Severity of Illness and the Relationship Between Intensive Care and Survival

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Abstract: Currently about 15 per cent of hospital costs are attributed to intensive care. Research using statistical models has not adequately demonstrated that therapy in intensive care units (ICUs) is associated with reductions in the probability of death. In a study of 613 consecutive admissions to a multidisciplinary ICU, we reevaluate the relationship between ICU care and survival using a new acute physiology scoring system to control for the severity of illness of the patient population.

When our severity of illness index was employed, we found a statistically significant and nonlinear relationship between the use of intensive medical care and the probability of survival. This statistical relationship produced a U-shaped curve with three distinct segments. The first segment exhibited an overall decrease in the probability of death with increasing therapy (275 admissions); the second segment, a fairly stable survival rate (281 admissions). Only in the third segment, where there were 57 admissions, did we find an overall increase in the probability of death as utilization of therapy increased.

These findings suggest that quantitative measurement of severity of illness, when used in clinical studies, could produce improved insights into the relationship between therapy and health outcomes. (*Am J Public Health* 1982; 72:449–454.)

Hospital-based intensive care accounts for about 15 per cent of hospital costs and is widely believed by physicians to be efficacious in treating individual patients.* However, studies of intensive care unit (ICU) populations have not been able to statistically demonstrate that the increased utilization of therapy in ICUs lowers the probability of death.[2–4] Likewise, analyses of area-wide data have in many instances failed to find a measurable health benefit related to the availability of health care resources.[5–9] In this paper we present results indicating that the impact of intense medical care on the probability of death is nonlinear and statistically measurable when the analysis controls for severity of illness.

Materials and Methods

Data Base

To perform the analysis, we collected detailed data on 613 consecutive admissions to the 16-bed medical and surgical ICU of the George Washington University Medical Center (GWUMC). The GWUMC ICU treats a wide variety of patients with acute medical and surgical problems with the exception of myocardial infarctions and burns.

During the eight-month study period, we collected information on the patient's past medical history; indications for ICU admission; the amount and type of therapy each patient received; the severity of acute illness; and outcome, defined as dead or alive when discharged from the hospital. Information regarding past medical history included age, sex, operative status, smoking history measured in pack years,** and the use of alcohol if it contributed to past or present medical problems.

To measure therapy we collected Therapeutic Intervention Scoring System (TISS) points during each shift the patient was in the ICU.[10] TISS uses assigned weights from 0 to 4 to grade approximately 75 various therapeutic, diagnostic, and monitoring tasks. The weights reflect the amount of time each task requires, as well as their complexity. Total TISS points, which are obtained by adding the weights, have been used as a measure of resource utilization in other ICUs.[11]

We also developed the Acute Physiology Score, derived from the Acute Physiology and Chronic Health Evaluation (APACHE), as an index of severity of illness.[12] This scoring system assigns weights from 0 to 4 for 34 potential physiological measurements, such as blood urea nitrogen, blood

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*Derived from data in reference 1.

**A pack year is the consumption of one pack of cigarettes a day over a one-year period.

TABLE 1—Probit Equations Predicting In-hospital Deaths

Independent Variables	Equation 1	Equation 2	Equation 3
Age over 40 (in years)	.0185	.0192	.0235
	(3.99)**	(4.14)**	(4.61)**
Sex (female = 1)	.110	.095	.133
	(.84)	(.72)	(.93)
Positive smoking history = 1	.226	.245	.342
(20 pack years)	(1.67)	(1.80)	(2.33)*
Recorded history of alcoholism = 1	.0751	.0933	.039
	(.43)	(.53)	(.21)
Surgical patient = 1	−.813	−.804	−.385
	(6.19)**	(6.08)**	(2.57)**
Therapeutic effort first 12 shifts	+.00317	−.00162	−.00611
in ICU (TISS points)	(5.28)**	(.79)	(2.65)**
Square of therapeutic effort (TISS	—	.00001205	.00001612
points)		(2.44)*	(2.96)**
Severity of illness (acute physiology score)	—	—	.0717
			(8.35)***
Constant	−1.420	−1.124	−2.165
	(8.31)**	(5.45)**	(8.05)**
Number of cases	613	613	613
Total misclassification rate	18.1%	17.8%	13.9%

