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# Predicting mortality in patients on continuous venovenous hemofiltration and hemodiafiltration

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#### **Abstract**

#### Introduction

The purpose of this study is to correlate levels of mortality in patients on CVVH/D with the degree of illness as determined by the APACHE II score. We also identified variables that were part of the APACHE II score that had the most significant impact on outcome. No study has looked at this particular question. This could give physicians, patients and families better information on which to base care decisions.

#### **Aims**

To identify and quantify variables that predict mortality in critically ill patients on CVVH/D.

#### Methods

#### General Description

The study was a retrospective descriptive analysis of all patients in the ICU's at Hartford Hospital who were on CVVH/D between January 1997 and December 1999.

#### **Patients**

There were 83 patients on CVVH/D during the specified time period with complete information. Those who were placed on this form of renal replacement therapy were considered too hemodynamically unstable to tolerate hemodialysis.

#### Data

Age, sex, past medical history, admission diagnosis, operations, number of failing organ systems and survival were recorded for all patients. The following data was obtained from the date of initiation of CVVH/D: sodium, potassium, creatinine, pH, PaO2, hematocrit, white cell count, Glasgow Coma Scale, temperature, heart rate, respiratory rate, and mean arterial pressure. The APACHE II score was calculated using the method described in Knaus et al. [5]

#### Statistical Analysis

Survivors and nonsurvivors were compared. Parametric data was analyzed using the student's t test with the Levene's test for equality of variance. The Mann-Whitney test was used for nonparametric data. A logistic regression analysis was done for the APACHE II score and age, after these were determined to be the most significant variables for determining mortality.

#### Results

Of the eighty-three patients for whom we were able to obtain all necessary data, twenty-two (26.5%) survived until hospital discharge. Table 1 describes the diagnoses in our population.

**Table 1** Diagnoses in Survivors and Nonsurvivors on CVVH/D

Diagnosis	Survivors	Nonsurvivors	
Cardiac	10	31	
Gastrointestinal	1	8	
Sepsis/SIRS	2	7	
Pneumonia	2	4	
Vascular	3	2	
Liver	0	4	
Trauma	2	2	
Pancreas	0	2	
Hematologic	1	1	
Neurologic	1	0	
Total	22	61	

Fifty-nine (71.1%) were surgical patients and twenty-four (28.9%) were medical. Survival was 28.8% in surgical patients and 20.1% in medical patients, which was not statistically significant (p = 0.221). Twenty-two (26.5%) patients had acute on chronic renal failure and sixty-one (73.5%) had acute renal failure. Survival was 31.8% in the former and 24.6% in the latter; again, this was not significant (p = 0.281). There were fifty-three (63.4%) males and thirty (36.6%) females; there was no difference in the male: female ratio between survivors and nonsurvivors.

All of the patients had at least three-organ system failure, including cardiovascular, renal and respiratory failure. Eleven patients had four organ system failure (nine had hepatic failure and two had anoxic brain injury) and all but one of these died.

At the time the decision was made to initiate CVVH/D, the APACHE II score and the age were significantly different (p < 0.01) between survivors and nonsurvivors (Table 2). The Chronic Health Problem score, pH, and creatinine were also significantly different (p < 0.05).

**Table 2** Comparison of Parameters for Survivors and Nonsurvivors

Parameter	Survivors		Nonsurvivors		р
	Mean	SD	Mean	SD	
APACHE II score	24.6	4.0	28.2	5.7	0.008
Age	54.6	16.7	64.7	14.9	0.010
Chronic Health	2.1	2.3	3.4	2.2	0.023
Problem score					
Temperature (C <sup>0</sup> )	36.7	1.2	37.0	0.8	0.311
Heart Rate	94	20	96	20	0.735
Mean Arterial Pressure	75	19	71	16	0.620

Respiratory Rate	14	5	16	7	0.550		
PH	7.38	0.06	7.34	0.08	0.026		
Sodium	136	8	138	6	0.353		
Potassium	4.4	0.7	4.5	0.8	0.574		
Creatinine	4.9	1.4	3.9	1.7	0.016		
White Cell Count	15.4	9.7	15.5	12.1	0.968		
Hematocrit	28.9	2.6	29.5	3.6	0.424		
Glasgow Coma Scale	8	3	8	3	0.663		
Number Organs Failed	3.0	0.2	3.2	0.4	0.413		
Boldface indicates significance with a p value of 0.050.							

Logistic regression analysis of the APACHE II score and age showed that APACHE II score less than or equal to 25 versus greater than 25, and age less than 60 versus greater than or equal to 60 were the most useful cutoff values. The odds of dying was 4.8 times higher for a person requiring CVVH/D if they were 60 years old or more than if they were younger than 60. The odds of dying was 3.7 times higher if their APACHE II score was greater than 25. Furthermore, an APACHE II score greater than 25 and age greater than or equal to 60 years (thirty-two patients) predicted mortality in 91% of these patients.

