TITLE

THE VALUE OF MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY IN *OBSTRUCTIVE JAUNDICE. A RETROSPECTIVE AND PROSPECTIVE STUDY AT* KENYATTA NATIONAL HOSPITAL

BY

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This dissertation is my original work and has not been presented for a degree in any other university.

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LIST OF ABBREVIATIONS

B.A	-	Biliary Atresia
C.B.D	-	Common Bile Duct
C.H.D	-	Common Hepatic Duct
C.T	-	Computed Tomography
E.R.C.P	-	Endoscopic Retrograde Cholangio Pancreatography
EUS	-	Endoscopic Ultrasound
HIV	-	Human Immunodeficiency Virus
I.O.C	-	Intra-operative Cholangiogram
I.V.C	-	Intravenous Cholangiogram
M.D.C.T	-	Multidetector Computed Tomography
M.I.P	-	Maximum Intensity Projection
M.R.C	-	Magnetic Resonance Cholangiogram
M.R.C.P	-	Magnetic Resonance Cholangio Pancreatography
M.R.I	-	Magnetic Resonance Imaging
N.H	-	Neonatal Hepatitis
N.P.V	-	Negative Predictive Value
O.C.G	-	Oral Cholangiogram
P.P.V	-	Positive Predictive Value
P.T.C	-	Percutaneous Transhepatic Cholangiography
R.F	-	Radiofrequency
S.P.S.S	-	Statistical Package for Social Scientist
T.E.	-	Time to Echo
T. R	-	Time to repeat
US	-	Ultrasound

ABSTRACT

Introduction: Diseases of the hepatobiliary tree are common all over the world and recently developed magnetic resonance imaging techniques are increasingly finding application in the evaluation of biliary and pancreatic diseases. Magnetic resonance cholangio-pancreatography (MRCP) has high spatial resolution and is used for rapid noninvasive and accurate imaging of the pancreaticobiliary tree. The objective of this study was to determine the ability of MRCP examination to accurately determine the site and etiology of biliary obstruction.

Methods: This cross-sectional study was designed to include former and current patients with clinical features of obstructive jaundice who subsequently underwent MRCP and definitive surgery over a 12 month period. Patients were mainly recruited from the surgical (liver) clinic at Kenyatta National Hospital. The methods involved comparative review of MRCP images as well as comparison between MRCP- and surgery-based diagnoses. The sensitivity of MRCP-based diagnosis was also determined. Statistical analysis was conducted using SPSS and involved both descriptive and inferential analysis. The chi-square test was mainly used for inferential analysis comparing cross tabulations for MRCP findings versus patient characteristics.

Results: Seventy-three (n = 73) patients with obstructive jaundice of whom 56.2% (41) were female participated in the study. The sample predominantly comprised adult patients with a mean age of 53.3 years (SD 17.9). MRCP was done, either alone or in combination with other imaging studies in 96% of patients. The most common sites of obstruction visualized on MRCP were the distal CBD (38.6%) and proximal CBD (34.3%). The leading causes of obstruction were tumors (53%), followed by calculi (20%) and strictures (17%). MRCP had high sensitivity for surgery confirmed diagnoses with sensitivities of 93.9%, 92% and 92% for tumor, calculi and stricture diagnoses confirmed by surgery.

Conclusions: MRCP has a high diagnostic accuracy in evaluating patients with obstructive jaundice. Therefore MRCP can be considered a valuable alternative to diagnostic ERCP. Further studies are required to determine the feasibility of using this method routinely in the diagnosis of obstructive jaundice in low income countries including Kenya.

GENERAL BACKGROUND

Diseases of the hepatobiliary tree are common all over the world and include gallstone and gallstone disease, gallstone pancreatitis, cholangitis and sphincter of Oddi dysfunction. Gallstones normally form in the gallbladder or within the bile ducts of the liver and often lead to obstruction. Gallstone disease is prevalent in those above 40 years and obese. Women of childbearing age who have had children are commonly affected. Other factors that may lead to gallstone formation include; rapid weight loss, oestrogen intake, lipid lowering agents and in diabetics. A patient may present with fever, chills, severe abdominal pain and jaundice.[1,2,3]

An abdominal ultrasound examination is the test most often used to interrogate a patient with obstructive jaundice. Also it determines the next suitable imaging examination for a patient's work-up. These other modalities include CT, MRI, and MRCP.[4,5]

In rural environments where the above mentioned technologies are missing; oral cholangiography (O.C.G) and intravenous (I.V.C) cholangiography complement the findings of ultrasound. O.C.G however has shortcomings worth of mention. In this examination bile ducts are not visualized because iodine is not concentrated in the ducts. Hence gallstones lodged in the ducts will go undetected.

The gallbladder may not be visualized if its cystic duct is obstructed by a calculi that prevents bile entering gallbladder. In inflammatory conditions, the gallbladder loses ability to concentrate bile and iodine. Also no information is availed about non-gallstone related diseases. O.C.G relies on a normally functioning liver.

Intravenous cholangiogram is useful in outlining the biliary tree. This procedure can be used to locate gallstones within bile ducts and identify other causes of obstruction e.g. strictures and tumours.

Use of iodine contrast medium poses a risk to patients who are allergic. I.V.C is limited when liver function is suboptimal.[6]

Magnetic Resonance Cholangiopancreatography (MRCP)

MRCP is a radiologic technique that produces images of the pancreaticobiliary tree that are similar in appearance to those obtained by invasive radiographic methods such as ERCP. The basic principle underlying MRCP is that body fluids, such as bile and pancreatic secretions, have high signal intensity on heavily T2-weighted magnetic resonance sequences. (i.e they appear white), whereas background tissues generate little signal. Both the multislice and single-slice methods can be performed in a single breath-holding session, and the data obtained with the two methods is complementary.

MRCP is equivalent in diagnostic accuracy to ERCP across numerous hepatobiliary pathologies. [7,8] MRCP is commonly used to evaluate the obstruction of the bile ducts or pancreatic ducts, for stones within the ducts or gallbladder, and for congenital anomalies of these structures.

In adult patients with persistent and unexplained signs and symptoms, such as cholangitis, pancreatitis, jaundice, recurrent abdominal pain, nausea and vomiting, a congenital anomaly of the pancreatic or bile duct must be considered and a low threshold for performing cholangiopancreatography is recommended. The most common congenital pancreaticobiliary abnormalities seen in adults are choledochal cysts, anomalous junction of the pancreatic and common bile ducts, aberrant biliary ducts and pancreas divisum. The following entities are rarely seen; annular pancreas, choledochoceles, multiple communicating intra and extrahepatic duct cysts. Recognition of congenital anomalies may aid in surgical planning and prevent inadvertent ductal injury.

Although congenital pancreaticobiliary anomalies are relatively uncommon, the increased prevalence of cholangitis, gallstones and cholangiocarcinoma seen with the various types of biliary cystic disease and junctional anomalies and the increased association of pancreatitis seen with pancreatic anomalies make recognition of variant anatomy clinically important. [9]

MRCP does not require the administration of any contrast materials and is a diagnostic procedure only. ERCP is used for diagnosis and treatment. ERCP may be necessary as a therapeutic intervention after MRCP. Such cases include in sphincterotomy and subsequent stone removal,

stent placement, balloon dilatation of strictures and tissue sampling. In such cases MRCP can be avoided, and patients are able to proceed immediately to treatment. However if no therapeutic intervention is found to be necessary, MRCP avoids the potential morbidity and mortality associated with ERCP. Therefore, MRCP is an appropriate non-invasive tool for interrogation of patients with suspected hepatobiliary pathology and when no or low likelihood of therapeutic intervention is anticipated.

MRCP is particularly useful where ERCP is difficult, harzardous or impossible (e.g patient with anatomical or structural impediments such as a previous gastroenteric anastomosis, or gastrojejunostomy. It is also an important option for patients with failed ERCPS.[4,5,10]

ERCP comes in handy as a non-therapeutic procedure in; localizing the site of duct leakage in pancreatic ascites, and collecting secretions for cytologic and chemical analysis. However it is contraindicated in severe cardiopulmonary disease and in acute pancreatitis whose cause is not gallstone disease.[11]

LITERATURE REVIEW

Shanmugam et al (2005) assessed the predictive value of MRCP in the diagnosis of biliary pathology. Clinical, laboratory and investigational data was evaluated from 351 patients undergoing MRCP at two hospital sites over a five year period. MRCP findings were compared to ERCP or operative findings and appropriate clinical endpoints. The predominant presentation was abdominal pain (n-190). Features of pancreatitis were present in 59, cholangitis in 26 and jaundice in 109 patients. Ultrasound was the initial investigation in 312 (89%) (176 were gallstone positive) common duct dilatation was evident in 114 patients and ductal calculi in 31. ERCP was successful in 212 of 283 (75%) patients. Significant ERCP induced pancreatitis occurred in 12 (5.6%). Comparison between MRCP and ERCP was not possible in 85 due to failure of either technique. Nine patients underwent other investigations including intraoperative cholangiogram (10C); percutaneous transhepatic cholangiogram (PTC) and were included. Of the 221 patients with full comparative data available, the MRCP showed a sensitivity of 97.98% and specificity of 84.4%. The authors stated that "MRCP is highly sensitive and specific for choledocholithiasis and avoids the need for invasive imaging in most patients with suspected choledocholithiasis.[12]

Vaishali et al (2004) evaluated 30 patients with biliary obstruction examined with MRCP. MRCP findings were confirmed on surgical exploration or clinical follow-up. MRCP had a sensitivity of 94.44%, specificity of 81.81%, positive predictive value of 89.47% and negative predictive value of 90% for the detection of malignant causes. The overall diagnostic accuracy for detection of level and cause of obstruction was 96.3% and 89.65% respectively.

