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Review Article

**REVIEW STUDY: MANAGEMENT OF LIVER CIRRHOSIS
IN PATIENTS WITH HEPATOCELLULAR CARCINOMA**

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Abstract:

Background: the majority of HCC patients are suffering from cirrhosis thus it's challenging to manage HCC because it's associated with chronic dysfunction of the liver.

Objective: This study aimed at studying the management procedures for liver cirrhosis among patients with hepatocellular carcinoma.

Methods: The online medical database was searched then the English articles from 2010 – 2020 were included in the review.

Results: There were 36 studies included that answered the question about the management procedures for liver cirrhosis among patients with hepatocellular carcinoma.

Conclusion: liver cirrhosis is a critical illness among HCC patients which hinders the management of HCC and can result in many complications. The severity of the liver disease and decompensation can affect the survival rates thus Child-Pugh is considered a sensitive and prognostic factor for defining the proper management technique among HCC patients.

Keywords: Management, liver cirrhosis, hepatocellular carcinoma (HCC).

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BACKGROUND:

Hepatocellular carcinoma (HCC) is a significant medical issue with high morbidity and mortality rates. It positions as the fifth most regular reason for malignant growth in males and the seventh in females ranging to 33% of all disease associated deaths and the main source of death in patients suffering from cirrhosis of liver [1, 2]. The reasons for this tumor harmonize with those of liver cirrhosis, in spite of the fact that there are epidemiological contrasts as indicated by the land zone considered [3, 4].

Cirrhosis is a typical issue around the world, representing huge mortality and clinic affirmation rate. The assessed predominance of cirrhosis in the United States was 0.15% of the populace [5]. Comparative numbers have been accounted for from European nations and much higher numbers are evaluated in generally African and Asian nations. Alcohol utilization and constant hepatitis C are the main sources of cirrhosis in western nations. Interminable hepatitis B is exceptionally endemic among Asian population and it is the commonest reason for liver cirrhosis [6].

Liver cirrhosis is considered as an advanced phase of hepatic fibrosis related with hepatic knobs that continuously disturbs the ordinary hepatic tissue and changes the liver to a high obstructive and resistant organ, this procedure lifts the sinusoidal weight resulting in debilitated hepatocyte capacity and expands the weight on the portal vein prompting hypertension. If the portal pressure increments, this increases the risk of creating complications identified with cirrhosis [7, 8]. This review is supposed to study the management procedures for liver cirrhosis among patients with hepatocellular carcinoma.

METHOD:

The data base was searched online for information related to the management of cirrhosis among patients with hepatocellular carcinoma then all the eligible English articles from 2010-2020 were collected, evaluated and included in this study.

RESULTS:

The study included 36 articles were included in this review that were published between 2010-2020 including RCTs, reviews, case-controlled studies and clinical trials.

- **Diagnosis of cirrhosis in relation to HCC:**

Cirrhosis of all etiologies may be complicated by HCC, but persistent hepatitis B virus (HBV) or hepatitis C virus (HCV) infection account for over 80% of HCC cases worldwide [9]. In Japan, the

United States, Latin America, Egypt and Europe, hepatitis C is the major cause of HCC. The incidence of HCC is 2-8% per year in patients with chronic hepatitis C and established cirrhosis. While in Asia, Africa, and in some eastern European countries, chronic hepatitis B is the prime cause of HCC, far outweighing the impact of chronic hepatitis C [10].

The vast majority of the patients with HCC have been suffering from cirrhosis. Overall information show that predominance of cirrhosis in people with HCC is around 80-90% [11]. Cirrhosis can be associated and complicated to HCC among 80% of HCC cases especially among hepatitis B infection (HBV) or hepatitis C infection (HCV) contamination [10].

It is necessary to examine the patients with HCC with a clinical analysis of cirrhosis including a definite assessment of cirrhosis manifestations and signs demonstrating nearness of cirrhosis, as enlargement of the stomach and sleeping disorders or, obvious liver or spleen. Lab examinations recommend assessing the variations from the norm for at least one of serum functions of the liver including bilirubin, albumin and prothrombin time. Also, the decrease in platelets count is sensitive in diagnosis of cirrhosis related portal hyper tension. Among patients with clinical highlights, laboratory and imaging findings and biopsy also must be considered to diagnose cirrhosis among HCC patients [12].

