S, et al. Contrast enhanced CT-scan to diagnose intrahepatic cholangiocarcinoma in patients with cirrhosis. *J Hepatol*. 2013;58:1188–1193.
60. Moller S, Bendtsen F, Christensen E, et al. Prognostic variables in patients with cirrhosis and oesophageal varices without prior bleeding. *J Hepatol*. 1994;21:940–946.
61. Gunsar F, Raimondo ML, Jones S, et al. Nutritional status and prognosis in cirrhotic patients. *Aliment Pharmacol Ther*. 2006;24:563–572.
62. Chinn KS, Hannon JP. Relationship of muscle protein to other components of the fat-free mass. *Am J Physiol*. 1966;211:993–997.

FURTHER READING

18. Signal SH, Stanca CM, Fernandez J, et al. Restricted use of albumin for spontaneous bacterial peritonitis. *Gut*. 2007;56:597–599.
63. Francoz C, Prie D, Abdelrazek W, et al. Inaccuracies of creatinine and creatinine-based equations in candidates for liver transplantation with low creatinine: impact on the model for end-stage liver disease score. *Liver Transpl*. 2010;16:1169–1177.
64. Plauth M, Schutz T, Buckendahl DP, et al. Weight gain after transjugular intrahepatic portosystemic shunt is associated with improvement in body composition in malnourished patients with cirrhosis and hypermetabolism. *J Hepatol*. 2004;40:228–233.
65. Tsien C, Shah SN, McCullough AJ, et al. Reversal of sarcopenia predicts survival after a transjugular intrahepatic portosystemic shunt. *Eur J Gastroenterol Hepatol*. 2013;25:85–93.

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