Prospective Trial of Supranormal Values of Survivors as Therapeutic Goals in High-Risk Surgical Patients*

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Survivors of high-risk surgical operations were previously observed to have significantly higher mean CI, $\dot{D}O_2$, and $\dot{V}o_2$ than nonsurvivors. The hypothesis was proposed that increased CI and $\dot{D}O_2$ are circulatory compensations for increased postoperative metabolism. We tested this hypothesis in two series. In series 1, prospectively allocated by services, mortality and morbidity of the control group were significantly greater than those of the protocol group. In series 2, patients who fulfilled previously defined high-risk criteria were preoperatively randomized to one of three monitoring/treatment groups: CVP-control group, PA-control group and PA-protocol group. Postoperative mortalities in the CVP-control and PA-control groups were not statistically significantly different, but PA-protocol group mortality was significantly reduced compared with its control group. The PA-protocol group had reduced complications, duration of hospitalization, duration in ICU, and mechanical ventilation, and reduced costs when the PA catheter was placed preoperatively and used to augment circulatory responses. ***(Chest 1988; 94:1176-86)***

PvO_2 = venous oxygen pressure; NR = not randomized; MAP = mean arterial pressure; WP = wedge pressure; LVSWI = left ventricular stroke work index; RVSWI = right ventricular stroke work index; LCWI = left cardiac work index; RCWI = right cardiac work index; SVRI = systemic vascular resistance index; PVRI = pulmonary vascular resistance index; $\dot{Q}sp/\dot{Q}t$ = pulmonary venous admixture; ANOVA = analysis of variance

The development of the balloon-tipped flow-directed pulmonary artery (PA) catheter by Swan and colleagues[1-3] has led to the widespread application of invasive hemodynamic monitoring in critically ill patients.[4-17] Although criteria for therapy have been tacitly assumed to be normal values, increased hemodynamic and oxygen transport variables observed in survivors[6,7,10-18] raise questions regarding therapeutic goals. Therapeutic goals for cardiac patients whose other vital organs are unimpaired may be different from those of the postoperative general surgical patient whose cardiac function is normal but whose metabolic demands are increased. The problems of the noncardiac general surgical patient may be of interest to the medical consultant and to the internist who inserts PA catheters to monitor these patients.

The critically ill surgical patient provides a unique opportunity to observe the development of one particular type of shock because elective surgical patients may be studied in the preoperative state, during the development of their circulatory crisis, and in the subsequent period where characteristic patterns of recovery or death evolve.[6,10,16-18] Bland et al[10] described the temporal sequence of hemodynamic and oxygen transport patterns in surviving and nonsurviving general surgical patients and from this physiologic database developed an empiric heuristic physiologic algorithm which then was demonstrated to satisfactorily predict outcome prospectively.[11] Therapeutic goals were developed from this predictor and the median values of the survivors.[6,10,16] Predictors based on the survivors' values were shown to have a high degree of accuracy in prospective testing.[11,14-16] Hankeln et al[18] have recently confirmed that the survival and nonsurvival patterns are predictably associated with outcome in a wider clinical mix and with less rigid time constraints.

The present study tests the hypothesis that the physiologic pattern empirically defined by the survivors may be the appropriate therapeutic goals for high-risk critically ill postoperative patients. In two prospective clinical trials, the outcomes of patients whose therapeutic goals were to maintain normal hemodynamic values were compared with those whose goals were to attain the supranormal values empirically observed in critically ill postoperative survivors.[6,10,14] In the first prospective series, patients were allocated by service; in the second prospective series patients

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Table 1—*Criteria for High Risk and Their Distribution to Therapeutic Groups*

Criteria	PA-Control		PA-Protocol		CVP	
	Series 1 (N = 151)	Series 2 (N = 30)	Series 1 (N = 101)	Series 2 (N = 28)	Series 2 (N = 30)	Not Randomized (N = 45)
Previous severe cardiorespiratory illness (acute MI, COPD, stroke, etc)	7	6	4	5	7	14
Extensive ablative surgery planned for carcinoma; *eg*, esophagectomy and total gastrectomy, prolonged surgery (>8 h)	39	4	17	7	6	3
Severe multiple trauma, *eg*, >3 organs or >2 systems, or opening 2 body cavities	29	0	21	1	0	0
Massive acute blood loss (>8 units), BV<1.5 L/m², Hct <20%	6	0	12	1	4	1
Age over 70 years and evidence of limited physiologic reserve of one or more vital organs	36	1	24	5	6	5
Shock, MAP<60 mm Hg, CVP<15 cm H_2O, and UO<20 ml/h	2	1	3	1	0	0
Septicemia, positive blood culture or septic focus, WBC>13,000, spiking fever to 101°F for 48 h, and hemodynamic instability	39	3	31	1	5	1
Respiratory failure, *eg*, PaO_2<60 on FIo_2>0.4, $\dot{Q}sp/\dot{Q}t$>30%, mechanical ventilation needed >48 h	0	2	0	0	4	0
Acute abdominal catastrophe with hemodynamic instability, *eg*, pancreatitis, gangrenous bowel, peritonitis, perforated viscus, GI bleeding	22	13	17	8	16	11
Acute renal failure (BUN>50 mg/dl, creatinine >3 mg/dl)	0	1	0	0	4	0
Late stage vascular disease involving aortic disease	5	6	2	5	2	2

were randomized preoperatively to either central venous or PA catheterizations, as well as to the two different therapeutic strategies. The two series are considered separately as they are directed to different problems.

Materials and Methods

Clinical Series: Entrance Criteria

This study was approved by the hospital's Institutional Review Board and informed consent was obtained from each patient; no proxy consents were used. Entrance criteria for selection of high-risk patients were previously defined as one or more of the high-risk criteria listed in Table 1. Over the past seven years, patients who met one or more of these criteria had been found to have a mortality rate close to 30 percent. Series 1 consisted of 276 operations on 252 high-risk general surgical patients; PA-monitoring in 96 (35 percent) of these was not started until the postoperative period. Patients were stratified into those whose hemodynamic monitoring was started preoperatively and those whose monitoring was started postoperatively. We also compared groups who preoperatively had relatively normal cardiac output values with those who had grossly abnormal preoperative cardiac output values.

