



ORIGINAL ARTICLE

Multi-detector computed tomography in evaluation of post-operative complications in hepatic transplantation recipients



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KEYWORDS

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Abstract *Purpose:* To evaluate the post-operative complications in patients underwent hepatic transplantation by using multi-detector computed tomography and MDCT angiography.

Patients and methods: This study included 30 adult recipients who underwent adult–adult living donor liver transplantation (LDLT). The study population included 27 males and 3 females who ranged in age from 38 to 63 years with a mean age of 49.8 years \pm 5. Sixteen patients were subjected to MDCT and 14 patients were subjected to MDCT according to transplantation surgical team.

Results: In this study, the complications were variable, vascular complications were in 16 patients (53.3%) the commonest, biliary complications in 8 patients (26.7%), recurrent HCC in 3 patients (10%), hepatic abscesses in 2 patients (6.7%) and lympho-proliferative disease which was the less common, statically significant value is seen of vascular complications were the commonest e.g. hepatic artery thrombosis, portal vein thrombosis, portal vein stenosis, hepatic artery stenosis and hepatic vein stenosis.

Conclusion: Multi-detector computed tomography and MDCTA of hepatic transplant recipients presenting with graft dysfunction yield valuable information that can be used to guide further management of the post-transplantation complications.

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1. Introduction

Liver transplantation is currently the treatment of choice for patients with severe acute or advanced chronic liver failure for which no other therapy is available. Liver failure can have a number of causes, including autoimmune hepatitis, chronic

viral hepatitis, alcoholic liver disease, metabolic diseases (hemochromatosis, Wilson's disease), cholestatic liver disorders (biliary cirrhosis, sclerosing cholangitis, biliary atresia), and severe acute liver failure due to viral hepatitis, drug-induced hepatitis (e.g., by acetaminophen or isoniazid), or hepatotoxins (1).

Patients with hepatocellular carcinoma, cholangiocarcinoma, or inoperable neuroendocrine metastases are also potential candidates for hepatic transplantation. The absolute contraindications for transplantation include acquired immunodeficiency syndrome, extra-hepatic malignant tumors, and active intravenous narcotic drug use or alcohol abuse (2).

These complications include acute rejection, biliary problems (leakage, stricture, stones or debris, obstruction, pneumobilia), vascular issues (arterial and venous stenosis or thromboses), lymphoproliferative disorders, recurrent tumors, periportal collar, splenic and hepatic infarction, hepatitis virus C infection, liver abscesses, right adrenal gland hemorrhage, focal fluid collections (seromas, hematomas, bilomas, localized ascites), and intraabdominal free fluid (3).

Multi-detector CT (MDCT) is recently accepted as a practical noninvasive diagnostic method in various complications following liver transplantation. The excellent spatial and temporal resolution combined with post-processing of the imaging data using a variety of three-dimensional reformatting techniques such as maximum intensity projection (MIP), shaded surface display, and volume rendering (VR) allows MDCT to detect both hepatic anatomy and pathology efficiently (4).

MDCT portal venography can display the entire portal venous system and help determine the extent and location of portosystemic collateral vessels in patients with portal hypertension and detected portal vein thrombosis and stenosis (5).

Moreover, MDCT has several advantages over other imaging modalities. Compared with catheter angiography, CT angiography is noninvasive and cost-effective. Unlike sonography, CT angiography is not as dependent on the operator's skill performing the study or on the patient's body habitus. Additionally, CT is more useful in detecting and monitoring sequential complications of hepatic pathology including hepatic ischemia/infarct, bile duct necrosis, bile leaks and abscesses (6).

2. Aim of the work

The aim of this study was to detect the post-operative complications in patients who underwent hepatic transplantations by using multi-detector computed tomography and MDCT angiography.

3. Patients and methods

3.1. Population

This study included 30 adult recipients who underwent adult–adult living donor liver transplantation (LDLT). The patients received only part of the donor's liver (right lobe).

The study population comprised 27 males and 3 females who ranged in age from 38 to 63 years with a mean age of 49.8 years \pm 5, from February 2014 to October 2014 and it was done at Tanat University Hospital, National Liver Institute and as outpatients, 16 patients were subjected to MDCTA

and 14 patients were subjected to MDCT according to transplantation surgical team.

An informed consent had been obtained from all participants in this study, and the ethics committee approval.

The studied patients (post-operative cases only) showed symptoms and signs of post-operative complications after LDLT. They were not accurately diagnosed by the routine ultrasonography or Doppler examinations as it's an operator depended and not as good as MDCT and MDCTA in detecting the liver parenchyma and its vascularity with some small branches and needed further MDCT and MDCTA assessment according to the transplantation surgical team.

Exclusion criteria for recipients in this study are high urea and creatinine level (renal impairment) and allergy to contrast media.

3.2. Methods

All inpatients were subjected to the following:

Routine post-operative evaluation schedule of the recipients:

During hospitalization daily follow-up (average 2 weeks duration) included:

Full clinical examination for post-operative complications such as wound at skin and sclera, detect rigid distended abdomen and leakage of any operative scar.

Laboratory investigations: Complete blood count (CBC), prothrombin time and activity, coagulations time, urea and creatinine level (renal function test), liver function test (SGOT and SGPT), bilirubin (direct and indirect) and hepatitis markers (HAV, HBV, HCV).

Imaging: Chest X-ray for any pleural effusion, abdominal ultrasound and colored Doppler performed twice daily in the first week and once daily during the rest of the hospital stay.

After hospital discharge:

The latter imaging MDCT and MDCTA evaluation was done on weekly basis during the first three months then on monthly basis till the end of six months and then every two months.

