The Selection of Donors in Living Donor Liver Transplantation Based on Results of Thrombophilia Screening Tests and Prophylactic Strategy for Venous Thromboembolic Events

[1]Abdul Wahab Dogar, [1]Azhar Hussain, [1]Kaleem Ullah, [2]Zubair Khan, [3]Hafiz M. Khan

[1]Gambat Liver Transplant Center, Gambat, Pakistan.
[2]UTHealth Houston, Houston , USA.
[3]AdventHealth Orlando, Orlando, USA.

ABSTRACT

The main aim of this study was to determine the frequency of hereditary thrombophilia in the Pakistani population and share our centers' safety and VTE prophylaxis protocols in live liver donors.

Thrombophilia testing was done on 567 living donor candidates. Donors were divided into the normal, borderline, and high-risk groups.

Among them, 21 (3.7%) donors were deficient in protein C, 14(2.5%) were deficient in anti-thrombin-III and 45(7.9%) were having Leiden factor-V mutation. Donor operation was performed on 44 candidates in the borderline group and 7 in the high-risk group. Complications after surgery were comparable between the 2 groups. One donor in the normal donor group developed pulmonary embolism, but none of the donors in either borderline or high-risk group developed VTE.

Donor operation is safe in donors in either borderline or high-risk groups, although more evaluations are required to determine the necessity and lowest safe levels of PC, PS, and AT-III of thrombophilia testing before surgery among living donor candidates.

CONTACT

Azhar Hussain, MBBS, MD.
Gambat Liver Transplant Center,
Gambat, Pakistan.
Email:
azharhussain0139@gmail.com
Phone: +923037156931
https://gambatlivertransplant.com/

INTRODUCTION

The highest priority in living donor liver transplantation (LDLT) is donor safety.

Vascular events after living donor liver transplantation (LDLT) are one of the most feared complications that usually lead to graft and patient loss.

The main aim of this study was to determine the frequency of hereditary thrombophilia in the Pakistani population and share our centers' safety and VTE prophylaxis protocols in live liver donors.

METHODS AND MATERIALS

In this retrospective cohort study, thrombophilia testing that includes protein S (PS), protein C (PC), antithrombin (AT) III, and anti-phospholipid antibody (APLA), was done in 567 living donor candidates between July 2016 and April 2020.

Donors were divided into the normal, borderline, and high-risk groups according to the Caprini score.

A conservative VTE prophylaxis with elastic stockings and intermittent pneumatic compression (IPC) was given postoperatively to donors in the normal donors group and majority of the borderline risk donors group.

A stringent VTE prophylaxis with Rivaroxaban alongside elastic stockings and intermittent pneumatic compression (IPC) was given postoperatively to donors in the the high-risk donors group.

The safety endpoints were VTE occurrence, bleeding complications or mortality.

RESULTS

Among 567 potential donors, 21 (3.7%) donors were deficient in protein C, 14(2.5%) were deficient in anti-thrombin-III and 45(7.9%) were having Leiden factor-V mutation.

31/416 (7.45%) were deficient in factor II. IgM & IgG Anti-phospholipids antibodies were positive in 2/567(0.4%) and 2/567(0.4%) respectively.

5 donors were excluded as both PC (%) and Anti-thrombin-III (%) activity were less than 50%.

Table 1. Comparison of demographics and surgical features of LLDs in donor groups