In series 2, 146 general surgical patients met one or more of these criteria and were eligible for the study. Of these 146 patients, 55 were operated on without randomization; ten of these went directly to the operating room as emergencies before informed consent could be arranged, and 45 patients were not randomized (NR group) by the choice of the service physicians because they were not considered ill enough to justify invasive monitoring. Three patients were randomized, but subsequently their operations were cancelled. The remaining 88 patients were prospectively allocated to one of the three groups designated by cards arranged according to a random numbers table by an outside person and placed in opaque sealed envelopes. The envelopes were opened in sequence as soon as the patient consented to the study.

During this period of observation, 7 percent of 2,086 patients operated on by the general surgical service were preoperatively identified on clinical grounds as being at high risk. This high-risk group accounted for 82 percent of the general surgical services' mortality.

Experimental Design

In series 1, patients were prospectively allocated to either a protocol or control service. One or two of the three adult general surgical services were prospectively designated as control services and the other one or two services as the protocol service according to a prearranged schedule developed prior to the beginning of each academic year; the protocol service was rotated to each of the three services and the principal investigator was also rotated between protocol and control services. The protocol group used supranormal therapeutic goals and was comprised of patients who were admitted when residents on the protocol services were on duty; the control group was comprised of patients treated by residents on the control services using normal values as goals (Table 2). Previous studies have documented comparable severity of illness and mortality among the three services.[19,20]

In series 1, the diagnoses, operations, age (control), 56 ± 21; protocol, 51 ± 19 [SD] years), gender (control, 61 percent males; protocol, 66 percent males), lowest blood pressure (control, 55 ± 24 mm Hg; protocol, 53 ± 22 mm Hg), time in hypotension (control, 2.2 ± 2.5 h; protocol, 2.4 ± 2.3 h), mean arterial pressures <50 mm Hg (control, 39 percent; protocol, 44 percent), and distribution of high risk factors (Table 1) were comparable between the two groups.

In series 2, patients were preoperatively randomized to one of three catheter/treatment groups: (a) CVP-control group: CVP-catheter placement and perioperative management using the normal

Table 2—*Therapeutic Goals for Groups*

Variable, Units	CVP and NR Groups	PA-Control	PA-Protocol
Similar goals for control and protocol groups			
Blood pressure, mm Hg	>120/80	>120/80	>120/80
CVP, cm saline	>4 and <12	>4 and <12	<15
Hct, %	>35	>35	>34
UO, ml/h	>30	>30	>30
HR, beats per minute	>60 and <120	>60 and <120	>60 and <120
Temperature, F	<102°	<102°	<102°
PaO_2, torr	>70	>70	>70
pH	>7.3 and <7.5	>7.3 and <7.5	>7.3 and <7.5
PvO_2, torr	. . .	>40	>40
PA pressure, mm Hg	. . .	>25/10	>25/10
Pulmonary WP, mm Hg	. . .	4-12	<18
Systemic vascular resistance, dyne•s/cm^5•m^2	. . .	1800-2600	>1450
Pulmonary vascular resistance, dyne•s/cm^5•m^2	. . .	45-250	45-250
Oxygen extraction, %	. . .	22-30	22-30
Major differences in the goals for control and protocol groups			
CI, L/min•m^2	. . .	2.8-3.5	>4.5
$\dot{D}O_2$, ml/min•m^2	. . .	400-550	>600
$\dot{V}o_2$, ml/min•m^2	. . .	120-140	>170

values of standard clinical parameters available by CVP as therapeutic goals, (b) PA-control group: pulmonary artery catheter placement and management using normal values of hemodynamic and oxygen-transport variables available by PA catheter monitoring as the goals of therapy, and (c) PA-protocol group: PA catheter placement using supranormal hemodynamic and oxygen-transport values as the goals of therapy (Table 2).

The monitoring team assisted the primary service in placing the

Table 3—*Comparison of Hemodynamic and Oxygen Transport Values in Control and Protocol Patients of Series 1**

	Preoperative Period		Postoperative Period (0-4 days)	
	Control	Protocol	Control	Protocol
Patients with normal preoperative values	(56 Data Sets)	(33 Data Sets)	(332 Data Sets)	(499 Data Sets)
Heart rate (beats per minute)	90 ± 19	90 ± 21	108 ± 18†	106 ± 20†
MAP (mm Hg)	98 ± 18	101 ± 18	92 ± 21‡	95 ± 18
Mean PA pressure (mm Hg)	18.3 ± 7.9	17 ± 9.6	24.4 ± 7.7†	21.1 ± 8.1†
CVP (mm Hg)	6 ± 4.7	6.3 ± 5.3	10.5 ± 6†	8.8 ± 5.2†
Pulmonary artery WP (mm Hg)	9.4 ± 5.6	8.9 ± 7.2	12.7 ± 5.7†	12.0 ± 6.5†
CI (L/min•m^2)	3.22 ± .75	3.29 ± .84	3.52 ± .98‡	3.79 ± 1.0†
Systemic vascular resistance (dynes•sec/cm^5•m^2)	2,409 ± 783	2,604 ± 633	1,999 ± 781†	1,946 ± 668†
PaO_2 (torr)	112 ± 58	101 ± 56	113 ± 49	121 ± 52‡
Arterial pH	7.42 ± .06	7.43 ± .05	7.43 ± .06	7.44 ± .07
Hct (%)	34.8 ± 4.4	33.9 ± 5.0	32.1 ± 5.2‡	33.3 ± 5.0
$\dot{D}O_2$ (ml/min•m^2)	473 ± 112	477 ± 124	495 ± 138	561 ± 148†
$\dot{V}o_2$ (ml/min•m^2)	126 ± 30	127 ± 39	139 ± 36‡	148 ± 41†
Data for the entire series	(92 data sets)	(73 data sets)	(593 data sets)	(836 data sets)
Heart rate (beats per minute)	96 ± 23	92 ± 20	110 ± 19†	108 ± 20†
MAP (mm Hg)	96 ± 18	101 ± 18	91 ± 20‡	92 ± 19†
Mean PA pressure (mm Hg)	8.3 ± 7.9	17.3 ± 8.5	22.4 ± 7.9†	21.7 ± 7.8†
Central venous pressure (mm Hg)	7.4 ± 6.1	7.1 ± 5.9	10.7 ± 6.2†	9.8 ± 6.1†
PA WP (mm Hg)	9.8 ± 6.2	9.7 ± 6.8	12.9 ± 5.9†	12.5 ± 6.5†
CI (L/min•m^2)	3.6 ± 1.1	3.85 ± 1.24	3.65 ± 1.13	4.45 ± 1.51†
Systemic vascular resistance (dynes•sec/cm^5•m^2)	2,194 ± 1,042	2,132 ± 839	1,964 ± 969‡	1,761 ± 747†
PaO_2 (torr)	114 ± 63	100 ± 49	108 ± 48	115 ± 56‡
Arterial pH	7.42 ± .08	7.43 ± .05	7.43 ± .07	7.44 ± .08
Hct (%)	34.1 ± 4.8	32.7 ± 5.6	31.5 ± 5.3‡	32.6 ± 4.9
$\dot{D}o_2$ (ml/min•m^2)	527 ± 159	542 ± 164	508 ± 166	598 ± 217
$\dot{V}o_2$ (ml/min•m^2)	138 ± 37	141 ± 52	135 ± 46	148 ± 38

*Values are mean ± SD.

