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Mario Antonini
Giorgio Della Rocca
Francesco Pugliese
Livia Pompei
Micaela Maritti
Cecilia Coccia
Alessandro Gasparetto
Raffaello Cortesini

Hemodynamic and metabolic effects of transjugular intrahepatic portosystemic shunt (TIPS) during anesthesia for orthotopic liver transplantation

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M. Antonini (✉) · G. Della Rocca
F. Pugliese · L. Pompei
M. Maritti · C. Coccia
A. Gasparetto
University of Rome "La Sapienza",
Institute of Anesthesiology and Reanimation,
Viale del Policlinico,
I-00161 Rome, Italy
Fax: + 39 6 446 3667

R. Cortesini
University of Rome "La Sapienza",
II Department of Surgery,
Viale del Policlinico,
I-00161 Rome, Italy

Abstract Recently, the transjugular intrahepatic portosystemic shunt (TIPS) has been advocated as a safe bridge to orthotopic liver transplantation (OLT). We retrospectively studied 53 consecutive cirrhotic patients who underwent OLT: 27 patients with TIPS were compared to 26 controls. Hemodynamic and oxyphoretic data (Fick method) were collected during six phases of OLT. There were no significant differences in demographic data and Child-Pugh class, nor in surgical time and blood product requirements before the anhepatic phase between TIPS patients and controls. In the TIPS group, we observed a marked hyperdynamic profile with a lower systemic vascular resistance index, higher cardiac index, and depressed oxygen consumption before native liver removal. During the same period, the TIPS group developed a greater acidosis and was treated with a larger amount of $NaHCO_3$. Following the anhepatic phase, no differences between the two groups were detected. All transplantations were successful, and no complications related to TIPS were observed. These results seem to be the consequence of a reduced liver function reserve with a direct hemodynamic effect due to the TIPS.

Key words TIPS, liver transplantation · Liver transplantation, TIPS · Portosystemic shunt, liver transplantation

Introduction

The transjugular intrahepatic portosystemic shunt (TIPS) is a reliable bridge to liver transplantation in patients with variceal bleeding. The TIPS is an expandable, flexible, metallic stent placed between a branch of the portal vein and the systemic venous system, and it reduces portal pressure and the risk of bleeding. TIPS therapy is highly successful and has a low incidence of complications. Since 1992 the number of liver transplantations in patients with TIPS has increased at our institution. The aim of the present study was to analyze the impact of TIPS on heemodynamics, oxyphoresis, and acid-base status during liver transplantation.

Methods

The records of 53 consecutive cirrhotic patients who underwent orthotopic liver transplantation (OLT) with the same surgical and anesthesiological staff at University of Rome "La Sapienza" between January 1991 and April 1995 were retrospectively studied. This research was approved by the local Ethics Committee, and informed consent was obtained from all patients. The study included 27 TIPS patients (group TIPS) and 26 control patients (group C). Demographic data, etiology of the liver disease, Child-Pugh classification, and relevant clinical findings are shown in Table 1. The temporal distribution of OLT in the two groups is shown in Fig. 1. The indications for TIPS were not selective. TIPS surgery was performed with Wall ($n = 17$), Nitinol-Strecker ($n = 9$), and Palmaz ($n = 1$) stents; six patients required balloon dilatation or an additional stent implantation. All patients showed an immediate reduction in portocaval pressure gradient greater than 50 %; moreover, these patients were completely free of hemorrhage while ascites

Table 1 Demographic data, etiology, Child-Pugh classification, and other diagnostic data in TIPS and control (C) groups (*PHC*, posthepatitis cirrhosis; *PHC-K*, carcinoma in posthepatitis cirrhosis)

Groups		TIPS	C
Patients	Number	27	26
	Sex	23 M–4 f	20 M–6 F
	Age in years (range)	48 (32–62)	42 (28–62)
	Weight in kg (SD)	72 (11)	73 (12)
Etiology	PHC	21	23
	PHC-K	5	2
	Other	1	1
Child-Pugh classification	B	20	21
	C	7	5
Diagnostic data[b]	Variceal bleeding	14 (52 %)	15 (58 %)
	Ascites	17 (63 %)	15 (58 %)
	Renal failure[b]	8 (30 %)	9 (35 %)

