Physiologic Determinants of Operative Survival After Portacaval Shunt

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Twenty cirrhotic patients with bleeding from esophageal varices were studied before, during, and after portacaval shunt. There were 12 survivors and eight nonsurvivors. Preoperative determination of hepatic function and classification by Child's criteria correctly predicted outcome only in those with very good and those with very poor hepatic function. However, the majority of patients had intermediate liver function, and their operative survival could not be predicted on this basis. Other parameters, however, did distinguish between survivors and nonsurvivors. Survivors had better preoperative cardiac contractility, shorter operations, less severe preoperative and intraoperative blood loss, and fewer emergency operations. Intraoperatively, survivors maintained cardiac index and oxygen delivery while nonsurvivors did not. After operation, survivors had increased cardiac index, oxygen delivery, and oxygen consumption above preoperative values, while nonsurvivors failed to attain this.

Analysis of these data suggests that determination of preoperative hepatic function alone will not provide accurate prediction of outcome from portacaval shunt, because there are multiple factors that determine outcome. The determinants identified in this study were 1) preoperative hepatic function, 2) degree of hemodynamic compensation from preoperative bleeding and shock, 3) magnitude of the intraoperative oxygen deficits, 4) hemodynamic reserve allowing for the compensatory postoperative state, and 5) nutritional status.

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THE PORTACAVAL SHUNT operation imposes a major physiologic stress upon the cirrhotic patient that frequently results in significant morbidity and mortality. Therefore, there has been considerable interest in identifying those factors that are important determinants of survival. The penultimate goal is to select for surgery those patients who are most likely to survive, but without excluding the majority of patients who would benefit from the operation.

Most studies on risk factors for portacaval shunt have identified preoperative hepatic function as the most important determinant of survival. Linton[1] first emphasized the importance of preoperative liver function. Child and Turcotte[2] subsequently identified a number of clinical factors that they felt reflected hepatic functional reserve, and they used these to stratify patients into risk groups. Child's classification of hepatic reserve has remained the standard for determining the risk of portacaval shunting, although there is some controversy whether certain measures of hepatic function may be better indicators than others.[3]

Nevertheless, success in identifying patients who will recover from the operation based on Child's classification has been disappointing.[4] Although patients with very good preoperative hepatic function are likely to survive and patients with very bad preoperative hepatic function are likely to die, most patients fall somewhere in between the extremes of hepatic function; these patients have an intermediate operative mortality of 40 to 60%.[5,6] Thus, except in the extremes, consideration of preoperative hepatic function has not been a good predictor of survival.

That a static profile of preoperative hepatic function does not accurately predict survival should not be surprising. Also relevant to survival must be the dynamic aspects of intraoperative hepatic damage and postoperative repair. Furthermore, liver function both affects and is dependent upon the patient's overall physiologic milieu. Consideration of preoperative hepatic function alone should not then be expected to determine accurately the eventual surgical outcome.

Del Guercio and his group[7] first studied the systemic hemodynamic responses of patients undergoing portacaval shunts. They demonstrated increased cardiac output after operation, and related this to outcome. Work from this laboratory on other general surgical operations has examined the physiologic responses to operations in general.[8] The results of these studies suggest that metabolic debts often accumulate intraoperatively be-

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cause of inadequate tissue oxygenation. The postoperative period in surviving patients is characterized by increased cardiac output and oxygen consumption; it is felt that these increases may represent physiologic compensation necessary to recover from intraoperative cellular and organ damage resulting from inadequate intraoperative cellular oxygenation. If these physiologic patterns pertain to cirrhotics undergoing surgery, then there may be parameters that can be identified, besides hepatic function, which are relevant to survival from portacaval shunt.

The present study describes clinical, hemodynamic, and oxygen transport variables in a series of cirrhotic patients undergoing portacaval shunt. Data are analyzed to determine the relative importance and the interrelationships of hepatic reserve and systemic hemodynamic responses to survival from portacaval shunt.