†$p<0.01$ between preoperative baseline values and their postoperative values by Student's t test for paired distributions.

‡$p<0.05$ between preoperative baseline values and their postoperative values by Student's t test for paired distributions.

catheters and in obtaining the measurements, but they had no direct clinical responsibility for patient management in any of the groups.

Physiologic Methods

Flow-directed, balloon-tipped PA catheters were placed percutaneously in study patients via an internal jugular or subclavian vein, and radial arterial catheters were put in place in the ICU before preoperative medication. Pulmonary arterial pressures, HR, MAP, CVP, and pulmonary capillary WP were measured. Cardiac output then was measured by thermodilution using a cardiac output computer (Model 9520, American Edwards Laboratories, Santa Ana, CA). Immediately after cardiac output was measured, arterial and mixed venous blood were sampled; pH, blood gas tensions, hemoglobin, hemoglobin saturation, and hematocrit were promptly measured. The LVSWI, SVRI, and PVRI, $\dot{Q}sp/\dot{Q}t$, $\dot{D}o_2$ defined as the product of CI and arterial oxygen content, ($\dot{V}o_2$), and oxygen extraction were calculated using standard formulas.[1-7] All flow and volume measurements were indexed to body surface area.

The measurements of each data set were taken within a 1- to 2-min period in order to calculate a complete set of oxygen transport and other derived variables for each of the various time intervals; 2,186 sets of data were obtained in 252 patients of the first series and 984 sets in the second series. Altogether over 100,000 measured and derived values were analyzed in the present study.

Definition of Therapeutic Goals and Strategies

Therapeutic goals in the control groups were normal values for those variables obtained from established normative standards and in current use in our institution. The relative priorities of the various physiologic variables measured in the CVP and PA-control groups were those of the current standard of care taught and practiced in the surgical department of our institution. In general, the maintenance of normal arterial and venous pressures as well as other hemodynamic variables were given priority.

In the PA-protocol group, by contrast, the therapeutic goals were supranormal values for cardiac output (>4.5 L/min•m²), $\dot{D}O_2$ (>600 ml/min•m²), and $\dot{V}o_2$ (>170 ml/min•m²), previously defined empirically from the median values of patients surviving critical surgical illnesses[6,10,14] (Table 2). Cardiac output and oxygen transport goals were given priority in the continuing management of these patients.

Therapy in both groups consisted of fluids including packed red blood cells, crystalloids and various colloids, inotropic agents—principally dobutamine, vasodilators including nitroprusside and nitroglycerine, and vasopressors such as dopamine and norepinephrine. The only difference in the therapy between the control and protocol groups was in the goals to which therapy was aimed.

Patients who preoperatively had abnormally high CI values (>5 L/min•m²) from associated severe sepsis and late stage cirrhosis were considered separately as they already were compensating in the preoperative state and had achieved spontaneously the therapeutic goals defined for the protocol patients.

Statistical Methods

Comparisons of mortality and morbidity figures were done using

Table 4—*Comparison of Preoperative and Postoperative Hemodynamic and Oxygen-Transport Values in Control and Protocol Groups of Series 2**

Variable	Preoperative Control Period		Postoperative Period		p Value
	Control	Protocol	Control	Protocol	
Patients with normal preoperative values					
Heart rate, beats per minute	89 ± 19	84 ± 13	100 ± 22	102 ± 19	
MAP, mm Hg	96 ± 19	95 ± 15	87 ± 24	90 ± 17	
CVP, mm Hg	5.9 ± 4.5	7.0 ± 3.5	9.2 ± 4.1	7.7 ± 4.5	
Mean PA pressure, mm Hg	20 ± 7.2	16.7 ± 7.6	20.8 ± 5.4	19.6 ± 7.7	
PA WP, mm Hg	9.8 ± 5.7	8.9 ± 4.3	12.3 ± 4.5	10.8 ± 6.1	
CI, L/min•m²	3.52 ± .81	3.62 ± .69	3.6 ± 1.12	4.25 ± 1.25†	<0.01‡
Systemic vascular resistance, dynes•sec/cm⁵•m²	2,329 ± 793	2,011 ± 651	1,819 ± 692	1,668 ± 654	
PaO_2, torr	139 ± 107	159 ± 109	148 ± 64	161 ± 82	
Arterial pH	7.41 ± .04	7.44 ± .07	7.42 ± .07	7.42 ± .07	
Hct, %	35.1 ± 3.8	36.6 ± 4.2	34.1 ± 3.5	33.5 ± 4.1	
$\dot{D}O_2$, ml/min•m²	541 ± 130	583 ± 90	561 ± 190	663 ± 232†	<0.01‡
$\dot{V}o_2$, ml/min•m²	121 ± 31	112 ± 24	118 ± 43	136 ± 44†	<0.01‡
Patients with hyperdynamic preoperative values					
Heart rate, beats per minute	102 ± 22	97 ± 28	101 ± 16	107 ± 26	
MAP, mm Hg	90 ± 14	98 ± 15	89 ± 10	99 ± 12	
CVP, mm Hg	9.3 ± 4.4	9.0 ± 4.4	11.7 ± 4.7	5.7 ± 4.1	
Mean PA pressure, mm Hg	17.3 ± 6.2	13.3 ± 2.3	21.9 ± 5.4	14.6 ± 4.2	
PA WP, mm Hg	10.7 ± 4.9	9.0 ± 1.7	12.4 ± 4.1	7.9 ± 3.4	
CI, L/min•m²	6.21 ± .59	5.37 ± .42	6.59 ± 1.57	5.83 ± .95	
Systemic vascular resistance, dynes•sec/cm⁵•m²	1,051 ± 221	1,311 ± 179	1,003 ± 301	1,308 ± 249	
PaO_2, torr	103 ± 60	88 ± 9	96 ± 31	116 ± 29	
Arterial pH	7.41 ± .10	7.46 ± .05	7.45 ± .04	7.45 ± .04	
Hct, %	28.1 ± 3.4	28 ± 3.5	31.9 ± 2.6	33 ± 4.7	
$\dot{D}o_2$, ml/min•m²	771 ± 121	661 ± 118	962 ± 240	875 ± 196	
$\dot{V}o_2$, ml/min•m²	147 ± 23	156 ± 43	149 ± 40	158 ± 38	

*Values are mean ± SD.