The authors concluded that the high diagnostic accuracy of MRCP in evaluating patients with obstructive jaundice indicates that it has the potential to become the diagnostic modality of choice in such patients.[13]

Takaya J et al (2007) studied the usefulness of MRCP in excluding biliary atresia as the cause of neonatal cholestasis. MRCP was done on four jaundiced neonates and infants aged from 38 days to 106 days. The diagnosis of Biliary Atresia BA (n=2) was confirmed with surgery, neonatal

hepatitis (n=2) was confirmed with surgery, liver biopsy and surgical cholangiography. Diagnosis of neonatal hepatitis (n=2) was confirmed on clinical follow up. One was diagnosed with surgical cholangiography. The CBD and the CHD were not visible on MRCP in two patients with BA. Two other patients with NH had their CHD and CBD clearly depicted using MRCP. MRCP accurately excluded BA as the cause of neonatal cholestasis. The authors hence concluded that MRCP can be used to depict the major biliary structures of neonates and small infants and to exclude BA as the cause of neonatal cholestasis by allowing visualization of the biliary tract.[14]

Hekimoglu K, Ustudag Y et al (2008) in a study compared the diagnostic potential of MRCP and ERCP with review of current literature. Out of 295 enlisted patients, 11 were excluded due to inadequate MRCP image quality and 15 excluded due to unsuccessful cannulation during ERCP. The participating patients were classified into four main groups; 1) Normal group 2) Stone disease group 3) Tumour group 4) Others. Group 1 consisted of 228 patients who had a normal pancreatico biliary tree on both MRCP and ERCP examinations. 18 patients in group II had an MRCP sensitivity of 88.9% and a100% specificity for diagnosing biliary stone disease. Its positive predictive value PPV and NPV and accuracy rates were 100% and 99.2% respectively. MRCP had a 100% sensitivity and 100% specificity for 20 patients in group III. It also had 100% PPV, 100% NPV and 100% total accuracy rates in this group. In three patients in group IV, the MRCP had a 100% sensitivity and specificity. Its PPV, NPV and accuracy were 100%, 100% and 100% respectively. The authors concluded that MRCP is being used with increasing frequency as a non-invasive alternative to ERCP and the diagnostic results of MRCP and ERCP are comparable with accuracy in various hepatobiliary pathologies.[15]

Taylor AC, Little AF, et al (2002) carried out a prospective study to assess the accuracy of MRCP as a non-invasive imaging tool in a large number of patients. Patients referred for ERCP were eligible for the study. MRCP was done 24 hours before ERCP. MRCP findings were compared with ERCP findings or when the initial ERCP was unsuccessful, with results of repeat ERCP, P.T.C or surgery.

The sensitivity, specificity, positive and negative predictive values for MRCP in the diagnosis of 46 choledocholithiasis patients were 97.9%, 89.0%, 83.6%, 98.6% respectively. 12 strictures cases were diagnosed by MRCP (sensitivity 100%, specificity 99.1%). The researchers concluded that MRCP is an accurate; non-invasive alternative to ERCP for imaging the biliary tree. Choledocholithiasis and biliary strictures can be reliably diagnosed or excluded by MRCP. Hence MRCP should be used increasingly in patients with suspected biliary obstruction to select those who require a therapeutic procedure. [16]

Hans SJ et al (2002) carried out a study to evaluate the usefulness of M.R.C for the diagnosis of biliary atresia in infantile cholestatic jaundice.

A total of 47 consecutive infants with cholestatic jaundice were included in the study. They found out that; extrahepatic bile ducts including the gallbladder, cystic duct, CBD, CHD were visualized in 23 of the 24 infants of the non-biliary atresia group. Extrahepatic bile ducts, except the gallbladder, were not depicted in any infant of the BA group. M.R.C had an accuracy of 98%, sensitivity of 100% and specificity of 96%, for the diagnosis of biliary atresia as the cause of infantile cholestatic jaundice.

Thus they concluded that; M.R.C is a very reliable non-invasive imaging modality for the diagnosis of biliary atresia. Hence in infants with cholestatic jaundice and due for exploratory laparatomy, M.R.C is recommended to avoid unnecessary surgery. [17]

Ferrari ES et al compared the reliability of US, M.R.I and other imaging techniques in the diagnosis of intrinsic biliary obstructive disease.

60 males and 71 females aged from 37 to 79 years with clinical features of biliary obstructive disease were included. Imaging studies were done on each patient using several different techniques. They found out that US is generally accurate in diagnostic imaging of obstructive biliary disease. MRCP and CT are significantly more accurate only in completing the staging of malignant stenosis. Thus the conclusion was; if the suspicion

posed by clinical and laboratory findings is not confirmed at US, the diagnosis must be achieved with the aid of MRCP or where MRCP does not provide a diagnosis, CT, so as to select candidates for therapeutic ERCP, P.T.C or surgery.[18]

Ali Ahmetoglu et al sought to evaluate the diagnostic utility of MDCT cholangiography with volume rendering in the evaluation of patients with suspected biliary tree obstruction.

MDCT was performed in 34 patients who were thought to have biliary obstruction. Portal venous phase scanning was initiated 70 sec after the IV infusion of 150ml of contrast agent, and no cholangiographic contrast agent was administered.

Three dimensional MDCT cholangiographic images were produced using volume rendering. ERCP was performed in 26 patients, percutaneous transhepatic cholangiography (P.T.C) was performed in five patients, 17 patients underwent biopsy or surgery. The findings on MDCT cholangiography were compared with those of ERCP, P.T.C, biopsy or surgery.

Correct diagnosis was made on MDCT cholangiography for 14 (93%) of the 15 patients with a biliary stone and in 16 (94%) of the 17 patients with malignant biliary obstruction. Microlithiasis in one patient could not be detected on MDCT cholangiography. One patient with polypoid adenocarcinoma and one patient with normal findings were incorrectly diagnosed with a biliary stone on the basis of MDCT cholangiography. In one of the two patients with a benign stricture, the stricture was incorrectly diagnosed as malignant. For the diagnosis of biliary stone, sensitivity and specificity of MDCT cholangiography were 93% and 89%, respectively. For the diagnosis of malignant obstruction, sensitivity and specificity were both 94%. The accuracy of the technique for the diagnosis of the cause of biliary obstruction was 83.3%.

Hence they concluded that MDCT cholangiography with volume renderingis a non invasive and fast imaging technique with high sensitivity and specificity for the diagnosis of the cause of biliary tree obstruction. It is a promising diagnostic tool for the assessment of patients with bile duct obstruction. [19]

ANATOMY OF THE HEPATOBILIARY SYSTEM

Interpretation of biliary disease needs one to be thoroughly knowledgeable on biliary anatomy, normal variants and common congenital disorders.

The radiologist thus plays an important role in the pre-operative preparation of a patient as he enables the surgeon to select the appropriate surgical technique for biliary exposure and drainage.

Biliary nomenclature

Central – refers to the proximity of ducts to the porta hepatis.

Peripheral - refers to intrahepatic bile ducts which extend into the hepatic parenchyma.

Proximal – the part of the biliary tree in relation to the liver.

Distal – the proximity of the portion of biliary tree to the bowel. [20]

Intrahepatic bile duct anatomy

Bile ducts arise as bile capillaries between hepatocytes and these together with branches of the portal vein and hepatic artery from the portal triad. Interlobular ducts join to form septal bile ducts which finally unite to form the left and right hepatic ducts. The left hepatic duct drains the three segments of the left lobe, the right hepatic duct drains the four segments of the right lobe. The drainage pattern of the caudate lobe varies however mostly (78%) it drains into both ducts. [21]

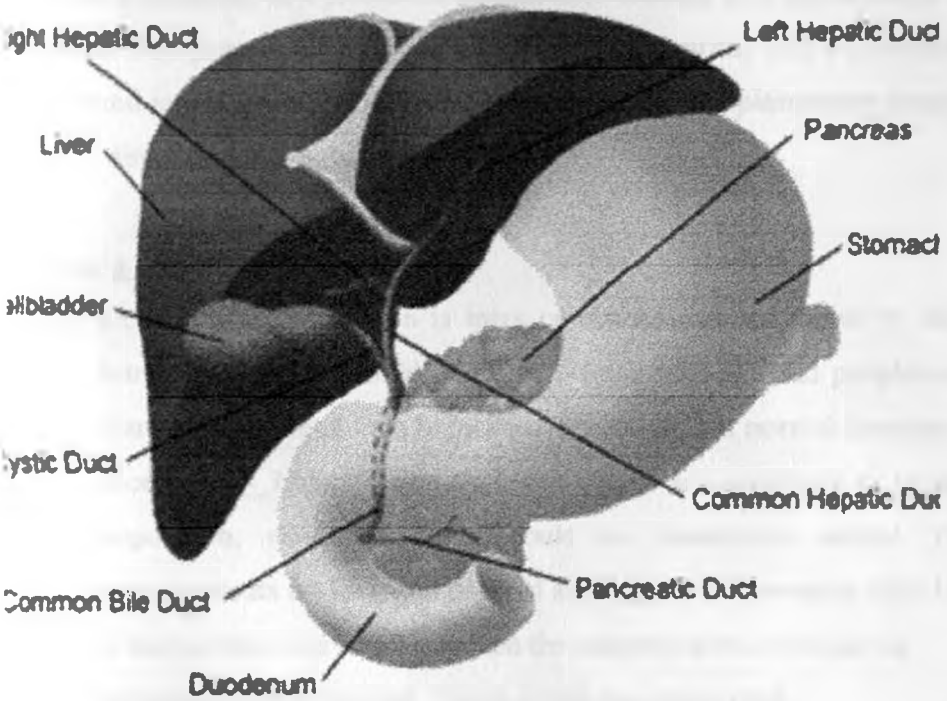
Extrahepatic bile duct anatomy

The right and left hepatic ducts combine to form the common hepatic duct. Together with the portal veins and hepatic artery, they course into the porta hepatis. The cystic duct courses postero-inferiorly from the gallbladder to joint the common hepatic duct and forms the common bile duct.

The bile duct then runs anterior to the portal vein and to the right of hepatic artery along the free right margin of the hepatoduodenal ligament to the duodenal bulb.

The common bile duct narrows distally as it terminates in the spincter of Oddi, creating a protrusion in the duodenal lumen known as ampulla of vater. The common bile duct and pancreatic duct may share a common orifice in 60% of individuals or have a separate orifice in 40%.[21]

Figure 1: Diagram shows normal hepatobiliary anatomy



Gall bladder

It is a pear shaped organ that lies in a fossa formed by the junction of the left and right lobes on the underside of the liver. Its function is to concentrate and store bile secretions from the liver. Its capacity ranges from 30-60mls. The position of the gallbladder fundus is inconsistent *however the neck is invariably positioned in the porta hepatis and major interlobar fissure. The* fundus may fold back on itself, (the phyrygian cap) and this is a
normal variant. Septa in the gallbladder may be partial or complete. Thick folds in the mucosa of the cystic duct form the spiral valves of Heister.

A gallbladder which measures more than 5cm in diameter is considered enlarged and it is contracted when less that 2cm in diameter. The wall of the gallbladder does not exceed 3mm when fully distended.

