REVIEW ARTICLE

CONTENTS

Portal hypertension and emergency care

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ABSTRACT

Aim: To evaluate the peculiarities of the course of complications and the provision of care for portal hypertension associated with the development of diuretic-resistant ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, and variceal bleeding.

Materials and Methods: This research is based on a review of the literature in PubMed, CrossRef, Google Scholar sources on complicated portal hypertension. Such complications of portal hypertension as spontaneous bacterial peritonitis, ascites, hepatorenal syndrome, variceal bleeding caused by sinistral portal hypertension are considered. The effectiveness of interventional treatment methods and laparoscopic surgical interventions has been demonstrated.

Conclusions: Diagnosis and treatment of patients with complicated portal hypertension requires a multidisciplinary approach, which is due to the diverse pathophysiological process of portal hypertension. The possibilities of providing emergency care to this category of patients depend on the level of medical training of the staff, the possibilities of medical and technical support in the provision of interventional care, the ineffectiveness of which necessitates surgical treatment using minimally invasive technologies.

KEY WORDS: portal hypertension, ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, bleeding

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INTRODUCTION

Portal hypertension, which occurs when the pressure gradient in the portal system exceeds 6 mm Hg, gradually leads to the development of complications that are accompanied by hospitalization and threaten the life of the patient. Complications in the form of ascites, hepatorenal syndrome, bleeding from the veins of the esophagus, stomach and other parts of the digestive tube, spontaneous bacterial peritonitis are difficult to diagnose and often require emergency care. Medical assistance for complicated portal hypertension is versatile, including drug support, interventional treatment, in case of ineffectiveness of which, surgical intervention is performed. The only radical method of treatment for patients with decompensated portal hypertension is liver transplantation.

AIM

To evaluate the peculiarities of the course of complications and the provision of care for portal hypertension associated with the development of diuretic-resistant ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, and variceal bleeding.

MATERIALS AND METHODS

This research is based on a review of the literature in PubMed, CrossRef, Google Scholar sources on complicated portal hypertension. Such complications of portal hypertension as spontaneous bacterial peritonitis, ascites, hepatorenal syndrome, variceal bleeding caused by sinistral portal hypertension are considered. The effectiveness of interventional treatment methods and laparoscopic surgical interventions has been demonstrated.

REVIEW AND DISCUSSION

Portal hypertension (PH), which is unceasingly developing, is caused by the formation of complications, among which ascites is the primary one that needs care.

PH and ascites are two crucial events in the natural history of liver cirrhosis, whose appearance marks a downward shift in the prognosis of the disease and over the years, several international and national societies have issued clinical practice guidelines for the diagnosis and management of PH and ascites [1].

The Japanese guidelines are based on the updated clinical guidelines for the treatment of cirrhosis and ascites, which are compared with the guidelines of Eu-

rope and the United States for the treatment of grade one to three ascites [2- 5].

Ascites — an abnormal accumulation of fluid in the peritoneal cavity — is present in up to 90% of patients with advanced cirrhosis, resulting in frequent hospitalisations due to debilitating episodes of pain and breathlessness [6]. About 20% of patients with cirrhosis have ascites at their first presentation, and 20% of those presenting with ascites die in the first year of the diagnosis [7].

Among the various risky complications of liver cirrhosis, refractory ascites is associated with poor survival of cirrhotics and persistently worsens their quality of life [8].

Palliative long-term drainage of the abdominal cavity in patients with cirrhosis with refractory ascites has an advantage over therapeutic paracentesis and consists on placing a tunnelled drain through the abdominal wall, with ultrasound guidance, and with the patient under local anaesthetic [9,10].

One of the essential points caused by ascites is an increase in pressure in the abdominal cavity, which leads to the deterioration of abdominal perfusion.

In critically ill patients, abdominal perfusion pressure (APP), resulting from the difference between mean arterial pressure and intra-abdominal pressure (IAP), correlates with improved survival however, there are reports of different clinical threshold values for APP ranging from 50 to 72 mm Hg [11]. Chronically increased IAP is present in the physiological state of pregnancy and in pathological states such as morbid obesity, decompensated heart failure and liver cirrhosis [12].

Less with that APP is a critical vital sign that assists the clinician in titrating volume restoration, administering vasopressors, and optimizing intra-abdominal pressure, thereby preventing the deleterious effects of persistent critical pressure [13].

The researchers concluded that APP can be considered a critical sign, so prevention and treatment of abdominal hypoperfusion in patients with decompensated cirrhosis is urgent, and mortality is higher among patients with hypoperfusion, independent of factors such as clinical severity, total bilirubin, and hepatic encephalopathy [14,15].