†$p<0.05$ between the postoperative values in the protocol group and the postoperative values of the control group by Student's *t* test for unpaired distributions.

‡$p<0.01$ between preoperative baseline and postoperative values in the PA-protocol group by Student's *t* test for paired distributions.

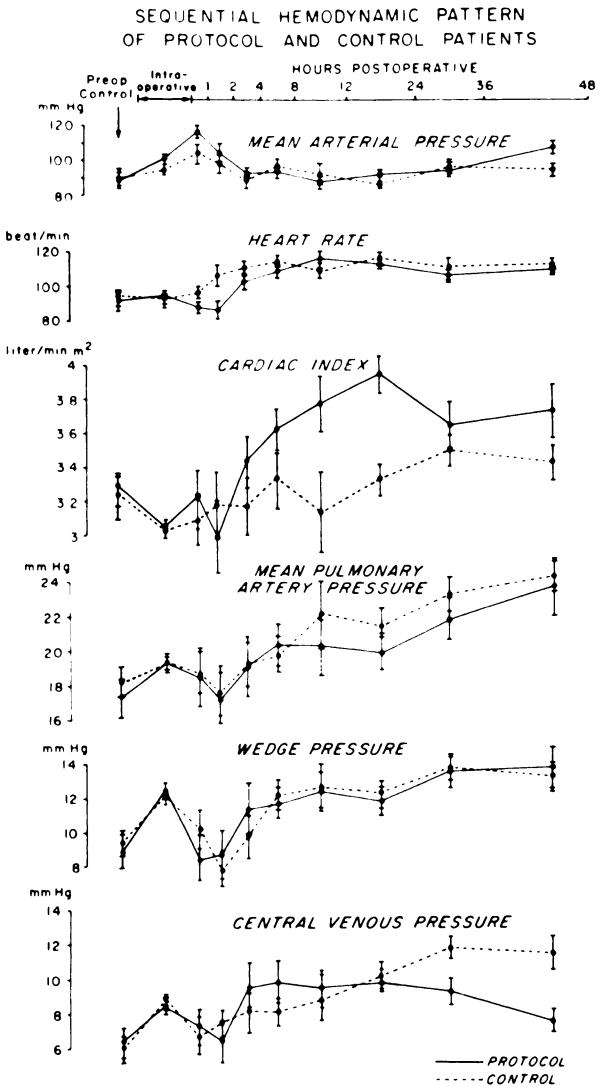

FIGURE 1. Sequential hemodynamic patterns of control and protocol patients in the preoperative, intraoperative and postoperative periods. *Dots* represent the mean values and *vertical lines*, the SEM. Note the appreciable increase in CI of the protocol patients beginning about 4 h postoperatively.

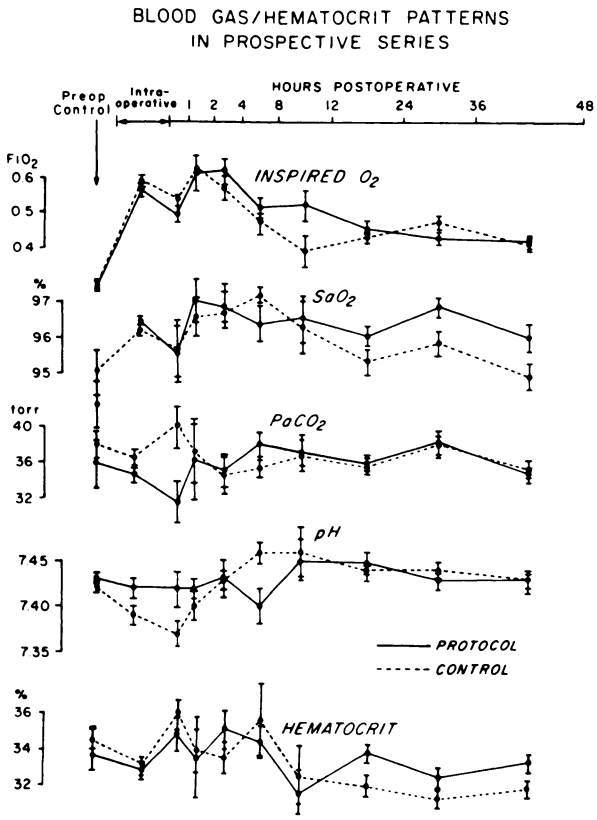

FIGURE 2. Sequential patterns of FIO_2, arterial blood gases, pH and hematocrit values in control and protocol patients in the preoperative, intraoperative and postoperative periods. There were no essential differences between the two groups.

chi square analysis with Yates' correction for small cell size where applicable.

Hemodynamic data comparisons within groups and between groups were analyzed using either paired or unpaired Student's *t* test and ANOVA with Newman-Keuls' test for significance of individual comparisons.

All p values were obtained using two-tailed tests.

RESULTS

Hemodynamic and Oxygen Transport Variables

Table 3 summarizes the hemodynamic and oxygen transport values of series 1 and Table 4 series 2. Data in the preoperative control period and in the immediate postoperative periods are shown for patients with relatively normal preoperative values and for the entire series of the hyperdynamic patients who had sepsis or late stage cirrhosis. Figures 1 to 3 illustrate the temporal sequential patterns in CI, $\dot{D}O_2$, $\dot{V}O_2$, as well as the most commonly monitored variables for series 1 and Figures 4 and 5 for series 2. The preoperative data demonstrate reasonable comparability between the control and the protocol patients. Postoperatively, however, significantly greater CI, $\dot{D}O_2$, and $\dot{V}O_2$ values were observed in protocol patients in both series. By contrast, there were no essential differences between the two groups in the other monitored variables.