The lumen of a normal gallbladder contains clear fluid and any particulate debri signifies pathology.[22]

HEPATOBILIARY PATHOLOGY

The role of imaging in a jaundiced patient is to identify and assess major bile duct obstruction. A patient may present with dark urine, pale stools, pruritus and a cholestatic liver function test. Ultrasound is the preferred method of examination. Supplementary examinations include CT, MRCP, direct cholangiography and ERCP.[23]

Aims of a radiological examination

(a) Determine if obstruction is intra or extrahepatic as shown by dilatation of the ducts. Intrahepatic ducts should measure 2-3mm centrally and peripherally should be smaller than adjacent portal vein branches. The maximum normal diameter of common bile duct should be $\leq$ 7mm. However lower values are employed in younger adults. In older population; values of 8mm could be considered normal. Post cholecystectomy measurements are less well defined and ducts could measure upto 10mm in diameter.[19]

(b) If duct obstruction is present then the anatomical level should be subsequently determined. Three levels are recognized;-

(i) Hilar-at or close to the confluence of right and left hepatic duct.

(ii) Mid common bile duct

(iii) Distal common bile duct.

Here below is a table of differential diagnosis of causes of bile duct obstruction at various levels.

Table 1: Causes of major bile duct obstruction

CAUSES OF MAJOR BILE DUCT OBSTRUCTION		
Anatomical location	**Malignant**	**Benign**
Hilar	-Gallbladder carcinoma -Hepatocellular carcinoma	- -
Low/Mid obstruction	-Pancreatic Carcinoma -Ampullar Carcinoma	- Pancreatitis.
Either	-Cholangiocarcinoma -Metastases -*Lymphoma*	-Stones -Mirrizzi's syndrome -*Post op strictures* -Primary sclerosing cholangitis -Parasites

(c) Afterwards imaging should evaluate malignant obstruction and the possibilities of resectability and biliary decompression options.

In malignant hilar obstruction; the radiologist should assess the proximal extent of structuring into the left and right hepatic ducts, any lobar atrophy, whether portal veins are patent and any intrahepatic/ extrahepatic metastases.

In low obstruction, tumour size should be assessed, vascular involvement (portal vein, superior mesenteric vein and superior mesentery artery) lymph node metastases and hepatic metastases.

BENIGN PATHOLOGIES OF THE BILIARY TREE

Choledocholithiasis

About 90% of bile duct stones are secondary; in that they have been passed from the gallbladder. Those that arise primarily from the bile duct are pigment stones and form the remaining percentage.[24]

PLATE 1: Cholelithiasis

MRCP shows multiple hypointense calculi [arrows] within a dilated CBD.

Hepatolithiasis

Majority of duct stones are extrahepatic. Intrahepatic stones or hepatolithiasis may occur oftenly associated with pathologies like benign strictures, primary sclerosing cholangitis, post operatively, pyogenic cholangitis and Caroli's disease.[25]

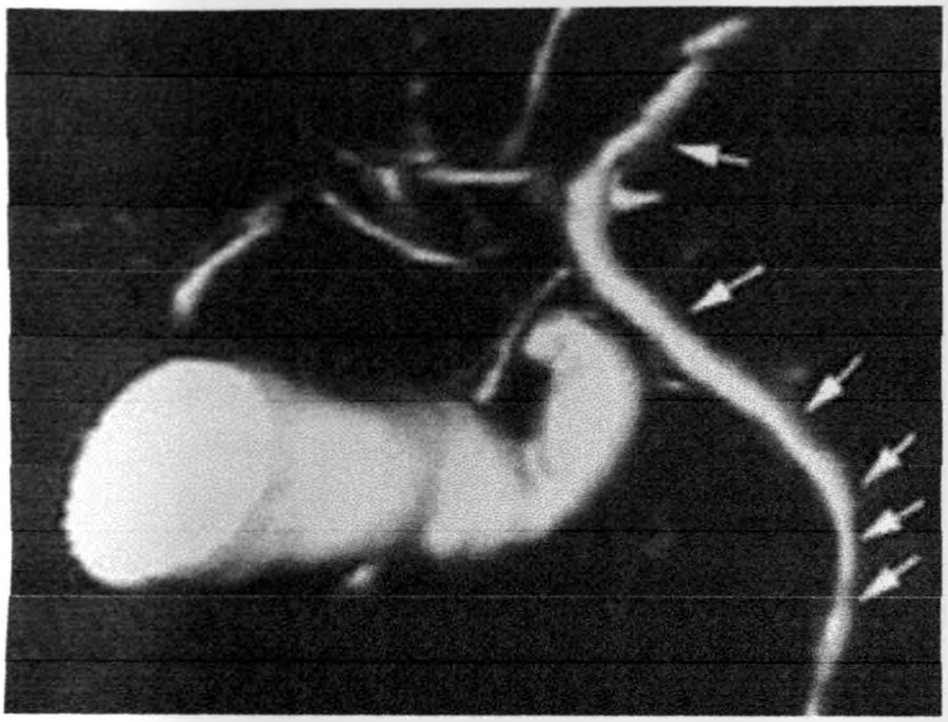
Post operative strictures

Result from cholecystectomy. They are about 1-2mm in length and oftenly involve the common duct, but can involve the right and left hepatic ducts. The duct stones develop proximal to stricture.[26,27]

Primary sclerosing cholangitis

Resulting stricturing involves multiple segments of intra/extra-hepatic ducts and is characterized in the common duct by diverticula-like out pouchings.[28]

PLATE 2: Primary sclerosing cholangitis



Coronal MRCP shows multifocal strictures, moderate dilation of the CBD

Acute bacterial cholangitis

Occurs secondary to partial bile obstruction. It is characterized by charcoat's triad namely; fever, right upper quadrant pain and jaundice. Gram negative organisms are the culprits.

Mirrizi syndrome

In this syndrome, a gallstone in the Hartmann's pouch or in the cystic duct compresses the common bile duct causing deranged liver function. The obstruction leads to inflammation and fibrosis resulting into further narrowing of the common bile duct. [29]

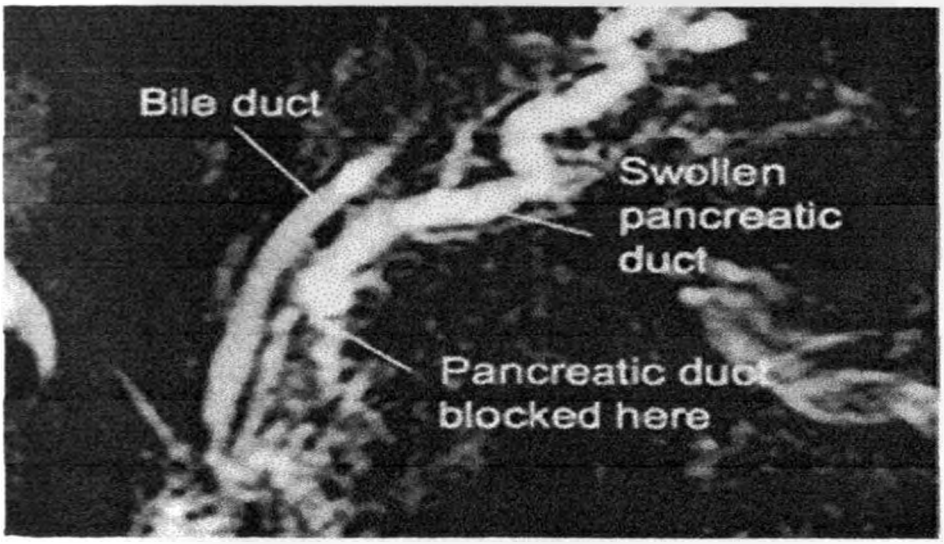
PLATE 3: Coronal cholangiogram

Shows a stone at the cystic duct/CHD junction in Mirizzi disease

Pancreatitis

Either acute or chronic produces biliary stricturing via fibrosis or inflammatory mass. [30]

PLATE 4: Coronal MRCP



Shows an atrophic pancreas with stricturing at its proximal ductal end-a case of chronic pancreatitis.

Parasitic Infections

Ascaris lumbricoides accesses the bile duct via the duodenal ampulla. They may be asymptomatic or lead to Cholangitis, Pancreatitis and Cholecystitis. Hepatic hydatid cysts may rupture into the biliary tree and obstruct it.

HIV Cholangiopathy

Develops in patients with an established diagnosis of HIV.

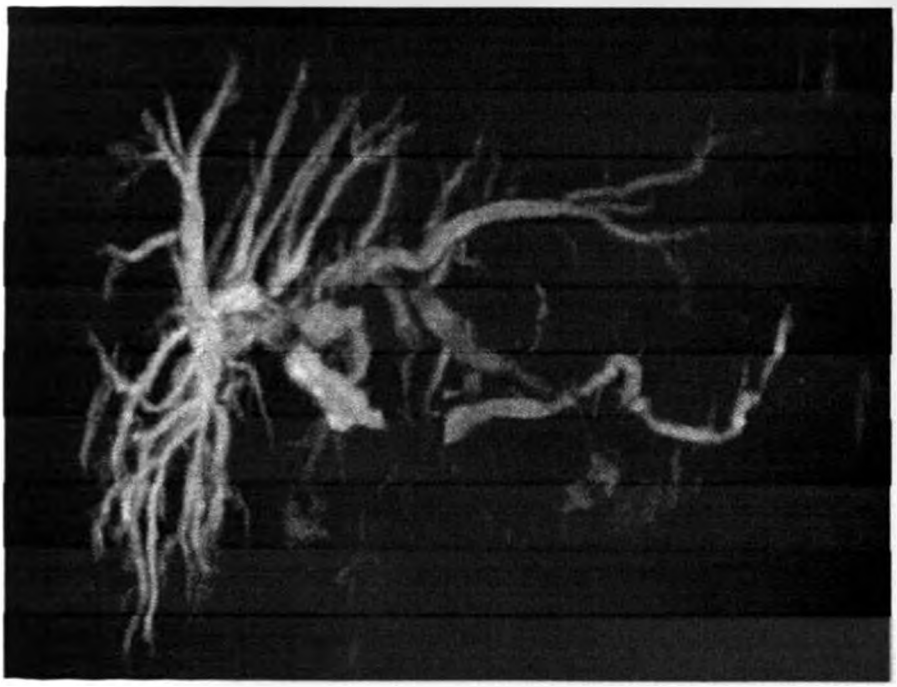
Cryptosporidium infection is commonly the cause. [30,31]