An increase in portal pressure, due to both the sinusoidal and presinusoidal components with the accumulation of ascitic fluid, leads to swelling of the intestinal wall and is accompanied by a violation of its permeability with subsequent formation of spontaneous bacterial peritonitis (SBP).

SBP is a term used to describe acute infection of ascites, an abnormal accumulation of fluid in the abdomen without a distinct or identifiable source of infection [16]. Ascites is a predominantly transudative fluid with weak opsonic activity, providing a favorable environment for bacterial growth in 10–30% of hospitalized patients [17].

A diagnosis of classic SBP is made if neutrophils count in the ascitic fluid is ≥250 cells/mm3, culture results are positive, and secondary causes of peritonitis are excluded [18]. SBP is most commonly (75%) caused by gram-negative aerobic organisms, with *Klebsiella pneumoniae* accounting for 50% of these, gram-positive aerobic microorganisms are responsible for the remainder of cases; the most common of these are *Streptococcus pneumoniae* or *Viridans group streptococci* [19].

Patients with SBP have Child-Pugh Class C chronic liver disease, have a 1-year survival rate of 45% and a 2-year survival rate of 35% [20].

In hospital settings, the non-infection-related mortality in SBP patients can be as high as 20-40 percent, and one to two years of mortality rates are 70 and 80 percent, respectively [21].

Thus, ascites, which complicates the course of portal hypertension, leading to an increase in intra-abdominal pressure, becomes even more dangerous for the patient's life due to its infection and requires treatment of both ascites itself and its bacterial component, as well as correction of intra-abdominal pressure. Another complication that occurs in patients with decompensated PH and ascites is hepatorenal syndrome (HRS), the provision of care for which is an extremely difficult task.

Renal failure is the leading cause of death in patients with SBP and develops in 30–40 percent of patients, but risk can be minimized by treatment with octreotide or midodrine is helpful if renal failure develops [22].

Until recently, HRS was categorized into 2 major types: the severe and rapidly progressing form of HRS (formerly called HRS type 1 [HRS-1]) marked by cirrhosis with ascites, and the milder, more slowly progressing form of HRS (formerly called HRS type 2 [HRS-2]) that is typically associated with refractory ascites [23,24].

HRS-acute kidney injury (AKI) is associated with a high mortality rate and can occur due to a precipitating event like bacterial infection and/or following acute liver injury stemming from causes such as alcohol abuse, drug use, hypovolemia from overuse of diuretics, and exacerbations of viral hepatitis [25,26].

AKI due to HRS has the highest short-term (30 days) mortality followed by AKI due to infection in decompensated cirrhosis and detection of AKI using creatinine kinetics-based definition may prompt an early appropriate intervention [27].

Preventive measures against the development of AKI in cirrhosis include avoidance of potentially nephrotoxic medications like nonsteroidal anti-inflammatory drugs, avoidance of excessive or unmonitored diuretics or nonselective beta-blockade, avoidance of large-volume para-

centesis without albumin replacement, and counseling patients to avoid alcohol use [28]. HRS patients treated with terlipressin experienced better clinical outcomes and a lower cost per treatment response vs other unapproved treatments [29-31].

Ascites, SBP, HRS, these complications of decompensated PH require constant monitoring with the need to provide emergency care, which is often provided with medication, while bleeding from varicose veins requires interventional or surgical measures.

Separately, sinistral portal hypertension (SPH) is distinguished, which is defined as increased pressure limited to the gastrosplenic side of the portal vein system and differs from other forms of portal hypertension in that liver function is preserved, the portal vein is open and treatment requires a multidisciplinary approach with surgery and interventional radiology [32]. For interventional radiology belongs splenic artery embolisation which is an effective treatment for gastric variceal bleeding secondary to SPH [33].

Esophageal variceal bleeding (EVB) is one of the most severe adverse events of liver cirrhosis [34].

Seven percent of patients with liver cirrhosis develop the symptom of esophagogastric fundic varices each year [35].

Patients with cirrhosis who are not treated prophylactically have a high risk of rebleeding within 1 year and a mortality rate of approximately 15%–20% within 6 weeks [36].

In recent years, some evidence suggests that endoscopic variceal ligation combined with endoscopic sclerotherapy can significantly reduce bleeding and recurrence of esophageal varices, with similar adverse events compared to endoscopic varices ligation alone [37,38].

Gastrointestinal bleeding is often encountered in patients with cirrhosis, with an incidence of 85% in Child Class C versus 45% in Child Class A and patients in Child Class C also have up to 30% mortality risk compared to other classes [39].

