Clinical And Laboratory Predictors Of Outcome After Acute Variceal Bleeding

Thesis

Submitted for partial fulfillment of

master degree in Internal medicine

By

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2009

ACKNOWLEDGEMENT

Before all and above all, thanks to ***GOD*** *for all things*

I *am greatly honoured to express my sincere gratitude, deepest appreciation to Prof. Dr.* ***M. Sherif Mogawer****, Professor of Internal Medicine and hepatology, Faculty of Medicine, Cairo University, for his outstanding guidance and kind support throughout the work .*

I *would like to express my deepest gratitude and appreciation to Prof. Dr.* ***Heba Morad Yousef****, Professor of Internal Medicine, Faculty of Medicine, Cairo University, for her generous help, guidance and faithful support.*

I *would like to thank all my fellow residents and dear house officers for the great help they offered throughout this work .*

I *would like to thank all patients who participated in this study and wish them a speedy recovery.*

I *dedicate this work to my family who supported me all through this work.*

May ***ALLAH*** *accept the work of all those and reward them for it.*

Atef abdel aziz

ABSTRACT

Background: Chronic liver diseases and cirrhosis have a 10-year mortality of 34-66%. Acute variceal hemorrhage (AVH) secondary to cirrhosis is the most important cause of mortality in cirrhosis. The prediction and evaluation of adequate hemostasis by non-endoscopic methods are desired by treating physicians.

Objective: The aim of this study to asses the validity of both *Baveno II/III* and *Baveno IV* criteria as well as to assess many other laboratory, endoscopic and ultrasonographic variables as predictors of variceal haemorrage.

Methods: This study included 50 cirrhotic patients (27 males, 23 females, mean age 43.8 ± 8 yrs) presented with their 1st attack of acute variceal bleeding. All patients were treated with injection sclerotherapy. The patients were divided into two groups: group I included 44 patients with successful treatment and group II which included only 6 patients with failed treatment. Full clinical examination was done for all these patients, as well as biochemical investigations in the form of CBC, liver function tests, kidney function tests and blood sugar level. Abdominal ultrasound and at least two upper GIT endoscopies were done for every patient.

Results: Comparison between the two groups showed that the mean *haemoglobin* and *haematocrit* as well as the *number of blood units* transfused correlate significantly with the incidence of treatment failure with a P value of *0.02, 0.02* and *0.0001* respectively. On the other hand, there was no significant difference in the platelets count or the coagulation profile between the two groups. We also found that the *degree of ascites* and the *portal vein diameter* were directly related to treatment failure with a P value of *0.04* and *0.02* respectively. In this study, the incidence of treatment failure was rising with increasing the grade of varices. As regarding the Baveno criteria, the overall accuracy of both Baveno II/III and Baveno IV criteria was nearly the same reaching about 82% and 83% respectively.

Conclusion: There is no significant difference in accuracy between Baveno II/III and Baveno IV criteria.

There are many variables like the mean haemoglobin and haematocrit, the number of blood units transfused, the degree of ascites, the portal vein diameter, the site and the grade of varices that can be taken as predictors of treatment failure in patients with variceal bleeding.

Keywords: Liver cirrhosis-predictors-Baveno-outcome of variceal bleeding.

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LIST OF ABBREVIATIONS

5HT	5 hydroxy tryptamine
AAAs	Aromatic amino acids
AAT	Alpha 1-antitrypsin
AFP	Alpha-fetoprotein
ALD	Alcoholic liver disease
ALT	Alanine aminotransferase
AMPA	Amino-3-hydroxy-5-methyl-4-isoxazol propionic acid
AST	Aspartate aminotransferase
ATN	Acute tubular necrosis
AVT	Antiviral therapy
BCAAs	Branched-chain amino acids
CGRP	Capsaicin-calcitonin gene-related peptide
Cho	Choline
CLD	Chronic liver disease
Cr	Creatine
CSPH	Clinically significant portal hypertension
CT	Computed tomographic scan
CTP	Child-Turcotte-Pugh score
DLCO	The diffusing capacity for carbon monoxide
DSRS	Distal splenorenal shunts
EEG	Electroencephalogram
EGD	Esophagogastroduodenoscopy
eNOS	Endothelial NO synthase
EVL	Endoscopic variceal ligation
FHVP	Free hepatic venous pressure
GABA	Gamma-aminobutyric acid
GGT	Gamma-glutamyl transpeptidase
Glx	Glutamine/glutamate
GOV	Gastroesophageal varices
H2S	Hydrogen sulphide
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HE	Hepatic encephalopathy
HPI	Hepatic perfusion index
HPS	Hepatopulmonary syndrome
HSC	Hepatic stellate cells
HVPG	Hepatic venous pressure gradient