3.3. Technique of MDCT and MDCTA in our study

Fourteen (14) patients were subjected to MDCT of the abdomen and (16) patients to MDCTA of the liver adopting the following technique.

We used MDCT machine: Siemens with 20 detectors at National Liver Institute for inpatients, and Siemens 64 dual source for outpatients.

Patients' laboratories data must be initially revised with particular interest in the results of the renal function tests and ask patient if he had a history of allergic reaction to any contrast media or any drugs.

All patients wore a cotton gown to be comfortable. They have been instructed to fast for food for 6–8 h before the exam, and they asked to continue adequate simple water intake up to 3 h prior to examination to ensure adequate hydration and to fill the stomach and bowel by water to help proper subtraction techniques and visualization of the target vessels.

Patients were asked to hold breath during examination when requested, to ensure their cooperation by asking them to take a deep inspiration and hold it for few seconds during the pre-contrast phase and during the three phases of acquisition for each and were allowed to breath quietly after that.

CT angiography was performed following target injection of 2 ml/kg of the patient's weight with a maximum of 150 ml of contrast medium at a flow rate 3.6–5 ml/s. The contrast medium used was low osmolar non-ionic contrast medium (Ultravist 300).

Patients were put in a comfortable supine position on the CT table in the "Head first" position with their arms resting comfortably above the head. An 18–20 gauge cannula was placed into a superficial vein within the antecubital fossa, or dorsum of the hand. Before the contrast material was injected, saline injections were administered at a high rate of flow, with the patient's arms in the scanning position. This was done to ensure the successful cannulation of the vein.

One scout was acquired in antero-posterior view. The examination was planned on these scouts from the level of the top of the right diaphragmatic cupula (Hepatic Dome) till 20 cm caudally or to iliac crest with a slice thickness about 6–8 mm in pre- and post-contrast sequences.

The pre-contrast series was taken by using about 8 mm nominal section thickness, a gantry rotation period 0.6 s, and a table speed of 15 ml per rotation. X-ray tube voltage was 120 kV, and the current was 270–300 mA s.

Tri-phasic CT was of three phases of scanning, the first phase called arterial phase which was done during the first 20 s of the study to visualize the celiac and superior mesenteric arteries especially the hepatic artery and its intra-hepatic branches, the second phase called porto-venous phase which was done of 60 s of contrast injection to visualize the portal venous system including the splenic and superior mesenteric veins as well as main portal vein and its intra-hepatic branches and the last phase called delayed phase which was done of

180 s of contrast injection to visualize the IVC and the intra-hepatic veins.

A contrast material bolus was followed by a saline bolus in order to reduce streak artifacts due to beam hardening. An antecubital vein was usually chosen, but other sites may also be used, in which case, it is necessary to re-calculate the delay time between starting the intravenous injection of contrast medium and the MDCTA acquisition.

3.4. Image analysis

All images were transferred to the workstation (Advantage Windows medical systems) for post-processing.

The pre- and post-contrast images were used to detect any parenchymal blood supply deficiency, infection, abscess or biliary dilatation. The images of the arterial, porta and venous phases were examined with proper visualization of these vascular structures.

This image was subtracted from the same images to get a set of images with no bones within. This step was repeated in all three phases of contrast injection. Images in different views were taken before and after bone subtraction. Three dimensional maximum intensity projections (MIP), volume rendering (VR), curved planar reformations were created at different angles mostly antero-posterior and oblique with zooming on areas of abnormal findings.

Table 1 Gender distribution in the studied 30 recipients with post-right hepatic lobe transplantation complications shows significant value in males than females.

Gender	Number of patients	Percentage (%)
Male	27	90.00
Female	3	10.00
Total number of patients	30	100.00
<i>Chi-square</i>		
χ^2	17.633	
<i>P</i> -value	<0.001*	

* < 0.05.

Table 3 Clinical presentation of the studied 30 recipients with post-right hepatic lobe transplantation complications shows statistically significant value of most common.

Clinical presentation	Number of patients	Percentage (%)
Abdominal pain	16	53.00
Abdominal rigidity and distention	15	50.00
Jaundice	8	26.67
Cachexia and weight loss	4	13.33
Fever	2	6.00
<i>Chi-square</i>		
χ^2	46.55	
<i>P</i> -value	<0.001*	

* < 0.05.

Table 2 Age distribution of the studied 30 recipients with post-right hepatic lobe transplantation complications shows significant value the commonest age was between 50 and 60 years.

Age	Number of patients	Percentage (%)
30 > 40 yrs	2	7
40 > 50 yrs	9	30
50 > 60 yrs	17	57
60 > 70 yrs	2	7
Total number of patients	30	100
<i>Chi-square</i>		
χ^2	20.400	
<i>P</i> -value	<0.001*	

* < 0.05.

Table 4 Type of complications of the studied 30 recipients with post-right hepatic lobe transplantation complications.

Types of complications	Number of patients	Percentage (%)
Vascular complications	16	53.33
Biliary complications	8	26.67
Recurrent HCC	3	10.00
Hepatic abscess	2	6.67
Neoplastic (lympho-proliferative disorder)	1	3.33
Total	30	100.00
<i>Chi-square</i>		
χ^2	25.667	
<i>P</i> -value	<0.001*	

* < 0.05.

Table 5 Distribution of vascular structure complications according to vascular complications in 30 recipients with post-right hepatic lobe transplantation complications shows statically significant value of hepatic artery thrombosis.