NEOPLASTIC BILE DUCT PATHOLOGY

Cholangiocarcinoma

This is an uncommon tumour which arises from bile duct epithelium and spreads via local infiltration. Approximately 60% arise in the hilar region and about 30% arise in the distal common duct. The remaining percentage constitutes multifocal or diffuse tumours. [32]

PLATE 5: Coronal MRCP

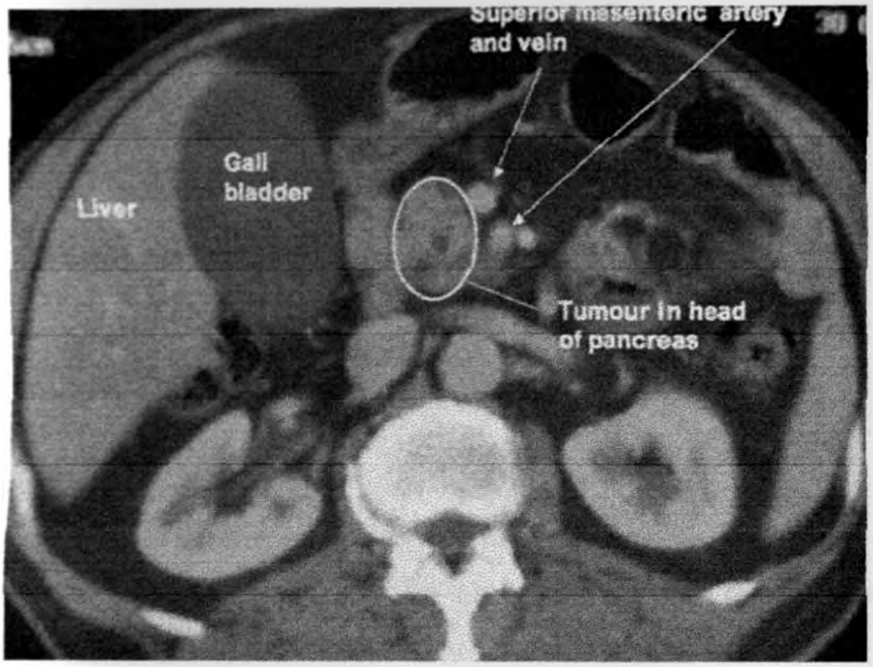


Shows a mass at the distal common bile duct obstructing both the CBD and pancreatic duct-a case of cholangiocarcinoma.

Pancreatic ampullary tumours

They cause distal biliary obstruction characterized by slight stricturing and shouldering.[30]

PLATE 6: Axial CT scan



Demonstrates a tumour at the head of pancreas obstructing the distal CBD

Metastases and lymphoma

These result in hilar or distal biliary obstruction. Melanoma characteristically causes intraductal metastases.

UNDERSTANDING M.R.I PHYSICS

- *Image generation*
- Contrast enhancement
- Special sequences
- *Advantages and disadvantages of M.R.I*

IMAGE GENERATION

What is MRI?

It is a rapidly expanding imaging modality. Being versatile and safe, MRI is increasingly becoming a popular diagnostic tool. The operational physical principles are complex, however a detailed knowledge of them is not required to interpret the images.

An MRI scanner does not require ionizing radiation but uses an extremely powerful magnet.

Here is a simple summary of the stages resulting in the MR image.

(a) Patient is positioned in the magnet

(b) A radiowave is briefly sent into the body an then switched off

(c) The patient then emits a signal

(d) This signal is then used to reconstruct the image.

Basic Physics

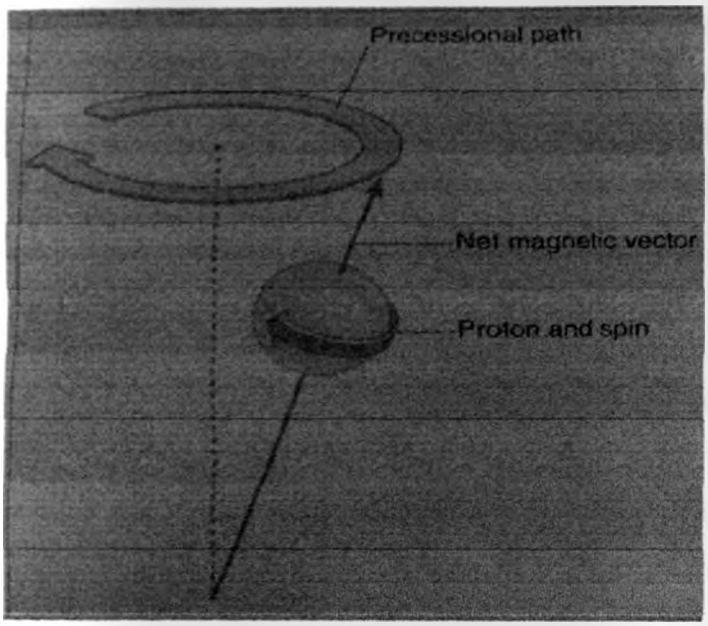
An understanding of the physics of MRI is desirable to appreciate how tissues are distinguished and accurately localized in the body. Also it helps to understand the principles of using the even increasing number of MRI sequences.

Hydrogen atoms or protons are a fundamental building block of all living tissues, principally in the form of water. Protons have an atomic number of 1- with an odd mass number and are MR active nuclei. Fortunately they are abundant in the body hence used and the best signal is received from them due to their large **magnetic moment**.

The proton has a single positive charge and spins on its own axis like the earth.

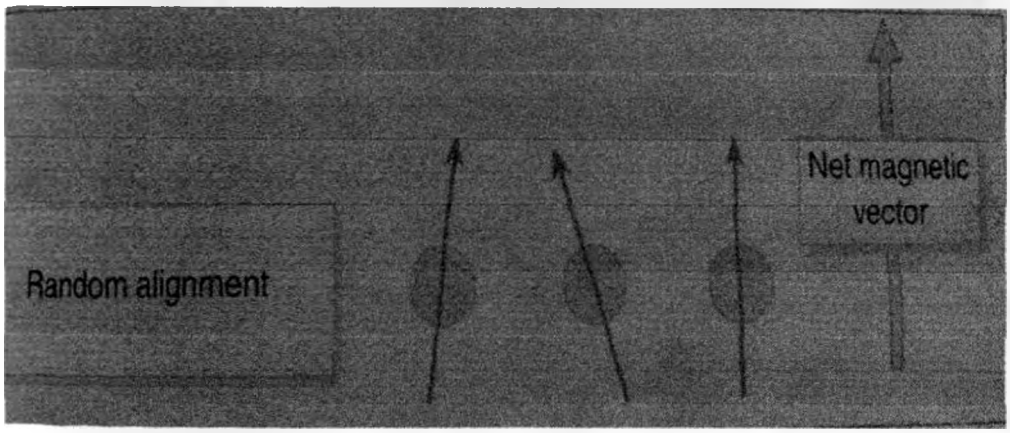
At the same time, it also precesses like a spinning top.

PLATE 7: Precession and net magnetic vector



A moving/spinning charge can be considered to be an electrical current and this in turn induces a **magnetic field**. Meaning:- there are billions of spinning protons in the body acting like tiny bar magnets. *Under normal conditions, all are* **randomly aligned** *with all their fields cancelling* each other out so they have no net magnetic moment.

PLATE 8: Precession and alignment



When the patient is in the MRI scanner (strong magnetic field), the nuclear magnetic moments align themselves in either the parallel or anti-parallel direction and in addition precess around the

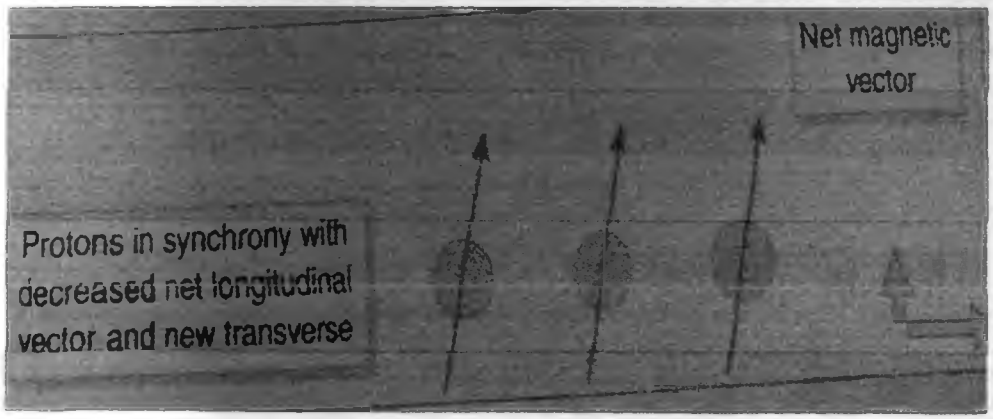
external field direction with frequency given by the Larmor equation. (F=KB). Where B is the magnitude of the applied magnetic field, K is the gyromagnetic ratio.

For hydrogen, the gyromagnetic constant equals 42.56 (mHz) per tesla.

The magnetic vectors will have their transverse plane projections all cancel out at each point in space because of their random motions. The vectors however, add up in the longitudinal direction giving the patient a back magnetization along the applied magnetic field. This is the equilibrium or relaxed state.

A short burst of energy (in milliseconds) is imparted to the protons in the form of a radiofrequency (RF) pulse. This is done through a coil. The RF pulse is of a specific frequency that can exchange energy with the proton, known as the resonance frequency, which has the same procession frequency as the proton. This can be calculated depending on what tissue is being imaged.

PLATE 9: Resonance



When the RF is turned off, the protons start to lose energy while returning to their natural, relaxed alignment within the external magnetic field. Longitudinal magnetization is regained, which is known as longitudinal or **T1 relaxation.** Transverse magnetization is lost, which is known as transverse or **T2 relaxation**. As a consequence a signal that the detector coils can pick up is given off. The rate at which T1 and T2 relaxations occur depends on the tissue in which protons lie. The resulting differences in signal intensity provide image contrast between tissues

in the body. In addition, the density of protons in a tissue will also determine the signal intensity.

Locating both the volume of tissue and then recognizing the X, Y and Z cor-ordinates of the signal generated by the protons depends on the use of three gradient coils. These apply a very weak magnetic field in addition to the main external field. Energy imparted to specific areas leads to establishment of location of subsequent signal.

Hydrogen nuclei are found throughout the body, in form of water. We know pathological processes result in local oedema, imaging sequences have been designed to highlight this difference between normal and pathological tissues.