The advance of decompensated cirrhosis is accompanied by jaundice, GIT bleeding, encephalopathy and ascites. The pace of decompensation is evaluated to be 3-5% every year with high mortality rates [13]. The seriousness of hepatic decompensation influences the treatment choices for HCC patients. Appraisal of the seriousness of cirrhosis is typically done utilizing the classification of Child-Pugh [14]. Also, patients who suffer from compromised hepatic replacement with Child-Pugh stage B are supposed to have higher adverse outcomes and effects with treatment in comparison with Child-Pugh A patients [15, 16].

- **Management of cirrhosis among HCC patients:**

Distinguishing and management of basic causes can decrease the development rates and can also reverse cirrhotic conditions clinically and histologically as well [17, 18]. Comparative outcomes are found in patients with redressed or decompensated cirrhosis because of using steroids in treatment of immune system hepatitis, using antivirals for management of HBV and using combination medications for treatment of HCV rewarded with blend treatment [19-21]. Although,

the job of antiviral treatment in patients with HCC isn't clear as most authority rules consider dynamic HCC as a contraindication to treatment. Anticipation of second complications ought to be accomplished by staying away from hepatotoxic prescriptions, herbal medications and cirrhotic patients with sero-negative vaccination against hepatitis A and B.

There is a lack of standard treatment pattern but various ongoing examinations show a gainful impact of usually utilized medications on management of cirrhosis and its complexities including beta blockers, statins, anti-infection agents and anticoagulation[19-21]. These medications can decrease the progression of fibrosis, varices and bacterial translocation. The management options depend on the severity of liver cirrhosis which is classified according to Child-Pugh class[22, 23].

- **Liver resection:**

The principal line treatment for patients with HCC and liver cirrhosis with Child-Pugh A is liver resection[24]. The mortality rates and blood transfusion prerequisites before the operation ought not surpass 2–3% and 10%, respectively[25, 26]. Thus there is a necessary need to be cautious while selecting patients who can tolerate the surgery to avoid other complications in liver function[24, 27]. Guidelines suggest assurance of indocyanine green degree of retention at 15 min or evaluation of the seriousness of portal hypertension with a cut-off estimation of $\leq 14\%$ is significant for hepatic resection however[28]. Assessing the severity of hepatic hypertension can be done using the Hepatic venous pressure gradient (HVPG) in patients with liver cirrhosis (HVPG ≥ 10 mm Hg)[29]. Among Patients no portal hypertension or high bilirubin levels, the 5-year survival (70%) rates can be higher than those suffering from portal hypertension (50%). Also, significant portal hypertension increased the mortality rates within 3-5 years after resection for HCC patients[30]. Thus, hepatic resection is only recommended in patients with good liver function and can strictly be operated only among 5-10% of HCC patients with liver cirrhosis[27]. Clinical trials must be conducted to expand the safety and curative options of hepatic resection among HCC patients with liver cirrhosis.

- **Ablation:**

Image guided local ablation can be done among patients with small tumors less than 5 cm and the Child-Pugh staging is A or B[27]. It can control local disease and increase the survival rates[24, 30].

- **Supportive care:**

Diet restrictions and pain control are efficient among cirrhotic patients to decrease the severity of pain and enhance better life. Treatment of the cause of liver decompensation and cirrhosis is a must for proper management of liver cirrhosis among HCC patients. A few investigations have indicated that continued hepatitis B infection (HBV) is related to higher danger of repeat after operative treatment[31] but the antiviral treatment can enhance the result among patients experiencing resection for HCC[32, 33]. Using interferon treatments for HCV is better for HCC patients even after resection or ablation which can decrease the need for liver transplantation[34].

Also, the multichines inhibitor sorafenib can be used among HCC patients with Child-Pugh A or higher B or C [35-37] and other small studies showed it can improve the portal hypertension syndrome[38-41]

- **Transarterial chemoembolisation:**

Among patients with compensated liver disease and HCC, the trans arterial chemoembolization is the first line of treatment in there is no extrahepatic spread or invasion in the vascular system[24]. but it is contraindicated among patients with Child-Pugh score > 8 , high bleeding risk, portal embolism [42]. It is supposed to decrease the ischemic damage and induced liver failure.

