Probability of Surviving Postoperative Acute Renal Failure

Development of a Prognostic Index

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Sixty-five patients who developed postoperative acute renal failure requiring hemodialysis were retrospectively analyzed to identify variables that could be used to predict outcome. Our aim was to identify patients who would have an unfavorable outcome despite hemodialysis and to identify those factors that might be altered to improve outcome. A linear discriminant function capable of segregating survivors from nonsurvivors in the retrospective analysis was subsequently validated in a prospective fashion using a second patient population. Variables used were age, sex, number of transfusions, interval from onset of acute renal failure to dialysis, type of surgery, preoperative hypotension, and the presence of cardiac failure. Scores were formulated for each patient and then segregated into three groups: patients with no precedence for survival, patients with an intermediate risk of dying, and patients with low risk of dying. Based on the univariant analysis, the interval from onset of acute renal failure to first dialysis and the maximum serum creatinine prior to first dialysis were the only factors that might be altered to change mortality. The prognostic index we have developed enables one to select patients without a chance of survival.

DESPITE MULTIPLE ADVANCES in the management of critically ill patients, acute renal failure (ARF) in the postoperative patient continues to have an exceptionally high mortality rate. Mortality figures in recent reports have been as low as 50% and as high as 100% depending on the patient population analyzed.[1-12]

Patients with postoperative ARF are likely to be involved in the syndrome of multiple organ failure. This type of patient consumes a large portion of the health-care dollars, technical resources, and manpower and many times does not survive, as recently described by Eiseman.[13] The database needed for making logical decisions to treat or not treat ARF in postoperative or trauma patients is essentially nonexistent. If such data were available, resources could be directed towards those patients with a chance for survival and emphasis in treatment placed on those factors that could alter mortality. We have developed a prognostic index that enables one to select patients without chance for survival as well as identify those factors that most affect mortality.

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Materials and Methods

The charts of 300 patients with ARF treated at the Medical Center Hospital of Vermont over a 9-year period (June 1973–December 1982) were reviewed. Of these 300 patients, 83 were surgical patients who developed ARF in the perioperative period and subsequently underwent hemodialysis. The first 65 patients from June 1973 to June 1980 constitute Group 1 and their data were used to derive a prognostic index.

The prognostic index was developed in 1980[14] and then prospectively validated on an additional 18 patients treated from July 1980 to December 1982, who constitute Group 2.

The following data were obtained for analysis:

1. Age, sex.
2. Length of hospitalization to include number of days in special care units.
3. Preexisting medical problems to include:
   (A) chronic renal insufficiency defined as a creatinine or blood-urea nitrogen (BUN) twice normal for greater than 1 month.
   (B) history of chronic renal failure that required dialysis or renal transplantation. (These patients were excluded from study.)
4. Date and type of all surgical procedures during this admission.
5. Presence of trauma directly preceding admission with calculated injury severity score (ISS) as described by Baker.[15]
6. Onset of ARF, defined as an increase in serum

TABLE 1. *Results of Univariate Analysis (Group 1)*

Variable	Alive	Dead	Significance
Cardiac failure	25%	66%	0.02
Number of systems failed	3.0	3.8	0.03
Number of transfusions	10 (50%)	10 (87%)	0.03
Noncavitary surgery	17%	2%	0.05
Age	41.2 ± 24	57.0 ± 17	0.01
Injury severity score	28.5 ± 8	42.0 ± 11	0.05
Creatinine prior to first hemodialysis	6.6 ± 1.7	8.2 ± 3.2	0.02
Interval acute renal failure (ARF) to hemodialysis	6.0 ± 2.8	8.6 ± 7.8	0.06
Aortic surgery	0%	25%	0.13
Preoperative chronic renal insufficiency	8%	3%	NS
Sepsis	66%	66%	NS
Emergent surgery	42%	45%	NS
Perioperative myocardial infarction	8%	5%	NS
Cardiovascular disease	33%	18%	NS
# of hemodialysis	5.7 ± 4.8	7.5 ± 7.8	NS
Interval from surgery to ARF	5.2 ± 4.6	3.9 ± 7.2	NS

creatinine and BUN of twice preoperative values or urinary output <400 ml/day after excluding pre- and postrenal causes.[1,16]

