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James Stephen Krinsley and Richard L. Jones

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Original Research

GLYCEMIC CONTROL

Cost Analysis of Intensive Glycemic Control in Critically Ill Adult Patients*

James Stephen Krinsley, MD, FCCP; and Richard L. Jones

Study objectives: **To assess the effect of an intensive glycemia management protocol on the cost of care of a heterogeneous population of critically ill adult patients.**
Design: **Economic analysis of a 1,600-patient "before-and-after" study of intensive glycemia management.**
Setting: **Fourteen-bed mixed medical-surgical adult ICU of a university-affiliated community teaching hospital.**
Patients: **Eight hundred consecutive admissions to the ICU prior to the institution of an intensive glucose management protocol were compared to the first 800 patients admitted to the ICU following institution of the protocol.**
Interventions: **Cost data were analyzed using the comprehensive database of the ICU as well as other hospital data repositories.**
Measurements and results: **The ICU database was used to quantify the major components of the cost of care. The analysis includes costs associated with ICU and non-ICU patient days, ventilator days, and laboratory, pharmacy, and radiology services. Comparing the baseline and treatment periods, there were decreases in patient days in the ICU; ventilator days; total laboratory, pharmacy and radiology costs; and post-ICU hospital length of stay. The net annualized decrease in costs during the treatment period was $1,339,500, or $1,580 per patient.**
Conclusions: **The institution of a program to intensively monitor glucose levels and treat even modest hyperglycemia in the ICU was associated with substantial cost savings. This finding, in conjunction with the previously demonstrated improvement in mortality and morbidity, strongly supports the adoption of this intervention as a standard of care in the ICU.**

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Key words: cost; glycemia management; hyperglycemia; ICU; length of hospital stay

Abbreviations: APACHE = acute physiology and chronic health evaluation; FY = fiscal year; IQR = interquartile range; LOS = length of stay

An emerging medical literature has described the adverse consequences of hyperglycemia in a variety of different clinical contexts. Hyperglycemia occurs commonly among patients with acute neurologic disease,[1–5] ischemic heart disease,[6–10] and a range of surgical and trauma diagnoses[11–13]; its mechanism has been attributed to numerous stress, counterregulatory, and iatrogenic factors.[14] A review[15] of 1,826 patients admitted to an adult medical-surgical ICUs demonstrated a strong association between increasing glucose levels during ICU admission and the risk of hospital mortality. The lowest hospital mortality occurred among patients with mean glucose levels of 80 to 100 mg/dL during their ICU stay; the rate of hospital mortality increased dramatically for every 20 mg/dL increment above this normal level.

There are relatively few studies in the literature reporting improved outcomes with control of blood glucose in the acute setting. Observational stud-

*From the Department of Medicine, Division of Critical Care, Stamford Hospital, Stamford, CT.
Dr. Krinsley is Director of Critical Care, and Mr. Jones is Chief Financial Officer, Stamford Hospital.
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Correspondence to: James Stephen Krinsley, MD, Director of Critical Care, Stamford Hospital, 190 West Broad St, Stamford, CT 06902; e-mail: jkrinsley@stamhealth.org

ies[16,17] of a large group of cardiac surgery patients suggest that tight glycemic control improves mortality and postoperative morbidity, especially infection rates. A landmark randomized controlled study[18] performed in a surgical ICU among 1,548 patients receiving mechanical ventilation, 63% of whom had undergone cardiac surgery, demonstrated 34% reduction in mortality and impressive changes in numerous organ system dysfunctions with an intensive regimen that targeted euglycemia. More recently, a before-and-after study[19] of intensive glucose management among a heterogeneous population of adult medical and surgical patients, targeting a range of 80 to 140 mg/dL, revealed a 29% decrease in mortality as well as a reduction in the development of new renal insufficiency and the number of patients requiring RBC transfusions.