Methods

Clinical Series

Twenty consecutive portacaval shunt operations performed at Harbor/UCLA Medical Center between 1977 and 1980 were studied. All patients had bleeding from esophageal varices caused by alcoholic cirrhosis. All of the patients were admitted to the hospital on an emergent basis with upper gastrointestinal bleeding. Histories and physical examinations indicated the presence of alcoholic cirrhosis, and liver biopsy confirmed this in selected cases. Acute alcoholic hepatitis was ruled out by serum transaminase determination and liver biopsy; no patient in this series had acute alcoholic hepatitis. Each patient had upper fiberoptic endoscopy performed during active bleeding, and each patient in this series had bleeding esophageal varices confirmed at endoscopy.

Patients presenting with variceal hemorrhage were admitted to the medical service, and aggressive medical therapy was initiated. This consisted of blood volume replacement, continuous intravenous pitressin infusion, and balloon tamponade with either a Linton or a Sengstaken–Blakemore tube. Surgical consultation was obtained at the discretion of the medical physicians; only a small percentage of patients presenting to this hospital with variceal bleeding had portacaval shunts.

Ten patients were operated upon as an emergency procedure because they continued to bleed despite maximum medical management; their mean age was 52.1 ± 3.0 (SE) years. These patients had multiple blood transfusions and usually had periods of hypotension prior to operation. Eight of the ten patients died after operation.

Ten patients responded to medical management, and bleeding stopped, but they were referred for surgery; their mean age was 44.8 ± 2.6 years. The indications in these cases were either that the patients had multiple previous bleeding episodes, or that the current bleeding episode required a large number of transfusions and was life-threatening. Following control of bleeding, these patients underwent a period of hospitalization to optimize nutrition, following which portacaval shunt was performed. Each of these ten patients survived and was discharged from the hospital.

Operative Management

All patients had general endotracheal anesthesia. The primary anesthetic agent was ethane in 13 cases, intravenous ketamine in four cases, and intravenous narcotics in three cases. The anesthesiologist had access to all measurements taken, and intraoperative therapy was titrated to optimize filling pressures and cardiac output.

The portacaval shunt was performed as an end-to-side anastomosis in 18 cases. There was one side-to-side anastomosis, and one H-graft. Portal pressure measurements were made with a water manometer through an omental vein or directly through the portal vein prior to and after construction of the shunt; simultaneous inferior vena cava pressure was also obtained in the same manner.

Following operation the patients were transferred directly to the surgical intensive care unit. Endotracheal intubation and mechanical ventilation was maintained after operation until adequate respiratory function was ensured. Intravenous fluids were titrated in an attempt to optimize blood pressure, urine output, and filling pressures (*i.e.*, normal blood pressure, urine output greater than 30 ml/hour, CVP and wedge pressure 10 to 15 mmHg).

Physiologic Measurements

In the immediate preoperative period, patients were classified as per Child and Turcotte[2] to estimate hepatic functional reserve. Clinical evaluation for the presence of ascites and encephalopathy was performed, the nutritional state was assessed, and bilirubin and albumin levels were drawn.

Intravenous catheters were placed and control hemodynamic measurements were made before operation in the intensive care unit. Arterial catheters were inserted in the radial arteries, and Swan–Ganz triple lumen flow-directed catheters were placed into the pulmonary arteries through the subclavian or jugular vein percutaneously. Cardiac ouput was measured by thermodilution using a cardiac output computor. Each set of

TABLE 1. *Preoperative and Intraoperative Clinical Features*

	Survivors	Nonsurvivors	P-Value
Days between bleeding and operation	25 ± 2.9*	3.5 ± 1.7	0.005
Preoperative blood transfusions (# units)	4.0 ± 0.5	12.2 ± 2.2	0.005
Duration of operation (hours)	5.31 ± 0.47	6.01 ± 0.56	—
Intraoperative blood loss (milliliters)	1850 ± 470	3730 ± 640	—