7. Etiology of ARF.
8. Date of onset of hemodialysis and number of dialyses.
9. Creatinine, BUN, and potassium (K+) at onset of dialysis.
10. Presence of failure of other organ systems:
    (A) respiratory failure as defined by Fulton and Jones,[17] which, in general, requires at least 120 hours of mechanical respiratory support of $F10_2$ of 0.5 or greater.
    (B) cardiac failure based on the criteria of Tilney,[7] which included a cardiac index Cl of ≤2.2, cardiogenic shock requiring pressor support in combination with elevated pulmonary artery wedge pressures, arrythmias that compromise cardiac output not metabolic in origin, or electrocardiogram (ECG) and enzyme evidence of perioperative myocardial infarction.
    (C) hepatic failure defined as a bilirubin greater than 2 mg/dl with elevation of liver enzymes to levels twice normal.[13,18]
    (D) gastrointestinal failure defined as bleeding stress ulcers requiring at least two units of blood in 24 hours.[2,12,13]
    (E) neurological failure defined as failure to respond to other than painful stimuli[7,18] or all grades of coma,[19]
11. Presence of sepsis defined by positive blood cultures in the clinical setting of hypotension with decreased systemic vascular resistance and increased cardiac index.
12. Whether surgery was elective or emergent.
13. Presence of significant preoperative hypotension.
14. Number of transfusions.
15. Use of hyperalimentation.
16. Postoperative complications to include:
    (A) coagulopathy.
    (B) pancreatitis.
17. Mortality.

Data Analysis

The data were evaluated for overall mortality for each group. Student's t-tests and chi-square tests were used to assess whether individual variables differed significantly between survivors and nonsurvivors at $p \leq 0.05$. Next a step-wise discriminant function analysis was performed to derive a linear discriminant function index that could be used to delineate between survivors and nonsurvivors using Group 1 data. To use the index derived from the discriminant function to classify patients, a criterion value must be chosen to separate patients with a high risk of death from those with a low risk of death. In establishing our criterion values, we used the usual value of the average of the mean index scores for survivors and nonsurvivors. To further quantify the chance for survival, posterior probabilities of mortality for each index score derived from the discriminant function were calculated. Similar scores and probabilities were then derived for patients in Group 2 in order to validate the index derived using Group 1 data. The distribution of the posterior probabilities for Groups 1 and 2 were compared using the Kolnogorov–Snivnov test,[20] while the actual classification matrixes for Group 1 and Group 2 were compared using the Mantel–Haenzel test.[21]

Results

Group 1—Derivation of the Linear Discriminant Function

The mortality for Group 1 was 81% (53 of 65 patients). All patients underwent surgery with 15 patients having multitrauma as the precipitation factor. There were 57 men, of whom 12 survived and eight women, all of whom died.

Initial screening of the variables by univariant chi-square methods (Table 1) indicated that four variables were significantly different ($p < 0.05$) between survivors and nonsurvivors: number of transfusions, number of organ systems failed, presence of cardiac failure, and noncavitary surgery. In addition, screening of continuous variables by t-test methods indicated that age, creatinine level prior to first hemodialysis, and injury severity score for trauma patients were significant at a $p \leq 0.05$. The interval from ARF to dialysis approached significance at p = 0.06 (Table 1).

The only single organ system failure that increased the risk of dying was cardiac failure. Although other individual organ systems failures were not by themselves significant, the total number of organ systems failed significantly effected survival (p = 0.03). For each additional system failed, mortality increased in a nonlinear fashion (Fig. 1). The mean number of systems failed for survivors was three and for nonsurvivors 3.8. Five or more systems failed was fatal in 13 of 14 patients.

The presence of pancreatitis or coagulopathys carried high mortality rates, but the number of patients in each category was too small for statistical significance. Fourteen of 15 patients with coagulopathys died and all five patients with pancreatitis died.

The type of surgery was quite varied among patients but overall did not vary significantly between survivors and nonsurvivors. Of the 14 patients undergoing surgery for abdominal aortic aneurysms (AAA), nine were ruptured, four elective, and one patient was reoperated on for a leaking suture line. None of the patients with AAA survived. Thirteen patients were postcardiac surgery with four survivors and nine nonsurvivors. Thirty-one patients had had nonvascular intra-abdominal surgery with four survivors and 27 nonsurvivors. Seven additional patients had miscellaneous extra-abdominal procedures of which four survived.

