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Predicting Weaning in Patients Requiring Long Term Mechanical Ventilation

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PREDICTING WEANING IN PATIENTS REQUIRING LONG TERM MECHANICAL VENTILATION

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VITA

The author, Linda M. Curgian, was born May 11, 1955 in Chicago, IL. She earned a Bachelor of Science degree with a concentration in biology from the University of Notre Dame in 1977, a Bachelor of Science in Nursing degree from Lewis University in 1979, and a Masters of Science Degree in Nursing from Yale University in 1981. In 1988 she was admitted to the Graduate School at Loyola University of Chicago where she pursued the Doctor of Philosophy degree with a double major in Research Methodology and Educational Psychology.

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CHAPTER I

INTRODUCTION

Mechanical Ventilatory Support (MVS)

Mechanical ventilatory support is one of the major supportive modalities used in critical care management of patients who are unable to spontaneously maintain an adequate respiratory status. MVS, one of the artificial life-support systems, entails connecting a person via a tracheal tube to a mechanical ventilator, formerly known as a respirator, which performs the majority of the work of breathing. MVS can be initiated in the critically ill patient for a variety of indications: 1) respiratory failure, 2) ventilatory failure, and 3) support of the respiratory system to decrease the work of breathing and allow better oxygen delivery to the other organ systems during systemic illness (Balk, 1991). A large number of complications are associated with MVS and can involve the pulmonary, cardiovascular, gastrointestinal, renal, hepatic, and neurological systems. The most frequent are infectious, nutritional, and hematological complications.

Weaning

In most cases the termination of MVS (or "weaning", or taking the patient off the ventilator) is accomplished in a straightforward manner when the process that precipitated the mechanical ventilation is resolved. However, a small percentage of intubated patients require weeks of mechanical ventilation and these patients are referred to as long term, chronic, or difficult to wean patients. Certain disease processes such as Chronic Obstructive Pulmonary Disease (COPD) put patients at high risk for complications and poor long-term prognosis (Menzies, Gibbons, and Goldberg, 1989). After several weeks, a tracheotomy tube (a tube surgically inserted into the trachea) is usually necessary. Tracheotomy is preferred over endotracheal tubes when the anticipated need of the artificial airway is greater than 21 days (Plummer and Gracey, 1989). Some researchers propose that a tracheostomy be performed in open-heart surgery patients after only seven days if they have failed to wean from mechanical ventilation; these patients can be viewed as "a desperately ill subset of cardiac surgery patients" (LoCicero, McCann, Massad, Joob, 1992, 990). Long term patients benefit from different approaches to weaning: increasing periods of time during which the patient receives no mechanical ventilation (breathes spontaneously), decreasing the amount of the patient's respiratory support, or a combination of both. It should be noted that previous studies have not clearly established the superiority of one method over another (Silver and Balk, 1991).

Criteria traditionally used for weaning patients from ventilators include arterial blood gases (ABG's), vital capacity (VC), inspiratory force (IF), minute ventilation (VE), fraction of inspired oxygen (FiO2), positive end-expiratory pressure (PEEP), pulse and cardiac rhythm, respiratory rate, level of consciousness, and nutritional status (Beaton and Bone, 1985). While these parameters in assorted combinations have been useful in the prediction of weaning in the population of acute ventilator patients (those requiring mechanical ventilation for less than one week) they have not been accurate predictors for the long term patient.

Yang and Tobin (1991) published two indices for the prediction of weaning for short term ventilator patients that received a great deal of attention. The first (and statistically better) quantified rapid, shallow breathing (RSB) as a ratio of the respiratory frequency (rate) to the tidal volume (volume exhaled after a normal inspiration); f/Vt was found to be accurate 89% of the time. In contrast, the CROP, an integrated index of thoracic compliance, respiratory rate, arterial oxygenation, and maximum inspiratory pressure had an accuracy of.78. Certainly the RSB index is a reflection of typical current practice and clinical judgement. Weaning trials will usually be suspended if the respiratory rate rises and/or the tidal volume decreases outside preset limits. It should be noted that the accuracy of these indices has not been established for long term patients. These indices may be useful in the prediction of outcome for a specific weaning trial on a day-to-day basis but may not be helpful in the final outcome prediction.

The discrepancies between predictors in acute and long term ventilators patients can be considered from several perspectives. The predictors in the acute care institution are looking at readiness to wean from MVS after a short time of MVS. Here, the patient has had an episode of acute respiratory failure and these indices focus on stability after a short term duration; the acute event leading to respiratory failure did not result in death and the person is stabilized enough for the clinician to consider that the person is ready to resume breathing on his own. On the other hand, the long term patient has also survived the initial insult leading to MVS but has been unable to maintain spontaneous ventilation after the acute event has resolved.

The inability to wean in long term ventilator patients can be attributed to a number of factors singularly or in association with each other. Overall there are three areas to consider: 1) prior medical history and the reason for initial intubation; 2) current physiological status, including respiratory parameters (ABG's, ventilator settings) as well as hematological, mental status, and nutritional considerations; and 3) other influences such as age, social status, and sex.

Severity of underling disease processes, pulmonary or non-pulmonary, can be a major impediment in the weaning process. Someone with a chronic, deteriorating muscular disease such as amyotrophic lateral sclerosis (ALS), Lou Gehrig's Disease, may have reached a point of ventilatory muscle weakness that precludes spontaneous ventilation. Acute illness, either new or prolonged, impacts immediate stability; a person may have originally had MVS initiated for a surgical procedure but post operative complications (hemorrhage or pneumonia) prolonged the need for MVS. In some cases the initial insult may have caused permanent destruction of an essential component of the respiratory system. A cerebral vascular accident (CVA) that effects the medulla or pons in the brain stem may interfere with neural control of respiration.

Survival

The issue of survival in patients requiring MVS has been systematically addressed in the literature. Most of the work has focused on acute MVS patients. Studies have shown that most clinicians have difficulty accurately predicting the survival of patients who require MVS (Kaelin, Assimacopoulos, and Chevrolet, 1987; Pearlman, 1987). Survival analyses have both clinical and social ramifications. Patients, families, and clinicians alike are interested in the life expectancy in terms of the appropriate allocation of emotional and financial resources.

The literature related to the survival of patients at large who required long term MVS is very scanty. The research that has been published on survival tends to look at very specific populations who are known survivors of MVS and exclude confounding variables or multiple diagnoses (Shachor, Liberman, Tamir, Schindler, Weiler, and Bruderman, 1989). Studies report people who required mechanical ventilation and use length of time or number of episodes of mechanical ventilation as descriptors rather than as main considerations or starting points of analyses. Survival to discharge from the hospital in patients who undergo 48 hours of mechanical ventilation is frequently described at 50% or less, particularly when multi-organ failure is present (Gracey, Gillespie, Nobrega, Naessens, and Krishman, 1987; Elpern, Larson, Douglass, Rosen, and Bone, 1989; Gillespie, Marsh, Divertie, and Meadows, 1986; Spincher and White, 1987).

While prognosis is typically thought of in terms of specific disease entities or diagnoses (such as cancer), those who require long term mechanical ventilatory support can be assigned a diagnosis of chronic respiratory failure, regardless of the events leading to the ventilator. It is then of interest to look at all those individuals as a group and examine the survival trends. From a social perspective, long term MVS patients can perhaps be conceptualized as having a chronic or terminal disease. Patients and families can incorporate a prognosis in the major decisions. It is important to note that many states have developed a legal means to remove an individual from life support.

One needs to consider the cost-benefit ratio in the treatment of those with chronic respiratory failure. The Mayo Clinic reported a mean loss of $20,915 per patient for 150 patients with a mean number of ventilator days of 13 and a mean length of stay of 28.7 days (Gracey, Nobrega, Naessens, and Krishan, 1989). These were considered long term patients. Even with a new reimbursement system from Medicare, the Mayo Clinic still lost $13,082 per patient. Douglass, Bone, and Rosen (1988) at Rush-Presbyterian-St.Luke's Medical Center also reported significant financial losses for 95 patients; even under a new reimbursement system the loss of $2.2 million ($23,158/patient) below cost was only reduced to $1.9 million ($20,000/patient).

Decisions regarding the intensity and duration of health care services are influenced in part by the expected outcome of treatment. Expectancies in this group are typically divided into two overlapping categories: weaning and death. This creates four theoretical categories: weaned and lived, weaned and died, did not wean and lived, did not wean and died. Finally, it should be noted that financial consideration in the age of spiraling health care costs are also important aspects when prescribing the level of care.

Purposes

This study was conducted at the Vencor-Chicago Hospital, one of 22 acute care hospitals in the Vencor Corporation chain. The uniqueness of the patient population received by this institution is that the patients who are admitted were all acutely ill and are not screened for "weaning potential". Furthermore, almost all had been on mechanical ventilators for more than 30 days and all were transferred from other referring hospitals. Other researchers (Gracey, Viggiano, Naessens, Hubmayr, Silverstein, and Koenig, 1992; Cordasco, Sivak, and Perez-Trepichio, 1991) have described their experiences with long term mechanical ventilation but the admissions were either pre-selected with respect to medical stability and/or readiness to wean or were all transferred from within the same or a limited numbers of institutions. On the contrast, all patients admitted to Vencor-Chicago Hospital received acute care (versus custodial care). They were weaned according to a standardized protocol which incorporates clinical judgment and time progressions (Appendix A). All patients were followed by pulmonologists with specialized training in the care of mechanically ventilated patients.

This study had three purposes. The first was to provide a description or "snapshot in time" of a diverse and very unique population of patients requiring long term mechanical ventilation. This detailed description included referral sources and length of stay and days on mechanical ventilation prior to transfer, original reason for mechanical ventilation, underlying diseases that may impede the weaning process, medical stability on admission including length of time needed to stabilize patient before beginning the weaning process, and outcomes related to weaning and survival. Of particular interest in this group of patients is survival. While aforementioned studies have described survival in specific samples, few have specifically studied people who have already survived thirty days of mechanical ventilation.

The second purpose of this study was to consider overall survival rates as well as survival with special consideration given to those who weaned (and did not wean) for two weeks from mechanical ventilation. Survival analyses typically use admission dates to the study as a starting point for the analysis which in this case would be admission to Vencor-Chicago Hospital. However, for many of the subjects used in the study the original date of acute care admission was available and a separate analysis could be done.

The final purpose of this study was to develop a statistical prediction model for weaning in a population that required long term mechanical ventilation. The model was validated using Monte Carlo procedures.