* Values are mean ± standard error of the mean.

measurements consisted of systemic and pulmonary arterial pressures, central venous and pulmonary arterial wedge pressures, cardiac output, arterial and mixed venous blood gases, hematocrit, hemoglobin, and oxygen saturation. These data sets were obtained at frequent intervals during the preoperative and intraoperative periods, and then repeated after operation when the patient returned to the intensive care unit and on the first postoperative day. Systemic vascular resistance, oxygen delivery (arterial oxygen content × cardiac index), oxygen extraction ration, and oxygen consumption were calculated using previously described standard formulas. All flow-related variables were indexed to preoperative body surface area.

After operation, the patients' clinical courses were documented, including days on the ventilator, sequential serum bilirubin determinations, and the occurrence and sequence of complications.

Statistical Analysis

The mean values for each variable were obtained for each patient in the preoperative, intraoperative, and postoperative periods. The mean and standard error of the mean for surviving and nonsurviving patients were calculated from the mean values of individual patients. Statistical significance of the values at each of the time periods was compared with their own preoperative control values within each group using the t-test for paired distributions. Statistical significance of comparisons between survivors and nonsurvivors was determined by the t-test for unpaired distributions.

Results

Preoperative Status

Preoperatively surviving patients had fewer blood transfusions, and were less frequently in shock. In addition, survivors had longer delays between the onset of variceal bleeding and the operation than did nonsurvivors, most of whom had portacaval shunt performed during the time of active variceal bleeding (Table 1).

Table 2 lists the clinical indicators of preoperative functional hepatic reserve. The nonsurvivors tended to have worse indices; but none of the variables alone had statistically different mean values for survivors and nonsurvivors. Combining the individual variables into Child's classification improved their discrimination somewhat; of the nonsurvivors, four patients were classified Child's Class B while four patients were Child's Class C. Of the survivors, five patients were classified Child's A and seven patients Child's B.

Preoperative hemodynamic measurements in both survivors and nonsurvivors revealed that cardiac index was greater than normal, and systemic vascular resistance was below the normal range. Before operation the survivors' mean arterial pressure was higher; this was associated with slightly higher cardiac index and systemic vascular resistance (Fig. 1).

Preoperative wedge pressures of the two groups were nearly equal. However, cardiac index was lower in nonsurvivors despite lower afterload estimated by systemic resistance. This is consistent with poorer preoperative ventricular contractility in nonsurvivors.

Although mean preoperative oxygen delivery was slightly lower in nonsurvivors, oxygen extraction was slightly higher, so that oxygen consumption was similar (Fig. 2).

Intraoperative Period

Nonsurvivors tended to have longer operations with more blood loss than did survivors (Table 1).

Intraoperative portal pressure measurements are listed in Table 3. Although portal pressures prior to portacaval shunting were somewhat higher in surviving patients, both systemic blood pressure and inferior vena caval pressures were also higher in survivors at the time of portal pressure measurement. Following the shunt, both groups fell to similar portal pressures.

Intraoperative hemodynamic monitoring showed that cardiac index was significantly lower in nonsurvivors

TABLE 2. *Preoperative Indicators of Hepatic Reserve*

	Survivors (N = 12)	Nonsurvivors (N = 8)
Bilirubin (mg/dl)	1.6 ± 0.3*	3.9 ± 1.8
Albumin (mg/dl)	3.1 ± 0.14	3.2 ± 0.21
Encephalopathy (Number (%))	1(8%)	2(25%)
Ascites (Number (%))	5(41%)	4(50%)
Prothrombin Time (seconds)	13.7 ± 1.6	14.2 ± 2.1

Preoperative clinical indicators of hepatic functional reserve at the time of portacaval shunt.

