Gut 1996; **39:** 600–604

Haemodynamic adaptation two months after transjugular intrahepatic portosystemic shunt (TIPS) in cirrhotic patients

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Abstract

***Background and Aims*—In portal hypertensive patients, transjugular intrahepatic portosystemic shunt (TIPS) acutely increases cardiac output and exaggerates peripheral vasodilatation. It has been suggested that the worsened hyperdynamic state may progress to high output heart failure. The aim was to evaluate the acute and short-term haemodynamic adaptation to this procedure.**

***Methods*—Systemic, splanchnic, and pulmonary haemodynamics were studied in 15 cirrhotic patients under stable haemodynamic conditions before placement of TIPS, then 15–30 minutes after and two months later. For inclusion in the final analysis, an uneventful post-TIPS at two months follow up and a stable portacaval gradient were required. The following variables were measured or calculated: portacaval gradient; cardiac index (thermodilution); systolic and diastolic mean arterial, atrial, pulmonary arterial, and wedged pulmonary capillary pressures; heart rate; and total peripheral and pulmonary vascular resistances. Blood flow in the shunt was measured using duplex Doppler ultrasound.**

***Results*—The portacaval gradient decreased by 56% and remained stable thereafter. Shunt blood flow was unchanged when measured immediately after TIPS and two months later. Immediately after TIPS there was a pronounced increase in cardiac index (+32%; $p<0.05$) in association with a decrease in peripheral and pulmonary vascular resistance (–21%; $p<0.05$ and –14%; NS). Two months later, whereas the initial rise in cardiac index was attenuated, peripheral vascular resistances remained similar and pulmonary vascular resistances decreased further (–33%; $p<0.05$) compared with immediate post-TIPS values.**

***Conclusions*—Hyperdynamic circulation worsened immediately after TIPS, with a progressive adaptation during follow up. The mechanisms of post-TIPS induced haemodynamic changes include an abrupt volume load resulting from splanchnic decompression and an increased delivery of gut derived vasodilators to the systemic circulation. The persistence of decreased peripheral and pulmonary vascular resistances despite the reduction in high cardiac output two months after TIPS suggests that vasodilatation is not solely a compensatory response to a TIPS induced increased preload. Vasodilatory substances shunted away from the liver probably play an important part in this phenomenon.**

(*Gut* 1996; **39:** 600–604)

Keywords: transjugular intrahepatic portosystemic shunt, haemodynamics, portal hypertension, cirrhosis, variceal haemorrhage, refractory ascites.

Cirrhotic patients with portal hypertension develop a hyperdynamic circulatory state characterised by peripheral vasodilatation, arterial hypotension, expansion of the plasma volume, high cardiac output, and increased regional flows.[1] Portal decompression, achieved either surgically[2] or through transjugular intrahepatic portosystemic stent shunt (TIPS) leads acutely to a further increase in cardiac output and exaggerates vasodilatation.[3–6]

The haemodynamic consequences of TIPS on the systemic circulation have not yet been fully characterised. Some studies suggest that the initial increase in cardiac output found immediately after TIPS tends to decline during subsequent weeks.[4 6] Conversely, one recent report found a progressive worsening of the hyperdynamic circulatory state within one month after TIPS placement.[7] Several factors might explain this discrepancy. In some studies, the initial haemodynamic evaluations were performed under general anaesthesia during TIPS placement; in other papers, changes in liver function or the degree of portal hypertension between the initial assessment and the haemodynamic studies performed several weeks later were not taken into account. Therefore, the reported changes need to be interpreted cautiously as all these variables may influence haemodynamic responses.

Because TIPS requires neither general anaesthesia nor laparotomy, it provides almost ideal conditions for the investigation of the haemodynamic response to portal decompression. Likewise, the assessment of systemic haemodynamics during the manometric controls routinely performed in the follow up of TIPS (to verify the persistence of effective portal decompression) allows a longitudinal evaluation of the longterm haemodynamic adaptation to TIPS.