All of the subjects were considered in the survival analyses, even those admitted for terminal care as they represent a portion of the population of those requiring long term mechanical ventilation. This analysis was contrasted to another survival analysis with the unweanable patients excluded. However, those terminal patients and those known to be "unweanable" (clinically did not receive a weaning trial) were excluded from the statistical prediction model for weaning.

CHAPTER II

LITERATURE REVIEW

First of all, it should be noted that a number of studies have been designed to examine weaning and survival among patients who require MVS. However, very few studies address the patient who requires MVS for greater than 29 days.

Descriptive Studies

Descriptions of experiences with prolonged respiratory care units are present in the literature. Early investigators attempted to demonstrate the need and cost efficacy of maintaining patients with extensive respiratory therapy modalities outside the Intensive Care Units (Indihar and Forseberg, 1982; Indihar and Walker, 1984). The majority of patients admitted to these units had a primary diagnosis of chronic airway obstruction, although they did not necessarily require mechanical ventilation, just intense respiratory care.

Two recent studies conducted at the Cleveland Clinic and the Mayo Clinic described populations that are similar to Vencor in terms of the operational definition of long term mechanical ventilation. That is, the patients required approximately 30 days of mechanical ventilation to be considered long term. However, in both reports, the patients were pre-screened and primarily transferred from within the same institution.

Researchers from the Cleveland Clinic reported the demographics of clinically stable long term ventilator dependent patients outside of the intensive care unit (Cordasco, Sivak, and Perez-Trepichio, 1991). The review included 99 patients serviced between 1988 and 1991 with the patients nearly equally divided into custodial (n=49) and rehabilitative (n=50) classifications. The overall number of ventilator days was not reported. Twenty-five patients did not survive, 25 were successfully weaned from mechanical ventilation, 30 required mechanical ventilation at home, and 19 were transferred to other institutions while still on ventilators.

Gracey, Viggiano, Naessens, Hubmayr, Silverstein, and Koenig (1992) described their experience with patients admitted to the chronic ventilator-dependent unit in the Mayo Clinic. The six bed unit opened in January, 1990 for those who could not be liberated after repeated attempts at weaning. The patients were screened for medical stability, absence of need for electrocardiographic monitoring, previous tracheostomy, and rehabilitation potential. The age of the patients ranged from 24-89 years. The 61 patients had a mean hospital length of stay of 38 days before admission and a mean of 34 ventilator days. The three major underlying diagnoses contributing to ventilator dependence was COPD (n=28), neuromuscular disorder (n=10), and restrictive lung disease (n=8). Patients had evidence of poor nutritional status as evidenced by a mean serum albumin of 2.77 with a standard deviation of 0.60. All of the patients were admitted from the Mayo Clinic services. The outcomes were as follows: 66% weaned; 8% required home mechanical ventilation; 21% required home oxygen; and 5% died in the hospital. The dismissal location was: 57% home; 15% chronic care facility; 2% remained in the unit; and 5% died.

<u>Survival Analysis Studies</u>

Before considering the issue of survival in long term mechanical ventilation, the mortality of ventilated patients in the ICU or acute setting should be considered. These patients first must survive the initial insult of acute respiratory failure before being labeled as chronic or long term.

From the onset, the prognosis is poor for those who require mechanical ventilation in the acute care setting. Early investigators reported that ventilated patients in the intensive care unit (ICU) had rates as low as 67% for survival of ICU treatment and 47% for discharge home in an institution where patients who did not require ventilation had a survival rate of 89% (Nunn, Milledge, and Singaraya, 1979).

Knaus (1989) used the Apache II index to predict outcome for 571 ventilated patients in a multi-center study. Of the 296 deaths, 142 (48%) were identified on admission to be at 75% or greater risk of hospital. After 3 days of ICU treatment, estimates for hospital mortality increased to 97%.

Patients with acute lung injury who required greater than 24 hours of mechanical ventilation were reported to have a mortality rate of 40 percent in uncomplicated cases and 81 percent when the acute lung injury was complicated by multisystem failure (Gillespie, Marsh, Divertie, and Meadows, 1986). Mortality rose to 89 percent when acute respiratory failure was seen in association with acute renal failure. Furthermore, while mortality was only 30 percent in patients with chronic obstructive pulmonary disease, 43 percent became ventilator dependent (Gillespie, Marsh, Diverie, and Meadow, 1986).

Complications of assisted ventilation may also lead to increased mortality. Intubation of the right main stem bronchus, endotracheal tube malformation, and alveolar hypoventilation were associated with decreased survival in a study of 354 episodes of mechanical ventilation with an overall survival rate of 64% (Zwillich, Pierson, Creagh, Sutton, Schatz,and Petty, 1974).

The issue of survival has been addressed in patients requiring long term mechanical ventilation. The definition of prolonged mechanical ventilation varies from study to study with ranges of one to more than 29 days.

Spicher and White (1987) retrospectively reviewed 250 consecutive patients with a minimum of ten days of ventilatory support and reported an overall survival rate of 39.2% at discharge, 28.6% at one year, and 22.5% at two years. Cardiac and pulmonary patients were found to have the worst prognosis; survival was the highest with post operative complication and neurological diseases as the cause of mechanical ventilation. Of those who were discharged alive, 39% were institutionalized and 32.7% were confined to their home.

Elpern, Larson, Douglass, Rosen, and Bone (1989) reported that only 31 (33%) of 95 non-surgical patients ventilated for three or more days survived to discharge. They were followed over the next three years and had a median survival rate of 13.5 months following discharge from the hospital. Only 9 of the original 30 alive at the end of three years. Length of MVS and hospitalization did not predict long-term survival in the elderly. Sanchor, Liberman, Tamir, Schindler, Weiler, and Brunderman (1989) followed long term survival of COPD patients following first mechanical ventilation for fifteen years and found a median survival rate of 23.5 months and an average survival rate of 44.9 months. They excluded patients from the study whose acute exacerbation was induced by trauma, CVA, adult respiratory distress syndrome, drug evidence or pulmonary edema which severely limits the generalizability of the study.

In a more recent study conducted at the Mayo Clinic, Gracey, Naessens, Krishan, and Marsh (1992) reported much more optimistic results for patients who were mechanically ventilated for more than 29 days. The mean number of in-hospital ventilator days was found to be 59.9 with a standard deviation of 36.7 days. This study is considerably different from the aforementioned studies in terms of the definition of prolonged mechanical ventilation. With the majority (82.6%) of the 104 patients being surgical patients, 60 survived to discharge with a 57.6 percent hospital survival rate.

Physicians can incorporate estimates of long-term mortality into the patient's plan of care but the decision to institute or withhold mechanical ventilation also includes the patient's desires, quality of life, and institutional policy. However, physician's predictions of outcome has great variability. Perkins, Jonsen, and Epstein (1986) report that physicians predicted death for only 41% of those who died but survival for 87% of adult survivors.

In a prospective study Kaelin, Assimacopoulos, and Chevrolet (1987) were unsuccessful at identifying features related to survival of patients with COPD who required mechanical ventilation. They found that the data generally available to the physician at the time of intubation was insufficient to predict survival for six months.

A summary of survival studies is displayed in Table 1. It illustrates a variety of clinical settings, most of which are from the acute hospital setting.

Table 1

Comparison of Survival Analyses

First Author Year	Subjects	n	Outcomes
Zwillich 1974	RICU	354	64% survived
Nunn 1979	ICU	100	67% survived ICU 47% survived discharge home
Gillespie 1986	MVS > 24 hours		Mortality Uncomplicated 40% Multisystem 87% With Renal 89%
Spincher 1987	min 10 days MVS	250	Survival 28.6% 1 year 22.5% 2 years
Elpern 1989	RICU	95	Survival to discharge 33% Over 3 years: median 13.5 mos
Sanchor 1989	COPD first MVS	50	Followed 15 years Median 23.5 mos Ave 44.9 mos
Gracey 1992	MVS >29 days	104	Hospital survival 57.6%

Predictive Indices

It is difficult to compare the predictive models across studies because researchers vary in their subject selection procedures and in their definitions of long term mechanical ventilation, weaning success, and weaning failure. Weaning "success" can range from a minimum 24 hours to two weeks without mechanical ventilatory support. Weaning "failure" can refer to death while on MVS or an extension of time on MVS from several weeks to four months. Tables 2 and 3 present an overview of subject selection and definition of weaning success across frequently cited studies.

Table 2

Overview of Subjects

First Author Year	N	Subjects
Yang 1991	100	ICU 8.2 + 1.1 days
Jabour 1991	38	ICU Mixed diagnoses MVS > 3 days
Shikora 1990	20	Consecutive MVS > 2 weeks
Yang 1989	41	ICU
Krieger 1989	269	Elderly > 70 years Pulmonary edema Abdominal surgery
Krieger 1988	44	MVS at least 48 hours
Pourriat 1986	37/15	COPD Tracheotomized MVS 8 + 3 days
Morganroth 1984	11	10 inpatients 11 instances Weaning time 11-43 days
Hilberman 1976	124	Post cardiac surgery
Sahn 1973	100	Ave duration MVS 37 hours (12-144)

Table 3

Definition of Successful Weaning

First Author Year	N	Definition of Success
Yang 1991	100	24 or more off MVS
Jabour 1991	38	Wean within 3 days of being clinically ready
Shikora 1990	20	Extubation within two weeks of start of study
Yang 1989	41	Not indicated
Krieger 1989	269	Fail if reinstituted
Krieger 1988	44	Off MVS 48 hours
Pourriat 1986	37/15	Success > 12 hours off MVS Fail < 10 hours off MVS
Morganroth 1984	11	24 hours or more
Hilberman 1976	124	24 hours or more
Sahn 1973	100	Extubation

Retrospective studies are far more common in the literature than prospective studies. It should be noted that the sample sizes, parameters, methods and statistical analyses vary considerably across the studies but all focus on the ability to predict the outcome of weaning trials. An overview of the predictive power of published indices is presented in Table 4.

