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NON-HUMAN TRANSPLANTATION OF LIVING LIVER GRAFT IN DIFFERENT POSSIBLE SITES

By
ALAA ISMAIL
Department of Surgery, Faculty of Medicine, Ain Shams University, Cairo 11566, Egypt (Correspondence: ahismail2002@gmail.com)

Abstract

Orthotopic liver transplantation became a standard operation. The recipients' number was increasing because of the wide indications. In many centers, many of the waiting patients died due to shortage of liver grafts. This study implanted living dog liver graft, in three different sites. The results showed that implantation as orthotopic non- auxiliary was better than the other sites.

Key words: Egypt, Liver transplantation, Dog, Recipient abdominal cavity

Introduction

No doubt, the chronic liver diseases are common worldwide, especially in developing countries, and cirrhotic patients' prognosis has had a resurgence of interest because of liver transplantations and new therapies for complications of end-stage cirrhosis (Cholongitas *et al,* 2005). Cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of hepatic architecture and regenerative nodules formation. Advanced cirrhosis is generally considered to be irreversible while early stages may regress with specific treatments aimed at underlying cause (Gines *et al,* 1987). There are more than a hundred different kinds of liver disease (D'Amico *et al,* 1986). Samuel *et al.* (1997) declared that acute and chronic liver diseases due to hepatitis viruses were the main indications for liver transplantation.

The commonest agents encountered in Egypt were liver flukes (Haseeb *et al,* 2002), mainly schistosomiasis (Abo-Madyan *et al,* 2004), viral hepatitis (Zakaria *et al,* 2007), especially HCV (Madwar *et al,* 1999), liver cancer (Hifnawy *et al*, 2004), and discovered hereditary (Gharib *et al,* 2011), or genetic variations (Motawi *et al,* 2013).

Starzl *et al.* (1963) in USA reported that the first human liver transplantations (LT) were performed from donation after cardiocirculatory death (DCD) in the 1960s. But, orthotopic liver transplantation (OLT) is the treatment of choice for patients with end-stage chronic liver diseases, acute liver failure, and some metabolic liver diseases from younger with trauma as cause of death, brain death, hemodynamic stability at the time of procurement, and absence of steatosis, chronic liver disease, and transmission disease (Feng *et al,* 2006). Another source of liver grafts resulted from the fact that the liver is composed of two half-liver, which was surgically divided. Each half-liver has its own portal vein, hepatic artery and bile duct. Partition of the liver may allow the obtaining of two grafts from a liver retrieved in a cadaver donor and of one graft from a living donor. In several centers, technique was markedly improved by using reduced size grafts from older heart-beating cadaver donors (De Jong *et al,* 1996).

This study aimed to assess the experimental feasibility resecting segment II from a living donor to be implanted in three different sites in the recipient abdominal cavity. The study evaluated three possible sites for partial liver transplantation.

Materials and Methods

The work was done on 30 adult male mongrel dogs weighed12-16Kg, kindly obtained from the Governmental Veterinary Hospital. They were clinically and laboratory examined to approve that they were healthy ones. Sodium pentobarbital was used for the induction of anesthesia which was maintained by endotracheal intubation and halothane.

Ethical consideration: This study was conducted in accordance with the guidelines for dealing with experimental animals (Helsinki, 1964) and approved by Ain Shams University, Egypt.

Technique of resection was standardized adopted (Couinaud, 1957) for the three types of recipient operations, by resected segment II & III with its left hepatic vein.

Preservation was done by flushing and cooling the graft via its portal vein and hepatic artery using 4^{O}C Ringers solution, and stored in cold Euro-Collins solution.

