IMPORTANCE OF PREOPERATIVE LIVER FUNCTION AS A PREDICTOR OF SURVIVAL IN PATIENTS SUPPORTED WITH THORATEC VENTRICULAR ASSIST DEVICES AS A BRIDGE TO TRANSPLANTATION

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Patient selection is crucial for the success of ventricular assist devices as a bridge to heart transplantation. *Purpose:* The objective of this study was to identify preoperative markers for survival and end-organ recovery in patients having a ventricular assist device. *Methods:* A retrospective study was performed on 32 severely ill patients with end-stage cardiac failure being mechanically bridged to heart transplantation with the Thoratec Ventricular Assist Device System (Thoratec Laboratories Corporation, Pleasanton, Calif) in a single center between 1984 and 1995. The preoperative cardiac index averaged 1.6 L/min per square meter with a pulmonary capillary wedge pressure of 29 mm Hg. Because of a high incidence of hepatic or renal dysfunction, or both (total bilirubin: 3.5 ± 6.2 mg/dL; creatinine: 2.0 ± 1.3 mg/dL), biventricular support was used in most patients (28/32). A total of 30 preoperative and 4 perioperative variables were evaluated for their association with survival and liver recovery. *Results:* Nineteen patients (59.4%) survived to transplantation and 13 died. All 19 patients undergoing transplantation were discharged alive with a 1-year survival of 94.4%. All patients without liver recovery died of multiorgan failure. Direct and indirect bilirubin measurements were the only significant predictors for survival to discharge ($P = .036, .045$); all other factors failed to show significance. As direct bilirubin levels increased (normal range, 3 times normal, and >3 times normal), patient survival decreased (82%, 56%, and 33%, respectively). In addition, bilirubin and liver enzyme levels before insertion of the assist device were significantly associated with liver recovery during support with the device. *Conclusion:* In our patient population with ventricular assist devices, liver function is the most predictive factor of patient survival in bridging to transplantation. (J Thorac Cardiovasc Surg 1998;116:633-40)

Ventricular assist devices (VADs) have become an accepted and effective therapy as a bridge to cardiac transplantation in selected patients with end-stage heart failure who would otherwise have died of their cardiac diseases. However, there remains the risk of dying of end-organ damage already present at the time of

implantation. Although VADs have been shown to be able to reverse end-organ failure in some patients,^{1,2} the pathophysiologic mechanisms of end-organ failure and its recovery are not fully understood, and clinical markers and thresholds beyond which recovery is unlikely to occur are often lacking.

One of the crucial major organs determining patient survival during VAD support is the liver. However, the role of hepatic function in patients with a VAD and the limits of reversibility are poorly understood. In a state of acute circulatory failure, decreased hepatic blood flow and increased hepatic venous pressure can lead to cellular hypoxia³ and a clinical picture similar to viral hepatitis, frequently called "ischemic hepatitis."^{4,5} Common abnormalities include the elevation of prothrombin time, liver enzymes, and sometimes bile duct enzymes and bilirubin.

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Table I. Analysis of continuous variables measured before VAD insertion between survivors and nonsurvivors and between patients with liver recovery and without liver recovery