(asymptotic t-ratios in parentheses; significance levels are approximate.)
*$P \leq .05$
**$P \leq .01$
***$P \leq .01^{-10}$

pressure, and PCO2, to reflect the severity of acute physiological abnormalities. The weights were determined a priori by a panel of experienced ICU physicians. The Acute Physiology Score reflects the level of physician concern created by the number and extent of abnormal measurements. We measured the Acute Physiology Score within the first 32 hours after the patient's admission to the ICU, the period when ICU patients are typically in their most serious condition.[12]

Study Population

Patients are admitted to this unit on request of their attending physician. All requests were reviewed by one of three full-time ICU directors, but only 23 admissions were denied or delayed during the study period, primarily because of a shortage of ICU nurses. Most patients are transferred to ICU care because their physicians believe they need more extensive therapy than is available on the hospital floors, or because the patient may be at risk of quickly developing the need for such therapy. Approximately 55 per cent of these patients received aggressive ICU therapy within 24 hours of ICU admission, while the other 45 per cent received only monitoring activities.

The average ICU patient in our sample was 57 years old,*** with 53 per cent of them being male. Over half (57 per cent) were admitted to the ICU following surgical procedures. Their diagnoses and indications for admission encompassed the entire range reported from other ICU surveys in tertiary care hospitals.[2–4,13,14] This included patients suffering from acute problems such as respiratory failure, drug overdoses, and shock, as well as chronic illnesses such as cancer. Their in-hospital mortality rate of 19.2 per cent is also comparable with other ICU surveys.[2,3,13,14]

A third of the population had a prior history of substantial smoking (20 pack years or more), while 14 per cent had alcoholism recorded in their chart as a significant health problem. The average number of TISS points received during the ICU stay was 136. The mean Acute Physiology Score was 15 with a range of 0 to 50.

Data Analysis

We began our analysis by examining the relationship of in-hospital survival and intense medical care as measured by TISS points, controlling for the age and sex of the patient but without including our severity of illness index. This is Equation 1 in Table 1. Variables measuring a history of smoking and of alcoholism were also included, as was a variable that distinguished surgical from medical patients. We then repeated the analysis, but TISS points were represented as a curve rather than a straight line by including a TISS squared term (Equation 2). Finally, we reestimated Equation 2 including our severity of illness index (Equation 3).

In all of these equations we used multiple regression analysis with in-hospital mortality as the dependent or target variable. Since the target variable in each case had only two possible values, alive or dead, probit analysis was used as the appropriate regression technique.[15,16] When using probit analysis, each independent variable is assumed to have an independent impact on variation in the probability of death.