The costs associated with intensive glycemic management in a critical care population have not been well described. The purpose of this article is to delineate changes in the cost of care associated with this intervention, using actual data from the 1,600-patient study.[19]

Materials and Methods

Patients and ICU Organization

Stamford Hospital is a 305-bed, university-affiliated community teaching hospital that serves as a major teaching affiliate of Columbia University College of Physicians and Surgeons. The 14-bed ICU treats a heterogeneous population of adult medical, surgical, and cardiac patients. Cardiovascular surgery is not performed at the institution. Although the unit is an "open" unit that allows any credentialed physician to admit patients, the Director of Critical Care and the Director of Surgery closely supervise the unit-based medical and surgical house staff who write all patient care orders. The ICU is highly data and protocol driven.

The clinical outcomes of the 1,600 patients in this study have been reported.[19] The 800 patients in the baseline population were admitted consecutively to the ICU between February 23, 2002, and January 31, 2003. The 800 patients in the treatment population were admitted consecutively between February 1, 2003, and January 10, 2004. The intervention promulgated in the second group was a protocol to maintain blood glucose levels in the 80 to 140 mg/dL range.

Data Analysis

A comprehensive ICU database was created in 1998 and has since tracked numerous demographic and clinical features for > 6,500 consecutive admissions. The database is linked to several hospital data repositories allowing detailed analysis of clinical and financial parameters. The database was queried to allow analysis of ICU length of stay (LOS) [measured in 0.1-day increments, rather than calendar days]; post-ICU LOS (measured in calendar days); duration of mechanical ventilation (measured in 0.1-day increments); APACHE (acute physiology and chronic health evaluation) II scores[20]; primary admitting diagnosis to the ICU (determined at the time of ICU admission by the Director of Critical Care or the Associate Director); final hospital discharge status of each patient; and all laboratory, pharmacy, and radiology costs.

Laboratory, pharmacy, and radiology costs were calculated by applying the appropriate fiscal year (FY) 2002, 2003, and 2004 Medicare Cost Report cost:charge ratios to the charge data captured in the database. The costs were calculated for each major diagnostic group (cardiac, respiratory, GI, septic shock, miscellaneous medical and surgical) and fully adjusted for any differences in the prevalence of mechanical ventilation. There were 292 patients during the baseline period and 230 patients during the treatment period who required mechanical ventilation at the onset of ICU stay. To adjust for this difference, costs in the latter period were recalculated assuming that the number of patients requiring ventilation had not changed, using the actual mean costs for ventilated and nonventilated patients. The "variable" cost of an ICU day and a non-ICU day were calculated by dividing the total cost for each type of bed during the fiscal year, after overhead allocations and adjustments were excluded, by the number of bed days for each category during that FY. This yielded a weighted average of $866.47 during the baseline period and $864.37 during the treatment period. The variable cost of a non-ICU day was $403 for the two periods. The cost of a ventilator day was calculated by reviewing charges and applying the appropriate cost:charge ratio. An adjustment for year-to-year charge inflation was made by reviewing the increase in charges from FY 2002 to 2003 and from FY 2003 to 2004. The reported costs are based on FY 2004, adjusted for inflation.

Some patients required readmission to the ICU after initial discharge from the ICU during their hospitalization. Cumulative data from all of the ICU admissions were analyzed. During the baseline period, 45 of the 800 patients were readmitted to the ICU once during their hospitalization and 6 were readmitted twice. During the treatment period, 35 of the 800 patients were readmitted to the ICU once, 4 were readmitted twice, 1 was readmitted three times, and 2 were readmitted four times to the ICU during their hospitalization.

The parameters were assessed for normality. For univariate analyses, continuous variables were compared using the Mann-Whitney rank-sum test (all comparisons were nonparametric) with the values expressed as a median and interquartile range (IQR), whereas categorical variables were compared using a χ^2 test. A p value of < 0.05 was considered statistically significant. All analyses were two tailed and performed using statistical software (Version 7.4.4.0; MedCalc Software; Mariakerke, Belgium). The Stamford Hospital Institutional Review Board approved this study.

