

การรักษาภาวะแทรกซ้อนจากการผ่าตัดปลูกถ่ายตับด้วยวิธีการทางรังสีร่วมรักษา

จิตราภรณ์ วงศ์วิวัฒน์ไชย*, วิริญจ เพชรจันทร์, วิเวียน คลังบุญครอง, อนุชา อาฮูญา, อรุณนิตย์ บุญรอด
ภาควิชารังสีวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น

Complications of Liver Transplantation with Successful Treatment by Interventional Radiology Techniques

Jitraporn Wongwiwatchai*, Virin Bejrachandra, Vivian Klungboonkrong, Anucha Ahooja, Arunnit Boonrod
Department of Radiology, Faculty of Medicine, Khon Kaen University

Received: 26 May 2020

Accepted: 7 August 2020

หลักการและวัตถุประสงค์: การผ่าตัดปลูกถ่ายตับเป็นทางเลือกในการรักษาโรคตับระยะสุดท้ายและตับวายเฉียบพลัน การตรวจพบและรักษาภาวะแทรกซ้อนจากการผ่าตัดในระยะแรกได้เพิ่มอัตราการรอดชีวิตหลังการผ่าตัดปลูกถ่ายตับ การศึกษานี้มีวัตถุประสงค์เพื่อศึกษาประสิทธิภาพของวิธีการทางรังสีร่วมรักษาในการรักษาภาวะแทรกซ้อนจากการผ่าตัดปลูกถ่ายตับ

วิธีการศึกษา: เป็นการศึกษาเชิงพรรณนาแบบย้อนหลังในผู้ป่วยที่มีภาวะแทรกซ้อนจากการผ่าตัดปลูกถ่ายตับซึ่งได้รับการรักษาด้วยวิธีการทางรังสีร่วมรักษาตั้งแต่กรกฎาคม พ.ศ. 2556 ถึง ตุลาคม พ.ศ. 2561 จำนวนทั้งสิ้น 13 ราย โดยทำการศึกษาข้อมูลประชากร ข้อบ่งชี้ในการผ่าตัดปลูกถ่ายตับ ชนิดการผ่าตัด ชนิดของภาวะแทรกซ้อน ระยะเวลาวินิจฉัยนับจากวันผ่าตัด วิธีการรักษาทางรังสีร่วมรักษา และผลการรักษา

ผลการศึกษา: ผู้ป่วยจำนวน 13 ราย ได้รับการรักษาภาวะแทรกซ้อนจากการผ่าตัดปลูกถ่ายตับด้วยวิธีการทางรังสีร่วมรักษา รวมทั้งสิ้นจำนวน 27 ครั้ง ประกอบด้วย การขยายหลอดเลือดดำด้วยบอลลูนในภาวะหลอดเลือดดำอุดตันฟีเรียเวนาคาวาตีบและหลอดเลือดดำพอร์ทัลตีบ (3 ครั้ง), การขยายหลอดเลือดแดงร่วมกับการใส่ขดลวดถ่างขยายและการละลายลิ่มเลือดในภาวะหลอดเลือดแดงตีบและหลอดเลือดแดงตีบอุดตัน (3 ครั้ง), หัตถการเกี่ยวกับการใส่สายระบายน้ำดีทางหน้าท้องในภาวะทางเดินน้ำดีตีบ (9 ครั้ง) และ การใส่สายระบายของเหลวที่เกิดหลังการผ่าตัดในช่องท้อง (12 ครั้ง) มีผลสำเร็จทางเทคนิคร้อยละ 100 ผลสำเร็จทางคลินิกร้อยละ 96.3

สรุป: รังสีร่วมรักษามีบทบาทสำคัญในการรักษาภาวะแทรกซ้อนจากการปลูกถ่ายตับเนื่องจากสามารถทำการรักษาได้ด้วยเทคนิคที่ไม่ต้องผ่าตัด มีการรุกรานน้อย มีผลสำเร็จทางเทคนิคและทางคลินิกสูง

Background and Objective: Liver transplantation is a treatment option for end-stage liver disease and acute liver failure. Early detection and treatment of post-operative complications have increased survival rates after liver transplantation. The objective of this study was to evaluate efficacy of the interventional radiology procedures in treatment of liver transplant complications.