***The largest portion of the patients (44 per cent) were between 50 and 70 years old.

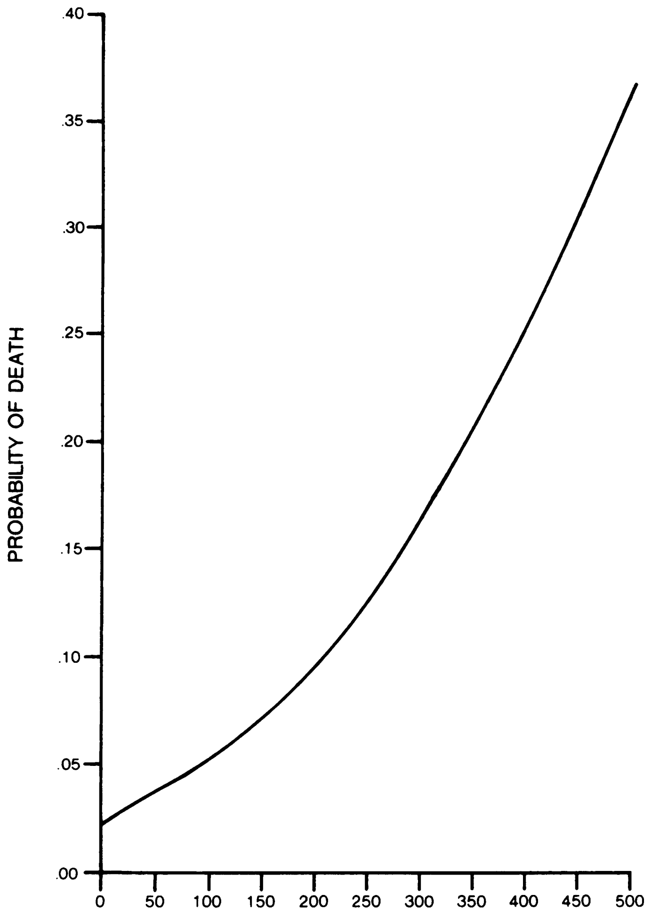

FIGURE 1—Relationship between Treatment and Survival Not Controlling for Severity of Illness (Derived from Equation #1)

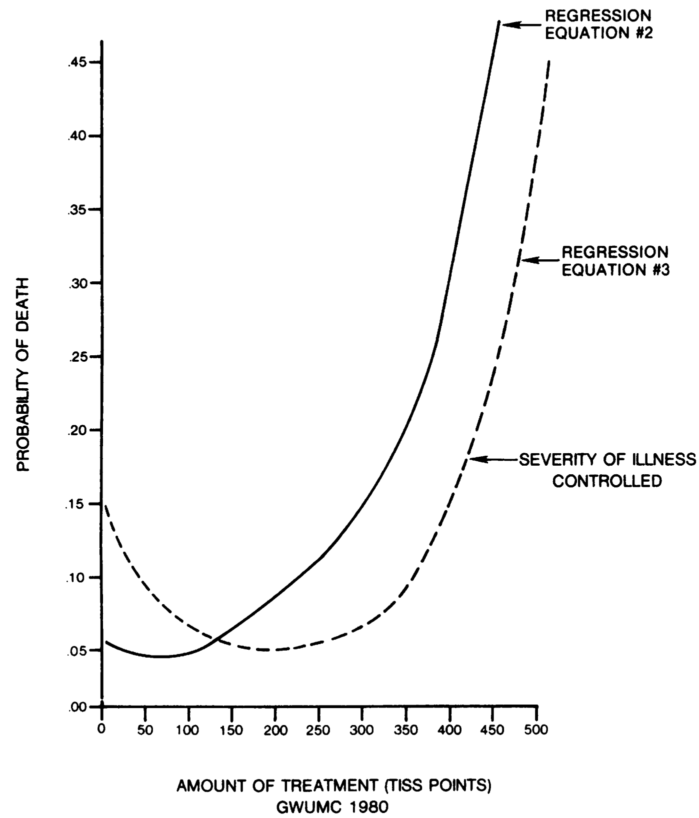

FIGURE 2—Relationship between Treatment and Survival with and without Control for Severity of Illness

The independent variables are defined and evaluated for statistical significance in Table 1. A variable was included to adjust for differences between medical and surgical patients, and a separate analysis was performed on cardiovascular patients. The entire analysis was repeated using ICU discharge status as the dependent variable.

Results

The first regression equation estimates the relationship between hospital survival, adjusted for age and sex, and TISS points received during the ICU stay up to 12 shifts (four days) of ICU care without controlling for severity of illness (Table 1). To examine whether our analysis is dependent on the number of shifts used, we also performed a sensitivity analysis in which the number of ICU shifts was varied (see next section). About 70 per cent of our ICU admissions were discharged within 12 ICU shifts.

As TISS points increase, so does the probability of an in-hospital death (see Equation 1, also Figure 1). The surgical variable in Equation 1 is statistically significant and indicates that surgical patients have a lower probability of death as compared to medical patients.[3,13] Age is the other statistically significant variable, and it indicates, as might be expected, that each year over 40 increases the probability of an in-hospital death.