#### Discussion

Mortality in patients requiring CVVH/D in the ICU is quite high because, by definition, these patients have at least two-organ system failure. In our series, all had at least three-system failure. However, most physicians and patients would probably agree that even a mortality of 60–80% does not constitute futile care. We set out to identify variables which might help us define subgroups in which CVVH/D is futile.

The APACHE II score was chosen because it is a broadly accepted and commonly used score for determining the degree of illness of patients in the ICU. Ideally, this score would have been calculated during the first twenty-four hours of admission to the ICU. However, the vast majority of our patients did not have complete data at that point in time. We were, however, able to obtain complete data sets for all of our patients at the time CVVH/D was started.

Also, the APACHE II score is ideally used to describe large groups of patients. The relatively small size of our group, therefore, weakens our conclusions. Nevertheless, this is the largest analysis of this type ever completed. Previous studies have looked at very small numbers of patients with specific diagnoses.

Gender and a history of chronic renal failure did not have an impact on mortality. Neither was there a difference between surgical and medical patients. As expected, nonsurvivors had a significantly higher APACHE II score at the time of initiation of CVVH/D than survivors. Age was the most important component of the APACHE II score; survivors were significantly younger than nonsurvivors. Survivors tended to have a higher pH and a lower Chronic Health Problem score than the nonsurvivors. And interestingly, the creatinine tended to be higher in the survivors; we cannot explain this finding. A larger sample size (two hundred) would be needed to include pH, the Chronic Health Problem score and creatinine in a logistic regression analysis.

A much larger multiinstitutional analysis or a metaanalysis would be required to more accurately define how acidosis, creatinine level, previous chronic health problems and specific diagnoses affect the ultmate outcome. However, this paper does show that the APACHE II score at the time of the initiation of CVVH/D and the age of the patient were important predictors of mortality in patients requiring CVVH/D. Whether further therapy, including CVVH/D, constitutes futile care in these patients, will still need to be decided by patients, their families and their physicians. We hope that this data will be of use in making this decision.

APACHE II scoring system, continuous venovenous hemodiafiltration, continuous venovenous hemofiltration, outcomes analysis

# Introduction

Patients who are ill enough to require admission to the ICU and who require CVVH/D have a mortality rate of 60–80% [1,2,3,4]. The few studies, which have looked at outcomes in patients on CVVH/D, have focused on particular subgroups of patients, and included burn victims, liver transplants and heart transplants [2,3,4]. They did not make any attempt to objectively determine how ill the patients were to begin with. Swartz et al. compared patients needing CVVH/D versus hemodialysis (HD)[1]. They believed that patients needing HD were not as ill as those on CVVH/D and thought the difference in mortality could be accounted for by this fact. However, they were unable to determine the (Acute Physiology and Chronic Health Evaluation) APACHE II scores and objectively confirm this suspicion.

The purpose of this study is to correlate levels of mortality in patients on CVVH and CVVHD with the degree of illness as determined by the APACHE II score. We also identified variables that were part of the APACHE II score that had the most significant impact on outcome. No study has studied this particular question. This could give physicians, patients and families better information on which to base care decisions, and would result in better utilization of resources and cost containment.

# Materials and Methods

# **General Description**

The study was a retrospective descriptive analysis of all patients in the medical and surgical ICU's at Hartford Hospital who were on CVVH/D between January 1997 and December 1999. Approval of the study was obtained from the Institutional Review Board at Hartford Hospital; informed consent was waived.

### **Patients**

There were 85 total patients on CVVH/D during the specified time period. The charts of two of the patients were unavailable; these were excluded. Those who were placed on this form of renal replacement therapy were considered too hemodynamically unstable to tolerate hemodialysis.

### Data

Age, sex, past medical history, admission diagnosis, operations, number of failing organ systems and survival were recorded for all patients. The following data was obtained from the date of initiation of CVVH/D: sodium, potassium, creatinine, pH, PaO2, hematocrit, white cell count, Glasgow Coma Scale, temperature, heart rate, respiratory rate, and mean arterial pressure. The APACHE II score was calculated using the method described in Knaus et al. [5] An attempt was made to obtain the same data from admission to the ICU as well, but very few patients had all of the necessary data.

# Statistical Analysis

Survivors and nonsurvivors were compared. Parametric data was analyzed using the student's t test with the Levene's test for equality of variance. The Mann-Whitney test was used for nonparametric data, including the APACHE II score and its component Chronic Health Problem score. A logistic regression analysis was done for the APACHE II score and age, after these were determined to be the most significant variables for determining mortality.

# Results

Of the eighty-three patients for whom we were able to obtain all necessary data, twenty-two (26.5%) survived until hospital discharge. Forty-one (49.3%) were cardiac patients (Table 1) and included those with coronary artery disease, myocardial infarction, congestive heart failure and valvular disease. Of the patients with SIRS, one had sepsis from necrotizing fasciitis. The gastrointestinal diagnoses included obstruction and bleeding. All of the liver patients were in failure and awaiting transplant. One pancreas patient had pancreatitis and one had a carcinoma. All of the vascular patients had an aortic aneurysm or occlusive disease. One trauma patient had rhabdomyolysis from pressure necrosis. The others had severe multisystem injuries after motor vehicle accidents.

