Original Article
DOI: https://doi.org/10.70749/ijbr.v2i02.112

INDUS JOURNAL OF BIOSCIENCES RESEARCH
https://induspublisher.com/IJBR
ISSN: 2960-2793/ 2960-2807

Crossref
OPEN ACCESS

Variceal Bleeding a Predictor of Mortality in Patient Admitted with Liver Cirrhosis

Syed Nadir Shah[1], Moneeb Ur Rehman[1], Hasil Khan[1], Javeria Mansoor[1], Fazal ur Rehman[1], Rida Manzoor[1], Sana Ullah Kakar[1]

[1]Department of Internal Medicine, Sandman Provincial Hospital Quetta, Pakistan.

ARTICLE INFO

Keywords

Variceal Bleeding, Liver Cirrhosis, Meld Score, Portal Hypertension, Mortality, Child PUGH, Chronic Liver Disease

Corresponding Author: Syed Nadir Shah
Department of Internal Medicine, Sandman Provincial Hospital Quetta, Pakistan.
Email: shahnadir2010@yahoo.com

Declaration

Author's Contributions: All authors contributed to the study and approved the final manuscript.
Conflict of Interest: The authors declare no conflict of interest.
Funding: No funding received.

Article History

Received: 03-10-2024
Revised: 22-10-2024
Accepted: 26-10-2024

ABSTRACT

This study aims to assess the risk of mortality in cirrhotic patients with acute variceal bleeding at a tertiary care hospital. Variceal bleeding is a common and life-threatening complication in liver cirrhosis, significantly contributing to early mortality. The study utilized a cohort design with 128 patients, divided into two groups: those with acute variceal bleeding (exposed) and those without (unexposed). Baseline clinical data, including Child-Pugh and MELD scores, were collected. The primary outcome was 30-day mortality. Key findings include a mean age of 55.7 ± 22.1 years, with 52.8% males and 56.3% from rural areas. The average Child-Pugh score was 10.1 ± 3.2, and the mean MELD score was 24.1 ± 10.1. The frequency of hematemesis and melena as presenting complaints was evenly split at 50%. Mortality was observed in 49.2% of the patients with variceal bleeding. Statistical analysis using chi-square tests revealed a significant association between variceal bleeding and increased mortality ($p < 0.05$). Confounding factors such as age, gender, and comorbid conditions were controlled through stratification, with relative risk calculations confirming the elevated mortality risk. This study highlights the critical need for timely interventions in cirrhotic patients with variceal bleeding and underscores the importance of comprehensive management strategies to reduce mortality in this high-risk population.

INTRODUCTION

The size of the varices is the most significant predictor of bleeding, with patients with big varices having the highest annual risk of experiencing their first bleeding (15%) (Garcia Tsao G et al., 2007). Several new modalities show promise, such as a combination of coil and glue injection for gastric varices that are bleeding or not bleeding. Skill is not necessary for this process. 2009, Augustin et al. noted that Numerous prognostic models have incorporated these characteristics. According to research conducted in 2009 by Abraides et al., these models can categorize patients according to their mortality risk and guide treatment choices, like using a more aggressive approach for patients at high risk. But they aren't used nearly enough, and that's in part because there isn't any third-party verification. The most common cause of mortality for those with cirrhosis is venous hemorrhage, an emergency affecting the digestive system. Reversing the bleeding and preventing additional problems caused by chronic liver disease are crucial for individuals with variceal hemorrhage to have a positive outcome. (Augustin S. et al., 2017; Augustin S. et al., 2011). However, a substantial mortality risk persists for patients with AVB (5'8). A multitude of prognostic models are available for use in predicting the

UGIB outcome. Clinical outcomes for patients with AVB are not well-predicted by the Rockall and Glasgow Blatchford score, a routinely used tool in UGIB; this score has mostly been validated for non-variceal IIGIB (NVB) (Reed EA, et al., 2014).