Pre-VAD variable	All patients	Survivors	Nonsurvivors	P value	Liver recovery	No liver recovery	P value
Age (y)	46.0 ± 9.6	45.4 ± 9.0	46.8 ± 10.6	>.2	46.4 ± 9.3	41.3 ± 8.7	.162
Weight (kg)	77.9 ± 15.3	81.1 ± 17.5	73.4 ± 10.6	>.2	81.3 ± 16.2	70.4 ± 9.5	.099
BSA (m ²)	2.0 ± 0.2	2.0 ± 0.2	1.9 ± 0.7	>.2	2.01 ± 0.2	1.87 ± 0.2	.199
CI (L/min/m ²)	1.6 ± 0.7	0.9 ± 0.7	1.7 ± 1.0	.033	1.0 ± 0.8	1.7 ± 1.0	.181
PCWP (mm Hg)	28.9 ± 6.2	30.3 ± 7.4	27.1 ± 3.9	>.2	30.3 ± 7.1	26.0 ± 3.9	>.2
Hct (%)	33.2 ± 5.1	33.4 ± 4.9	33.0 ± 5.6	>.2	33.8 ± 5.1	33.6 ± 5.4	>.2
WBC (nl)	13.6 ± 5.7	15.0 ± 6.4	12.3 ± 4.3	>.2	14.3 ± 6.5	14.1 ± 4.1	>.2
Platelets (nl)	144 ± 95	171 ± 107	107 ± 55	.112	166 ± 105	95 ± 63	.103
PT (s)	15.7 ± 3.4	15.0 ± 2.8	16.6 ± 4.0	>.2	15.0 ± 2.8	17.1 ± 3.8	>.2
AST (U/L)	422 ± 793	272 ± 573	631 ± 1013	>.2	248 ± 546	985 ± 1176	.016
ALT (U/L)	387 ± 782	222 ± 415	620 ± 1097	>.2	211 ± 405	914 ± 1263	.016
AP (U/L)	73 ± 41	70 ± 20	78 ± 60	>.2	69 ± 19	94 ± 72	>.2
GGT (U/L)	76 ± 76	71 ± 33	84 ± 117	>.2	70 ± 32	112 ± 142	>.2
LD (U/L)	831 ± 884	642 ± 555	1092 ± 1178	>.2	605 ± 539	1578 ± 1293	.038
Protein (mg/dL)	5.5 ± 0.9	5.5 ± 0.9	5.6 ± 0.8	>.2	5.5 ± 0.9	5.3 ± 0.8	>.2
Albumin (mg/dL)	3.0 ± 0.8	3.0 ± 0.6	3.0 ± 1.0	>.2	3.0 ± 0.7	2.8 ± 0.9	>.2
Total bilirubin (mg/dL)	3.5 ± 6.2	1.6 ± 1.6	5.8 ± 9.0	.062	1.7 ± 1.8	8.5 ± 10.7	.001
Direct bilirubin (mg/dL)	1.6 ± 3.0	0.7 ± 0.8	2.8 ± 4.3	.036	0.7 ± 0.9	4.0 ± 4.9	.001
Indirect bilirubin (mg/dL)	2.0 ± 3.5	0.9 ± 0.9	3.4 ± 5.1	.045	1.0 ± 1.1	4.5 ± 6.0	.008
BUN (mg/dL)	36.2 ± 19.7	33.7 ± 17.9	39.6 ± 22.2	>.2	33.2 ± 17.7	46.9 ± 24.4	.165
Creatinine (mg/dL)	2.0 ± 1.3	1.9 ± 0.8	2.0 ± 1.8	>.2	1.9 ± 0.8	2.5 ± 2.2	>.2
AST/LD ratio	0.38 ± 0.3	0.33 ± 0.27	0.46 ± 0.44	>.2	0.32 ± 0.27	0.58 ± 0.50	.091
ALT/LD ratio	0.40 ± 0.5	0.36 ± 0.40	0.45 ± 0.58	>.2	0.34 ± 0.39	0.64 ± 0.65	.177

VAD, Ventricular assist device; BSA, body surface area; CI, cardiac index; PCWP, pulmonary capillary wedge pressure; Hct, hematocrit; WBC, white blood cells; PT, prothrombin time; AST, aspartate transaminase; ALT, alanine transaminase; AP, alkaline phosphatase; GGT, gamma-glutamyl transferase; LD, lactate dehydrogenase; BUN, blood urea nitrogen.

Because of the importance of patient selection, a number of publications have evaluated pre-VAD markers of survival in patients with significant end-organ failure, but with no consistent findings.^{1,6-9} This article focuses on the importance of liver function in patients having a VAD. On the basis of a single-center experience, we analyze different liver function variables to assess which of them are predictive of patient survival and liver recovery.