Type of vascular structure complication	Number of patients	Percentage (%)
Hepatic artery thrombosis	8	50
Portal vein thrombosis	3	18.75
Portal vein stenosis	2	12.5
Hepatic veins stenosis	2	12.5
Hepatic artery stenosis	1	6.25
Total number of patients	16	100

Chi-square
 χ^2 9.625
P-value 0.047*

* < 0.05.

3.5. Statistical analysis

Data were collected, revised, verified, and then edited on personal computer. The data were then analyzed statistically using SPSS statistical package version 12. The following tests were done: \bar{X} = Mean – Median. SD = Standard Deviation. *T*-test for independent samples. χ^2 = Chi-square test. A (*P*) value of less than 0.05 was considered significant.

4. Results

Twenty patients were referred to Radiology department at National Liver institute as inpatients, 10 patients were out-patients. In the current study, male patients were 27 and female patients were only 3, and this was with significant value that males more than females as seen in Table 1.

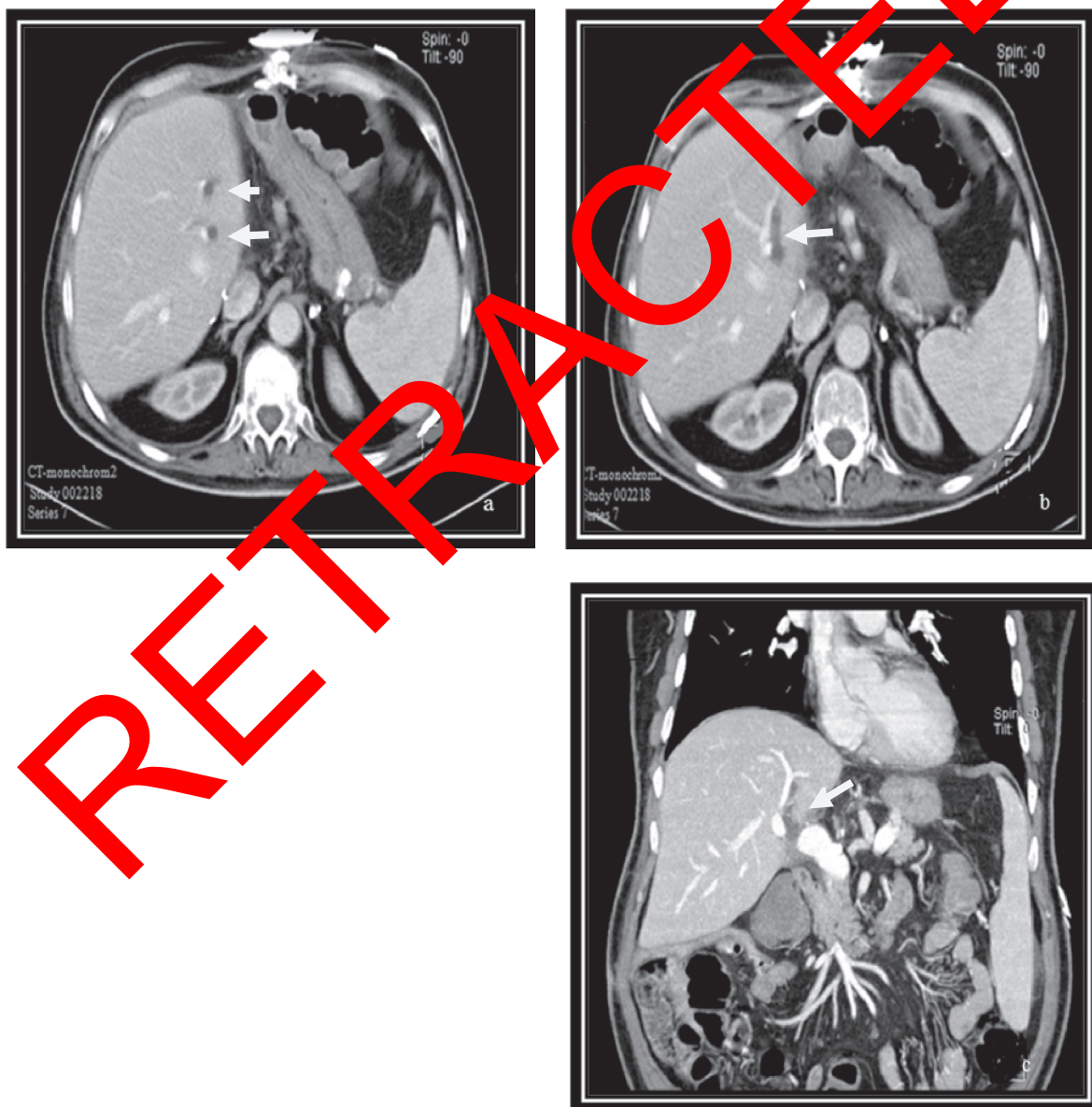


Fig. 1 Axial MDCTA showing intra-hepatic biliary radical dilatation at anterior segment more than posterior (arrow in a, b) coronal MDCTA showing common hepatic duct is seen dilated more than normal (arrow in c).

This study enrolled 30 patients. Their age ranged from 38 to 63 years with a mean age of 49.8 years \pm 5.9, 28 patients and the most common age was between 50 and 60 years (Table 2).

The most common clinical presentations were upper abdominal pain and rigidity in 16 patients, yellowish coloration of skin and sclera in eight patients, 4 patients presented with weight loss and cachexia, fever in two patients, and statically significant value of most common clinical presentation with, more than one complain may be present in the same patient and this will be demonstrated in Table 3.

In this study, the complications were variable, vascular complications were in 16 patients (53.3%) the commonest, biliary complications in 8 patients (26.7%), recurrent HCC in 3 patients (10%), hepatic abscesses in 2 patients (6.7%) and lympho-proliferative disease which was the least common. The highest statically significant value was that of vascular complications as shown in Table 4.