THE IMAGING SEQUENCES

Image sequences are made up of differing combinations of RF pulses and signal sampling timing. Signal intensity changes with time.e.g T1 relaxation curve, a signal sampled sooner is less intense than one sampled later. More importantly, the difference in signal intensity between fat and water is greatest if the signal is sampled soon after the RF is switched off, thus providing tissue contrast. If the sampling time is too long, this results in no difference in signal intensity between two tissues. Reverse is true for T2 relaxation curve.

Points to remember;

- *All tissues have different T1 and T2 relaxation times*
- All tissues have different proton densities

Three common sequences help distinguish tissues from one another.

1) T1 –weighted –utilizes differences in T1 relaxation times between tissues.
2) T2 weighted –utilizes differences in T2 relaxation times between tissues.
3) Proton –density utilizes differences in proton density between tissues.

The sequence used in a certain image can be appreciated by the scan appearance and the scanning parameters. The signal is recorded as grey scale imagery (black, white and shades of grey).

The following is a basic guide to scanning parameters;

TR (time to repetition) is the time between sequential RF pulses

TE (time to echo) is the time between sequential RF ending and when signal is sampled.

T1 weighted image; (short TR < 500ms, short TE <50ms). It offers good spatial resolution and is useful for anatomy. Fat is bright, water/simple fluid is dark, hemorrhage is bright, melanin bright, grey matter –grey, cerebral white matter white.

T2 weighted image: Long TR > 1500ms, long TE >80ms).

Its sensitve to local oedema –useful in identifying pathology.

Fat is bright, water/simple fluid is bright, cerebral gray matter is grey. Cerebral white matter is dark.

Proton density: Long TR > 1500ms, short TE <50ms).

Fat is bright

Water/simple fluid is dark.

Cerebral grey –grey; white: dark [33,34]

MAGNETIC RESONACNE CHOLANGIOPANCREATOGRAPHY EXAMINATION

Once again this examination demonstrates biliary and pancreatic ducts by MRI. Various sequences are used. All rely on heavily T2-weighted sequences which effectively eliminate signal from all tissues except stationary free –water protons. Thus, images display fluid containing structures as bright (high signal).

MRCP can be added to a conventional MRI examination of the abdomen.

TECHNIQUES FOR MRCP

Thick –slab single shot fast spin echo images and thin multislice HASTE images are employed. The thick-slab technique provides an overview of bile duct anatomy and has multiplanar capabilities. Thin –slice images improve the visualization of fine structures.

Thick-slab images are obtained with a very long TE (940m sec) in order to completely suppress background tissue.

A well positioned imaging slab will allow the slab thickness to be reduced to around 50mm, which gives a better image quality than a thicker slab.
Thin slice images (4mm) are obtained at a moderate TE, approximately 96m sec. Note that small caliber ducts are lost with longer TE. Thin slice images should be reviewed both as individual slices and after maximum intensity projection. (M.I.P) reconstruction. Parallel saturation bands and fat suppression are used with both sequences.

Images are acquired during breath-holding. Coronal or oblique images are often most useful. Since conventional MRCP is not reliant on contrast excretion it is suitable for jaundiced patients.

More recently MR has been combined with hepatobiliary contrast agents. These include mangafodipir trisodium, gadobenate dimeglumine and gadoxetic acid disodium. These agents shorten T1 relaxation providing positive contrast images on T1 weighted sequences. Imaging is performed 30 minutes after IV infusion to allow hepatocyte uptake and biliary excretion. Thus it offers functional and anatomical information. However it depends on near –normal hepatocyte function.

Since T1-weighted MR sequences are used, it is possible to use near –isotrophic three-dimensional gradient-echo acquisitions, which allow greater image manipulation than do conventional MRCP sequences.

Applications for contrast-enhanced MR cholangiography include liver donor transplant work up, assessment of bile leaks and biliary communication with cysts, and the demonstration of segmental obstruction.

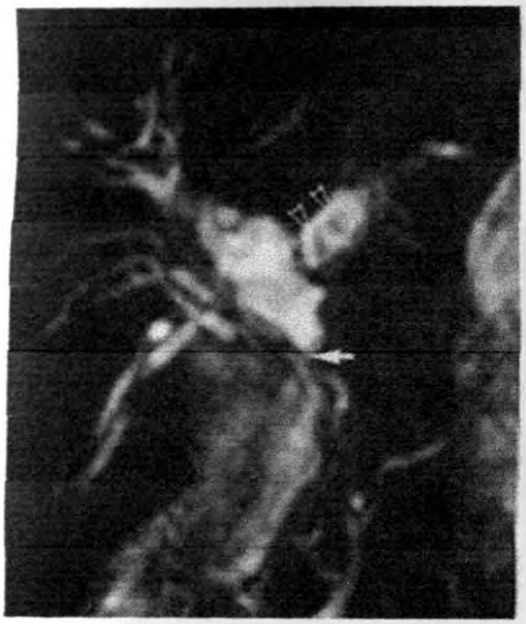
Diagnostic pitfalls of MRCP include pseudo-filling defects, pseudodilatation and non-visualization of the ducts. Filling defects are usually due to stones, air, tumours, haemorrhage or sludge.

In frequent causes of filling defects include susceptibility artifact from adjacent clips, metallic bile duct stents, folds and flow voids.

Pseudo dilatation can occur if the cystic duct crosses the common bile duct or courses parallel to it or if extradural fluid-filled structures (e.g intestines, pseudo cysts, gallbladder) are volume averaged with the ducts.

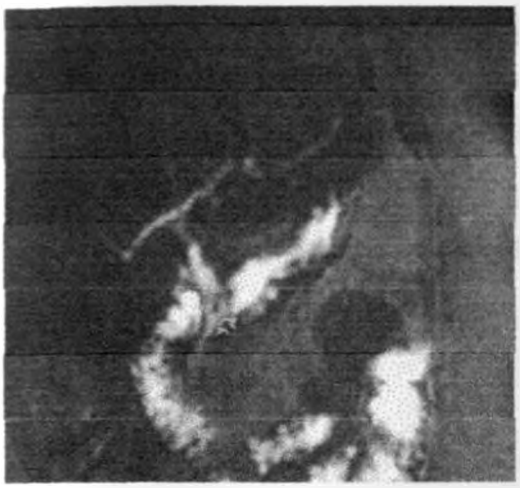
Non visualization of the intrahepatic bile ducts may be a normal finding due to non-distension, however non-visualization of extrahepatic bile ducts may be due to obscuration by extraductal fluid-filled structures (e.g intestine, pseudocysts, gallbladder), intravenous administration of manganese or pneumobilia.[35,36]

PLATE 10: Pneumobilia



Three dimensional MIP reconstruction image. It shows two filling defects (arrow heads) in the left hepatic ducts secondary to pneumobilia from a choledochojejunostomy (arrow). Multifocal strictures and dilatation are due to primary sclerosing cholangitis.

PLATE 11: Pseudo-dilatation



Single shot fast spin echo MRCP image shows pseudo dilatation and a pseudo-filling defect of the extrahepatic bile duct (arrow) due to medial insertion of the cystic duct.

PLATE 12: Duct non-visualization

Thick-section single shot fast spin –echo MRCP image shows the gallbladder (arrow) obscuring the common hepatic duct.

ADVANTAGES OF MRI

- Uses no ionizing radiation; the RF and Magnetic fields so far have not been found to cause significant harm.
- Has Multiplanar, multiaxial capability. Thus a plane can be specifically oriented to the anatomy being examined.
- High contrast resolution between soft tissues and between normal and pathological tissues.

DISADVANTAGES

- Patients with ferromagnetic substances are ineligible for examination.
- Long acquisition time leads to motional artifacts.
- It is less suitable for examining bony structures, cortical bone contains little water, hence returns very little signal. It is dark in all sequences.
- M.R.I is less suitable for the acutely or critically ill patient who needs extensive monitoring of vital signs. All monitoring equipment must be M.R.I scanner compatible. (33,34)

STUDY OBJECTIVES

Broad objectives

The main objective of this study is to determine the ability of M.R.C.P examination to accurately determine the site and etiology of biliary obstruction.

Specific objectives

- To determine the pattern of M.R.C.P findings in obstructive jaundice.
- To evaluate the regional distribution of the various causes of obstructive jaundice in the biliary tree.
- Determine the age and sex distribution, the relative frequency of the lesions causing obstructive jaundice.

MATERIALS AND METHODOLOGY

Study Area

Study was conducted at the radiology and surgical departments of Kenyatta National Hospital, University of Nairobi and Plaza Imaging Solutions.

Study Design

This was a retrospective and prospective study.

Study population

The study was designed to include former and current patients with clinical features of obstructive jaundice who subsequently underwent MRCP and definitive surgery. Patients were mainly recruited from the surgical (liver) clinic at Kenyatta National Hospital.

Sample size

Statistical formula used in calculation of sample size; at confidence interval of 95% and a margin error of 5% and prevalence rate of hepatobiliary diseases at 2%; the sample size was calculated by the formula.

$N = (1.96/m)^2 P(1-P)$

Where P = proportion of prevalence

N = Sample size

M = Proportion of margin of error

Using this formula the sample size (n) was 30 subjects.

Sampling method

M R C P and definitive surgery results of patients with clinical features of obstructive jaundice were obtained for a period of 12 months.

Inclusion Criteria

Pediatric and adult patients with obstructive jaundice undergoing MRCP and surgery at Kenyatta National Hospital radiology and surgery departments.

Exclusion criteria

Patients with obstructive jaundice but who did not undergo surgery to confirm M.R.C.P findings.

Patients with non-obstructive jaundice.

Study limitations

Data collection and retrieval was hampered by lack of computerization.

Some patients opted to undergo surgery at other health institutions of their own choice thus making follow up difficult.

Due to financial or other personal reasons, some patients with obstructive jaundice diagnosed on M.R.C.P did not undergo surgery. Results were not be available to confirm M.R.C.P. findings.

Time lag between the time of M.R.C.P examination and date of definitive surgery led to progression of pathology creating discrepancies in M.R.C.P and surgical findings.

Data Management

Data collection

Qualified radiologists diagnosis and surgeon's intra-operative findings were filled in the pretested questionnaire by the researcher.

Data analysis

Statistical Package for Social Scientists (SPSS) was used for data analysis.

Subsequently, tables, pie charts and graphs were used to present the data.

Images, when available were presented for some cases.

MRI equipment used in KNH/PLAZA

Both use Philips Brilliance 16 slice CT machines. This type of machine offers;

High quality imaging, fast reconstruction, task automation and evolved ways to minimize radiation dose.