Gastric varices infrequently bleed compared to oesophagal varices, they may lead to massive bleeding resulting in hemorrhagic shock and death in 25-55% of cases due to the rapid flow of blood in the varices and the inflow and outflow vessels [40].

Balloon-occluded retrograde transvenous obliteration(BRTO) appears feasible and successful in patients with poor hepatic functional reserve or hemorrhagic diathesis.

Transjugular intrahepatic portosystemic shunt (TIPS) is a nonsurgical intervention to reduce portal pressure by creating a low-resistance channel between the portal and systemic circulations.

TIPS can significantly decrease the level of the portal pressure gradient (PPG), but it is only considered a treatment choice after failed first-line treatment.

Patients with a portal venous pressure ≥25 mmHg or at high-risk of the first-line treatment failure and mortality, the primary goal is to reduce the level of portal venous pressure, which indicate TIPS can be applied as a first-line treatment to prevent further life-threatening conditions.

TIPS treatment has been extensively used in the treatment of variceal bleeding for more than two decades; however, TIPS treatment increases the incidence of hepatic encephalopathy, which was reported as 16% to 31% in post-TIPS patients.

Gauri Mukhiya et al, evaluated the efficacy and safety of TIPS combined with gastric coronary vein embolization (GCVE) for cirrhotic portal hypertensive variceal bleeding and compare outcomes of first-line with second-line treatment, coil with glue, and single-covered with double stents.

However, whether TIPS or BRTO is more beneficial for GVB patients, especially regarding the overall survival rate, still needs to be discovere.

Mini-invasive surgical technologies expand the possibilities and are successfully used in the treatment of patients with portal hypertension and its complications.

During the last three decades the Sugiura procedure and other nonshunting operations have been widely performed as the operations of choice for bleeding esophageal varices in Japan.

Surgery is usually performed in patients with PH with a high risk of variceal bleeding in China using individualized and precise total laparoscopic surgical procedure based on 3D remodeling for PH.

Esophagogastric devascularization and splenectomy are safe and effective to treat PH secondary to liver cirrhosis and it can be performed successfully in elderly patients and achieve a curative effect that is not inferior to young patients. Laparoscopic Hassab's procedure is a feasible treatment for esophagogastric varices with PH in terms of both short- and long-term results.

Thus, PH occurs when hemodynamics is disturbed in the portal system and is accompanied by the development of complications that potentiate each other and negatively affect the results of diagnosis and treatment.

CONCLUSIONS

Diagnosis and treatment of patients with complicated PH requires a multidisciplinary approach, which is due to the diverse pathophysiological process of portal hypertension. The possibilities of providing emergency care to this category of patients depend on the level of medical training of the staff, the possibilities of medical and technical support in the provision of interventional care, the ineffectiveness of which necessitates surgical treatment using minimally invasive technologies.