[a] Some patients have multiple diagnoses
[b] Creatinine clearance < 50 ml · min^{-1}

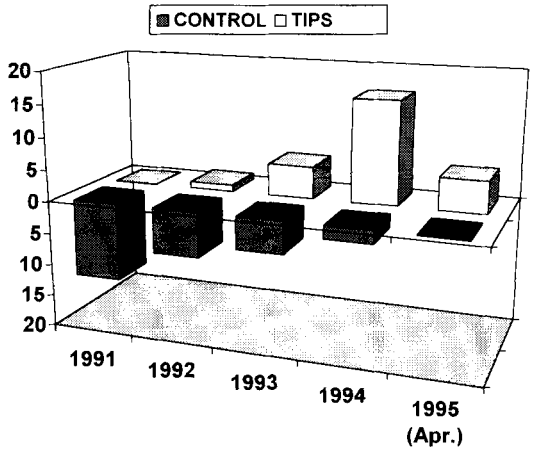


Fig. 1 Temporal distribution of liver transplantation in TIPS and control (*C*) groups

and renal function always improved. The median time interval between the TIPS procedure and liver transplantation was 50 days (range 1–270 days). TIPS patency was assessed by Doppler color ultrasound when patients were scheduled for OLT and confirmed by examination of the hepatectomy specimen.

All patients received oral benzodiazepines as premedication, and general anesthesia was induced with fentanyl (5 μg · kg^{-1}), droperidol (0.04 mg · kg^{-1}), and sodium thiopental (2–3 mg · kg^{-1}). Pancuronium bromide (0.08 mg · kg^{-1}) was used as a muscle relaxant. Anesthesia was maintained with isoflurane (0.8 %–1.2 %) supplemented by fentanyl in O_2 air ($FiO_2 = 0.5$). Mechanical ventilation, with positive end-expiratory pressure equal to 5 cmH_2O, was performed with a Siemens Servo 900D to obtain mild hypocapnia ($ETCO_2$ 4.8–5 kPa). To maintain body temperature, all patients were placed on a heating blanket and all of the intravenous lines were warmed. Lost blood was replaced with packed red cells (RBC) to maintain the hemoglobin level at 10 g · dl^{-1}. Volemic replacement was obtained with normal saline and fresh frozen plasma (FFP) in accordance with filling pressures and laboratory data. Calcium chloride was administered in boluses as indicated by the Ca + + plasma levels. Base excess (BE) values determined sodium bicarbonate administration. A continous infusion of dopamine (2 μg · kg^{-1} · h^{-1}) and aprotinin (500000 u · h^{-1}) was established throughout the entire procedure. Inotropes were never used. Venovenous bypass (Biomedicus) was done in all cases.

Hemodynamic and oxyphoretic data with acid-base status (pH, BE) and $NaHCO_3$ administration were collected during six different phases: basal (after anesthesia induction and before isoflurane administration), hepatectomy, preanhepatic (at onset of venovenous bypass), anhepatic, early neohepatic (5 min after graft revascularization), and neohepatic. Moreover, surgical hepatectomy time and blood product requirements were determined before the native liver was removed. All values are shown as mean (SD). Cardiac output was measured in triplicate by thermodilution. The following parameters were calculated according to body surface area: cardiac index (CI), systemic (SVRI) and pulmonary (PVRI) vascular resistances, arterial oxygen delivery (O_2AVI), and oxygen consumption (VO_2I). These parameters and the oxygen extraction ratio (O_2ER) were obtained by standard computerized formulas (software CLICS Spacelabs). Statistical significance was assessed using Student's *t*-test for unpaired data (SPSS plus). A *P* value less than 0.05 was deemed significant.