In the present study we evaluated the effect of TIPS on the splanchnic, pulmonary, and

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Accepted for publication 9 May 1996

systemic circulation immediately after TIPS and two months later in patients with a stable portocaval pressure gradient (PCPG) to characterise the process of haemodyamic adaptation after uncomplicated TIPS. The pattern of sequential systemic haemodynamic changes after TIPS should shed light not only on the pathophysiology of portal decompression but ultimately on the mechanisms implicated in the systemic haemodynamic derangements that accompany portal hypertension.

Methods

INCLUSION CRITERIA

A total of 51 patients underwent TIPS insertion between January 1992 and June 1994. Of them, 15 cirrhotic patients undergoing TIPS were included in this prospective study. The inclusion criteria were: (*a*) a stable haemodynamic condition for at least 24 hours before TIPS placement; (*b*) the absence of pre-existing cardiac failure (clinical examination, electrocardiogram (ECG), chest radiograph, echocardiogram); (*c*) the absence of renal failure or neoplastic disease, vasoactive medication, and active alcoholism.

Inclusion in the final analysis also required: (*a*) an uneventful post-TIPS at two months follow up; (*b*) the absence of a significant change in PCPG ($PCPG_{(2\ mo)}$-$PCPG_{(post\text{-}TIPS)}$ ≤3 mm Hg) during the follow up period.

PATIENT POPULATION

All patients (12 men and three women, mean age 57 (SD 8)); range 49 to 73 years) had cirrhosis established by biopsy. The aetiology of cirrhosis was alcohol related in 10 patients, autoimmune in one, cryptogenic in two, and two patients with HBsAg+. According to the Child-Pugh criteria, there were two class A, eight B, and five C patients. Placement of TIPS was performed for refractory ascites (n=7), variceal bleeding refractory to endoscopic sclerotherapy (n=7), and bleeding secondary to portal hypertensive gastropathy (n=1). During this period, 41 patients were excluded from the present study for the following reasons: shunt stenosis (n=9), death within two months (n=8); use of vasoactive drugs (n=5); active alcoholism (n=2); haemodynamic instability before TIPS (n=15); progressive liver failure (n=1); hepatorenal syndrome (n=1). The present study is part of a protocol approved by the local ethics committee. Patients were informed in detail about the procedures and gave written consent.

TIPS PROCEDURE

In all cases TIPS was performed after sonographic evaluation documenting the patency of the portal vein. Placement of TIPS was carried out as previously described.[8] Briefly, under local anaesthesia the right internal jugular vein was punctured, and through it the right (or middle) hepatic vein was entered with a 9-French Cournand catheter (Cook, Bloomington, IN, USA). Free and wedged hepatic vein pressures were measured and recorded. A modified Ross trans-septal needle (Cook, Bloomington, IN, USA) was employed to create an intrahepatic tract from the hepatic to the right portal vein branch, which was subsequently entered with a guide wire and cannulated. The intraparenchymal tract was dilated by balloon and fixed by deploying either a Palmaz stent (Johnson and Johnson, Warren, NJ, USA), a Wallstent (Schneider, Minneapolis, MI, USA), or both according to the anatomical conditions. The procedure was performed without general anaesthesia. Fentanyl was used for analgesia and sedation during the parenchymal tract balloon dilatation step. The use of radio-opaque contrast medium was kept to a minimum (range 50–150 ml); mesenteric arteriograms were not performed. Adequate stent function was confirmed at the end of the procedure by portography as well as PCPG measurement.

HAEMODYNAMIC EVALUATION

The systemic haemodynamic status was assessed (*a*) immediately before, (*b*) 15–30 minutes after TIPS, and (*c*) two months (62 (SD 7) days) later. A Swan-Ganz thermodilution catheter was used to measure cardiac output, right atrial pressure (RAP), pulmonary arterial pressure (PAP), and wedged pulmonary capillary pressure (WCcP). Pressure measurements were done in duplicate and recorded with a Gould Statham polygraph (Oxnard, CA, USA); cardiac output was the average of five thermodilution curves provided by a microcomputer (Abbott Laboratory, North Chicago, IL, USA). Arterial pressure, pulse rate, ECG, and digital oxygen saturation were monitored continuously. The PCPG (mm Hg), mean arterial pressure (MAP) (mm Hg), cardiac index (l/min/m^2), and total peripheral and pulmonary vascular resistance (TPR, PVR: dyne·s·cm^{-5}) were calculated from standard formulae. Follow up during two months included outpatient clinical and biochemical evaluation every two weeks. Doppler ultrasound was performed every 30 days and included portal venous and stent flow measurements by a trained operator (ML) unaware of PCPG data, as previously reported.[9]