IGV	Isolated gastric varices
INR	International normalized ratio
IPVDs	Intrapulmonary vascular dilatations
ISMN	Isosorbide mononitrate
IVC	Inferior vena cava
LAS	Liver angioscintigraphy
LFTs	Liver function tests
L-NAME	N(G)-nitro-L-arginine methyl ester
MAO A	Mono amin oxidase A
MAO B	Mono amin oxidase B
MARS	Molecular adsorbent recirculating system
MELD	Model for End-stage Liver Disease
mI	Myoinositol
MRI	Magnetic resonance imaging
NAA	N-acetyl aspartate
NAFLD	Nonalcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NCT	Number connection test
NMDA	N-methyl-D-aspartate
NO	Nitric oxide
OLT	Orthotopic liver transplantation
PRPS	Per-rectal portal scintigraphy
PRSI	The per-rectal portal shunt index
PVT	Portal vein thrombosis
SBP	Spontaneous bacterial peritonitis
SHE	Subclinical hepatic encephalopathy
TIPS	Transjugular intrahepatic portosystemic shunt
TMP-SMX	Trimethoprim-sulfamethoxazole
TPO	Thrombopoietin
UNOS	The United Network for Organ Sharing
VEGF	Vascular endothelial growth factor
WHVP	Wedged hepatic venous pressure

INTRODUCTION AND AIM OF THE WORK

Chronic liver diseases and cirrhosis are now being recognized as an important cause of morbidity and mortality world-wide. Established cirrhosis has a 10-year mortality of 34-66% **(Burroughs et al., 2009).** Cirrhosis and chronic liver disease were the 10th leading cause of death for men and the 12th for women in the United States in 2001, killing about 27,000 people each year **(Anderson and Smith, 2003)**.

At least two-thirds of patients with liver cirrhosis develop oesophageal varices during the course of their disease, and severe upper gastrointestinal (GI) bleeding is a common complication of portal hypertension, affecting 30-40% of patients with cirrhosis **(Tacke et al., 2007).**

Acute variceal hemorrhage (AVH) secondary to cirrhosis is to date the most important cause of mortality in cirrhosis **(Burroughs et al., 2009)**. Therefore, the optimal management of variceal bleeding remains a great challenge to hepatologists, gastroenterologists, endoscopists, interventional radiologists, and surgeons **(Yu and Zhao-shen, 2009).**

The prediction and evaluation of adequate hemostasis by non-endoscopic methods are desired by treating physicians and till now there is no simple noninvasive method which accurately predicts esophageal variceal bleeding **(Chitapanarux et al., 2007)**

Many criteria and definitions to evaluate failure to control and prevent variceal bleed were developed in Baveno Consensus Workshops I –III (**De Franchis, 2003)**.

Some of these criteria are rather difficult to apply and do not reflect adequately the situation in clinical practice; therefore, new definitions and criteria were proposed at Baveno-IV workshop in 2005 **(Zuberi et al., 2007)**.

AIM OF THE WORK:

The aim of this study to asses the validity of both **Baveno II/III** and **Baveno IV** criteria and to assess the accuracy of many other clinical, laboratory, endoscopic and ultrasonographic variables as a good predictors of treatment failure among a group of Egyptian patients presented with bleeding oesophageal varices.

Review of Literature

Chapter One

Portal circulation

PORTAL CIRCULATION

THE PORTAL SYSTEM OF VEINS :

The portal system includes all the veins which drain the blood from the abdominal part of the digestive tube (with the exception of the lower part of the rectum) and from the spleen, pancreas and gall bladder to the liver via the portal vein (figure 1). There, it ramifies like an artery and ends in the capillary-like vessels (sinusoids), from which the blood is conveyed to the inferior vena cava by the hepatic veins (through two sets of capillaries). In the fetus; and for a short time after birth, valves can be demonstrated in the tributaries of the portal vein, as a rule they soon atrophy and disappear, but in some subjects they persist in a degenerate form **(Gray, 1989).**

The Portal vein: The right branch of the portal vein enters the right lobe of the liver, but before doing so generally receives the cystic vein. The left branch, longer but of smaller caliber than the right, crosses the left sagittal fossa, gives branches to the caudate lobe, and then enters the left lobe of the Iiver. As it crosses the left sagittal fossa it is joined in front by a fibrous cord, the ligamentum teres (obliterated umbilical vein), and is united to the inferior vena cava by a second fibrous cord, the ligamentum venosum (obliterated ductus venosus) **(Fruechtc and Zwiebel, 1992).**

Tributaries of the portal vein are :

Lienal.

Superior Mesenteric.

Coronary.

Pyloric.

