Impact of Portal Vein Thrombosis on Adult to Adult LDLT: 8 Years Experience

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Abstract: Background and Objective: Living donor liver transplantation (LDLT) for patients with portal vein thrombosis (PVT) involves technical difficulty. Its presence has frequently been presented as a relative or absolute contraindication in LDLT by numerous groups. The aim of this study is to demonstrate our experience in dealing with patients with preexisting PVT and its effect on the outcome of transplantation. Methods: From October 2001 to September 2009, 210 LDLT were performed by our team. Thirty one patients with intraoperatively confirmed nontumoral PVT formed the study group. The thrombus was removed by a simple technique of eversion thrombectomy. Anticoagulation was started after surgery to be stopped 6 months after confirmation of absence of PVT. A comparative analysis with intraoperative and postoperative variables was performed with 179 patients without PVT transplanted in the same period. Results: PVT was diagnosed preoperatively in 15 (48%) patients. The commonest type was grade II, occurring in 13(41.9%) patients. Total thrombectomy was successful in 29 cases and partial in two cases, but with adequate portal flow.The overall complications, Infections and portal vein rethrombosis were higher in patients with preexisting PVT but this was not associated with increase in ICU or hospital stay. PVT did not affect patient survival (70.6% and 60.2%, one and three year survival rate in patients with PVT vs. 81% and 62% in patients without PVT). Conclusion: PVT increases surgical difficulties and postoperative morbidity (PV rethrombosis, infections) but does not have an influence on patients survival.

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Key words: Impact of Portal Vein Thrombos, Adult , Adult LDLT ,Years Experience.

1. Introduction

Orthotopic liver transplantation (OLT) is now an accepted and efficient therapy for end-stage liver diseases. Portal vein thrombosis (PVT) is a complication of chronic liver diseases that occurs in approximately 5–15% of these patients[(1)].

At the beginning of OLT history, PVT was considered an absolute contraindication, till 1985, when the first report of a successful transplantationin two patients with PVT was published[(2)]. Nowadays, the presence of PVT is no longer considered a contraindication for LT, as many improvements have been made in the field of perioperative management and surgical technique, including vein grafts to overcome this problem[(3)].

Living donor liver transplantation (LDLT) has emerged as one of a variety of approaches to overcome the current lack of organ donation in the face of growing waiting lists and as the only modality in the absence of the cadaveric programs in some countries.

In LDLT, there are technical difficulties due to the need of distal dissection of vascular pedicle of the hilum and restricted availability of a vein graft. The presence of PVT in the recipient has frequently been presented as a relative or absolute contraindication in LDLT by numerous groups[(4, 5)].

To address this issue, an international survey[(6)] was performed to examine the attitude of transplant teams relative to LDLT in the setting of preexisting PVT in the potential recipient. They found that, 5 centers considered it to be an absolute contraindication (10.7%), 24 centers a relative contraindication (51%), and 18 as not being a contraindication (38.3%).

Aim of the study is to review our experience of performing LDLT in patients with PVT, in order to evaluate the feasibility of thrombectomy, and its influence on post-operative outcome.

2. Patients and method

From October 2001 to September 2009, 210 LDLT were performed at Wady El Nile and Ain Shams Specialised University Hospital including 31 patients with intraoperatively confirmed nontumoral PVT formed the study group. Patients with hepatocellular carcinoma (HCC) were excluded.

Preoperative assessment of liver transplant candidates for portal vein patency included both Doppler ultrasonography and abdominal computed tomography (CT) scan with CT portography (Figs. 1-4). Ultrasonography (US) is usually the investigation of choice, with a sensitivity and specificity ranging between 60% and 100% [(7)] ; it can

reveal the presence of solid, hyperechoic material into a distended portal vein or its tributaries, the presence of collateral vessels or a cavernoma. Doppler imaging can confirm the absence of flow in part or all the vassal lumen, and if present, a cavernomatous transformation[7]. Incidentally, US is less reliable in determining the extension of the thrombus to the mesenteric circulation. Instead, CT scanning can easily obtain this information, and, can estimate the impairment of the bowel and other adjacent organs. CT scanning is able to demonstrate hyperattenuating material in the portal vein lumen and the absence of enhancement after contrast injection. In addition, in hypoperfused areas, hepatic enhancement appears increased during the arterial phase and decreased during the portal phase[7].