Subsequent to construction of correlation matrices, a step-wise linear discriminant function analysis was performed to derive an index that would delineate between survivors and nonsurvivors. Variables were added to the function in a manner that would increase the ability of the function to discriminate between survivors and nonsurvivors. The analysis was concluded when addition of more variables did not increase the accuracy of discrimination. The following linear discriminant function (LDF) was derived:

$$\text{LDF} = \text{A (age)} + \text{B (\# of transfusions)} + \text{C (cardiac surgery)} + \text{D (cardiac failure)} + \text{E (sex)} + \text{F (vascular surgery other than AAA)} + \text{G (interval from ARF to dialysis)} + \text{H (preoperative hypotension)} + \text{I}.$$

The variables were encoded as shown in Table 2.

The distribution of scores is shown in Figure 2. The scores range from −2.04 to 3.95 with a mean of −0.130. The mean LDF score for survivors was 1.76 and for nonsurvivors −0.423. The value used for predictive purposes was the average of the means or 0.669. Patients with a score less than 0.669 had greater than a 50% chance of dying and were classified as nonsurvivors. Patients with a score greater than 0.669 had greater than a 50% chance of being a survivor and were classified as a survivor regardless of actual outcome (Table 3). Two survivors were incorrectly classified as nonsurvivors. Posterior probabilities were then performed to assign a probability of being a nonsurvivor for each score (Fig. 2). A score of −0.686 or less entails at least a 95% probability of being a nonsurvivor. No survivors scored less than −0.686 while 26 of 53 (49%) nonsurvivors did. The lowest score by a survivor was −0.0132; the patient had a 19% probability of being a survivor.

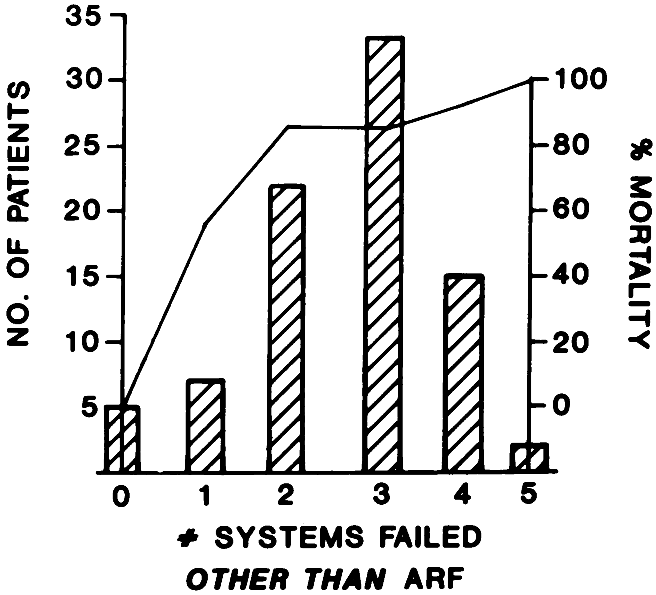

FIG. 1. The histogram represents the number of patients with 0 to 5 organ systems failed other than acute renal failure (ARF). The curve represents actual per cent mortality for each group. Data are from Groups 1 and 2.

TABLE 2. *Linear Discriminant Function Variable Codes and Coefficient Constants*

Constant	Variable	Significance*
A = 0.034	Age: actual age in years	0.0089
B = −0.472	# of transfusions: 5 = 1, 5–10 = 2 11–20 = 3, 20 = 4	0.0006
C = 1.43	Cardiac surgery; No = 0, Yes = 1	0.0002
D = −1.21	Cardiac failure; No = 0, Yes = 1	0.0000
E = 1.44	Sex; male = 1, female = 0	0.0000
F = 1.09	Vascular surgery†; No = 0, Yes = 1	0.0001
G = −0.050	Interval in days from onset acute renal failure to dialysis	0.0001
H = −0.75	Preoperative hypotensin; No = 0, Yes = 1	0.0001
I‡ = 3.19		

* Significance level addition of variable adds to function.
† Other than abdominal aortic surgery.
‡"I" represents the constant for the equation and is not associated with a variable.