* Values are means ± standard errors. None of the differences are statistically significant.

than survivors during operation; in fact, cardiac index tended to increase intraoperatively in survivors and decrease in nonsurvivors as compared with preoperative values. Mean wedge pressures were slightly lower intraoperatively in nonsurvivors, suggesting that decreased preload as well as decreased contractility may have contributed to decreased cardiac index (Fig. 1).

Both survivors and nonsurvivors decreased oxygen consumption during operation. These decreases in oxygen consumption were to similar levels, despite significantly higher oxygen delivery in surviving patients. Oxygen extraction decreased in both groups, but more in survivors, to account for the decreased oxygen consumption (Fig. 2).

Postoperative Period

After operation, survivors were hospitalized a mean of 13 ± 4 days. Six of the 12 patients had uncomplicated postoperative courses, while six patients had one or more complications including ascites in four patients, encephalopathy in three patients, pneumonia in two patients, and staphylococcal sepsis from an infected radial

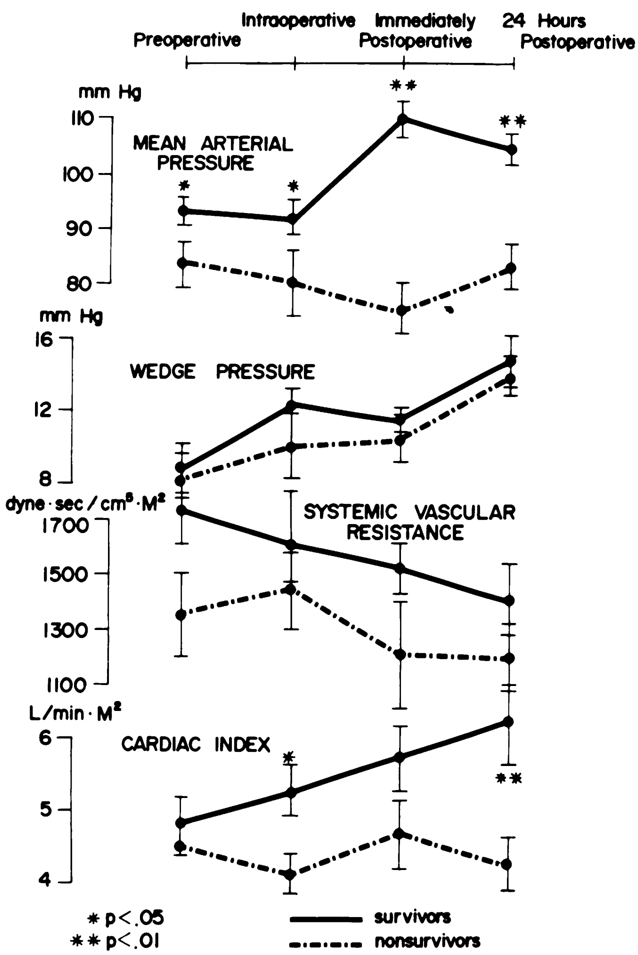

FIG. 1. Sequential determinations of hemodynamic variables of survivors and nonsurvivors are compared. Values are mean ± SE of the mean. Note the intraoperative and postoperative differences in cardiac index values.