Material and methods: This retrospective study included 13 patients with post liver transplantation related complications, which were treated with interventional radiology procedures from July 2013 to October 2018. Demographic data, indications for liver transplantation, type of liver transplantation, liver transplantation related complications, onset of complications, interventional radiology procedures and result of treatment were collected.

Results: Between July 2013 to October 2018, 13 patients undergoing 27 procedures were identified, including venoplasty for inferior vena cava and portal vein stenosis (n=3), angioplasty and stent placement without/with thrombolysis for hepatic artery stenosis and hepatic artery thrombosis (n=3), percutaneous transhepatic biliary drainage related procedures (insertion, exchange, and irrigation) for biliary stricture (n=9) and percutaneous drainage related procedures (insertion and exchange) for intraabdominal collections (n=12). Technical and clinical success rates were 100% and 96.3%, respectively.

*Corresponding author : Jitraporn Wongwiwatchai, 123 Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen Thailand 40002. Email: jitrawo@kku.ac.th, pjitraporn@gmail.com

คำสำคัญ: การผ่าตัดปลูกถ่ายตับ; ภาวะแทรกซ้อน; รังสีร่วมรักษา

Conclusion: Interventional radiology procedures have an important role in the management of post-operative complications of liver transplantation under non-operative and minimally invasive techniques with high technical and clinical success rates.

Key words: Liver transplantation, complication, interventional radiology

ศรินครินทร์เวชสาร 2563; 35(5): 561-567. • Srinagarind Med J 2020; 35(5): 561-567.

Introduction

Liver transplantation (LT) becomes a standard treatment for end-stage liver disease including decompensated hepatic cirrhosis, hepatocellular carcinoma (HCC) and acute fulminant hepatic failure¹. Advances in surgical techniques, organ preservation, immunosuppressive therapy, and early detection of post-operative complications have increased survival rates after liver transplantation². The 5-year survival rate after LT has been reported at 70.1-74.6%^{3,4}. The studies reported LT related complications up to 25%⁵⁻⁸, including vascular and non-vascular complications, which are the major cause of graft failure. Vascular complications include arterial complications (hepatic artery thrombosis [HAT], hepatic artery stenosis [HAS] and hepatic artery pseudoaneurysm), portal vein complications (portal vein stenosis and thrombosis), inferior vena cava (IVC) and hepatic venous complications (IVC stenosis and thrombosis, hepatic vein stenosis and thrombosis). Non-vascular complications include biliary complications (biliary stricture, biliary necrosis, bile leakage) and intraabdominal fluid collections. In the past, most of these complications were treated with surgical management. Fortunately, as the technical advancement in the field of interventional radiology (IR) emerged over the past decades, it contributes many efficient procedures that can deal with these complications, especially, in the non-operative and minimally invasive fashion.

In Thailand, there are a few studies of LT with post-operative complications treatment. The purpose of this study was to evaluate efficacy of the interventional radiology procedures for treatment complications following liver transplantation.

Material and Methods

Patients

A retrospective study included all patients who underwent LT with post-operative complications which were treated with IR procedures in our hospital from July 2013 to October 2018. The study protocol was approved by the local Ethics Committee for Human Research with a waiver of informed consent. The data were collected from medical records, including demographic data, indications for LT, types of LT, LT related complications, onset of complications, length of hospital stay and status of all patients. Findings from diagnostic imaging, follow-up imaging and IR treatments (procedures, technical success rate, complications) were collected from PACS (Picture Archiving and Communication System).