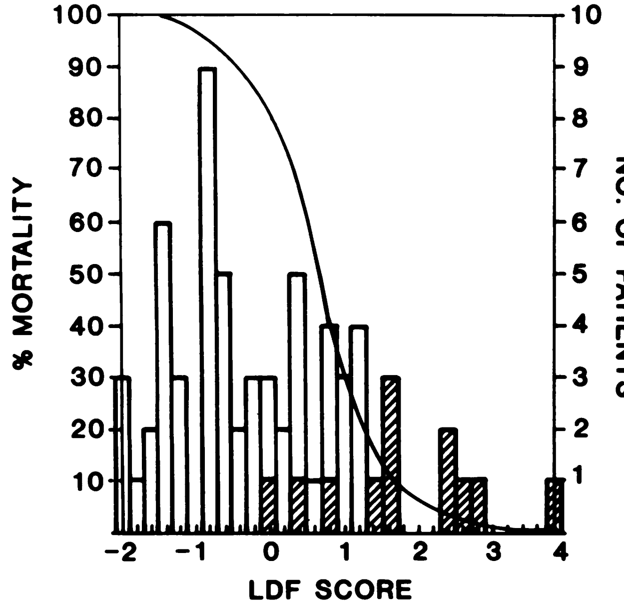

FIG. 2. Distribution of scores: Group 1, the histogram represents the number of patients with each score. Cross-hatched area represents survivors. The curve represents per cent mortality based on posterior probabilities for each score.

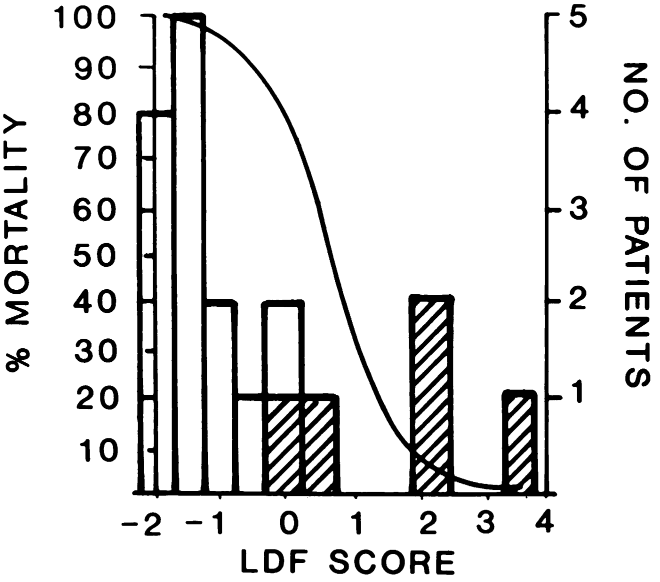

FIG. 3. Distribution of scores: Group 2, the histogram represents the number of patients with each score. Cross-hatched area represents survivors. The curve represents per cent mortality based on posterior probabilities for each score.

Group 2–Validation of Index

Group 2 mortality was 73% or 13 of 18 patients. There were 15 men, of whom five survived and three women, all of whom died. No patients had trauma as the precipitating event. The mean age of survivors was 50.6 years and nonsurvivors 70.4 years ($p < 0.05$). Deaths occurred in five of eight nonvascular abdominal surgery patients, two of three cardiac surgery patients, three of four ruptured AAA patients, and three of three elective AAA. Linear discriminant function from −3.29 to 3.95, with a mean of +1.68 for survivors and −1.46 for nonsurvivors. The overall mean was −0.60. Distribution of scores are shown on Figure 3. The lowest score by a survivor was −0.279.

TABLE 3. *Accuracy of the Linear Discriminant Function (LDF) Score in Predicting Survival or Nonsurvival of Acute Renal Failure Patients*

		Predicted Status	
Group	Actual Status	Alive*	Dead†
1	Alive (12)‡	83%§ (10)	17% (2)
	Dead (53)	19% (10)	81% (43)
2	Alive (5)	80% (4)	20% (1)
	Dead (13)	0% (0)	100% (13)

* Patients with a LDF score greater than 0.669. This score represents the average of the mean scores for alive and dead patients.

† Patients with a LDF score less than 0.669.

‡ Actual number of patients in each group.

§ Percentage of actually alive or dead patients predicted to be alive or dead.

Linear discriminant function scores for each group were then segregated as to actual outcome. Comparison of index scores between Groups 1 and 2 indicate that no differences were apparent for survivors ($p = 0.87$). For those patients who did not survive, Group 2 had a somewhat more negative mean value when compared to Group 1 ($p = 0.02$) and all scores were less than the criterion value of 0.669.

