Cardiovascular Effects of Veno-Venous Bypass during Hepatic Transplantation

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Abstract

***(J. Extra-Corpor. Technol.* 19[3] p. 268-273 Fall 1987, 12 ref). A series of 42 orthotopic hepatic transplant patients were reviewed retrospectively to determine the cardiovascular effects of heparinless veno-venous bypass using a constrained vortex pump. Pump flows and cardiac outputs fell progressively during bypass. During the bypass period the vascular volume became hemoconcentrated as indicated by increases in hematocrit, colloid osmotic pressure, serum osmolality, and serium sodium. The changes in colloid osmotic pressure were inversely related to the bypass pump flow. Transient hemodynamics occurring at the onset of bypass included decreases in temperature, heart rate, arterial pressure, and increases in pulmonary artery pressure, central venous pressure and T wave amplitude. Core temperature changed at the rate of −0.89°C per hour during the bypass period as compared to −0.31°C during the previous phase of the procedure. Veno-venous bypass may improve hemodynamic stability during the anhepatic phase of the procedure, but the abdomen and lower extremities may be less than optimally perfused.**

Introduction

The history of veno-venous bypass begins with the recognition of venous congestion, inadequate urine output, and excessive bleeding from venous hypertension during experimental liver transplantation in dogs.[1,2] The first use of active venous drainage with a pump was reported by Calne et al. in 1979.[3] These investigators heparinized patients who could not tolerate clamping of the inferior vena cava during the hepatectomy, and employed a pump oxygenator circuit that drained blood from the femoral vein and returned it to the femoral artery. Unfortunately, this procedure resulted in uncontrollable bleeding that could not be reversed adequately by protamine. However, they reported increased hemodynamic stability and decreased bank blood utilization from autotransfusion into the oxygenator.

In 1982, Toledo-Pereyra and MacKenzie[4] reported the use of a roller pump to actively decompress the abdomen and lower extremities during canine orthotopic hepatic transplantation. They surgically constructed a portacaval shunt and connected the bypass line to the iliac vein with the return from the pump to the external jugular vein. Abdominal venous pressure was decreased significantly compared to the passive shunt technique, and 24 hour survival improved, which was also attributed to the active bypass circuit.

Denmark et al. in 1953 reported the successful application, in the laboratory, of heparinless bypass using a constrained vortex pump.[5] This was followed by successful application of the same technique in humans by Griffith et al.[6] and Shaw et al.[7] in 1984. Blood was drained from the portal vein and the femoral vein, and returned via the pump into the axillary vein. This mode of veno-venous bypass is the dominant technique employed routinely during clinical orthotopic hepatic transplanatation in many centers.

Calne et al.[8] reported that 2 of 7 patients, in whom veno-venous bypass was instituted using the method reported by Griffith et al.,[6] except for returning the blood to the brachial vein, had bypass flows that were too low to sustain bypass. They proposed that bypass be used only on a few selected patients, not routinely for every transplant, and that the centrifugal pump be used to drain the femoral vein and return the blood to the femoral artery.

The routine use of veno-venous bypass remains a controversial topic. Proponents claim that bypass augments venous return enhancing cardiovascular stability, decreases blood loss, and improves renal function

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during the anhepatic phase.[7] Opponents claim that hemodynamic and metabolic problems resulting from venous stasis can be adequately managed without resorting to bypass.[9,10] Further, they report no excessive intraoperative blood loss from venous hypertension, or postoperative problems with renal function.

Hypothermia during hepatic transplantation is a major concern. The use of an extracorporeal circuit without a heat exchanger may potentiate the heat loss during the anhepatic phase. The classic heat exchanger may be a liability in the sense of exposing unheparinized blood to a large potentially thrombogenic surface area. The possibility of fibrin deposition and subsequent release of emboli into the patient is an unacceptable risk.

The purpose of this review of 52 successive liver transplant patients was to investigate the hemodynamics and changes in body temperature associated with veno-venous bypass.

Materials and Methods

Forty-two consecutive adult patients undergoing hepatic transplantatation for end stage liver disease were reviewed retrospectively. Routine hemodynamic and metabolic monitoring included: radial or brachial arterial pressure measurements; pulmonary artery and central venous pressures, and cardiac output measurements from thermal dilution Swan Ganz catheters; heart rate; simultaneous measurement of ECG leads II and V5; esophageal, rectal and pulmonary artery temperature; mass spectrometer for analysis of inspired and exhaled gases; arterial blood gases; NA^+, K^+, Ca^{++}, glucose, serum and urine osmolarity; and colloid osmotic pressure. Coagulation was monitored by thrombelastography and coagulation profiles.