Table 4

Overview of Predictive Indices

First Author Year	N	Criteria	Positive Predictive Power	Negative Predictive Power
Yang 1991	100	f/Vt CROP	.78 .71	.95 .70
Jabour 1991	38	Weaning Index	.96	.95
Shikora 1990	20	VO2sb-VO2mv	1.00	.63
Yang 1989	41	VTsb/fsb NIP, fsb,Cdyn & a/AO2	.79 .87	.83 .72
Krieger 1989	269	NIP	.92	.21
Krieger 1988	44	Resp alterans, RIP	1.00	.96
Pourriat 1986	37	Pdi,breath/Pdi,max	.60	.67
Morganroth 1984	11	Adverse Factor Score Ventilator Score	.86	.93
Hilberman 1976	124	NIP,VC,Rrs,Crs, NIP,VC	.60 .58	.95 .92
Sahn 1973	100	NIP,VC,VE	.71	1.00

Investigators who have studied short term ventilator dependent patients have reported the development of indices to predict weaning. Respiratory pattern has been demonstrated to be a useful predictor for success or failure in weaning trials. One notable exception failed to demonstrate differentiation between groups in COPD patients (Pourriat, Lamberto, Hoang, Fournier, and Vasseur, 1986). Measurement of passive pulmonary mechanics, cardiac function, arterial blood gases have been found to be poor predictors of respiratory adequacy (Hilberman, Kamm, Martz, and Osborn, 1976).

Krieger and Ershowsky (1988) utilized noninvasive respiratory inductive plethysmography (RIP) to continuously monitor and record the breathing patterns of 44 intensive care patients who required MVS. Respiratory alterans was present in 11 patients, all of whom failed weaning trials. An increase in the respiratory rate of >11 breaths per minute occurred in eight of fourteen failure periods and in four of 60 control periods. An elevation of total compartmental displacement/tidal volume (TDC/Vt) >.22 occurred in 11 of fourteen failure tracings. The investigators concluded that the presence of 2/3 abnormal parameters occurring over a one-hour time period had a diagnostic accuracy approaching 99% in these 44 patients, 30 of whom were successfully extubated. While the RIP had both outstanding positive predictive power (1.00) and negative predictive power, it is unlikely that this index would gain widespread use because special equipment not typically found at the bedside was required to perform measurement.

Yang and Tobin (1988) were among the first to develop an index that included a number of important physiological functions. The Integrated Index combined dynamic compliance (Cdyn), maximal inspiratory pressure (MIP), arterial-to-alveolar PO2 ratio, and respiratory frequency (f) to achieve a positive predictive value of .87 which was higher than any of the factors considered alone. The second index specifically appraised rapid, shallow breathing patterns by calculating tidal volume/frequency (Vt/f). Patients with a Vt/f <10 had an 83% likelihood of failing a weaning trial.

Yang and Tobin (1991) followed up with a prospective study of two indexes predicting the outcome of trials of weaning from mechanical ventilation in 100 intensive care patients who required MVS for 8.2 days. The first index quantified rapid shallow breathing as the ratio of respiratory frequency to tidal volume; the second (CROP) integrated thoracic compliance, respiratory rate, arterial oxygenation, and maximal inspiratory pressure (Pimax). Weaning was defined as successful in the patient who was able to sustain spontaneous breathing for at least 24 hours after extubation. The study concluded that rapid, shallow breathing was the most accurate predictor (compared to CROP and traditional measures) of failure to wean while its absence was the most accurate predictor of success. One limitation of this study was that the criteria used for "successfully" weaned patients was only 24 hours off MVS. There were no reports as to the continued course (whether or not MVS needed to be reinstituted) or as to survival rates.

Studies have also been reported on patients who require prolonged MVS. The operational definition of prolonged mechanical ventilation varies from study to study. In one of the earlier studies, Morganroth, Morganroth, Nett, and Petty (1984) created two indices, the Adverse Factor Score and the Ventilator Score when traditional spontaneous ventilatory measurements were not useful in predicating a successful weaning from prolonged mechanical ventilation. For eleven instances, the two scores were summed for a total score; the weighting of the scores for both scales was based on the authors'clinical judgement rather than statistical procedures. The data needed to completely score all the questions on the scales was extensive and required some invasive monitoring; the authors themselves did not have 100% of the criteria available. The positive and negative predictive powers were found to be 0.86 and 0.93 respectively. Prolonged MVS was defined as ventilator dependence for 30 or more days.

Menzies, Gibbons, and Goldberg (1989) reviewed 95 COPD patients with acute respiratory failure; 55 required MVS for more than two weeks; 72 of the total 95 successfully weaned for 72 hours. Weaning was associated with premorbid level of activity, FEV1, albumin level, negative inspiratory force (NIF), and respiratory rate during T-piece trial. Survival was associated with premorbid level of activity, FEV1, serum albumin, and severity of dyspnea (shortness of breath). The limitation of this study was that it considered all patients together rather than separating the easy from the difficult to wean patients. Another inherent problem with this index is that pre-morbid parameters are not readily available for many patients.

Shikora and associates (1990) examined the work of breathing (WOB) as a predictor of weaning and extubation in a prospective study of 20 ventilator dependent patients, 19 of whom required MVS for greater than two weeks due to their inability to tolerate weaning trials. Five of the eight patients with WOB < 15% were extubated within two weeks of the study while none (n=12) with a WOB greater than 15% were successfully weaned. The researchers reported that using a reference value for the WOB of 15%, the study had a sensitivity of 100% and a specificity of 80%. Successful weaning was not clearly defined in terms of length of time off the ventilator. Nine of the fifteen patients in the study did eventually wean and five died.

Krieger, Ershowsky, Becker, and Gazeroglu (1989) evaluated conventional parameters (spontaneous respiratory rate, tidal volume, minute ventilation, maximum inspiratory pressure, pH, PaCO2, PaO2, and PaO2/FiO2) but with specific consideration for the elderly. All parameters had good positive predictive value but poor negative predictive value. This is contrary to the findings of Sahn and Lakshminarayan (1973).

Another study refuted the usefulness of the tradtional weaning parameters and reported that patients who had decreased urine volume, lower respiratory quotients, and positive blood cultures were more likely to require reintubation (Tahvanainen, Salmenpera, and Nikki, 1983).

Overall, the review of the literature contained few predictive indices for patients who required long term mechanical ventilation. Even the traditional criteria for weaning from mechanical ventilation have not consistently been validated although they may still be used in clinical practice as guidelines.

CHAPTER III

METHOD

Hypotheses

The following null hypotheses were tested:

1. There will be no difference in the survival curves between those patients who wean from long term mechanical ventilation compared to those who do not wean from mechanical ventilation.

2. There will be no difference in the weaning outcome for those patients who require long term mechanical ventilation across initial reason for mechanical ventilation (Adult Respiratory Distress Syndrome, Sepsis, COPD, Surgery, Neuromuscular Disease, CVA, and multiple diagnoses).

3. There will be no difference in the weaning outcome for those patients who require long term mechanical ventilation across significant preexisting medical conditions (Cancer, COPD, Coronary Artery Disease, Decubiti, Congestive Heart Failure, Renal Failure, Depresses Mental Staus, and Neuromuscular Disease).

4. There will be no difference in the weaning outcome for those who require long term mechanical ventilation across physiological variables (respiratory rate, arterial carbon dioxide level, pH, arterial oxygen level, hemoglobin, white

blood cell count, lymphocyte count, polymorphonucleocytes, temperature, and albumin).

5. There will be no difference in the weaning outcome for those who require long term mechanical ventilation across social variables (age, marital status, sex).

Subjects

Data were collected on all 166 patients admitted to Vencor-Chicago hospital between February 7, 1991, and February 7, 1992. All patients were transferred from a total of 65 different acute care hospitals. It should be noted that a total of 21 patients were excluded from the analysis. Three were under the age of 18, three invoked the Health Care Surrogate Act, and fifteen were not on a mechanical ventilator at the time of admission. All the remaining 145 patients were included in the descriptives of the population and survival analyses. However, twenty-eight of the remaining 145 patients were deemed unweanable on admission due to underlying medical conditions (cancer, n=20 and neuromuscular disease, n=8) were excluded in a separate survival analysis and from the prediction model. All but seven of the 145 were discharged before the end of the data collection period.

Procedure

Data were collected by chart review for all the patients between August 31, 1992, and January 31, 1993.

Hospital treatment plans were not altered in any way during the conduction of this study.

Consent Procedures and Safeguards

This study was approved by the human investigations committees of Loyola University and Rush University. It was determined that there were no known potential risks to subjects. All data from the chart reviews were collected in such a way as to ensure the confidentiality. The findings were reported in the aggregate to ensure anonymity. Finally, it should be noted that given the nature of the design of the study that written informed consent was not obtained for each subject.

Design and Data Analysis

The variables available for analyses included physiologic parameters, significant premorbid conditions, weaning and mechanical ventilation parameters, outcomes, and demographics. The dependent variables of primary interest were weaning from mechanical ventilation and disposition at discharge. "Successful" weaning was defined as two weeks without mechanical ventilatory support.

Each of the samples were systematically described in an effort to provide a "snapshot in time" of patients who require prolonged mechanical ventilatory support. This description consisted of composite frequencies with a comparison between those who did and did not wean for a two week period of time.

Six survival analyses were performed to describe survival of long term MVS patients. These analyses differed in starting point of analysis or patient inclusion. Succinctly, the survival analyses were as follows:

1. All patients using Vencor admission dates as the start date (n=145).
2. All patients using initial ventilation date from the acute care referring hospital (where the data were available) as the start date.
3. All patients divided into those weaned and not weaned using Vencor admission as the start date.
4. All patients divided into weaned and not weaned using initial ventilation date from the acute care referring hospital as the start date.
5. "Unweanable patients" (history of cancer or neuromuscular disease) excluded from the population (n=28) using Vencor admission dates as the start date.
6. "Unweanable patients" excluded from the population divided into those weaned and not weaned using Vencor admission as start date.

For the prediction model the subjects were randomly selected by the SPSS program into one of two groups. In the first group, a series of multiple regression equations were used to select significant variables; these predictor variables were then tested in the second sample using a combination of multiple regression and discriminant analyses.

Monte Carlo computer analyses were then performed. One hundred samples of 58 cases were randomly drawn and the stability of the predictive power was tested using discriminant analysis for the two variables RR and DECUB. A second Monte Carlo analysis was done on 100 samples of 58 randomly selected cases using discriminant analysis which included PH, PCO2, TEMPGR, and TEMPLS.

CHAPTER IV

RESULTS

Descriptives

All 145 patients, admitted from 58 different referring acute care hospitals, who were on mechanical ventilators were included inn the data described here. Forty-five percent (n=65) were males and 55% (n=80) were females. Twenty-four percent (n=35) were single, 30% (n=43) were married, 28% (n=41) were widowed, and 6% (n=9) were divorced. On admission, 30% (n=43) had orders to "Do not resuscitate". The mean age was 70.6 years (S.D.=13.9) for all patients (n=145), 71.2 (S.D.=13.9) for those who did not wean for two weeks (n=112), and 67.9 (S.D.=14.2) for those who did wean two weeks from mechanical ventilation.