For Equation 2, we include a square as well as a linear measure of TISS points (see Figure 2). This enables us to represent TISS points as a curve. The remaining variables in Equation 2 are the same as those in Equation 1. The TISS squared term is statistically significant and positive in sign while the linear TISS term is negative but insignificant. Thus, again we find that increases in therapy relate to a statistically higher probability of death. Other research without controls for illness severity has also found a positive relationship between increases in therapy and the probability of death.[2-4]

In Equation 3 we again investigate the statistical relationship between TISS points and survival, this time controlling for severity of illness. We did this by introducing an explicit measure of severity of acute illness (the Acute Physiology Score) into Equation 3. Equation 3 shows that severity of illness as measured by the Acute Physiology Score is statistically related to outcome ($t = 8.35$; $p < .01^{-10}$), as are the linear and square measure of TISS.

The introduction of the physiology score changes the statistical relationship between TISS points and outcome. The TISS and TISS squared variables are both highly significant ($p < .01$), implying a U-shaped curve that appears

TABLE 2—Death Rates (in per cents) by Acute Physiology Score and TISS Points

Acute Physiology Score	Therapy Ranges (TISS Points)			All Patients
	Less than 100	100 to 280	More than 280	
Less than 10	5% (151)	5% (59)	0% (1)	5% (211)
10 to 14	5% (60)	11% (73)	43% (7)	10% (140)
15 to 19	24% (29)	8% (64)	31% (13)	15% (106)
20 to 24	33% (18)	21% (43)	33% (12)	26% (73)
25 to 29	50% (8)	46% (13)	86% (7)	57% (28)
30 or more	91% (11)	70% (27)	76% (17)	76% (55)
All patients	14% (277)	18% (279)	53% (57)	19% (613)

Note: (Frequency in Parentheses)

to have three distinct segments. Equation 3 also has a lower misclassification rate (13.9 per cent) than Equations 1 and 2 (18.1 and 17.8 per cent respectively). Using Equation 3 we derive a U-shaped curve for nonsmoking, average-age, male medical patients with a physiology score of 15—the average physiology (see Figure 2).

The first segment of the U-shaped curve shows a sharp decline in the probability of death as TISS points increase from 0 to about 100. The second segment, between about 100 and approximately 280 TISS points, shows a probability of death that remains fairly stable (the flat of the curve). It is only at approximately 280 TISS points that the probability of death increases substantially despite increases in TISS points (the third segment of the curve).

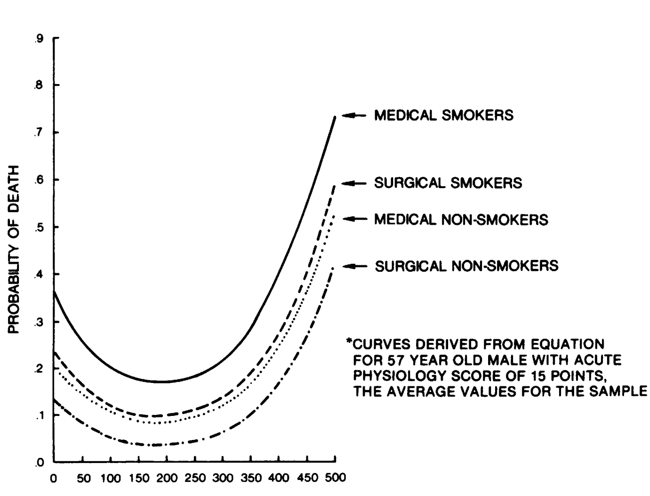

FIGURE 3—Impact of Operative Status and Smoking on Relationship between Treatment and Survival, Controlled for Severity of Illness*

We explored the three segments of the curve in Figure 2 in terms of the number of ICU admissions and total number of TISS points received in each segment. The results indicate that 45 per cent of admissions and 19 per cent of TISS points were within the declining segments of the curve. Only 9 per cent of admissions were in the third segment, where the probability of death increased. This third segment, however, did account for 24 per cent of total TISS points delivered in the ICU.

