DEVELOPMENT OF A HEMODYNAMIC DATABASE IN SEVERE TRAUMA PATIENTS TO DEFINE OPTIMAL GOALS AND PREDICT OUTCOME.

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We have developed a large database of invasive and noninvasive hemodynamic monitoring of acutely ill trauma and surgical patients, beginning in the emergency room (ER): a) to describe early survivor and nonsurvivor patterns of emergency patients in terms of cardiac, pulmonary, and tissue perfusion deficiencies; b) to measure quantitatively the net cumulative amount of deficit or excess of the monitored functions that correlate with survival or death; and c) to use discriminant analysis to predict outcome and evaluate the biological significance of monitored deficits.

METHODS
Development of Databases
Databases for acute injury patients (N=316), elective high risk surgery, noninvasively monitored patients (N=374), invasively monitored patients (N=809), septic shock patients (N=378), and hemorrhage only patients (N= 87) have been developed to describe the primary injuries or illnesses, the hemodynamic patterns by invasive and noninvasive methods and their outcomes, including survival/nonsurvival, organ failure, and other complications. Noninvasive monitoring was begun in the ER and followed to the OR, radiology department and ICU; invasive pulmonary artery catheterization (PAC) was instituted when clinically indicated in ICU patients. The time and place of monitoring was related to the time elapsed after ER admission, the time of operations, the times of ICU admission and discharge, and the time of hospital discharge or death [1-4].

Each therapeutic intervention was designated by time, dose, duration of infusion, and related to the time after admission. Each therapy was given one-at-a-time (except for clinical exigencies) with hemodynamic monitoring before, during and after its administration. The noninvasive database has >8000 time lines for 54 columns describing the clinical and hemodynamic patterns of 28 clinical subsets with specified co-morbid conditions, 18 hemodynamic variables, and >2500 therapeutic interventions with values obtained before, during, and after each therapy. The sequential patterns of survivors and nonsurvivors were described in time elapsed from ER admission. We use, as weighting criteria, the p values of differences in the temporal patterns of survivors' and nonsurvivors' values in each subset, for example, for subsets of patients with and without head injuries, blunt vs. penetrating trauma, truncal and nontruncal trauma, age stratifications, prior cardiac, respiratory, hepatic, and renal dysfunction or organ failure, etc. Finally, the hemodynamic responses to standardized test doses of whole blood or packed red cell transfusions given over 1-hour provided quantitative measures of each patient's cardiac reserve capacity, expressed as changes in cardiac index relative to corresponding change in PA occlusion (wedge) pressure or central venous pressure
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Noninvasive Hemodynamic Monitoring Systems
The monitoring systems were an improved noninvasive thoracic electric bioimpedance cardiac output device, a pulse oximeter, a noninvasive blood pressure device, and transcutaneous O_2 and CO_2 sensors to reflect tissue perfusion/oxygenation. These continuously monitored noninvasive measurements were used to prospectively evaluate circulatory patterns in 151 consecutively monitored severely injured patients beginning with admission to the ER.

RESULTS
Therapeutic Goals
Specific goals of therapy, based on empirical findings of survivors, were: cardiac index > 4.5 L/min/m2; systolic blood pressure > 120 mmHg; pulse oximetry > 96%; transcutaneous oxygen $PtcO_2$/FiO_2 ratio >200; heart rate < 100 beats/min. Survivors had increased hemodynamic and oxygen

transport values. Table I compares the mean ($\pm$ SEM) of all noninvasive hemodynamic values of survivors and nonsurvivors of trauma patients during the initial resuscitation period, suggesting that these responses compensated for prior inadequacies of tissue perfusion and oxygenation (1-4).

Table 1. Noninvasive Hemodynamic Values for Survivors and Nonsurvivors in Initial Resuscitation

Variable, unit	Optimal Value	Survivors (N=103) Mean $\pm$ SEM	Nonsurvivors (N=48) Mean $\pm$ SEM	P value
CI, L/min/m^2	4.0	4.14 $\pm$ 0.02	3.87 $\pm$ 0.03	0.001
MAP, mmHg	85	88 $\pm$ 0.37	80 $\pm$ 0.69	0.066
SapO$_2$, %	98	99 $\pm$ 0.05	96 $\pm$ 0.26	0.001
PtcO$_2$/FiO$_2$, torr	200	206 $\pm$ 2.9	93 $\pm$ 2.6	0.001

CI cardiac index, MAP mean arterial pressure, SapO$_2$ arterial hemoglobin saturation by pulse oximetry, PtcO$_2$/FiO$_2$ transcutaneous oxygen tension indexed to FiO$_2$

Quantitative Assessment of Noninvasive Variables as Net Cumulative Amount of Excess or Deficit

The total overall deficit or excess of each noninvasively monitored variable was evaluated by comparing its normal or optimal value with its temporal pattern during the observation period. This was done by mathematically integrating over time the area between the continuous display of each fluctuating variable and either normal or optimal values. The net cumulative deficits or excesses were calculated for each individual patient and for both survivor and nonsurvivor groups as time-integrated areas between the curve produced by continuously monitored variables and their normal or reference values. Table 2 compares the mean net cumulative deficits or excesses of hemodynamic values during the initial period of resuscitation of severely traumatized patients.