Final weaning outcome at discharge (n=138) was considered at three endpoints: weaned for 24 hours (Oneday), weaned for 72 hours (Threeday), and weaned for two weeks (Twoweeks). The results for the 138 discharged patients are in Table 5. The seven patients still in house were not included because final weaning outcome was not known. It should be noted that this assessment is a time progression and that all of the patients who weaned for two weeks were also included in the totals for one and three days.

Table 5

Successful Weaning Outcomes for All Discharged Patients

Weaning Outcome	n	Percent
One day	53	36.6
Three days	45	31.0
Two weeks	26	17.9

The disposition of the entire sample at the end of data collection is presented in Table 6. The majority of patients admitted during the year (71.7%) died while inpatients at Vencor.

Table 6

Disposition of All Patients (n=145)

Died at Vencor	104	71.7%
Alive at discharge	34	23.4%
Still inpatients	07	4.8%

Disposition can be further described as a function of weaning outcome at discharge (n=138), Table 7. This number excludes the patients who were still inpatients.

Table 7

Disposition by Weaning Outcome

		Not weaned two weeks	Weaned two weeks
Died at Vencor	n	88	14
	%	64	10
Alive at discharge	n	24	12
	%	17	9

Information was collected with respect to the patient's significant medical history for the following variables: Cancer, Chronic Obstructive Pulmonary Disease (COPD), Coronary Artery Disease (CAD), decubiti (DECUB), Congestive Heart Failure (CHF), Renal Failure (RENAL), depressed mental status (MENTAL), and neuromuscular disease (NM). These descriptive findings are summarized in Table 8 for all patients and then subdivided by weaning outcome where it was known. It should be noted that some subjects had multiple diagnoses. These diagnoses were taken from the transfer records from the referring hospital. In some instances multiple diagnoses may have been underestimated because only the primary diagnoses were listed. Also, some patients developed other significant medical diagnoses during their hospital course at Vencor.

Table 8

Significant Medical History (n=145)

Diagnosis	n	Percent of total	Not weaned two weeks n	Weaned two weeks n
Cancer	20	13.8	20	0
COPD	56	38.6	44	9
CAD	34	23.4	27	5
DECUB	85	58.8	65	16
CHF	62	42.8	51	8
RENAL	27	18.6	23	4
MENTAL	28	19.3	19	9
NM	8	5.5	8	0

The initial reasons used for receiving mechanical ventilation are described in Table 9. The reasons were classified into the following areas: Chronic Obstructive Pulmonary Disease (COPD), Adult Respiratory Distress Syndrome (ARDS), surgical complication (SURG), Sepsis, Neuromuscular (NM), Cerebral Vascular Accident (CVA), and multiple diagnoses (MULTI). It should be noted that data for four patients were missing. Again, final weaning outcome was not known for in patients still in the hospital. The total are greater than 100% because multiple reasons listed for mechanical ventilation.

Table 9

Reason for Mechanical Ventilation (n=141)

Reason	n	Percent of total	Not weaned two weeks n	Weaned two weeks n
COPD	25	17.2	20	4
ARDS	67	46.2	49	16
SURG	11	7.6	7	3
SEPSIS	46	31.7	35	9
NM	4	2.8	2	1
CVA	17	11.7	14.	3
MULTI	39	26.9	28	9

Information was also collected with respect to a number of physiological variables within 48 hours of admission: respiratory rate (RR), arterial PH (pH), arterial carbon dioxide levels (PaCO2), arterial oxygen level (PaO2), hemoglobin (HGB), white blood cell count (WBC), percent polymorphonucleocytes (POLY), total lymph count (Lymph), albumin (ALB), spontaneous respiratory rate (SRR), spontaneous tidal volume (SVT), and minute ventilation (Minute).

Table 10

Physiological Variables

Variable Normal Range		Total	Not Weaned	Weaned
RR	MEAN	21.15	20.82	23.81
12-24	STD DEV	8.69	8.65	8.44
	n	140	109	26
pH	MEAN	7.43	7.43	7.44
7.35-	STD DEV	.07	.08	.05
7.45	n	140	110	25
PaCO2	MEAN	43.17	43.19	42.48
36-44	STD DEV	12.03	12.42	11.02
mmHg	n	140	110	25
PaO2	MEAN	99.93	96.00	109.16
80-100	STD DEV	32.39	30.04	35.29
mmHg	n	139	109	25
HGB	MEAN	9.99	10.02	9.96
12-18	STD DEV	1.47	1.51	1.26
gm/100 ml	n	138	107	26
WBC	MEAN	13510.7	13855.9	12467.9
3500	STD DEV	6531.6	6979.2	3824.0
-11000	n	140	109	26
POLY	MEAN	77.64	77.97	76.34
36-72	STD DEV	10.03	10.41	8.24
	n	117	90	23
LYMPH	MEAN	1881.46	1888.95	1876.00
>1000	STD DEV	1308.15	1379.77	1043.40
	n	135	90	25
ALB	MEAN	2.54	2.45	2.64
3.5-5.5	STD DEV	.72	.65	.57
	n	68	49	13
SVT	MEAN	361.24	361.66	376.71
Varies	STD DEV	130.74	131.24	133.91
	n	76	60	14
MINUTE	MEAN	10.29	10.42	9.53
5-9 L/min	STD DEV	3.41	3.58	2.50
	n	113	89	20
SRR	MEAN	17.74	18.09	14.83
12-24	STD DEV	9.65	9.55	8.54
	n	84	64	20

For analysis, the variable temperature was dichotomized into temperature greater than 99.6 degrees Fahrenheit (TEMPGR) and temperature less than 97.6 degrees Fahrenheit (TEMPLS). This was done to partition temperature into ranges that were outside the norm of 98.6. Table 11 provides a summary description of the dichotomized data set.

Table 11

Temperature

	n	Percent of total n=144	Not weaned two weeks n	Weaned two weeks n
TEMPGR	36	26.2	30	6
TEMPLS	30	20.7	27	3

In addition, comparative information from a limited number of initial metabolic studies performed on the patient are displayed in Table 12: energy expenditure (MEE), oxygen consumption (VO2), carbon dioxide production (VCO2), and respiratory quotient (RQ).

The metabolic cart necessary for measurement of these variables was not available for patients admitted early in the study. Furthermore, only the results of those metabolic studies performed within two weeks of admission were included in the data set. It was felt that studies done after that time might not accurately reflect the admission status of the patient.

Table 12

Metabolic Studies

		Total n=49	Not Weaned n=35	Weaned n=14
MEE	MEAN	1147.79	1152.00	1137.21
	STD DEV	284.92	248.93	385.68
VO2	MEAN	161.76	161.60	162.14
	STD DEV	42.42	36.84	55.64
VCO2	MEAN	153.91	155.77	149.28
	STD DEV	38.74	35.34	47.34
RQ	MEAN	.97	.98	.94
	STD DEV	.17	.18	.12

Information was also collected regarding the hospital course and length of stay (LOS). In order to consider ventilatory stability, the number of days were counted from admission until the patient could tolerate standard baseline ventilator settings per the weaning protocol of SIMV 6 Pressure Support 10 (DAY1 Change). The number of days were also counted from admission until the patient could begin weaning trials of CPAP/Pressure per the weaning protocol (Day1 CPAP). The length of hospital stay at Vencor and at the referring acute care hospitals were also calculated. For several patients who were transferred for a procedure to another hospital for several days during their tenure at Vencor, the LOSV reflects initial admission date to ultimate discharge date. The results are displayed in Table 13.

Table 13

Hospital Course

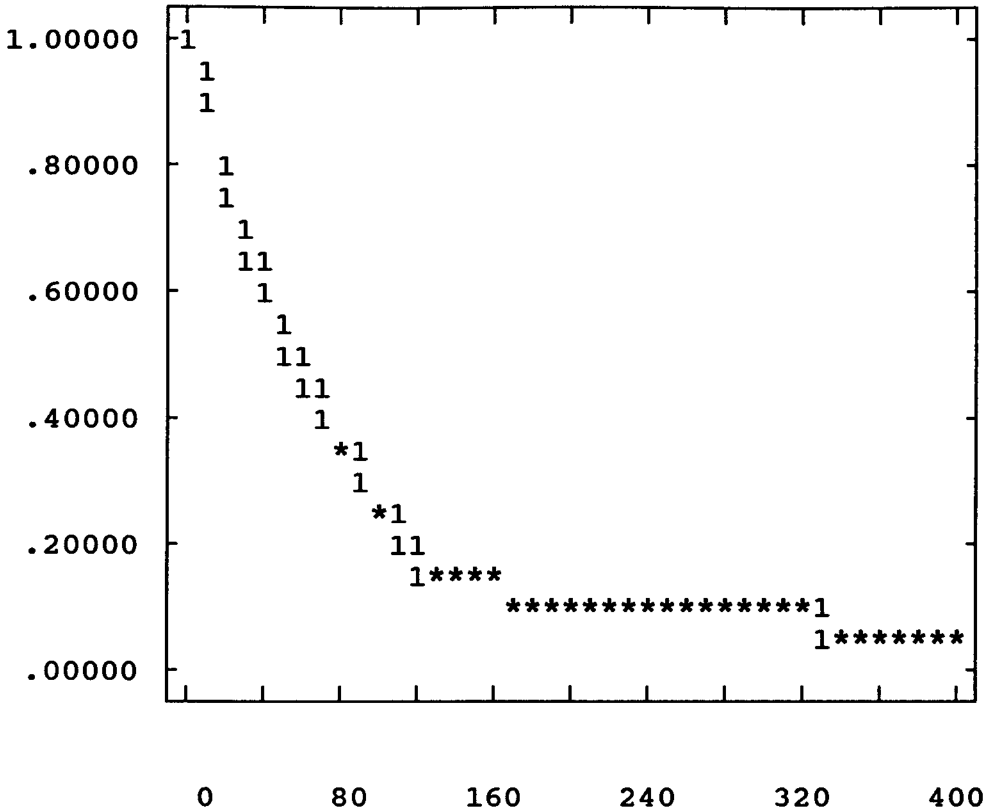
		Total	Not Weaned	Weaned
Day 1 Change	MEAN	4.2	4.8	2.7
	STD DEV	5.6	6.8	2.1
	n	121	90	26
Day 1 CPAP	MEAN	11.2	10.9	8.0
	STD DEV	16.9	14.1	14.3
	n	98	71	26
LOS Vencor	MEAN	68.8	58.7	110.5
	STD DEV	75.6	72.7	78.0
	n	135	109	26
LOS Acute Care	MEAN	120.3	111.4	157.2
	STD DEV	85.9	86.7	78.6
	n	131	102	26

Survival Analyses

Survival analyses were performed by length of stay from admission at Vencor (LOSV) and for the combined total length of stay at Vencor plus the acute care hospital (LOST) for those cases in which the information was available on the medical record. The graph of the survival function using admission to Vencor as the starting point is shown in Figure 1. All 145 subjects entered the survival analysis at the starting interval. For those who were not yet discharged, the end of the data collection date (1-31-93) was substituted to estimate survival. The median survival time for these data is 51.50 days.