Results

All patients in both groups had successful transplantations, and complications due to the TIPS were not detected. The surgical hepatectomy time was 188 min (SD 39) in the TIPS group and 212 min (SD 49) in the control group (P = NS). The total blood product requirements until the anhepatic phase were, respectively, 2.6 l (SD 1.7) in the TIPS group and 2.5 l (SD 1.7) in the C group, without statistical differences. Hemodynamic and oxyphoretic data are shown in Tables 2 and 3. In the basal, hepatectomy, and preanhepatic phases, a significantly lower SVRI was observed in the TIPS group than in the control group. In TIPS patients CI, mean pulmonary arterial pressure (MPAP), and (PAWP) were significantly higher during the hepatectomy phase. VO_2I was lower in the basal and hepatectomy phases in the TIPS group, although O_2ER was lower in the hepatectomy phase only. As for the acid-base status (Fig. 2), base excess and pH were significantly lower in the TIPS group during the preanhepatic phase ($P < 0.01$).

Table 2 Hemodynamic parameters in the different phases of OLT (CI_x cardiac index; HR_x heart rate; MAP_x mean arterial pressure; $SVRI_x$ systemic vascular resistance index; CVP_x central venous pressure; $MPAP_x$ mean pulmonary arterial pressure; $PVRI_x$ pulmonary vascular resistance index)

Phases	Group	CI ($l \cdot min^{-1} \cdot m^{-2}$)	HR (beats $\cdot min^{-1}$)	PAWP (mm Hg)	MAP (mm Hg)	SVRI (dyne $\cdot$ sec $\cdot$ $cm^{-5} \cdot m^{-2}$)	CVP (mm Hg)	MPAP (mm Hg)	PVRI (dyne $\cdot$ sec $\cdot$ $cm^5 \cdot m^{-2}$)
Basal	TIPS	5.2 (1.5)	89 (15)	11 (3)	76 (16)	1152 (337)*	6 (3)	16 (5)	75 (37)
	C	4.9 (1.8)	95 (21)	10 (4)	85 (23)	1394 (421)	6 (2)	16 (5)	101 (67)
Hepatectomy	TIPS	6.3 (1.2)*	99 (10)	13 (3)*	81 (9)	978 (251)*	8 (2)	18 (3)*	70 (23)
	C	5.5 (1.4)	93 (13)	11 (4)	85 (12)	1207 (391)	7 (3)	16 (4)	83 (37)
Preanhepatic	TIPS	6.0 (1.4)	103 (11)	10 (3)	79 (10)	1013 (290)*	8 (3)	14 (4)	66 (31)
	C	5.4 (1.3)	94 (13)	9 (4)	84 (11)	1219 (411)	6 (4)	13 (5)	93 (51)
Anhepatic	TIPS	4.8 (1.1)	104 (10)	7 (3)	82 (11)	1327 (360)	8 (3)	12 (3)	88 (35)
	C	4.3 (0.9)	97 (15)	7 (2)	82 (10)	1492 (437)	6 (2)	12 (3)	101 (42)
Early neohepatic	TIPS	7.1 (1.6)	103 (9)	14 (6)	78 (11)	809 (242)	10 (4)	20 (7)	74 (28)
	C	7.1 (1.6)	100 (14)	13 (5)	78 (14)	819 (253)	10 (4)	19 (6)	78 (39)
Neohepatic	TIPS	6.3 (1.3)	99 (9)	13 (3)	81 (10)	962 (233)	8 (2)**	19 (4)	74 (27)
	C	5.8 (1.3)	97 (14)	11 (4)	79 (13)	1048 (347)	6 (3)	17 (4)	79 (35)

* $P < 0.05$; ** $P < 0.01$

Table 3 Mixed venous saturation (SVO_2), arterial oxygen delivery (O_2 AVI), oxygen consumption (VO_2 I), and oxygen extraction ratio (O_2 ER; Fick method) in the different phases of OLT