Surgical operation: The donor operation was performed through a midline incision. Round ligament, falciform ligaments were divided. Using an operative microscope, the terminal 2cm of left hepatic vein were dissected from the surrounding parenchyma and encircled. Then, the upper left portion of the hepatic artery, hepatic duct and portal vein was achieved. According to the animal, two to three glissonian pedicals going from the horizontal portion of the left glissonian pedicle to the quadrate lobe were ligated and divided, as well as one or two short pedicles going to Spigelian lobe. Then, without clamping the vascular structures going to liver left part, liver capsule was incised along a line between the right side of the round ligament and the right side of the end of the left hepatic vein. Transaction was done step by step using a Kelly clamp with ligature or coagulation of each pedicle; it was conducted posteriorly and slightly to the left ending in front of caudate portion right border of Spigelian lobe. Technique allowed maintaining normal blood to the liver left part during the parenchymal transection.

Finally, the left branches of hepatic artery and portal vein and left hepatic vein clamped and divided. After a warm ischemia time of less than 2min, the graft was flushed and cooled via the left portal branch and the left hepatic artery using 200ml of 4^{O}C Ringer's solution and immediately transplanted. In donor, the stumps of left portal branch, and left hepatic duct were either ligated or sutured. Before abdomen was closed without drainage, inspection of the remaining liver in all cases showed a small area of congestion on its left and anterior part, close to the transaction plane.

1- Auxiliary heterotopic partial liver transplantation of a bi-segmental graft from a living donor in the splenic bed: Both donor and recipient operation were simultaneously done. The liver graft was flushed cooled via its portal vein and its hepatic artery using 4^{O}C Ringer's lactate solution during operation. The graft was implanted in the splenic bed of the recipient after removal of the spleen and leaving a long stump of splenic artery and vein. Splenic vein was flushed by 1/10.000 heparinized saline solution before its clamping to prevent thrombosis. The liver graft was rotated 180' in the frontal plane so that the end of the hepatic vein was in down ward position; also the graft was rotated 180 degree in the vertical plane so that the cut surface of the graft is facing medially. The graft was implanted in the splenic bed by anastomosing its left portal branch end-to-end to the splenic vein using 6-0 prolene continuous suture. The hepatic artery was anastomosed end-to-end to the splenie artery using 6-0 prolene continuous suture. The hepatic vein was anastomised end-to-end to proximal end of the left renal vein after its thorough dissection and ligation very near to the kidney hilum. The hepatic duct of the graft-was implanted end-to-side on a Roux-ewn-Y in a jejunal loop. The portal vein of the recipient was narrowed to half of its diameter to allow blood to flow to the graft. At the operation end careful haemostasis was done and the abdomen was closed by ordinary technique. The dogs were then extubated as soon as it awoke.

2- Auxiliary heteropic partial liver transplantation of bisegmental graft from a living donor in the right paravenebral gutter: The recipient operation was done by a midline incision. The harvesting procedure itself was standardized in all types of operations. The right paravertebral gutter was carefully dissected to find a bed suitable for the graft size. Mobilization of portal vein and exposure of infra-hepatic inferior, vena cava was an essential step. The graft was placed in the space after its rotation 180 degree in the frontal pl-

ane so as to bring hepatic vein downward and hepatic pedicle upward. Hepatic vein of the graft was anastomosed end-to-end side to right anterior surface of the inferior vena cava below the site of the right renal vein. Portal branch of the graft was anastomosed end-to-end to the portal vein of the recipient. The hepatic duct was implanted end-to-side as a Roux-en-Y in a jejnal loop. Dogs were infused by 750 ml lactated Ringer's solution, because of the dissection of the P.C. gutter.

3- Orthotopic non auxiliary partial liver transplantation of bisegmnetal graft from living donor: The recipient operation started by complete dissection of the liver and total hepatectomy without its vascular supply, i.e. leaving vessels in its place after clamping. The clamped and transected hepatic veins while recipient I.V.C. was clamped above and below, the liver was preserved in continuity. Confluence of the three hepatic veins was left opened while small hepatic veins were ligated. Graft was implanted by anastomosing the hepatic vein end-to-side of I.V.C. at the site of recipient veins, using 5-0; prolene suture Graft hepatic artery was anastomosed to the recipient hepatic artery end-to-end using 5-0 prolene suture. Portal vein was anastomosed end-to-end to recipient portal vein, using 6-0 prolene suture. Clamps were removed and bleeding or biliary leakages were managed. Duct was reconstructed as end-to-side choledo-chojejunostomy by using a Roux-en-Y loop with insertion of T tube. Dogs were infused by 500ml Ringer's solution & 500ml plasma expanders as ooze occurred during operation.