Diagnosis and treatment procedures

A routine post-operative color Doppler ultrasound (CDS) of the transplanted liver performs on post-operative day 0 to day 7. If there is any suspicious abnormality, further computed tomography (CT) or magnetic resonance imaging (MRI) would be requested for a definite diagnosis. IR treatments include venoplasty for IVC and portal vein stenosis, percutaneous transluminal angioplasty (PTA) and stent placement without/with thrombolysis for HAS and HAT, percutaneous transhepatic biliary drainage (PTBD) and percutaneous collection drainage (PCD) related procedures (insertion, exchange, and irrigation) for biliary stricture and intraabdominal collections, respectively. The detail of the IR procedures was reviewed based on the images and reports in the database performed by three interventional radiologists.

Definition

Technical success was defined as the ability to

perform successful for each interventional procedure. Clinical success was defined as after treatment post LT complications, the patients had no symptoms-related or resolved complications being treated.

Statistics

The data were analyzed using mean, standard deviation, frequency, and percentage. Overall survival rate after liver transplantation was analyzed using Kaplan-Meier curve log analysis.

Results

Thirteen patients with 15 liver transplantation (from 111 patients with 114 LT) underwent treatment of complications related to LT in our interventional radiology unit between July 2013 to October 2018. There were 12 males (92.3%) and 1 female patient

(7.7%) with a mean age of 50.69 ± 11.53 years (range, 20–64 years). Two patients had liver re-transplantation due to graft failure. Mode of liver transplantation was cadaveric LT for all patients. The indications for transplantation were HCC (n = 6), cirrhosis (n = 7) and graft failure (n = 2).

In these 13 patients, there were 16 complications following LT. The complications were divided into two groups, vascular (n = 6, 37.5%) and non-vascular complications (n = 10, 62.5%) (Table 1). The IR procedures were performed for a total of 27 procedures, including venoplasty for IVC and portal vein stenosis (n = 3) (Figure 1), PTA and stent placement without/with thrombolysis for HAS and HAT (n = 3) (Figure 2), PTBD related procedures (insertion, exchange, and irrigation) for biliary stricture (n = 9) and PCD related procedures (insertion and exchange) for intraabdominal collections (n = 12) (Table 2).