Technique

Ascertain that there were no contraindications for M.R.C.P in an individual patient.

ETHICAL CONSIDERATION

Numerous ethical considerations were considered in the process of this research.

Kenyatta National Hospital ethical committee was requested to approve the research proposal.

Patient's personal information e.g. names were not to be used in the study in order to uphold confidentiality. Information acquired would not be used for any other purpose besides in the clinical management of patients and academics.

M.R.C.P was one of the step-ladder examinations (others included ultrasound, CT, standard M.R.I) requested by the physician in the diagnostic work-up of a patient with obstructive jaundice.

No other extra examination was done on a patient unless so requested.

Patients were requested to provide an informed consent in writing.

RESULTS

Seventy-three (n= 73) patients with jaundice and suspected biliary obstruction were included in the study. The demographic characteristics of patients are shown Table 2 below. There were 32 males and 41 females (male-female ratio, 0.8:1). The ages of the patients ranged from 5 months to 85 years with a mean of 53.3 years (SD 17.9). The study enrolled only 4 patients below 18 years of age including 3 infants, and most patients were aged between 40 to 50 years (26%) and above 50 years (58.9%).

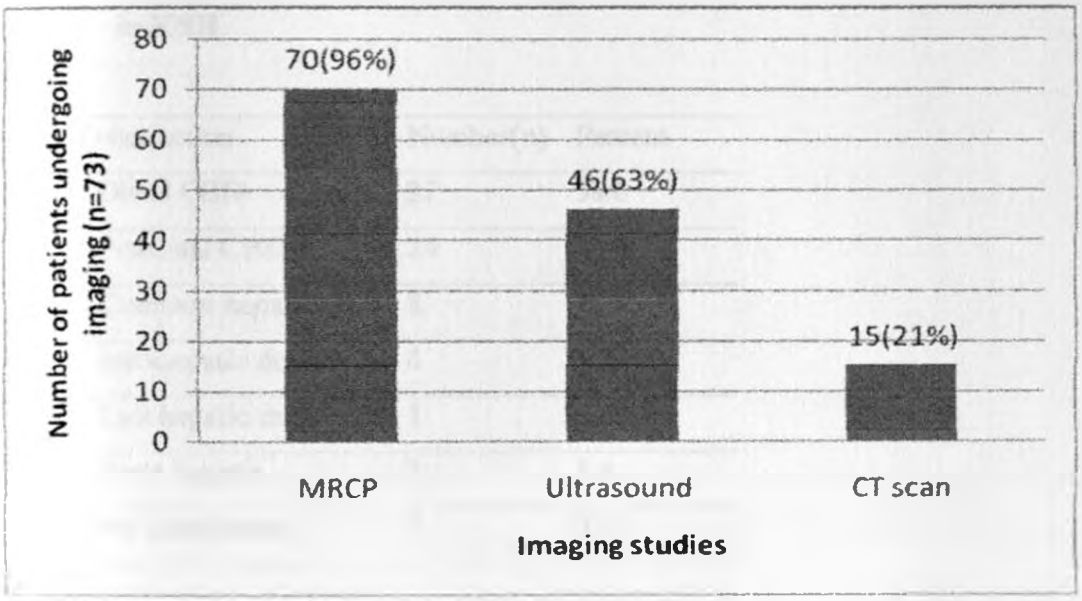
Table 2: Demographic characteristics of patients with obstructive jaundice enrolled in the study

Characteristic	Number	Percent
Gender		
Male	32	43.8
Female	41	56.2
Age category		
Below 1 year	3	4.1
1 to 5 years	0	0
6 to 17 years	1	1.4
18 to 30 years	2	2.7
30 to 40 years	5	6.9
40 to 50 years	19	26
50 years and above	43	58.9

Imaging studies

As shown in Figure 2, a total of 131 imaging studies frequently in combination were conducted among the 73 patients in the study.

Figure 2: Types of imaging studies conducted among 73 patients with obstructive jaundice at KNH



MRCP was done either in combination or alone in 96% of patients. Thirty-eight (52.8%) patients underwent both MRCP and ultrasound investigations, while seven (9.7%) patients were investigated using all the three imaging studies: MRCP, ultrasound and CT scan. A similar number of patients (n=7) were investigated using both MRCP and CT scans.

Ultrasound and CT scan were rarely used alone in the study. Only one patient was investigated using ultra sound alone and a second patient investigated using CT scan alone. These two patients were excluded from further analysis since the primary comparison was based on MRCP and surgery findings.

Site of obstruction

The sites of obstruction, visualized using MRCP, in the hepatobiliary system of 70 patients with obstructive jaundice are presented in Table 3. No obstruction was visualized on MRCP for 5 (7.1%) out of the 70 patients with obstructive jaundice.

Table 3: Site of obstruction in patients with obstructive jaundice investigated using MRCP *in KNH*

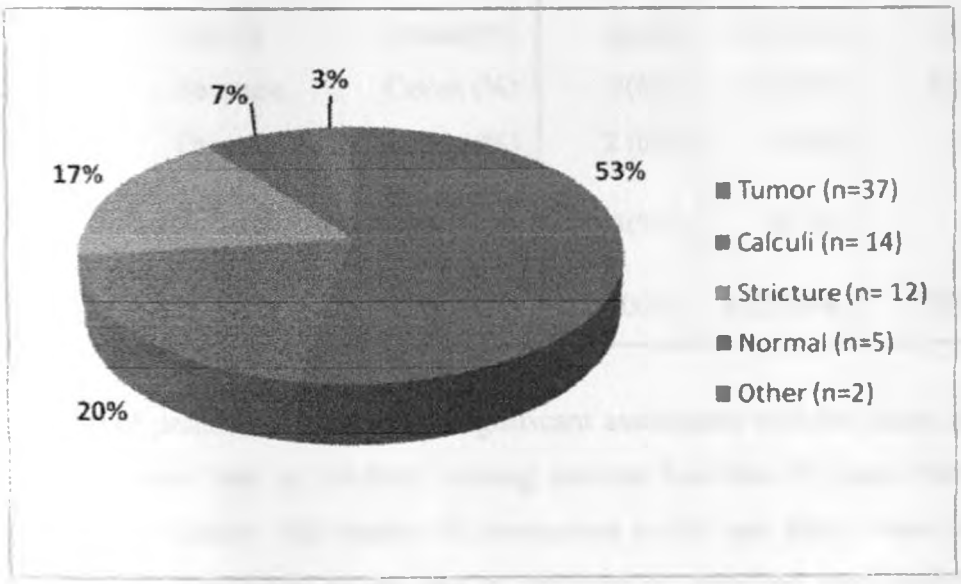
Site of obstruction	Number(n)	Percent
Distal CBD	27	38.6
Proximal CBD	24	34.3
Common hepatic duct	8	11.4
Intrahepatic ducts	4	5.7
Left hepatic duct	1	1.4
Porta hepatis	1	1.4
No obstruction	5	7.1
Total	70	100

Obstruction commonly occurred at the distal CBD and proximal CBD, with 38.6% and 34.3% of all patients, respectively, having obstruction at these two sites (Table 3). This was followed by the common hepatic duct and intrahepatic ducts which accounted for 11.4% and 5.7% of obstruction, respectively. One patient had an obstruction in the left hepatic duct and another patient's obstruction occurred at the porta hepatis.

Cause of obstruction

The causes of biliary obstruction among patients in the study determined using MRCP are shown in Figure 3. The MRCP readings of five (7%) patients were normal implying that these patients did not have any biliary obstruction despite their clinical diagnosis of obstructive jaundice.

Figure 3: Causes of obstruction diagnosed by MRCP among 70 patients investigated at KNH



Initially, 37 (53%) patients were diagnosed to have obstruction caused by tumors based on clinical and/ or MRCP findings. The next most common cause of suspected obstruction visualized using MRCP was calculi in 20% (n=14) of patients followed by stricture (n = 12, 17%).

Table 4 below shows that the cause of obstructive jaundice was significantly associated with gender of patients (*Chi* =12.2, df =4, p =0.009). Seventy-two percent of male patients had obstruction caused by tumors, compared to only 39% of females who also had obstruction due to tumors. Conversely, female patients were more likely to have strictures (25% versus 6%) and calculi (27% versus 6%) compared to male patients.

Table 4: Association between cause of obstruction and gender of patients with obstructive jaundice

			Gender		Total	Chi square (df)	P value
			Male	Female			
Cause of obstruction	Tumor	Count (%)	23(72%)	16(39%)	39(53.4%)	12.2(4)	0.009
	Calculi	Count (%)	2(6%)	11(27%)	14(20%)		
	Stricture	Count (%)	2(6%)	10(25%)	12(16%)		
	Others	Count (%)	2 (6%)	1(2%)	3(4%)		
	No obstruction	Count (%)	3(9%)	3(7%)	6(8%)		
Total		Count (%)	32(100%)	41(100%)	73(100%)		

The age of patients also showed a significant association with the cause of obstructive jaundice (Fisher's exact test, $p = 0.016$). Among patients less than 18 years there was no obstruction caused by a tumor. The causes of obstruction in this age group were either calculi (n=2) or stricture (n=1) and one patient had no obstruction visualized using MRCP. Conversely, most (70%) obstructions in patients above 50 years of age were caused by tumors. The causes of obstruction were almost evenly distributed between stricture, calculi and tumors between the ages of 30 and 50 years.

Surgery

Surgery was done in 54 (83%) patients out of the 65 patients studied. One patient declined surgery, while another patient was unfit for surgery or too weak to undergo the surgical procedure. Other reasons for failure to undergo surgery in enrolled patients included alternative procedures i.e. successful removal of calculi via ERCP in 3 patients. Three deaths occurred before the scheduled operations. No reason was stated for failure to operate on one patient.

The surgical diagnoses among the 54 patients undergoing surgery are compared with the initial MRCP diagnoses in Table 5 below.

Table 5: Comparative results of surgery and MRCP finding in patients treated through surgery (n = 54)

Finding	MRCP	Surgery	ERCP
Tumor			
Cholangiocarcinoma*	18	13	
Duodenal tumor		1	
Tumor of left lobe of liver, stomach, intestines		1	
Ca stomach with nodal metastases		1	
Ca stomach, obstruction due to porta hepatic nodes		1	
Calculi		1	
Ca head of pancrease*	15	13	
Periampullary tumor		1	
Pancreatic head fibrosis		1	
Stricture*	12	11	
Cholangiocarcinoma		1	
Calculi*	14	8	3
Stricture		1	
No stones		2	

* MRCP diagnosis

MRCP tumor diagnosis versus surgical findings

Overall,MRCP correctly diagnosed tumours as the cause of obstruction in 93.9%

MRCP correctly diagnosed 13 cases of cholangiocarcinoma confirmed by surgery and further 13 cases of carcinoma of head of pancreas also confirmed by surgery (Table 5). The resulting sensitivity of MRCP for diagnosing cholangiocarcinoma and carcinoma head of pancreas was 79%.