Results

Demographic and clinical characteristics of the baseline and treatment populations have been described previously.[19] The two groups were well matched overall in regards to age, gender, race, distribution of admitting diagnoses, prevalence of diabetes and APACHE II scores. Table 1 lists the major diagnostic categories of the patients. The percentage of patients undergoing mechanical ventilation at any time during their ICU stay was 40.6% during the baseline period and 33.6% during the treatment period. The percentage of patients who required mechanical ventilation at the onset of their

Table 1—*Diagnostic Categories of Patients**

Services	Baseline	Treatment
Medical	502	525
Cardiac	169	175
Respiratory	115	125
GI	63	64
Septic shock	43	45
Other	112	116
Surgical service	298	275

*Data are presented as No.

ICU stay was 36.5% and 28.8% for baseline and treatment periods, respectively. Table 2 reports the age and APACHE II scores of patients requiring mechanical ventilation and those not requiring mechanical ventilation during the two periods.

ICU Days and LOS

The number of ICU days can be calculated two ways: by calendar day and by actual number of hours in the ICU (reported in 0.1-day increments in the database). Table 3 delineates ICU days using the two methodologies. ICU LOS, measured by actual number of hours in the ICU, decreased from median of 2.0 days (IQR, 1.0 to 4.3) during the baseline period to 1.7 days (IQR, 0.9 to 3.5 days) during the treatment period ($p = 0.005$). LOS decreased from a median of 1.5 days (IQR, 0.8 to 2.5) to 1.3 days (IQR, 0.8 to 2.3) days among patients not requiring ventilation ($p = 0.138$) and from a median of 4.2 days (IQR, 1.6 to 9.6) to 3.4 days (IQR, 1.6 to 9.2) among patients requiring ventilation ($p = 0.222$).

Post-ICU Days and Duration of Hospitalization After ICU Discharge

There were 712 ICU survivors during the baseline period and 731 ICU survivors during the treatment period. Table 4 reports the number of hospital days before discharge for the two groups and the median duration of their post-ICU hospitalization. All non-ICU days following the last discharge from the ICU are included. The "Materials and Methods" section details the number of patients requiring readmission to the ICU after initial discharge.

Table 2—*Age and APACHE II Scores of the Patients Grouped by Ventilation Status**

Variables	Baseline	Treatment	p Value†
Age			
No ventilation at ICU admission	68 (51–79)	65 (50–77)	0.217
Ventilation at ICU admission	72 (56–82)	73 (56–81)	0.981
APACHE II			
No ventilation at ICU admission	12 (8–17)	12 (8–18)	0.739
Ventilation at ICU admission	23 (16–29)	22 (16–29)	0.511

*Data are presented as median (IQR).
†Mann-Whitney rank-sum test.

Table 3—*ICU Days*

Variables	Baseline	Treatment	Reduction, %
Calendar days (range)	4,171 (1–47)	3,586 (1–60)	13.9
No. of hours	79,351	65,688	17.2

Ventilator Days and Duration of Ventilation

The number of days of mechanical ventilation can be calculated two ways: by calendar day and by actual number of hours of mechanical ventilation. All episodes of mechanical ventilation during each hospitalization are included in this analysis. The total number of calendar days and hours of mechanical ventilation were 2,135 (range, 1 to 36 days) and 41,690 during the baseline period and 1,427 (range, 1 to 57 days) and 27,389 during the treatment period, representing relative reductions of 33.2% and 34.3%. Duration of mechanical ventilation per patient decreased from median of 2.0 days (IQR, 0.7 to 7.1) during the baseline period to 1.7 days (IQR, 0.6 to 5.3) during the treatment period ($p = 0.045$).

Resource Utilization

Table 5 reports the median resource (laboratory, pharmacy, and diagnostic imaging) costs per patient during the two periods, stratified by ventilation status. These inflation-adjusted data are derived from the captured charge data, with appropriate application of the Medicare cost:charge ratios for each category of charge and each FY. There was a nonsignificant decrease in resource costs among nonventilated patients in the treatment period and a large decrease in resource costs among the ventilated patients, driven by significant decreases in imaging and laboratory costs.

Table 4—*Duration of Hospitalization After ICU Discharge*

Variables	Baseline	Treatment	p Value*
Floor days before discharge (range), No.	5,366 (1–124)	5,185 (1–119)	
Days†	5 (3–9)	4 (2–8)	0.054

*Mann-Whitney rank-sum test.
†Data are expresses as median (IQR).