Fifty-nine (71.1%) were surgical patients and twenty-four (28.9%) were medical. Survival was 28.8% in surgical patients and 20.1% in medical patients, which was not statistically significant (p = 0.221). Twenty-two (26.5%) patients had acute on chronic renal failure and sixty-one (73.5%) had acute renal failure. Survival was 31.8% in the former and 24.6% in the latter; again, this was not significant (p = 0.281). There were fifty-three (63.4%) males and thirty (36.6%) females; there was no difference in the male:female ratio between survivors and nonsurvivors.

All of the patients had at least three-organ system failure, including cardiovascular, renal and respiratory failure. In this study we defined patients with cardiovascular failure as those who needed inotropic, pressor and/or mechanical support. Those with renal failure required renal replacement therapy. Those with hepatic failure were coagulopathic, encephalopathic and/or jaundiced. Those with respiratory failure required ventilatory support. Those with brain failure included those with anoxic brain injury. Eleven patients had four organ system failure (nine had hepatic failure and two had anoxic brain injury) and all but one of these died. This last was a man who had anoxic brain injury after a cardiac arrest who eventually went to a nursing home. The difference in the number of organ system failures in the survivors and nonsurvivors was not significant (p = 0.413).

At the time the decision was made to initiate CVVH/D, the APACHE II score and the age were significantly different (p < 0.01) between survivors and nonsurvivors (Table 2). The Chronic Health Problem score, pH, and creatinine were also significantly different (p < 0.05).

Logistic regression analysis of the APACHE II score and age showed that APACHE II score less than or equal to 25 versus greater than 25, and age less than 60 versus greater than or equal to 60 were the most useful cutoff values. The odds of dying was 4.8 times higher for a person requiring CVVH/D if they were 60 years old or more than if they were younger than 60. The odds of dying was 3.7 times higher if their APACHE II score was greater than 25. Furthermore, an APACHE II score greater than 25 and age greater than or equal to 60 years (thirty-two patients) predicted mortality in 91% of these patients.

# Discussion

Mortality in patients requiring CVVH/D in the ICU is quite high. This is not to imply that CVVH/D is the cause. The high mortality is expected, since these patients, by definition, have at least two-organ system failure. In our series, all had at least three-system failure. However, most physicians and patients would probably agree that even a mortality of 60–80% does not constitute futile care. We set out to identify variables, which might help us define subgroups in which CVVH/D is futile.

The APACHE II score was chosen because it is a broadly accepted and commonly used score for determining the degree of illness of patients in the ICU. Ideally, this score would have been calculated during the first twenty-four hours of admission to the ICU. However, the vast majority of our patients did not have complete data at that point in time. We were, however, able to obtain complete data sets for all of our patients at the time CVVH/D was started.

Also, the APACHE II score is ideally used to describe large groups of patients. The relatively small size of our group, therefore, weakens our conclusions. Nevertheless, this is the largest analysis of this type ever completed. Previous studies have looked at very small numbers of patients with specific diagnoses. Oeseph et al. studied heart transplant patients; those needing CVVH or HD (six on CVVH and two on HD) had a mortality of 63.5%. These were too few to compare survivors and nonsurvivors. Mortality in the patients without renal failure was 9%. Leblanc et al. studied sixteen burn patients with renal failure; all received CVVH/D. Mortality was 82%; the mean APACHE II score at admission was 18.4 and the mean burn surface area was 58%. Again, there were not enough patients to compare survivors and nonsurvivors. Fiore et al. looked at eleven liver transplant patients requiring CVVH. A copy of the manuscript was not available for evaluation. There were not enough patients in our population to determine if specific diagnoses had an impact on survival.

Gender and a history of chronic renal failure did not have an impact on mortality. Neither was there a difference between surgical and medical patients. As expected, nonsurvivors had a significantly higher APACHE II score at the time of initiation of CVVH/D than survivors. Age was the most important component of the APACHE II score; survivors were significantly younger than nonsurvivors. Survivors tended to have a higher pH and a lower Chronic Health Problem score than the nonsurvivors. And interestingly, the creatinine tended to be higher in the survivors; we cannot explain this finding. A larger sample size would be needed to include pH, the Chronic Health Problem score and creatinine in a logistic regression analysis. A power analysis determined that two hundred patients would be required and we have not had that many on CVVH/D at Hartford Hospital.

A much larger multiinstitutional analysis or a metaanalysis of data from several institutions would be required to more accurately define how acidosis, creatinine level, and previous chronic health problems affect the ultmate outcome. Also, such a study would enable us to determine if specific diagnoses have any impact on survival.

However, this paper does show that the APACHE II score at the time of the initiation of CVVH/D and the age of the patient were important predictors of mortality in patients requiring CVVH/D. An APACHE II score greater than 25 and age greater than or equal to 60 years (thirty-two patients) predicted mortality in 91% of these patients. Whether further therapy, including CVVH/D, constitutes futile care in these patients, will still need to be decided by patients, their families and their physicians. We hope that this data will be of use in making this decision.

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