Assessment of prognosis in patients with liver cirrhosis admitted to Hepatology ICU

Thesis

submitted for partial fulfillment of the M.D. Degree of internal medicine

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2013

Acknowledgement

First, I would like to express my deepest gratitude and thanks to almighty; **ALLAH** most Gracious most Merciful whose magnificent help was the main factor in accomplishing this work.

I would like to express my sincere gratitude and deep appreciation to Prof. Dr.**Nouman EL Garem**Professor of internal medicine ,faculty of medicine ,Cairo university for his continuous scientific guidance, unlimited help, the precious time and effort she devoted in the supervision of the present work.

I'm delighted to express my deep gratitude and sincere thanks to, Prof. Dr.**AmanyA.MaqsoudSholkamy**Professor of internal medicine faculty of medicine Cairo university for her great help, experienced guidance, endless support, precious advice and kind supervision throughout the period of the work

I'm greatly indepted to Prof.Dr **Mohamed Ahmed AboSeif**Professor of internal medicine faculty of medicine BeniSueif University , for his continuous interest, helpful cooperation and effective advice throughout the entire work.

Finally but not the least, thanks to my family and special thanks to my **boys** who exerted true effort in helping me to complete this work.

Abstract

Background: Cirrhotic patients have many critical situations .The recognition of risk factors that can stratify a population of cirrhotic patients into subgroups with different survival is of great prognostic value for the clinician. Numerous attempts have been made to develop a reliable prognostic survival model for cirrhosis. *(Chatzicostas et al 2003)*Some current ICU prognostic models [APACHE,OSF and SOFA] were used to stratify cirrhotics into risk categories, but few cirrhotics were included in the original model development. *(Cholongitas et al 2006)*Liver-specific scores [CTPand MELD] might be useful in these circumstances.

Objectives: evaluate whether ICU prognostic models perform better compared with liver-disease specific ones in cirrhotics admitted to ICU and defining the predictors of poor mortality in a group of cirrhotic patients admitted to Hepatology intensive care unit.

Methods: The survival/mortality of 301 cirrhotic patients admitted from July2007 to March 2012was respectively studied. The CTP, MELD, and APACHE II scores were computed for each patientwithin the first 24 hours of their admission. Patient disposition was classified as either survival or non survivors. Group comparisonsbetween survivors and non-survivors were carried out using multiple logistic regressions to identify risk factors directly correlated with mortality. Finally, sensitivity, specificity, positivePredictive and negative predictive values were computed for the three prognostic scoring systems.

Results: 172 patients non-survivors (57.1%) and 129 patients were survivors (42.9%). CTP, APACHE Π and MELD mean scores of survivors (10.2, 22.7, 21.8
Respectively) werelower than non-survivors (11.3, 26.6 and 31.4, respectively) (p<0.001). Sensitivity of CTP, APACHEΠand MELD were (75.6%, 72% and 86.6% respectively), the overall predictive accuracy ofMELD was81% greater than the CTP (67%) and APACHE Π (71%) scores. Usage of mechanical ventilation and vasopressors were associated with high mortality.

conclusion: The present study showed that MELD score has the highest overall predictive accuracy among the three scoring systems. However, it is prudent to say, that these scoring systems should always go hand in hand with critical clinical analysis and good decision making.