Results

Seven dogs died, four either at operation end or two days after due to acute anemia resulted from repeated hemorrhagic episodes during transection of the liver parynchyma and in availability of blood transfusion. The other three died 4-10 days after operation due to severe intra-abdominal infection The remaining 23 dogs were alive 3 months post operation. Three of them were systematically killed. No abdominal complications were noted. Macroscopically, the remaining liver right part was slightly enlarged as compared to time of surgery, but their surface, color and consistency were normal. Microscopically, liver histological sections were normal. The immuneospressive drugs to all recipient dogs started during operation with dose according to the body weight. Three months post operation; three dogs from each group were sacrificed for follow-up macroscopically and microscopically. Other dogs lived normal life. Mortality rate was 20% in dogs submitted to partial orthotopic liver transplantation. Post-operative death from bleeding was due to graft congestion in one dog led to subcapsular hemorrhage, second dog due leakage vena cava anastomosis, and third due to bleeding from cut surface of graft liver.

Details were given in tables (1, 2, & 3) and figures (1, 2, 3, & 4)

Table 1: Complications due to types liver transplantation

Operation complications	APLT in splenic n=10	ALPT in right paravertebral gutter n=10	Partial LTX n =10
Bleeding	2/10	3/10	3/10
Sepsis	1/10	2/10	1/10
Graft necrosis	1/10	1/10	--
Venous thrombosis	2/10	--	--

ALPT= Auxillary Partial Liver Transplantation, LTX=Orthotopic Liver Transplantation

Table 2: Mortality and its causes in three types of partial liver transplantation

Cause of death Type of Operation	Bleeding	Sepsis	Graft Necrosis	Venous Throm bosis	Mortality %
Aplt in spenic bed	2	1	1	2	60%
Aplt in right para vertebral gutter	1	2	-	-	30%
Parial LTX					

Table 3: Operative infusion

Type of Operation infusion	APLT in splenic bed	ALPT in right paravertebral gutter	Partial LTX
Ringer's Lactate solution	500 ml	750	500 ml
Plasma expanders	--	--	500 ml

Discussion

Generally speaking, the liver transplantation faced a live donor problem (Welech, 1955). Wangensteen (1951) did the first removal of all liver located to the falciform ligament right side or about 85% of it. Absolon *et al.* (1965) did the first auxiliary heterotopic liver transplantation. Starzyl *et al.* (1975) in trisegmentectomy extended right hepatic lobectomy to removal liver true right lobe in continuity with most or all medial left lobe segment. Bismuth (1982) found 2 technical conceptions of typical hepatectomies were with preliminary vascular control (Lortat-Jacob) & hepatictomies with primary parenchymatous transection (Ton That Tung). Otte *et al*. (1989) reported that as to liver, the pediatric donors can be accepted from one month of age, but liver harvested from older child and even young adult can be transplanted into small children after ex-vivo reduction of the graft size. Multi-organ procurement from the same donor provided valuable organs if unaesthetic management of the donor was appropriate. Active transplant program needed international cooperation possible by the organ exchange organizations.

In the present study, graft was implanted in 3 sites. The first one was auxiliary heterotopic in the splenic bed, with enough space for the graft after splenectomy, the stumps of the recipient vessels after graft rotation of 180 degree in horizontal plane. Also, heparin locally in splenic vein was important in preventing complications after splenectomy. The recipient portal vein was narrowed to the half of its diameter to oblige the portal blood to flow to the graft. So, this site was easy to find space for the graft, but with high incidence of vascular thrombosis (20%). Two dogs died from bleeding due to lack of blood transfusion, and high incidence of venous thrombosis due to the long splenic vein and stagnation of blood inside. Lygidakis (1988) reported that construction of a long side-to-side anastomosis between the inferior caval vein of the receiver and the inferior caval vein of the graft provided a free and unimpeded outflow from the graft and prevents kinking at the anastomotic site.