The bypass circuit consisted of a Bio-Medicus model 520 console and a model 600 Bio-Pump (154 ml volume) with 3/8-inch internal diameter tubing. The inlet tubing to the Bio-Pump was a 7 foot length of Gish Medifex 3/8 × 3/32-inch tubing. The patient return was composed of a 8-inch length of the Gish tubing, the Bio-Medicus Bio-Probe Insert (model DP38), and a 5-foot length of Tygon 3/8 × 3/32 inch tubing. The bypass circuit was primed with 440 ml of room temperature Plasmalyte A.

Gott shunts were placed into the femoral and portal veins, connected together with a Y adapter and to the pump inflow tubing. The blood was returned by the pump into the axillary vein. Bypass was initiated just prior to clamping the suprahepatic cava. Bio-Pump flow was determined by increasing the speed until no further increase in flow could be obtained. Complete sets of measurements related to this study were acceptable only when they were obtained within 20 minutes of the start of the anhepatic phase, approximately 15 minutes following the onset of bypass to allow the settling of hemodynamic transients, within 15 minutes prior to termination of portal bypass, and 10 minutes prior to revascularization of the donor organ. In addition, a series of cardiac outputs and resistances were obtained along with pump flow rates every 10 minutes during the bypass period. Pulmonary artery temperature; heart rate; ECG lead V5; central venous, pulmonary artery and systemic arterial pressures were recorded continuously during the bypass period.

The contribution of the bypass circuit to heat loss was examined further using the standard pump circuit and a constant temperature bath set at 36.9°C (± 0.23). Thermistors were located at the inlet and outlet of the circuit to measure the temperature drop. Room temperature and pump flow were varied.

Results

Upon examination of the data from patients reviewed for this study, 1 patient had bypass terminated after only a few minutes due to inadequate flow through the bypass circuit (less than 1 liter/minute for an adult is deemed inadequate). One patient died during the bypass procedure. Five patients had only femoral vein bypass due to either clotted portal veins or anticipated technical difficulties concerning the placement of the cannula.

Veno-venous bypass was conveniently divided into 4 phases for purposes of this study. The onset of veno-venous bypass (BYPASS) was followed by the termination of portal bypass (PORTAL) about 54.1 minutes (± 14.3, n = 32) later, in those patients in whom full bypass, femoral vein + portal vein, was instituted. The point in the procedure where blood flow was restored to the donor organ (UNCLAMPING) occurred 68.7 minutes (± 13.6, n = 39) after the start of the bypass procedure. The termination of veno-venous bypass (TERMINATION) occurred on the average of 81.5 minutes (± 18.5, n = 39) following the onset of bypass. The pump flows for patients receiving full bypass (portal + femoral veins) and partial bypass (only femoral vein) are given in Table 1. As bypass progressed, the pump flow in the full bypass group decreased. The pump flow for the partial bypass group appears to have increased with time. However, the initial bypass flow of 1.7 liters/minute increased to 2.1 liters/minute at approximately 20 minutes following the onset of bypass, and then deteriorated to 2.04 liters/minute by the time that bypass was terminated.

Upon the initiation of veno-venous bypass, transient hemodynamic effects were recorded that lasted

Table 1

Bio-Pump Rates Associated with the Phases of Full Veno-Venous Bypass. Data Are Expressed as the Mean ± 1 Standard Deviation.

	Bypass (n = 35)	Portal (n = 32)	Unclamping (n = 32)
Bio-Pump Flow (liters/minute)	2.49 ± 0.58	2.25 ± 0.55	1.76 ± 0.52
Difference	−0.21 ± 0.52	−0.53 ± 0.58	
Significance	$P < 0.025$	$P < 0.001$	

Bio-Pump Flow Rates Associated with the Phases of Veno-Venous Bypass for Only Femoral Vein Bypass. Data Are expressed as the Mean ± 1 Standard Deviation.

	Bypass (n = 5)	Unclamping (n = 3)
Bio-Pump Flow (liters/minute)	1.72 ± 0.73	2.04 ± 0.83
Difference	.32 ± 0.23	
Significance	$P < 0.05$	

less than 45 seconds. Mean peak temperature changes in the pulmonary artery of approximately −3.8°C (−10.7% ± 3.4, n = 25) were accompanied by decreases in heart rate (−18.7% ± 6.9, n = 25) and arterial blood pressure (−15.1 ± 8.5, n = 25). The T wave amplitude of the ECG increased (232% ± 122, n = 22) along with the pulmonary artery pressure (15.0% ± 13.3, n = 25) and the central venous pressure (27.6% ± 24.6, n = 25). The magnitude of these changes was related to how rapidly the bypass flow approached the maximum pump flow, and the magnitude of the pump flow relative to the cardiac output. The greater the initial pump flow in relationship to the cardiac output, the more pronounced was the bolus effect of cold volume loading to the myocardium.