Methods

Patients. At California Pacific Medical Center, from 1984 to 1995, 48 patients with acute or chronic heart failure were mechanically supported with the Thoratec VAD System (Thoratec Laboratories Corporation, Pleasanton, Calif). Of these, 32 patients (29 male and 3 female) received the device as a bridge procedure to heart transplantation and will be analyzed further in this study; the remaining 16 patients were supported after cardiectomy for weaning from cardiopulmonary bypass and are not included in this study. The ages of the bridge-to-transplant group ranged from 30 to 61 years with a mean age of 46 years. Dilated cardiomyopathy was diagnosed in 13, ischemic cardiomyopathy in 8, acute myocardial infarction in 8 patients, and postpartum cardiomyopathy, hemochromatosis, and mitral valve disease in 1 patient each. Six patients had undergone other cardiac operations before VAD implantation. Average body surface area

was 1.9 m² (range 1.6-2.6 m²) and average weight was 78 kg (range 51-126 kg).

Preoperative status and indication for support. All patients in this study were candidates for cardiac transplantation and were selected for VAD support at a stage of the disease where death or permanent end-organ damage was likely to occur before a donor heart was available. Hemodynamic guidelines for implantation were cardiac index less than 1.8 L/min per square meter, mean arterial pressure less than 70 mm Hg, and left atrial pressure greater than 20 mm Hg despite appropriate use of conventional therapies.

Before implantation, all patients were receiving maximal inotropic support and the average cardiac index was 1.6 L/min per square meter with an average pulmonary capillary wedge pressure of 28.9 mm Hg. Fifty percent of patients had prior cardiac arrests, 88% were supported with intra-aortic balloon pumps, and 69% were intubated and mechanically ventilated. More than half of the patients had substantial liver failure before implantation, with 18 patients (56%) having elevation of both transaminases and 19 (59%) having pathologic total bilirubin levels.

Mechanical circulatory support system. The Thoratec VAD System was used as a biventricular system in 28 patients (88%) and as a left VAD in 4 patients. The system consists of paracorporeally placed prosthetic ventricles with a 65-mL stroke volume connected to the heart and great vessels via cannulas crossing the chest wall and a pneumatic drive con-

sole.¹⁰ The left VAD inflow was achieved from the left ventricular apex in 24 patients and from the left atrium in 8 patients; the right VAD inflow was from the right atrium; outflow of the VADs was through 14-mm preclotted polyester grafts to the ascending aorta and pulmonary trunk, respectively. The average support duration in the 11-year study period was 18.5 days with a maximum of 149 days.

The study was conducted under investigational device exemption regulations, with protocol and patient consent forms approved by the institutional review board of the hospital and the US Food and Drug Administration. Informed consent was obtained from either the patient or next of kin.

Factors analyzed. The following 30 preoperative factors were evaluated regarding their association with 2 end points (patient survival to discharge and liver recovery): age, sex, body surface area, weight, diagnosis, cardiac index (either measured by thermodilution or, in ventricular fibrillation, considered 0), pulmonary capillary wedge pressure, pre-VAD cardiac operations, preoperative mechanical ventilation, preoperative intra-aortic balloon pump, pre-VAD cardiac arrest, previous support with a different system such as a centrifugal pump or extracorporeal membrane oxygenation, and 18 laboratory values determined directly before implantation of the device (Table I). Additionally, several intraoperative and postoperative factors were analyzed: inflow cannulation site on the left side, univentricular or biventricular support, and reoperation for bleeding.

Liver recovery was defined as the return of the transaminases (aspartate aminotransferase [AST] and/or alanine aminotransferase [ALT]) to within normal limits within a maximum of 14 days after implantation, regardless of subsequent death due to reasons other than liver failure. Two of the 32 patients were excluded from this subanalysis because liver function first recovered and then deteriorated again in association with other complications; one patient who died during the operation was also excluded. To analyze the time course of liver recovery, total bilirubin and AST concentrations during the first 3 weeks of support were also evaluated in all patients who were supported by the device for 7 days or more.