To more directly explore this U-shaped relationship, we calculated death rates within broad groupings of Acute Physiology Scores across three ranges of TISS points representing the three apparent segments of the curve found in Equation 3. These groupings, as shown in Table 2, do not control for such variables as age, operative status, or a positive smoking history, as did Figure 2, which was derived from the regression analysis. Except for low Acute Physiology Scores (0 to 14), the data indicate that the relationship between probability of death and TISS points is U-shaped and similar to that found in Figure 2. For example, admissions with an Acute Physiology Score of 15 to 19 receving 0 to 100 TISS points had a death rate of 24 per cent; those receiving between 100 and 280 TISS points had a death rate of 8 per cent; while those receiving more than 280 TISS points had a death rate of 31 per cent.

Using our data and the results of regression analysis, we derived curves for surgical and medical admissions‡ (Figure 3). The lower curve in Figure 3 is for post-surgical, nonsmoking, average-age (57 years) male ICU patients with an Acute Physiology Score of 15 (average for the population studied). The other curves in Figure 3 indicate that medical

‡We also reestimated Equation 3 separately for medical and surgical patients. The signs of both variables and their statistical significance were unchanged. The turning point, i.e., the minimum value, of the curve was at 182 TISS points for surgical patients and 198 TISS points for medical patients as compared to 190 TISS points for the combined analysis.

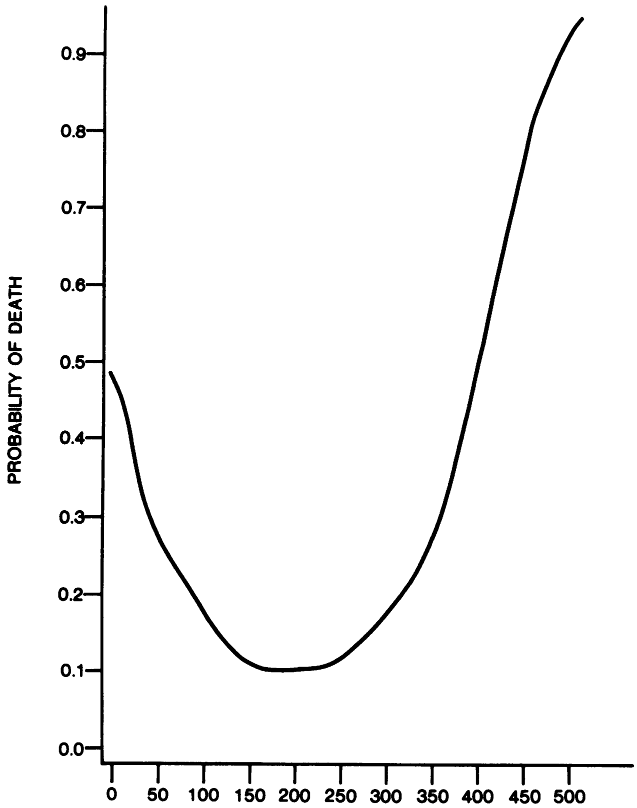

FIGURE 4—Relationship between Treatment and Survival Controlling for Severity of Illness for 234 Cardiovascular Patients

patients with these same characteristics have a higher probability of dying as compared to surgical patients. A 20-pack-year history of smoking increases the probability of death by about 6 percentage points for both medical and surgical admissions.

The statistical results from Equation 3 indicate that age increases the probability of in-hospital death from 5 per cent for a typical 40-year-old to 18 per cent for a 70-year-old, assuming the same severity of illness. This result is very close to that found in a recent survey examining survival following burns.[17] As in that study, our analysis did not find any statistical relationship between survival and the patient's sex.

Sensitivity Analysis

We subjected these results to a number of sensitivity tests to investigate their integrity. To evaluate our choice of using TISS points received during the first 12 ICU shifts to measure therapy, we expanded the analysis to include the initial 36 shifts (less than 9 per cent of all ICU admissions stay beyond 36 shifts). This does not change the U-shaped pattern of the curve. However, it does increase the percentage of TISS points accounted for by the 9 per cent of patients within the third or ascending segment of the curve from 24 per cent to 33 per cent. We also found that using TISS points for fewer shifts (after 6 and 9 shifts) did not alter the basic relationships. Up to approximately 12 shifts, the statistical significance of the TISS variable increases as more shifts are included in the analysis.