Hepatic artery thrombosis, portal vein thrombosis, portal vein stenosis, hepatic artery stenosis and hepatic vein stenosis were suspected in 16 patients as vascular complications and they were sent by the surgical team to the radiology department as shown in Table 5.

Colored Doppler ultrasound was referred to 10 patients and showed a hyperechoic lesion inside hepatic artery in 5 cases with no wave is detected, no wave nor velocity in hepatic artery in 3 cases with no thrombus inside lumen in hepatic artery, PV couldn't be visualized or detected in 2 cases, and thus these patients were sent for MDCTA as it's more accurate and diagnostic.

Hepatic infarctions in 3 patients were detected secondary to vascular complications, hepatic artery thrombosis was the etiology in 2 cases and hepatic vein stenosis was the etiology in 1 case, and infarctions appear as hypodense wedge shaped area of the liver graft with no enhancement detected inside.

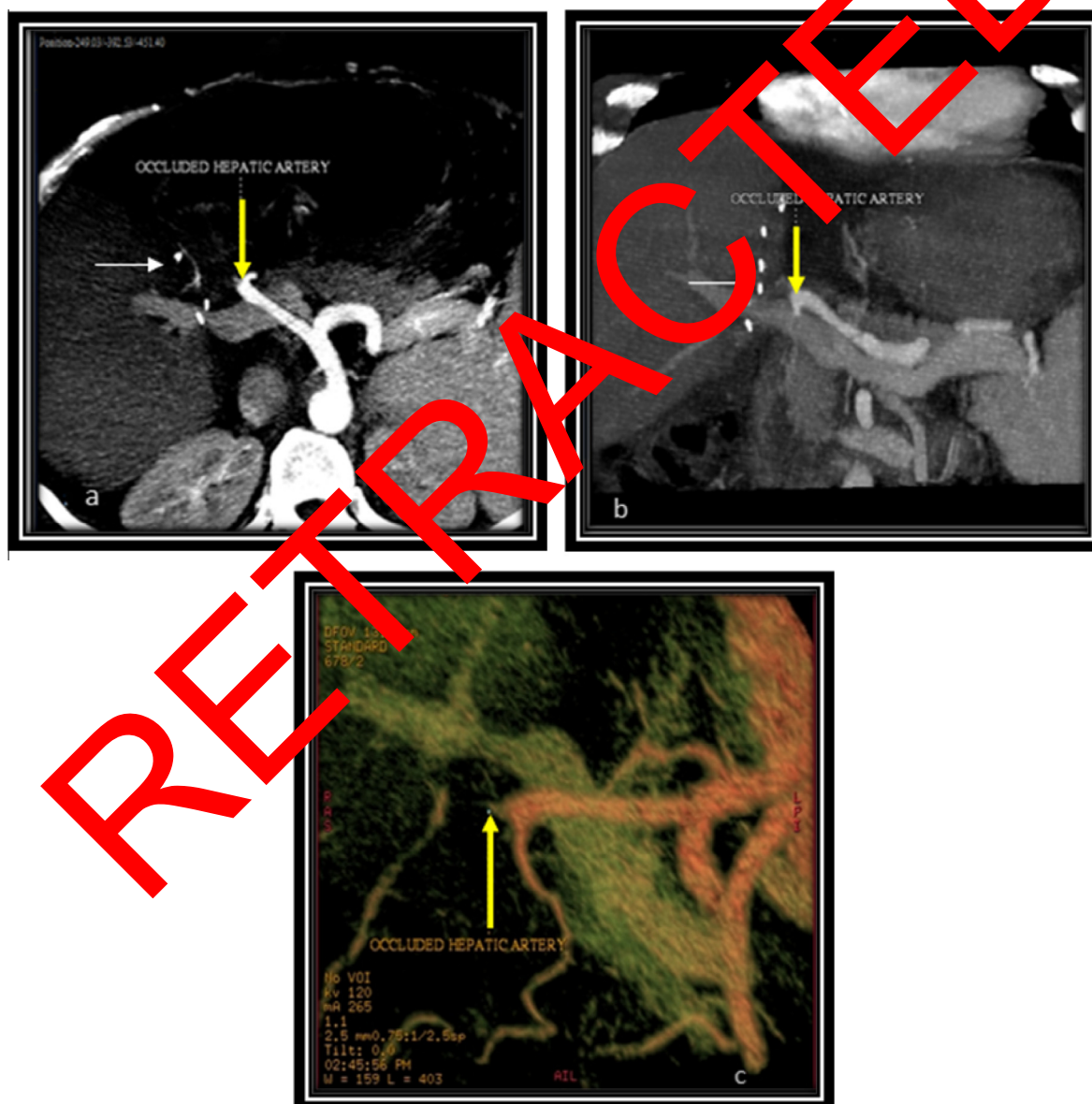


Fig. 2 Axial and coronal MDCTA MIP shows the common hepatic artery lumen arising from celiac trunk is totally occluded (yellow arrow in a) and clips are noted (white arrow in a, b). Volume rendering (VR) MDCTA image shows that the hepatic artery is totally occluded (arrow in c).

The 8 cases with suspected hepatic artery thrombosis were referred to the Radiology Department. The diagnosis of hepatic artery thrombosis was confirmed by the MDCTA examination.

Six of these cases were sent for urgent conventional angiography examination and thrombolytic therapy with successful relief of thrombosis. Two of these 6 cases had recurrent thrombosis and were operated upon surgically, while other 2 cases were sent for surgical intervention from the start with success in relief of thrombosis.