The median delay between the last Doppler ultrasound examination and the transplantation was one week. Patients with confirmed PVT were classified into four grades according to the extent of thrombosis assessed intraoperatively, as described by Yerdel *et al.*[8]. (Figure 5): grade 1 :< 50% PVT without obstruction of the superior mesenteric vein (SMV); grade 2: grade 1 but >50% PVT; grade 3: complete PV and proximal SMV thrombosis; grade 4: complete PV and entire SMV thrombosis.

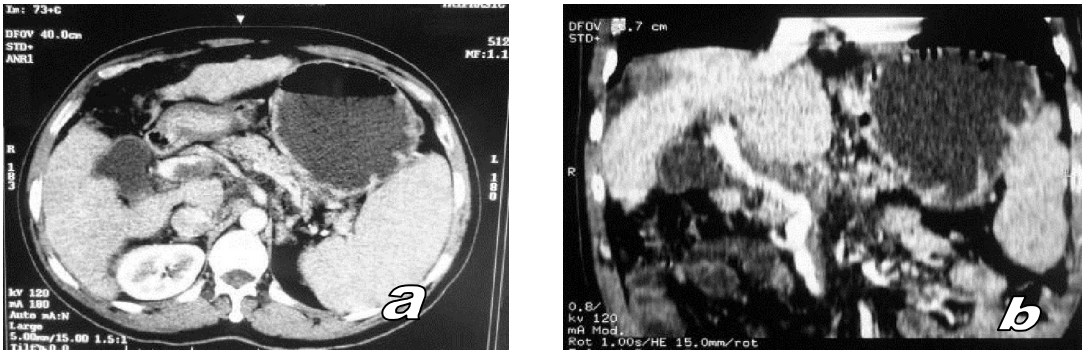


Figure (1): Male patient 55 years old liver cirrhosis and right hepatic lobe HCC. **(a)** Axial CT cuts in porto-venous phase showing partial eccentric main PV thrombus. (b) Coronal reconstruction in portovenous phase showing partial eccentric PV thrombosis which extend to involve the superior mesenteric vein causing eccentric thrombosis as well.

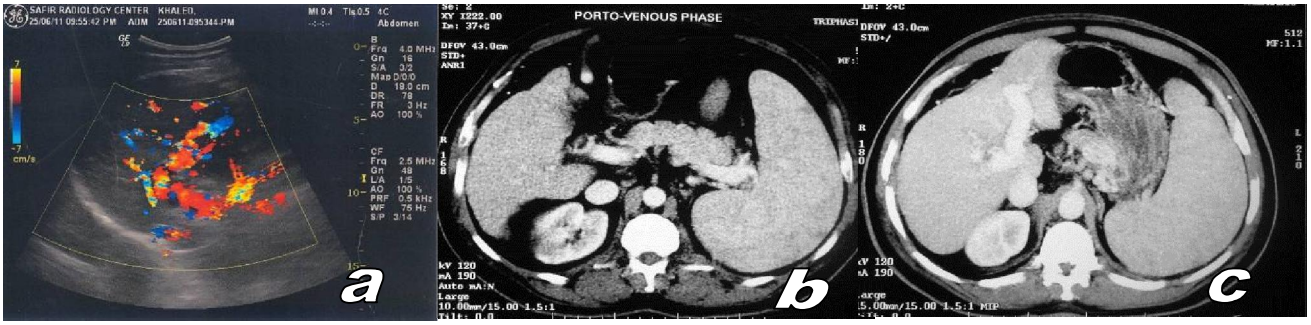
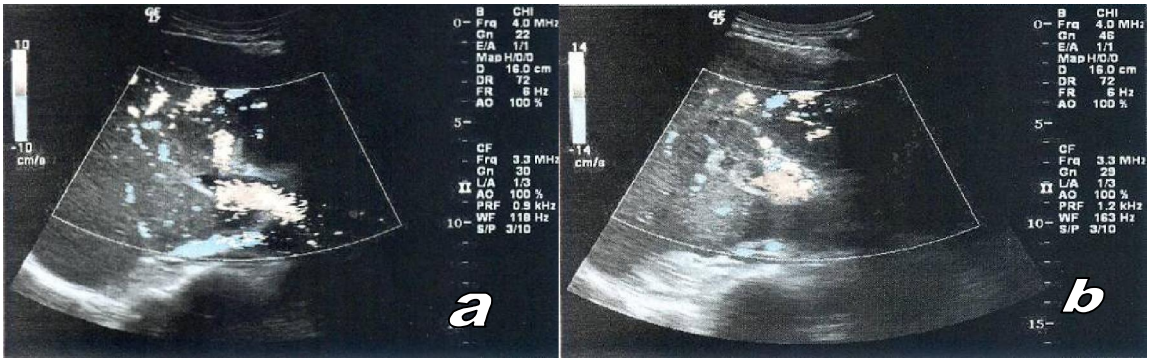