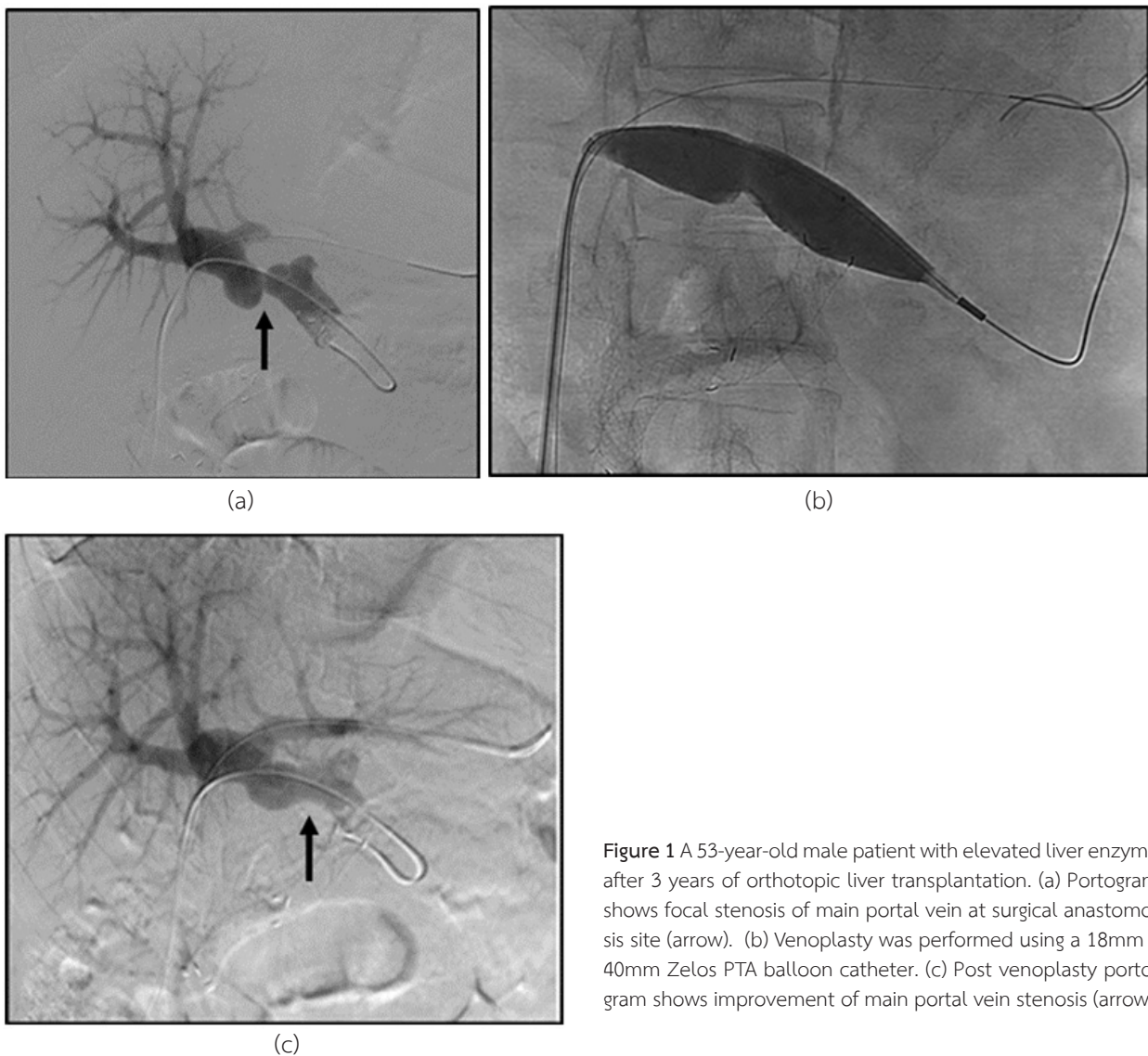


Figure 1 A 53-year-old male patient with elevated liver enzyme after 3 years of orthotopic liver transplantation. (a) Portogram shows focal stenosis of main portal vein at surgical anastomosis site (arrow). (b) Venoplasty was performed using a 18mm x 40mm Zelos PTA balloon catheter. (c) Post venoplasty portogram shows improvement of main portal vein stenosis (arrow).

Table 1 Post liver transplantation complications

Type of complications	Number (%)
Vascular	6 (37.5)
Hepatic artery stenosis	2 (12.5)
Hepatic artery thrombosis	1 (6.25)
Portal vein stenosis	2 (12.5)
IVC stenosis	1 (6.25)
Non-vascular	10 (62.5)
Biliary stricture	2 (12.5)
Intraabdominal collection	8 (50)

Abbreviations: IVC = inferior vena cava

The technical success rate of the IR treatment was 100%. The clinical success rate was 96.3% (26 from all 27 procedures). There was one patient with massive ascites and IVC re-stenosis after IVC venoplasty for 1 month. There was no significant immediate complication from the IR treatment, except one case of HAS with vasospasm following PTA and stent placement. No major complication or death-related procedure was occurred. The overall survival rate at 1, 3 and 5 years were 91.67%, 76.39% and 38.19%, respectively.

Discussion

Both vascular and non-vascular complications following LT remain a significant number despite the increased patients' survival rate. Without adequate treatment, the patients usually end up with re-transplantation or even mortality. IR procedures play an important role as the treatment of choice for these complications due to their advantage of minimal invasive way of treatment.

Incidence of hepatic artery complications has been reported about 4-25%^{1,2}. These complications may result in arterial insufficiency of the transplanted liver. Mortality rates are greater than 80% without emergent re-transplantation or revascularization. The majority of HAS occurs at the surgical anastomosis and related to surgical technique, including clamp injury, kinking vessel and thrombus formation^{5,6}. Hepatic artery serves as the only vascular supply for the biliary system, thus hepatic artery complications usually easily result in biliary ischemia following stricture and eventually biliary necrosis, biloma formation and intrahepatic abscess. Similarly, two of our patients had experienced HAS at the anastomotic site (onset 10 days to 3 months after LT), and eventually developed biliary necrosis and bilomas. One of them had a severe deranged liver function and lead to re-transplantation. This raises our concern about the importance of early diagnosis and

