vations probably exceeds those in the paper of Savarese *et al.*

When performing a cumulative bolus dose-response study, potency may be calculated in several ways. First, all data from every patient can be pooled and linear regression analysis performed on the total number of observations. An alternative method, if two or more doses per patient are administered, is to perform regression analysis on the data from each subject and to average the calculated individual ED50 and ED95 values. These two methods produce similar, but not identical, estimates of potency, even when the number of observations in all patients is the same. Since it is unclear to this investigator that one method clearly has greater validity than the other, both estimates of potency are included in table 1.

In summary, the evoked adductor pollicis MMG and the 1st dorsal interosseous EMG may be used essentially interchangeably in determining the depth of nondepolarizing neuromuscular blockade. The calculated ED95 of metocurine as measured by the MMG is between 0.25 and 0.27 mg/kg. Calculating the ED95 of metocurine from the EMG will result in a very slight (approximately 7%) overestimation of its potency.

This study also suggests that, without a preload applied to the muscle under investigation, the EMG may significantly overestimate the sensitivity to nondepolarizing neuromuscular blocking drugs. This possibility needs further substantiation, especially if EMG studies are to be used in evaluating future generations of nondepolarizing blocking drugs.

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Pediatric Orthotopic Liver Transplantation: Multifactorial Predictions of Blood Loss

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Orthotopic liver transplantation is an established method of therapy for pediatric patients with end-stage liver disease. Because of the magnitude of the operation, blood loss can be substantial. Blood for this procedure must be available on a 3–4-h notice.

Retrospective investigations have quantified intraoperative blood loss for pediatric patients. In two previous reports, blood usage during liver transplantation in pediatric patients ranged from 2 to 59 units,[1] and averaged 3.9 blood volumes.[2] No study, though, has attempted to identify factors that might predict blood loss as well as survival in children. Such data might indicate roughly how many units the blood bank should have prepared for each patient, as well as the extent of venous access and monitoring that should be prepared before a case. We have collected clinical and laboratory information, as well as intraoperative blood loss data, to

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TABLE 1. Preoperative Information Collected For Each Patient

Age
Pathologic diagnosis (acute *vs* chronic)
History of previous major abdominal operation
Bleeding varices
Degree of encephalopathy
Presence of ascites
Need for ICU prior to time of transplant
Nutritional status
Retransplant
Planned segmental or whole liver transplant
Prothrombin time (PT)
Partial thromboplastin time (PTT)
Platelet count
Serum albumin levels

identify factors which significantly correlate with both a high level of intraoperative blood loss and survival.

MATERIALS AND METHODS

We studied 17 patients under 15 yr of age who underwent 21 liver transplants between November, 1984, and June, 1986. The data collection protocol was approved by our institutional Human Subjects Review Board. The same anesthesia and surgical team performed all transplants. Preoperative data collected for each patient is outlined in table 1.

In patients without an iv, anesthesia was induced with halothane, nitrous oxide, and air; thiamylal was used for patients with an established iv. Anesthesia was maintained with isoflurane, oxygen, and air. Pancuronium was injected iv for muscle relaxation. Three large-bore ivs and a radial arterial line were inserted. Blood was administered as a mixture of one unit packed red cells with one unit fresh frozen plasma, because these patients were in liver failure which is associated with clotting abnormalities; in addition, we anticipated the need for massive blood transfusion. Plasmalyte (20 cc/kg) was administered iv at the beginning of the case to provided optimal filling of intravascular volume. If a child was 0–2 yr of age, blood volume was calculated as 80 ml/kg; if a child was 2–15 yr of age, blood volume was calculated as 70 ml/kg. In determining blood replacement therapy, we attempted to keep systolic blood pressure within 10% of its preoperative value, and hematocrit at 30–35%. There is a tendency to administer a large amount of fluids during the procedure which could result in dilutional thrombocytopenia. Therefore, we administered platelet concentrates after transfusion of one estimated blood volume. Platelet concentrates were also administered if hemostasis seemed inadequate.

Surgical technique consisted of a bilateral subcostal incision with extension of the incision apex to the xiphoid. The native recipient liver was removed after cross clamping the inferior vena cava, the portal vein, and the hepatic artery; venous-venous bypass was not employed. Prior to reperfusion, the donor liver was flushed with 500 ml 5% albumin in saline *via* the portal vein. Hemostasis was achieved by direct suture ligation, electrocoagulation, and infrared coagulation. A Roux-en-Y choledochojejunostomy was performed. We determined the amount of blood administered during the procedure; the number of blood volumes administered was then calculated by dividing the amount of blood administered by the child's calculated blood volume. One month after surgery, survival was noted.