Hepatic artery thrombosis appeared as filling defect in CT scan with no enhancement could be seen.

Hepatic infarction was detected in this study as secondary complication due to hepatic artery thrombosis in 2 cases, and 3 cases referred for confirming the diagnosis of portal vein thrombosis were sent to Radiology department after the transplantation.

The diagnosis of portal vein thrombosis was confirmed by the MDCTA in the 3 cases with 1 of them had SMV thrombosis as well, and these cases were sent for surgical intervention with successful relief of thrombosis, yet recurrent thrombosis occurred in all of them. Thrombosis appeared on MDCTA as filling defect in the course of the portal vein.

Two cases referred for suspected portal vein stenosis were detected by MDCTA. Both cases were sent within the first month after transplantation. These 2 cases were treated with conservative treatment with no intervention, as they had no clinical signs of portal hypertension.

The stenotic portal vein appeared on MDCTA as narrowing of the lumen with small thread of enhancement with no filling.

The 2 cases referred with suspected hepatic vein stenosis were found to have hepatic vein stenosis by MDCTA. They were sent within the first 2 months after transplantation. One of these cases also developed hepatic infarction. They were referred for conventional angiographic examination with angioplasty and balloon dilatation.

The stenotic hepatic vein appeared on MDCTA as narrowing of the lumen with small thread of enhancement with no filling.

The case with suspected hepatic artery stenosis was urgently sent for conventional angiography where angioplasty was done. The stenotic artery appeared as narrowing of the lumen with small thread of enhancement in the hepatic artery lumen, and all these complications will be demonstrated in Figs. 1–4.

In this study 8 out of 30 cases were referred to radiology department for assessment of biliary complications, which included bilomas and biliary obstruction. Biliary complications were about 26.7% of all complications. Biliary stricture (with intra-hepatic biliary radical dilatation) and bilomas were seen in their previous ultrasonography examinations. Multi-detector CT was needed for confirming the diagnosis and excluding any other missed findings.

Five out of 8 cases sent for detection of biliary complications were found to have biloma after ultrasonography which was not diagnostic as it showed a well defined collection. They were referred for MDCTA examination to assess the extension of these bilomas, to exclude retro-gastric extension and to detect good axis of drainage. Aspiration was done; and sent to laboratory that confirmed the diagnosis.

In MDCTA bilomas appeared as a well defined fluid density collection without air which was seen inside the fluid.

Three out of 8 cases sent for detection of biliary complications were found to have intra-hepatic biliary radical dilatation due to biliary stricture with no definite CT evidence of biliary obstruction.

Biliary strictures were applied in the three cases with relief of biliary obstruction. There was no statically significant to types of biliary complications as will be demonstrated in Table 6 and Fig. 5.

In the current study, 3 cases developed recurrent focal lesions of hepatocellular carcinoma in the transplanted liver. No re-transplantation operation was done.

The recurrence of HCC was very aggressive and spread all over the liver graft and in MDCT, it appeared as well defined focal lesions with irregular peripheral enhancement and central breaking down/or cystic degeneration.

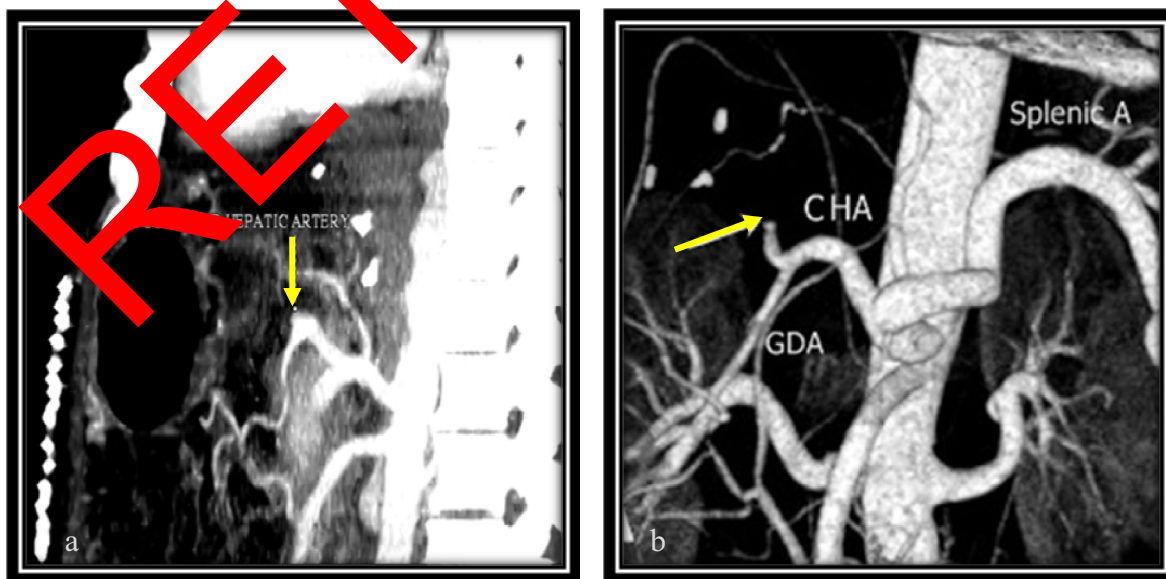


Fig. 3 Sagittal MDCTA MIP image shows occluded common hepatic artery (CHA) (arrow in a). Coronal MDCTA volume rendering (VR) image shows hepatic artery thrombosis distal to the origin of the Gastro-Duodenal artery (GD) (arrow in b).