REFERENCES

1. Italian Association for the Study of the Liver (AISF). Portal Hypertension and Ascites: Patient-and Population-centered Clinical Practice Guidelines by the Italian Association for the Study of the Liver (AISF). Dig Liver Dis. 2021;53(9):1089-1104. doi: 10.1016/j.dld.2021.06.021. DOI
2. Yoshiji H. Management of cirrhotic ascites: Seven-step treatment protocol based on the Japanese evidence-based clinical practice guidelines for liver cirrhosis 2020. Hepatol Res. 2023. doi: 10.1111/hepr.13937. DOI
3. Yoshiji H, Nagoshi S, Akahane T et al. Evidence-based clinical practice guidelines for liver cirrhosis 2020. Hepatol Res. 2021;51(7):725-749. doi: 10.1111/hepr.13678. DOI
4. Yoshiji H, Nagoshi S, Akahane T et al. Evidence-based clinical practice guidelines for Liver Cirrhosis 2020. J Gastroenterol. 2021;56(7):593-619. doi: 10.1007/s00535-021-01788-x. DOI
5. Aithal GP, Palaniyappan N, China L et al. Guidelines on the management of ascites in cirrhosis. Gut. 2021;70(1):9-29. doi: 10.1136/gutjnl-2020-321790. DOI
6. Macken L, Mason L, Evans C et al. Palliative long-term abdominal drains versus repeated drainage in individuals with untreatable ascites due to advanced cirrhosis: study protocol for a feasibility randomised controlled trial. Trials. 2018;19(1):401. doi: 10.1186/s13063-018-2779-0. DOI
7. Fleming KM, Aithal GP, Card TR, West J. The rate of decompensation and clinical progression of disease in people with cirrhosis: a cohort study. Aliment Pharmacol Ther. 2010;32(11-12):1343-50. doi: 10.1111/j.1365-2036.2010.04473.x. DOI
8. Fleming KM, Aithal GP, Card TR, West J. The rate of decompensation and clinical progression of disease in people with cirrhosis: a cohort study. Alimentary pharmacology & therapeutics. 2010;32(11-12):1343–1350. doi:10.1111/j.1365-2036.2010.04473.x. DOI
9. Cooper M, Pollard A, Pandey A et al. Palliative Long-Term Abdominal Drains Versus Large Volume Paracentesis in Refractory Ascites Due to Cirrhosis (REDUCe Study): Qualitative Outcomes. J Pain Symptom Manage. 2021;62(2):312-325.e2. doi: 10.1016/j.jpainsymman.2020.12.007. DOI
10. Macken L, Bremner S, Gage H et al. Randomised clinical trial: palliative long-term abdominal drains vs large-volume paracentesis in refractory ascites due to cirrhosis. Aliment Pharmacol Ther. 2020;52(1):107-122. doi: 10.1111/apt.15802. DOI
11. Cheatham ML, White MW, Sagraves SG et al. Abdominal perfusion pressure: a superior parameter in the assessment of intra-abdominal hypertension. J Trauma. 2000;49(4):621-6. doi: 10.1097/00005373-200010000-00008. DOI
12. De Laet IE, Malbrain MLNG, De Waele JJ. A Clinician's Guide to Management of Intra-abdominal Hypertension and Abdominal Compartment Syndrome in Critically Ill Patients. Crit Care. 2020;24(1):97. doi: 10.1186/s13054-020-2782-1. DOI
13. Evans L, Rhodes A, Alhazzani W et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. Crit Care Med. 2021;49(11):e1063-e1143. doi: 10.1097/CCM.0000000000005337. DOI
14. Pereira RA, Esteves AF, Cardoso FS et al. Abdominal perfusion pressure in critically ill cirrhotic patients: a prospective observational study. Sci Rep. 2023;13(1):8550. doi: 10.1038/s41598-023-34367-6. DOI
15. Hasan I, Nababan SHH, Handayu AD et al. Scoring system for predicting 90-day mortality of in-hospital liver cirrhosis patients at Cipto Mangunkusumo Hospital. BMC Gastroenterol. 2023;23(1):190. doi: 10.1186/s12876-023-02813-4. DOI
16. Song DS. [Spontaneous Bacterial Peritonitis]. Korean J Gastroenterol. 2018;72(2):56-63. Korean. doi: 10.4166/kjg.2018.72.2.56. DOI
17. Aithal GP, Palaniyappan N, China L et al. Guidelines on the management of ascites in cirrhosis. Gut. 2021;70(1):9-29. doi: 10.1136/gutjnl-2020-321790. DOI
18. European Association for the Study of the Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. J Hepatol. 2010;53(3):397-417. doi: 10.1016/j.jhep.2010.05.004. DOI
19. Oey RC, van Buuren HR, de Jong DM et al. Bacterascites: A study of clinical features, microbiological findings, and clinical significance. Liver Int. 2018;38(12):2199-2209. doi: 10.1111/liv.13929. DOI
20. Ameer MA, Foris LA, Mandiga P, Haseeb M. Spontaneous Bacterial Peritonitis. 2023 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024: 28846337.
21. Li H, Wieser A, Zhang et al. Patients with cirrhosis and SBP: Increase in multidrug-resistant organisms and complications. Eur J Clin Invest. 2020;50(2):e13198. doi: 10.1111/eci.13198. DOI
22. Fernández J, Angeli P, Trebicka J et al. Efficacy of Albumin Treatment for Patients with Cirrhosis and Infections Unrelated to Spontaneous Bacterial Peritonitis. Clin Gastroenterol Hepatol. 2020;18(4):963-973.e14. doi: 10.1016/j.cgh.2019.07.055. DOI
23. Salerno F, Gerbes A, Ginès P et al. Diagnosis, prevention and treatment of hepatorenal syndrome in cirrhosis. Gut. 2007;56(9):1310-8. doi: 10.1136/gut.2006.107789. DOI
24. Chaney A. A Review for the Practicing Clinician: Hepatorenal Syndrome, a Form of Acute Kidney Injury, in Patients with Cirrhosis. Clin Exp Gastroenterol. 2021;14:385-396. doi: 10.2147/CEG.S323778. DOI
25. Velez JCQ, Therapondos G, Juncos LA. Reappraising the spectrum of AKI and hepatorenal syndrome in patients with cirrhosis. Nat Rev Nephrol. 2020;16(3):137-155. doi: 10.1038/s41581-019-0218-4. DOI
26. Lenz K, Buder R, Kapun L, Voglmayr M. Treatment and management of ascites and hepatorenal syndrome: an update. Therap Adv Gastroenterol. 2015;8(2):83-100. doi: 10.1177/1756283X14564673. DOI