Patients were grouped according to their status for each discrete variable being evaluated. For continuous variables, they were divided into two groups based on the median value of the variable. Blood loss was compared between groups for each variable using Student's t test; for the variables where three discrete groups were evaluated, analysis of variance was employed.[3]

Patients were also divided into two groups based on whether their age was less than or equal to the median age or greater than the median age. Continuous variables were compared using Student's t test; for discrete variables, groups were compared using chi-square with a correction for continuity.[3]

Multiple linear regression analysis was used to determine the most significant preoperative factors for blood loss.[4,5] In this analysis, blood loss was the dependent variable and the preoperative factors listed in table 1 were the independent variables. Forward selection was used to select variables: the first variable considered for entry into the equation was the one with the largest positive or negative correlation, depending on the dependent variable, blood loss; subsequent variables were included until the criterion for inclusion (the coefficient of the entered variable was significantly different from 0) was no longer met. Discriminant analysis was used to determine which factors (preoperative factors as well as intraoperative blood loss) were significant in determining survival after 1 month; variable selection was similar to that used for the multiple linear regression analysis.[4]

RESULTS

From November, 1984, to June, 1986, 21 liver transplants were performed on 17 children. The average patient age was 2.7 yr of age. The diagnoses of patients with acute liver disease included acute hepatitis (N = 3) and acute rejection (N = 3). The diagnoses of patients with chronic liver disease included biliary atresia (N = 11), alpha-1-anti-trypsin deficiency (N = 3), and tyrosinemia (N = 1). The average amount of blood administered was 3.4 blood volumes. A histogram illu-

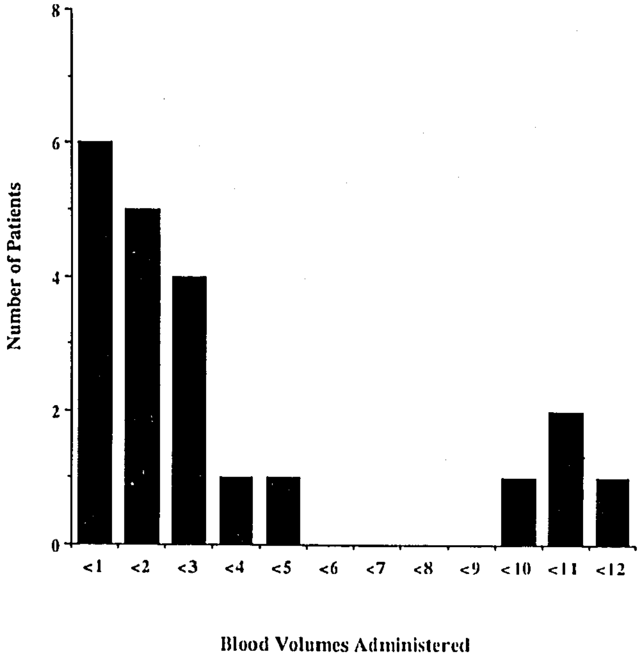

FIG. 1. Histogram showing distribution of blood volumes administered.

strates the distribution of blood volumes (fig. 1). Two peaks are evident, *i.e.*, patients lost either relatively little or large amounts of blood.

Summary data for all variables are listed in tables 2 and 3. The results of the *t* test and analysis of variance comparisons are listed in tables 4 and 5. When blood loss was compared by grouping patients based on the median value for the continuous variables or according to their specific group for the discrete variables, significant differences were found according to age, preoperative prothrombin time, presence of encephalopathy, history of bleeding varices, pathological diagnosis, planned segmental transplant, and presence in ICU prior to transplant. Patients who were alive 1 month after surgery also required less blood during their transplant operations.

When patients were grouped according to age, the only variable that differed significantly between the two groups was nutritional status ($P < 0.05$). In the group of patients whose age was less than or equal to the median, four patients were well, one patient was mildly depleted, and six were depleted. In the group of patients whose age was greater than the median, three were well, six were mildly depleted, and one was depleted.