Figure 1

Survival from Vencor Admission-All Patients



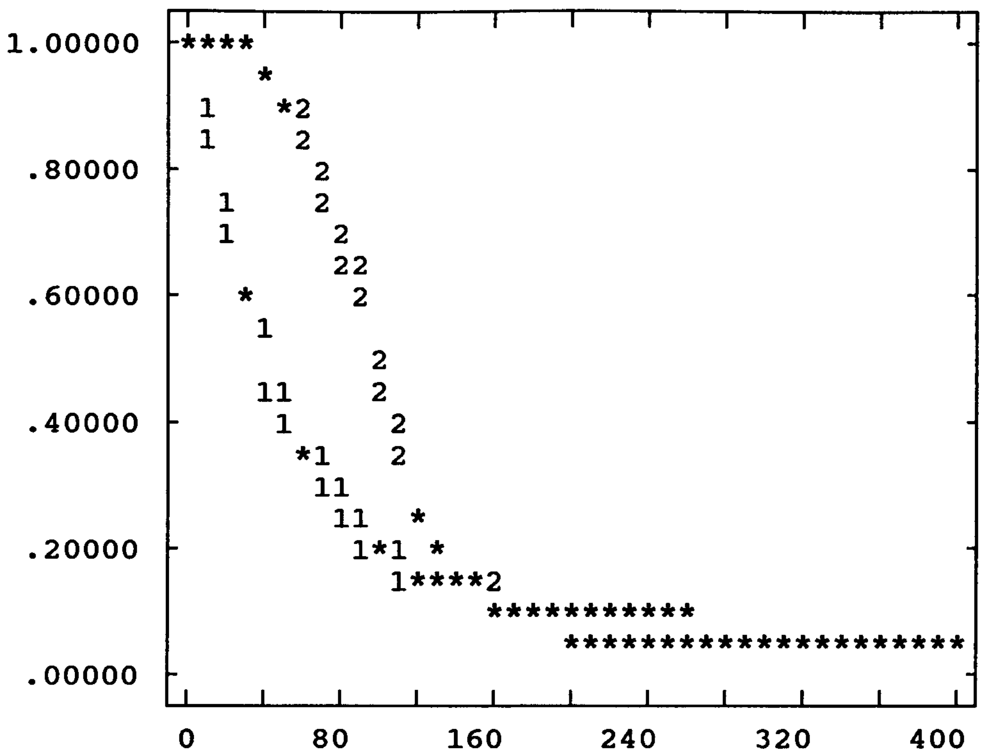
Note. Median Survival Time 51.50 days

All patients were then divided into those who weaned (two weeks) and those who did not. The graph depicting these findings is presented in Figure 2. The median survival time for those who did not wean for two weeks (n=114) was found to be 38.13. The median survival time for those who did wean (n=26) was found to be 95.00. A comparison of survival times using the Lee-Desu Statistic was 18.31 with 1 degree of freedom, p=.0000.

Figure 2

Survival from Vencor Admission by Weaning Outcome-

All Patients



Note. Graph symbols

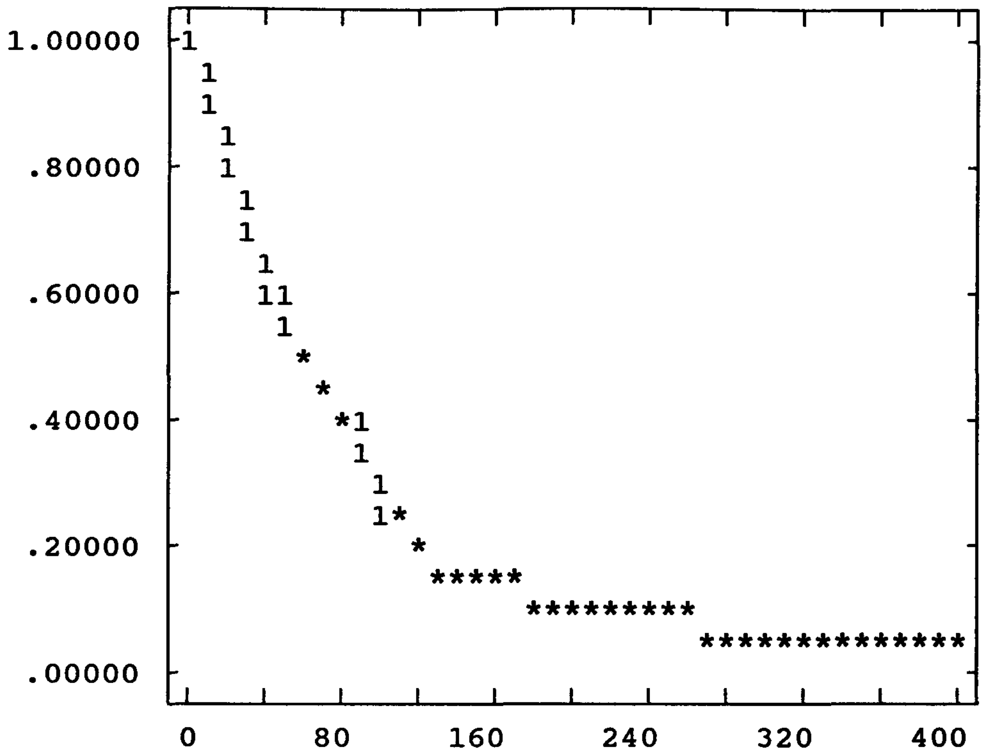
1 Did not wean Median survival time 38.15

2 Did wean Median survival time 95.00

The analyses depicted in Figures 1 and 2 were repeated excluding the "unweanable" patients (n=28). The "unweanable" patients were those with significant medical histories for cancer and neuromuscular disease. Figures 3 and 4 display the graphic presentations.

Figure 3

Survival from Vencor-"Unweanable" Excluded

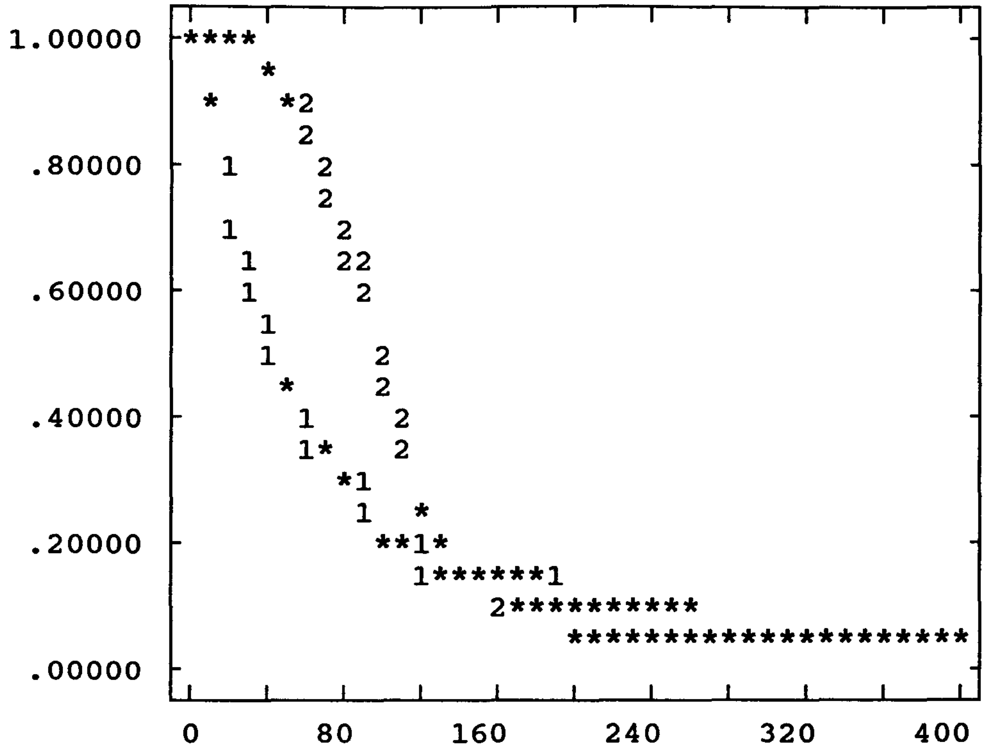


Note. The Median Survival Time 57.50

Again the patients were divided into those who weaned and those who did not wean for two weeks. The graph depicting these findings, which exclude the unweanable patients, is displayed in Figure 4. The median survival time for those who did not wean was found to be 40.83 (n=87). The median survival time for those who did wean remained 95.00 days (n=26).

