Arterial Lactate and Bilirubin as Clinical Predictors of Survival in Critically III Patients Treated with Continuous Renal Replacement Therapy: A Retrospective Analysis

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A. Study Purpose and Rationale

Acute renal failure in the ICU setting is present in up to 30% of patients, and is a significant cause of mortality despite advances in the treatment in renal replacement therapy. Mortality ranges between 40-70% for patients who develop renal failure in the ICU. Treatment for these patients consists of either standard intermittent hemodialysis (IHD) or continuous hemodialysis, or CVVHD (continuous veno-venous hemodiafiltration). This latter therapy has been FDA approved since the mid- I 980's and has allowed physicians to treat hemodynarnically unstable patients who would otherwise not tolerate IHD. The survival of patients initiated on CVVHD in this hospital for the last 3 years is not known; in the literature mortality with CVVHD ranges between 3656% (Sasaki et al, 2001; Cole et al 2000; van Bommel et al 1995; Bellorno et al 1994).

CVVHD is intended as a bridge until renal function returns, or until patients are stable enough to tolerate regular intermittent hemodialysis. However, given the high mortality in these patients, CVVHD appears to be often initiated after a "window of opportunity" has passed, and the CVVHD has no impact on survival; instead, the intervention becomes one of simply delaying or complicating end-of-life decisions for patients, their families, and their doctors. Identifying a stage of illness where CVVHD ceases to have an impact on patient survival would be a valuable tool for doctors, both in managing patients and in discussions with families about end-of-life care. Likewise, CVVHD is a limited resource, which should be used judiciously; prognostic indicators would be helpful to help use this resource more effectively.

At present there is no formally recognized way to screen patients for CVVHD, and the initiation of this treatment depends on the summary of clinical judgment from doctors, after discussion with the family and patient if possible. A variety of studies have attempted to identify which ARF patients are more likely to benefit from the initiation of CVVHD, but these are observational in nature and have provided conflicting data. Severity of illness scores (such as APACHE 11), co-morbid illnesses, number of organ failures, age, and ventilation status, among others, have been analyzed as mortality predictors in patients with ARF in the ICU without consistent results.

Brivet et al (1996) found that age, previous health status, hospitalization before ICU course, delayed occurrence of ARF, sepsis, oliguria and APACHE 11 score were associated with worse prognosis, but not to a degree that would help with decision making. Several studies have failed to find association between APACHE 11 scores and outcome of acute renal failure in the ICU (Schwik et al, 1997; Schaefer et al 199 1). Fewer studies have looked at predictors of outcome in relation to CVVHD. Takahira et al (200 1) found that the APACHE 11 score on day 3 of CVVHD, but not on the first day, was able to predict future mortality. Van Bommel et al (1995) found that in 60 peri-op pts treated with CVVHD, there was an association between hospital death and higher APACHE 11 scores, mechanical ventilation, vasopressor support and septicemia, but found there was no way to identify with certainty those patients most likely to benefit from CVVHD. In one study, age was not a predictive factor; Bellomo et al (1994) found that elderly patients (>65) did as well as equally sick younger patients when treated with CVVH in the ICU.

Sasaki et al (200 1) found that in an observational uncontrolled study of 41 patients treated with CVVHD (23 of whom survived to hospital discharge), a bifirubin level >I 0 mg/dI or arterial lactate level >3.5 mmol/L may be used to predict hospital mortality for patients initiated on continuous renal

replacement therapy. These cut-off values provide an 83.3% sensitivity and 90.9% specificity. There was also a strong association between death and hepatic failure.

Our hypothesis is that elevated arterial lactate and bilirubin can predict death with at least 85% accuracy in patients with ARF in the ICU treated with continuous renal replacement. A secondary analysis of the data will be performed to identify any other possibly predictive clinical indicators such as APACHE 11 score, number of organ failures, underlying diagnose, urine output, or other physiologic data.

B. Study Design and Statistical Analysis

This will be a retrospective study. In this study we will identify all the patients with acute renal failure placed on CVVHD in one of four ICUs in the Columbia-New YorkPresbyterian Hospital, from January 1999-December 2001. This should amount to approximately 400 patients. Their charts will be pulled and Web-cis data will be retrieved in regards to the information listed below. Subjects will be divided into two groups, survivors and non-survivors, at the time of discharge from the hospital. It is expected that there will be approximately 180 survivors and 220 non-survivors, an estimate reached by reviewing our personal experience and published data. The values for bilirubin and arterial lactate last obtained prior to initiating CVVHD will be recorded.

To detect an accuracy of at least 85% for elevated bilirubin and arterial lactate, we will need at least 369 patients by chi-square test.

The charts will also be reviewed for secondary analyses; age, sex, race, etiology of renal failure, data on APACHE 11 score, number of organ failures, underlying disease, urine output, pH, presence of mechanical ventilation, central venous pressure and cardiac index will be collected and used in a multivariable logistic regression to determine predictors for hospital mortality.

C. Study Procedure

As noted, this will be a retrospective analysis in the form of chart and computer data review by the investigator. The chart will be reviewed until death of the patient or discharge from the hospital.

D. Medications:

none

E. Medical Device:

Prisma continuous hemodiafiltration unit, via venous-venous access with a double lumen catheter into either the femoral, subclavian or internal jugular vein. Specifications of each patient's dialysis, as recommended by the consulting nephrologists, will vary according to flow rate of the dialysate, blood, and ultrafiltrate; and the composition of the dialysate.

F. Study Questionnaire:

See attached for the data abstraction form.

G. Study Subjects:

Study subjects will be all patients from January 1999-December 2001 treated with continuous renal replacement (hemodiafiltration) in one of the four Columbia-New York Presbyterian Hospital intensive care units, for the treatment of ARF. Exclusion criteria shall include: no previous dialysis, age <20, metastatic cancer, brain death. Any patient undergoing other blood purification such as plasma

exchange, intermittent hemodialysis, or hemofiltration (without dialysis) will not be included, as well as any patients who underwent CVVHD for any non-renal indications.

H. Recruitment:

All patients who have undergone CVVHD in 2001 will be identified through the dialysis unit, which records all patients it dialyzes in the ICU.

I. Confidentiality of Study Data:

Patient's data will be recorded anonymously by a unique code number, and data will be secured in a location accessible only to the investigators.

J. Potential Conflict of Interest:

There is no relationship to be disclosed between the investigators and the makers of the CVVHD machine or companies that make the assays for bilirubin and lactate.

K. Location of the Study:

Study will be performed within CPMC.

L. Potential Risks:

There are no potential risks to the subjects given the retrospective nature of the study.

M. Potential Benefits:

There are no potential benefits to the subjects, other than a potential benefit to society in general.

N. Alternative Therapies:

none

O. Compensation to Subjects:

There will be no compensation for subjects whose charts are reviewed. P. Costs to subjects: none. Q. Minors as research subjects: There will be none. R. Radiation: none.

P. References:

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