The most significant changes in physiologic variables that occurred as a result of veno-venous bypass are illustrated in Table 2. Most notable were the con-

Table 2

Physiological Variables Related to the Phases of Veno-Venous Bypass and the Changes in these Variables Between the Phases. Data are expressed as the Mean ± 1 Standard Deviation.

	Prebypass (n = 34)	Bypass (n = 34)	Portal (n = 26)	Unclamping (n = 26)
Heart Rate (Beats/Minute)	94.04 ± 13.51	93.66 ± 14.94	94.38 ± 15.16	91.93 ± 15.39
Difference	−0.37 ± 10.19	0.03 ± 10.31	−1.89 ± 5.66	
Significance	NS	NS	NS	
Art. Pressure (mmHg)	72.56 ± 10.99	77.49 ± 13.10	71.73 ± 11.64	76.57 ± 15.17
Difference	4.92 ± 13.01	−4.35 ± 11.01	4.31 ± 14.27	
Significance	$P < 0.005$	$P < 0.05$	NS	
Cardiac Output (liters/minute)	7.70 ± 2.45	5.81 ± 1.72	5.14 ± 1.41	4.89 ± 1.58
Difference	−1.89 ± 2.07	−0.57 ± 0.72	−0.64 ± 1.15	
Significance	$P < 0.001$	$P < 0.001$	$P < 0.025$	
Sys Vasc Res (dyne sec/cm^5)	700.8 ± 270.6	996.3 ± 349.4	1016.4 ± 395.6	1179.2 ± 478.2
Difference	295.5 ± 251.6	28.1 ± 204.4	225.7 ± 311.5	
Significance	$P < 0.001$	NS	$P < 0.005$	

tinual decreases in cardiac output and increases in peripheral and pulmonary resistances as bypass progressed. Table 3 indicates the same data for the partial bypass group (femoral vein only), illustrating the same trends. Physiologic control mechanisms maintained arterial pressure well despite continued decreases in cardiac output.

Clinical laboratory data and hemostasis profiles were obtained during the bypass period. Statistically significant changes were noted in the activated partial thromboplastin time (APTT), which decreased 10.5 seconds (± 18.4, n = 39), hemocrit, which increased 1.9 percent (± 1.9, n = 39), colloid osmotic pressure, which increases 1.7 mmHg (± 1.9, n = 26), serum osmolarity, which increased 2.1 mOsm (± 5.1., n = 32), sodium, which increased 1.2 mEq/liter (± 2.1, n = 41), and base deficit, which increased 2.1 mEq/liter (± 1.6, n = 39). Excluding the clotting profile data and the base deficit, the remaining data indicate hemoconcentration of the vascular volume. The increase in base deficit suggested that blood flow to the abdomen and lower extremities was not optimal, or at least not as good as during the preanhepatic phase of the surgical procedure. Changes in all variables were examined for a relationship to blood product during bypass, changes in cardiac output during bypass, and changes in pump flow. A highly significant linear relationship was uncovered between changes in colloid osmotic pressure and pump flow, demonstrating that as pump flow decreased, the colloid osmotic pressure increased.

In an attempt to identify the physiologic factors that determined the pump flow, in addition to the routine continuous measurements, pump flows and cardiac outputs were recorded every 10 minutes during the bypass period from 12 patients. A best subset regression was performed on the data from each patient and for all patients grouped together. There were no simple linear relationships, or simple linear combinations of variables that adequately accounted for the pump flow. For any individual patient a single factor could be correlated with pump flow, but the factor was different for each patient. When the patients were grouped together the strongest contributor to the correlation was cardiac output, which had a correlation coefficient of 0.50.

Heat loss during bypass was examined by comparing the rate of temperature change prior to bypass, with the temperature change that occurred during bypass. The pulmonary artery temperature prior to bypass decreased at a rate of 0.31°C/hr (± 0.17, n = 24) compared to 0.89°C/hr (+ 0.37, n = 24) during bypass.

In addition, a constant temperature water bath was set up in conjunction with the bypass circuit. The temperature drop across the bypass circuit was measured under different pump flow rates and different room temperatures. The heat loss from the circuit was

Table 3

Physiologic Variables Related to the Phases of Veno-Venous Bypass without Portal Bypass, and the Changes in these Variables between the Phases. Data Are Expressed as the Mean ± 1 Standard Deviation.