Figure 4

Survival from Vencor Admission by Weaning Outcome- "Unweanable" Excluded



Note. Graph symbols

1 Did not wean Median Survival Time 40.83

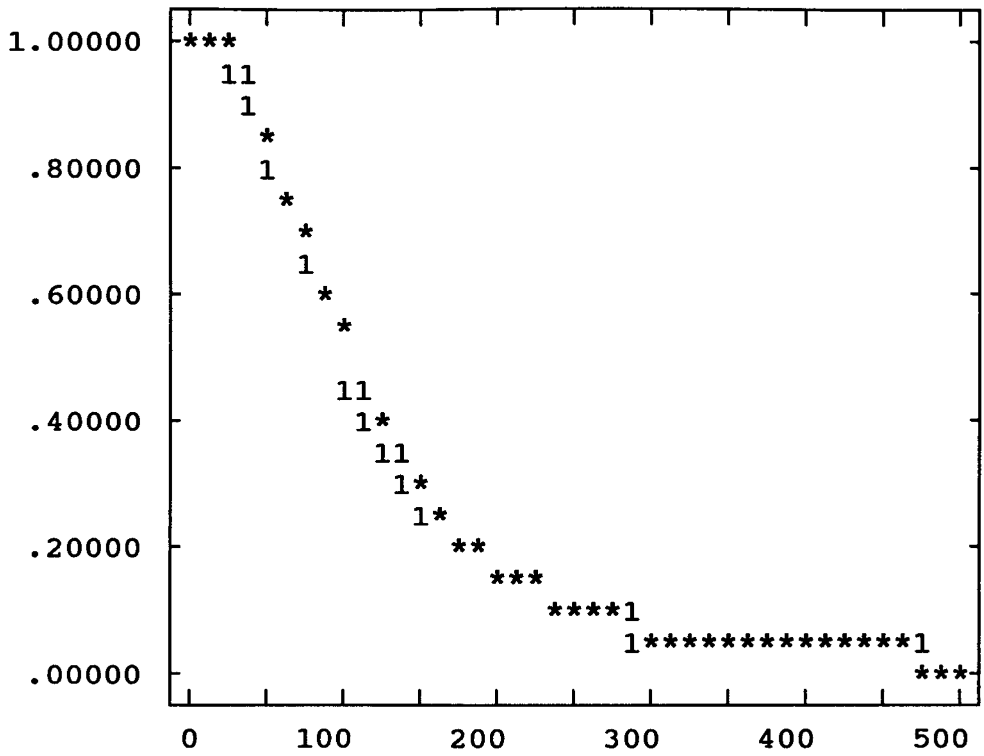
2 Did wean Median Survival Time 95.00

The comparison of the survival experience using the Lee-Desu statistics was 14.492 with 1 degree of freedom, p=.0001. The graphs were significantly different.

Survival was also considered using the admission date to the acute care referring hospital as the starting date (Figure 5). Due to missing data, only 136 subjects were entered into this analysis. The median survival time is 102.50 days.

Figure 5

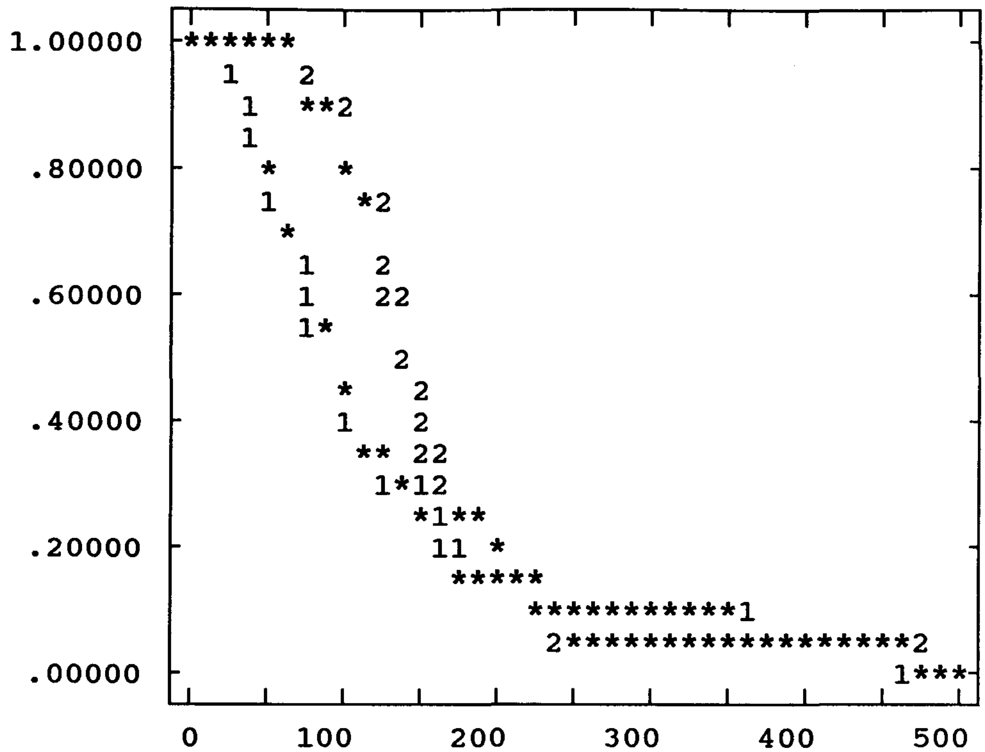
Survival from Acute Care Admission -All Patients



Note. Median Survival Time 102.5.

The patients were then divided into those who weaned two weeks and those who did not. The graph is displayed in Figure 6. The median survival time for those who did not wean for two weeks (n=106) was found to be 92.14. The median survival time for those who did wean (n=26) was found to be 140.00. A comparison of survival times using the Lee-Desu Statistic is 10.75 with 1 degree of freedom, p=.0010.

Figure 6
Survival from Acute Care Admission by Weaning Outcome-All Patients



Note. Graph Symbols

1 Did not wean   Median survival time 92.14

2 Did wean   Median survival time 140.00

Prediction Model

Regression Equations.

The prediction model was developed using multiple regression equations with the dependent variable of weaning from mechanical ventilation for two weeks. The analysis was limited by the amount of missing data in medical records.The computer program randomly assigned the cases into two groups. The first group was used to determine the variables for inclusion.

A series of multiple regression analyses were run to compress the number of variables. The equations using the independent variables of demographics, previous medical history, and initial reason for mechanical ventilation did not yield significant F statistics. However, the variable history of decubiti did consistently yield a significant beta weight even in the non-significant equations. However, only the equation for the physiological variables produced significant F. Variables for the model were chosen conceptually and based on significant beta weights. They included respiratory rate (RR), pH, carbon dioxide level, both temperature variables (TEMPLS,TEMPGR), and history of decubiti (DECUB).

Regression Analyses

These variables were used to regress the line of best fit in the second group. The descriptive statistics are displayed in Table 14 and the Correlation/Covariance Matrix in Table 15 (n=51). None of the independent variables have very high correlations with the dependent variable two weeks. The only two independent variables which have a moderate degree of correlation between them (.43) is PH and PCO2 which is expected since pH is the negative logarithim of PCO2.

Table 14

Multiple Regression Descriptive Statistics

	Mean	Std Dev
TWOWEEKS	.294	.460
DECUB	.569	.500
PCO2	43.118	12.604
PH	7.425	.077
RR	22.216	8.801
TEMPLS	.176	.385
TEMPGR	.255	.440

Table 15

Correlation, Covariance Matrices

	TWOWEEKS	DECUB	PCO2	PH	RR	TEMPLS	TEMPGR
TWOWEEKS	1.00	-.22	-.15	.19	.34	-.19	-.08
	.21	-.05	-.85	.01	1.45	-.03	-.02
DECUB	-.22	1.00	-.22	-.03	.28	-.01	.15
	-.05	.25	-1.37	-.00	1.235	-.00	.03
PCO2	-.15	-.22	1.00	-.43	-.29	-.11	-.01
	-.86	-1.36	158.8	-.416	-31.85	-.54	-.07
PH	.19	-.03	-.43	1.00	.04	.03	.14
	.01	-.00	-.42	.01	.03	.00	.01
RR	.34	.28	-.29	.04	1.00	.04	.02
	1.36	1.24	-31.85	.03	77.45	.14	.08
TEMPLS	-.18	-.01	-.11	.02	.04	1.00	-.27
	-.03	-.00	-.54	.00	.14	.15	-.05
TEMPGR	-.08	.15	-.01	.14	.02	-.27	1.00
	-.02	.03	-.07	.01	.08	-.05	.19

The independent measures RR and DECUB were found to have the highest zero order correlation with the dependent measure Two Weeks.

Regression analysis using the enter method yielded an equation with an R square of.31, F=3.29, F significant .009. However, only two of the variables had significant beta weights (RR and DECUB). These results are displayed in Table 16.

Table 16.

Beta Weights

Variable	B	SE B	Beta	T	Sig T
TEMPGR	-.141398	.139573	-.135241	-1.013	.3166
PCO2	-.002107	.005446	-.057724	-.387	.7006
DECUB	-.301906	.123968	-.328160	-2.435	.0190
TEMPLS	-.304061	.156632	-.254395	-1.941	.0587
RR	.021810	.007046	.417101	3.095	.0034
PH	.994605	.855709	.165643	1.162	.2514
(Constant)	-7.223001	6.481139		-1.114	.2711

Discriminant Analysis

The objective of the discriminant analysis is to determine if the linear combination of the independent variables can discriminate between the two groups (Weaned and Not Weaned for Two Weeks). The purpose for running a discriminant analysis here is to determine the predictive accuracy of the model.

The Wilk's method was used to run the discriminant analysis. This is a stepwise procedure that selects only significant variables and allows one to find the optimal subset to discriminate. The maximum number of discriminant functions is (# groups-1). The Summary Table of Wilk's Lambda entered in two steps is presented in Table 17.

Table 17

Wilk's Lambda Summary Table

STEP	ENTERED	REMOVED	IN	LAMBDA	SIG.
1	RR		1	.884	.012
2	DECUB		2	.758	.001

The structure matrix is displayed in Table 18. This structured matrix represents the pooled within-groups correlations between discriminating variables and the Canonical Discriminant Function. The variables are ordered by size of correlation within the function.

Table 18

Structure Matrix

Variable	Correlation
RR	0.641
DECUB	- 0.480

The test of equality of group covariance matrices was done using Box's M. The Box's M of .550 was not found to be significant (p=.91) which is good because a significant Box's M increases the probability of a Type I error. It tests the assumption that within group variance can be pooled (i.e., homogeneity). The Standardized Canonical Discriminant Function Coefficients, that illustrate the relative size of the relationships, were found to be -.82 for DECUB and .94 for RR.

Finally, the classification results are displayed in Table 19.

Table 19

Classification Results-Two Variables-Split Sample

Actual Group	Number of Cases	Predicted Not Weaned	Predicted Weaned
Not weaned	38	26 68.4%	12 31.6%
Weaned	16	6 37.5%	10 62.5%
Ungrouped	1	1 100%	0 0%

The overall percent of "grouped" cases correctly classified was 66.67%. It is interesting to not that the best hit rate was for the true negatives. The sensitivity, specificity, positive predictive value and negative predictive value were found to be .63, .68, .45, and .81 respectively.

