Platelet count to spleen diameter ratio and platelet count to spleen area ratio as predictors of esophageal varices in patients with liver cirrhosis

Thesis

Submitted for partial fulfillment of Master Degree in ***Tropical Medicine***

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Acknowledgement

*First, thanks are all due to **Allah** for Blessing this work until it has reached its end, as a part of his generous help throughout our life.*

*I would like to express my deep appreciation to **Prof. Dr. Mohamed Awad Mansour**, Professor of Tropical Medicine, Ain Shams University for his detailed and constructive comments, professional guidance and for his valuable support throughout this work.*

*I am deeply grateful to, **Dr. Ashraf Mohammad Al Breedy,** Lecturer of Tropical Medicine, Ain Shams University. I am indebted to his constructive criticism and continuous unlimited help and for giving me the privilege to work under his supervision. I appreciate his active participation in providing me with a lot of knowledge.*

I would like to express my deepest thanks to all patients and all the staff members in Ain Shams endoscopy unit in Ain Shams Hospital for their help and cooperation to accomplish this work.

I am deeply grateful to my family, for their helpful assistance and moral support.

Last but not least, I would like to express my gratitude and appreciation to all those who helped me directly or indirectly in accomplishing this work.

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List of Abbreviations

AASLD	:	American Association for the Study of Liver Disease
ALP	:	Alkaline phosphatase
ALT	:	Alanine Transaminase
APRI	:	Aspartate transaminase-to-Platelet Ratio Index
ARFI	:	Acoustic Radiation Force Impulse Imaging
AST	:	Aspartate Transaminase
AUC	:	Area Under The Curve
CSPH	:	Clinically Significant Portal Hypertension
CT	:	Computed Tomography
CTP	:	Child-Turcotte-Pugh score
DIA	:	Digital-Image Analysis
EGD	:	Esophagogastroduodenoscopy
EV	:	Esophageal Varices
EVL	:	Endoscopic Variceal Ligation
FHVP	:	Free Hepatic Venous Pressure
GAVE	:	Gastric Antral Vascular Ectasia
GI	:	Gastrointestinal
GOV	:	Gastroesophageal Varices
GV	:	Gastric Varices
HB	:	Hemoglobin
HBV	:	Hepatitis B Virus
HCV	:	Hepatitis C Virus

List of Abbreviations (Cont.)

HVPG	:	Hepatic Venous Pressure Gradient
IGV	:	Isolated Gastric Varices
INR	:	International Normalized Ratio
IVC	:	Inferior Vena Cava
LS	:	Liver Stiffness
MRE	:	Magnetic Resonance Imaging Elastography
MRI	:	Magnetic Resonance Imaging
NASH	:	Non-Alcoholic Steatohepatitis
NIEC	:	North Italian Endoscopic Club
NPV	:	Negative Predictive Value
NSAIDs	:	Non-Steroidal Anti-Inflammatory Drugs
P/A ratio	:	Platelet count/spleen Area ratio
P/D ratio	:	Platelet count/spleen Diameter ratio
PBC	:	Primary Biliary Cirrhosis
PHG	:	Portal Hypertensive Gastropathy
PPG	:	Portal Pressure Gradient
PPV	:	Positive Predictive Value
PT	:	Prothrombin Time
PTFE	:	Polytetrafluoroethylene
PV	:	Portal Vein
PVD	:	Portal Vein Diameter
PVT	:	Portal Vein Thrombosis

List of Abbreviations (Cont.)