Key words: liver cirrhosis, CTP,MELD,APACH Π

list of abbreviations

ALD → Alcoholic liver disease

APACHE →acute physiology and chronic health evaluation

AUC →Area under the resultant curve

BCS→ budd- chirari syndrome

CCA → cholangiocarcinoma

CTP →Child- Turcotte-Pugh

ET-1 → Endothelin -1

FAP → familial amyloid polyneuropathy

FHVP →Free Hepatic Venous Pressure

GABA→ Gamma - amino butyric acid

HCC →hepatocellular carcinoma

HE→ : hepatic encephalopathy

HHT→ hereditary hemorrhagic telangiectasia

HPS→ hepatopulmonary syndrome

HRS →Hepatorenal syndrome

HSC → Hepatic stellate cells

HVPG → Hepatic venous pressure gradient

INR →international normalized ratio

ICU →intensive care unit

MELD→ model of end stage liver disease

MODS→ multiple organ dysfunction score

MPM → mortality probability models

NASH → Non-alcoholic steatohepatitis

PCLD → polycystic liver disease

POPH → portopulmonary hypertension

PT→ prothrombin time

ROC → Receiver operating characteristic

SAAG→ serum- ascites albumin gradient

SAPS → simplified acute physiology score

SOFA →sequential organ failure assessment.

WHVP → Wedged hepatic vein pressure

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AIM OF THE WORK

1. Defining the predictors of poor mortality in a group of cirrhotic patients admitted to Hepatology intensive care unit.

2. To evaluate whether ICU prognostic models perform better compared with liver-disease specific ones in cirrhotics admitted to ICU.

LIVER CIRRHOSIS

The word "cirrhosis" derives from Greek kirrhos, meaning "tawny"(the orange-yellow color of the diseased liver). While the clinical entity was known before. It was Rene Laennec who gave it the name "cirrhosis" in his 1819 work in which he also describes the stethoscope. ***(Roguin, 2006)***

DEFINITION:

Cirrhosis of the liver is an irreversible disorder characterized by diffuse hepatic fibrosis and the conversion of normal liver architecture into abnormal nodules. It represents a sustained healing response to chronic injury from a wide variety of causes**. *(Sherlock, Dooley, 2002)***

This process distorts the normal liver architecture, interferes with blood flow through the liver and disrupts the biochemical functions of the liver. ***(Mathews et al, 2006)***

The condition often develops insidiously without giving rise to symptoms and it is thought that about 30-40% of cases are clinically latent. It may therefore be categorized on clinical grounds as:

l- Compensated cirrhosis, in which the patient is asymptomatic and the condition is discovered during biochemical screening. Routine clinical examination or abdominal surgery for another condition.

2- Decompensated cirrhosis, in 'which the most frequent manifestations are jaundice, ascites, encephalopathy and gastric or esophageal hemorrhage.

INCIDENCE:

Cirrhosis is the twelfth leading cause of death by disease killing. About 26,000 people each year in USA. Also, the cost of cirrhosis in terms of human suffering, hospital costs, and lost productivity is high. Cirrhosis is generally irreversible once it occurs, and treatment generally focuses on preventing progression and complications. In advanced stages of cirrhosis the only option is a liver transplant. ***(Anderson, Simth, 2003)***

PATHOLOGY:

The changes in cirrhosis usually affect the whole liver however in biliary cirrhosis (e.g. primary biliary cirrhosis) they can be patchy. They include progressive and widespread death of liver cells associated with inflammation and fibrosis, leading to loss of the normal liver architecture. Destruction of the liver architecture causes distortion and loss of the normal

hepatic vasculature with the development of portosystermic vascular shunts and the formation of nodules rather than lobules due to the proliferation of surviving hepatocytes. The evolution of' cirrhosis is gradual and progressive unless the etiological agent is withdrawn for example, by abstinence from alcohol. ***(Ferrell, 2000)***

Cirrhosis can be classified histologically into three types:

1-Micro-nodular cirrhosis is characterized by small nodules about 3 mm in diameter and is seen in alcoholic cirrhosis.

2-Macro nodular cirrhosis is characterized by larger nodules of various Sizes.

3-Mixed.

CAUSES:

Cirrhosis has many possible causes; sometimes more than one cause is present in the same patient. In the Western World, chronic alcoholism and hepatitis C are the most common causes.