The second site was implanted in the right paracolic gutter. But, there was much difficulty to dissect a space for the graft without much bleeding and dogs were infused by 750ml Ringer lactated solution which saved two out of three, which developed bleeding during operation. Also, two dogs developed severe, abdominal sepsis and died from dissection of the para colic gutter which caused in spread of bacterial secondary infection. Bismuth and Houssin (1984) reported that due of the rarity of child donors; in cases of adult donors room requirement for the liver graft was a major technical obstacle to liver transplantation in children. They performed an orthotopic transplantation with an adult liver that was reduced to left lobe. Absence of technically-related complications suggests that this procedure might facilitate the performance of liver transplantation in children.

In the third site which was orthotopic non-auxiliary; expecting bleeding during hepatectomy of the recipient liver, the dogs were infused by 500ml plasma expanders. This infusion amount saved 2 I.V.C., only clamping of the portal vein before hepatectomy without excision of the recipient I.V.C. This agreed with Ringe *et al.* (1988) reported that reduced-size liver transplantation was safely with the described type of hepatic vein reconstruction, when large donor organs were used for small children.

No doubt, the liver transplants are reasonably safe procedures with good survival rates (Samuel and Feray, 2000). Nevertheless, many factors can influence the patients' chances of a successful surgery, and determine how long they live after surgery. These factors include their overall health, lifestyle habits, and additional conditions (Ferreira *et al*, 2013). Also, Zarrinpar and Busuttil (2013) reported that for people, especially children after liver transplantation must maintain general health through proper nutrition, rest, exercise, and stress reduction. Avoid people who have infectious diseases especially peo-

ple with active viral infections, such as chicken pox, mumps, measles, mononucleosis, tuberculosis, colds, or the flu. Take medications to prevent infection, as prescribed.

Conclusion

Removal of live animal liver part was not a risky operation; its complications were minimal. In orthotopic non auxiliary partial liver transplantation of a bi-segmental liver graft with conservation of the vena cava of the recipient would probably be preferable, its only problem is bleeding which can be corrected by blood transfusion

References

Abo-Madyan, AA, Morsy, TA, Motawea, S M, 2004: Efficacy of Myrrh in the treatment of schistosomiasis (*haematobium* and *mansoni*) in Ezbet El-Bakly, Tamyia Center, El-Fayoum Governorate, Egypt. J. Egypt. Soc. Parasitol. 34, 2: 423-46.

Absolon, KB, Hagihari, PF, Griffen, WO, Lillehei, RC, 1965: Experimental and clinical heterotopic liver homotransplantation. Rev. Int. Hepatol. 15, 8:1481-90.

Bismuth, H, 1982: Surgical anatomy and anatomical surgery of the liver, World J. Surg. 6: 3-9.

Bismuth, H, Houssin, D, 1984: Reduced size ortho-topic liver graft in hepatic transplantation in children. Surgery 95:367-70.

Cholongitas, E, Papatheodoridis, GV, Vangeli, M, Terreni, N, Patch, D, *et al,* 2005: Systematic review: The model for end-stage liver disease-should it replace Child-Pugh's classification for assessing prognosis in cirrhosis? Aliment. Pharmacol. Ther. 22, 11/12:1079-89.

Couinaud, C, 1957: Le foie; études anatomiques et chirurgicales. Printed Book, Masson, Paris

D'Amico, G, Morabito, A, Pagliaro, L, Marubini, E, 1986: Survival and prognostic indicators in compensated and decompensated cirrhosis. Dig. Dis. Sci. 31:468-72.

Feng, S, Goodrich, NP, Gresham, JL, Dykstra, DM, Punch, JD, *et al,* 2006: Characteristics associated with liver graft failure: the concept of a donor risk index. Am. J. Transplant. **6**:783-90.