STATISTICAL ANALYSIS

Data are expressed as means (SD). Comparisons between variables measured before TIPS, immediately after TIPS, and two months later were performed using the Wilcoxon signed rank test. $P<0.05$ was considered significant.

Results

CLINICAL AND BIOCHEMICAL DATA

There were no immediate complications after the TIPS procedure. No recurrent bleeding was detected during the two month observation period and patients undergoing TIPS

Hepatic, pulmonary, and systemic haemodynamics before and after TIPS (mean (SD))

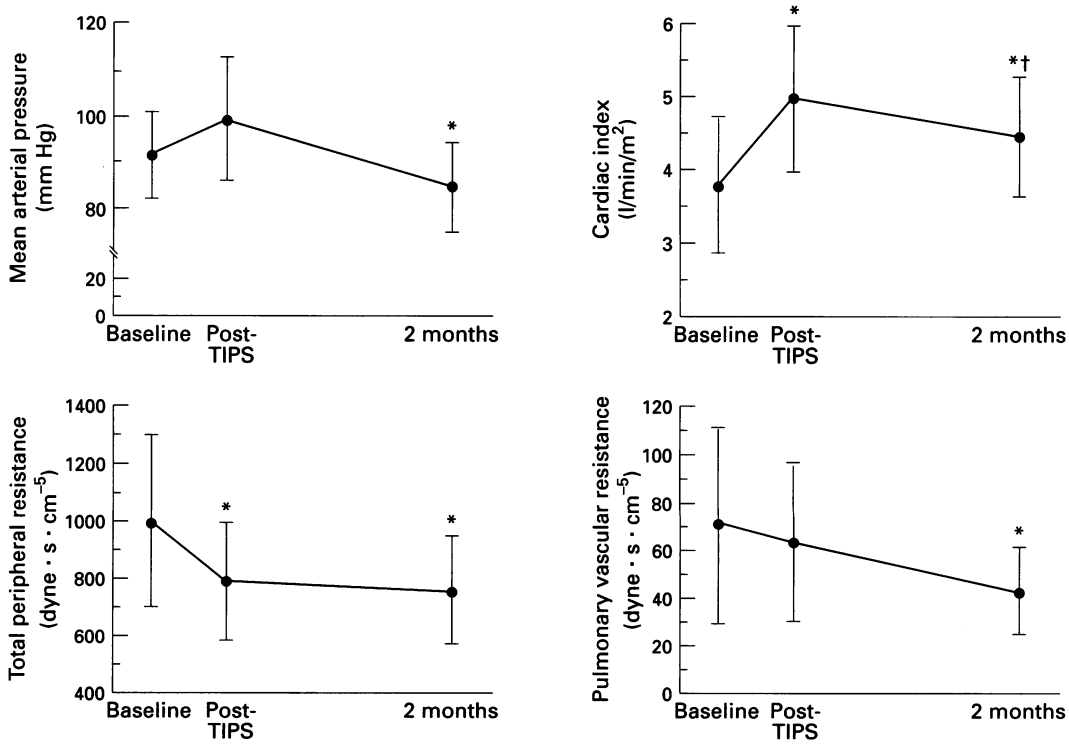
	Before TIPS	*Immediately after TIPS*	*2 Months after TIPS*	*p Value**	*p Value†*	*p Value‡*
Systolic arterial pressure (mm Hg)	130 (15)	144 (20)	129 (15)	0·018	NS	0·041
Diastolic arterial pressure (mm Hg)	73 (9)	77 (13)	63 (10)	NS	0·018	0·002
Mean arterial pressure (mm Hg)	92 (10)	100 (14)	85 (9·7)	NS	0·038	0·003
Heart rate (beats/min)	87 (13)	89 (10)	84 (12)	NS	NS	NS
Right arterial pressure (mm Hg)	3·2 (3·9)	6·9 (4·1)	4·6 (2·1)	0·001	0·025	NS
Wedged pulmonary pressure (mm Hg)	5·3 (1·4)	11·6 (1·6)	11·3 (1·2)	0·001	0·010	NS
Pulmonary arterial pressure (mm Hg)	11·1 (4·9)	18·4 (6·0)	15·0 (3·6)	0·001	0·013	NS
Cardiac index (l/min/m^2)	3·8 (0·9)	5·0 (1·0)	4·5 (0·8)	0·001	0·018	0·036
Portocaval gradient (mm Hg)	23·9 (0·9)	10·6 (2·9)	11·1 (2·9)	0·001	0·001	NS
Total peripheral resistance (Dyne·s·cm^{-5})	999 (301)	793 (206)	761 (183)	0·002	0·005	NS
Pulmonary vascular resistances (Dyne·s·cm^{-5})	74 (41)	64 (33)	43 (18)	NS	0·050	NS
Stent blood flow (ml/min)		1745 (758)	1691 (609)			NS

