INTRODUCTION

Biliary strictures are most often caused by inflammatory or neoplastic disorders involving the pancreas, biliary tree, gallbladder, or ampulla ***(Stewart et al., 2001).***

Bile duct stricture is an uncommon but challenging clinical condition requiring a coordinated multidisciplinary approach involving gastroenterologists, radiologists, and surgical specialists. Bile duct strictures may be asymptomatic but, if ignored, can cause life-threatening complications, such as ascending cholangitis, liver abscess, and secondary biliary cirrhosis. Strictures of the bile duct can be benign or malignant. Benign strictures develop when the bile ducts are injured. The injury may be due to surgery or trauma to the abdomen, pancreatitis, bile duct stones or a chronic disease, such as primary sclerosing cholangitis. Malignant strictures usually are the result of either a primary bile duct cancer or extrinsic compression of the bile ducts by a neoplasm in an adjacent organ, such as the gallbladder, pancreas, or liver ***(Pande, 2004).***

Determining the cause of a stricture of the main bile duct, either benign or malignant in nature, is a prerequisite for treatment. The diagnosis of malignant biliary strictures rests on the identification of tumor cells obtained using various methods. Percutaneous fine needle aspiration

requires the presence of a tumor mass ***(Choi et al., 1989).*** Cytology performed directly on bile allows detection of malignant cells in only 6-26% of cancer cases ***(Foutch, 1994)***. The use of serum markers of malignancy is of little help. CA 19-9 is not specific for malignancy in associated cholangitis ***(Pearce et al., 1994)*** and serum anti-p53 antibodies are detectable in only 5% of cholangio-carcinomas ***(Laurent-Puig et al., 1995).***

Therefore, new methods, such as molecular biology, are required to improve the differential diagnosis of benign and malignant biliary strictures before surgery ***(Saurin et al., 2000).***

Mutations of the ***Ki-ras oncogene*** have been described in several human carcinomas~~, including pancreas and bile duct cancers~~ ***(Hruban et al., 1997)***. These point mutations appear to be of biological significance in the complex process of cell transformation ***(Bos, 1989).*** Therefore, when detected, they provide additional information on malignancy. Such point mutations mainly reside in the first tw___o nucleotides of codon 12, making their detection by polymerase chain reaction (PCR) feasible. However, the usefulness of detecting Ki-*ras* mutations has not yet been evaluated in a large prospective series of patients with benign and malignant biliary strictures ***(Saurin et al., 2000)***.

AIM OF THE WORK

The aim of this work is to study the clinical value of detection of biliary Ki-*ras* gene mutation in the diagnosis of patients with malignant biliary strictures.

ANATOMY OF THE BILIARY TREE AND PANCREAS

Understanding of the biliary and pancreatic tracts anatomy is essential for radiologists, endoscopists and others who are involved in the diagnosis and treatment of the biliary and pancreatic diseases ***(Pelligrini and Duh, 1991).***

The anatomy of the biliary tract can be divided into an intra and extra-hepatic parts:

1- Intra-hepatic biliary system:

Bile is secreted by the hepatocytes into the bile canaliculi, which drain into true biliary ductules. These ductules then unite to form the segmental bile ducts ***(Lindner, 1987).***

The intra-hepatic ducts are tributaries of the corresponding hepatic ducts which form part of the major portal tracts and which penetrate the liver invaginating Glisson's capsule at the hilus ***(Smadja and Blumgart, 2001).***

Bile ducts are usually located above the corresponding portal branches, whereas hepatic arterial branches are located inferior to the veins. The right liver

and the left liver are respectively drained by the right and left hepatic ducts, which converge at the liver hilus to the common hepatic duct. All these biliary and vascular elements are liable to anatomical variations ***(Smadja and Blumgart, 2001).***

2- Extra-hepatic biliary system:

The extra-hepatic bile ducts are represented by the extra-hepatic segments of the right and left hepatic ducts joining to form the biliary confluence and the main biliary channel draining to the duodenum. The accessory biliary apparatus, which constitutes a reservoir, compromise the gall bladder and cystic duct. The extra-hepatic segment of the right duct is short but the left duct has a much longer extra-hepatic course ***(Smadja and Blumgart, 2001).***

The common bile duct:

The junction of the cystic and hepatic ducts forms the common bile duct. Its length varies from 5-15 cm (mean value of 7.5 cm long) depending on the position of the entrance of the cystic duct, 6 mm in diameter ***(Williams et al., 2002).***

The duct is divided arbitrarily into four portions:

1- Supra-duodenal portion:

Its average length is 2.5 cm. It lies between the two leaves of the hepato-duodenal ligament infront of the epiploic foramen (foramen of Winslow), to the right of

hepatic artery and anterior to the portal vein ***(Smadja and Blumgart, 2001).***

2- Retro-duodenal portion:

Its average length is 1.5 cm. It lies between the superior margin of the first part of the duodenum and the superior margin of the head of the pancreas. It passes behind the first part of the duodenum with gastro-duodenal artery on its left and runs in a groove on the posterior surface of the head of the pancreas, sometimes embedded in the pancreatic tissue ***(Williams et al., 2002).***

3- Pancreatic portion:

It is related to the head of the pancreas, either lying entirely retro-pancreatic or traversing its substance ***(Behar, 1995).***

Its average length is 3 cm. It has many variations. 44% is partly covered by a tongue of the pancreas, 30% is completely within the pancreatic substance, 16.5% is uncovered on the pancreatic surface and 9% is completely covered by two tongues of the pancreas ***(Gaj et al., 2003).***

4- Intra-mural portion:

Its average length is 1.1 cm. It passes obliquely through the duodenal wall together with the main pancreatic duct ***(Williams et al., 2002).***

The terminal portion of the common bile duct is related to the pancreatic duct. They join to form a common channel just before entering or at the duodenal wall. Both ducts are separated by a septum along their entire course in about 20% of cases and never form a common channel draining into the papilla by separate ostia. The common bile duct diameter narrows from 10 to 6 mm as it transverse the duodenal mucosa ***(Anson and McVay, 1977).***

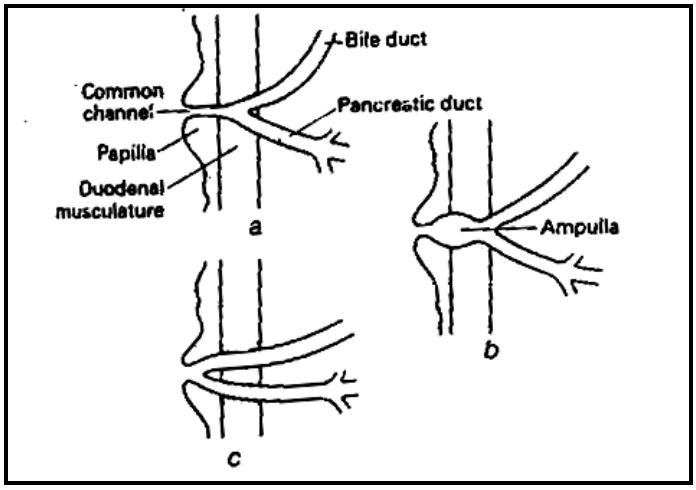

Figure (1): Configuration of the lower end of the common bile and pancreatic ducts. Quoted from **(*Cuschieri, 1995*).**

The ampulla of Vater and sphincter of Oddi:

The ampulla of Vater is a localized dilatation of the common channel; which is formed by the junction of the lumens of common bile duct and pancreatic duct. Its length varies from 3 to 14 mm, depending on whether the junction takes place outside or within the duodenal wall.

The Vaterian segment includes the lower 2.5-3 cm of the common bile duct, the distal part of the pancreatic duct, the ampulla or common channel and the major duodenal papilla. These structures are surrounded by a condensation of circular and longitudinal smooth muscle fibers often referred to as the sphincter of Oddi. The inferior sphincter is the strongest component and is also known as the papillary muscular ball. It surrounds the terminations of the bile and pancreatic ducts and the common channel. The middle sphincter is the longest and the thinnest of the components and surrounds the trans-duodenal and a variable portion of the trans-pancreatic portions. The superior sphincter consists of localized thickenings of the middle sphincters around the bile and pancreatic ducts, at the proximal end of the sphincter complex ***(Cuschieri, 1995).***

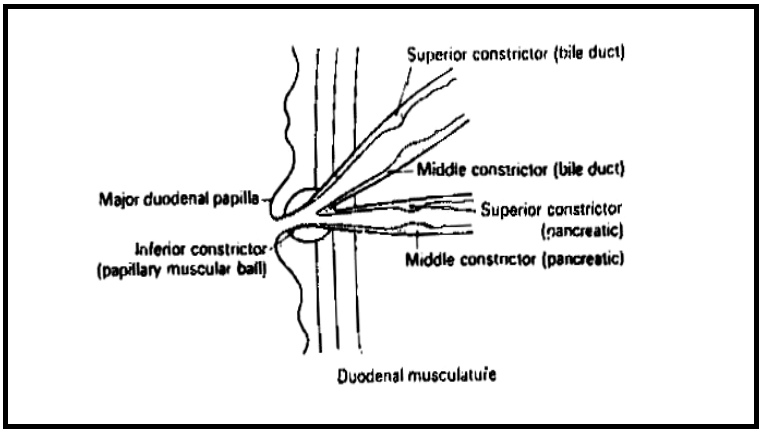

Figure (2): Diagrammatic representation of the components of the sphincter complex (sphincter of Oddi). Quoted from ***(Cuschieri, 1995).***