Statistical methods. Comparisons of continuous variables between survivors and nonsurvivors and between patients with and without liver recovery, respectively, were performed with a Mann-Whitney test. For comparisons of discrete variables, Pearson's χ^2 test and Fisher's exact test were used. In addition, patients were divided into 3 groups on the basis of total and direct bilirubin values: normal, up to 3 times normal, and more than 3 times normal. For these groups, univariate logistic regression was carried out to identify odds ratios. Multivariate logistic regression of the data was not performed because of the small numbers of patients. In the analysis of laboratory factors, 1 patient had to be excluded because no preoperative tests were available. All statistical analyses were performed with the Crunch statistical data package (Crunch Software Corporation, Oakland, Calif) on a standard personal computer.

Results

Survival. Of the 32 patients receiving a VAD as a bridge to transplantation, 19 (59.4%) survived to trans-

Table II. Analysis of discrete factors before VAD insertion between survivors and nonsurvivors

	Survivors	Non-survivors	Survivors (%)	P value
Diagnosis				
Dilated cardiomyopathy	7	6	53.8	>.2
Acute myocardial infarction	6	2	75.0	
Ischemic cardiomyopathy	5	3	62.5	
Other	1	2	33.3	
Previous cardiac operation				
Yes	2	4	33.3	.194
No	17	9	66.7	
Preop cardiac arrest				
Yes	9	7	56.3	>.2
No	10	6	62.5	
Preop IABP				
Yes	16	12	57.1	NA
No	3	1	75.0	
Previous support with other system				
Yes	1	3	25.0	NA
No	18	10	64.3	
Preop mechanical ventilation				
Yes	6	4	60.0	>.2
No	13	9	59.1	
Sex				
Male	17	12	58.6	NA
Female	2	1	66.7	

IABP, Intra-aortic balloon pump; NA, test not applicable because of small number in 1 group.

plantation and 13 (40.6%) died while being supported with the device. All patients without liver recovery died of multiorgan failure associated with highly pathologic liver function values during VAD support. All 19 patients who survived to receive a heart transplant were subsequently discharged from the hospital. In the late follow-up period, 5 patients died 6 months and 2, 7, 9, and 11 years after transplantation, respectively, giving a 1-year survival after transplantation of 94.4%. Causes of death while supported with the device were multiorgan failure (7), sepsis (3), pneumonia (1), pulmonary embolism (1), and right ventricular failure (1).

Association of preoperative factors with survival.

The analysis of preoperative factors is shown in Tables I and II. In general, the average values measured in nonsurvivors appeared different from those in the survivors, but as a result of high standard deviations these differences were not statistically significant. Only direct and indirect bilirubin values were significant, with group averages approximately 4 times higher in the nonsurvivors (2.8 ± 4.3 and 3.4 ± 5.1 mg/dL, respectively) compared with those of the survivors (0.7 ± 0.8 and 0.9 ± 0.9 mg/dL); the difference in total bilirubin values approached signifi-

Fig 1. Pre-VAD total bilirubin in survivors and nonsurvivors. All patients' individual values are depicted on the *left* (P value: Mann-Whitney test). Survival in percent of patients divided into 3 groupings of normal, 3 times normal or less, and greater than 3 times normal range is shown on the *right*. Logistic regression revealed a significant difference between these groupings ($P = .04$) with an odds ratio of 3.3 (95% confidence interval: 1.05-10.32).

cance with a P value of .06 (Table I). Cardiac index between the groups was also significantly different, but with the survivors having a lower cardiac index. Leaving out patients in ventricular fibrillation before implantation (where cardiac index is assumed to be 0) and calculating only the values measured by thermodilution, the difference was no longer statistically significant (10 survivors with an average cardiac index of 1.4 ± 0.3 L/min per square meter versus 9 nonsurvivors with an average cardiac index of 1.9 ± 0.8 L/min per square meter).