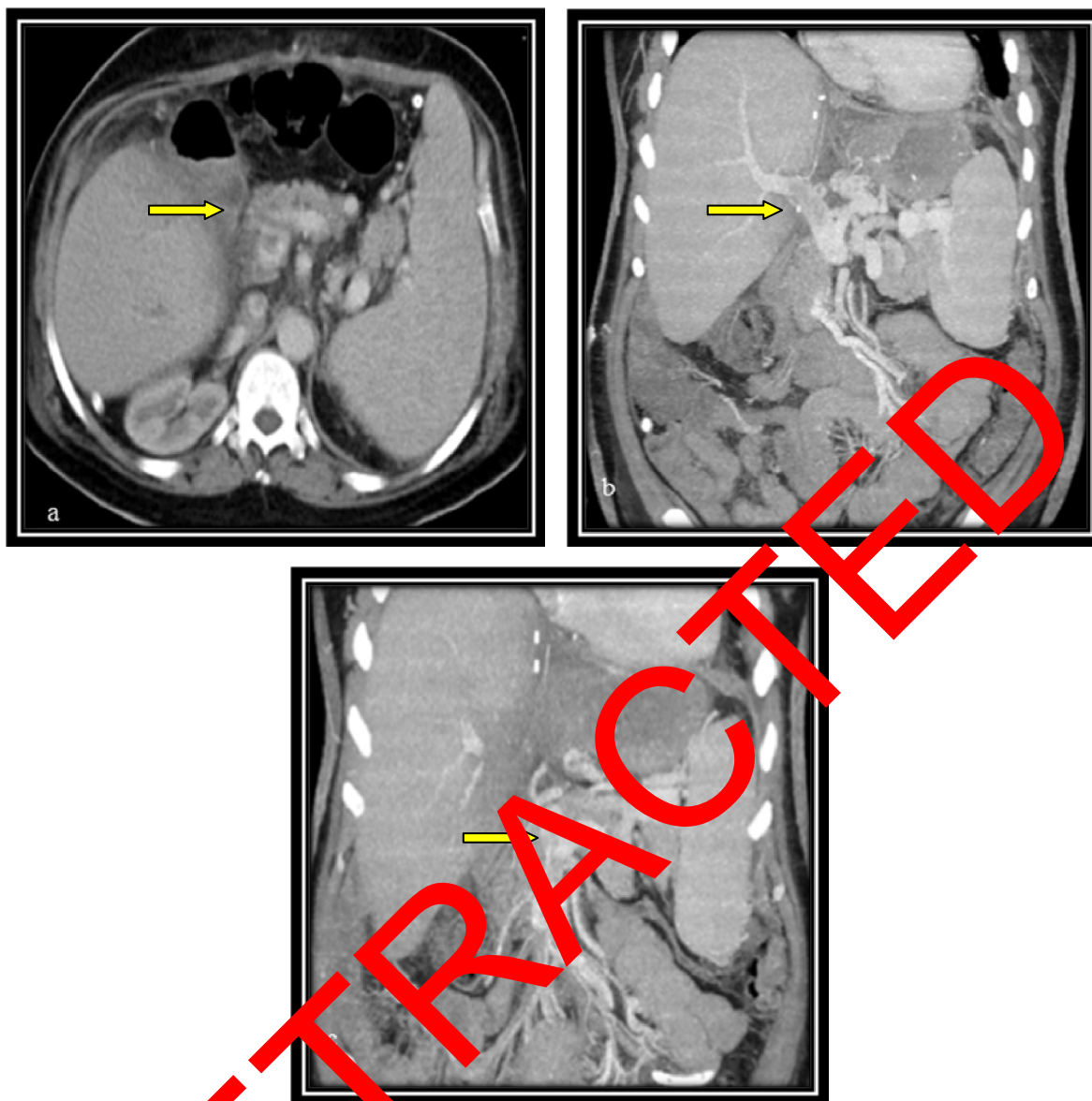


Fig. 4 Axial MDCTA image shows partial filling defect in the portal vein, denoting partial thrombus (arrow in a). Coronal MDCTA MIP image also shows partial portal vein thrombosis at its extra-hepatic part (arrow in b). Coronal MDCTA MIP shows that the thrombus is extending to superior mesenteric vein (arrow in c).

In recent study, 2 patients were referred from the transplantation unit for assessment of hepatic abscess.

Multi-detector CT confirmed the development of abscess in both patients after drainage was done and it was sent to laboratory that confirmed diagnosis and heavy antibiotic therapy were taken.

The hepatic abscess in MDCT is well defined thick walled fluid collection with/without air-fluid level and may be multilocular.

One case developed Non-Hodgkin lymphoma, after transplantation was done, and 2 lymph nodes were seen at porta-hepatis and 2 subpleural nodules at chest (Fig. 6).

5. Discussion

CT is useful for the evaluation of complications such as abscess (intrahepatic or extrahepatic); extent of hepatic

necrosis or intrahepatic abscesses following and fluid collections secondary to bile leak. Multi-detector CT permits a good assessment of liver parenchyma and other abdominal organs, and the evaluation of biloma, bleeding, abdominal or hepatic abscesses and can identify biliary duct dilatation, even if the anastomosis is not easy to depict. MDCT angiography is the best option for confirming the ultrasonographic suspicion of early and late vascular complications (7).

The present study found that the post-operative complications of hepatic transplantation are more common in males than females, males represented about 90% and females represented about 10%, and this contributed with study carried by Chung-Mau et al. (8), who studied 41 patients and males were 86% and females were 14%.

In this study the commonest age was > 60 years and this agreed with study carried out by Levy and Somasundar (9), who found that 83% were younger than 60 years of age.

Table 6 Type of biliary complications in 30 recipients with post-right hepatic lobe transplantation complications in relation to all biliary complications.