Table 2 Interventional radiology procedures in post liver transplant complications

Interventional radiology procedures	Number (%)	Technical success	Clinical success	Complication (%)
Venoplasty in PV stenosis and IVC stenosis	3 (11.1)	3	2	0
Angioplasty with stent placement in HAS	2 (7.4)	2	2	1 (vasospasm)
Angioplasty with thrombolysis and stent placement in HAT	1 (3.7)	1	1	0
PTBD related	9 (33.3)	9	9	0
- PTBD insertion	2 (7.4)	2	2	
- PTBD exchange	4 (14.8)	4	4	
- PTBD irrigation	3 (11.1)	3	3	
PCD related	12 (44.4)	12	12	0
- PCD insertion	10 (37.0)	10	10	
- PCD irrigation	2 (7.4)	2	2	
Total	27	27 (100%)	26 (96.3%)	1 (3.7%)

Abbreviations: PV = portal vein, IVC = inferior vena cava, HAS = hepatic artery stenosis, HAT = hepatic artery thrombosis, PTBD = percutaneous transhepatic biliary drainage, PCD = percutaneous drainage

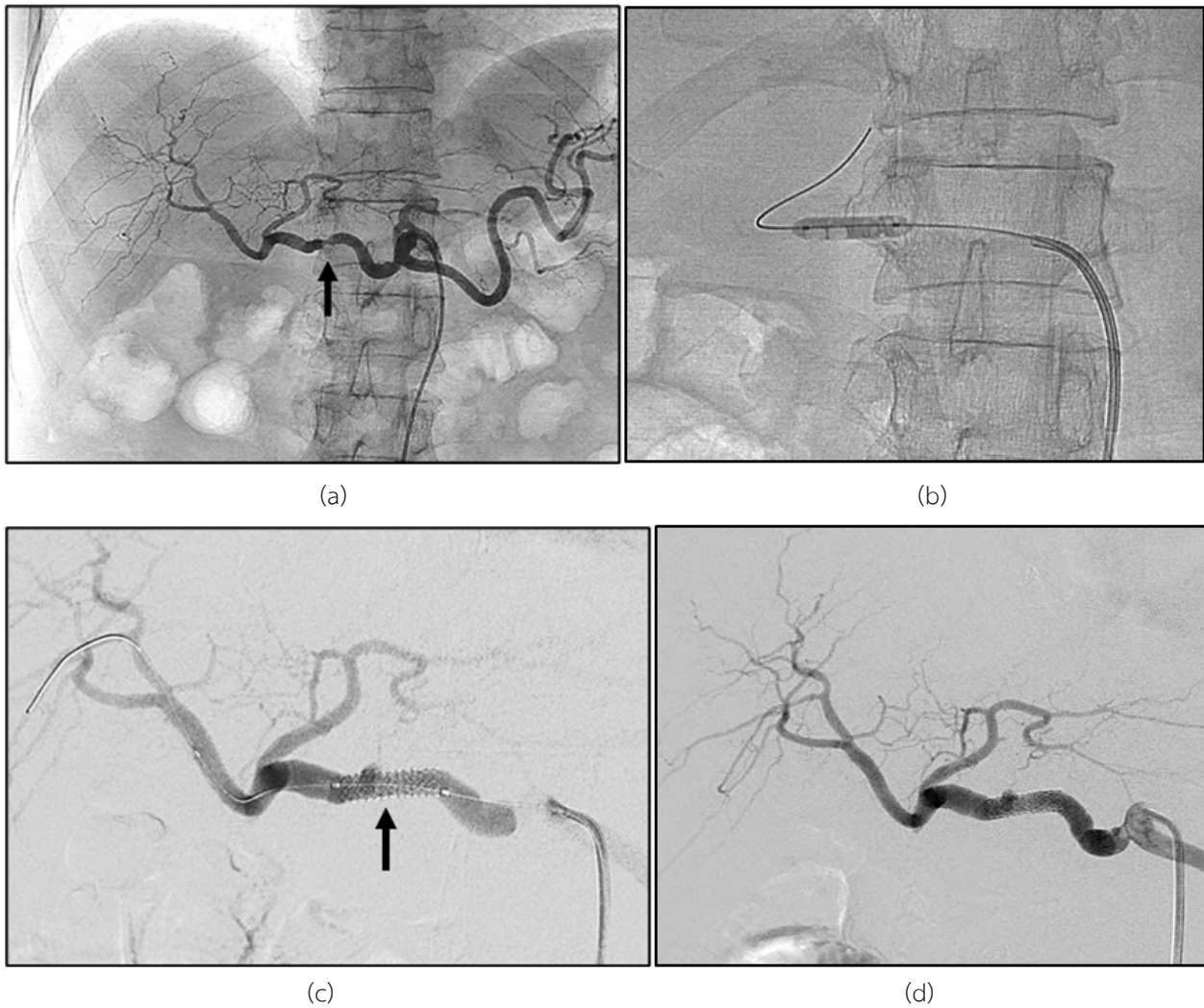


Figure 2 A 58-year-old male patient presented with deranged liver function and CT diagnosis of hepatic artery stenosis (Post-operative day 25) (a) Celiac angiogram showed focal stenosis at hepatic artery anastomosis (arrow). (b) During balloon angioplasty at anastomotic site (c) Placement of a 5mm x 19mm monorail pre mounted stent (Express SD, Boston Scientific) covered anastomotic stenosis (arrow) (d) Post stenting celiac angiogram shows patent hepatic artery stent without residual stenosis.

revascularization, which might reduce the risk of graft failure and re-transplantation.

In HAS, transfemoral angiograms are performed for diagnosis, following by PTA with or without stent placement. Primary patency rates after PTA and stent placement at 6 months are 50% and 69%, respectively⁹. Complications include spasm, dissection, occlusion and pseudoaneurysm formation. One of our cases developed vasospasm proximally to anastomotic stenosis during balloon angioplasty removal. His serial CDS and CT angiography show patency of hepatic artery and stent during a follow-up of 25 months.

Portal venous complications, including anastomotic stenosis or thrombosis following orthotopic LT, have been reported to be below 3%^{5,6}. Portal vein stenosis can be detected in the immediate

