## PREDICTORS OF RECURRENCE OF VARICEAL BLEEDING AFTER INITIAL ENDOSCOPIC TREATMENT

Thesis
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#### بسم الله الرحمن الرحيم

# قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

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#### **List of Abbreviations**

APC	Argon Plasma Coagulation
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
BCS	Budd-Chiari Syndrome
CSPH	Clinically Significant Portal Hypertension
CT scan	Computerized Tomographic Scan
ECG	Electrocardiography
EGD	Esophagogastrodudenoscopy
EST	Endoscopic Sclerotherapy
ET	Endothelin
EVL	Endoscopic Variceal Ligation
eNOS	Endothelial Nitric oxide Synthase
FHVP	Free Hepatic Venous Pressure
GIT	Gastro Intestinal Tract
HVPG	Hepatic Venous Pressure Gradient
IPH	Idiopathic Portal Hypertension
ISDN	Isosorbide Dinitrate
ISMN	Isosorbide Mononitrate
IVC	Inferior Vena Cava
MRI	Magnetic Resonance Imaging
NIEC	Northern Italian Endoscopic Club
NO	Nitric Oxide Nitric Oxide N
NOS	Nitric Oxide Synthase
PH	Portal Hypertension
RCT's	Randomized Controlled Trials
rfVIIa	Activated Recombinant Factor VII
TB	Tuberculosis
TIPS	Transjugular Intrahepatic Portosystemic Shunt
WHVP	Wedged Hepatic Venous Pressure

### Aim of the work

The aim of this work is to study different demographic, clinical, biochemical, ultrasonographic and endoscopic variables as predictors of recurrence of variceal bleeding after successful endoscopic treatment of the first attack of variceal bleeding by injection sclerotherapy.

### Introduction

#### **Introduction**

Portal hypertension is a common clinical syndrome with chronic liver disease and is characterized by a pathological increase in the portal

pressure. Porto-systemic collaterals develop as a result of portal hypertension (*Paquet*, 2000).

Clinically, the most significant collaterals are the intrinsic veins of the gastro-esophageal junction, which are located close to the mucosal surface. They are the collaterals most likely to bleed when dilated because of increased blood flow (*Hegab & Luketic*, 2001). Gastro-esophageal varices occur in approximately 50% of patients with hepatic cirrhosis. The presence and severity of varices is related to the cause, duration and severity of cirrhosis. Variceal bleeding is a major complication that occurs in 25 to 35% of patients with cirrhosis and it is associated with a high rate of illness and death in these patients. Efforts to treat this condition have included sclerotherapy, band ligation and various medications including beta-blockers, nitrates, alpha -adrenergic blockers, spironolactone, pentoxifylline, and molsidomine (*Villanueva et al.*, 2001).

While an improvement in mortality associated with active bleeding has been reported (*Chalasani et al.*, 2003), the long term natural history of subjects who have survived an index bleed remains poor (*D'Amico & de Franchis*, 2003).

Specifically, recurrent variceal hemorrhage is associated with an increased risk of development of liver failure, encephalopathy and sepsis which contribute to mortality (*D'Amico & de Franchis*, 2003).

Any bleeding that occur more than 48 hours after initial admission for variceal bleeding and is separated by at least 24-hour bleed-free

period is considered to represent recurrence of bleeding (rebleeding). Rebleeding that occurs within 6 weeks of onset of an acute bleed represents early rebleeding, while bleeding episodes that occur at later times are defined as late rebleeding episodes (*de Franchis*, 2000).

Among the survivors of the first bleeding, 30% experienced rebleeding. Red color sign and heavy drinking are independent risk factors for the first variceal bleeding (*Park et al.*, 2004).

Bleeding esophageal varices contribute to the estimated 32,000 deaths annually attributed to cirrhosis (*Hegab& Luketic*, 2001).

The role of endoscopy in bleeding varices is both diagnostic and therapeutic (*Bohnacker et al.*, 2000).

Endoscopic injection sclerotherapy has been established as one of the most important modalities in the treatment of bleeding esophageal varices (*Osman et al.*, 2001).

Gastric varices and portal hypertensive gastropathy are important complications of portal hypertension (Sarin & Agarwal, 2001).

Treatment of patients at highest risk for bleeding is critical because of the high risk of death with each episode of variceal hemorrhage. The goal of treatment of portal hypertension is decreased variceal flow, which is achieved by reducing either portal venous inflow or resistance to portal outflow (*Hegab & Luketic*, 2001).

The veins of the gastro-esophageal junction are classified as intrinsic, extrinsic, and venae comitantes. The intrinsic veins form a sub-epithelial and sub- mucosal plexus starting at the gastric cardia and

running the length of the esophagus. In healthy persons, these veins drain into the extrinsic plexus through perforating veins 2 to 3 cm above the gastro- esophageal junction. Flow through the perforating veins is unidirectional toward the extrinsic plexus and systemic circulation (Hegab & Luketic, 2001).

When portal hypertension develops, however, the valves of the perforating veins become incompetent and allow reversal of flow from the extrinsic to the intrinsic system (*Hegab & Luketic*, 2001).

Varices of the gastro-esophageal junction usually are classified by location as esophageal or gastric (1). Esophageal varices consist of three or four large trunks that are further characterized by size (*Table 1*).

This classification is important because the larger the varix, the more likely it is to bleed. (2) Gastric varices, on the other hand, are by convention classified only by location. Most likely to bleed are the isolated variceal clusters of the fundus, which often are caused by splenic vein thrombosis or spontaneous splenorenal collaterals (*Hegab & Luketic*, 2001).

#### Table 1. Classification of gastroesophageal varices

#### (1) Esophageal:

\*Small, straight.

\*Enlarged, tortuous; occupy less than one third of the lumen.

\*Large, coil-shaped; occupy more than one third of the lumen.