To further examine the comparability of the classification probabilities between Groups 1 and 2, data were cross-tabulated for each group based on patient status and predicted outcome. Scores less than 0.669 were classified as nonsurvivors and scores greater than 0.669 as survivors (Table 3). Comparison of the performance levels of the classifications for Group 1 and Group 2 data indicate a substantial similarity in discrimination between survivors and nonsurvivors ($p = 0.50$).

Discussion

Prior to the advent of hemodialysis, ARF carried a mortality in excess of 90%.[22] Improvements in hemodialysis as well as general medical support of the critically ill have considerably improved the outcome of isolated ARF.[19] However, ARF occurring in the postoperative patient is still associated with a high mortality.[1–12] The surgical patient with ARF frequently has multiple organ failure. The poor prognosis of ARF in the setting of multiple organ failure has been described by Eiseman[13] as well as others.[18,19] Tilney,[7] in describing patients with

ARF following repair of ruptured abdominal aortic aneurysms, stated "all patients subjected to this combination will experience progressive, sequential organ system failure and eventually succumb."

Since the incidence of postsurgical ARF remains fairly constant in certain populations, (approximately 2% in cardiac surgery series,[5,22] 2% in elective abdominal aortic aneurysms, and 20% in ruptured aneurysms,[6]), data upon which logical decisions can be made concerning treatment are necessary. With the development of sophisticated statistical analytic techniques such as multivariant analysis, numerous investigators have attempted to develop prognostic indices for critically ill patients with ARF. McLeish,[23] using univariant analysis, identified age, nonoliguric renal failure, and number of medical complications as important prognosticators while Baek[16] concluded that age was insignificant. Luft and colleagues,[24] using a stepwise discriminant function program, concluded that age greater than 70 years, interruption of renal blood flow, and preoperative renal dysfunction were the only reliable prognostic variables in patients with ARF following aortic aneurysm repair. However, Porter[25] claimed that preoperative renal dysfunction was of little significance. Routh et al.[31] attempted to use a clinical scoring system as described by Civetta, which quantified the severity of illness in patients with ARF. While Routh identified old age, sepsis, and gastrointestinal disease as important adverse variables, he was unable to define a subset of patients without chance of survival. Eiseman[13] reported a 70% mortality with two or more organ systems failed but a total of at least three systems was necessary to reach this level of mortality in our patient series (Fig. 1). The presence of hepatic failure with ARF in our patients was not universally fatal as previously reported.[2] However, pancreatitis associated with ARF in our patients was fatal.[27,28] Preoperative renal dysfunction did not influence outcome, though Luft[24] has suggested that this is a critical factor in patients undergoing abdominal aortic aneurysm surgery. Sepsis in itself did not increase mortality, though sepsis likely plays a major role in the etiology of ARF as suggested by Eiseman[29] and Fry.[18] We found creatinine level prior to the first dialysis and the interval to the onset of dialysis as the only significant factors based on univariant analysis that could be altered to potentially affect outcome. This supports the data of Conger,[9] who found in trauma patients a 64% mortality when dialysis was instituted at the first signs of ARF compared to 80% for those patients dialyzed late. This suggests that when patients with postoperative ARF are to be hemodialyzed that dialysis be instituted early.

By using a linear discriminant analysis, we are attempting to use patient specific data to identify as many nonsurvivors as possible without misclassifying survivors.

TABLE 4. *Tripartite Distribution of Scores for Each Group Segregated According to the Mean Scores for Survivors and Nonsurvivors*

	Linear Discriminant Function (LDF) Score		
	−0.423*	−0.423–+1.76	+1.76†
Group 1			
Survivors	0%	58%	42%
Nonsurvivors	57%	43%	0%
Group 2			
Survivors	0%	40%	60%
Nonsurvivors	85%	15%	0%

* Mean LDF score for nonsurvivors in Group 1.
† Mean LDF score for survivors in Group 1.

The linear discriminant analysis has the ability to assess the probability of dying for any given patient developing acute renal failure in the postsurgical period (Fig. 1). Additionally, the LDF is of value in enabling one to identify variables that can be altered to affect outcome.

In reviewing the variables that were included in the LDF, an apparent discrepancy appears. First, some variables that were statistically significant on univariant analysis are not included while some variables not significant are included. Multivariant analysis such as that used in the LDF analysis compares groups of variables instead of single variables. A variable may be insignificant on univariant analysis but when grouped with others, significance is reached. The concept of multivariant analysis is to study how groups of variables are related. This helps to unmask the effect that variables have on one another. Variables that are related need not both be used in the LDF. Thus, only the interval from ARF to dialysis and not the creatinine level prior to dialysis was used.