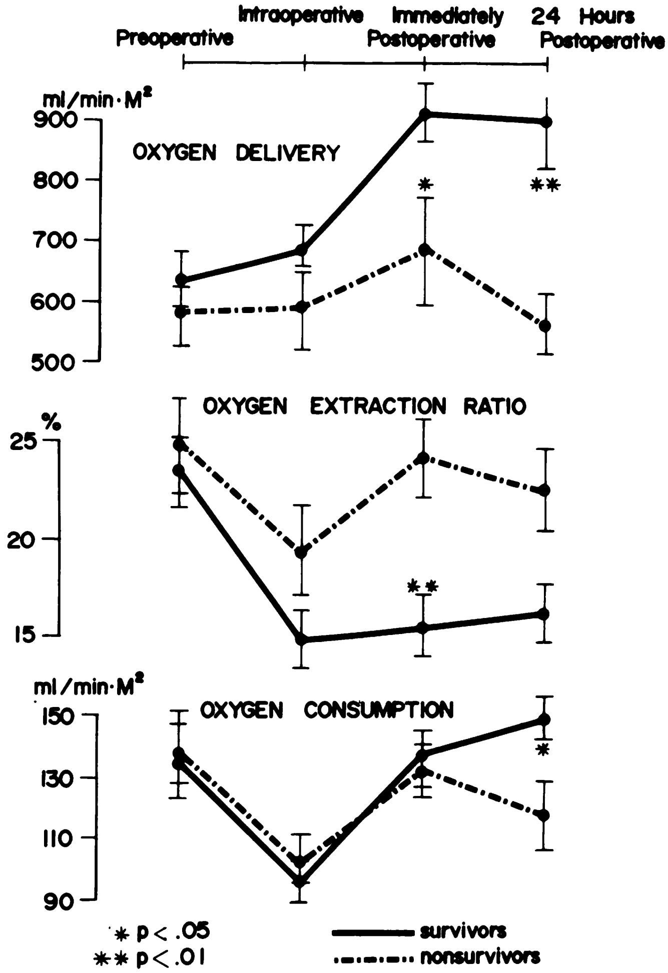

FIG. 2. Sequential determinations of oxygen transport variables are compared in survivors and nonsurvivors. Shown are mean ± SE. Note especially the postoperative increases of oxygen delivery and oxygen consumption in surviving patients.

TABLE 3. *Intraoperative Portal Pressures*

	Survivors	Nonsurvivors	P-value
Preshunt portal pressure ($cm\ H_2O$)	45 ± 1.5*	39 ± 2.5	0.05
Preshunt inferior vena cava pressure ($cm\ H_2O$)	18 ± 3.2	14 ± 3.8	—
Postshunt portal pressure ($cm\ H_2O$)	21 ± 1.6	20 ± 11	—
Postshunt inferior vena cava pressure ($cm\ H_2O$)	20 ± 3.0	16 ± 3.6	—

Portal and inferior vena caval pressures taken before and after portacaval shunts.

* Values are mean ± SE.

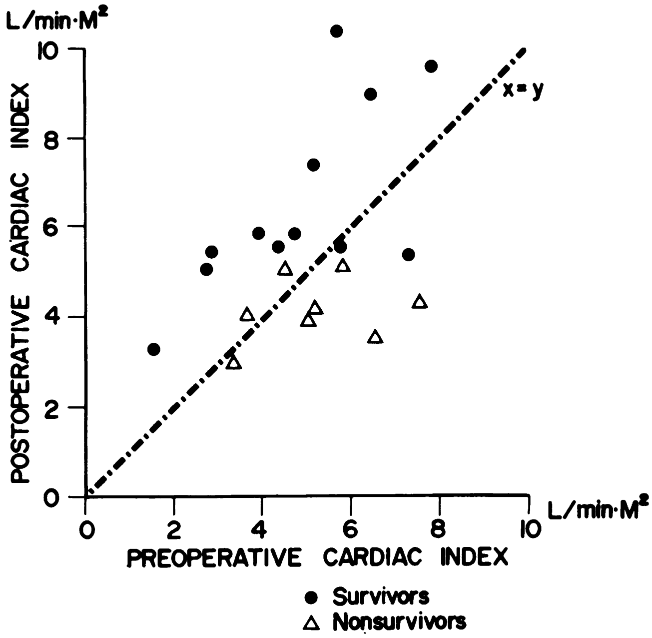

FIG. 3. The maximum postoperative cardiac index is plotted against the preoperative cardiac index for each of the 20 patients. Note that nearly all surviving patients increased cardiac index above preoperative values while few nonsurvivors accomplished this.

artery catheter in one patient. Nine of the survivors were extubated within 24 hours following operation, while three patients were maintained on the ventilator three to eight days. Bilirubin levels reached an average peak of 4.2 ± .8 mg/dl after operation, usually on the fourth to eighth postoperative day, then progressively decreased; at discharge the mean bilirubin was 2.2 ± .6 mg/dl, only slightly higher than preoperative levels.