Multiple linear regression analysis revealed that presence in the ICU prior to transplant and previous abdominal operation were significant factors for predicting blood loss. The regression coefficient for ICU was 6.34 ($P < 0.001$), 3.81 for previous abdominal operation ($P < 0.002$), and the constant was −1.40 (NS). By multiplying the coefficients by their associated variable (0 = "no", 1 = "yes") and then adding the constant, it is possible to estimate blood loss for the operation. The standardized coefficients, which are the coefficients for the variables when they are standardized to a mean of 0 and a standard deviation of 1, indicate the relative importance of the variable in predicting blood loss. These coefficients were 0.82 for presence in the ICU prior to transplant and 0.47 for previous abdominal operation. Discriminant analysis revealed that ICU and retransplant were significant factors for predicting 1-month survival. The discriminant coefficient for retransplant was 1.47, 2.13 for presence in the ICU, and the constant was −0.99. By multiplying the coefficients by their associated variable (0 = "no", 1 = "yes") and then adding the constant, a score is obtained; a score less than 0 predicts survival. Using the discriminant analysis on our 21 transplants, 71% of cases could be correctly classified as to their survival status. Standardized coefficients for the analysis were 0.59 for retransplant and 0.94 for presence in the ICU. The standardized coefficients, again, are coefficients for the variables when they are standardized to a mean of 0 and a standard deviation of 1, and here indicate the relative importance of the variable in predicting survival.

TABLE 2. Summary Data for Characteristics of the Continuous Variables of 21 Pediatric Liver Transplant Recipients

	Mean	S.D.	Median
Age (years)	2.7	2.2	1.8
Prothrombin time (seconds)	18.4	8.3	15.1
Partial thromboplastin time (seconds)	43.2	23.5	32.5
Blood administered (blood volumes)	3.4	3.8	1.9
Serum albumin (g/dl)	3.0	0.5	3.0
Platelets (#/mm^3 × 10^3)	177	143	131

Normal value for our laboratories: Prothrombin time: 11.2–13.2 s; partial thromboplastin time: 20.0–28.5 s; serum albumin: 3.5–5.0 g/dl; platelets: 150–450/mm^3.

TABLE 3. Summary Data for Characteristics of the Discrete Variables of 21 Pediatric Liver Transplant Recipients

	No	Yes
Previous abdominal operation	6	15
Encephalopathy	12	5 mild, 4 severe
History of bleeding varices	14	7
Acute disease	16	5
Planned segmental transplant	18	3
Retransplant	17	4
ICU prior to transplant	14	7
Malnutrition	7	7 mild, 7 severe
Ascites	9	12
One-month survival	6	15

TABLE 4. Comparison of Blood Loss for Individual Continuous Variables

Variable	Blood Loss in Blood Volumes [Blood Volumes (±SD)]			Significance
	Median for Variable	≤Median	>Median	
Age (years)	1.8	5.03 (4.58)	1.68 (1.18)	<0.025
Prothrombin time (seconds)	15.1	1.51 (1.23)	5.55 (4.48)	<0.005
Partial thromboplastin time (seconds)	32.5	2.18 (2.98)	4.82 (4.15)	NO
Serum albumin (g/dl)	3.0	4.11 (4.07)	2.53 (3.27)	NO
Platelets (#/mm^3 × 10^3)	131	4.13 (4.31)	2.67 (3.06)	NO

DISCUSSION

This analysis was undertaken to determine the factors important for predicting both blood loss and survival of children undergoing liver transplants. In our series, blood replacement was guided by arterial blood pressure as well as the desire to keep the hematocrit between 30–35%. Intraoperatively, we were aggressive in our use of fresh frozen plasma as well as platelet concentrates; most of these patients were in liver failure, which is associated with clotting abnormalities; also, there was a tendency for massive blood transfusion. Since the decision to perform the transplant must be made using preoperative data, these are the data we used in our analysis of blood loss. Based on this analysis, a patient who is young (less than 2.5 yr of age), with a high prothrombin time (PT) (>15), with mild or severe encephalopathy, bleeding varices, acute liver disease, a planned segmental transplantation, and/or is in an ICU prior to transplantation, will tend to bleed more than if the opposite were true. Two variables that we found important, PT and encephalopathy, overlap with those previously reported to be predictive of blood loss during liver transplantation in adults.[1,2] These variables, as well as ICU status, reflect the severity of hepatic dysfunction and, therefore, would logically be risk factors for blood loss in both the pediatric and adult patient. In adults, malnutrition correlates with high blood loss, and the use of venous-venous bypass correlates with low blood loss. Current technology does not permit the use of venous-venous bypass in small children. Perhaps with the development of this technology, blood loss in pediatric liver transplantation can be further reduced.