A second discriminant analysis using all six variables was run to determine if the same significant variables would be identified as in the multiple regression (DECUB and RR) and to see if the predictive accuracy would change. The examination of Wilk's Lambda Summary Table (see Table 20) indicates that all of the variables were included except PCO2.

Table 20

Wilk's Lambda Summary Table-Six Variables-Split Sample

STEP	ENTERED	IN	LAMBDA	SIG.
1	RR	1	.88801	.0164
2	DECUB	2	.78123	.0027
3	TEMPLS	3	.73786	.0024
4	PH	4	.70919	.0028
5	TEMPGR	5	.69223	.0043

The overall structure matrix is displayed in Table 21. This matrix represents the pooled within-groups correlations between discriminating variables and the Canonical Discriminant Function. The variables are ordered by size of correlation with the function. Respiratory rate was found to have the highest correlation with DECUB, PH, and TEMPLS clustering together.

Table 21

Structure Matrix-Six variables-Split Sample

Variable	Correlation
RR	-0.53259
DECUB	0.33787
PH	-0.29152
TEMPLS	0.28378
PCO2	0.13450
TEMPGR	0.12236

Once again, the test of equality of group covariance matrices was done using Box's M. The Box's M of 19.96 was not significant (p=.32).

The Standardized Canonical Discriminant Function Coefficients are displayed in Table 22.

Table 22

Standardized Canonical Discriminant Function Coefficients-Six Variables-Split Sample

Variable	Coefficient
DECUB	0.672
PH	-0.405
RR	-0.877
TEMPLS	0.531
TEMPGR	0.299

Finally, the classification results are displayed in Table 23.

Table 23

Classification Results-Six Variables-Split Sample

Actual Group	Number of Cases	Predicted Not Weaned	Predicted Weaned
Not weaned	36	27 75%	9 25%
Weaned	15	3 20%	12 80%
Ungrouped	1	1 100%	0 0%

The overall percent of "grouped" cases correctly classified was 76.47%. It is interesting to note that the best hit rate was found to be for the weaned group at 80%. The sensitivity, specificity, positive predictive value and negative predictive value were .80,.75,.57, and .90 respectively.

Monte Carlo Procedures

One hundred samples of size 58 were randomly selected by the computer from the population. The Macro commands are contained in Appendix B. The SPSS package generated 100 discriminant analyses using the Wilk's method for two separate sets of independent variables. The first set included the variables RR and DECUB the second set contained the additional variables PH, PCO2. TEMPGR, and TEMPLS.

Monte Carlo-Two Variables.

The first set of 100 discriminant analyses included the variables DECUB and RR. Both of these were found to be significant in the original discriminant analysis. However, analysis of the 100 equations yielded the following distribution of significant variable inclusion (Table 24). Only 69 of the samples produced variables that qualified for analysis.

Table 24

Variable Inclusion and Standardized Canonical Discriminant Function Coefficient-Two Variables

	n	RR Coef Mean	RR Coef STD DEV	DECUB Mean	DECUB STD DEV
RR	42	1.00	0.00	------	------
DECUB	13	------	------	1.00	0.00
BOTH	14	.64	.41	.52	.48

The random selection of samples appears to have chosen approximately equal numbers of Weaned and Not Weaned patients for Two Week cases. The hit rates by variable inclusion in the equation are displayed in Table 25.

Table 25

<u>Hit Rates-Two Variables</u>

Variables Included	Number of Equations	n Not Weaned Mean STD DEV	n Weaned Mean STD DEV	Hit Rate Mean STD DEV
RR	42	41.24 2.20	12.88 2.13	66.25 6.24
DECUB	13	42.00 3.03	13.08 3.01	48.58 4.50
BOTH	14	39.78 2.54	13.71 2.64	56.47 4.20
	69	41.09 2.50	13.09 2.36	57.83 7.37

<u>Monte Carlo-Six Variables.</u>

One hundred random samples were used to run the Wilk's method Discriminant analysis. This time, 86 samples generated variables that qualified for the analysis. However, the total 100 samples produced 30 different combinations of 1 to 5 significant variables. The variables were included as significant in the 86 samples in descending order: RR 60.5% (n=54), DECUB 37.2% (n=32), TEMPLS 37.2% (n=32), PH 25.6% (n=22), PCO2 25.6% (n=20), and TEMPGR 19.7% (n=17). The overall hit rate (range 30.4 to 71.4) of all 86 analyses was 58.24% with a standard deviation of 7.93.

It is extremely interesting to note that none of the analyses produced the same combination of significant variables that was found in the original model development (RR, DECUB, PH,TEMPLS,TEMPGR). The equations are classified by number of significant variable produced in Tables 26 through 30.

Table 26

One Variable-Monte Carlo

Variable Included	Number of Samples	Hit Rate Mean	Hit Rate STD DEV
DECUB	3	50.40	8.00
PH	4	54.93	5.34
PCO2	3	58.53	2.57
RR	21	60.55	5.69
TEMPLS	3	32.86	2.66

Table 27

Two Variables-Monte Carlo

Variable Included	Number of Samples	Hit Rate Mean	Hit Rate STD DEV
RR TEMPLS	4	59.75	4.19
DECUB TEMPLS	3	55.36	1.50
DECUB RR	3	58.03	0.42
TEMPLS TEMPGR	3	52.40	5.71
DECUB TEMPGR	3	56.97	9.45
PCO2 RR	2	60.45	4.31
PH RR	4	57.00	9.31
PH PCO2	1	56.40	0.00

Table 28

Three Variables-Monte Carlo

Variable Included	Number of Samples	Hit Rate Mean	Hit Rate STD DEV
DECUB PH PCO2	3	56.27	2.83
DECUB RR TEMPLS	3	63.17	8.22
RR TEMPLS TEMPGR	3	69.10	2.17
PCO2 RR TEMPLS	3	64.00	6.24
DECUB PCO2 RR	1	64.70	0.00
DECUB PH TEMPLS	2	62.85	0.07
DECUB TEMPLS TEMPGR	1	55.60	0.00
DECUB PH RR	2	60.00	0.57
DECUB PH TEMPGR	1	57.40	0.00
PH RR TEMPGR	2	54.65	6.57

Table 29

Four Variables-Monte Carlo

Variable Included	Number of Samples	Hit Rate Mean	Hit Rate STD DEV
DECUB RR TEMPLS TEMPGR	1	51.90	0.00
PCO2 RR TEMPLS TEMPGR	1	70.50	0.00
DECUB PH PCO2 RR	1	57.70	0.00
DECUB PH PCO2 TEMPLS	1	62.50	0.00
DECUB PCO2 RR TEMPLS	1	59.20	0.00

Table 30

Five Variables-Monte Carlo

Variable Included	Number of Samples	Hit Rate Mean	Hit Rate STD DEV
DECUB PH PCO2 TEMPLS TEMPGR	1	65.40	0.00
DECUB PH PCO2 RR TEMPLS	1	55.60	0.00

CHAPTER V

DISCUSSION

Description of the Sample and Survival

This chapter begins with a discussion of the demographics of the overall sample and the survival analyses. The data presented confirm the presence of a heterogeneous sample. These 145 patients were admitted from 58 different hospitals; the mean length of stay (LOS) at the referring hospital was long at 120.3 (SD=85). The medical histories and reason for initial ventilation were found to be greatly varied across patients (Tables 8 and 9). With the exception of decubiti with a 58.8% prevalence rate, no one underlying medical disease predominates in the sample. This finding is different from the other studies reported in the literature.

Although decubitus is not typically considered a primary diagnosis (unless one is admitted specifically for wound infection or surgical wound repair), it does reflect underlying disease. Patients at risk for skin breakdown are generally immobile, malnourished and/or infected for a long period of time. It is most likely for that reason that it surfaced as a predictor in later analyses. That is to say that the presence of decubiti can reflect a chronic, unhealthy underlying condition.

Table 5 illustrates successful weaning outcomes by different endpoints. The prognosis, considered from any of the endpoints, is not encouraging. The overwhelming majority will not wean from long term mechanical ventilation. The percentage of "successfully" weaned varies dramatically between the endpoints of one day and two weeks. This finding reinforces the difficulty we encounter when we attempt to compare studies reported in the literature. Most studies do not report the incidence of reintubation in their success rates. The weaning success rate found here is lower than that reported by Gracey et al. (1992) and Cordasco, Sivak, and Perez-Trepichio (1990). A striking difference between this population and other reports is that Vencor does not pre-screen for medical stability and rehabilitation potential. Furthermore, both the Mayo Clinic and the Cleveland Clinic admitted their patients in transfer from their own institutions.

The data on disposition is just as bleak (Tables 5 and 6). Over 71% of the patients died while still inpatients. Only 9% of the patients were weaned and alive at discharge. Although long term mechanical ventilator patients are sometimes considered hardy because they beat the initial survival odds, prognosis remains poor. The mortality rate described here is more similar to the outcomes reported in the intensive care units (Spicher and White, 1987;Gillespie, Marsh, Divertie, and Meadows, 1986; Elpern, Larson, Douglass, Rosen, and Bone, 1989).

Tables 10, 11, and 12 illustrate the overall medical stability and the toll of chronic ventilatory support. The mean WBC is above normal which typically reflects an infected state. Low hemoglobin and albumin are usually predictors of poor weaning outcome because of impaired oxygen transport and malnutrition. Furthermore, albumin reflects the clinical picture from 20 days prior to the blood draw. The situation may have changed for better or worse. Almost 47% of the patients were admitted with temperatures outside the normal range. Overall, the patients could be considered chronically acutely ill on admission to Vencor.

It is unfortunate that more metabolic studies were not available for analyses (n=51). During the preliminary runs of multiple regression, these variables accounted for a great deal of the variance although the equations did not produce significant F ratios. This finding was most likely due to the missing data sets that dropped the cases for analysis. Less than 50% of the patients had data sets related to metabolic studies.

A comparative examination of the survival curves appearing in Figures 1-6 graphically display the bleak prognosis. Although those who wean have a longer median survival rate (95.00) compared to those who did not wean

(38.15), their chances of survival are not good Figures 1-2). Even when the patients termed "unweanable" due to cancer and neuromuscular diseases were dropped from the analyses (Figures 3 and 4), the median survival time for those who did not wean only rose from 38.15 to 40.83 days. When interpreting survival analysis curves it is important to remember that it is the median survival time rather than the arithmetic mean that it analyzed. While the average overall length of stay at Vencor is 68.8 days, the median survival time is 51.5 days.