A common clinical chronic progressive disease that progresses slowly and has a high death rate due to one or more reasons is liver cirrhosis. It ranks eighth among primary diseases in terms of economic cost said by Scaglione S et al. (2015), the world's largest cause of liver-related death, and the fifth most common cause of adult fatalities. Two prognostic stages for cirrhosis—compensated cirrhosis and decompensated cirrhosis—are recognized for this diverse disease (Westbrook RH at el., 2014). There are no outward signs in the early stages because of the vital liver compensatory function. Subsequently, portal hypertension and liver function impairment become the main symptoms, affecting several systems. Portal hypertension in cirrhosis occurs When there is greater hepatic vascular resistance to portal blood flow. (Tetangco EP at el., 2016; Garcia-Pagan JC et al., 2012). When the HVPG is less than 12 mmHg, actual variceal hemorrhage is unlikely to happen, and when it is more than 20 mmHg, failure to stop bleeding and higher mortality are predicted (Groszman Risk stratification and tailored care were the main topics of discussion at the most recent of these conferences, known as Baveno VI, which was held in 2015 4. (de Francis R, 2015).

REVIEW OF LITERATURE

Repeat bleeds are more dangerous and underline the efficacy of treatment procedures and the necessity of their timely providing. Based on the study carried out by Reverter et al. (2014), Hemorrhage is indeed significantly linked to the cirrhotic patients' early mortality rate, especially variceal bleeding. From the available research, it is found that the mortality after a variceal bleed ranges between 15 to 20 % at six weeks (Banares et al. , 2013). Lowering mortality rates means that interventions have to be provided and initiated in a timely and effective manner (Garcia-Tsao et al. , 2017). For achieving secondary prophylaxis, the high risk patients should be treated with trans jugular intrahepatic portosystemic shunt (TIPS) and non-selective beta blockers and are recommended to undergo endoscopic band ligation (Villanueva et al. , 2016). The studies show that these actions significantly raise mortality and decrease the probability of rebleeding (Merkel et al. , 2017). It might be feasible to improve the patients' prognosis, for instance, by exploring the efficacy of new vasoactive agents, the TIPS technique further, as well as by developing individual treatment strategies based on patients' gene and molecular profiles (Ge et al. , 2019). In addition, new therapies for variceal hemorrhage and cirrhosis may be developed by pursuing the research on the roles of gut microbiota (Bajaj, 2019). Patients who have suffered from the variceal bleeding normally present with hemodynamic compromise, melena and hematemesis. For de Franchis (2015), endoscopic examination remains the gold standard in the diagnosis of varices and variceal hemorrhage because of the direct visualization and treatment capability. The diagnosis of cirrhosis and the determination of its clinical stage CTP class patients are compensated; however, those that belong to CTP-B/C class are mainly decompensated (Garcia-Tsao G et al., 2017). Using terlipressin, somatostatin, or octreotide in this combination of endoscopic and pharmaceutical treatment demonstrated similar efficacy, according to a major RCT (Seo YS et al., 2014). Once the patient is receiving medication and has been stabilized, an endoscopy is required to identify the bleeding source. The best time for an endoscopy in cirrhotic individuals with upper gastrointestinal (GI) bleeding has not been investigated by randomised trials. (Franchis R De et al., 2015). Using prokinetic drugs (erythromycin) in conjunction with placing a nasogastric tube to clean and empty the stomach are two steps that could expedite and simplify endoscopic therapy. Nonetheless, there isn't much data to back up its usage. Sprayable hemostatic powders (Hemospray, Endo Clot) have been introduced recently for gastrointestinal endoscopy to induce a rapid stop to bleeding. Through the combination of forming a mechanical barrier, absorbing elements of serum fluid to concentrate clotting factors, and initiating the clotting cascade, they promote hemostasis (Haddara S et al., 2016; Hagel AF et al., 2017). We have shown in our previous work (P = 1170) that in HCC patients who are having LC complications, a lower serum sodium content is a helpful predictor (H. Nishikawa, R. Kita, T. Kimura et al., 2015). Current reports have concentrated on evaluating the effectiveness of noninvasive techniques using long-term follow-up studies linked to LC-related clinical outcomes. However, we previously reported that the GSAindex, which is based on the ratio of the liver's uptake to that of the liver plus heart at 15 minutes, the heart's uptake to that at 3 minutes, and this ratio calculated from 99mTc-labeled diethylene triamine pentaacetate-galactosyl human serum albumin (99mTc-GSA) scintigraphy, A liver fibrosis glycobiomarker with a distinct fibrosis-related glycoalteration has recently been demonstrated to be the Wisteria floribunda agglutinin-positive human Mac-2-binding protein (WFA+-M2BP) (T. Toshima, K. Shirabe, T. Ikegami et al., 2015).