Variables	Normal Group (n=516)	Borderline Group (n=44)	High Risk Group (n=7)	P value
Mean age (Years)	23.43 ± 5.53	23.91± 5.25	26.86 ± 6.54	0.17
Mean BMI (Kg/m²)	21.40 ± 7.99	20.5 ± 2.71	21.53 ± 3.29	0.69
Gender				
Male	290(56.2%)	24(54.5%)	4(57.1%)	0.97
Female	226(43.7%)	20(45.4%)	3(42.8%)	
Marital status				
Unmarried	351(68.1%)	25(56.9%)	5(71.4%)	0.06
Married	165 (31.9%)	19 (43.1%)	2(28.5%)	
Donors relation to recipients				
Son	63 (12.2%)	6 (13.6%)	1(14.2%)	0.008
Brother	99 (19.1%)	5 (11.3%)	2(28.5%)	
Nephew	25 (4.8%)	5(11.3%)	1(14.2%)	
Daughter	35 (6.7%)	5 (11.3%)	0	
Sister	32 (6.2%)	5 (11.3%)	0	
Father	88 (17.1%)	3 (6.8%)	0	
Swap	10 (1.9%)	0	0	
Others	157(30.4%)	11 (25.0%)	3(42.8%)	
Type of Graft				
Modified right lobe graft	437 (84.6%)	36 (81.8%)	6(85.7%)	NS
Modified extended right lobe graft	62 (12.0%)	8 (18.1%)	1(14.2%)	
Left lobe graft	4 (0.7%)	7 (15.9%)		
Left lateral segment graft	11 (2.1%)	0	0	
	6(1.1%)	0	0	
GRWR	1.26 ± 0.63	1.4 ± 0.68	1.2 ± 0.63	NS
Mean warm ischemia time (minutes)				
Mean operation time (hours)	10.99 ± 6.09	10.68 ± 4.08	13.86 ± 7.26	
Mean blood loss (ml)				
Blood transfusions (no of patients/ %)	407.94 ± 64.86	412.27 ± 89.11	422.86 ± 62.37	
	516	44	7	NS
				0.76
Personal History of Thrombosis	0	0	0	--
Family History of Thrombosis	0	0	1	--

Table 2: Various outcomes in LLDs in donor groups

Variable	Normal Group (n=516)	Borderline Group (n=44)	High Risk Group (n=7)	P value
Total number of complications	62 (12.0%)	15 (34.1%)	2(28.5%)	0.43
Grade 1 & 2				
-Wound infections	20 (3.8%)	3 (6.8%)	2(28.5%)	
-Wound hematoma	2 (0.3%)	1 (2.2%)	0	0.001
-UTI	4 (0.7%)	2 (4.5%)	0	
-Fever	3 (0.5%)	2 (4.5%)	0	
-Paralytic ileus	2 (0.3%)	1 (2.2%)	0	
Grade 3A				
-Bile leakage	6 (1.1%)	1 (2.2%)	0	
-Bile duct stricture	3(0.5%)	0	0	0.15
-Post-op bleeding	3 (0.5%)	1 (2.2%)	0	
-Pleural effusion/Aspiration	9 (1.7%)	1 (2.2%)	0	
-ERCP & Stenting	3 (0.5%)	1 (2.2%)	0	
Grade 3B				
- Re-open	6(1.1%)	1 (2.2%)	0	0.45
Grade 4A				
- Need ICU care/ ventilator	1 (0.1%)	1 (2.2%)	0	0.95
Grade 4B				
-Multi-organ failure	0	0	0	--
Grade 5	0	0	0	--
Mean ICU stay (Days)	3 ± 1	2.53 ± 1	3 ± 1	0.15
Mean hospital stay (Days)	6 ± 2	5 ± 2	6 ± 2	0.17
Mortality	0	0	0	--

DISCUSSION

This is the first report to determine the importance for risk stratification approaches for VTE prophylaxis on the basis of thrombophilia tests for LDLT donors in a large cohort to the best of our knowledge.

Fifty-one living donors having marginal or high-risk results of thrombophilia screening tests underwent right lobe hepatectomy due to the absence of an alternative donor. Contrary to other LDLT centers, our center protocols are to manage with conservative measures postoperatively.

For the high-risk group (having both Protein C and Protein S levels greater than 50%, at least), we performed seven donors who underwent right lobe hepatectomy with Rivaroxaban cover due to the absence of an alternative donor and emergent nature of LDLT in their recipients.

None of the high-risk donors in both groups ever had any VTE-related complications or symptoms during their pre-operative period and this also supported us on clinical grounds to make decisions about the cautious use of pharmacological prophylaxis against VTE.

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