Figure (2): male patient 50 years old, liver cirrhosis **(a)** color Doppler examination showing patent main PV and left PV branch showing normal color flow pattern yet the right PV branch shows no color flow denoting its thrombosis. **(b)** Axial CT portography at extrahepatic level showing patent contrast enhanced opacified main portal vein with no evidence of thrombosis. **(c)** Axial CT portography at intrahepatic level showing patent contrast enhanced opacified left portal vein yet the right portal branch was not opacified and showed no contrast enhancement demoting it thrombosis.



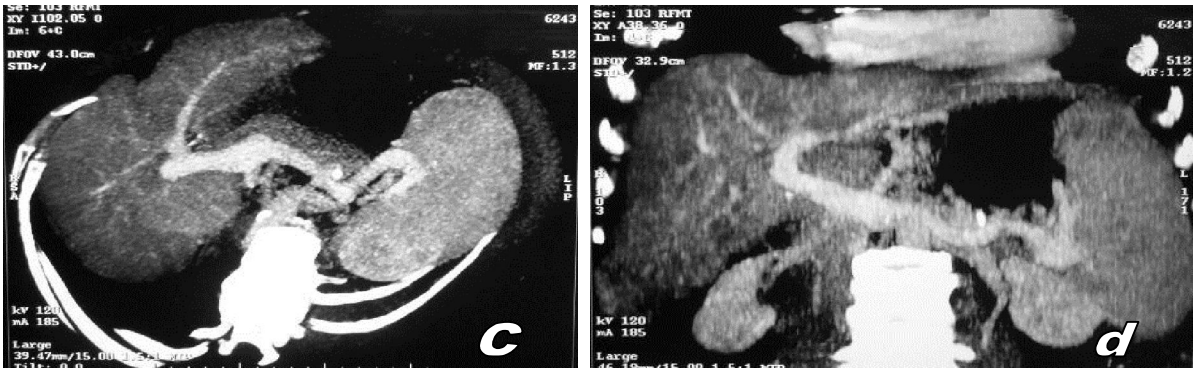


Figure (3): Female patient 56 years old, with liver cirrhosis. **(a)** Color Doppler examination showing patent main PV with normal color flow pattern with no evidence of thrombosis. **(b)** Color Doppler examination showing echogenic thrombus seen in right portal branch and no color flow denoting its thrombosis. **(c)** CT portography, axial cut showing patent opacified main portal and left portal vein branch, yet, non-opacified right portal vein branch denoting its thrombosis. **(d)** CT portography coronal reconstruction showing patent opacified main portal and left portal vein branch, yet non-opacified right portal vein branch.