Figs 1 and 2 show the values of pre-VAD total and direct bilirubin of all patients individually on the *left* and their survival divided into 3 groupings (normal range, up to 3 times normal, more than 3 times normal) on the *right*. The survival decreased stepwise from 82% to 56% to 33% with increasing direct bilirubin levels (Fig 2). The differences between the groups for both variables were significant (see illustrations), although when total bilirubin is analyzed, survival remained at 69% to 70% until values of more than 3 times normal were achieved, at which point survival decreased to only 25%.

Association of intraoperative and postoperative factors with survival. As shown in Table III, there was no statistically significant association between intraoperative and postoperative factors and survival; however, of 4 patients who needed reintervention for bleeding, only

1 survived. The 3 who died had extremely high preoperative total bilirubin levels, with a median of 6.2 mg/dL.

Association of preoperative factors with liver recovery. The results of the analysis between patients with and without liver recovery are given in Table I on the *right side*. Patients with high total, direct, and indirect bilirubin, AST, ALT, and lactate dehydrogenase (LD) levels had a significantly higher likelihood of dying of liver failure than did those without elevated levels. Weight and AST/LD ratio were approaching significance (ie, P value between .1 and .05).

Postimplantation course. The change of total bilirubin and AST in survivors and nonsurvivors during the first 3 weeks of support is depicted in Fig 3. In the majority of survivors, total bilirubin level rose slightly during the first few days and recovered to normal or near-normal values within 7 to 10 days of support; however, in most nonsurvivors it increased to highly pathologic values during this period. AST showed a gradual decline to normal values within approximately 10 days in survivors, whereas there was high variability and frequently initial increase in nonsurvivors.

Discussion

Analysis for patient survival. This study shows that preimplantation liver function has an important impact

Fig 2. Pre-VAD direct bilirubin in survivors and nonsurvivors. Analogous to Fig 1, individual values are shown on the *left* (P value: Mann-Whitney test), survival in percent of patients divided into 3 groupings of normal, 3 times normal or less, and greater than 3 times normal range on the *right*. With logistic regression, difference between the groupings was significant ($P = .04$) with an odds ratio of 3.0 (95% confidence interval: 1.07-8.31).

on the survival of patients undergoing mechanical bridging to transplantation. Both the direct and indirect fractions of bilirubin were significantly associated with survival in our patients. Total bilirubin failed to show significance and had a slightly higher P value (.062) than either of its portions. This difference was due to 2 patients in whom only the total bilirubin level was available for analysis. Omitting these patients, total bilirubin was also significantly ($P = .022$) related to survival.

A low preoperative direct bilirubin level appears to be the best predictor of survival in our study. In the 3 groupings (Fig 2), the odds ratio for direct bilirubin level was 3.0, indicating that, with all other factors remaining equal, for each categoric increase in direct bilirubin, a patient was 3 times less likely to survive. In our study population, patients with a preoperative direct bilirubin level of more than 3 times normal had a survival of 33.3%, and patients having a total bilirubin level of more than 3 times normal had a survival of only 25%, compared with 82% and 70% survival-to-transplantation for patients with normal direct and total bilirubin levels, respectively. However, as the *left sides* of Figs 1 and 2 illustrates best, even patients with extremely elevated levels have a chance to survive. The

Table III. Analysis of intraoperative and postoperative factors between survivors and nonsurvivors

Discrete variables	Survivors	Non-survivors	Survivors (%)	P value
Univentricular or biventricular support				
LVAD	3	1	75.0	NA
BVAD	16	12	57.1	
Cannulation site left inflow				
Left ventricular apex	13	10	56.5	>.2
Left atrium	6	3	66.7	
Reoperation for bleeding				
Yes	1	3	25.0	NA
No	18	10	64.3	

LVAD, Left ventricular assist device; BVAD, biventricular assist device; NA, test not applicable because of small number in 1 group.