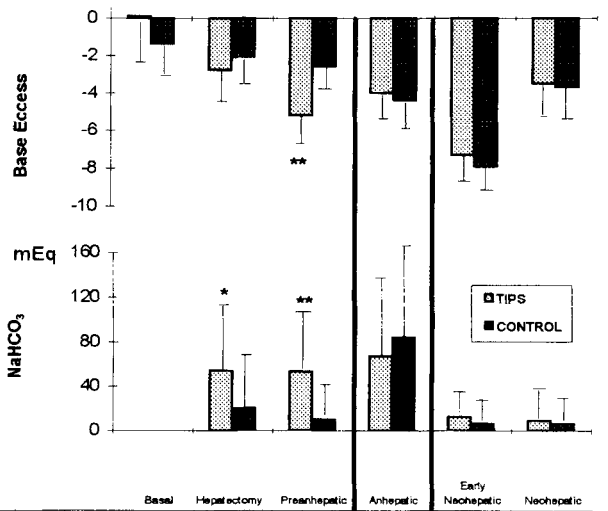
Phases	Group	SVO_2 (%)	O_2AVI (ml $\cdot min^{-1} \cdot m^{-2}$)	VO_2I (ml $\cdot min^{-1} \cdot m^{-2}$)	O_2ER (%)
Basal	TIPS	88.1 (4.6)	747 (245)	98 (19)**	14.1 (4.0)
	C	85.9 (4.9)	839 (300)	122 (31)	15.8 (4.8)
Hepatectomy	TIPS	90.3 (3.6)	895 (216)	105 (19)**	12.4 (3.2)*
	C	88.1 (3.9)	920 (241)	122 (23)	14.5 (4.3)
Preanhepatic	TIPS	90.6 (3.0)	790 (190)	104 (28)	13.4 (2.8)
	C	88.8 (4.8)	824 (218)	113 (36)	14.4 (4.6)
Anhepatic	TIPS	90.4 (2.9)	652 (137)	90 (26)	13.6 (2.6)
	C	89.2 (3.3)	658 (136)	90 (19)	14.1 (3.2)
Early neohepatic	TIPS	89.1 (6.1)	995 (242)	139 (39)	14.7 (5.6)
	C	89.3 (3.7)	1088 (215)	147 (32)	13.9 (4.1)
Neohepatic	TIPS	88.4 (4.0)	851 (176)	129 (31)	15.6 (3.8)
	C	87.1 (4.0)	841 (178)	132 (26)	16.2 (3.6)

* $P < 0.05$; ** $P < 0.01$

Sodium bicarbonate administration (mEq) in the TIPS and control groups was, respectively, 54 (SD 60) vs 20 (SD 49) during the hepatectomy phase ($P = 0.028$) and 53 (SD 54) vs 10 (SD 28) during the preanhepatic phase ($P < 0.001$; Fig. 2). No differences between the two groups were detected in the anhepatic phase or after liver graft reperfusion.

Discussion

The role of TIPS as a bridge to transplantation, if confirmed in the future, will increase the number of OLTs in patients with intrahepatic portosystemic shunts because these stents remain functional longer than 4 years [2]. TIPS reduces portal venous pressure and blood flow through esophagogastric varices, reducing the risk of bleeding. TIPS is of particular value in the treatment of clinical ascites; good results have also been reported in patients with both ascites and hepatorenal syndrome [6], as our experience also confirmed. TIPS is a much less invasive procedure than surgical portosystemic shunt implantation and, because the totally intrahepatic stent is removed with the native liver, there is no further technical complication during liver transplantation [4, 8]. Although Martin et al. [6] and Woodle et al. [9] reported that TIPS markedly reduced surgical operative time and transfusion requirements during OLT, in agreement with Freeman et al. [3] we did not observe any significant differences in either case. On the other hand, deterioration of hepatic function as a result of decreased portal venous perfusion is a potential risk. However, hepatic synthetic function is generally maintained because TIPS improves nutritional status reducing portal hypertension and mobilizing ascites [2]. Martin et al. [6] noted a progressive loss of liver volume, a pro-