Gharib, AF, Karam, RA, Pasha, HF, Radwan, MI, Elsawy, WH, 2011: Polymorphisms of hemochromatosis, and alpha-1 antitrypsin genes in Egyptian HCV patients with and without hepatocellular carcinoma. Gene 489, 2:98-102.

Gines, P, Quintero, E, Arroyo, V, *et al,* 1987: Compensated cirrhosis: Natural history and prognostic factors. Hepatology 7:122.

Haseeb, AN, el-Shazly, AM, Arafa, MA, Morsy, AT, 2002: A review on fascioliasis in Egypt. J. Egypt. Soc. Parasitol. 32, 1:317-54.

Hifnawy, MS, Mangoud, AM, Eissa, MH, Nor Edin, E, Mostafa, Y, *et al*, 2004: The role of aflatoxin-contaminated food materials and HCV in developing hepatocellular carcinoma in Al-Sharkia Governorate, Egypt. J. Egypt. Soc. Parasitol. 34, 1:S479-88.

Ferreira, L, Santos, LF, Anastácio, LR, Lima, AS, Correia, MITD, 2013: Resting energy expenditure, body composition, and dietary intake: a longitudinal study before and after liver transplantation. *Transplantation* 96:579-85.

Madwar, MA, El-Gindy, I, Fahmy, HM, Shoeb, NM, Massoud, BA, 1999: Hepatitis C virus transmission in family members of Egyptian patients with HCV related chronic liver disease. J. Egypt. Publ. Hlth. Assoc. 74, 3/4:313-32.

Motawi, TK, Shaker, OG, Ismail, MF, Sayed, NH, 2013: Genetic variants associated with the progression of hepatocellular carcinoma in hepatitis C Egyptian patients. Gene 527, 2:516-20.

Otte, JB, Squifflet, JP, Carlier, MC, de Hemptinne, B, Gianello, P, *et al,* 1989: Organ procurement in children, surgical, anaesthetic and logistic aspects. Intensive Care Med. 15, 1:S67-70.

Ringe, B, Pichlmayr, R, Burdelski, M, 1988: A new technique of hepatic vein reconstruction in partial liver transplantation. Transpl. Int. 1, 1: 30-5.

Samuel, D, Feray, C, J, 2000: Recurrent hepatitis C after liver transplantation: clinical and therapeutical issues. Viral. Hepat. 7, 2:87-92.

Samuel, D, Feray, C, J, 2000: Recurrent hepatitis C after liver transplantation: clinical and therapeutical issues. Viral. Hepat. 7, 2:87-92.

Samuel, D, Feray, C, Bismuth, H, 1997: Hepatitis viruses and liver transplantation. J. Gastroenterol. Hepatol. 12, 9/10:S335-41.

Starzl, TE, Marchioro, TL, Vonkaulla, KN, Hermann, G, Brittain, RS, *et al,* 1963: Homotransplantation of the liver in humans. Surg. Gynecol. Obstet. 117:659-76

Zakaria, S, Fouad, R, Shaker, O, Zaki, S, Hashem, A, *et al,* 2007: Changing patterns of acute viral hepatitis at a major urban referral center in Egypt. Clin. Infect. Dis. 44, 4:e30-6

De Jong, IJ, Reinders, ME, Kranenburg, J, de Meester, J, Persijn, GG, 1996: Multiorgan do-

nation in The Netherlands: limited by consent and policy. Transpl. Int. 9, 4:430-2.
Welch, CS, 1955: A note on transplantation of the whole liver in dogs. Transplant. Bull. 2:54-9
Wangensteen, OH, 1951: Proceed. 3rd Natl. Cancer Conf.; JB, Lippincott Co., Philadelphia,
Lygidakis, NJ, 1984: A new technique of partial auxiliary heterotopic liver transplantation. Neth. J. Surg. 36, 1:24-6.
Zarrinpar, A, Busuttil, RW, 2013: Liver transplantation: Past, present and future. Nature Rev. Gastroenterol. Hepatol. **10**, 7:434-40.

Explanation of figures

Fig. 1: Segmented anatomy of human liver.
Figs. 2, 3, & 4: Illustrative author hand drawing