Validation of the LDF is necessary before clinical application. The LDF derived from Group 1, when applied to a second population of patients, accurately segregated patients. Statistically, the classification probabilities for each group were the same. When applied to Group 2, four of five survivors (80%) and all 13 nonsurvivors (100%) were correctly identified for a predictive accuracy of 95%. This does not mean that one can predict a 100% probability of dying for any patient with a score less than 0.669. However, by the use of posterior probabilities, one may select scores that segregate patients into categories with high, intermediate, and low risk of dying. (Table 4) The scores used are the means of survivor and nonsurvivor for Group 1. A score less than −0.423 would represent patients with no precedent for survival between −0.423 and 1.76 an intermediate risk, and greater than 1.76 a low risk for dying. No survivors and 62% of nonsurvivors are in Category 1; 53% of survivors and 38% of nonsurvivors are in Category 2; and 47% of survivors and no nonsurvivors are in Category 3.

The individual data from the two survivors in Group 1 who were originally misclassified are quite similar. Both had heart surgery at age 66; three other systems failed, including cardiac; and both patients were septic while receiving their first dialysis at a creatinine less than 6 mg/dl. They received low LDF scores because of the long interval from the onset of ARF to dialysis. The results of the Pearson correlation coefficients showed that the creatinine level prior to the first dialysis and the interval from the onset of ARF to dialysis are correlated in a positive direction at $p < 0.10$. Thus, patients with fulminant ARF who receive dialysis late would have a high value for each variable. These two patients had low creatinines at first dialysis despite a long interval from ARF to dialysis. Neither patient had severe ARF and, indeed, the patient with the lowest score required only one dialysis before return of renal function. The one survivor in Group 2 who was misclassified as a nonsurvivor was a 63-year-old man who underwent emergent surgery for a leaking AAA. He had two other failed systems and underwent dialysis in his second anuric day at a creatinine of 4.9 mg/dl. The explanation for this low score is the presence of significant preoperative hypotension necessitating multiple transfusions. Of note, he is the only AAA patient who developed ARF to survive in either group.

The mortality rate of 80% in the series presented here is higher than that in the current literature. An extensive review by Brown and colleagues[32] revealed a mortality rate of 57% in 1994 patients collected from multiple series and a 62% mortality in their own patients. The difficulty in comparing mortality data from multiple series is that each series contains patients of varying qualifications, not all of whom received dialysis and those receiving dialysis did so for differing indications. In the series presented here, all patients were postoperative and underwent hemodialysis.

The cost of postoperative renal failure requiring dialysis is considerable. Certainly, patients with postsurgical ARF fall into the group as discussed by Drucker et al.,[26] where 8% of the patients consumed 25% of surgical dollars spent. Because of the significant economic issues involved, Cullen has commented that resources for the critically ill are finite and decisions on who will receive treatment may have to be made in the future.[30] These same issues prompted Butkus[33] to comment in a recent editorial ". . . Attention should be given to defining which combination of factors are potentially reversible and which circumstances always foretell a fatal outcome. In this way, appropriate value judgments can be made before dialysis is instituted, sparing endless costs and grief when dialysis may not be indicated." This expenditure would be warranted if all patients had equal chance for survival. But in the setting of ARF superimposed upon multiple organ failure, a significant number of patients consume a large share of resources and have little or no chance for survival. The availability of objective data to identify patients with no chance for survival could result in a significant economic savings as well as decreasing the physical and mental anguish associated with a prolonged but ultimately fatal postoperative course. Additionally, our analysis allows one to study factors that influence survival in a group of patients in which clinical impression and basic intuition does not enable one to accurately determine which patients have a chance for survival and who should be fully supported.

Summary

In summary, a review of 65 patients with perioperative ARF requiring hemodialysis revealed a 81% mortality. Eight variables differed significantly between survivors and nonsurvivors at a $p \leq 0.05$. The significant variables were multiple organ failure, multiple transfusions, cardiac failure, time interval from surgery to onset of ARF, patient age, type of surgery, injury severity score, and creatinine level prior to first dialysis. A linear discriminant function was derived to separate survivors and nonsurvivors. The linear discriminant function was validated prospectively with a second group of 18 patients. The prognostic index derived allows one to segregate patients into those with little chance of survival, those with an intermediate chance of survival, and those with a good chance of survival.

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