Wilcoxon signed rank test: *p before *v* immediately after TIPS; †p before TIPS *v* months; ‡p immediately after TIPS *v* 2 months.

for intractable ascites benefited from the treatment although ascites was not eradicated. No other clinical complications were detected in these cases. The Child-Pugh score remained unchanged during follow up (9·0 (2·1)) before TIPS *v* 8·3 (2·2) at two months; NS). Likewise, serum albumin (26·1 (1·0) *v* 28·8 (1·5) g/l; NS), bilirubin (28·6 (4·7) *v* 38·2 (5·6) μmol/l; NS), and International normalisation ratio (1·33 (0·06) *v* 1·36 (0·05); NS) before TIPS and two months post-TIPS were comparable.

SPLANCHNIC, PULMONARY, AND SYSTEMIC HAEMODYNAMICS

The Table and Figure depict the splanchnic, pulmonary, and systemic haemodynamic data at baseline, immediately after TIPS, and at two month follow up. The efficacy of acute portal decompression achieved through TIPS was evidenced by the significant decrease in PCPG (23·9 (1·3) *v* 10·6 (0·8) mm Hg; p<0·001); PCPG remained stable at two months (11·1 (0·7) mm Hg). Stent flow immediately after TIPS was comparable with that obtained at the two month follow up (1745 (202) *v* 1691 (167) ml/min; NS). An initial increase in cardiac index was observed acutely post-TIPS (mean change: +34%; 95% confidence intervals (95% CI) +22% to +46%). It decreased two months later (mean change: −8%; 95% CI 0% to −16%) but remained higher than before TIPS (mean change: +22%; 95% CI +8% to 36%). There was a decrease in TPR immediately after TIPS (mean change: −18%; 95% CI −10% to −26%); at two months, it remained lower than baseline (mean change: −20%; 95% CI −9 to −31%) and similar to post-TIPS values. A tendency for MAP to increase after TIPS placement was noted but the difference was not significant; two months later it decreased to a value lower than baseline (mean change: −7%; 95% CI −1 to −13%) but similar to that after TIPS. There were large increases in RAP and WPcP after TIPS (mean change +214% (95% CI +111% to 317%) and +245% two months later; it was significantly decreased compared with pre-TIPS values (mean change: −20%; 95% CI: −4% to −36%).



*Haemodynamic evolution after TIPS. *p<0·05 v baseline values; †p<0·05 v values immediately after TIPS.*

Discussion

It has been long recognised that cirrhosis is associated with a hyperdynamic circulation characterised by an increased cardiac output and systemic vasodilatation.[1] It has been hypothesised that this hyperkinetic state might be related to increased concentrations of vasodilator substances not metabolised by the liver such as glucagon, vasointestinal polypeptide, prostacyclins, and nitric oxide; a decreased production of vasoconstrictors by the diseased liver could also play a part.[10]

The influence of surgical portocaval shunts on systemic haemodynamics has been evaluated previously[11–13] but interpretation of the data is difficult due to the influence of important confounding variables such as general anaesthesia and surgical stress.