Table 5—*Resource Costs per Patient Based on Ventilation Status at the Onset of ICU Stay**

Variables	Baseline	Treatment	p Value†
Laboratory			
Total	1,091 (512–2,269)	795 (397–1,719)	< 0.001
No ventilation	725 (364–1,290)	573 (286–962)	0.004
Ventilation	2,032 (1,286–4,300)	1,693 (1,008–3,052)	0.012
Pharmacy			
Total	475 (165–1,361)	405 (164–1,037)	0.099
No ventilation	309 (131–781)	348 (125–711)	NS
Ventilation	1,020 (367–2,489)	808 (297–2,199)	NS
Imaging			
Total	1,062 (354–2316)	848 (308–1,822)	0.003
No ventilation	657 (208–1,769)	597 (226–1,533)	NS
Ventilation	1,707 (773–3,360)	1,348 (557–2,400)	0.004
Total			
Total	2,832 (1,296–5,757)	2,145 (1,142–4,577)	< 0.001
No ventilation	1,715 (939–3,369)	1,560 (938–2,809)	NS
Ventilation	5,483 (3,110–11,326)	4,661 (2,339–9,499)	0.029

*Data are presented as median (IQR) values US$. NS = not significant.
†Mann-Whitney rank-sum test.

Costs Associated With the Glucose Management Protocol

The cost of promulgating the glucose management protocol includes personnel costs, insulin acquisition costs, and the cost of any related disposable supplies. The number of nursing hours decreased from 49,105 during the baseline period to 46,867 in the treatment period. The Medicare cost report was used to assign a weighted average for daily variable unit costs, including salaries, but before allocation for "fixed" expenses of $866.47 during the baseline period and $864.37 during the treatment period. These latter figures were used in the calculations summarized in Table 6. Insulin is not a charge item in our ICU; therefore, the exact cost of insulin administered to the patients cannot be determined. The yearly acquisition cost for regular insulin ranges between $5,000 and $7,000 for the entire hospital. An estimate of $1,000 during the baseline period and $2,500 during the treatment period is used in the calculations of total cost. The exact cost of additional disposable supplies related to glucose management, such as IV tubing, cannot be determined from the ICU database. A liberal estimate of $25,000 during the baseline period and $50,000 during the treatment period is assumed. There were three monitors (Accu-Chek; Roche Diagnostics; Indianapolis, IN) used in the ICU during both periods.

Summary of Cost Savings

The total cost of care during the two periods is compared in Table 6 by combining the following components: duration of ICU admission, duration of hospitalization after the last ICU discharge, duration of mechanical ventilation, and resource utilization costs. The number of ventilator days is adjusted to account for the difference in frequency of mechanical ventilation use at the beginning of ICU admis-

Table 6—*Components of the Total Cost of Care in US$**

Variables	Baseline	Treatment	Cost Savings Unadjusted	Cost Savings Adjusted†
ICU days	3,618,700	3,105,400	513,300	348,400
Ventilator days	1,612,000	1,070,300	541,700	328,600
Post-ICU days	2,163,600	2,097,200	66,400	66,400
Imaging	1,392,700	1,100,600	292,100	259,700
Pharmacy	1,025,700	905,600	120,100	43,900
Laboratory	1,586,700	1,250,300	341,400	243,800
Insulin and supplies	26,000	52,500	(26,500)	(26,500)
Total	11,425,400	9,581,900	1,848,500	1,264,300
Savings per patient			2,311	1,580

*Based on the assumptions that the unit cost of 1 ICU day is $866.47 (baseline) and $864.37 (treatment); the unit cost of 1 non-ICU day is $403; the unit cost of 1 ventilator day is $750. ‡Data in parentheses represent costs (a loss, not a savings).
†ICU days, ventilator days, and resource costs adjusted for the difference in the prevalence of ventilation at the onset of each period.

sion during the two periods. The annualized adjusted total cost savings amounted to $1,339,500. The mean adjusted cost savings per patient was $1,580. Table 7 analyzes these components for each diagnostic category. There were substantial savings demonstrated among the surgical, cardiac, and GI groups, and smaller net deficits among the septic shock, miscellaneous medical, and respiratory patients.