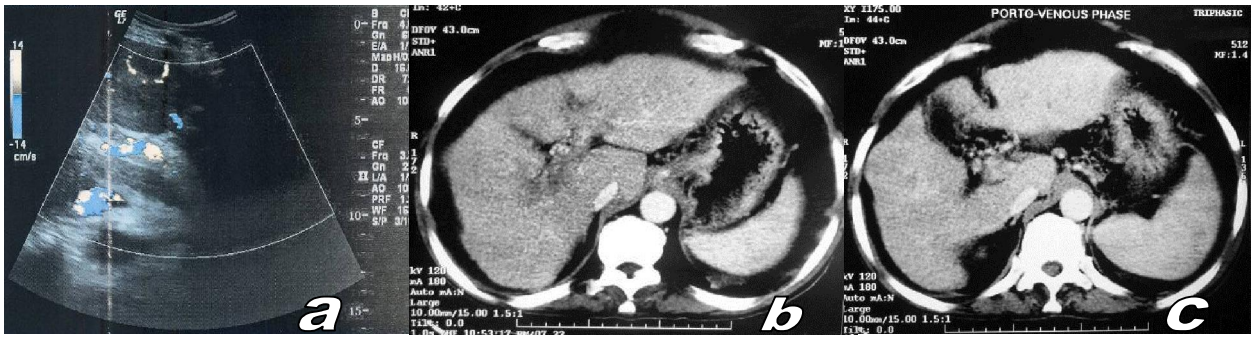


Figure (4): Male patient 58 years old, with liver cirrhosis. (a) Color Doppler examination showing patent hepatic artery with normal color flow pattern, yet the main portal vein showing intraluminal echogenic thrombus with no color flow signal denoting its thrombosis. (b) CT portography, axial cut showing non-opacified left and right portal vein branches denoting their thrombosis. (c) CT portography, axial cut showing non-opacified main portal vein denoting its thrombosis.

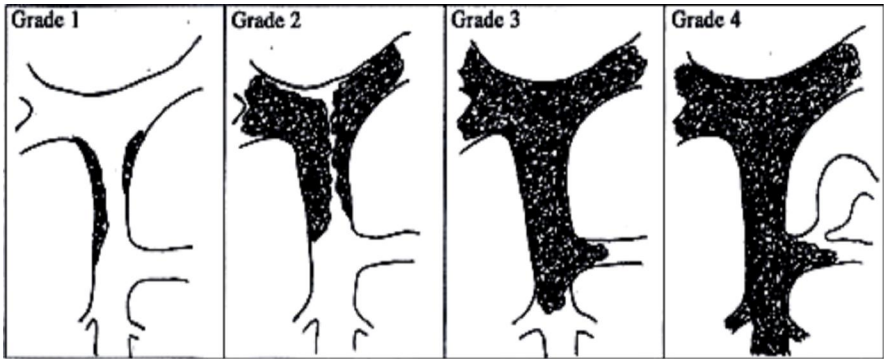


Figure (5): PVT grades according to Yerdel *et al.*[8].

Surgical technique:

Partial or complete PVT may be detected before or during surgery. In either case, our technique is the same. The hilum is dissected first, with isolation of the right and left hepatic arteries which aretied and transected as long as possible, followed by transection of the bile duct. This allows for an intimate exposure and dissectionof the portal vein in its entirety. The portal vein is manually and visually examined to determine the extent ofinvolvement by the thrombus. A portal clamp is applied at its lower part followed by transection of its right and left branches. The vein is maintained open by three tonsil clamps applied to its edge,and then the cleavage

plane between the thrombus and the intima was found. The clot was progressively and circumferentially freed (Figure 6), with the aid of a tonsilclamp by everting the venous wall, by clamping the free edge of the clot with a tonsil. This maneuver was extended to the splenic and/or superior mesenteric veins if necessary. After the clot had been pulled out, portal patency was assessed by introduction of the surgeon's index finger or a Hegar dilator. Usually, this technique allowed the entire clot material to be removed. Before completing the anastomosis, the blood flow in the recipientportal vein was verified by removing the clamp. The portal vein wasflushed with blood in order to eliminate residual or newly formed clots.Subsequently, portal flow was restored by end-to-end portal anastomosis and its patency was checked at the end of the operation by intra-operative Doppler ultrasound.