There were, however, two false-positive tumor readings by MRCP and five tumor misclassifications (Table 4). One case classified as cholangiocarcinoma was found to be calculi on surgery and another case classified as carcinoma head of pancreas by MRCP was diagnosed as pancreatic head fibrosis during surgery.

Misclassification of tumor type was more frequent in cholangiocarcinoma (n=4) compared to carcinoma involving head of pancreas (n=1). Surgical findings that had been initially classified

as cholangiocarcinoma included cancer of the stomach with metastases (n=3) and duodenal tumor (n=1).

MRCP stricture diagnosis versus surgical findings

Eleven (92%) out of the 12 cases of MRCP diagnosed with biliary strictures were confirmed during surgery (Table 5). The sensitivity of MRCP for diagnosing strictures was 92%. As shown in Table 5 there was one false positive stricture diagnosed by MRCP. This false diagnosis was confirmed to be a tumour - cholangiocarcinoma- during surgery.

MRCP calculi diagnosis versus surgical and ERCP findings

As indicated in Table 3, MRCP showed that 14 patients had calculi. Out of these 11 diagnoses were confirmed to be calculi by surgery (n=8) and ERCP (n =3). The sensitivity of MRCP for diagnosing calculi confirmed by either surgery or ERCP was 92%. There were three false positives, confirmed to be either stricture (n = 1) or a definite diagnosis of no calculi (n = 2) made during surgery.

Table 6: Overall diagnostic accuracy of MRCP in various studies done over the world

	Level of Obstruction	**Cause of Obstruction**
KNH/PLAZA IMAGING	100%	92 %
Vaishali et al (2004)	96.3%	89.65 %
Lannicelli et al (2006)	100%	88 %
Vupadhyaya et al (2006)	95.45%	87.5 %

PLATE 13: 68year old female with gallstone impacted in the common bile duct

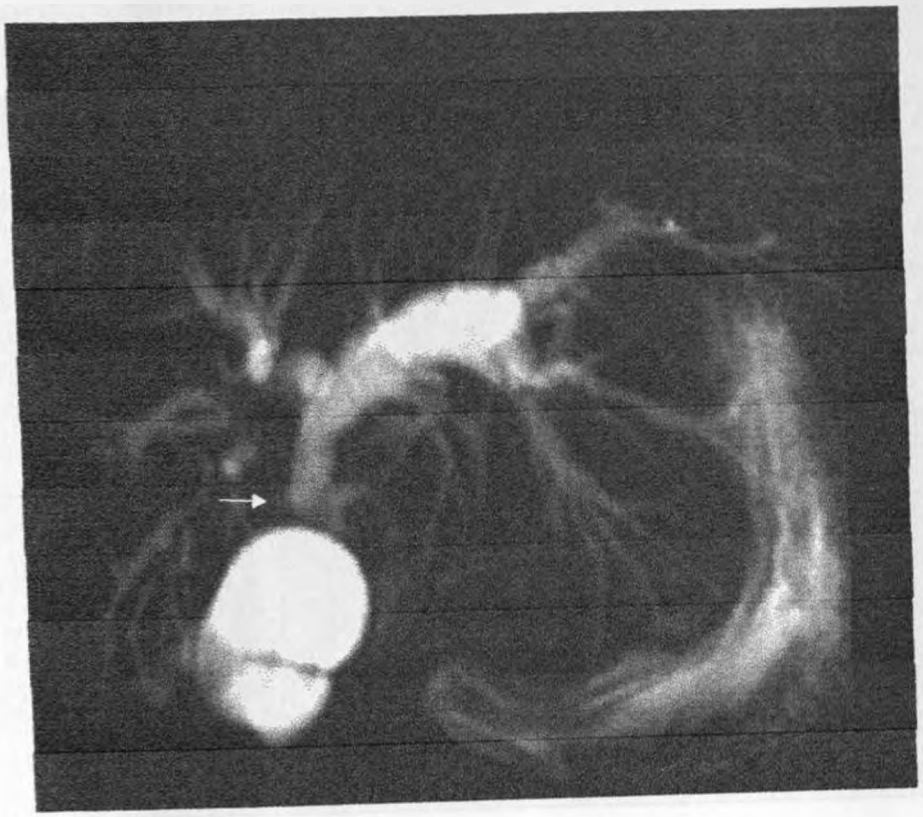


PLATE 14: 77 year old female with gallbladder cholangiocarcinoma obstructing the common bile duct

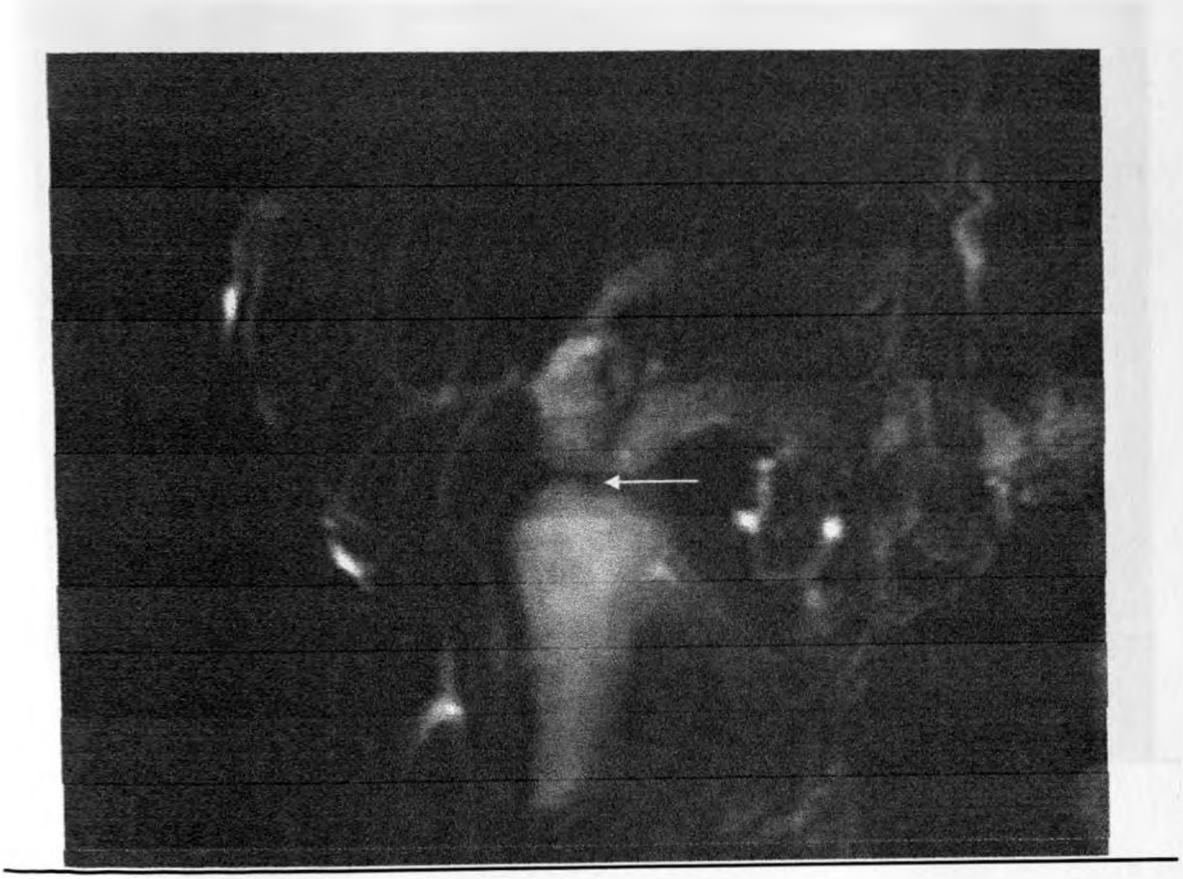


PLATE 15: 52 year old with male with klaskin tumour obstructing the hepatic ducts confluence