To further evaluate the results, we redefined the outcome (dependent variable) as ICU death rather than hospital death and reestimated our equations. Again the basic relationship was similar to the one shown in Equation 3.

We then studied a more homogeneous subset of the ICU population, patients admitted for cardiovascular disease. As a group, they were more severely ill than the overall patient group, with an Acute Physiology Score averaging 17 as compared to the mean of 15 ($p < .05$). The result of this analysis was similar to the overall results in Equation 3; but, as seen in Figure 4, the resulting curve derived from the equation drops more quickly and rises faster than the curve for all ICU admissions.

We also compared the predictive power of the equation for cardiovascular patients to that for all patients. Equation 3 had an overall misclassification rate of 14 per cent, a false positive rate (predicted to live but died) of 12 per cent, and a false negative rate (predicted to die but lived) of 27 per cent. When only cardiovascular patients were analyzed (equations not shown), the misclassification rate fell to 10 per cent (the false positive rate was 8 per cent, and the false negative rate was 20 per cent). This suggests that subsequent analysis using more homogeneous patient groups may produce more precise results.

Discussion

ICUs provide a wide range of services, from monitoring stable patients to treating critical illnesses.[13] Although long-term survival and quality of life are important concerns, a principal role of ICUs is improving short-term survival.[3,4,11,13] Previous studies examining ICU populations have not been able to statistically identify the relationship between increases in ICU therapy and reductions in the probability of death. Our results suggest a U-shaped, nonlinear relationship exists.

The initial downward sloping segment of the curves in Figures 2 and 3 suggests that some patients respond rapidly to treatment with the use of a small amount of ICU resources. This group of patients accounts for 45 per cent of admissions and uses only 19 per cent of total therapy. Patients within this group include persons treated for acute diabetic ketoacidosis, those recovering from neurosurgical procedures, and those admitted following cardiac arrests or with reversible shock.

The second segment of the curve accounts for about the same percentage of admissions (46) as the declining segment of the curve but uses substantially more therapy (57 per cent of total TISS points). For this group, the overall probability of death remains relatively stable as the number of TISS points delivered increases. Patients in this segment include those suffering from acute but reversible renal failure or shock. Others are patients recovering from extensive surgery such as open heart procedures.

The third segment of the curve, where the probability of death increases despite increasing therapy, represents many critically ill patients for whom initial therapy is unsuccessful or in whom complications or another illness develop. This group consists of multiple trauma patients and those with prolonged respiratory or multi-system failure.

This relatively small percentage of the total ICU population who have poor outcomes does account for a disproportionate amount of total ICU resources.[2-4] But while this patient group is important, they have drawn attention away from the 91 per cent of the admissions in the first two segments of the curve.

We are not suggesting that these results are evidence that patient survival was due solely to ICU treatment. Many patients who survived might have achieved a similar outcome without intensive care. Methods such as a controlled clinical trial are required to identify those patients for whom ICU admission was lifesaving.

These findings illustrate that using a severity of illness index allows for more precise statistical analysis of the relationship between intensive medical therapy and outcome. Controlling for severity of illness could allow more appropriate comparisons of patients treated in different intensive care settings, or with different medical technologies. This could facilitate the more precise measurement of the effect on patients of new medical technologies or on changes in treatments over time. It also has important implications for determining the ICU needs in different hospital settings.

Our severity of illness index also holds substantial promise for use in clinical trials to control for case-mix differences among diverse patient populations. The strength of the Acute Physiology Score in such uses is its relatively objective and precise quantification of the impact of comorbid events and secondary diagnoses. An important antecedent to such use, however, should be more extensive multi-institutional validation studies. Clinicians are justifiably skeptical of multivariate analyses of heterogeneous groups of patients which might confound differences in disease state with severity of illness. It is important to establish the measurement reliability and predictive validity of these instruments in multiple hospitals and to establish that the results hold up within narrow, homogeneous diagnostic categories. Preliminary work on more homogeneous patient categories, such as that reported on cardiovascular patients and other work in progress, is promising in that the predictive power seems to improve as the patient category is more narrowly defined.

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