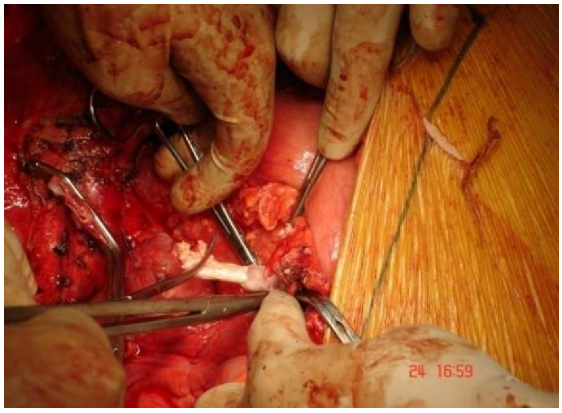


Figure (6): Holding the edge of portal vein opened by three tonsil clamps

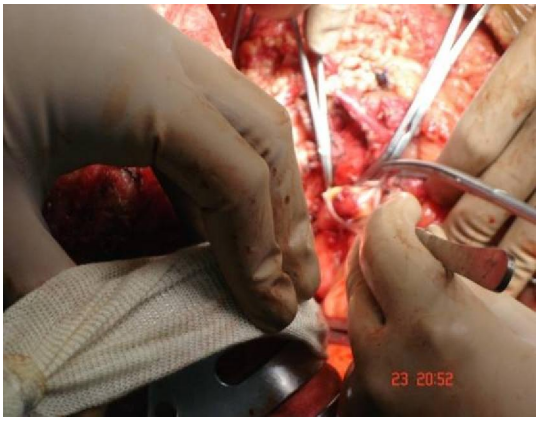


Figure (7): Dissection between the intima and the thrombus.

Hepatectomy was performed in all cases using the piggy-back technique.The choice between right or left lobe grafts depends on the graft recipient weight ratio (GRWR) and residual liver volume (RLV). A minimal 0.8 GRWR and 30% RLV criteria was applied.

Immunosuppression consisted of tacrolimus or cyclosporine and low-dose steroids. Anticoagulation was started postoperatively with enoxaparin1 mg/kg every 12 hours when INR>1.5 and platelet >20.000 with no evidence of bleeding tendency. Warfarin sodium was begun 1 week before discharge adjusting the INR between 2 and 3, to be stopped 6 months after confirmation of absence of PVT.

Post-operative arterial and venous patency was evaluated routinely using Doppler ultrasound at 24 h, daily for one week, weekly for one month, monthly for three months, and then as necessary. In case of any doubt of PVT, CT portography was done.

Intraoperative and postoperative variables analysed were: grade of PVT, thrombectomy whether partial or complete, type of graft, GRWR, blood requirements, cold ischemia time, operative time, recurrence of PVT, postoperative complications, early and late postoperative deaths, and survival. A comparative analysis was performed with 179 patients without PVT transplanted in the sameperiod.

Statistical analysis was performed using the analysis of variance or chi-squared test. The actuarial survival rate was calculated with the nonparametric Kaplan-Meier method and was compared with the Wilcoxon test throughout the study. Quantitative data are presented as median (range) and were analyzed using Kruskal-Wallis test. *P* values of less than 0.05 were considered significant.

3. Results

The pre-operative characteristics of the whole study group are shown in (Table 1).The incidence of PVT at the time of LT was 15%.Compared to patients without PVT, there were no differences in age, sex and Model for end stage liver disease (MELD) score, whereas the indication for LT was less frequently none viral hepatitis in PVT group.

PVT was diagnosed preoperatively in 15 (48%) patients; while in 18 (58%) was accidently discovered intra operatively. The commonest type was grade II, occurring in 13(41.9%) patients (Table 2). Total thrombectomy was successful in 29 cases. In two cases, (type III and IV) the remnant of the thrombus inside the SMV could not be extracted completely and a small residual thrombus was left but with adequate portal flow and reassessed at the end of the operation by intraoperative Doppler U/S. One patient needed ligation of the collaterals in gastro splenic ligament to increase the portal flow.None of them developed portal vein

rethrombosis.

On comparing the intra operative data between non PVT and PVT groups (Table 3), ischemia time was the only significant factor which was more prolonged in the PVT group (p=0.014). However blood transfusion requirements and operative time were nearly similar in both groups.

Table 1. Patient characteristics

	PVT (N=31)	Non-PVT (N=179)	p-value
Age (yr)	50 (28-64)	50(18-64)	0.36
Gender (M/F), n (%)	27(87)/4(13)	153(85.4)/26(14.6)	0.17
MELD	18(11-44)	16(7-29)	0.06
Etiology, n (%)			
HCV	29(93.5)	151(84.3)	0.11
HBV	1(3.2)	3(1.6)	
HBV+HCV		3(1.6)	
Other	1(3.2)	22(12.3)	
Graft			
Right lobe, n (%)	28 (90.3)	177(98.8)	0.09
Left lobe, n (%)	3(9.7)	2(1.1)	
GRWR	1.2(0.6-1.8)	1.2(0.7-1.9)	0.15

Continuous variables are reported in median and range.
PVT, portal vein thrombosis; MELD, Model for end stage liver disease ;HCV, hepatitis C virus; HBV, hepatitis B virus;; GRWG, graft recipient weight ratio.