		Basal	Hepatectomy	Preanhepatic	Anhepatic	Early Neohepatic	Neohepatic
pH	TIPS	7,43 (0,07)	7,40 (0,06)	7,37 (0,05)*	7,40 (0,05)	7,31 (0,06)	7,40 (0,06)
	C	7,41 (0,06)	7,41 (0,04)	7,41 (0,04)	7,38 (0,05)	7,29 (0,05)	7,40 (0,06)
BE	TIPS	0,1 (4,0)	-2,8 (3,0)	-5,2 (2,6)**	-4,0 (2,3)	-7,3 (2,3)	-3,5 (3,1)
	C	-1,4 (2,7)	-2,1 (2,4)	-2,6 (2,0)	-4,4 (2,4)	-7,9 (2,1)	-3,7 (2,8)
$NaHCO_3$	TIPS	-	54 (60)*	53 (54)**	67 (73)	12 (22)	9 (28)
(mEq)	C	-	20 (49)	10 (28)	84 (84)	6 (21)	6 (22)

Fig. 2 Base excess and $NaHCO_3$ administration during liver transplantation in TIPS and control (*C*) groups. pH is shown in the table at the bottom

longation of caffeine-antipyrine clearance, and an increased incidence of encephalopathy without any significant change in serum bilirubin, prothrombin time, or albumin levels. Although TIPS is a calibrated portosystemic shunt, it presents the disadvantages of the non-selective shunts, i.e., a gradual decrease in hepatic mass and quantitative hepatic function [6]. Therefore, the indication in patients with a poor hepatic functional reserve is highly questionable [1] and may be justified only in emergencies.

The aim of our study was to retrospectively compare intraoperative hemodynamic effects of TIPS during OLT between two groups of cirrhotic patients treated during different periods of time, as we have been experiencing a progressive replacement of cirrhotic patients with TIPS-treated cirrhotic patients as transplant candidates. Nevertheless, we believe that our observations are of some value because: a) both study groups showed comparable severity in liver disease according to their Child-Pugh classification, (b) surgical and anesthesiologic management were identical, (c) hepatectomy time and blood requirements did not show significant differences, and (d) all differences between groups were eliminated with removal of the native liver.

Ozier et al. [7] demonstrated in anesthetized patients that TIPS placement induced an increase in preload, CI, and O_2AVI without changes in VO_2I, measured with indirect calorimetry. Only a few of these observations were confirmed in the preoperative hemodynamic profile of liver transplant patients studied by Lopez-Olaondo et al. [5], who did not find any differences in CI or peripheral resistances between TIPS patients and controls. Our results suggest a specific intraoperative hemodynamic pattern in patients with TIPS before the anhepatic phase showing a marked hyperdynamic profile with a lower SVRI, higher CI, and reduced VO_2I. The significantly higher values of PAWP and MPAP during hepatectomy could have been a direct effect of the intrahepatic stent. As the native liver was removed, the two groups became absolutely identical. The differences in hemodynamic and oxygenation data could only have been due to a higher degree of liver failure in TIPS patients. Nevertheless, TIPS may affect hemodynamic and oxyphoretic parameters in such critical situations as isoflurane anesthesia, positive pressure ventilation, and surgery. As a clinical consequence, a larger amount of sodium bicarbonate was administered in the TIPS group before the anhepatic phase, even though it was not sufficient for a complete correction of acidosis at the onset of venovenous bypass (preanhepatic phase).

In conclusion, TIPS is effective in controlling ascites and bleeding varices in patients with acceptable liver function who are awaiting transplantation. During liver transplantation patients with TIPS become more acidotic before the anhepatic phase and have a marked hyperdynamic circulation as well as a reduced oxygen consumption. The lack of intraoperative surgical complications related to TIPS that was observed in our series gives TIPS a great advantage compared with classic portocaval shunts. The expected decrease in surgical operative time and transfusion requirements have yet to be confirmed.

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