- **Liver transplantation:**

Liver transplantation is suggested for little tumors and severely impaired liver function. Thus, the transplantation procedure is the main treatment methodology that can manage HCC and liver cirrhosis[43]. High survival rates were found among HCC and cirrhotic patients when compared to transplanted patients with no tumors or non-threatening indications[27, 44].

CONCLUSION:

In this literature review, liver cirrhosis is a critical illness among HCC patients which hinders the management of HCC and can result in many complications. The severity of the liver disease and decompensation can affect the survival rates thus Child-Pugh is considered a sensitive and prognostic factor for defining the proper management technique among HCC patients. More studies are needed to evaluate the cons and pros of the available HCC medications on the liver functions if there are signs of cirrhosis.

REFERENCES:

1. Fitzmaurice C, Akinyemiju TF, Al Lami FH, Alam T, Alizadeh-Navaei R, Allen C, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted

- Life-Years for 29 Cancer Groups, 1990 to 2016: A Systematic Analysis for the Global Burden of Disease Study. *JAMA oncology*. 2018;4(11):1553-68. doi:10.1001/jamaoncol.2018.2706.
2. Njei B, Rotman Y, Ditah I, Lim JK. Emerging trends in hepatocellular carcinoma incidence and mortality. *Hepatology (Baltimore, Md)*. 2015;61(1):191-9. doi:10.1002/hep.27388.
 3. Goh GB, Li JW, Chang PE, Chow KY, Tan CK. Deciphering the epidemiology of hepatocellular carcinoma through the passage of time: A study of 1,401 patients across 3 decades. *Hepatology communications*. 2017;1(6):564-71. doi:10.1002/hep4.1059.
 4. Wallace MC, Preen D, Jeffrey GP, Adams LA, Jero, hepatology. The evolving epidemiology of hepatocellular carcinoma: a global perspective. 2015;9(6):765-79.
 5. Schuppan D, Afdhal NH. Liver cirrhosis. *Lancet (London, England)*. 2008;371(9615):838-51. doi:10.1016/s0140-6736(08)60383-9.
 6. Qua CS, Goh KL. Liver cirrhosis in Malaysia: peculiar epidemiology in a multiracial Asian country. *Journal of gastroenterology and hepatology*. 2011;26(8):1333-7. doi:10.1111/j.1440-1746.2011.06732.x.
 7. Poordad FF. Presentation and complications associated with cirrhosis of the liver. *Current medical research and opinion*. 2015;31(5):925-37. doi:10.1185/03007995.2015.1021905.
 8. Long B, Kozyfman A. The emergency medicine evaluation and management of the patient with cirrhosis. *The American journal of emergency medicine*. 2018;36(4):689-98. doi:10.1016/j.ajem.2017.12.047.
 9. Liu J, Ma Z, Liu Y, Wu L, Hou Z, Li W. Screening of potential biomarkers in hepatitis C virus-induced hepatocellular carcinoma using bioinformatic analysis. *Oncology letters*. 2019;18(3):2500-8. doi:10.3892/ol.2019.10578.