The junction between the two ducts, the common bile and pancreatic ducts, is classified into the following types:

a- Junction of the ducts is high. The common channel may or may not be dilated to form "ampulla" (86%).

b- The common channel is short. No ampulla is present (5%).

c- The common bile and pancreatic ducts enter the duodenum separately. No ampulla is present (9%).

(Schwartz, 2002)

Surface anatomy of the bile duct:

The position of the bile duct is indicated on the anterior abdominal wall by a line starting 5 cm above the tans-pyloric plane and 2 cm to the right of the median plane and descending vertically for 7.5 cm ***(Williams et al., 2002).***

Cystic duct:

The cystic duct connects the neck of the gall bladder to the common hepatic duct. It is 0.1 to 0.4 cm in diameter and 0.5 to 8 cm in length. In 70% of cases, the cystic duct enters the common hepatic duct directly. Sometimes, it runs parallel to or spiral around the common hepatic duct before entering it. The cystic duct usually enters the right side of the common hepatic duct, but it can course distally and

enter the posterior or the left side of the common hepatic duct ***(Lindner, 1987).***

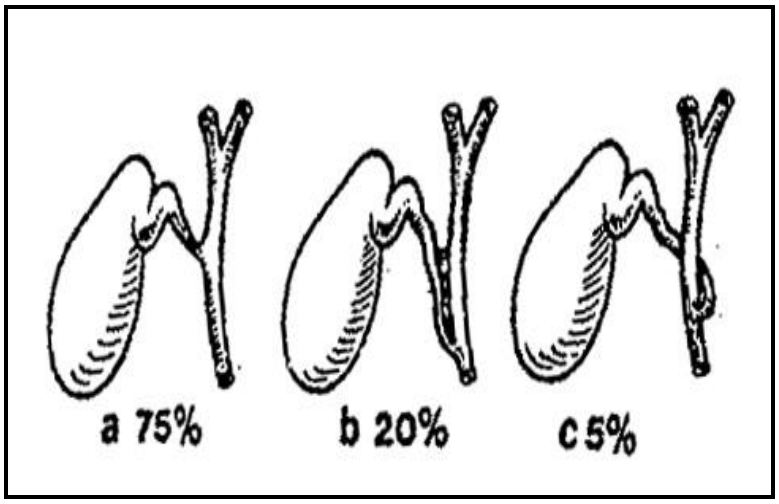

Figure (3): Different types of union of cystic duct and common hepatic duct: a, angular union, b, parallel union; c, spiral union. Quoted from ***(Lindner, 1987).***

The mucosa forms 4 to 10 crescentic folds or spiral valves of Heister. Their function is to prevent excessive distention or collapse of the duct during rapid changes in the intra-ductal pressure. These valves maintain continuous pressure gradient between the gall bladder and hepatic duct, facilitating slow but steady bile flow in either direction ***(Bannister, 1995).***

Gall bladder:

It is a globular or pear-shaped viscus with a capacity of about 50 ml and consists of three parts; fundus, body and

neck. It lies in the gall bladder fossa on the visceral surface of the right lobe of the liver, adjacent to the quadrate lobe. The liver is thus its main anterior relation. Its other important clinical relations are the anterior abdominal wall, duodenum and transverse colon ***(Last, 1994).***

Its bulbous blind end, the fundus, projects a little beyond the sharp lower border of the liver and touches the parietal peritoneum of the anterior abdominal wall at the tip of the ninth costal cartilage, where the trans-pyloric plane crosses the right costal margin, at the lateral border of the right rectus sheath ***(Last, 1994).***

Blood supply:

Arterial supply: The gall bladder is supplied by a single cystic artery, which normally arises from the hepatic artery. However, its origin may vary greatly. It may arise from an aberrant hepatic artery, from the left hepatic artery, or from one of the other branches of the celiac artery. Occasionally, it originates from superior mesenteric artery. As soon as the hepatic artery reaches the gall bladder by running along the superior aspect of the cystic duct, it divides into two branches. One traverses the peritoneal surface and the other lies between the gall bladder and the inferior surface of the liver ***(Behar, 1995).***