100% posttransplantation survivals (through hospital discharge) achieved with these patients indicate that preoperative liver dysfunction is no longer an issue in patients who survived with the aid of VAD support to qualify for heart transplantation.

A number of studies have previously been published

Fig 3. Total bilirubin and AST in survivors and nonsurvivors during the first 3 weeks after VAD implantation. Analyzed is a subset of patients with a minimum VAD support of 7 days ($n = 18$). Values are expressed as means $\pm$ standard error of the mean.

on patient selection for VAD support—with the Thoratec VAD,¹ with other devices,^{2,6,8,9,11} or with mixed device populations.^{7,12,13} In some of these reports, a statistical evaluation of preoperative risk factors has been performed, but only the St Louis group,⁷ the Columbia group,⁹ and the Thoratec multicenter¹ results give statistically significant predictors for survival.

In the St Louis data, white blood count, platelet count, and preimplantation dialysis were significantly associated with survival.⁷ These factors were not significant in our analysis (however, pre-VAD dialysis was not evaluated). The lack of significance of liver function tests in the St Louis series might be due to a different patient selection regimen resulting in fewer patients with severe liver failure, as the mean bilirubin level of the nonsurvivors was 1.2 mg/dL, compared with 5.8 mg/dL in the present study. Preoperative hepatic function in our patient population is also more severely compromised than in other studies reported in the literature,^{2,14, 15} implying that some patients in this report may not be representative of patients being selected for bridge to transplantation at other centers.

The present study analyzes data of a single center, which is a subset of the Thoratec multicenter data.¹ In the multicenter study, blood urea nitrogen and previous

cardiac operation were found to be significant predictors of survival. In our center, blood urea nitrogen was not a significant factor, and although patients with previous operations had a lower survivorship, this difference did not reach statistical significance. However, bilirubin also showed a trend toward significance ($P = .07$) in the multicenter report.¹ Patients with a pre-VAD bilirubin concentration of more than 5 mg/dL had a survival of only 33%, suggesting a considerable effect of liver function on survival. Again, comparing the preoperative bilirubin levels, the patients in our subpopulation had comparably worse preoperative hepatic function (mean bilirubin averaging 5.8 mg/dL among nonsurvivors compared with 3.6 mg/dL in the multicenter group).

A consistent observation in all studies is that preoperative cardiac function (eg, cardiac index, left ventricular ejection fraction, pulmonary capillary wedge pressure) is not a significant predictor of survival, although central venous pressure greater than 16 mm Hg was included as a risk factor in the Columbia report.⁹ In our analysis, patients with a lower cardiac index even appeared to have a better chance of survival. A possible explanation may be that the decision for support in patients with extremely low cardiac output or in ventricular fibrillation is being made immediately, whereas those patients with long-standing borderline cardiac function might remain in circulatory failure for too long, leading to more severe end-organ damage.

The majority (88%) of the analyzed patients at our center—and in fact all patients with impaired hepatic function—have been supported with biventricular VADs. Biventricular support has the potential not only to restore blood flow to the liver, which is commonly accepted as the main reason for ischemic hepatitis,⁴ but also to directly relieve hepatic congestion, which is the other pathophysiologic mechanism leading to hepatic damage in cardiac failure.³ Our results are consistent with the findings in another multicenter publication on the Thoratec VAD,¹⁰ that patients requiring biventricular support are more severely ill and have slightly reduced, but still acceptable, survival.

Our results, although in only 4 of our patients, also suggest that patients who received VADs after support with other devices had reduced survival (only 1/4). These patients could have had increased total bilirubin levels related to hemolysis from the previous support. If so, that could have had some impact on the data.

Variables of hepatic function. It is appropriate to review the relevance of different liver function variables and to discuss their predictive value for liver recovery, because the study population seems to be one with a high degree of liver failure.