Prediction Model

The subjects included in this study appear to be different than those subjects in other studies with respect to time on ventilator (see Table 2) in that these patients required extended periods of mechanical ventilation and had an average length of stay at the acute referring hospital of 120.3 days (standard deviation of 85.9). Unfortunately the medical records were not always complete with regards to the date of initial ventilation, therefore it was not possible to calculate the number of ventilator days for a significant number of subjects.

The definition of successful weaning used in this study was also more stringent than those reported in Table 3. The success rate here varies from 36.6% for one day to 17.9% for two weeks. Two weeks was used as the criterion for the prediction model in this study because it makes better clinical sense. That is, the patients had been on mechanical ventilators too long to realistically consider 24 hours off the ventilator as "weaned". Twenty seven of the 53 patients who weaned for one day did not wean for two weeks.

Split Sample Discriminant Analyses.

Recall that the original prediction model was developed by first randomly selecting the 117 subjects into two groups. In the first group multiple regression was used to compress the variables by categories. Six potentially significant variables were identified: History of decubiti (DECUB), respiratory rate (RR), arterial carbon dioxide level (PCO2), arterial pH (PH), temperature greater than 99.6 (TEMPGR), and temperature less than 97.6 (TEMPLS). Using the enter method of multiple regression, only two of the variables, DECUB and RR, were found to have significant beta weights. The equation was found to be statistically significant (p=.009) and accounted for 31 percent of the variance in the dependent measure of weaned for two weeks.

Based on the multiple regression results, the variables RR and DECUB were entered into the discriminant analysis using the Wilk's methods. Wilk's was chosen over the direct method (which forces all the variables in the analysis) in order to determine if they would both be significant in the prediction of weaning. The prediction model using the two variables DECUB and RR was able to correctly classify group membership 66.67% of the time with a sensitivity, specificity, positive predictive value and negative predictive value were .63, .68, .45, and .81 respectively. This finding is fairly comparable to other studies (Table 4). Per usual, it is easier to predict those who will not wean than those who will. In fact, that is the reason patients with cancer and neuromuscular disease were excluded from the analyses. Clinically, it is known they would not wean. Inclusion would have increased the ability to predict those who will not wean but would not add to predictability of those who will wean or who are in the grey area.

In order to further investigate whether or not the multiple regression identified all the significant variables, a discriminant analysis was done entering all six of the variables. Indeed the results were found to be different than the multiple regression in that five of the six variables entered significantly into the discriminant analysis. Only PCO2 failed to enter using the Wilk's method. In this second discriminant analysis run on the same group, the overall hit rate improved to 76.47%. The positive predictive value improved; the weaned group had a hit rate of 80%. The sensitivity, specificity, positive predictive value and negative predictive value also showed improvement at .80,.75,.57, and .90 respectively.

Based on the above analyses, there is considerable evidence to support a prediction model for the weaning of patients requiring long term mechanical ventilation.

Monte Carlo Discriminant Analyses.

Statistical textbooks (Stevens, 1986) caution the use of stepwise discriminant analyses like the Wilk's because the results can be positively biased, especially if the subject/variable ratio is small (<5). Monte Carlo studies have shown that unless sample size is large relative to the number of variables, both the standardized coefficients and correlations are very unstable.

Two Monte Carlo studies were done on the data set, one for each of the two discriminant analyses. In both, 100 samples of 58 cases were randomly selected from the total population.

In the first one, the variables DECUB and RR were entered using the Wilk's methods. The results were somewhat surprising because the subjects to variable ratio was found to be large (58:2) at about 30:1. The variables were not strong enough to qualify for analyses in almost one third of the samples drawn (31 of 100). The remaining 69 analyses were distributed unequally among three sets of included variables (Table 24). The combination of both DECUB and RR was only generated in 14 of the 60 samples; the overall hit rate of these samples had a mean of 56.47 and a standard deviation of 4.20. The original classification of 66.67% does not even fall within the first standard deviation of the Monte Carlo analysis. The best overall hit rate was seen where only RR rate was entered (n=42, 61% of all analyses) at 66.3% with a standard deviation of 6.24. In the analyses where DECUB was entered, the mean hit rate of 48.5% and standard deviation of 4.50%. When one considers that the prior probability of classification by chance alone is .500, flipping a coin may be about as accurate of a predictor as DECUB.

The second Monte Carlo analysis using all six variables and the Wilk's method also demonstrated great instability. A less stable model would have been predicted because the subject to variable ratio decreased from 29:1 to 58:6 or 29:3. However, this is still greater than the recommended minimum of 5:1 but less that the preferred of 20:1 (Stevens, 1986).

This time, only 14 samples failed to produce variables that qualified for analysis. The multiple combinations of variables and their hit rates were previously displayed in Tables 26 to 30. The original split sample discriminant analysis had a hit rate of 76.47%. None of the 86 analyses performed achieved a hit rate as high as this (range 30.4 to 71.4). And even though 30 different combinations of significant variables were generated, not one matched the original split sample.

Although no formal analyses were done, the hit rates across analyses is approximately the same in the 50-60% range with the notable exceptions of TEMPLS (32.86%) and the combination of PCO2, RR, TEMPGR, TEMPLS (70.51%). An interpretation of this result could be that all of the variables are predicting weaning to some extent. However, a prediction model with a hit rate of 50-60% is not very useful in the clinical setting.

Summary

In this study a unique sample of patients who require long term mechanical ventilation was described. Demographics and survival analyses were presented.

Discussion of Results Related to Testing the Null Hypotheses.

The results will be discussed as they relate to the null hypotheses.

1. The null hypothesis that there would be no difference in the survival curves for those patients who wean and do not wean from long term mechanical ventilation was rejected.
2. The results of the multiple regression failed to reject the null hypothesis that there would be no difference in the weaning outcome for those who required long term mechanical ventilation across initial reason for ventilation.
3. The null hypothesis that there would be no difference in the weaning outcome for those who required long term mechanical ventilation across significant preexisting medical conditions was rejected due to the preexisting

medical condition of history of decubiti.

4. The null hypothesis that there would be no difference in the weaning outcome for those who require long term mechanical ventilation across physiological variables was also rejected. The physiological variables of respiratory rate, arterial carbon dioxide, arterial pH, and temperature were identified as predictors.

5. The study failed to reject the null hypothesis that there would be no difference in the weaning outcome for those who require long term mechanical ventilation across social variables.

Monte Carlo Studies.

The two Monte Carlo studies presented illustrated many of the problems associated with the validation of prediction models. Even though the variables and sample size did not violate the typical recommendations, the results revealed unstable replications. It would be interesting to perform a Monte Carlo study on some of the other indices reported in the literature.

Limitations of the Study.

The major limitation of this study was the amount of missing data. While it can be acknowledged that incomplete medical records does not necessarily equate with incomplete care, it was disappointing to drop cases from analyses based on this alone.

Another limitation was the potentially subjective nature of the data related to underlying disease processes and initial reason for mechanical ventilation. The transferring physician selected the reported information. With the large variation in referring hospitals (58 for the 145 patients), and the unknown number of different referring physicians, it is difficult to ascertain the consistency with which major illnesses were diagnosed.

Future Research.

Two general recommendations will be made regarding the development of prediction models for patients requiring long term mechanical ventilation (prospective studies and large sample sizes).

Prospective data collection by a consistent health care provider is essential. One of the biggest disappointments was the amount of missing data and incomplete records in the retrospective chart reviews. It would also be of value to prospectively study the survival of patients who are discharged from the hospital.

The Monte Carlo studies make the need for larger sample sizes and cross validation glaringly apparent. The physiological variable respiratory rate consistently surfaces as significant. However, it needs to be established whether it is a predictor in and of itself versus a reflection of current clinical practice. Respiratory rates outside the normal range may preclude weaning so that the patient never initiates the weaning process. Future analyses could dichotomize the variable of respiratory rate (similar to temperature) with reference to rates above and below the normal respiratory rate.

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APPENDIX A

WEANING PROTOCOL

Unless otherwise directed by physician's order, the following weaning steps will be utilized by Respiratory Care personnel.

Step #1	Settings:	IMV=0/CPAP=0, PS+10 x 2 hours
Step #2	Settings:	IMV=0/CPAP=0, PS+10 x 4 hours
Step #3	Settings:	IMV=0/CPAP=0, PS+10 x 8 hours
Step #4	Settings:	IMV=0/CPAP=0, PS+10 x 12 hours
Step #5	Settings:	IMV=0/CPAP=0, PS+8 x 8 hours
Step #6	Settings:	IMV=0/CPAP=0, PS+8 x 12 hours
Step #7	Settings:	IMV=0/CPAP=0, PS+5 x 4 hours
Step #8	Settings:	IMV=0/CPAP=0, PS+5 x 8 hours
Step #9	Settings:	IMV=0/CPAP=0, PS+5 x 10 hours
Step #10	Settings:	IMV=0/CPAP=0, PS+5 x 12 hours
Step #11	Settings:	IMV=0/CPAP=0, FB x 4 hours, then ABG
Step #12	Settings:	IMV=0/CPAP=0, FB x 8 hours
Step #13	Settings:	IMV=0/CPAP=0, FB x 12 hours
Step #14	Settings:	IMV=0/CPAP=0, FB x 16 hours
Step #15	Settings:	IMV=0/CPAP=0, FB x 16 hours

APPENDIX B

COMMANDS FOR MACRO

```
//STEP EXEC SPSS,PRM=240K
//DATAIN DD DSN=@W34LMC.WEANS.SPSSYSTM,DISP=SHR
//SYSIN DD *

DEFINE RAN (ARG1 = !TOKENS(1)
           /ARG2 = !TOKENS(2))
!DO !I = !ARG1 !TO !ARG2
GET FILE = DATAIN
SELECT IF NOT (HNM EQ 1)
SELECT IF NOT (HCA EQ 1)
TEMPORARY
SAMPLE 58 FROM 117
DISCRIMINANT GROUPS=TWOWEEKS (0,1)/
   VARIABLES=HDECUB RR/
   METHODS=WILKS/
   STATISTICS=ALL
!DOEND
!ENDDEFINE
SET SEED=2005000
RAN ARG1=1 ARG2=100
```

APPROVAL SHEET

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The final copies have been examined by the director of the dissertation and the signature which appears below verifies the fact that any necessary changes have been incorporated and that the dissertation is now given final approval by the Committee with reference to content and form.

The dissertation is therefore accepted in partial fulfillment of the requirement for the degree of Doctor of Philosophy.

4/8/93
Date

Jack A. Kavanagh
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