Nonsurvivors died on the average of 12.4 ± 2.7 days following operation. There were an average of 4.0 ± 0.4 complications per patient prior to death; respiratory failure, jaundice, ascites, and hepatic coma were the most common. At death, the mean bilirubin was 26 ± 6 mg/dl.

Hemodynamic data are illustrated in Figures 1 and 2. During the postoperative period, survivors increased mean arterial pressure, while the mean arterial pressure of nonsurvivors was significantly lower. Systemic vascular resistance decreased after operation in both groups, compared with preoperative values. The mean postoperative cardiac index increased over preoperative values in survivors (Fig. 3). Thus, cardiac index was significantly greater in survivors than in nonsurvivors, especially on the day following surgery.

Similarly, oxygen delivery increased markedly over preoperative levels in survivors, and was much higher than in nonsurvivors, who failed to increase oxygen delivery above preoperative values. Oxygen extraction was initially higher in nonsurvivors so that oxygen consumption was maintained near preoperative levels. However, by the day following operation, oxygen extraction in nonsurvivors had decreased somewhat, and oxygen consumption had fallen to below preoperative levels. On the other hand, survivors increased their oxygen consumption above preoperative values, and had significantly higher oxygen consumption than did nonsurvivors on the day following operation.

Discussion

Evaluation of preoperative hepatic function was not helpful in predicting survival from portacaval shunt for the majority of the patients in this study (Table 4). No single measure of hepatic function discriminated survivors from nonsurvivors, and the combination of these into Child's Classification predicted only for those with the extremes of hepatic function; that is, those with extremely good parameters survived, while those with extremely poor parameters did not. The majority of the patients, who fell between these extremes, had a 64% chance of survival; thus, this approach was not very useful as a predictor for these patients. The data from the current study help explain why evaluation of preoperative hepatic function should not be expected to accurately predict survival. In addition to preoperative hepatic reserve, there are other important physiologic considerations that are essential for survival from the portacaval shunt operation.

The intraoperative period is a time when severe stress on body metabolism is sustained. This metabolic injury is not only to the liver, but to other cells and organs in the body as well. The metabolic stress is reflected by decreased oxygen consumption intraoperatively. This decreased oxygen consumption is, in part, caused by decreased metabolic demands during anesthesia. However, the decreased oxygen consumption appears to be more than just decreased demands, and to represent inadequate cellular oxygenation, leading to cellular and organ damage.[8,9] Surviving patients have a physiologic

TABLE 4. *Child's Classification: Relationship to Survival*

Child's Classification	Number of Patients	% of Survival
A	5	100
B	11	64
C	4	0

The relationship of stratification by Child's Classification and survival. Note that the majority of patients were classified as Child's B, and that survival was not predicted accurately in these class B patients.

compensatory state after operation: they stimulate cardiac output to increase blood flow above preoperative levels, thereby providing increased supply of oxygen and nutritional substrates to damaged tissues, and thereby allowing metabolic repair of hypoxic damage.

This physiologic pattern held true in this series. Organ damage occurred in all patients, even survivors, whose serum bilirubin invariably increased after operation. However, in surviving patients there were increases in cardiac index and oxygen consumption after operation, representing a compensatory state, and subsequent improvements in hepatic function followed. Nonsurvivors may have had more severe insults intraoperatively, since they had longer operations with more blood loss. Thus, their cumulative intraoperative oxidative deficits may have been greater. In addition, nonsurvivors failed to increase cardiac index and oxygen consumption after operation. Unlike survivors who had improvement in hepatic function, nonsurvivors failed to recover from the surgical metabolic insult and had progressive hepatic failure. Furthermore, it was not only the liver that was so affected; each of these patients had sequential failure of other vital organs as well.