Rationale of the Study

The prognostic indicators of mortality in patients with cirrhosis having variceal bleeding is an important area

for outcome improvement. This information can serve in clinical practice to assist with treatment selection, patient stratification for aggressive therapies as well as aid health care resource allocation. Despite the identification of many prognostic models and risk factors, there is still need for large studies that would consolidate all these variables together along with a validation of their eventual predictive power in different clinical scenarios.

OBJECTIVE

The objective of this Study is to determine the association between variceal bleeding and mortality in patients with liver cirrhosis admitted to a tertiary care hospital. The study aims to identify whether the presence of acute variceal bleeding significantly increases the risk of mortality within 30 days of admission compared to cirrhotic patients without variceal bleeding. By using a cohort study design, the research will involve collecting and analyzing baseline clinical and demographic data, calculating Child-Pugh and MELD scores, and following patients for a defined period. This investigation seeks to provide valuable insights into the prognostic implications of variceal bleeding in liver cirrhosis, ultimately guiding clinical management and improving patient outcomes in this high-risk population.

Operational Definition

Liver Cirrhosis

It will be labelled as positive if there is presence of 3 or more features On abdominal ultrasound:

- Reduction in longitudinal diameter of 1eft and right lobe of the liver (Lcft lobe <90mmand right lobe <70mm) on ultrasound.
- Ultrasound shown irregularity in liver surface/nodularity of liver surface.
- Decrease echogenicity comparison with right kidney on ultrasound.
- Presence of more than l00ml of ascitic fluid.
- Anterior-posterior diameter of portal vein >l3mm on ultrasound.

Acute Variceal Bleeding

Acute variceal bleeding will be defined as a bleed in a known case liver cirrhosis, with the presence of hematemesis, within 24 hours of presentation, and/or ongoing melena, with the melenic stool within 24 hours. It will be confirmed by endoscopy as dilated, longitudinal mucosal folds running down the lengh of esophagus, with active bleeding.

Mortality

Patient will be followed till 30 days for the assessment of mortality. (Or) the ratio of the total number of deaths in a year in a given population from a particular cause, group of causes, or all causes, to the total population (WHO).

MATERIAL & METHODS

Study Design

The study design is cohort study.
A cohort study is an observational research design that tracks a group of individuals over time to investigate the effects of specific factors (e.g., exposure to a particular risk factor) on their health outcomes. Individuals in a cohort share a characteristic or lived experience, such as birth year or geographic area.

Sample Size

The required sample size for this study is 128 (64 in each group)
Sample size was calculated by using WHO sample sizc calculator. By using the frequency of mortality in patient with and without variceal bleeding in patient with liver cirrhosis was 18% and 2.9% respectively {10), power 80% and level of significance 5%.

Sampling Technique

Consecutive sampling

Sample Selection

Inclusion Criteria

- **Age:** Patient of age >18 years.
- **Gender**: Both genders.
- **Patient**: patients admitted with liver cirrhosis.
- **Expose**: Patient with acute variceal bleeding.
- **Un-expose**: Patient without variceal bleeding.

Exclusion Criteria

- Patient with hepatocellular carcitroma.
- Patient with history of coagulopathy.
- Patier.rt with chronic renal failure,

DATA COLLECTION

Study will be started after taking approval from College of Physicians and Surgeons Pakistan (CPSP) and ethical review committee ol the institute. All patient admitted with liver cirrhosis and fulfilling the inclusion criteria will be enroll in the study. Before enrollment complete details of the study will be explain to the patient and written inform consent will be taken. At the time of enrollment baseline clinical and demographic details such as age, gender, residence, family monthly income, height, weight, BMI, comorbid. smoking and presenting

complaint will be taken and noted in a predesigned performa. All patient will be divided into two groups i.e expose (patient with acute variceal bleeding) and unexposed (patient without variceal bleeding). ChildPUGH score and MELD (Model for End-Stage Liver Disease) score will be calculated in all patient. All patients will be managed as per hospital protocol during stay in the hospital. All patients will be full till 30 days for the assessment of mortality. This structured data collection process ensures comprehensive and consistent information is gathered, facilitating robust analysis of the association between variceal bleeding and mortality in patients with liver cirrhosis.