At their maximum values, CI, $\dot{D}O_2$ and $\dot{V}O_2$ were 5.6 ± 1.3 L/min•m², 847 ± 267 ml/min•m², and 185 ± 46 ml/min•m², respectively, for PA-protocol patients. Thus, the maximum changes in these three variables irrespective of time were well above the therapeutic goals specified by the protocol and were higher than those of the PA-control group.

Hyperdynamic patients had elevated flow and flow-related variables in the preoperative control period. These values were well maintained in the immediate postoperative period in both series.

Table 5 compares values of the survivors and non-survivors; the data are consistent with previously

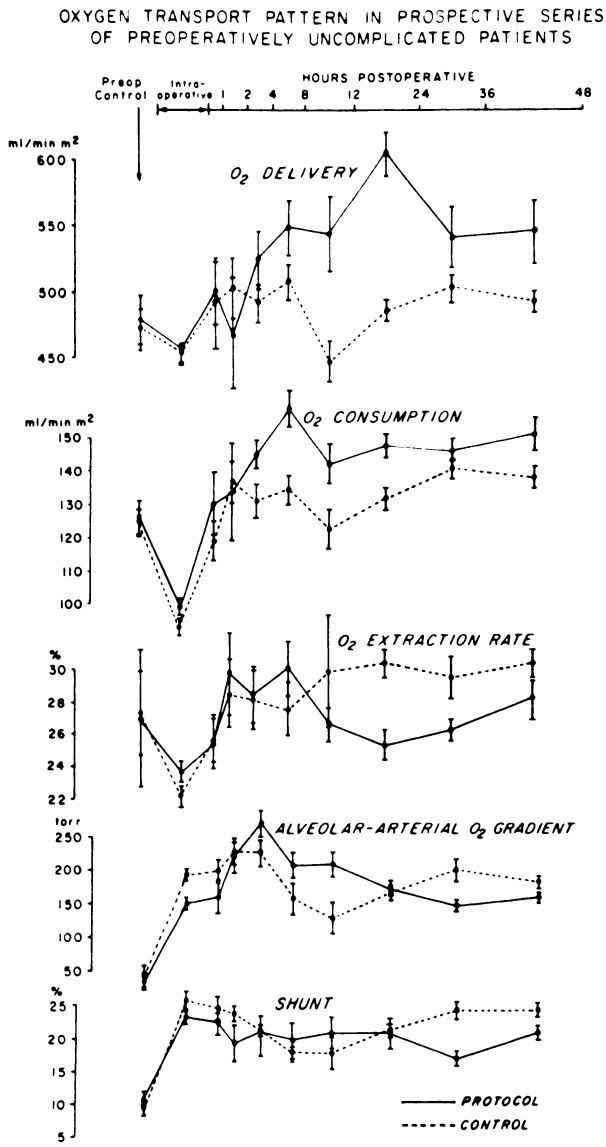

FIGURE 3. Sequential patterns of oxygen transport variables of control and protocol patients in the preoperative, intraoperative and postoperative periods. Note the appreciable increase in $\dot{D}o_2$ and $\dot{V}o_2$ patterns of the protocol patients beginning about 4 h postoperatively. The oxygen extraction rate is higher in the control group beginning about 12 h postoperatively.

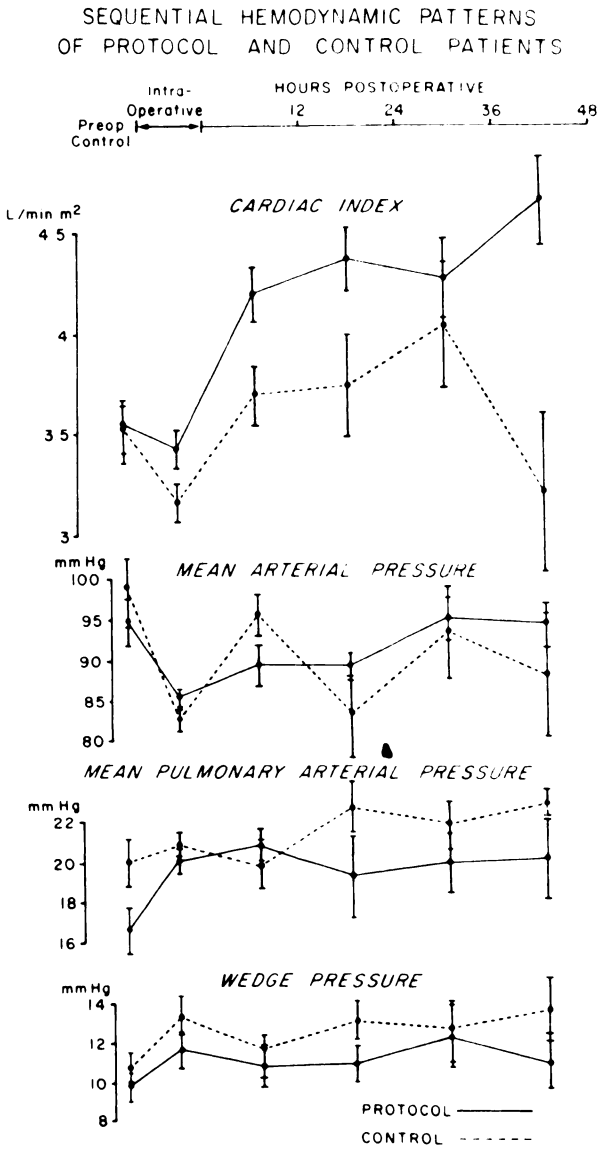

FIGURE 4. Sequential patterns of CI, MAP, mean PA pressure, and pulmonary arterial WP for PA-control and PA-protocol patients in the preoperative, intraoperative and during the immediate postoperative period. Differences in CI in the 36- to 48-h period were significant ($p<0.05$) by the two-tailed Student's t test.

reported studies[6,10,14,17,18] demonstrating greater responses in cardiac output, cardiac output-related values, and oxygen transport values.