 10. Ferenci P, Fried M, Labrecque D, Bruix J, Sherman M, Omata M, et al. World Gastroenterology Organisation Guideline. Hepatocellular carcinoma (HCC): a global perspective. *Journal of gastrointestinal and liver diseases : JGLD*. 2010;19(3):311-7.
 11. Cabrera R, Nelson DR. Review article: the management of hepatocellular carcinoma. *Alimentary pharmacology & therapeutics*. 2010;31(4):461-76. doi:10.1111/j.1365-2036.2009.04200.x.
 12. Runyon BA. A Primer on Detecting Cirrhosis and Caring for These Patients without Causing Harm. *International journal of hepatology*. 2011;2011:801983. doi:10.4061/2011/801983.
 13. 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):1343-50. doi:10.1111/j.1365-2036.2010.04473.x.
 14. Busco S, Buzzoni C, Mallone S, Trama A, Castaing M, Bella F, et al. Italian cancer figures--Report 2015: The burden of rare cancers in Italy. *Epidemiologia e prevenzione*. 2016;40(1 Suppl 2):1-120. doi:10.19191/ep16.1s2.P001.035.
 15. Marrero J, Lencioni R, Kudo M, Ye S, Nakajima K, Cihon F, et al. Global Investigation of Therapeutic Decisions in Hepatocellular Carcinoma and of its Treatment with Sorafenib (GIDEON) second interim analysis in more than 1,500 patients: Clinical findings in patients with liver dysfunction. 2011;29(15_suppl):4001-.
 16. Culleton S, Jiang H, Haddad CR, Kim J, Brierley J, Brade A, et al. Outcomes following definitive stereotactic body radiotherapy for patients with Child-Pugh B or C hepatocellular carcinoma. 2014;111(3):412-7.
 17. Turco L, Villanueva C, La Mura V, García-Pagán JC, Reiberger T, Genescà J, et al. Lowering Portal Pressure Improves Outcomes of Patients With Cirrhosis, With or Without Ascites: A Meta-Analysis. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2020;18(2):313-27.e6. doi:10.1016/j.cgh.2019.05.050.
 18. Suk KT. Hepatic venous pressure gradient: clinical use in chronic liver disease. *Clinical and molecular hepatology*. 2014;20(1):6-14. doi:10.3350/cmh.2014.20.1.6.
 19. Leonardi F, Maria N, Villa E. Anticoagulation in cirrhosis: a new paradigm? *Clinical and molecular hepatology*. 2017;23(1):13-21. doi:10.3350/cmh.2016.0110.
 20. Tsochatzis EA, Bosch J, Burroughs AK. New therapeutic paradigm for patients with cirrhosis. *Hepatology (Baltimore, Md)*. 2012;56(5):1983-92. doi:10.1002/hep.25915.
 21. Wang SZ, Ding HG. [New therapeutic paradigm and concepts for patients with cirrhotic refractory ascites]. *Zhonghua gan zang bing za zhi = Zhonghua ganzangbing zazhi = Chinese journal of hepatology*. 2017;25(4):249-53. doi:10.3760/cma.j.issn.1007-3418.2017.04.003.
 22. Dănulescu RM, Stanciu C, Trifan A. Assessing the risk of decompensation by ascites and spontaneous bacterial peritonitis in cirrhosis. *Revista medico-chirurgicala a Societatii de Medici si Naturalisti din Iasi*. 2014;118(2):320-6.
 23. Fernández J, Acevedo J, Castro M, Garcia O, de Lope CR, Roca D, et al. Prevalence and risk