Bilirubin. In severe hepatocellular disease caused by congestive heart failure, particularly predominantly right-sided failure, a certain elevation of bilirubin concentration is common. However, high values of more than 5 mg/dL are rare and seen only in severe centrilobular necrosis, especially in acute failure.³ Although classically one should expect mainly unconjugated (indirect) hyperbilirubinemia owing to the difficulty of the liver parenchyma to conjugate bilirubin, in most patients both direct and indirect bilirubin levels rise. The reason for the elevation of the direct fraction is a secretory abnormality of unknown biochemical mechanism.¹⁶

In our study, the preoperative direct bilirubin fraction appears to be a better predictor of patient survival than total or indirect bilirubin. A possible reason might be the additional rise of the indirect fraction by hemolysis, which plays a role in hepatic congestion, but can also be increased by therapies such as intra-aortic balloon counterpulsation.

Transaminases. In isolated hepatic congestion, transaminases rise only slightly. However in ischemic hepatitis, with a decrease in blood flow, a more than 5-fold rise is frequent. This is strongly associated with the pathologic finding of centrilobular necrosis.¹⁷ ALT is the more specific variable for liver recovery, because AST is also released from damaged myocardium, skeletal muscle, brain, and kidneys. However, in our patients AST and ALT both were significant predictors for liver recovery.

LD. Inasmuch as all cells contain LD as an essential enzyme, its rise is relatively nonspecific, although well recognized in ischemic hepatitis in particular.⁴ In our study, it was not a significant predictor for survival, although it was a predictor for liver recovery. The LD isoenzyme 5 fraction might have been an even better marker for liver status, but no data were available.

AST/LD and ALT/LD ratio. Cassidy and Reynolds¹⁸ reported that the AST/LD ratio and, perhaps even more important, the ALT/LD ratio can help differentiate between viral and ischemic hepatitis. The authors suggested that this could be due to less release of LD in viral hepatitis, because only hepatocytes in zone 1 were damaged, compared with all zones (although zone 3 in particular) in ischemic injury. We tested these ratios in our patient population with the underlying hypothesis that the ratios would be higher in more severe hepatocellular disease. Both ratios were indeed higher in patients whose livers did not recover, although the difference did not reach statistical significance.

Biliary tract enzymes. The reason for the rise of alkaline phosphatase and gamma-glutamyl transferase levels in heart failure is thought to be pressure-induced intrahepatic biliary obstruction, and it is therefore mainly associated with elevated hepatic venous pressures.³

Both enzymes are rather mildly elevated even in severe ischemic hepatitis and had no relevant predictive ability for survival or liver recovery in our patients.

Protein and albumin. Serum albumin levels reflect long-term hepatic function. They often remain within normal limits in ischemic hepatitis¹⁹ and do not correlate well with the degree of actual hepatic damage.³ Serum albumin levels can also be acutely influenced by many factors (ie, the altered fluid status in heart failure or iatrogenic factors). Protein and albumin therefore did not show good predictive ability.

Prothrombin time. Prothrombin time is usually prolonged earlier than partial thromboplastin time because of a deficiency of factor VII, the vitamin K-dependent coagulation factor with the shortest half-life. Although it is widely used clinically as a marker for severity of liver damage, in our patients the difference between survivors and nonsurvivors was not significant. Also, no association between preoperative prothrombin time and incidence of reoperation for bleeding was found.

Importance of patient selection and early VAD support. In conclusion, pre-existing severe liver failure was prevalent in our patient population being mechanically bridged to transplantation with the Thoratec VAD. Preoperative liver function was identified as the most important predictor of survival, with total bilirubin and, in particular, its direct portion being the best predictors. However, a few patients with highly impaired liver function recovered during VAD support, and thus no threshold value was found that should absolutely lead to exclusion of a patient. In our experience, we have found that biventricular support is highly recommended in extremely ill patients such as those presented in this report. The encouraging survivals in patients without liver failure (eg, 82% survival to transplantation for patients with normal direct bilirubin levels) reinforces the importance of early VAD intervention to restore circulatory support before the onset of irreversible organ failure.

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