Type of biliary complications	Number of patients	Percentage (%)
Biloma	5	62.50
Biliary stricture	3	37.50
Total	8	100.00
<i>Chi-square</i>		
χ^2	0.125	
<i>P</i> -value	0.723	

In this study, we found the most common indications of liver transplantation were cirrhosis due to HCV, primary cholestatic liver disease (PCLD), primary biliary cirrhosis (PBC) and HCC in percentage about 60%, 20%, 13.5% and 6.7% respectively. This agreed with Ito et al. (10), who found the indications of hepatic transplantation were cirrhosis in about 60%, and second cause was primary cholestatic liver disease in 20% and primary biliary cirrhosis in 16.3%.

The present study, stated that the clinical presentation as: abdominal pain in 24 patients, rigid abdomen and distention in 15 patients, jaundice in 8 patients, cachexia and weight loss in 4 patients and finally fever in 3 patients neither conclusive nor specific for each complication. This concurred with study done by Ito et al. (11), who found that the clinical presentations of post-hepatic transplantation as: abdominal pain, distention and fever were neither specific nor diagnostic for the complications.

In the present study, abdominal pain in recipient was the commonest and presented in more than one complication and this was agreed by study done by Craig et al. (12), that found abdominal pain is of important value as it was represented in more than one complication.

This study found that the post-hepatic transplantation complications in 53.3% of all patients occurred within 3 months and in 46.7% occurred after 3 months post-operative, and this was in agreement with study carried out by Rennert et al. (13), who found post-hepatic transplantation complications might occur early (< 3 months) or late (> 3 months) after transplantation with no relation between time and the type of complication.

The recent study found the vascular complications were 53.3% of all complications which are the most common complications after liver transplantation in recipients. According to Gad et al. (14), that stated that the incidence of VC was 21.6% 36 patients out of 167 patients were the commonest complications in his study.

Vascular problems such as thrombosis and stenosis of the hepatic artery (HA), portal vein (PV) and hepatic vein (HV) are among the most serious complications reported after LT and are more frequently seen among recipients of LDLT. These complications can lead to increased morbidity, graft loss, and patient death as reported by Duffy et al. (15).

In the current study, hepatic artery thrombosis presented in 8 patients out of 30 patients and this agreed with study done by Kayah et al. (16), in which hepatic artery thrombosis was in 16 patients out of 110 patients.

According to Calzavara et al. (17), the hepatic artery thrombosis is one of the most common and potentially most dangerous arterial complications.

In MDCT, hepatic artery thrombosis appeared as filling defect with abrupt stoppage of the artery, and this matched with the study done by Girometti et al. (18), abrupt interruption of the hepatic artery, hepatic artery thrombus itself not enhanced.

In this study, portal vein (PV) thrombosis was seen in 10% of all patients and this concurred with study done by Endoire et al. (19), who studied that portal vein thrombosis incidence ranged from 2% to 26%.

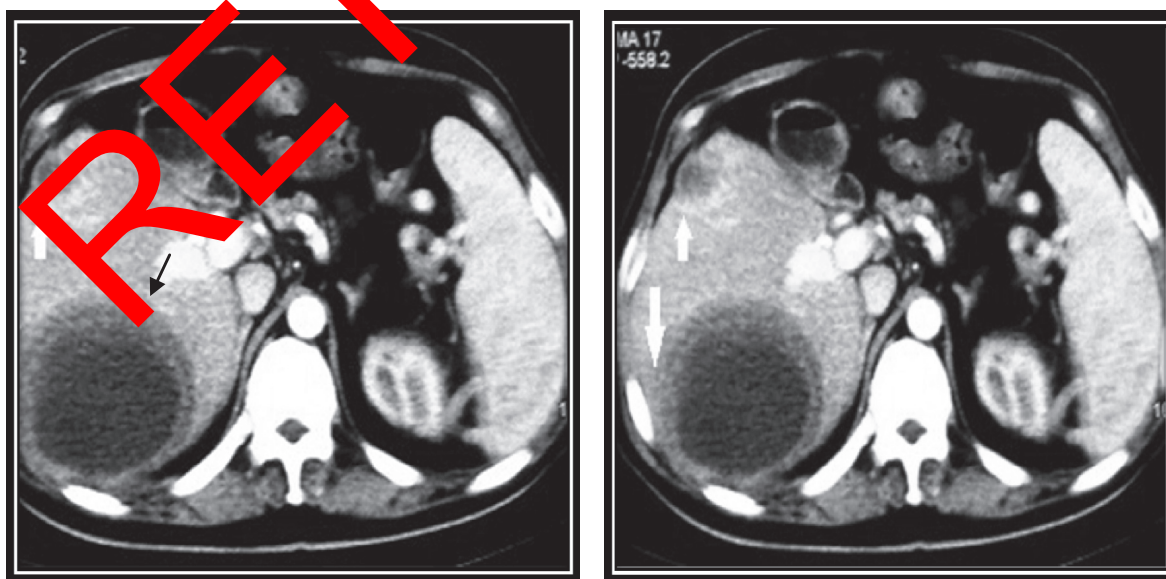


Fig. 5 Axial MDCTA image shows two well defined rounded hypo-attenuating lesions in segments V and VI of the liver graft with double target appearance biloma (arrows in a, b). Aspiration was done and confirmed the diagnosis.