DATA ANALYSIS

Data is entered in excel and analyzed by using SPSS version 26. Quantitative variables such as age, height, weight, BMI, family monthly income, child PIJGH score, MELD score and duration of hospital stay will be reported as mean and standard deviation. Qualitative variables such as gender, residence. comorbid, smoking, presenting compliant and mortality will be reported as frequency and percentage. Mortality will be compared between expose and unexposed group by using chi-square test and relative risk will be calculated. Confounding variables such as age, gender, residence, family monthly income, BMI, comorbid, smoking, presenting complaint, Child score, MELD score and duration of hospital stay will be controlled through stratification. Post stratification chi-square test will be applied taking p-value <0.05 as significant. Relative risk will also be calculated.

RESULTS

In this study, 128 patients are included to assess the Risk of mortality in patient with variceal bleeding. Data regarding different variables such as; height, weight, BMI, family monthly income, child PUGH score, MELD score, gender, residence. comorbid, smoking, presenting complaint and mortality are collected through the Proforma at Bolan medical complex hospital, Quetta and the results were analyzed as:The mean ± SD of age was 55.70 ± 22.068 with C.I (51.8….59.56) years The mean ± SD of weight was 90.05 ± 24.084 with C. I (85.83……94.26) kg The mean ± SD of height was 4.31 ± .606 The mean ± SD of BMI was 26.40 ± 0.487 with C.I (25.43…27.36) The mean ± SD of Child PUGH score was 10.13 ± 3.234 with C.I (9.56…10.69) The mean ± SD of MELD score was 24.09 ± 10.141 with C.I (22.32….25.87) The mean ± SD of MELD score was 64531.25 ± 27403.643 with C.I (59738.23…69324.27) In the Frequency distribution table of gender 65 (52.8%) were male while 63 (49.2%) were female patients In the Frequency distribution table of Residence 56 (43.8%) were urban while 72 (56.3%) were rural patients.In the Frequency distribution table of comorbid 37 (28.9%) said yes while 91 (71.1%) said no. In the Frequency distribution table of smoking 60 (46.9%) said yes while 68 (53.1%) patients said no.In the Frequency distribution table of presenting complaint 64 (50%) said Hematemesis while 64 (50%) said melena.

In the Frequency distribution table of mortality 63 (49.2%) said yes while 65 (751.8%) said no.

Table 1
Frequency distribution of comorbid

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	melena	37	18.8	28.9	28.9
	hematemsis	91	46.2	71.1	100.0
	Total	128	65.0	100.0	
Missing	System	69	35.0		
Total		197	100.0		

Table 2
Frequency distribution of smoking

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	60	30.5	46.9	46.9
	No	68	34.5	53.1	100.0
	Total	128	65.0	100.0	
Missing	System	69	35.0		
Total		197	100.0		

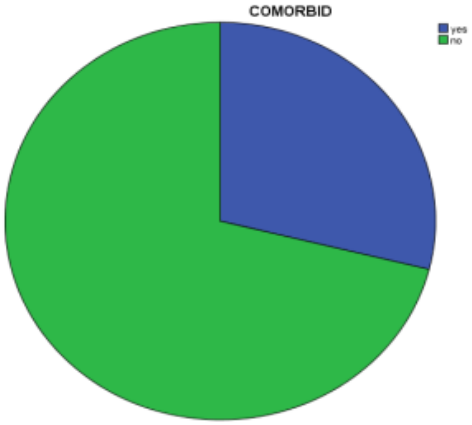
Table 3
Frequency distribution of presenting complaint

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	64	32.5	50.0	50.0
	No	64	32.5	50.0	100.0
	Total	128	65.0	100.0	
Missing	System	69	35.0		
Total		197	100.0		

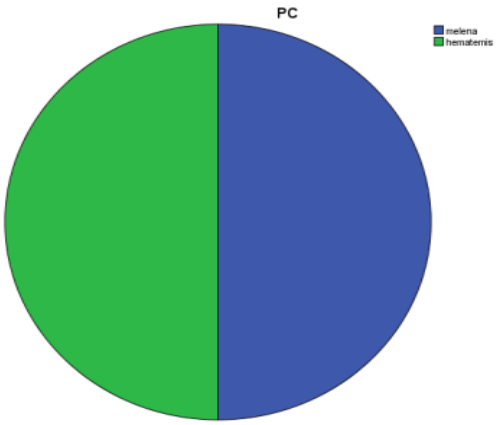
Table 4
Frequency distribution of mortality