27. Kumar U, Kumar R, Jha SK et al. Short-term mortality in patients with cirrhosis of the liver and acute kidney injury: A prospective observational study. Indian J Gastroenterol. 2020;39(5):457-464. doi: 10.1007/s12664-020-01086-z. DOI
28. Flamm SL, Wong F, Ahn J, Kamath PS. AGA Clinical Practice Update on the Evaluation and Management of Acute Kidney Injury in Patients With Cirrhosis: Expert Review. Clin Gastroenterol Hepatol. 2022;20(12):2707-2716. doi: 10.1016/j.cgh.2022.08.033. DOI
29. Carter JA, Huang X, Jamil K et al. Cost-effectiveness of terlipressin for hepatorenal syndrome: the United States hospital perspective. J Med Econ. 2023;26(1):1342-1348. doi: 10.1080/13696998.2023.2260693. DOI
30. Pitre T, Kiflen M, Helmeczi W et al. The Comparative Effectiveness of Vasoactive Treatments for Hepatorenal Syndrome: A Systematic Review and Network Meta-Analysis. Crit Care Med. 2022;50(10):1419-1429. doi: 10.1097/CCM.0000000000005595. DOI
31. Huang X, Bindra J, Chopra I et al. Treatment-Related Cost Analysis of Terlipressin for Adults with Hepatorenal Syndrome with Rapid Reduction in Kidney Function. Adv Ther. 2023;40(12):5432-5446. doi: 10.1007/s12325-023-02674-z. DOI
32. Abraham M, Doshi S, Asfari MM et al. Isolated Gastric Variceal Hemorrhage Secondary to Idiopathic Sinistral Portal Hypertension. Cureus. 2021;13(7):e16165. doi: 10.7759/cureus.16165. DOI
33. Li L, Zhao X. Treatment of rare gastric variceal bleeding in acute pancreatitis using embolization of the splenic artery combined with short gastric vein. Case Rep Gastroenterol. 2012;6(3):741-6. doi: 10.1159/000345962. DOI
34. Sharma M, Singh S, Desai V et al. Comparison of Therapies for Primary Prevention of Esophageal Variceal Bleeding: A Systematic Review and Network Meta-analysis. Hepatology. 2019;69(4):1657-1675. doi: 10.1002/hep.30220. DOI
35. Su J, Zhang H, Ren M et al. Efficacy and Safety of Ligation Combined With Sclerotherapy for Patients With Acute Esophageal Variceal Bleeding in Cirrhosis: A Meta-Analysis. Front Surg. 2021;8:664454. doi: 10.3389/fsurg.2021.664454. DOI
36. Wang AJ, Zheng XL, Hong JB et al. Cap-Assisted Endoscopic Sclerotherapy vs Ligation in the Long-Term Management of Medium Esophageal Varices: A Randomized Trial. Clin Transl Gastroenterol. 2020;11(12):e00285. doi: 10.14309/ctg.0000000000000285. DOI
37. Wang J, Chen S, Naga YM et al. Esophageal Variceal Ligation Monotherapy versus Combined Ligation and Sclerotherapy for the Treatment of Esophageal Varices. Can J Gastroenterol Hepatol. 2021;2021:8856048. doi: 10.1155/2021/8856048. DOI
38. Retracted: Additional Benefits Conferred by Endoscopic Sclerotherapy to Liver Cirrhosis Patients Receiving Endoscopic Variceal Ligation. Evid Based Complement Alternat Med. 2023;2023:9758732. doi: 10.1155/2023/9758732. DOI
39. Rodge GA, Goenka U, Goenka MK. Management of Refractory Variceal Bleed in Cirrhosis. J Clin Exp Hepatol. 2022;12(2):595-602. doi: 10.1016/j.jceh.2021.08.030. DOI
40. Waguri N, Osaki A, Watanabe Y. Balloon-occluded retrograde transvenous obliteration for treatment of gastric varices. World J Hepatol. 2021;13(6):650-661. doi: 10.4254/wjh.v13.i6.650. DOI

CONFLICT OF INTEREST

The Authors declare no conflict of interest

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