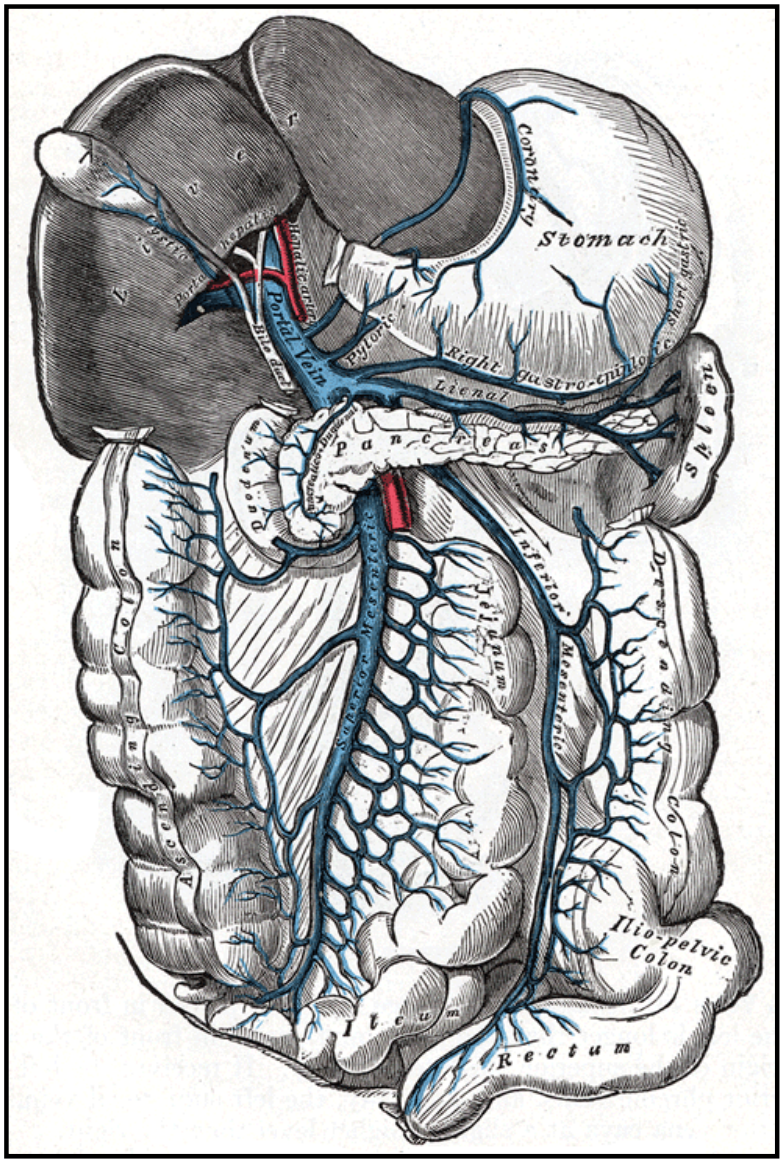
Cystic.

Parumbilical.

The lienal vein(vein Iienalis; splenic vein) commences by five or six large branches which return the blood from the spleen. These unite to form a single vessel, which passes

from left to right, grooving the upper and back part of the pancreas, below the lineal artery, and ends behind the neck of the pancreas by uniting at a right angle with the superior mesenteric to form the portal vein. It receives the short gastric veins, the left gastroepiploic vein, the pancreatic veins, and the inferior mesenteric veins **(Sherlock and Doollcy 1997).**

(Figure: 1) The portal vein and its tributaries.
(Henry Gray (1825–1861). Anatomy of the Human Body. 1918.)



The short gastric veins (gastricae breves), four or five in number, drain the fundus and left part of the greater curvature of the stomach, and pass between the two layers of the gastrolienal ligament to end in the lienal vein or in one of its large tributaries **(Gardner, 1975) .**

The Left gastroepiploic vein (vein gastroepiploica sinistra): Receives branches from the antero-superior and postero-inferior surfaces of the stomach and from the greater omentum; it runs from right to left along the greater curvature of the stomach and ends in the commencement of the Iienal vein.

The Pancreatic veins (veins pancreaticae): Consist of several small vessels, which drain the body and tail of the pancreas, and open into the trunk of the lineal **vein (Warwick and Williams, 1989) .**

The Inferior mesenteric vei: (vein mesenterica inferior) returns blood from the rectum and the sigmoid, and descending parts of the colon. It begins in the rectum as the superior hemorrhoidal vein, which has its originin the hemorrhoidal plexus, and through this plexus communicates with the middle and inferior hemorrhoidal veins. The superior hemorrhoidal vein leaves the lesser pelvis and crosses the left common iliac vessels with the superior hemorrhoidal artery, and continues upward as the inferior mesenteric vein. It then passes behind the body of the pancreas and opens into the lienal vein. Sometimes it ends in the angle of union of the lienal and superior mesenteric veins. It receives the sigmoid veins (from the sigmoid and iliac colon) and the left colic vein (from the descending colon and left colic flexure) **(Gray, 1989).**