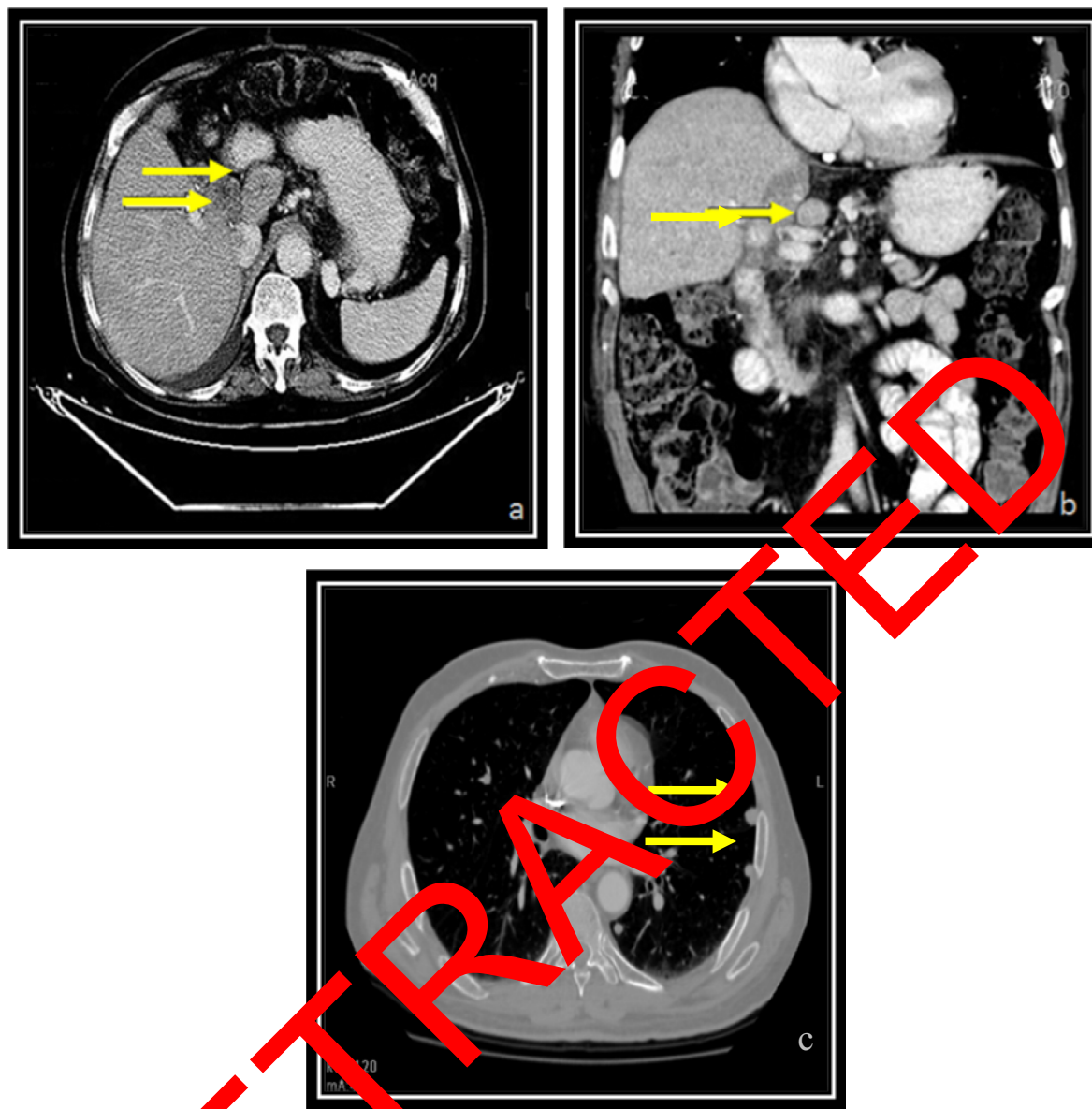


Fig. 6 Axial arterial MDCT image shows two lymph nodes with peripherally enhancing wall and necrotic center at the porta-hepatis (arrows in a). Coronal reformatted images showing the lymph node (arrows in b). Axial CT chest cuts show multiple lung nodules, some being sub-pleural in location (arrows in c).

On MDCTA, PV thrombosis appeared as partially filling defect in the course of the portal vein and this was conceded with study carried out by Kamel et al. (20), who stated portal vein thrombus was hypodense with partial filling defect as partially thrombosis.

On MDCTA, hepatic vein stenosis appeared as narrowing of the lumen of the vein, and this conceded with Hwang et al. (21), that stated that hepatic vein stenosis appeared as focal narrowing of the vein.

The stenotic artery on MDCTA appeared as narrowing of the lumen with small thread of enhancement in the hepatic artery lumen. This agreed with a study done by Park et al. (22), who commented on narrowing as short segmental or focal luminal narrowing of the hepatic artery.

Russ and Karani (23), pointed that biliary complications occurred in approximately 13–19% of recipients following hepatic transplantation.

In the current study, biloma was seen in 5 patients represented about 16.7%, and this is in agreement with Todo et al. (24), that had studied on 308 patients and found 25 of the patients had biloma about 8.1%.

In MDCT, bilomas appeared as a well defined fluid density collection, with/without air loculi seen inside the fluid that was in agreement with study carried out by Tutar et al. (25), that had described biloma as hypodense fluid collection in the graft liver parenchyma.

The present study stated 3 cases were found to have biliary obstruction and this was in agreement with a study carried by Sharma et al. (26), that found biliary obstruction after transplantation with an incidence of biliary strictures of 5–15% of all patients.

In present study, recurrent hepatocellular carcinoma (HCC) occurred in about 10% of patients, and this coincided with the study done by Chok et al. (27), that found that

recurrent HCC after liver transplantation represented in about 17.3%.

Conflict of interest

Authors declare that there are no conflicts of interest.

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