S. Alb	:	Serum Albumin
SEMS	:	Self-Expandable Metal Stents
TB	:	Total Bilirubin
TE	:	Transient Elastography
TIPS	:	Transjugular Intrahepatic Portosystemic Shunt
US	:	Ultrasonography
VBL	:	Variceal Band Ligation
VEGF	:	Vascular Endothelial Growth Factor
WBCs	:	White Blood Cells
WHVP	:	Wedged Hepatic Venous Pressure

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Introduction

Portal hypertension commonly accompanies the presence of liver cirrhosis, and the development of esophageal varices (EV) is one of its major complications. The prevalence of EV in cirrhotic patients ranges between 24% and 69% according to the degree of liver dysfunction ***(De Franchis and Primignani, 2001).*** The incidence of EV development is approximately 5% per year in patients with cirrhosis and the progression from small to large varices occur in 10% to 20% of cases after 1 year ***(De Franchis, 2003).*** In Egypt, it was found that the incidence of varices among portal hypertension patients was 77% ***(Hunter et al., 1998).***

Variceal haemorrhage occurs in 25 to 40% of patients with cirrhosis and varices ***(Grace, 1992),*** the frequency of bleeding from large varices is 30%-53% compared with 5%-18% for small varices ***(De Franchis, 2003).*** Bleeding EV is the most common cause of upper GI haemorrhage in Egypt as it represented 53.3% of total bleeding cases ***(Esmat et al., 2004).***

The mortality from each episode of variceal bleeding is estimated to be 17-57 % ***(Jensen, 2002).*** Within the first two years of detection of varices, the incidence of the first attack of bleeding ranges from 20 to 40 % of all cases. This makes the

prevention of esophageal variceal bleeding is the cornerstone of long-term management of patients with liver cirrhosis ***(D'Amico et al., 2001).***

The American Association for the Study of Liver Disease (AASLD) and the Baveno V Consensus Conference on portal hypertension recommended that cirrhotic patients should be screened by esophagogastroduodenoscopy (EGD) for the presence of EV when liver cirrhosis is diagnosed ***(Garcia-Tsao et al., 2007 and De Franchis, 2010).***

In addition, repeated EGD is recommended at 3 year intervals in patients without varices and compensated cirrhosis and at 2 year intervals in patients with small varices so as to evaluate the development or progression of this feature. Furthermore, if there is evidence of hepatic decompensation, EGD should be repeated annually ***(De Franchis, 2000).***

These recommendations imply a considerable burden on endoscopies and related costs as they require that patients repeatedly undergo an unpleasant invasive procedure, even though the majority of subjects undergoing screening EGD either do not have varices or have varices that do not require prophylactic therapy ***(D'Amico and Morabito, 2004).*** On the other hand, many patients refuse repeated endoscopies because of discomfort and fear of transmission of or contribution to

infection as it is associated with disruption of the natural barriers ***(Bosch et al., 2003).*** Moreover, sedation of a cirrhotic patient to perform endoscopy may be hazardous ***(McGuire, 2001).***Therefore, considerable interest in developing models to predict the presence of EV especially high risk varices by non-endoscopic methods.

Aim of the Work

The aim of this study is evaluation of the utility of the platelet count/spleen diameter ratio and platelet count/spleen area ratio to predict for the presence of EV in cirrhotic patients.

Chapter (I)

Portal Hypertension

Portal hypertension is a frequent syndrome – most often caused by chronic liver diseases – which is characterized by an increased portal pressure gradient (PPG; the difference in pressure between the portal vein and the inferior vena cava [IVC], which represents the perfusion pressure of the liver with portal blood). The increased portal pressure leads to other consequences, such as splenomegaly, growth of an extensive network of portal-systemic collaterals that shunt portal blood flow to the systemic circulation by passing the liver and development of a hyperkinetic circulatory state. In normal conditions the PPG ranges between 1 and 5 mmHg. Portal hypertension becomes clinically significant (associated with risk of clinical complications) when the PPG increases to 10 mmHg or above. Values between 5 and 9 mmHg represent subclinical portal hypertension ***(Bosch et al., 2009).***