	Prebypass (n = 5)		Bypass (n = 5)		Unclamping (n = 4)
Heart Rate (Beats/Minute)	105.32 ± 27.72		100.46 ± 21.43		93.88 ± 22.97
Difference		−4.86 ± 7.75		−3.12 ± 9.34	
Significance		NS		NS	
Art. Pressure (mmHg)	73.84 ± 12.14		71.36 ± 17.73		77.0 ± 13.14
Difference		−2.48 ± 9.51		12.18 ± 10.61	
Significance		NS		$P < 0.025$	
Cardiac Output (liters/minute)	8.26 ± 2.74		5.34 ± 1.81		4.70 ± 1.34
Difference		−2.92 ± 1.57		−0.85 ± 1.18	
Significance		$P < 0.001$		NS	
Sys Vasc Res (dyne sec/cm^5)	669.2 ± 222.7		1001.4 ± 414.6		1191.1 ± 390.9
Difference		332.2 ± 356.5		323.8 ± 181.9	
Significance		$P < 0.05$		$P < 0.01$	

calculated from the data obtained using distilled water in the circuit. Actual heat loss from the circuit, if blood had been flowing through it, was estimated by substituting the specific heat and specific gravity of blood into the circulation. The estimated heat loss for blood flowing through the circuit at a rate of 2.5 liters/minute and a room temperature of 18.3°C, is approximately 5 kilocalories per minute.

Discussion

The hemodynamic data presented above is in good agreement with the more general view of bypass presented by Shaw et al.[7] The most significant finding from the data presented here is that while veno-venous bypass may provide enhanced cardiovascular stability during the anhepatic phase, bypass does not result in perfectly adequate perfusion of the abdomen and lower extremities. Falling cardiac outputs and bypass flows while arterial pressure is maintained are indicative of physiologic control mechanisms responding to decreased circulating blood volume. Hemoconcentration also supports the concept of shrinking circulating blood volume, possibly by filtration of fluid out of the intravascular space in the gut. Bypass flow has been shown to effect the changes in colloid osmotic pressure during the bypass period. Low flows, that are responsible for the largest changes in colloid osmotic pressure, probably result in increased venous pressure in the gut causing infiltration of fluid out of the vasculature into the interstitial space. Increased venous pressure would also decrease the pressure gradient across the vasculature and hence the blood flow, with the possible result of an accumulating base deficit from hypoperfusion.

Transient cardiovascular effects noted upon initiation of veno-venous bypass are related to cold volume loading of the heart, and possibly acute hemodilution of the coronary circulation, that results in a transiently hypoeffective heart. The brief duration of these effects does not cause a problem with the management of the patient.

An unsuccessful attempt was made to directly identify measurable physiologic parameters that would determine the bypass flow. In this regard, a reasonable hypothesis would be that pump flow is determined by cannula and vessel size that drain the venous system, along with the regional mean circulatory filling pressure. This is analogous to the relationship between cardiac output, resistance to venous return, and the mean circulatory filling pressure, as described by Guyton et al.[11] Unfortunately, regional mean circulatory filling pressure cannot be measured directly in these patients, nor can it be computed from the measured parameters.

The apparent improvement in the APTT during bypass could not be related to blood product administration, but might be a result of activation of factors V and VIII as they came in contact with the surfaces of the bypass tubing.

While the almost three times greater rate of fall in patient temperature during bypass could be related to multiple factors—including decreased metabolism from removal of the liver and possible hypoperfusion of the bowel; and the cold donor organ sitting in the body cavity—the heatloss from the extracorporeal circuit may be significant or even dominant. Data obtained from investigation of the flow rate and room temperature effects upon heat loss from the bypass circuit, indicate that even under the best conditions with low pump flow rates, the heat lost from the bypass circuit exceeds the normal basal heat production of an unanesthetized 70 Kg man. The magnitude of heat loss from the bypass circuit is a function of the pump flow and the room temperature.

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Questions from the Audience

Question: Frank Scalia, Monroe, LA: Regarding temperature loss with your patient, how are you reinfusing or keeping up with the volume with the patient? Are you using a RID system?
Response: Actually, we do have a RID system. A home brewed RID system that does heat the blood up to 37 degrees.
Comment: When I was in Virginia we were doing livers. We incorporated a heat exchanger in our RID system, which worked fairly decently.
Response: We have a system that uses a cardioplegia system with a heating coil in the reservoir that we're using. We keep it warm all the time.