Chronic hepatitis C. Infection with the hepatitis C virus causes inflammation of the liver and a variable grade of damage to the organ that over several decades can lead to cirrhosis. Cirrhosis caused by hepatitis C is the most common reason for liver transplant. Egypt reports the highest prevalence of HCV worldwide, ranging from 6% to more than 40% among regions and demographic groups ***(Lehman &Wilson, 2009***).

- *Chronic hepatitis B.* The hepatitis B virus causes liver inflammation and injury that over several decades can lead to cirrhosis. Hepatitis D is dependent on the presence of hepatitis B and accelerates cirrhosis in co-infection. ***(wolf et al 2012)***

- *Alcoholic liver disease* (ALD). Alcoholic cirrhosis develops for between 10% and 20% of individuals who drink heavily for a decade or more. ***(Kim et al,2010)*** Alcohol seems to injure the liver by blocking the normal metabolism of protein, fats, and carbohydrates.

- *Non-alcoholic steatohepatitis* (NASH). In NASH, fat builds up in the liver and eventually causes scar tissue. This type of hepatitis appears to be associated with diabetes, protein malnutrition, obesity, coronary artery disease, and treatment with corticosteroid medications. This disorder is similar to that of alcoholic liver disease but patient does not have an alcohol history. Biopsy is needed for diagnosis.

- *Primary biliary cirrhosis*. May be asymptomatic or complain of fatigue, pruritus, and non-jaundice skin hyper pigmentation with hepatomegaly. It is more common in women. ***(wolf et al 2012)***

- *Primary sclerosing cholangitis*. PSC is a progressive cholestatic disorder presenting with pruritus, steatorrhea, fat soluble vitamin deficiencies, and metabolic bone disease. There is a strong association with inflammatory bowel disease (IBD), especially ulcerative colitis.

- *Autoimmune hepatitis*. This disease is caused by the immunologic damage to the liver causing inflammation and eventually scarring and cirrhosis. ***(wolf et al 2012)***

- *Hereditary hemochromatosis*. Usually presents with family history of cirrhosis, skin hyper pigmentation, diabetes mellitus, pseudo gout, and/or cardiomyopathy, all due to signs of iron overload.

- *Wilson's disease*. Autosomal recessive disorder characterized by low serum ceruloplasmin and increased hepatic copper content on liver biopsy. May also have Kayser-Fleischer rings in the cornea and altered mental status.

- *Alpha 1-antitrypsin deficiency* (AAT). Autosomal recessive disorder. Patients may also have COPD, especially if they have a history of tobacco smoking. ***(wolf et al 2012)***

- *Cardiac cirrhosis*. Due to chronic right sided heart failure which leads to liver congestion.

- Galactosemia

- Cryptogenic causes (18%)

- Granulomatous disease (eg, sarcoidosis)

- Glycogen storage disease type IV

- Cystic fibrosis

- Hepatotoxic drugs or toxins

PATHOPHYSIOLOGY:

The liver plays a vital role in synthesis of proteins (e.g., albumin, clotting factors and complement), detoxification and storage (e.g., vitamin A). In addition, it participates in the metabolism of lipids and carbohydrates.

Cirrhosis is often preceded by hepatitis and fatty liver (steatosis), independent of the cause. If the cause is removed at this stage, the changes are still fully reversible. ***(Elsharkawy et al., 2005)***

The pathological hallmark of cirrhosis is the development of scar tissue that replaces normal parenchyma, blocking the portal flow of blood through the organ and disturbing normal function. Recent research shows the pivotal role of the stellate cell, a cell type that normally stores vitamin A, in the development of cirrhosis. Damage to the hepatic parenchyma leads to activation of the stellate cell, which becomes contractile (called myofibroblast) and obstructs blood flow in the circulation. In addition, it secretes TGF-β_1, which leads to a fibrotic response and proliferation of connective tissue. Furthermore, it secretes TIMP 1 and 2, naturally occurring inhibitors of matrix metalloproteinases, which prevents them from breaking down fibrotic material in the extracellular matrix. ***(Iredale JP, 2003)***