- factors of infections by multiresistant bacteria in cirrhosis: a prospective study. *Hepatology* (Baltimore, Md). 2012;55(5):1551-61. doi:10.1002/hep.25532.
24. Cancer EAFTSOTLEOFRATO. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. *Journal of hepatology*. 2012;56(4):908-43. doi:10.1016/j.jhep.2011.12.001.
 25. Yip VS, Poon RT, Chok KS, Chan AC, Dai WC, Tsang SH, et al. Comparison of Survival Outcomes Between Right Posterior Sectionectomy and Right Hepatectomy for Hepatocellular Carcinoma in Cirrhotic Liver: A Single-Centre Experience. *World journal of surgery*. 2015;39(11):2764-70. doi:10.1007/s00268-015-3146-x.
 26. Shiba H, Ishida Y, Fujiwara Y, Wakiyama S, Gocho T, Ito R, et al. Comparison of hepatocellular carcinoma with cirrhosis patients undergoing hepatic resection between hepatitis B and C infection. *Hepato-gastroenterology*. 2013;60(127):1746-8.
 27. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. *Hepatology* (Baltimore, Md). 2011;53(3):1020-2. doi:10.1002/hep.24199.
 28. Vos JJ, Wietasch JG, Absalom AR, Hendriks HG, Scheeren TWJA. Green light for liver function monitoring using indocyanine green? An overview of current clinical applications. 2014;69(12):1364-76.
 29. Fullwood D. Portal hypertension and varices in patients with liver cirrhosis. *Nursing standard* (Royal College of Nursing (Great Britain) : 1987). 2012;26(48):52-7; quiz 8. doi:10.7748/ns2012.08.26.48.52.c9230.
 30. Berzigotti A, Reig M, Abraldes JG, Bosch J, Bruix JH. Portal hypertension and the outcome of surgery for hepatocellular carcinoma in compensated cirrhosis: a systematic review and meta-analysis. 2015;61(2):526-36.
 31. Lee JI, Kim JK, Chang HY, Lee JW, Kim JM, Chung HJ, et al. Impact of postoperative hepatitis B virus reactivation in hepatocellular carcinoma patients who formerly had naturally suppressed virus. *Journal of gastroenterology and hepatology*. 2014;29(5):1019-27. doi:10.1111/jgh.12472.
 32. Li N, Lai EC, Shi J, Guo WX, Xue J, Huang B, et al. A comparative study of antiviral therapy after resection of hepatocellular carcinoma in the immune-active phase of hepatitis B virus infection. *Annals of surgical oncology*. 2010;17(1):179-85. doi:10.1245/s10434-009-0694-z.
 33. Kubo S, Takemura S, Sakata C, Urata Y, Uenishi T. Adjuvant therapy after curative resection for hepatocellular carcinoma associated with hepatitis virus. *Liver cancer*. 2013;2(1):40-6. doi:10.1159/000346214.
 34. Liver EAfSo. EASL Recommendations on Treatment of Hepatitis C 2015. *Journal of hepatology*. 2015;63(1):199-236. doi:10.1016/j.jhep.2015.03.025.
 35. Lee SH, Song IH, Noh R, Kang HY, Kim SB, Ko SY, et al. Clinical outcomes of patients with advanced hepatocellular carcinoma treated with sorafenib: a retrospective study of routine clinical practice in multi-institutions. 2015;15(1):236.
 36. Sohn W, Paik Y-H, Cho J-Y, Lim HY, Ahn JM, Sinn DH, et al. Sorafenib therapy for hepatocellular carcinoma with extrahepatic spread: treatment outcome and prognostic factors. 2015;62(5):1112-21.
 37. Iavarone M, Cabibbo G, Piscaglia F, Zavaglia C, Grieco A, Villa E, et al. Field-practice study of sorafenib therapy for hepatocellular carcinoma: a prospective multicenter study in Italy. *Hepatology* (Baltimore, Md). 2011;54(6):2055-63. doi:10.1002/hep.24644.
 38. Yang YY, Liu RS, Lee PC, Yeh YC, Huang YT, Lee WP, et al. Anti-VEGFR agents ameliorate hepatic venous dysregulation/microcirculatory dysfunction, splanchnic venous pooling and ascites of NASH-cirrhotic rat. 2014;34(4):521-34.
 39. D'Amico M, Mejías M, García-Pras E, Abraldes JG, Garcia-Pagan JC, Fernández M, et al. Effects of the combined administration of propranolol plus sorafenib on portal hypertension in cirrhotic rats. 2012;302(10):G1191-G8.
 40. Pinter M, Sieghart W, Reiberger T, Rohr-Udilova N, Ferlitsch A, Peck-Radosavljevic M. The effects of sorafenib on the portal hypertensive syndrome in patients with liver cirrhosis and hepatocellular carcinoma—a pilot study. *Alimentary pharmacology & therapeutics*. 2012;35(1):83-91. doi:10.1111/j.1365-2036.2011.04896.x.
 41. Hidaka H, Nakazawa T, Kaneko T, Minamino T, Takada J, Tanaka Y, et al. Portal hemodynamic effects of sorafenib in patients with advanced hepatocellular carcinoma: a prospective cohort study. *Journal of gastroenterology*. 2012;47(9):1030-5. doi:10.1007/s00535-012-0563-6.
 42. Sieghart W, Huckle F, Peck-Radosavljevic MJ. Transarterial chemoembolization: modalities, indication, and patient selection. 2015;62(5):1187-95.
 43. Forner A, Llovet JM, Bruix J. Hepatocellular carcinoma. *Lancet* (London, England). 2012;379(9822):1245-55. doi:10.1016/s0140-6736(11)61347-0.
 44. Mazzaferro V, Bhoori S, Sposito C, Bongini M, Langer M, Miceli R, et al. Milan criteria in

liver transplantation for hepatocellular carcinoma: an evidence-based analysis of 15 years of experience. Liver transplantation : official publication of the American Association for the Study of Liver Diseases

and the International Liver Transplantation Society. 2011;17 Suppl 2:S44-57. doi:10.1002/lt.22365.