Our patients were in the ICU prior to the transplant because of multisystem organ failure, including bleeding, coma, and/or respiratory failure. We demonstrated that presence in the ICU correlated with blood loss and was a significant predictor for operative mortality within 1 month. Our study is based on the results of one transplant center. Certainly, in other centers, other factors may be involved in determining whether a patient is admitted to the ICU, as well as predicting 1-month operative mortality. Selecting the appropriate time for liver transplantation is a complex issue. Transplantation should be avoided very early in the course of the patient's disease because the disease process may spontaneously abate or be reversed; yet it should not be performed in such an advanced stage that the surgical procedure doesn't have a fair chance of success.[6] A much larger series, involving many transplant centers, is necessary to validate our findings.

The primary diagnosis of acute hepatitis correlates positively with blood loss in this series, yet has been negatively associated with bleeding in series on adult liver transplantation.[2] In our study, the children with acute hepatitis all had overwhelming liver failure with attendant coagulopathy and encephalopathy. Perhaps adults with this diagnosis in other series have had a more indolent course. Segmental liver transplantation, which also correlates with high blood loss, was under-

TABLE 5. Comparison of Blood Loss for Individual Discrete Variables. Numbers are Listed as Blood Volumes (±SD)

Variable	No	Yes	Significance
Previous abdominal operation	1.77 (0.78)	4.10 (4.26)	no
Encephalopathy	1.53 (1.24)	mild 5.47 (4.96) severe 6.60 (4.52)	<0.025
History bleeding varices	1.76 (1.25)	6.79 (4.88)	<0.005
Acute disease	2.66 (3.14)	5.91 (4.80)	<0.05
Planned segmental transplant	2.61 (2.96)	8.37 (4.83)	<0.005
Retransplant	3.24 (3.67)	4.26 (4.54)	no
ICU prior to transplant	1.59 (1.25)	7.12 (4.44)	<0.0005
Malnutrition	2.77 (3.59)	mild 1.93 (1.39) severe 5.61 (4.83)	no
Ascites	2.31 (3.19)	4.28 (4.04)	no
One month survival	6.00 (5.25)	2.41 (2.50)	<0.05

taken in two of the three children with acute hepatitis because a size-matched liver was unavailable. When a larger series has been accumulated, a multivariate analysis will be necessary to determine if primary diagnosis is truly an independent variable in predicting intraoperative blood loss in pediatric liver transplantation.

Why the younger patients require more blood is not clear. Patients who are sicker will receive their transplants when they are younger; the younger patients in our group tended to have a poorer nutritional status. Certainly, only the younger patient, for whom a smaller liver is much more difficult to obtain, will require a segmental liver transplant, and patients who received a segmental transplant did bleed more. Patients undergoing segmental transplantation may also tend to bleed more along the cut liver edge. However, none of these patients died from uncontrollable bleeding, and the fact that a patient received a segmental transplant did not predict survival. Significantly, blood loss, when included in the criteria for survival after 1 month, was not a predictor, in contrast to the strong correlation of blood loss and fatal outcome observed in adults.[7,8]

Proper timing of a transplant is important in reducing blood requirement and improving survival rates. Further prospective work is necessary to define appropriate timing. Additional controlled prospective studies are needed to ascertain whether modalities, such as the use of venous bypass, or a more defined use of blood products through techniques such as thromboelastography, will further decrease blood utilization.

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Separation of the Hub from the Shaft of a Disposable Epidural Needle

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With the development and widespread use of disposable needles for spinal and epidural anesthesia, separation of the hub from the shaft of the needle or needle breakage has become a rare event. The hubs of most of these needles are made of plastic and glued to the metal shaft with epoxy. However, a few manufacturers still provide disposable needles having metal hubs, and these are "crimped" onto the metal shaft as was done with reusable needles. While breakage of old reusable needles at the shaft-hub junction was a known complication in the past,[2,3] it has not been reported since the development of disposable needles. The following case illustrates the fact that separation of the hub from the shaft of a needle is also possible, especially if one uses disposable needles with metal hubs.

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REPORT OF A CASE

A 21-yr-old, gravida 2, para 1, 80-kg woman with a height of 62 inches, BMI = 32, presented for cesarean section because of non-progression of labor. The history and physical examination were unremarkable except that the patient's spinous processes were difficult to palpate because of her size. Premedication consisted only of 30 cc of oral sodium citrate. In the operating room, the appropriate monitors were applied, and the patient was placed in the sitting position. Following preparation and draping of the back, local infiltration of the skin and subcutaneous tissues with creation of a skin wheal was accom-