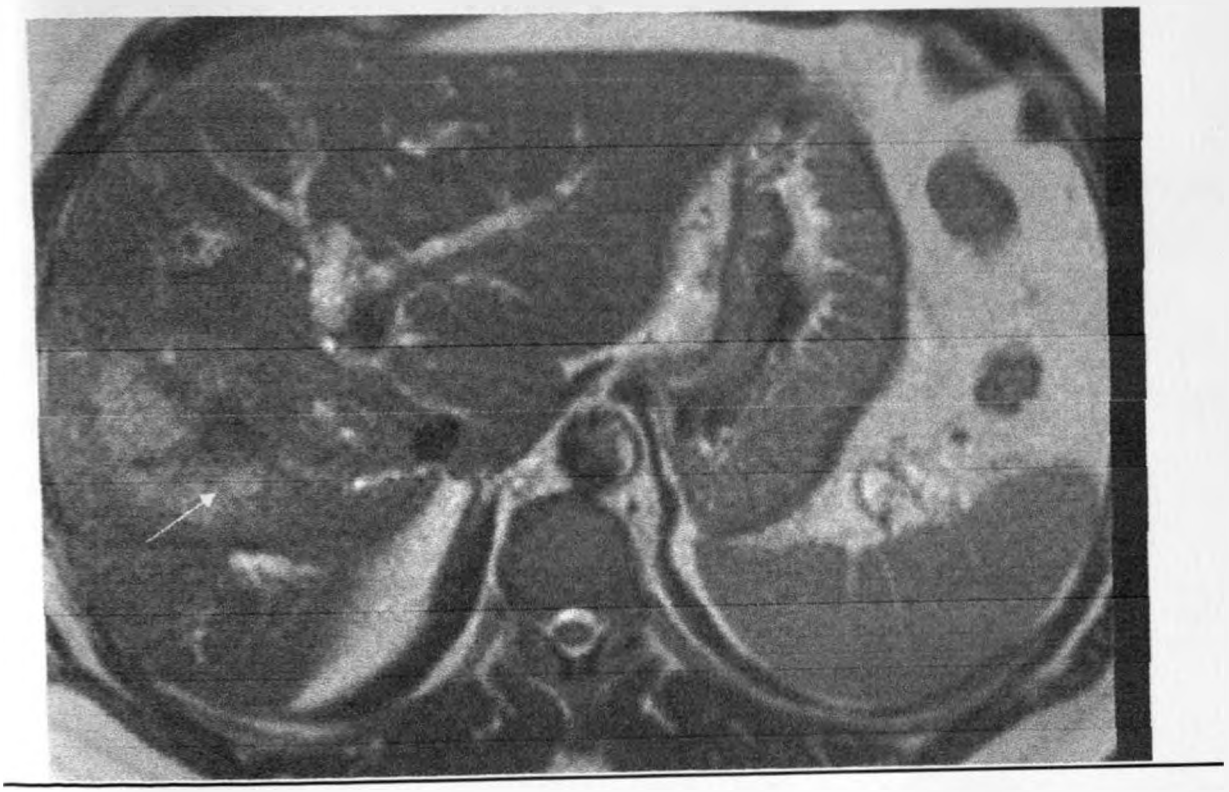
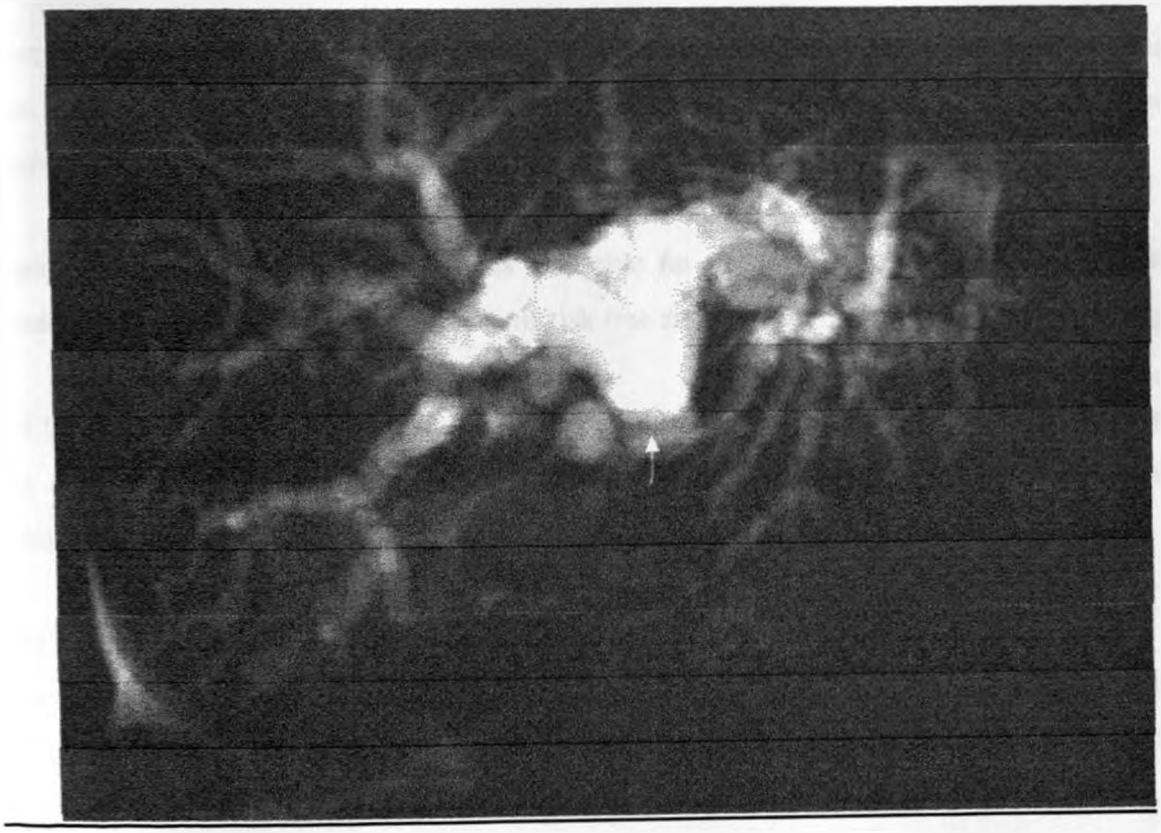


PLATE 16: 62 year old with proximal common bile duct stricture



DISCUSSION

Since the advent of laparascopic surgeries, preliminary evaluation of the biliary tree has assumed even greater importance in patient at risk of obstructive jaundice (especially due to choledocholithiasis) and may help to avoid intra-operative difficulties.

Inspite of different diagnostic modalities available for detecting site and cause of obstructive jaundice, currently no single method is both risk free and with high sensitivity and specificity.

ERCP which has been at the helm of investigating cases of obstructive jaundice carries potential risk of complications e.g pancreatitis, bleeding from sphincterectomy sites and duodenal obstruction.

MRCP approaches the ideal imaging modality.
In my study, multimodality imaging was done in 96% of patients. In such cases requesting clinicians employed MRI/MRCP as a problem solving tool; where either ultrasound or CT alone or in combination had failed to answer the clinical question.

In two cases; one patient was investigated using ultrasound alone and another by CT. upon follow up; both had classic clinical signs and symptoms of cholelithiasis. The clinicians decided to intervene surgically.

Results from this study indicate that MRCP has a 100% sensitivity in detecting the site of obstruction and 92% sensitivity for diagnosing the cause of obstruction.

The above compares favourably with studies done in other parts of the world.
Vaishali et al ([13]) found that, the diagnostic accuracy of MRCP was 96.3% and 89.65% for the site and cause of obstruction respectively.

Lannicelli et al had 100% and 88% sensitivity respectively ([40]) while Vupadhyaya et al had 95.45% and 87.5% respectively ([41]).

The slight discrepancy in the above results could be due to the MRI machines used in examining patients.

MRI technology is advancing; field strengths are higher, gradient switching is faster which makes better image resolution with improved accuracy. This study had the privilege of using the latest version of MRI technology.

Thus MRCP is able to present a detailed visualization of the anatomy of the un obstructed biliary tract. This is essential for planning surgery and post operative management.

No cause of obstruction was detected in five cases despite dilated bile ducts.
This may illustrate the drawbacks of MRCP. Bile ducts may remain dilated soon after and obstructing calculus is passed. MRCP may fail to detect a small calculus or a stenotic ampullar of Vater.

MRI/MRCP could diagnose obstruction due to tumours in 93.9% of cases (KNH /PLAZA study) H.E. Adameka et al 81% ([42]). This technique has the potential of producing excellent cross sectional images of the biliary tract and other abdominal viscera. Findings suggestive of malignancy e.g metastases, lymphadenopathy, ascites are readily visualized.

92% of obstructing calculi were detected in the KNH/PLAZA study. In similar researches; Hekimoglu K et al ([15]) Taylor AC et al ([16]) had sensitivies of 88.9% and 97.7% respectively.

Three false positive cases were diagnosed. The diagnosis of a calculus is based on the basis of visualizing an intraluminal signal poor mass causing obstruction.
A stricture, mucosal fold, small intramural tumour or intraluminal gas would produce the same.

In three patients, interventional endoscopic procedure was necessary. Unfortunately MRCP could not offer this.

Strictures were detected in 92% of the cases in KNH/MRI study, Taylor AC et al 100% ([16]) H.E Adameka et al 100% ([42]).

Most of the strictures were due to prior inflammatory processes.

Late hospital presentation in the study could have led to subsequent architectural distortion of the normal biliary duct anatomy making image interpretion difficult.

CONCLUSION

Thus results from various studies indicate that MRCP has a high diagnostic accuracy in evaluating patients with obstructive jaundice. Hence, it is recommended as the next diagnostic modality of choice in such patients.

RECOMMENDATION

Most of the strictures (inflammatory) in this study were secondary to prior cholecystectomy due to gallstones. More information needs to be gathered to explain this outcome.

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APPENDIX A: PATIENT CONSENT FORM

My name is Dr. John Ngololo Mutisya, a master of medicine student in the department of Diagnostic imaging and Radiation Medicine at the University of Nairobi. I am carrying out a study on M.R.C.P findings in obstructive jaundice.

I would like to recruit you in this study. Information obtained from you will be treated with confidentiality. Only your hospital number will be used. Results of the study will be used to inquire on clinical management of patients with obstructive jaundice.

Please note that your participation is voluntary and you have a right to decline or withdraw from the study.

Signature _____

Date _____

I certify that the patient has understood and consented participation in the study.
Dr John Ngololo Mutisya

Signature _____

Date _____

APPENDIX B: KIBALI CHA MGONJWA

Jina langu ni Daktari John Ngololo Mutisya, mwanafunzi wa masomo ya upigaji picha za mwili katika chuo kikuu cha Nairobi. Nafanya uchunguzi wa magonjwa ya kufungana kwa mfereji ya maini. Naomba ruhusa kwako ili nitumie majibu yako kwa uchunguzi ninaofanya. Majibu yatashungulikiwa kisiri. Nitatumia nambari yako ya hospitali tu ili kukutambulisha. Mwishowe maoni ya uchunguzi wangu yatasaidia kwenye utibabu wa wangojwa wenye shida hii ya kufungana mifereji ya maini.

Hauwajibiki kukubali hila hakuna uchuguzi mwingine utakaotekekelezwa juu yako.

Kama umekubali, tafadhali weka sahihi hapa chini

Sahihi _____

Tarehe _____

Nadhibitisha kwamba nimemueleza mgonjwa juu ya uchunguzi na amenipatia kibali.

Daktari John M. Ngololo

Sahihi _____

Tarehe _____

APPENDIX C: BUDGET

No.	Requirement	Cost (Kshs)
1.	Stationery, typing and photocopying	20,000/=
2.	Secretarial services	10,000/=
3.	Analysis of Data	30,000/=
4.	Scanning and printing of documents	20,000/=
5.	Binding of documents	5,000/=
6.	Data collection expenses	18,000/=
7.	Transport	10,000/=
8.	Contingency expenses	20,000/=
	TOTAL	**133,000/=**

The above expenses are to be met by the researcher.

APPENDIX D : QUESTIONNAIRE

1. Patients number

2. Age ☐

4. Sex ☐

5. Previous history of surgery Yes No

6. History and duration of jaundice

7. Presenting symptom Present Absent

   Fever

   Chills

   Jaundice

   Abdominal pain

8. M.R.C.P findings

   (a) Cause of obstruction

   (b) Site of obstruction

9. Surgical findings