Table 2. Mean Net Cumulative Deficits or Excesses of Monitored Values of Survivors and Nonsurvivors in the Initial Period of Resuscitation

Variable	SURVIVORS (N=103)		NONSURVIVORS (N=48)		P-Value
	Mean	SEM	Mean	SEM	
CI, L/m^2	+81	52	-232	138	0.007
MAP, mmHg.h	-10	13	-57	24	0.078
SapO$_2$, %.h	-1	0.3	-8	2.6	0.006
PtcO$_2$/FiO$_2$, torr.h	+313	87	-793	175	0.001

CI cardiac index, MAP mean arterial pressure, SapO$_2$ hemoglobin saturation by pulse oximetry, PtcO$_2$/FiO$_2$ transcutaneous arterial tension indexed to FiO$_2$,

Outcome Prediction by Discriminant Analysis

The time-integrated data were sufficiently robust to be analyzed by discriminant function. The following variables were selected by stepwise discriminant analysis (PROC STEPDISC): a) cumulative PtcO$_2$/FiO$_2$, b) Glasgow coma score, c) cumulative SapO$_2$ values and d) cumulative cardiac index. The discriminant function, Z, was derived for an individual patient: Z = 0.0011a + 0.3300b + 0.0656c + 0.0423d; where ")a to)d are defined above. Classification of the survivors was: Z>2.36.

Table 3 shows the stepwise discriminant analysis; 95 percent of the survivors and 62% of the nonsurvivors were correctly classified in the early period after the initial resuscitation (Table 4). There were 23/151 (15.2%) misclassifications at this time. Cross-validation studies by the jackknife method were performed. There were 14/76 (18.4%) misclassifications in the cross-validation study, compared with 23/151 (15.2%) of the series as a whole, which was reasonably satisfactory.

Table 3. Stepwise Discriminant Analysis

Step Entered	Partial R^2	Prob>F	Cumulative R^2 *
1. Cumulative $PtcO_2/FiO_2$	0.210	.0001	0.2099
2. GCS	0.188	.0001	0.3581
3. Cumulative $SapO_2$	0.053	.0047	0.3921
4. Cumulative CI	0.031	.0336	0.4107

Classification of survivors, Z>2.36; where Z = 0.0011 (Cumulative $PtcO_2/FiO_2$) + 0.3300 (GCS) + 0.0656 (Cumulative $SapO_2$) + 0.0423 (Cumulative CI) * Pillai's trace/(# groups -1)

Table 4. Classification Summary for the Series (N=151)

	Predicted to Die		**Predicted to Live**		**Total**	
Actual Outcome	N	(Row%)	N	(Row%)	N	(Col%)
Died	30	62.5%	18	37.5%	48	31.8%
Lived	5	4.9%	98	95.1%	103	68.2%
Total (%)	35	23.2%	116	76.8%	151	100.0%

Misclassification: 23/151=15.2%

CONCLUSIONS

 Noninvasive monitoring systems provided continuous on-line displays of data in the early post admission period from the ER to the OR, and to the ICU for early recognition of circulatory dysfunction in acute emergency conditions. Survival was predicted by discriminant analysis models based on quantitative assessment of the net cumulative deficits of cardiac index, arterial hypoxemia, and tissue perfusion. These deficits were significantly greater in the nonsurvivors.

The data are consistent with the physiologic concept that the initial hemodynamic findings were low flow or unevenly distributed microcirculatory flow with poor tissue perfusion/oxygenation. These are initially precipitated by hypoxemia, hypovolemia, acidosis, and the adrenomedullary stress response. The poorly perfused, acidotic capillary endothelial wall activates macrophages, stimulates systemic immune response syndrome (SIRS), and produces reactive oxygen substances (ROS), that may contribute to the development of ARDS and other organ failures.

Our approach is that early identification of the initiating hemodynamic mechanisms allows their correction with concomitant reversal of shock, and with improved outcome. We now propose to supplement discriminant analysis with a stochastic control program, which is a more powerful research tool applicable to more extensive use of monitored variables in a wider variety of acutely ill patients. The stochastic control program provides objective, quantitative information on likelihoods of survival or death before, during, and after each therapeutic modality.

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