Discussion

Close monitoring and intensive treatment of hyperglycemia has become an emerging standard of care among critically ill patients in the last several years. Observational studies[16,17] among a large cohort of cardiovascular surgery patients have demonstrated substantial decreases in wound infection rates and hospital mortality when patients are treated with continuous IV insulin with the goal of achieving euglycemia. Findings from a study by Van den Berghe et al,[18] performed in 1,548 surgical ICUs patients requiring mechanical ventilation, most of whom had undergone cardiac surgery, provided evidence from a prospective, randomized controlled trial that tight glycemic control yielded impressive reductions in mortality and multiple morbidity. The decreases in the rates of blood stream infections, prolonged antibiotic use, renal replacement therapy, prolonged mechanical ventilation, and prolonged ICU stay likely translated into substantial cost savings to the institution. Most recently, a before-and-after trial[19] of intensive glucose monitoring and management in 1,600 consecutive patients admitted to the mixed medical-surgical-cardiac ICU of a university-affiliated community hospital reported a 29.3% reduction in hospital mortality in the treated patients, as well as a decrease in the development of new renal insufficiency, the need for RBC transfusions, and a decrease in the ICU LOS. This report analyzes the major components of the cost of care for these 1,600 patients. To our knowledge, there has been no other economic analysis of the consequences of tight glycemic control in a critically ill population.

The main strength of this article is the comprehensive nature of the data reported, allowing the capture of all the major components of the cost of care. This is attributable to the robust and powerful nature of the ICU database, created in 1998 and now including detailed information regarding $> 6,500$ consecutive admissions to the unit. The database measures LOS and ventilator duration in 0.1-day increments, avoiding the inaccuracies inherent in calendar-day measurements. APACHE II scoring is performed by the director of critical care or his associate, ensuring accuracy and consistency. The data reported include information from any readmissions to the ICU that may have occurred during the hospitalization. Laboratory, pharmacy, and imaging charges are complete due to the linkages between the ICU database and the central billing database. Charge data are converted to costs using inflation adjustments and the appropriate cost:charge ratios generated by the Medicare cost reports for each FY.

There are some limitations to the analysis that must be explored. The study has a "before-and-after," not randomized, controlled prospective design. However, the 800 patients in the baseline group were well matched to the 800 patients in the treatment group, with no significant differences in age, gender, distribution of admitting diagnoses or severity of illness, as reflected by the APACHE II score. The number of patients requiring mechanical ventilation at the onset of ICU admission was slightly higher among the patients in the baseline group than among the patients in the treatment group; the cost analysis adjusted all the components of care for this difference. Finally, the resource utilization costs were derived by the indirect methods described above. Though this is standard methodology, it does not yield an exact measure of cost, only the best estimate.

The savings associated with the intensive glucose management program were not shared equally among the different groups of patients. The largest net savings occurred among surgical, cardiac, and GI patients. The largest net deficit occurred among the small group of patients (43 in the baseline group and 45 in the treatment group) with septic shock. Notably, however, the mortality rate among this group of the most severely ill patients was 60.5% among the baseline patients and 33.3% among the treatment patients ($p = 0.020$).[19] Perhaps the higher costs among the septic patients in the treatment group occurred because a subset of new "expensive" survivors was created. The data and study design do not allow this hypothesis to be tested explicitly.

The quantity of savings associated with this intervention, $1,580 per patient, may understate the actual savings. The categories of resource utilization measured in this study—laboratory, pharmacy, and radiology—do not encompass all ICU costs. Indeed, a recent review[21] of data from 253 hospitals that included 51,009 patients quantified the cost of intensive care admission using a large administrative database. The authors estimated the total cost of the first day of ICU admission as $10,794 for patients requiring mechanical ventilation and $6,667 for those patients not requiring mechanical ventilation.[21] The corresponding costs for day 2 were $4,796 and $3,496, and for all subsequent days were

Table 7—*Components of the Total Cost of Care in US$, Grouped by Diagnostic Category**