Table 2. Degree and management of portal vein thrombosis

Grade	**n-value**	**Complete thrombectomy**
I, n (%)	**7(22.5%)**	**7**
II, n (%)	**13(41.9%)**	**13**
III, n (%)	**9(29%)**	**8**
IV, n (%)	**2(6.4%)**	**1**

Table 3. Intraoperative data of both groups

	PVT	Non PVT	p- value
RBC transfusion(U)	6 (0-28)	5 (0-40)	0.1
Ischemia time (min)	(35-175)	76 (50-214)	0.014
Operative time(min)	660(360-780)	570(320-930)	0.3

Variables are reported in median and range
PVT, portal vein thrombosis; RBC, red blood cells.

Influence on morbidity and mortality

The median follow up period is 14 months (1-79). Three patients 3/31(9.6%) developed re thrombosis in the early (within 2 weeks) postoperative period. Two of them, developed partial PVT on Day 2, 15 which was confirmed by duplex and elevation of the liver enzymes. They were successfully treated by medical treatment in the form of full hepiraniztion. Re-canalization occurred after 2 weeks, 2 months respectively with normalization of the graft function.One patient developed complete re-thrombosis on the 2nd day postoperative, confirmed by CT portography. This patient was urgently explored followed by transient clamping of the 3 venous outflow (right hepatic vein, vein of segment 5 and right posterior inferior hepatic vein), and hepatic artery. Thrombectomy followed by re anastomosis of PV and ligation of collaterals. The patient died on day 10 with renal and hepatic failure due to thrombosis of the segment 5 vein with development of the small for size syndrome (SSS).

On comparing the postoperative morbidity in patients with or without PVT (Table 4),the incidence of re thrombosis was significantly higher(p< 0.003) in the PVT group(9.6%versus 0.55%) .Two patients in the none PVT group developed portal vein stenosis postoperatively on day 31 and 45 with successful treatment by ultrasound guided dilation

with stent insertion. The incidence of infection was significantly higher (p<0.001) in the PVT group (n=19/31, 61%) than none PVT group46/179(31%). No difference was found between the two groups as regard the incidence of reoperation, postoperative bleeding ICU and hospital stay.

The overall morbidity in PVT group was significantly higher (p0.001) compared to none PVT group(23/31, 74.1%; versus 60/179, 33.5%)

Mortality occurred in 11 (35%) patients in the PVT group with only one patient developed portal vein re-thrombosis. The major cause of death was sepsis (n=6, 46.1%). Other causes included SSS (n=2, 6.4%), Bleeding (n=1, 3.2%), Hepatic artery thrombosis (n=1, 3.2%), and Cerebrovascular stroke (n=1, 3.2%).

The survival analysis (Figure 8.) showed that the 1 and 3years survival rates were 70.6% and 60.2%, respectively in PVT group compared to 81% and 62% in none PVT group however there was no statistical difference (p> 0.3) between the two groups.

Table 4. Percentages of postoperative complications with presence or absence of PVT

	PVT	Non PVT	p-value
Reoperation, n (%)	5/31(16%)	18/179(10%)	0.5
Bleeding, n (%)	1(3.2%)	9(5%)	0.3
PV complications, n (%)			
Re thrombosis	3/31(9.6%)	1(0.55%)	0.003
Stenosis	0	2(1.1%)	
Renal dialysis, n (%)	4(13%)	17/179(9.4%)	0.6
Infections, n (%)	19/31(61%)	46/179(31%)	0.001
Overall complications	23/31(74.1%)	60/179(33.5%)	0.001
ICU stay (days)	8(0-48)	7(0-56)	0.7
Hospital stay (days)	24(0-60)	28(2-61)	0.8

Continuous variables are reported in median and range
PVT, portal vein thrombosis; PV, portal vein