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	63	32.0	49.2	49.2
	No	65	33.0	50.8	100.0
	Total	128	65.0	100.0	
Missing	System	69	35.0		
Total		197	100.0		

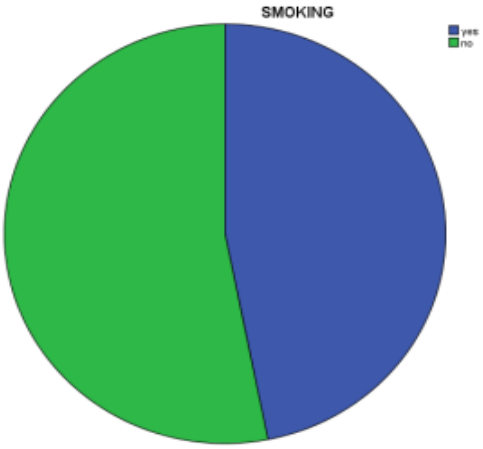
Graph 1
Frequency of comorbid



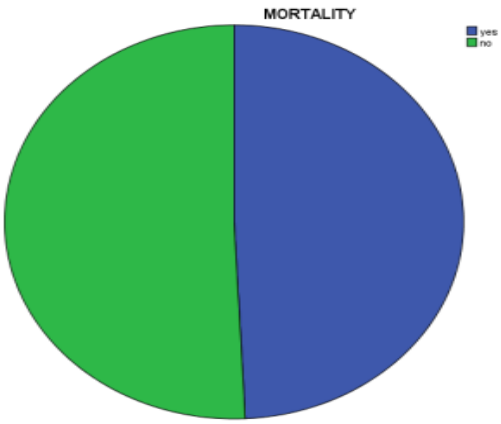
Graph 2
Frequency of presenting complaint



Graph 3
Frequency of smoking



Graph 4
Frequency of mortality



DISCUSSION

This study aimed to assess the risk of mortality in patients with variceal bleeding admitted with liver cirrhosis. A total of 128 patients were included, with data collected on various demographic and clinical variables. The findings provide valuable insights into the factors associated with mortality in this patient population. The mean age of the patients was computed to be 55. 70 ± 22. 068; however, the 95% CI for the mean age ranged from 51. 84 to 59. 56. The high-risk character of variceal bleeding in this cohort was highlighted by the observation of mortality in 63 individuals (49.2%). Important the stratification of MELD scores did not provide a significant p-value (p = 0.870), indicating that MELD scores were not a reliable indicator of death in this particular population. Overall, this study emphasizes how difficult it is to forecast death in individuals who have both variceal bleeding and liver cirrhosis. Prominent correlations between monthly income and presenting symptoms imply that clinical presentation and socioeconomic status are important determinants of patient outcomes. In order to increase survival in this susceptible group, more research and focused treatments are required due to the high documented death rate.

CONCLUSION

The findings of the current study develop significant implications pertaining to service to prognosis and understanding of patients with liver cirrhosis especially in prognosis of variceal burst. The demographic study revealed that patient was older with a mean age of 55. 70 years, this index underlined the general trend towards increased prevalence of liver cirrhosis among elderly. The mean BMI of the patients was 26. 40; the patients measured an average of 4. 31 feet tall and weighed, on average, 90. 05 kilograms. These consequences indicate that a sizeable portion of the research sample was either fat or overweight, which could have aggravated the severity of liver disease. In clinical aspects, the mean MELD score and Child-Pugh score, which are vital indexes concerned with the severity of liver disease and predicting death, were 24. 09 and 10. 13, individually. Bearing in mind the results of this study, it can be concluded that it is necessary to consider soci-economic indicators as essential for the effective treatment and prognosis management of patients suffering from liver cirrhosis. These components provide all round details of the patient demographic information and may be used to individualize some of the treatments which maybe given to the patient. The presenting complaints in half the cases were of hematemesis, and in the other half, it was melena. In particular, nearly half of the patients experienced fatality, which means that variceal hemorrhage in the present group is potentially life-threatening. Important insights were obtained from the stratification of several factors: The results showed that smoking and gender do not determine mortality, thus casting doubt on which these variables as the primary indicators of outcomes in this case.