Outcome Data

Table 6 summarizes the outcome data of the control and protocol groups of the first series which had sufficient numbers of patients to stratify into clinical subgroups. There were 168 operations on 151 control patients, 57 (38 percent) of whom died and 108 operations on 101 protocol patients, 21 (21 percent) of whom died ($p<0.05$). The data of each subgroup are listed in Table 6 and in general show improved mortality in protocol patients in subgroups with sufficient numbers. In series 1, seven of the 67 protocol patients with normal preoperative values died; three of these patients had delayed insertion of their PA catheters that averaged 56 h after the end of their operation. Five patients had overwhelming medical problems: one patient had massive intraoperative blood loss associated with delayed transfusion. An 82-year-old man had perforated gastric cancer with widespread metastases and peritonitis. An 80-year-old man had postoperative hemorrhage after abdominoperineal resection for rectal cancer, which necessitated subsequent surgery that led to peritonitis, severe hemorrhagic pancreatitis with ARDS and cardiac arrest. Finally, an 81-year-old woman had peritonitis following

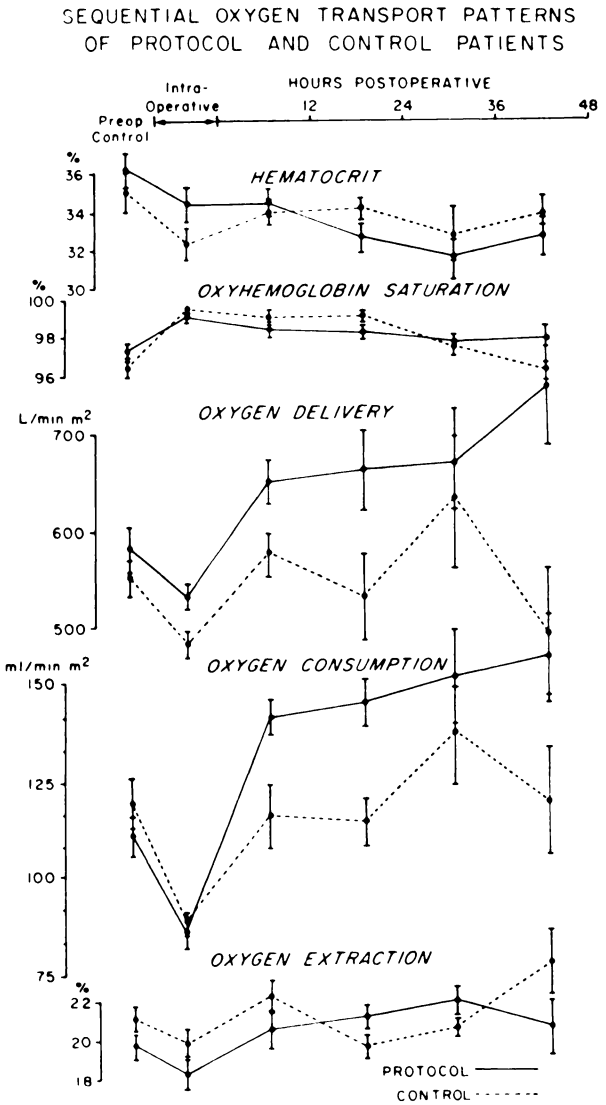

FIGURE 5. Sequential patterns of hematocrit, oxyhemoglobin saturation, $\dot{D}o_2$, $\dot{V}o_2$, and oxygen extraction in the preoperative, intraoperative and during the immediate postoperative period. Differences in oxygen delivery in the 36- to 48-h period, and in $\dot{V}o_2$ in the 12- to 24-h period were significant ($p<0.05$) by the two-tailed Student's *t* test.

resection of a gangrenous infarcted ileal segment. Three of these patients had delayed or inadequate fluid administration and their management was in poor compliance with the protocol.

Table 7 summarizes the outcome data of series 2. The mortality rates were: 23 percent for the CVP-control group, 33 percent for the PA-control group, and 4 percent for the PA-protocol group. The single death in the protocol group was that of a 67-year-old man scheduled for esophagogastrectomy who at operation was found to have carcinomatosis and all that was done was a biopsy and closure. He died two weeks later of cancer, but because he did not leave the hospital alive, he was considered a protocol failure. The difference in the mortality rates was statistically significant when the PA-protocol group was compared with the PA-control group (4 *vs* 33 percent, $p<0.01$), as well as with both CVP plus PA-control groups (4 *vs* 28 percent, $p<0.02$); it was marginally significant when the PA-protocol group was compared with the CVP-control group (4 *vs* 23 percent, $p<0.10$); the CVP group mortality was not significantly different from that of the PA-control group (23 *vs* 33 percent, $p<0.20$).

Complications were observed less frequently in patients treated by the protocol in both series (Table 8). Both the proportion of patients who had complications and the average number of complications per patient were lowest in the PA-protocol group ($p<0.05$). There was a higher incidence of patients with multiple complications in the control group of both series.

There were 17 patients (57 percent) in the CVP group who in the opinion of the primary service developed indications for PA catheterization for management in the postoperative period; seven (29 percent) of these patients subsequently died.

Of the 55 patients in the second series who fulfilled the entrance criteria but were not randomized, ten were operated on immediately; four of these died. This group was too small for further statistical analysis. The remaining 45 patients (NR group) were not considered sufficiently ill in the opinions of their primary service resident and attending staff to warrant invasive monitoring and declined the study. Ironically, despite the initial reluctance, 27 (60 percent) of these patients subsequently had a PA catheter placed by their primary service, usually after they developed lethal postoperative complications. This nonrandomized, nonemergency group had the highest mortality and morbidity (Tables 7 and 8).

Table 6 compares mortality of patients whose monitoring was begun preoperatively with that of patients whose monitoring was started postoperatively in the first series. The data is stratified in those with normal, high, and low preoperative CI values. Table 9 summarizes the mortality rates for both series and the intervening control periods over a 7½-year study.

Catheter Complications

There were transient dysrhythmias (almost always premature ventricular complexes) on insertion of the PA catheter in 12 percent, local infection or inflammation at the catheter site in 5 percent, and positive blood cultures drawn from the PA catheters in 44 percent of the septic patients. There were no major or permanent complications that could be attributed to the PA catheters.