Variables	Baseline	Treatment	Cost Savings Unadjusted	Cost Savings Adjusted†
Medical service				
Cardiac, No.	169	175		
ICU days	597,300	539,400	57,900	38,800
Ventilator days	228,000	167,300	60,800	35,200
Post-ICU days	328,800	274,000	54,800	54,800
Imaging	276,300	221,000	55,300	50,800
Pharmacy	186,300	141,300	45,000	39,000
Laboratory	268,800	210,300	58,500	43,400
Total	1,885,500	1,555,300	332,200	262,000
Net per patient			1,931	1,523
Respiratory, No.	115	125		
ICU days	742,100	718,300	23,800	(30,100)
Ventilator days	463,000	411,700	51,200	(23,700)
Post-ICU days	482,000	417,900	64,100	64,100
Imaging	229,100	217,600	11,500	(900)
Pharmacy	191,100	197,700	(6,600)	(34,800)
Laboratory	342,800	334,000	8,800	(13,700)
Total	2,450,100	2,297,200	152,800	(39,100)
Net per patient			1,273	(326)
GI	63	64		
ICU days	269,500	204,800	64,700	40,800
Ventilator days	110,300	37,500	72,800	49,900
Post-ICU days	124,900	116,100	8,800	8,800
Imaging	105,300	81,400	23,900	11,500
Pharmacy	69,800	56,700	13,100	800
Laboratory	126,000	94,300	31,700	14,400
Total	805,800	590,800	215,000	126,200
Net per patient			3,386	1,987
Septic shock	43	45		
ICU days	219,200	243,800	(24,500)	(57,400)
Ventilator days	135,800	92,300	43,500	500
Post-ICU days	97,900	228,900	(131,000)	(131,000)
Imaging	105,200	89,600	15,600	21,700
Pharmacy	140,000	85,600	54,400	44,700
Laboratory	129,100	120,800	8,300	(5,100)
Total	827,200	861,000	(33,700)	(126,600)
Net per patient			(780)	(2,890)
Other medical, No.	112	116		
ICU days	382,100	409,700	(27,600)	(43,900)
Ventilator days	186,600	97,500	89,100	63,200
Post-ICU days	251,100	419,100	(168,000)	(168,000)
Imaging	180,200	187,700	(7,500)	(7,600)
Pharmacy	92,000	86,600	5,400	(700)
Laboratory	159,800	153,400	6,400	(1,900)
Total	1,251,800	1,354,000	(102,200)	(158,900)
Net per patient			(896)	(1,394)
Surgical service	298	275		
ICU days	1,410,500	983,700	426,800	408,300
Ventilator days	488,300	264,000	224,300	203,500
Post-ICU days	878,900	641,200	237,700	237,700
Imaging	496,600	303,300	193,300	184,200
Pharmacy	346,500	337,700	8,800	(5,100)
Laboratory	560,200	337,500	227,700	206,700
Total	4,181,000	2,867,400	1,318,600	1,235,300
Net per patient			4,602	4,312

*Based on the assumption that the unit cost of 1 ICU day (′indirect cost) is $866.47 during the baseline period and $864.37 during the treatment period; the unit cost of 1 non-ICU day is $403; and the unit cost of 1 ventilator day is $750 (both periods). Data in parentheses represent costs (a loss, not a savings).

†ICU days, ventilator days, and resource costs adjusted for the difference in the prevalence of ventilation at the onset of each period.

$3,968 and $3,184, respectively. Using the assumptions detailed in Table 6, the mean daily cost of the components of care measured in this study was $2,708 for the 1,600 patients.

In summary, this study reports the cost implications of an intervention, intensive glycemic control in critically ill adult patients, that has substantial beneficial effects on patient morbidity and mortality. The substantial annualized savings that accrued to the institution, conservatively estimated at $1,339,500, or $1,580 per patient, were due to decreases in all major categories of resource utilization. Extension of these findings to large numbers of ICUs could have a major impact on national health-care expenditures. These findings provide further impetus for the emergence of tight glycemic control as a standard of care among the critically ill.

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