REFERENCES

1. Bajaj, J. S. (2019). Altered gut microbiota in patients with cirrhosis and its relationship to the development of infections. *Clinical Liver Disease*, *13*(5), 154-157. https://10.1002/cld.827
2. Bernard, B., Grangé, J.-D., Khac, E. N., Amiot, X., Opolon, P., & Poynard, T. (1999). Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with gastrointestinal bleeding: A meta-analysis. *Hepatology*, *29*(6), 1655–1661. https://doi.org/10.1002/hep.510290608
3. Bosch, J., Abraldes, J. G., Berzigotti, A., & García-Pagan, J. C. (2009). The clinical use of HVPG measurements in chronic liver disease. *Nature Reviews Gastroenterology & Hepatology*, *6*(10), 573–582. https://doi.org/10.1038/nrgastro.2009.149
4. Brocchi, E., Caletti, G., Brambilla, G., La Mantia, L., Lupinacci, G., & Pisano, G…. (1988). Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. A prospective multicenter study. *The New England journal of medicine*, *319*(15), 983–989. https://doi.org/10.1056/NEJM198810133191505
5. Burroughs, A. K., & Triantos, C. (2008). Predicting failure to control bleeding and mortality in acute variceal bleeding. *Journal of Hepatology*, *48*(2), 185–188. https://doi.org/10.1016/j.jhep.2007.11.006
6. Carbonell, N., Pauwels, A., Serfaty, L., Fourdan, O., Lévy, V. G., & Poupon, R. (2004). Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. *Hepatology*, *40*(3), 652–659. https://doi.org/10.1002/hep.20339
7. D'Amico, G., Garcia-Pagan, J. C., Luca, A., & Bosch, J. (2006). Hepatic Vein Pressure Gradient Reduction and Prevention of Variceal Bleeding in Cirrhosis: A Systematic Review. *Gastroenterology*, *131*(5), 1611–1624. https://doi.org/10.1053/j.gastro.2006.09.013
8. D'Amico, G. (2003). Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and

prognostic indicators. *Hepatology*, *38*(3), 599–612. https://doi.org/10.1053/jhep.2003.50385