Cost Analysis

The hospital charges in the second series averaged $31,438 for patients in the nonrandomized group, $30,748 for the CVP group, $37,335 for the PA-control

Table 5—*Comparison of Hemodynamic and Oxygen Transport Values of Surviving and Nonsurviving Patients in the Preoperative and Postoperative Periods**

Values	Preoperative Period		Postoperative Period (0-4 Days)	
	Survivors (99 Data Sets)	Nonsurvivors (41 Data Sets)	Survivors (1,233 Data Sets)	Nonsurvivors (813 Data Sets)
HR (beats per minute)	91 ± 21	102 ± 23	109 ± 19†	109 ± 19.9‡
MAP (mm Hg)	99 ± 16	95 ± 22	97 ± 17	84 ± 20†
Mean PA pressure (mm Hg)	16.9 ± 8.6	18.9 ± 8.8	20.8 ± 7.6†	24.1 ± 7.9†
CVP (mm Hg)	6.1 ± 5.1	10.3 ± 6.7	9.2 ± 5.6†	12.0 ± 6.4
PAWP, wedge pressure (mm Hg)	8.8 ± 6.1	11.9 ± 6.5	11.6 ± 5.7†	14.5 ± 6.5‡
CI (L/min•m²)	3.76 ± 1.19	3.6 ± 1.18	4.21 ± 1.27†	3.36 ± 1.26
SI (ml/m²)	42.7 ± 15.2	36.3 ± 12.5	39.8 ± 12.9‡	31.6 ± 12.5‡
SVRI (dynes•sec/cm⁵•m²)	2,182 ± 785	2,154 ± 1,320	1,812 ± 686†	1,976 ± 1,120
PVRI (dynes•sec/cm⁵•m²)	184 ± 109	240 ± 151	195 ± 128	253 ± 175
LCWI (kg•m/m²)	5.0 ± 1.7	4.5 ± 1.6	5.5 ± 1.9‡	3.9 ± 1.8‡
RCWI (kg•m/m²)	0.81 ± .44	1.03 ± .52	1.17 ± .53†	1.1 ± .47
LVSWI (g•m/m²)	59 ± 20	45.9 ± 15.9	52.1 ± 2.02†	36.8 ± 19†
RVSWI (g•m/m²)	9.2 ± 5.4	10.4 ± 5.4	11.1 ± 5.3†	10.1 ± 4.9
PaO_2 (torr)	104 ± 53	122 ± 69	113 ± 48	109 ± 51
SaO_2 (%)	94.5 ± 3.5	94.9 ± 2.7	95.6 ± 3.1†	94.1 ± 6.8
$PaCO_2$ (torr)	35 ± 7	36 ± 11	36 ± 7	35 ± 9
pH, arterial	7.43 ± .05	7.42 ± .11	7.44 ± .06	7.43 ± .09
Hct (%)	34.3 ± 5.6	31.8 ± 3.6	32.4 ± 4.9†	31.5 ± 5.5
$\dot{D}O_2$ (ml/min•m²)	548 ± 162	500 ± 159	601 ± 189†	461 ± 173
$\dot{V}O_2$ (ml/min•m²)	141 ± 49	135 ± 30	153 ± 41†	136 ± 46
O_2 extraction ratio (%)	26.7 ± 8.2	28.1 ± 7.4	26.7 ± 7.2	32.0 ± 10.9†

*Values are mean ± SD.
†$p<0.01$ by Student's t test compared with their preoperative baseline values.
‡$p<0.05$ by Student's t test compared with their preoperative baseline values.

group and $27,665 for the PA-protocol group. The average patient expenditure distributed over the survivors was $50,525 for the nonrandomized group, $40,106 for the CVP group, $58,950 for the PA-control group and $28,690 in the PA-protocol group.

Discussion

The cardiac output, $\dot{D}O_2$ and $\dot{V}O_2$ values were higher in the protocol patients than in the control patients, while the other monitored variables were not appreciably different, indicating that there was reasonable

Table 6—*Comparison of Mortality in Subgroup of Control and Protocol Patients Whose Studies Were Started Preoperatively with Those Whose Studies Were Started Postoperatively**

	Control Group									Protocol Group											
	Started Preop†			Started Postop‡			Subtotal			Started Preop			Started Postop			Subtotal			Total		
	No.	Died	%	No.	Died	%	No.	Died	%	No.	Died	%	No.	Died	%	No.	Died	%	No.	Died	%
Normal preop values	79	21‖	27	39	12	31	118	33¶	28	42	4‖	9.5	25	3	12	67	7¶	10	185	40	22
Septic/Cirrhotic (CI>4 L/min•m²)	18	9	50	7	5	71	25	14	56	15	3	20	7	3	43	22	6	27	47	20	43
Severe trauma/stress (CI>4 L/min•m²)	9	1	11	13	6	46	22	7	32	13	4	31	2	1	50	15	5	33	37	12	32
Elderly/hemorrhage (CI<2.4 L/min•m²)	0	0	0	2	2	100	2	2	100	3	2	67	0	0	0	3	2	67	5	4	80
Miscellaneous§	1	1	100	0	0	0	1	1	100	0	0	0	1	1	100	1	1	100	2	2	100
Total	107	32	30	61	25	41	168	57¶	34	73	13	18	35	8	23	108	21¶	19	276	78	28

*Patients are stratified according to various clinical subsets with normal and abnormal preoperative CI values.
†Preop represents the data of patients in whom the pulmonary artery catheter was placed preoperatively.
‡Postop represents the data of patients in whom the pulmonary artery catheter was placed postoperatively.
§The miscellaneous group included one control patient with massive pulmonary embolism and one protocol patient with blunt abdominal trauma, severe head injury and progressive neurologic deterioration; both died.
‖$p<0.05$ protocol vs control group by chi square test.
¶$p<0.01$ protocol vs control group by chi square test.

Table 7—*Summary of Clinical Data of Series 2*

	Nonrandomized (N = 45)	CVP-Control (N = 30)	PA-Control (N = 30)	PA-Protocol (N = 28)
Age, yr	56.9 ± 2.5	55.2 ± 3.0	53.4 ± 2.5	56.4 ± 3.1
Sex, males/females (%)	45/55	64/36	39/61	75/25
Hospital days	21.9 ± 1.7	22.2 ± 2.8	25.2 ± 3.4	19.3 ± 2.4
ICU days	14.0 ± 1.7	11.5 ± 1.7	15.8 ± 3.1	10.2 ± 1.6*
Ventilator days	6.5 ± 1.3	4.6 ± 1.4	9.4 ± 3.4	2.3 ± 0.5*
Intraoperative death	0	0	1	0
Postoperative deaths, No. (%)	17 (38%)	7 (23%)	10 (33%)	1 (4%)†

*p<0.05 compared with its control group.
†p<0.01 compared with its control group.

compliance with the protocol. The higher CI and $\dot{D}O_2$ values are consistent with the concept that this pattern represents compensatory increases in circulatory function needed to meet the increased metabolic requirements reflected by $\dot{V}O_2$. The present study suggests that this augmented circulatory response represents appropriate goals of therapy for the critically ill noncardiac surgical patient. However, the protocol, defined by median values of survivors may be overly aggressive for elderly patients with limited capacity for physiologic compensation and it may be unattainable or ineffective for overwhelming lethal disease.