Venous drainage: The venous drainage is more complex. No single cystic vein, but multiple small veins

run towards the liver surface or the cystic duct and then join the veins of the common bile duct before entering into the portal venous system ***(Behar, 1995).***

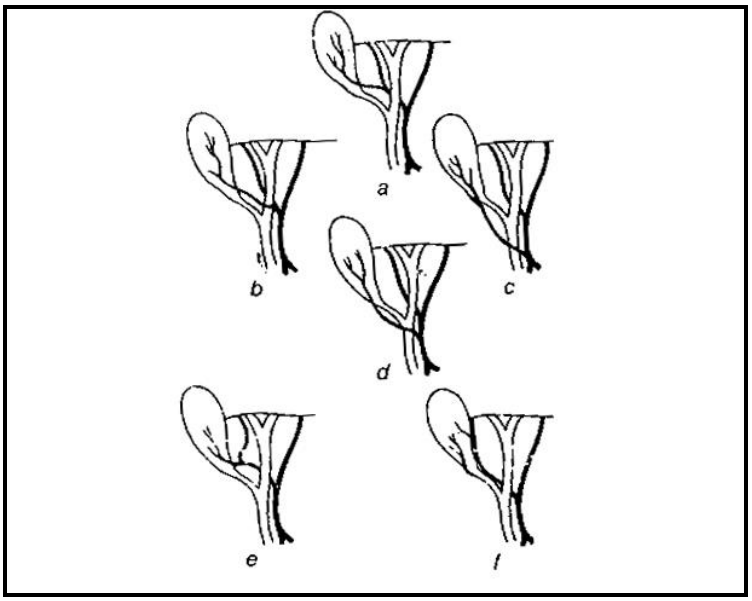

Figure (4): Anomalies of the cystic artery. Quoted from ***(Cuschieri,1995).***

Lymphatic drainage: It follows a pattern similar to that of venous return; the small lymphatics run along the liver surface of the gall bladder towards the cystic duct and into the lymph node around this duct. Eventually, the lymphatics go to the lymph nodes of the hepatic hilum ***(Behar, 1995).***

Nerve supply:

Like other gastrointestinal structures, the gall bladder receives motor and sensory parasympathetic and sympathetic innervation. The sympathetic nerves originate from T7 to T10 and reach the gall bladder and extra-hepatic bile ducts by way of the splanchnic nerves ***(Cai and Gabella, 1993).***

ANATOMY OF THE PANCREAS

Structure:

The pancreas is soft, lobulated, grayish pink gland, 15 cm long, extending nearly transversly behind the stomach, from the duodenum to the spleen. Its broad right extremity is the head and is connected to the main part of the body by a slightly constricted neck; its narrow left extremity forms the tail. It passes obliquely to the left and slightly forwards, across the posterior wall of the abdomen, in the epigastric and left hypochondric regions ***(Bannister, 1995).***

The structures related to the pancreas are best considered with respect to its different parts, as follows:

Head:

Flattened antero-posteriorly, lying within the duodenal curve. Its upper border is overlapped by the superior segment of the duodenum, the other borders being grooved by the adjacent margin of the duodenum. Sometimes a small part of the head is embedded in the wall of the descending part of the duodenum. From the lower and left part of the head the hook-like uncinate process projects upwards and to the left behind the superior mesenteric vessels ***(Bannister, 1995).***

Anterior surface: Is at first in contact with the transverse colon, separated only by loose connective tissue. The uncinate process is crossed anteriorly by the superior mesenteric vessels ***(Bannister, 1995).***

Posterior surface: Is related to the inferior vena cava, the terminal parts of the renal veins and the right crus of the diaphragm. The uncinate process lies in front of the aorta. The bile duct is lodged either in a supero-lateral groove on the posterior surface or in a canal within the gland's substance ***(Bannister, 1995).***

Neck:

It is about 2 cm long. Its posterior surface is in relation with the superior mesenteric vein and the beginning of the portal vein ***(Basmajian, 1980).***

Body:

Prism-like in section, having three surfaces; anterior, posterior and inferior.

Anterior surface: Is covered by peritoneum continuous antero-inferiorly with the anterior ascending layer of the greater omentum and is separated from the stomach by the omental bursa.

Posterior surface: Devoid of peritoneum. It is in contact with the aorta and the origin of the superior