In the present work we found that the increase in cardiac index immediately after TIPS is partially reversed two months after the procedure. Furthermore, the two month haemodynamic evaluation disclosed a dissociation of the TIPS effect on cardiac index and TPR; TPR decreased immediately after TIPS and remained stable thereafter.

Placement of TIPS provides suitable conditions to study the haemodynamic consequences of portal decompression in portal hypertensive patients, based on the absence of other interfacing factors – namely, laparotomy and general anaesthesia. The usefulness of this approach is enhanced if analysis of the haemodynamic pattern after TIPS is restricted to patients free of confounding factors such as infection, active haemorrhage, progressive liver failure, shunt occlusion, or stenosis. To attain the best conditions for comparison, in the present series patients were included only if they were haemodynamically stable at the time of TIPS placement. Similarly, minimal amounts of radio-opaque contrast material and analgesics were used to maintain an adequate haemodynamic baseline. An uneventful post-TIPS follow up period with no changes in hepatic function, unaltered shunt patency, and constant PCPG was also required. We routinely perform the first invasive haemodynamic control two months after TIPS. This time was selected to avoid the initial changes in liver function usually characterised by a transient increase in prothrombin time and serum bilirubin,[14 15] changes which usually regress within four to six weeks. Evaluations carried out after this time point can be blurred by the the progression of the liver disease itself; indeed the degree of liver failure has been shown to be a major determinant of the haemodynamic abnormalities in cirrhotic patients.[16]

Placement of TIPS is followed by an immediate increase in the preload due to the delivery of a high splanchnic blood flow into the systemic circulation. In the present study, splanchnic blood flow was found to be almost twice as high as in normal subjects. In addition, shunting abolished the hepatic extraction of gut derived vasoactive substances normally metabolised by the liver. However, some of these substances are still inactivated or excreted by the lungs.[10] This could explain a dissociation in the effects of TIPS on the systemic and pulmonary circulation found after the procedure. Moreover, cardiac performance is impaired in cirrhotic patients[17] irrespective of the cause of liver disease; in alcoholic cirrhotic patients cardiomyopathy could also influence cardiac function.[18]

Thus the haemodynamic effects after TIPS result from a complex interaction between these different variables. It can be hypothesised that immediately after TIPS, the influence of the volume load is predominant, leading to a large increase in cardiac output, and a rise in RAP, PAP, and WPcP with a compensatory vasodilatory response in the systemic and pulmonary circulations. Haemodynamic adaptation then occurs during the two months after shunting. The decrease in cardiac index found at that time reflects an adaptation of the cardiac handling to the volume preload. Peripheral vasodilatation remains present probably due to shunting of gut derived vasodilatory substances; pulmonary vasodilatation worsens because these substances exert their vasoactive action before their inactivation by the lungs.

The relative influence of volume load and of vasoactive substances on systemic haemodynamics can be seen in animals and cirrhotic patients in the following situations. In rats studied in the early phase after portal vein ligation, vasodilatation was present before the rise in cardiac output had occurred.[19] After liver transplantation in cirrhotic patients, peripheral vasodilatation disappears, presumably because the new liver metabolises gut derived vasodilators, but cardiac output remains increased probably related to a residually enlarged splanchnic vascular bed.[20]

Future studies should be directed at characterising the factors implicated in the haemodynamic changes after TIPS. These include the measurement of vasodilating substances as well as a more detailed assessment of the cardiac function itself.

We thank Dave Guerette and Jacques Bernard for excellent technical support, Bernard Rocheleau for the preparation of the figures, and Manon Bourcier for editing the manuscript. This project was supported by the Medical Research Council of Canada. LS is a recipient of a grant from the University Hospital of Geneva, Switzerland.

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