perioperative period or even many years after transplantation with the majority of cases are asymptomatic and detected on routine screening ultrasound. If symptoms are present, the clinical signs of portal hypertension, such as variceal bleeding, ascites, or splenomegaly would be observed. In our two patients, they had late presentation with altered hepatic function and treated with portal venoplasty via transhepatic approach. Transjugular approach has been reported in patients with severe coagulopathy and/ or ascites for reducing the risk of bleeding¹⁰.

IVC stenosis or thrombosis is observed less than 1% of the LT patients, which mostly occur at the anastomosis site. In our institution, a large-sized balloon catheter is used for IVC venoplasty, but IVC re-stenosis occurred within 1 month. Inflation of multiple balloon catheters has been reported when

a single large-sized balloon is not enough¹¹. The report showed venoplasty can achieve technical success in restoring anastomotic patency in close to 100%, but frequent re-stenosis. In resistant stenosis, stent placement may be needed¹².

Biliary stricture occurs either anastomotic or non-anastomotic site. While anastomotic stricture occurs related to technical factors, non-anastomotic stricture usually related to other causes, such as hepatic arterial insufficiency, infection, blood group incompatibility and primary sclerosing cholangitis. Role of IR in treating biliary stricture usually preserved for cases with choledocho-jejunostomy anastomosis or cases that failed ERCP^{10,13,14}. One of our patients underwent choledocho-jejunostomy anastomosis was sent for PTBD. Other treatment options such as cholangioplasty or biliary stent placement was not done in our patients.

Intraabdominal collections could be seroma, hematoma or biloma, which are commonly observed near areas of vascular and biliary anastomosis, as well as perihepatic spaces and usually found during the first day after transplantation, which were found in nearly all of our cases. In our institution, intraabdominal collections were treated with PCD. Resolution of clinical signs and symptoms are seen in all cases.