9. de Franchis, R., & Primignani, M. (2001). NATURAL HISTORY OF PORTAL HYPERTENSION IN PATIENTS WITH CIRRHOSIS. *Clinics in Liver Disease*, *5*(3), 645–663. https://doi.org/10.1016/s1089-3261(05)70186-0
10. Feu J. C. Garcia-Pagan, Bosch, J., Luca, A., Angels Escorsell, Rodés, J., & Josep Terés. (1995). Relation between portal pressure response to pharmacotherapy and risk of recurrent variceal haemorrhage in patients with cirrhosis. *The Lancet*, *346*(8982), 1056–1059. https://doi.org/10.1016/s0140-6736(95)91740-3
11. Garcia- Pagán, J.-C., Gracia-Sancho, J., & Bosch, J. (2012). Functional aspects on the pathophysiology of portal hypertension in cirrhosis. *Journal of Hepatology*, *57*(2), 458–461. https://doi.org/10.1016/j.jhep.2012.03.007
12. Garcia-Pagan, J. C., Caca, K., Bureau, C., Laleman, W., Appenrodt, B., Luca, A., Abraldes, J. G., Nevens, F., Vinel, J. P., Mössner, J., & Bosch, J. (2010). Early Use of TIPS in Patients with Cirrhosis and Variceal Bleeding. *New England Journal of Medicine*, *362*(25), 2370–2379. https://doi.org/10.1056/nejmoa0910102
13. Garcia-Tsao, G., Groszmann, R. J., Fisher, R. L., Conn, H. O., Atterbury, C. E., & Glickman, M. (1985). Portal pressure, presence of gastroesophageal varices and variceal bleeding. *Hepatology*, *5*(3), 419–424. https://doi.org/10.1002/hep.1840050313
14. Garcia-Tsao, G., Sanyal, A. J., Grace, N. D., & Carey, W. (2007). Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology*, *46*(3), 922–938. https://doi.org/10.1002/hep.21907
15. Garcia–Tsao, G. (2001). Current management of the complications of cirrhosis and portal hypertension: Variceal hemorrhage, ascites, and spontaneous bacterial peritonitis. *Gastroenterology*, *120*(3), 726–748. https://doi.org/10.1053/gast.2001.22580
16. Ge, P. S., Runyon, B. A., & Kamath, P. S. (2019). Modern medical management of cirrhosis. *Current Opinion in Gastroenterology*, *35*(3), 197-202.
17. Ginès, P., Solà, E., Angeli, P., Wong, F., Nadim, M. K., & Kamath, P. S. (2018). Hepatorenal syndrome. *Nature Reviews Disease Primers*, *4*(1), 1–17. https://doi.org/10.1038/s41572-018-0022-7
18. Graham, D. Y., & Smith, J. L. (1981). The course of patients after variceal hemorrhage. *Gastroenterology*, *80*(4), 800–809. https://pubmed.ncbi.nlm.nih.gov/6970703/
19. Groszmann, R. J., Bosch, J., Grace, N. D., Conn, H. O., Garcia-Tsao, G., Navasa, M., Alberts, J., Rodes, J., Fischer, R., Bermann, M., Rofe, S., Patrick, M., & Lerner, E. (1990). Hemodynamic events in a prospective randomized trial of propranolol versus placebo in the prevention of a first variceal hemorrhage. *Gastroenterology*, *99*(5), 1401–1407. https://doi.org/10.1016/0016-5085(90)91168-6
20. Groszmann, R. J., Garcia-Tsao, G., Bosch, J., Grace, N. D., Burroughs, A. K., Planas, R., Escorsell, A., Garcia-Pagan, J. C., Patch, D., Matloff, D. S., Gao, H., & Makuch, R. (2005). Beta-Blockers to Prevent Gastroesophageal Varices in Patients with Cirrhosis. *New England Journal of Medicine*, *353*(21), 2254–2261. https://doi.org/10.1056/nejmoa044456
21. Groszmann, R. J., Garcia-Tsao, G., Bosch, J., Grace, N. D., Burroughs, A. K., Planas, R., Escorsell, A., Garcia-Pagan, J. C., Patch, D., Matloff, D. S., Gao, H., & Makuch, R. (2005). Beta-Blockers to Prevent Gastroesophageal Varices in Patients with Cirrhosis. *New England Journal of Medicine*, *353*(21), 2254–2261. https://doi.org/10.1056/nejmoa044456
22. Lefkowitch, J. H. (2005). Morphology of Alcoholic Liver Disease. *Clinics in Liver Disease*, *9*(1), 37–53. https://doi.org/10.1016/j.cld.2004.11.001
23. McCormick, P. A. (2001). Improving prognosis following a first variceal haemorrhage over four decades. *Gut*, *49*(5), 682–685. https://doi.org/10.1136/gut.49.5.682
24. Reverter, E., Tandon, P., Augustin, S., Turon, F., Casu, S., Bastiampillai, R., Keough, A., Llop, E., González, A., Seijo, S., Berzigotti, A., Ma, M., Genescà, J., Bosch, J., García–Pagán, J. C., & Abraldes, J. G. (2014). A MELD-Based Model to Determine Risk of Mortality Among Patients With Acute Variceal Bleeding. *Gastroenterology*, *146*(2), 412-419.e3. https://doi.org/10.1053/j.gastro.2013.10.018
25. Ripoll, C., Groszmann, R., Garcia–Tsao, G., Grace, N., Burroughs, A., Planas, R., Escorsell, A., Garcia–Pagan, J. C., Makuch, R., Patch, D., Matloff, D. S., & Bosch, J. (2007). Hepatic Venous Pressure Gradient Predicts Clinical Decompensation in Patients With Compensated

Cirrhosis. *Gastroenterology*, *133*(2), 481–488. https://doi.org/10.1053/j.gastro.2007.05.024

Ripoll, C., Groszmann, R. J., Garcia-Tsao, G., Bosch, J., Grace, N., Burroughs, A., Planas, R., Escorsell, A., Garcia-Pagan, J. C., Makuch, R., Patch, D., & Matloff, D. S. (2009). Hepatic venous pressure gradient predicts development of hepatocellular carcinoma independently of severity of cirrhosis. *Journal of Hepatology*, *50*(5), 923–928. https://doi.org/10.1016/j.jhep.2009.01.014