The results of series 2 indicate no significant difference in outcome between high-risk surgical patients managed perioperatively with PA catheters and those managed with CVP catheters, unless the PA catheter data are used to augment rather than simply normalize circulatory parameters. Institution of PA catheter monitoring selectively after complications or physiologic decompensations occur did not significantly affect group outcome. In contrast, cardiorespiratory data obtained beginning with the preoperative and intraoperative period may provide crucial early warning of

Table 8—*Complications*

	Series 1		Series 2			
	Control (N = 151)	Protocol (N = 101)	Nonrandomized (N = 45)	CVP-Control (N = 30)	PA-Control (N = 30)	PA-Protocol (N = 28)
Complications in the therapeutic groups						
Respiratory failure	64	33	11	7	9	1
Renal failure	29	9	10	7	7	
Sepsis and septic shock	44	23	11	6	9	
Hepatic failure	6	3	2	2	2	
Cardiac arrest	11	5	3		2	
Pulmonary edema	8	4	2		3	2
Pleural effusion	2	2	2	2	3	3
Wound infection	5	4	2	2	2	1
DIC	13	5	2		2	
Acute MI	5	1	3			
Evisceration	6	1		1		
Abdominal abscess	13	2	1	1		
Postoperative hemorrhage	11	3	1	1		1
Pancreatitis	14	3		1		1
Gastric outlet obstruction	0	0				1
Urinary tract infection	0	0		1		1
Cerebral infarct	0	1	1			
Pulmonary embolism	1	0				
No. of complications	232	98*	52	31	39	11*
Complications per patient	1.54	0.97	1.16	1.03	1.3	0.39
Frequency of multiple complications						
Patients with complications	99 (66%)	61 (61%)	28 (62%)	15 (50%)	15 (50%)	8 (28%)†
Patients with 0 complications	52 (34%)	40 (39%)	17 (38%)	15 (50%)	15 (50%)	20 (71%)
Patients with 1 complication	42 (28%)	38 (38%)	13 (29%)	7 (23%)	3 (10%)	5 (18%)
Patients with 2 complications	21 (14%)	14 (14%)	8 (18%)	3 (10%)	4 (13%)	3 (11%)
Patients with 3 complications	20 (13%)	6 (6%)	5 (11%)	2 (7%)	4 (13%)	0
Patients with 4 or more complications	15 (10%)	3 (3%)	2 (4%)	3 (10%)	4 (13%)	0

*p<0.01 between the protocol and each of the control groups by chi square analysis.
†p<0.05 between the protocol and each of the control groups by ANOVA and Newman-Keuls test.

Table 9—*Summary of Mortality of the Prospective Series*

Series	Date	Control		Protocol	
		Number	Deaths	Number	Deaths, %
Series 1	1/78-6/80	168	57 (34%)	108	21 (19%)
Control period between trials	6/80-5/83	239	66 (28%)	. . .	. . .
Series 2	5/83-5/84	105	34 (32%)	28	1 (4%)
Control period after trials	5/84-5/85	160	40 (25%)	. . .	. . .
Total		672	197 (29%)	136	22 (16%)

potential circulatory decompensation for high-risk patients.[9] Clearly, the risk-benefit of PA catheters used to augment physiologic compensations is favorable as the PA catheter complications were relatively few and transient.

The PA catheters are most often placed for the management of patients who have compromised cardiovascular function. The population studied in this report is different in that the primary indication for invasive monitoring was high-risk surgery rather than a primary cardiovascular disease. Our data indicate that in these circumstances, the accepted normal hemodynamic standards are applied too broadly. Normalization of hemodynamic values appropriate for the cardiac patient may be inappropriate for the general surgical patient in the perioperative period.

Blood pressure, heart rate, hematocrit, CVP, ECG, urine output, and blood gases are conventional measurements that are well recognized descriptors of acute crises as well as the end stages of circulatory failure. Although these variables should be monitored and corrected if abnormal, they are neither sensitive nor accurate descriptors of circulatory decompensation in the perioperative period.[9-13] However, the use of PA catheters in surgical patients is considered to be highly controversial because of the lack of adequately controlled clinical trials. Recently, Robin[21] has called attention to the fact that use of PA catheters has assumed epidemic proportions without clinical trials establishing improved outcome from their use. Moreover, hospitals and third-party payers view PA catheterization in the surgical patient as a potentially morbid and unnecessary expense.

The present study reaches the opposite conclusion; PA catheterization is highly efficacious in terms of both patient outcome and cost containment when used as part of a management plan to augment physiologic circulatory function in the perioperative period. Nonetheless, the overwhelming majority of PA catheterizations performed in general surgical patients are not used to obtain the right heart catheterization data crucial to evaluation of oxygen transport; in fact, about 95 percent of such perioperative catheterizations are used only to obtain WP data (personal communication, Helmut F. Kaspar, MD, Medicare Physician Support Section, Transamerica-Occidental Insurance Co., August 1985). Under these conditions of use, the present study suggests that PA catheterization is not better than CVP monitoring when normalization of hemodynamic values is the therapeutic goal.

We conclude that "normal" hemodynamic values are appropriate for normal unstressed subjects, but the cardiorespiratory patterns of postoperative patients who have survived critical illnesses are more appropriate goals for selected high-risk postoperative patients. The PA catheter is an efficacious and cost-effective tool in the perioperative management of critically ill surgical patients when systemic oxygen transport data is used to augment, rather than simply normalize, the patient's circulatory status. We believe that in the high-risk patient, PA catheterization should be instituted preoperatively and that the important cardiorespiratory values be prophylactically augmented beginning in the preoperative and continued into the intraoperative and immediate postoperative periods. There is a compelling need for this approach, despite the current medical-economic climate encourages less frequent use of invasive procedures. Our study suggests that this conservative approach to patients undergoing high-risk surgical procedures is a false economy both fiscally and in terms of patient outcome.

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