There were several reasons why nonsurvivors may have failed to increase cardiac index and oxygen consumption. The first is that nonsurvivors before operation had poorer cardiac reserve than did survivors. Cardiac reserve in the cirrhotic patient undergoing operation has special importance, because even before operation these patients have increased cardiac index, and a subsequent postoperative increase in cardiac index above preoperative levels requires supernormal cardiac reserve capacity. There are several possible explanations for decreased cardiac reserve in the nonsurvivors. First, the mean age of nonsurvivors was higher, and thus their intrinsic cardiac function may have been limited. Secondly, most of the nonsurvivors had just been subjected to upper gastrointestinal bleeding and shock prior to operation; under these circumstances ventricular function may have been severely compromised.[10]

Besides failing to adequately increase cardiac index, there are additional reasons why nonsurvivors were unable to increase oxygen consumption; these relate to peripheral oxygen transport. Since the stress of operation may have been superimposed upon the stress of the preoperative variceal bleeding, there may have been resulting microcirculatory flow maldistribution limiting cellular oxygenation.[11] Further, the combined insults of shock and surgery may have caused additional severe cellular damage, so that the requirements for repair were even greater, while the ability of the cells to utilize oxygen were even less. Finally, the multiple preoperative blood transfusions may have altered the P_{50} of hemoglobin dissociation, so that circulating oxygen was less available to the tissues.

Thus, the identifiable physiologic determinants of survival from the portacaval shunt operation are as follows.

1. *Preoperative hepatic reserve.* The liver suffers an insult during portacaval shunting, not only from loss of portal venous blood flow, but also from decreases in arterial flow during operation, and from a poorly understood generalized metabolic insult from surgery and anesthesia. The reserve capacity of the liver is clearly important for recovery from these intraoperative insults.
2. *Compensation from preoperative bleeding and shock.* Metabolic damage results from preoperative variceal bleeding and shock; the metabolic stress of operation itself constitutes a second major insult which requires additional major physiologic compensations. A combination of preoperative and intraoperative insults may cause cellular and organ damage that is too great for repair, or for which the potential for the necessary physiologic compensation is not adequate. Therefore, a therapeutic delay between the bleeding and the operation to allow metabolic recovery is of benefit.
3. *Degree of oxygen deficit intraoperatively.* A brief operation with limited blood loss represents a shorter period of metabolic stress, and will require less compensation for recovery. The anesthetic management also plays an important role, but the choice of anesthetic agents and techniques that minimize metabolic stress remains unclear. Certainly aggressive physiologic monitoring to optimize intraoperative blood flow and oxygen consumption seems warranted.
4. *Hemodynamic reserve.* The ability of the patient to compensate from the stress of the portacaval shunt operation requires considerable cardiopulmonary reserve in order to increase cardiac index and oxygen delivery to supernormal levels. Furthermore, the peripheral oxygen transport system including the arterial oxygen content, the oxyhemoglobin dissociation characteristics, the microvascular flow, the interstitial diffusion gradients, and the intracellular metabolic machinery, all must be in a state allowing increased metabolic activity to repair incurred damages in multiple organ systems.
5. *Nutritional state.* Although not directly addressed by this study, it is clear from other studies that the preoperative nutritional state of these patients may affect survival.[12] Patients who are malnourished before operation or who become so after operation may lack substrate and energy necessary for metabolic repair and will, therefore, experience multiple organ failure.

In summary, survival from the portacaval shunt operation is a complex process. Although preoperative evaluation of hepatic function is extremely important, it cannot be expected to predict survival accurately because other physiologic variables are also important. Evaluation of these other variables may improve the ability to predict survival and, thus, to select patients for operation more appropriately. Furthermore, a fuller understanding of the physiologic interactions occurring during and after portacaval shunt should help direct therapy to improve preoperative management, to minimize intraoperative damage, and to optimally support postoperative compensations.

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