Anatomy of the Portal Venous System : *Fig. (1)*

The liver has the most complicated circulation of any organ. According to the anatomical peculiarity of the double afferent blood supply of the liver, 75%-80% of the blood entering the liver is partially deoxygenated venous blood supplied by the portal vein, which collects all the blood that

leaves the spleen, stomach, small and large intestine, gallbladder and pancreas. The hepatic artery accounts for the remaining 25% with well-oxygenated blood ***(Vollmar & Menger, 2009)***.Total hepatic blood flow ranges between 800 and 1200 mL/min, which is equivalent to approximately 100 mL/min per 100 g liver wet weight. Although the liver mass constitutes only 2.5% of the total body weight, the liver receives nearly 25% of the cardiac output. The valveless portal vein is a low pressure/low resistance circuit, while the hepatic artery supplies the liver with arterial blood in a high pressure/high resistance system ***(Greenway & Stark, 1971).***

The portal vein is formed by the union of the superior mesenteric vein and the splenic vein (splenic veins drain the splanchnic and splenic beds) just posterior to the head of the pancreas at about the level of the second lumbar vertebra ***(Andrew, 2011).***

Numerous small tributaries connect the portal and systemic venous systems, and these can evolve into major collateral channels when portal hypertension supervenes. Formation of such collaterals is triggered when portal pressure rises above the normal level of 5 to 10 mmHg ***(Morris & Wood, 2000).***

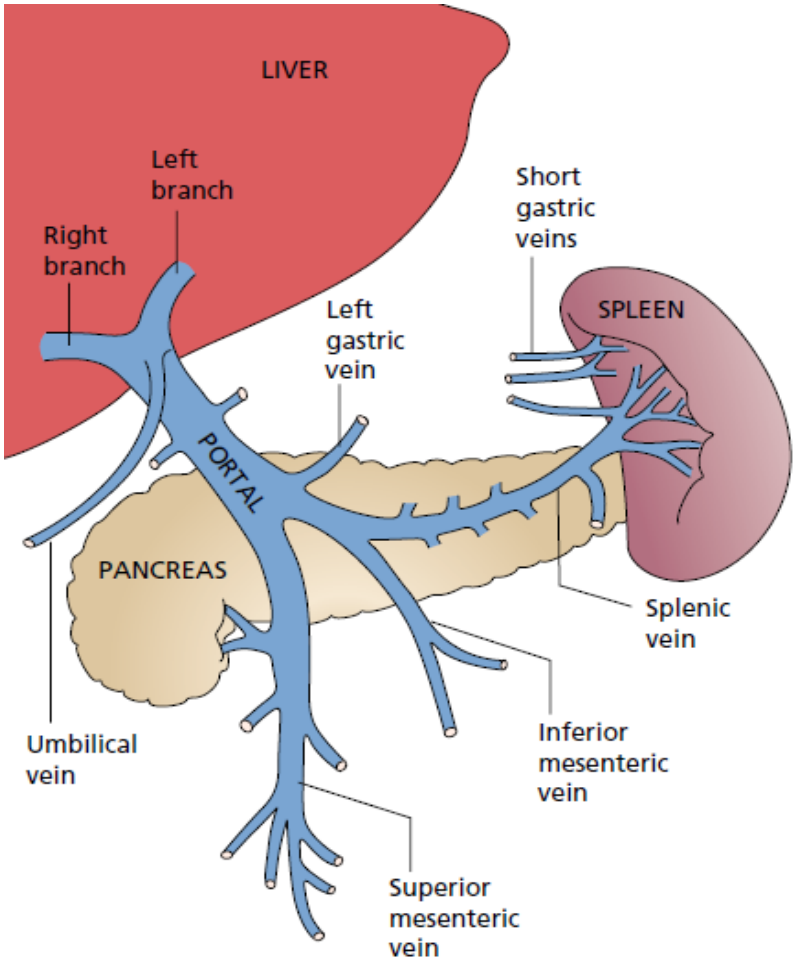

Fig. (1): The anatomy of the portal venous system. The portal vein is posterior to the pancreas ***(Andrew, 2011)***.

The most important of these portal-systemic channels are:

- The left gastric or coronary vein, which connects the esophagocardiac venous plexus with the splenic or portal vein.
- The short gastric and left gastroepiploic veins, which connect the esophageal and gastric plexus with the splenic vein.