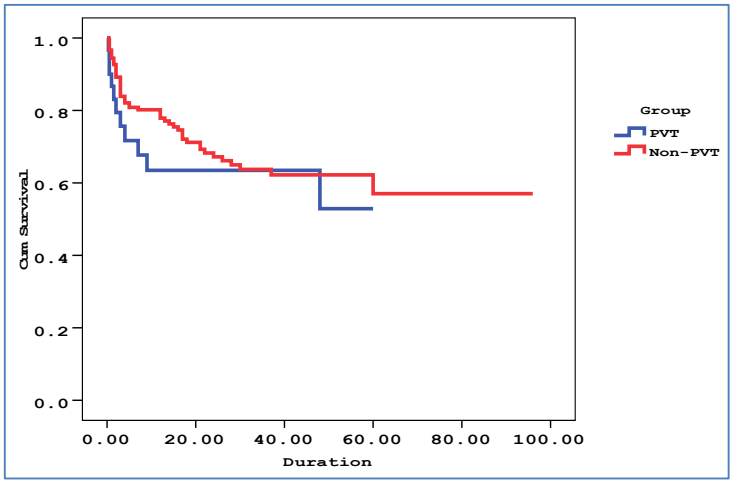


Figure (8): Overall patient survival rates in patients with and without

4. Discussion

Greater experience with LT and the description of several technical options have led PVT to beconsidered as a surgical challenge, rather than a contraindication for LT[9].

Theincidence of PVT among patients undergoing LT ranges from 2% to 26%, dependingon the reported series[10,11]. These differences are due to different diagnostic criteria andthe different study periods. There is a tendency in recent years towards an increasedincidence of PVT in patients undergoing LT[12]. In our series, it was 15%.

Imaging the portal vein is an important goal of pre-OLT patient evaluation and is usually based on Doppler ultrasonography, which is easily available, inexpensive and non-invasive but, its accuracy in detecting PVT ranges from 26% to 87%. This is explained by a high incidence of false negatives due

to the extension of PVT, the identification of portal collaterals as the PV, and the post-US thrombosis of the PV while patients are awaiting transplantation[13]. In our patients, although we use routinely both Doppler and CT portography, our detection rate of PVT preoperatively was 42%. This is similar to the results obtained by Dumortier *et al*[13], who had the rate of pre-OLT diagnosis of PVT of 44.7%.

An adequate portal inflow to the graft is essential for good liver function. Different approaches have been proposed to restore PV patency at the time of OLT, such as thrombectomy, the use of venous interposition grafts, the use of PV collaterals, and cavoportalhemitransposition[14]. In absence of cadaveric programs, eversion thrombectomy, represents the simplest way to restore portal flow. In our experience, thrombectomy with good portal flow restoration wasapplicable in most cases with the exception of grade 4 in which partial thrombectomy was done in one case and complete thrombectomy in the other.

When the portal flow is adequate in the setting of a small residual thrombus in the SMV and/or splenic vein after removal of the main thrombus, it is controversial whether or not to secure a perfect, but dangerous, further thrombectomy or to leave an incomplete, but safe thrombectomy. The two patients in our series with partial thrombectomy did not show portal rethrombosis in the follow up period.

The greater technical difficulty in a patient with preexisting PVT may be associated with longer operation time, anhepatic phase, and higher transfusion requirements[15]. In our patients,transfusion requirements and operative time were similar in both groups but longer Ischemia time in patients with preexisting PVT. The difficult hilar dissection in these patients may push us to rapidly control the pedicle which may have a reflection on minimizing operative time and blood loss.

It has been reported in the literature that OLT in patients with PVT is associated with a higher rate of complications, such as hepatic artery thrombosis, relaparotomy, pancreatitis, sepsis, and renal failure[8]. In our patients, the overallcomplications, Infections and portal vein rethrombosis were higher in patients with preexisting PVT but this was not associated with increase in ICU or hospital stay.

Although the incidence of portal vein rethrombosis was higher in patients with preexisting PVT (3/31, 9.6% vs. 1/179, 0.55%) this was not associated with direct effect on the outcome of these patients as two of them had partial thrombosis and was successfully treated with anticoagulant therapy and the third one died from SSS.

We observed that PVT did not affect patient survival (70.6% and 60.2%, one and three year survival rate in patients with PVT vs. 81% and 62% in patients without PVT), confirming most of the reports in the literature[13,16].

In conclusion, PVT increases surgical difficulties and postoperative morbidity (PV rethrombosis, infections) but does not have an influence on patients` survival. Grade IV had poor out come and may need venous Jump grafts or cadaveric OLT.

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