The advantage of these IR procedures is the ability to treat the complications via a percutaneous approach with minimally invasive technique for preserve the function of transplanted liver. There is reducing the need for further surgical intervention or re-transplantation with less morbidity and mortality. There are several limitations of this study. It is retrospective study at a single institution with small sample size. There is no comparison of the treatment results and post procedural complications with surgical management.

Conclusion

Interventional radiology procedures have an important role in the management of post-operative complications of liver transplantation under non-operative and minimally invasive techniques with high technical and clinical success rates. No major complication or death-related procedure was occurred.

Compliance with ethical standards

Funding: No funding was received for this report.

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in reports involving human participants were in accordance with the ethical standards of the institutional research committee number HE621049 and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of report formal consent is not required.

Informed consent: Informed consent was not obtained.

Reference

1. Thai Transplantation Society.. THAI TRANSPLANT CARE (TTC) LIVER. (2015). [cited May 25, 2020]. Available from: http://www.transplantthai.org/upload/170815114538293_MNB.pdf
2. Song ATW, Avelino-Silva VI, Pecora RAA, Pugliese V, D'Albuquerque LAC, Abdala E. Liver transplantation: Fifty years of experience. *World J Gastroenterol* 2014; 20(18): 5363–74.
3. OPTN/SRTR 2016 Annual Data Report: Liver - Kim - 2018 - American Journal of Transplantation - Wiley Online Library [Internet]. [cited May 25, 2020]. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1111/ajt.14559>
4. Castroagudín JF, Molina E, Bustamante M, Tomé S, Otero E, Martínez J, et al. Orthotopic liver transplantation for hepatocellular carcinoma: a thirteen-year single-center experience. *Transplant Proc* 2008; 40(9): 2975–7.
5. Piardi T, Lhuire M, Bruno O, Memeo R, Pessaux P, Kianmanesh R, et al. Vascular complications following liver transplantation: A literature review of advances in 2015. *World J Hepatol* 2016; 8(1): 36–57.
6. Pérez-Saborido B, Pacheco-Sánchez D, Barrera-Rebollo A, Asensio-Díaz E, Pinto-Fuentes P, Sarmentero-Prieto JC, et al. Incidence, management, and results of vascular complications after liver transplantation. *Transplant Proc* 2011; 43(3): 749–50.
7. Pascher A, Neuhaus P. Bile duct complications after liver transplantation. *Transpl Int* 2005; 18(6): 627–42.
8. Andrews JC. Vascular complications following liver transplantation. *Semin Intervent Radiol* 2004;21(4): 221–33.

9. Endovascular Treatment of Hepatic Artery Stenosis After Liver Transplantation - PubMed [Internet]. [cited Jun 19, 2020]. Available from: <https://pubmed.ncbi.nlm.nih.gov/23332988/>
10. Miraglia R, Maruzzelli L, Caruso S, Milazzo M, Marrone G, Mamone G, et al. Interventional radiology procedures in adult patients who underwent liver transplantation. *World J Gastroenterol* 2009; 15(6): 684–93.
11. Amesur NB, Zajko AB. Interventional radiology in liver transplantation. *Liver Transpl* 2006; 12(3): 330–51.
12. Settmacher U, Nüssler N, Glanemann M, Haase R, Heise M, Bechstein W, et al. Venous complications after orthotopic liver transplantation. *Clinical Transplantation* 2000; 14(3): 235–41.
13. Mehrzad H, Mangat K. The Role of Interventional Radiology in Treating Complications following Liver Transplantation. *ISRN Hepatol* [Internet]. 2012 Dec 3 [cited May 25, 2020];2013. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4890878/>. doi: 10.1155/2013/696794
14. Kothary N, Patel AA, Shlansky-Goldberg RD. Interventional radiology: management of biliary complications of liver transplantation. *Semin Intervent Radiol* 2004; 21(4): 297–308.

